Required Textbook

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Gastrointestinal Physiology

Lecture 1

Organization & General Principles of Gastrointestinal Physiology

(Chapter 62)

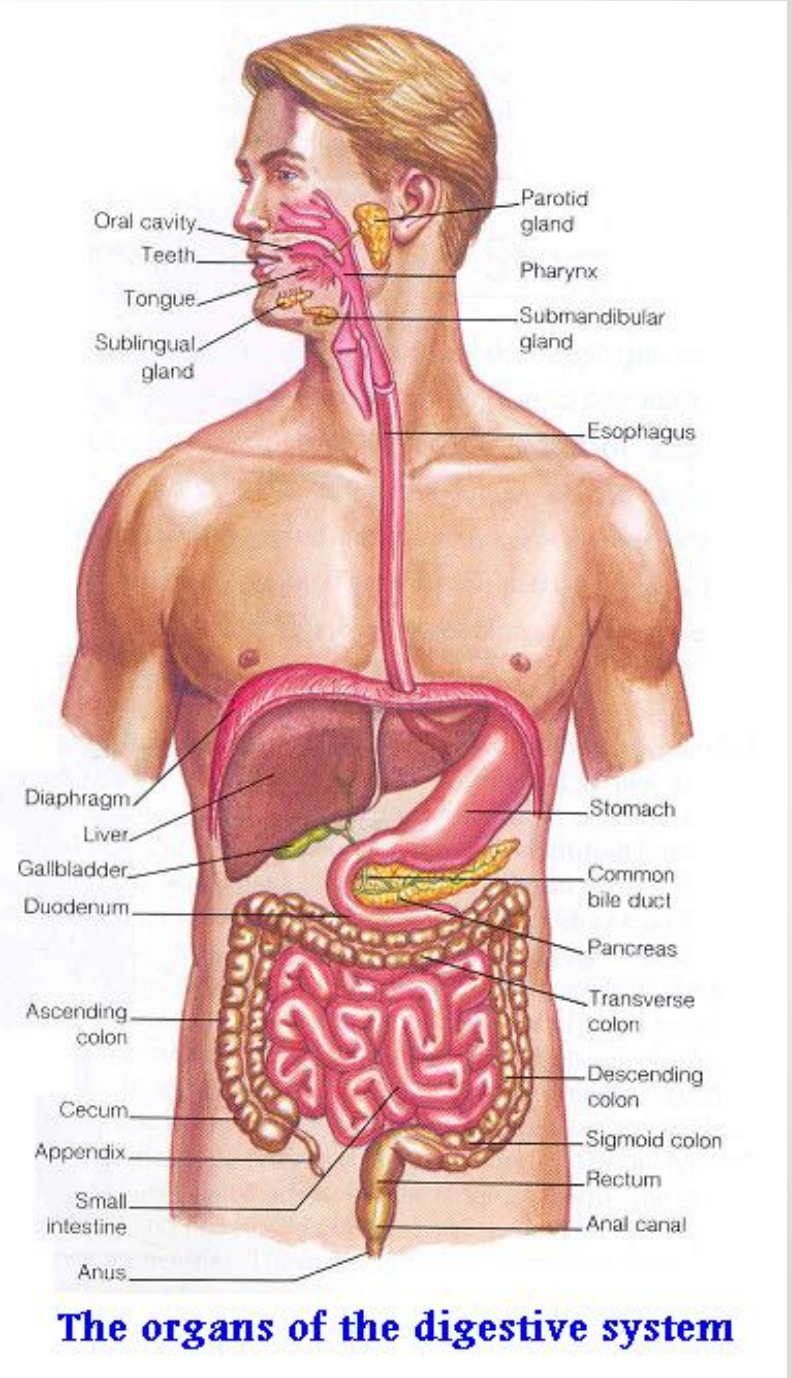
Dr. Hayam Gad

Associate Professor of Physiology

Learning Objectives

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

The gastrointestinal system consists of the gastrointestinal tract (GIT) and associated organs that produce secretions



