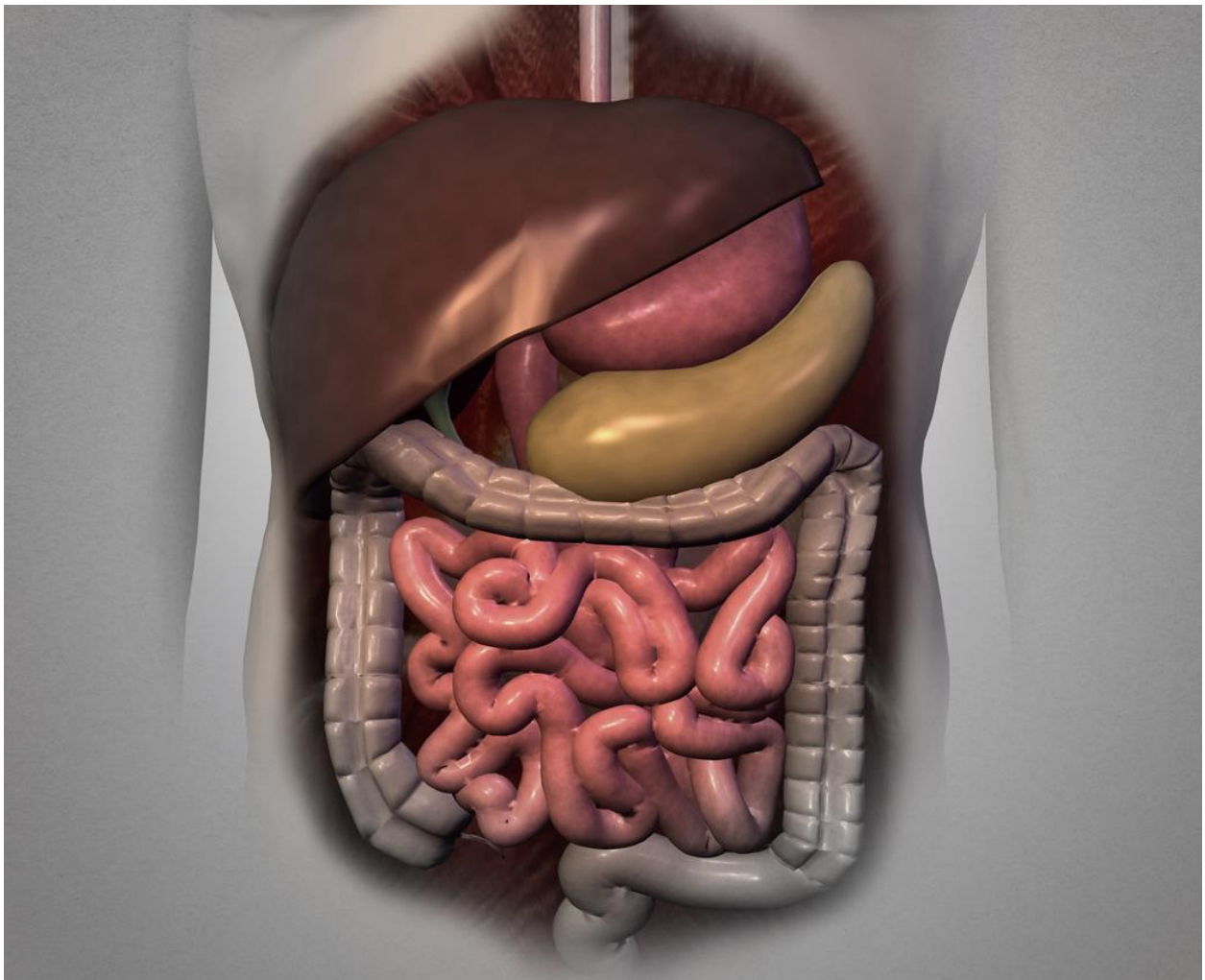

GIT Block

Physiology Team 431

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Organization & General Principles of Gastrointestinal Physiology