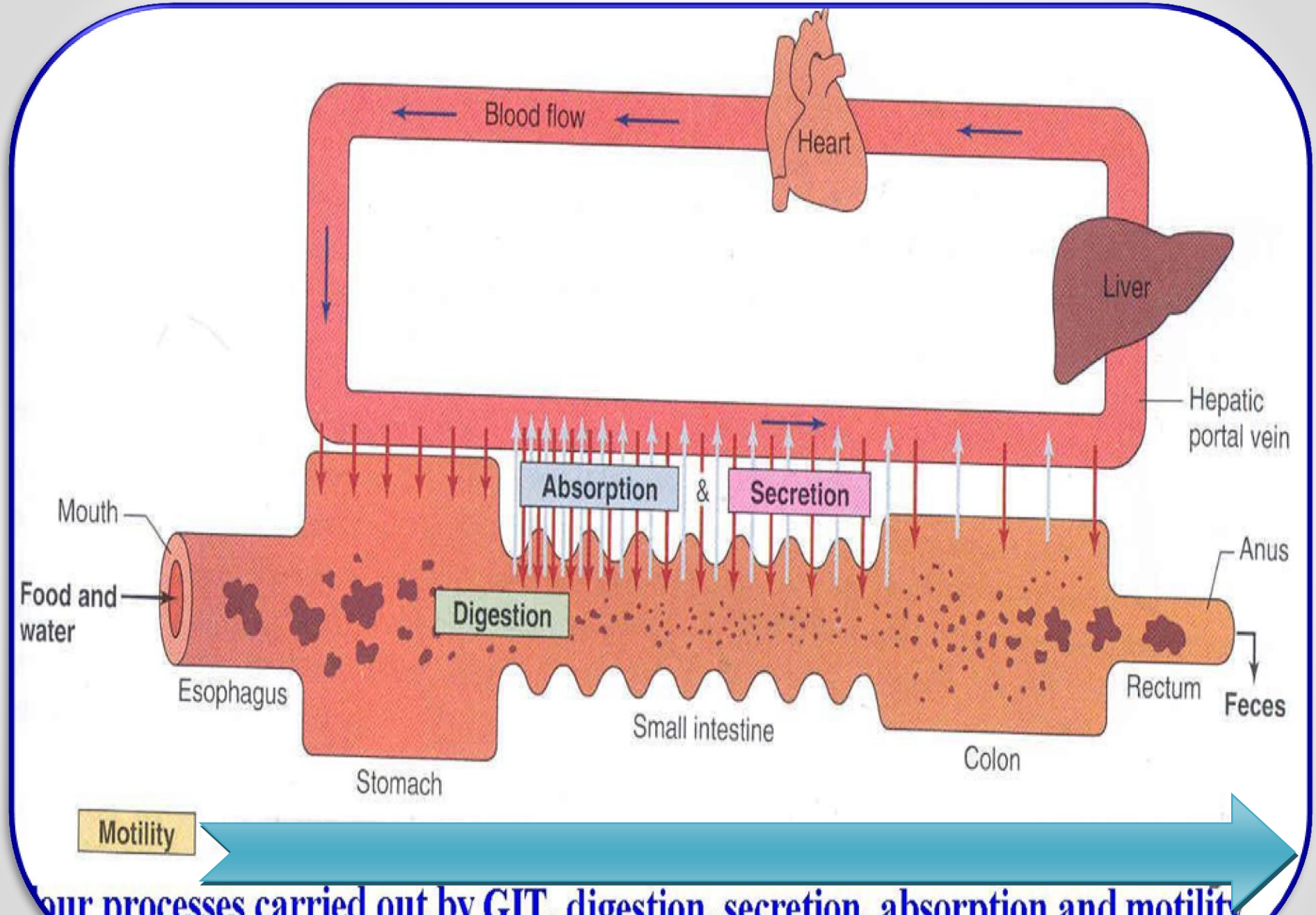
Gastrointestinal Function

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



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

General Principles of Gastrointestinal Motility

Physiologic Anatomy of the Gastrointestinal Wall

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

(1) The serosa

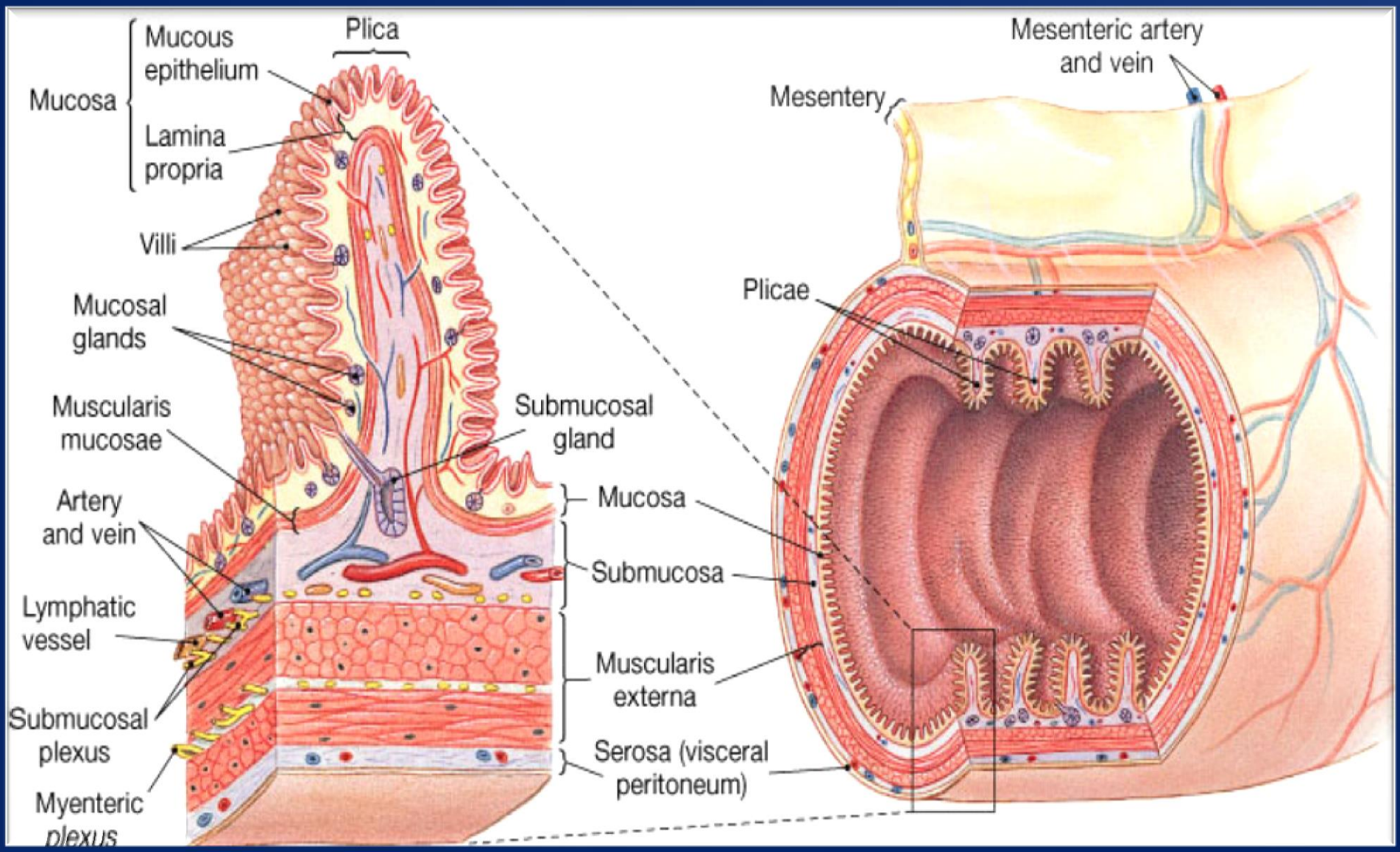
(2) longitudinal muscle layer

(3) Circular muscle layer

(4) The submucosa

(5) The mucosa.

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


Mucosa
Mucous epithelium
Lamina propria
Plica
Villi
Mucosal glands
Muscularis mucosae
Submucosal gland
Artery and vein
Lymphatic vessel
Submucosal plexus
Myenteric plexus
Mucosa
Submucosa
Muscularis externa
Serosa (visceral peritoneum)
Mesenteric artery and vein
Mesentery
Plicae

The General Characteristics of Smooth Muscle

1- Two smooth muscle classification

- **Unitary type**

- Contracts spontaneously in response to stretch and in the absence of neural or hormonal influence (such as in stomach and intestine)
- Cells are electrically coupled via gap junctions

- **Multiunit type**

- Contracts spontaneously in response to neural input, but not in response to stretch (such as in esophagus & gall bladder)

2- Types of contraction

✓ **Phasic contractions (rhythmical)**

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

✓ **Tonic contractions**

- Maintained contraction without relaxation; such as in orad region of the stomach, lower esophageal, ileocecal and internal anal sphincters.
- Not associated with slow waves.

3- Two main muscle layers

A. Longitudinal Smooth Muscles:

B. Circular Smooth Muscles:

3- Two main muscle layers

A. Longitudinal Smooth Muscles

- Contraction of this type shortens the segment of the intestine and expands the lumen.
- They are innervated by enteric nervous system (ENS), and mainly by excitatory motor neurons.
- The Ca^{++} influx from outside is important in the activity of this type of muscle.

3- Two main muscle layers

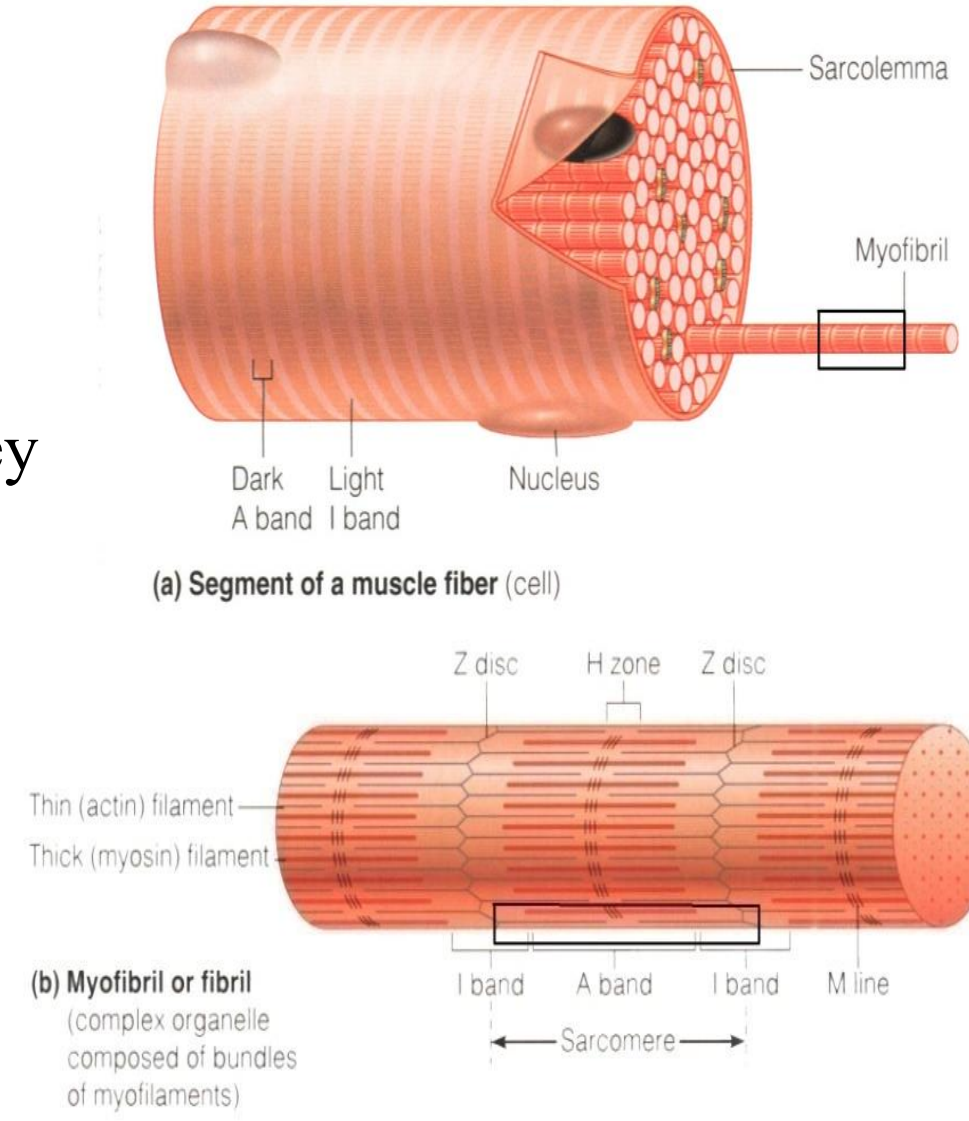
B.Circular Smooth Muscles:

- They are thicker and more powerful than longitudinal muscle.
- More gap junctions are available than in longitudinal muscle.
- Contraction of this type reduces the diameter of the lumen and increases its length.
- They are innervated by ENS, both excitatory and inhibitory motor neurons.
- Intracellular release of Ca^{++} is more important.

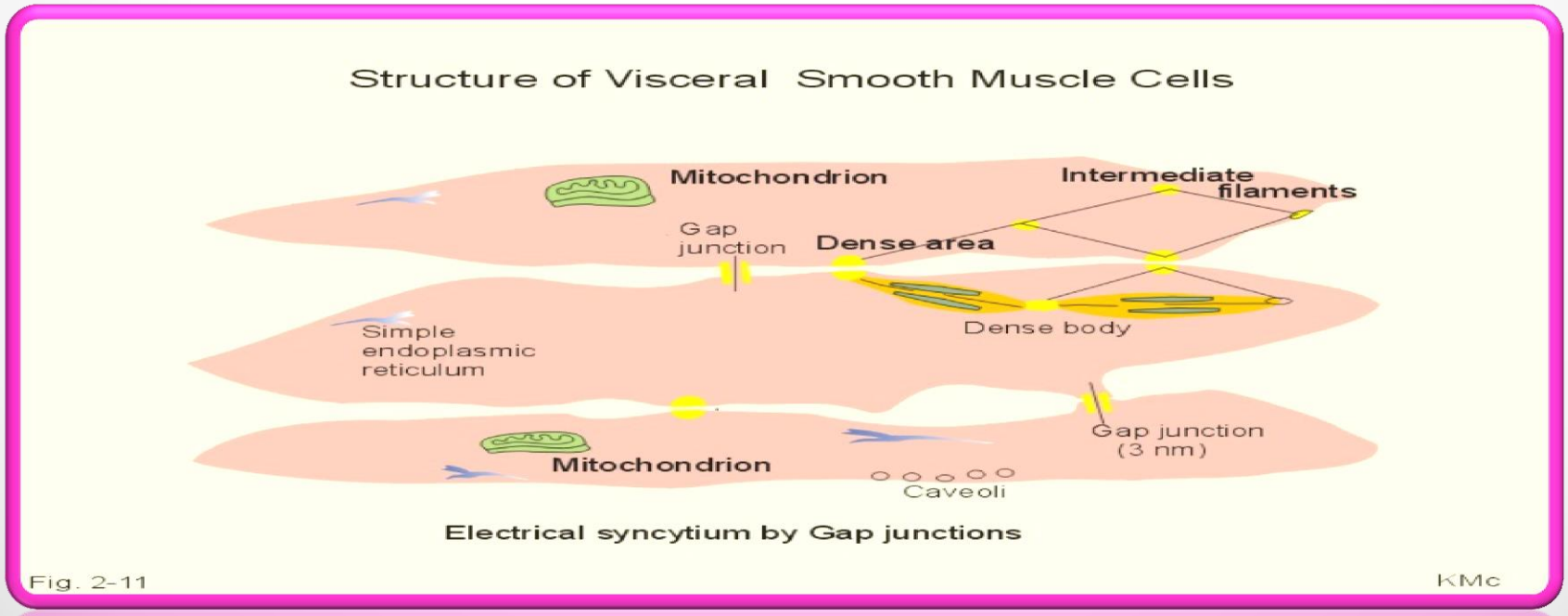
The Specific Characteristics of Smooth Muscle

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 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.
- 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.

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:
  (a) *Slow waves*
  (b) *Spikes*.

A- The slow waves- basic electrical rhythm

- These waves are not action potentials. Instead, they are slow spontaneous change in RMP (cyclic waves of depolarization & repolarization).
- Their intensity varies between 5-15 mv.
- Their frequency ranges between 3/min. in stomach body to 12/min in duodenum and change to 8/min. in terminal ileum.
- They do not directly cause contraction.
- Spikes of action potential are superimposed on the depolarization phase of slow waves followed by contraction