Required Textbook

Textbook of Medical Physiology

Eleventh Edition

Guyton & Hall

Black= slides

Red= important

Green=males notes

Blue= explanation

Learning Objectives:

Physiologic Anatomy of the Gastrointestinal Wall

The General Characteristics of Smooth Muscle

The Specific Characteristics of Smooth Muscle

Gastrointestinal Smooth Muscle Functions as a Syncytium•

:Electrical Activity of Gastrointestinal Smooth Muscle•

.Changes in Voltage of the Resting Membrane Potential•

.Calcium Ions and Muscle Contraction•

.Tonic Contraction of Some Gastrointestinal Smooth Muscle•

Control of Gastrointestinal Function

(Neural control (Autonomic and Enteric Nervous Systems•

Hormonal control•

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 (salivary glands, gall bladder and pancreas..)

Gastrointestinal Function:

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

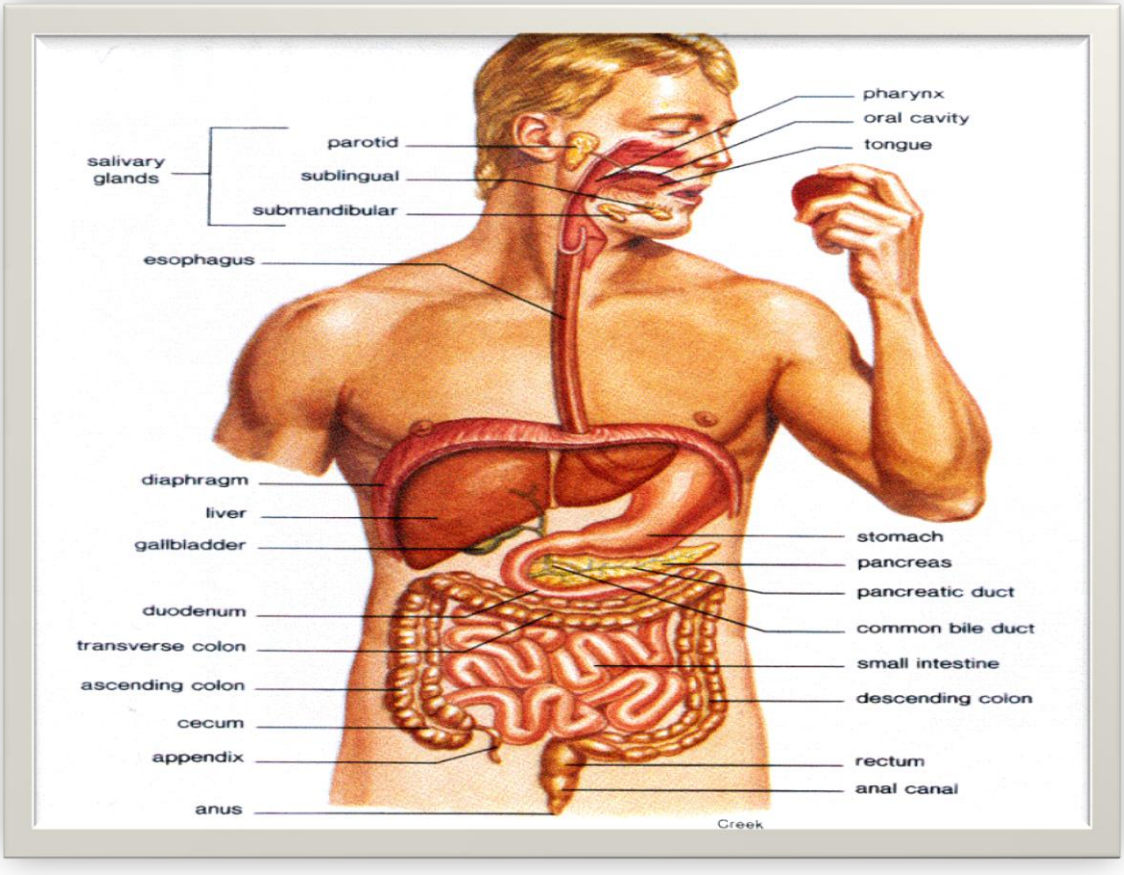
1.Movement of food through the alimentary tract (motility). Motility from mouth to anus (forward movement)