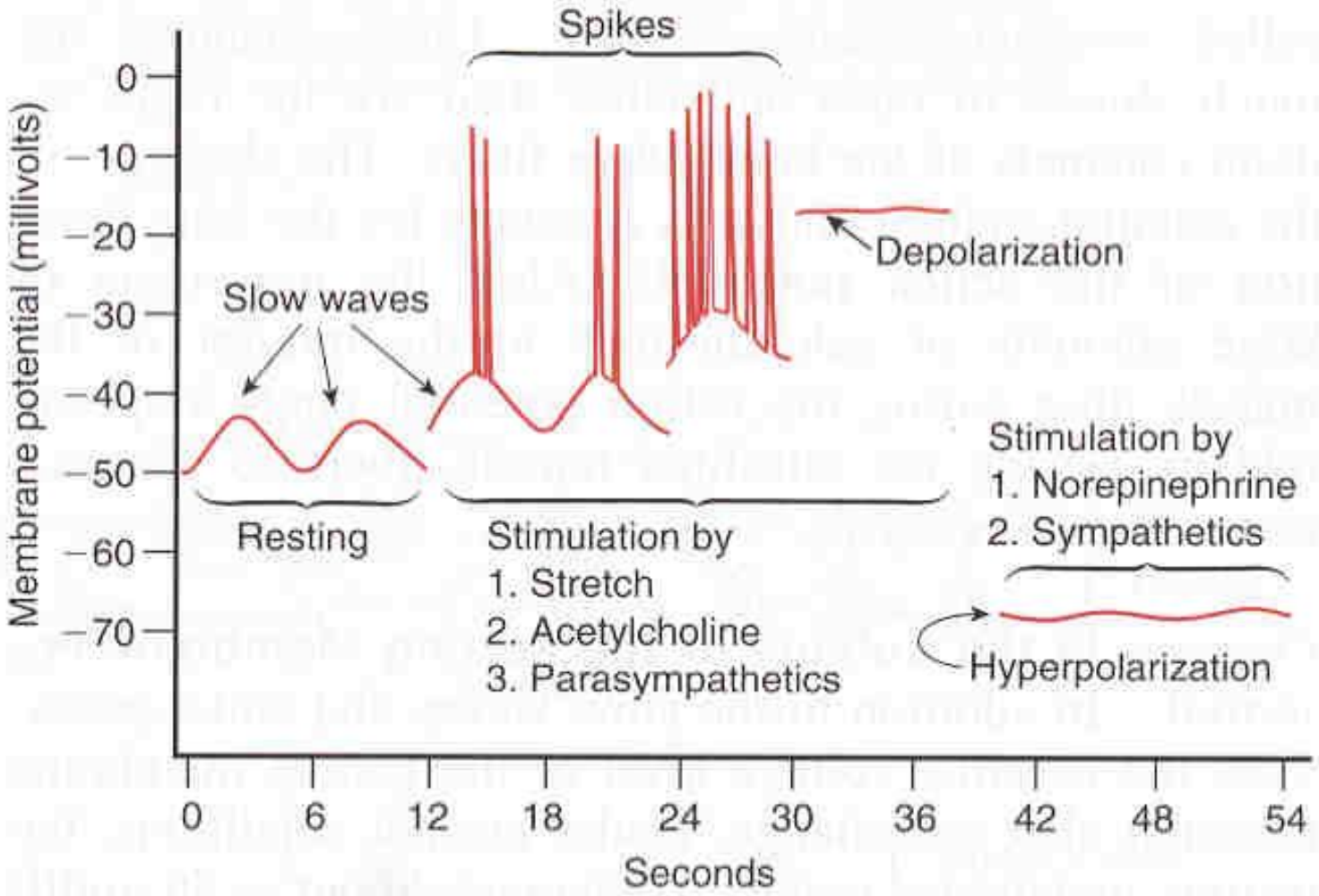
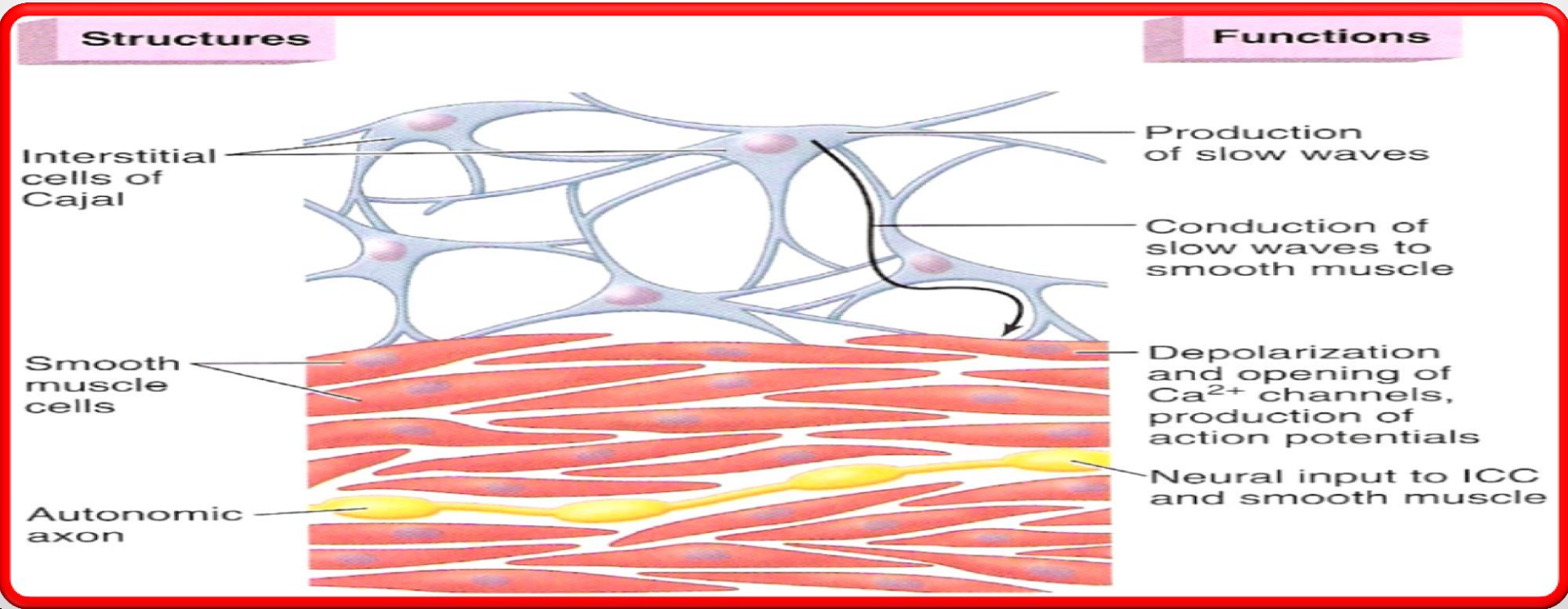


FIGURE 62–3

Membrane potentials in intestinal smooth muscle. Note the slow waves, the spike potentials, total depolarization, and hyperpolarization, all of which occur under different physiologic conditions of the intestine.

* They are generated by **interstitial cells of Cajal, ICC** (the GI pacemaker), located between the longitudinal & circular muscle layers. 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.

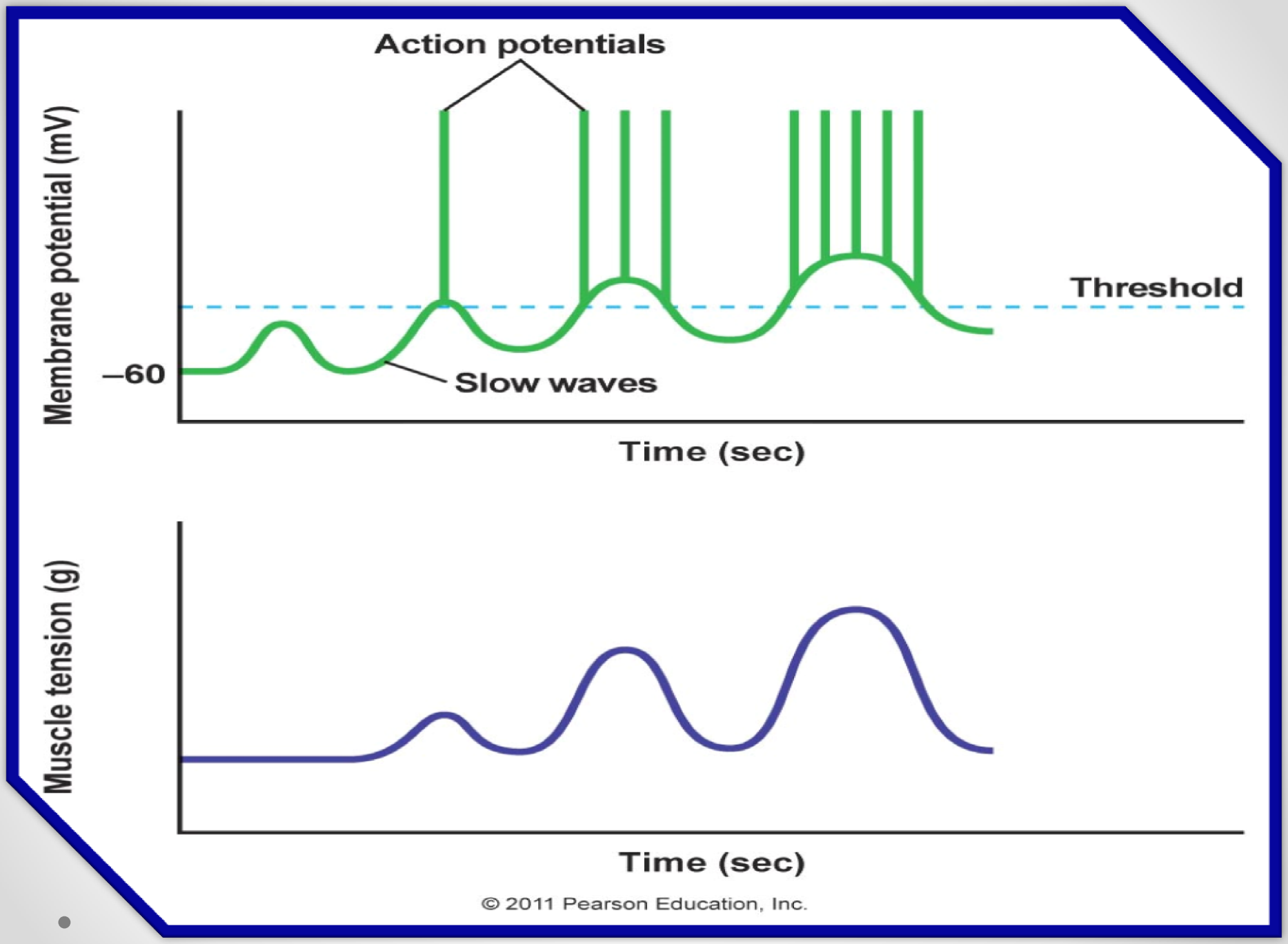
* Parasympathetic ↑ the amplitude and frequency of slow waves. Sympathetic ↓ their amplitude and frequency.



B- The spike potentials

* They are true action potentials that occur when RMP rises above -40 mv [RMP= -50- (-60) mv].
* They are more prolonged than those of skeletal muscles.
* 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^{+} (Ca^{++}-Na^{+} channels). They open slowly. Ca^{++} that enters cells helps to initiate contraction.

  (N.B: slow waves do not cause Ca^{++} entry).
* They usually do not propagate more than a few mm. Instead slow waves are propagated & spike potentials occur at the peak of slow waves.
* The higher the slow wave potential rises, the greater the frequency of the spike potentials, usually ranging between 1 and 10 spikes per second.



3. Changes in Voltage of the Resting Membrane Potential.

The resting membrane potential averages about

-56 mv [-50- (-60) mv] but multiple factors can change this level:-

- When the potential becomes less negative, which is called *depolarization* of the membrane, the muscle fibers become more excitable.
- When the potential becomes more negative, which is called *hyperpolarization*, the fibers become less excitable.

Factors that depolarize the membrane-that is, make it more excitable-are:

(1) Stretching of the muscle
(2) Stimulation by acetylcholine
(3) Stimulation by parasympathetic nerves that secrete acetylcholine at their endings
(4) Stimulation by several specific gastrointestinal hormones.

Factors that hyperpolarize the membrane and make the muscle fibers less excitable-are:

(1) Norepinephrine or epinephrine
(2) Stimulation of the sympathetic nerves that secrete mainly norepinephrine at their endings.

4. Calcium Ions and Muscle Contraction.

- Smooth muscle contraction occurs in response to entry of Ca^{++} into the muscle fiber.
- The slow waves do not cause Ca^{++} to enter the smooth muscle fiber (only Na^{+}). Therefore, the slow waves by themselves usually cause no muscle contraction.
- Instead, it is during the spike potentials, generated at the peaks of the slow waves, that significant quantities of Ca^{++} do enter the fibers and cause most of the contraction.

5. Tonic Contraction of Some Gastrointestinal Smooth Muscle.

- Some smooth muscle of the GI exhibits *tonic contraction* as well as or instead of rhythmical contractions. It is continuous, **not associated with the basic electrical rhythm of the slow waves** but often lasting several minutes or even hours.
- **Tonic contraction is sometimes caused by**

1. Continuous repetitive spike potentials.
2. Hormones.
3. Continuous entry of Ca^{++} into the interior of the cell brought about in ways not associated with changes in membrane potential.

Control of GIS functions

I- Neural control

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

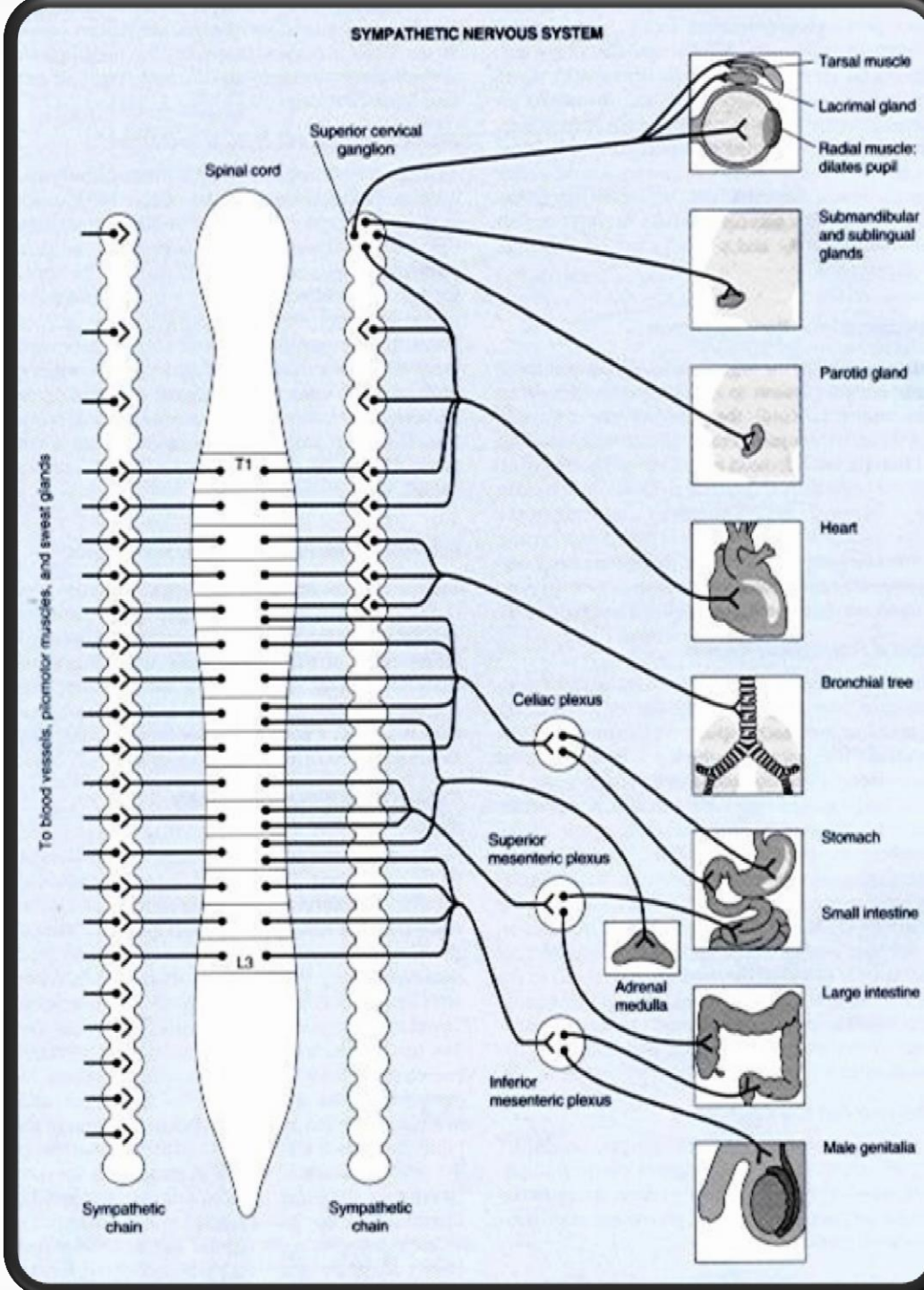
II- Hormonal control

I- Autonomic control (the extrinsic nervous system):