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



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 (outer) muscle layer

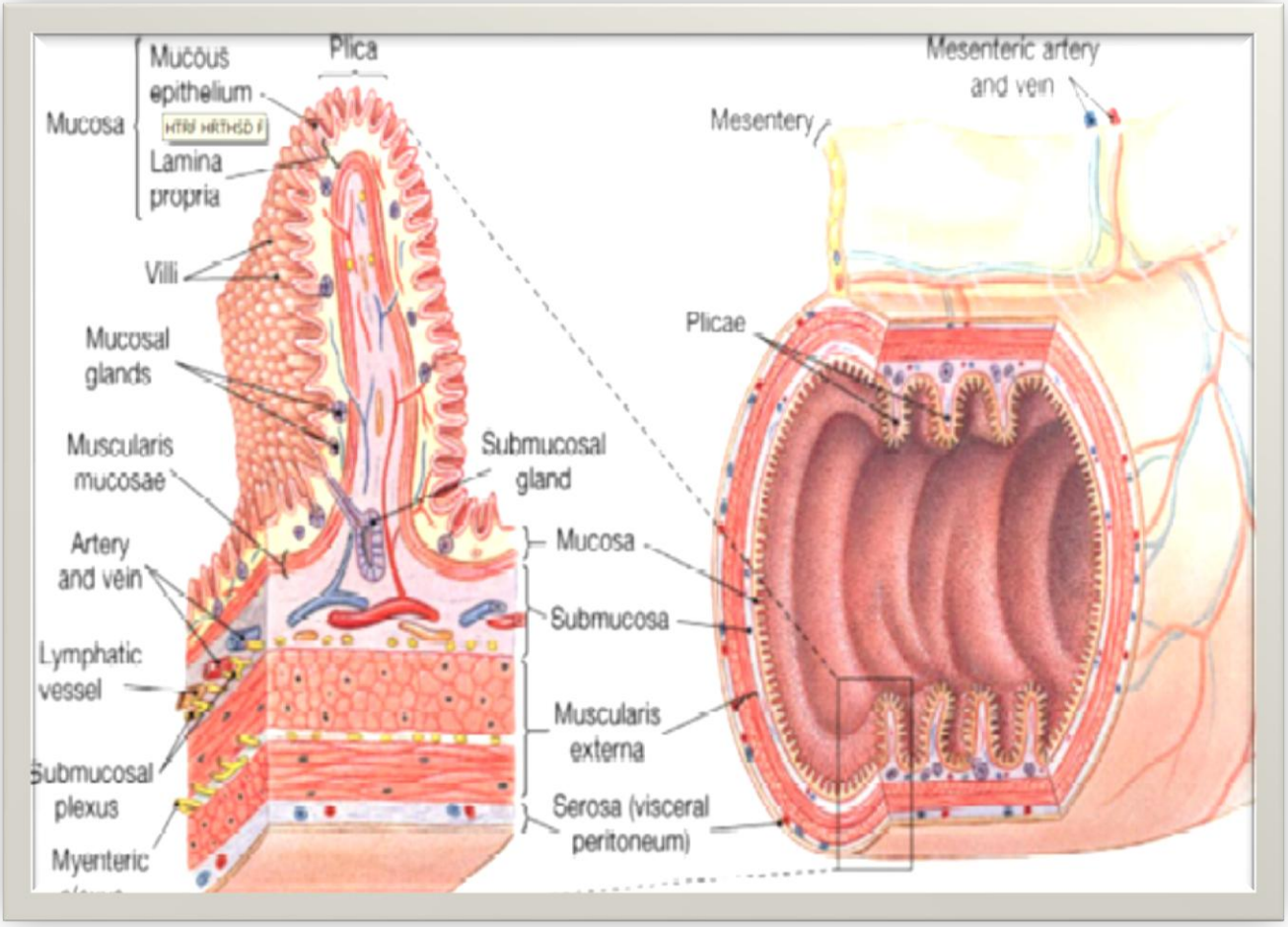
(3)Circular (inner) muscle layer

} Between them is myegenic plexus

(4)The submucosa (has glands, vessels and submucosal plexus)

(5)The mucosa.