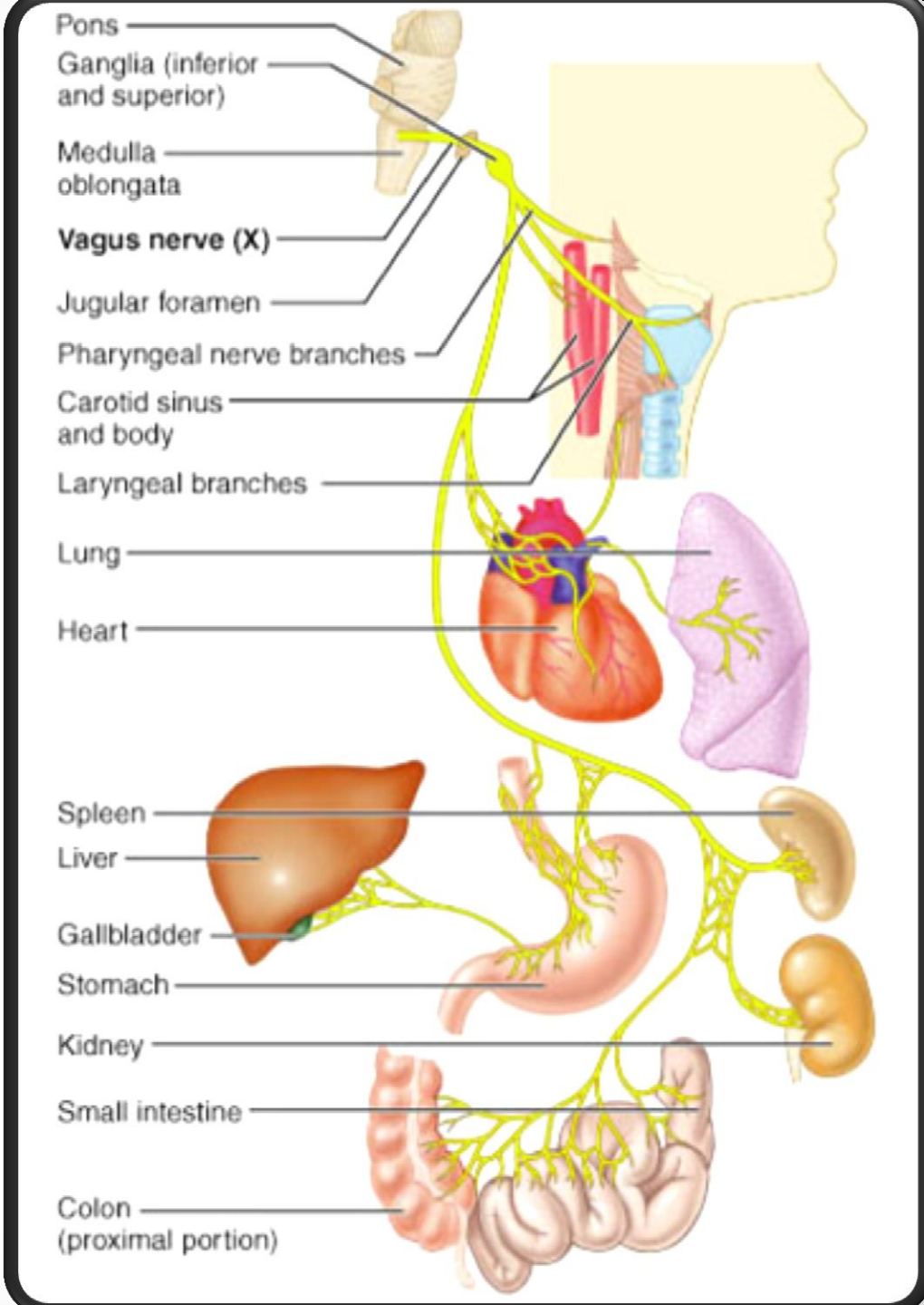
A- Sympathetic (What is its function?)

B- Parasympathetic (What is its function?)

Sympathetic Innervation



Parasympathetic Innervation



Enteric Nervous System

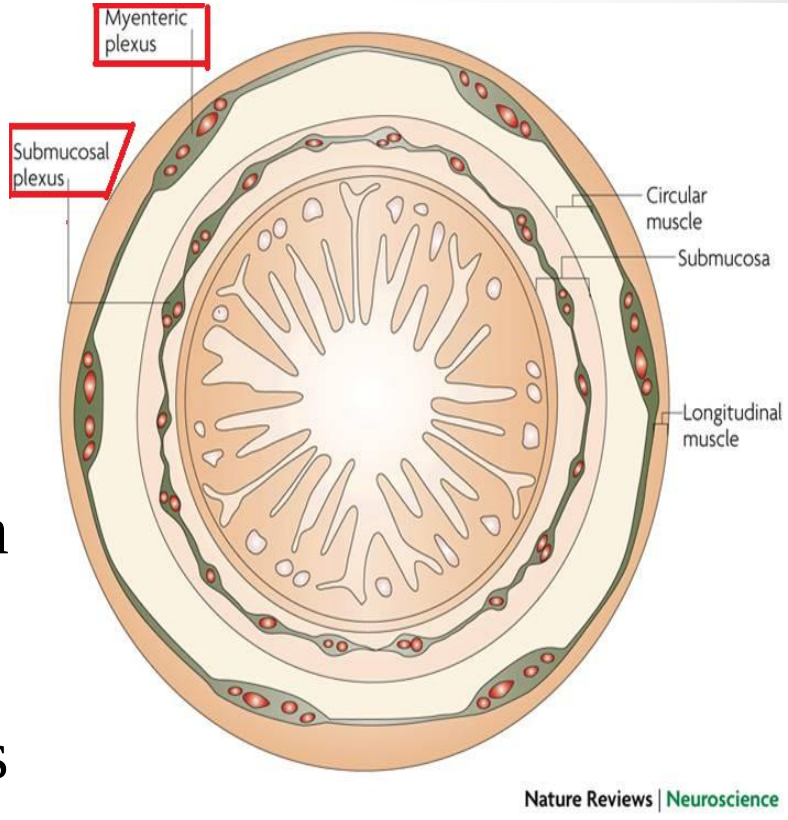
- *Enteric Nervous System* is the nervous system of GI tract.
- It lies entirely in the wall of the gut, beginning in the esophagus and extending all the way to the anus.
- It has as many neurons as spinal cord (about 100 million).

Enteric Nervous System

It is composed mainly of two plexuses:

(1) **The *myenteric (*Auerbach's)plexus** lies between the longitudinal and circular muscle layers) controls mainly the gastrointestinal movements.

(2) **The *submucosal (Meissner's) plexus*** lies in the submucosa, controls mainly gastrointestinal secretion and local blood flow.



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.

Differences Between the Myenteric and Submucosal Plexuses

The *myenteric plexus*

- 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 gut wall
- Has *excitatory* and *inhibitory* motor neurons (fiber endings secrete an inhibitory transmitter, e.g., *vasoactive intestinal polypeptide)*

The submucosal plexus

- Controls local *intestinal secretion,* local *absorption*, and local *contraction of the submucosal muscle* that causes various degrees of infolding of the gastrointestinal mucosa.

Types of Neurotransmitters Secreted by Enteric Neurons

- The specific functions of many of GI neurotransmitters are not well known, but some research workers have discovered the effects of some of these substances as following:

1. Excitatory Motor Neurons Evoke Muscle Contraction & Intestinal Secretion:

A. Neurotransmitters of motor neurons:

i. Substance P
ii. Ach

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

i. Ach
ii. VIP
iii. Histamine

2. Inhibitory Motor Neurons Suppress Muscle Contraction:

Neurotransmitters:

i. ATP

ii. NO

iii. VIP

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

II- 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	Site of Secretion	Stimuli for Secretion	Actions
Gastrin	"G" cells of the stomach	Small peptides and amino acids Distention of the stomach Vagal stimulation (GRP)	↑ 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

Functional Types of Movements in GIT

- Two types of movements occur in the gastrointestinal tract:

1) Propulsive movements (peristalsis)

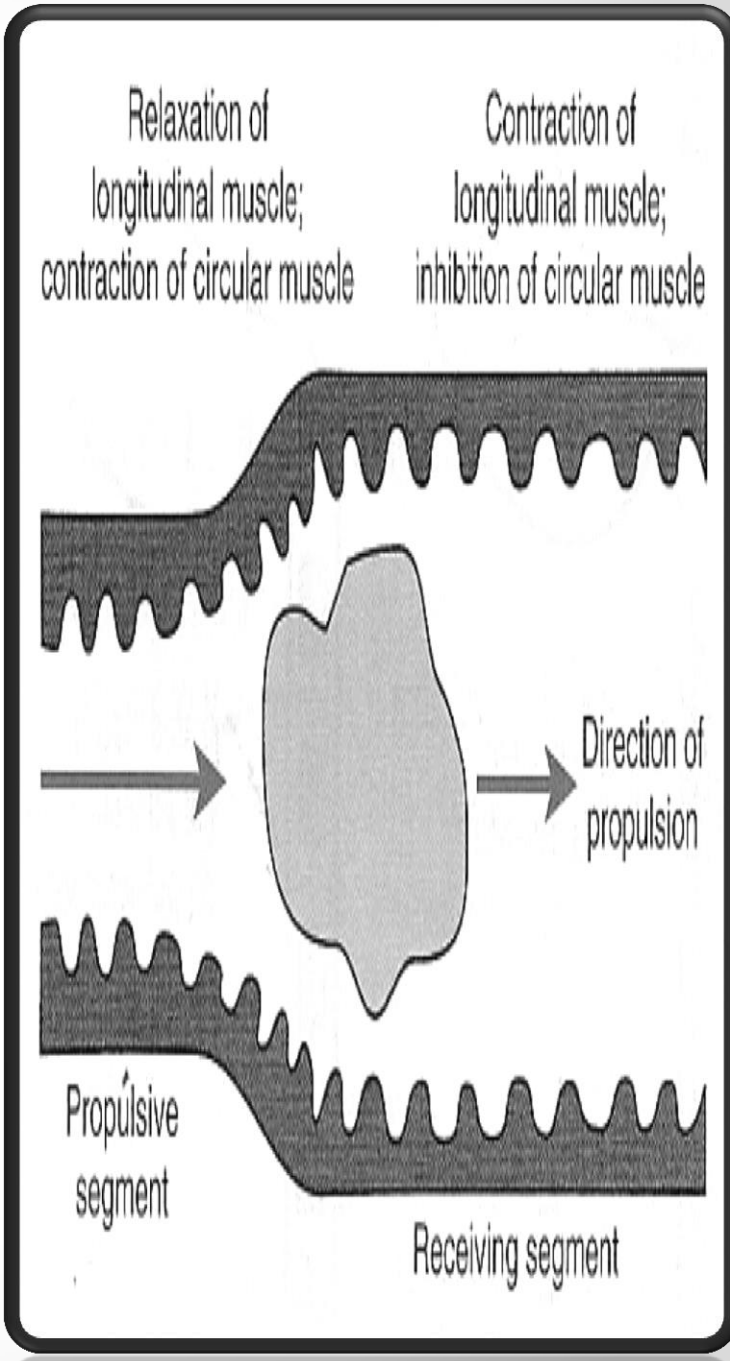
- Organizes propulsion of material over variable distances within the GI lumen
- A contraction ring appears around gut, then moves forward.
- Usual stimulus is distention. Other stimuli include chemical or physical irritation of the epithelial lining in the gut.
- Myenteric plexus is important
- Atropine (cholinergic blocker) depresses propulsion.

❖ Receiving segment ---contraction (longitudinal M.)
---relaxation (circular M.)

❖ Propulsive segment ---contraction (circular M.)
----relaxation (longitudinal M.)

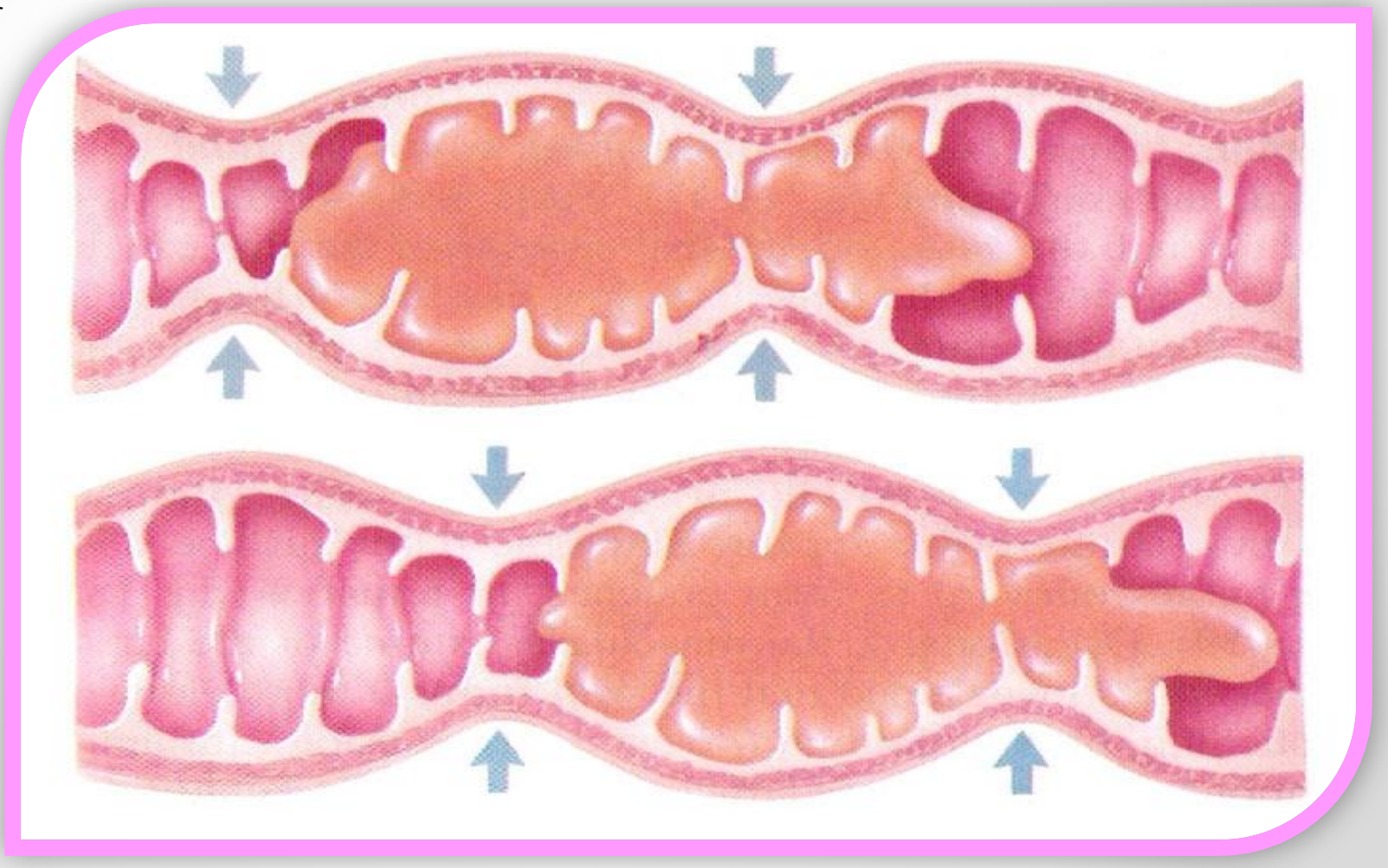
Peristaltic Reflex and the "Law of the Gut."

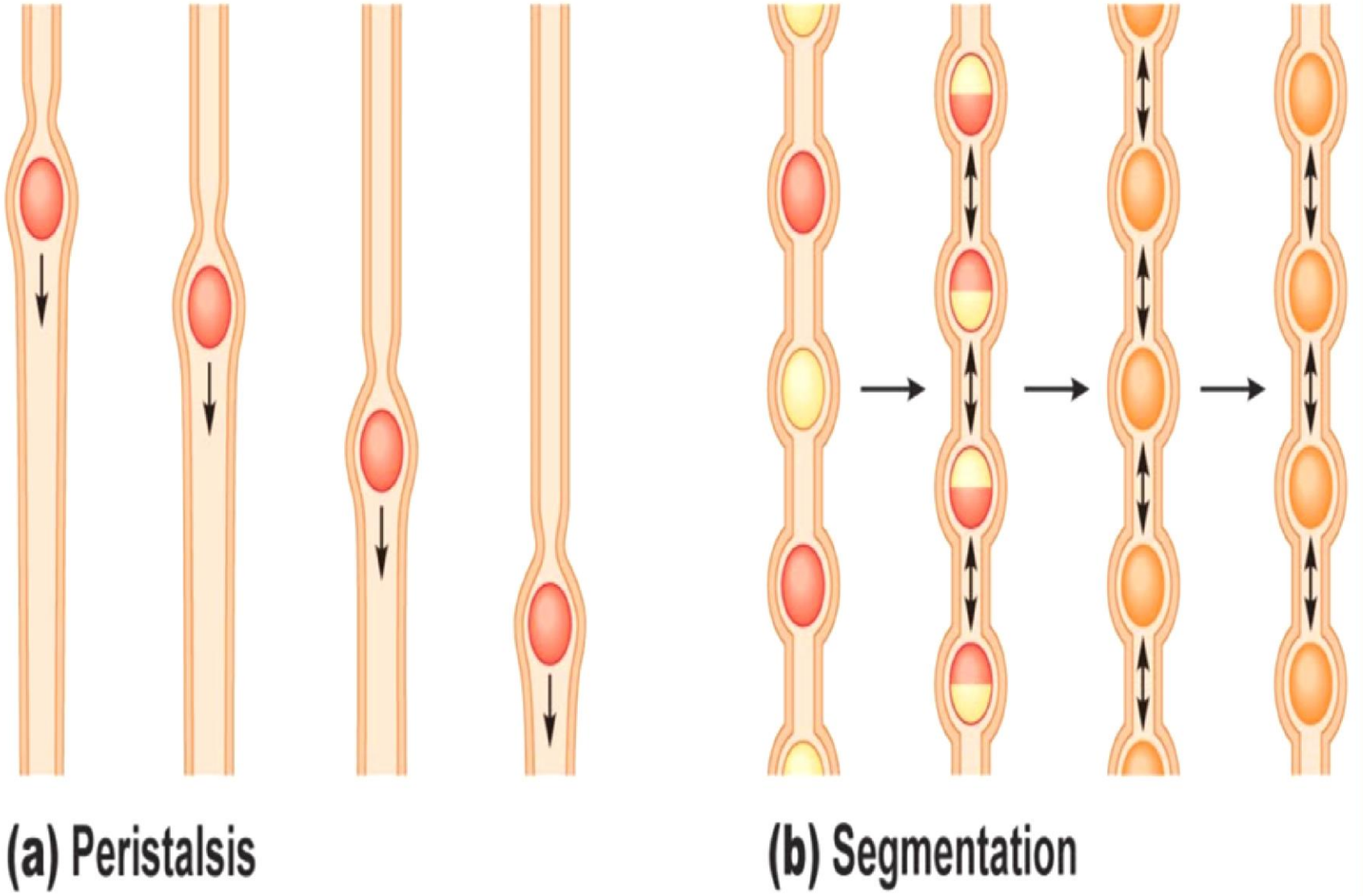
When a segment of the intestinal tract is excited by distention and thereby initiates peristalsis, the contractile ring causing the peristalsis normally begins on the orad side of the distended segment and moves toward the distended segment, pushing the intestinal contents in the anal direction for 5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



2) Mixing movements (segmentation)

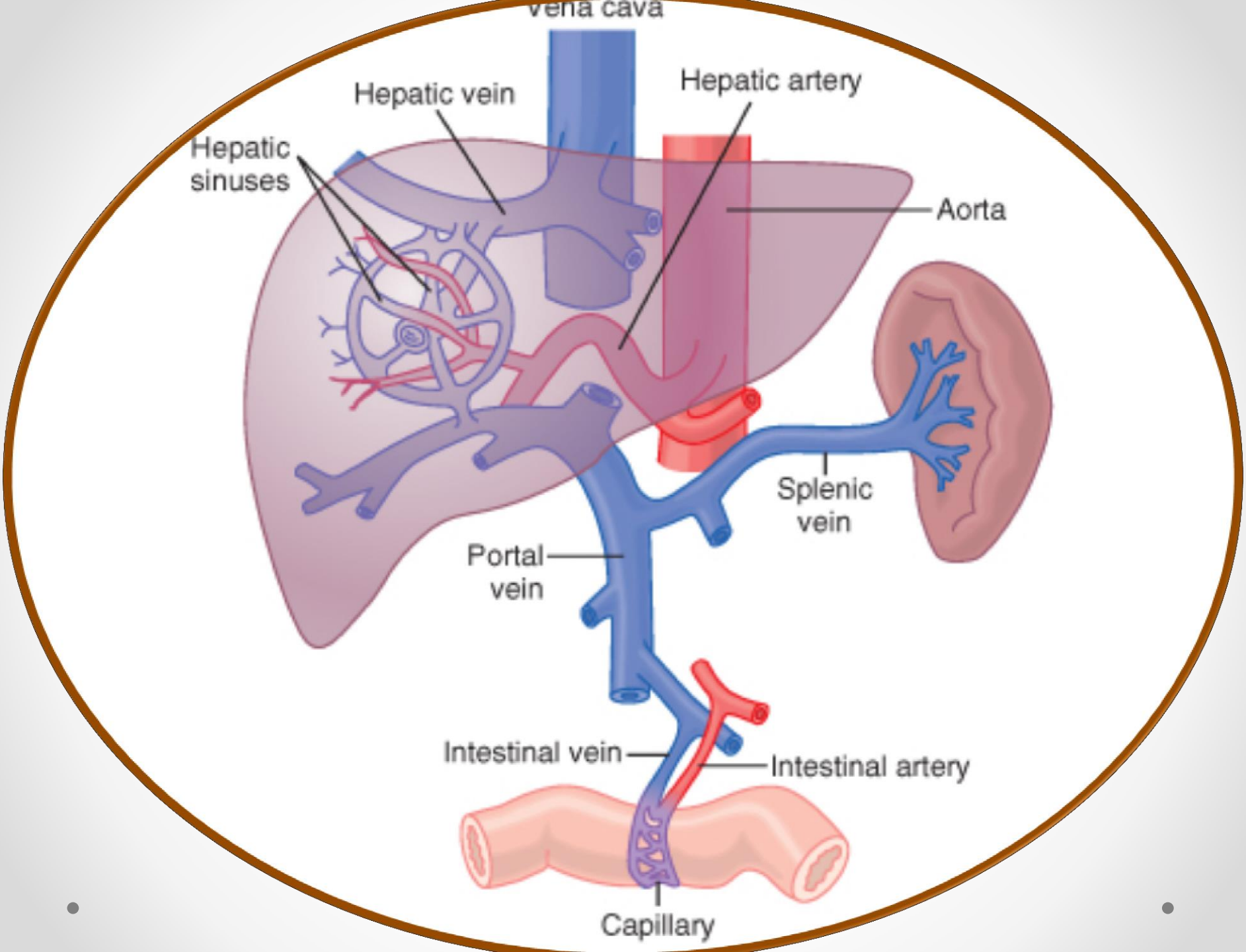
- Blend different juices with the chyme
- Bring products of digestion in contact with absorptive surfaces





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.


Vena cava
Hepatic vein
Hepatic artery
Hepatic sinuses
Aorta
Splenic vein
Portal vein
Intestinal vein
Intestinal artery
Capillary

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 GIT 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.


Thank You