In addition, sparse bundles of smooth muscle fibers, the mucosal muscle, lie in the deeper layers of the mucosa (The contraction of these fibers produce mucosal folds)



The General Characteristics of Smooth Muscle (not only in GIT)

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 (like cardiac muscles)

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(distal part of stomach) and small intestine.

Tonic contractions

•Maintained contraction without relaxation; such as in orad region of the stomach (oral or proximal part), lower esophageal, ileocecal and internal anal sphincters; e.g. lower esophageal sphincter is only relaxed during swallowing and internal anal is only relaxed during defecation)

•Not associated with slow waves (explained later)

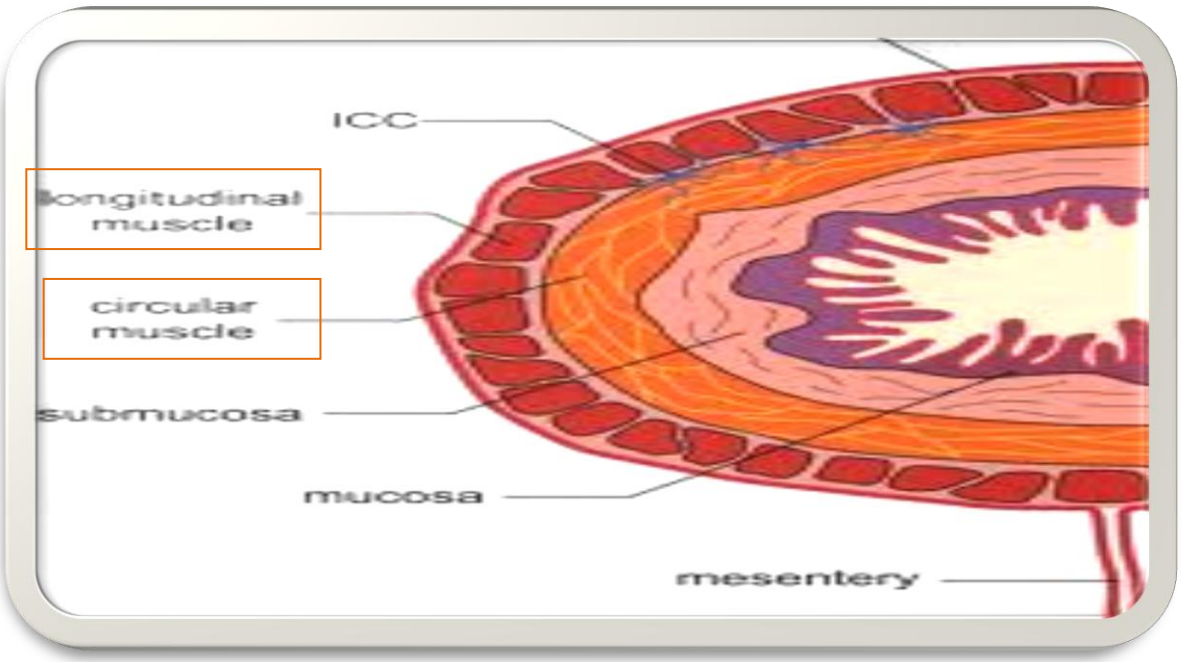
3-Two main muscle layers (present also in vessels)

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. (little inhibitory)

- The Ca^{++} influx from outside (extracellular) is important in the activity of this type of muscle.



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. (equally)

- Intracellular release of Ca^{++} is more important.

The Specific Characteristics of Smooth Muscle

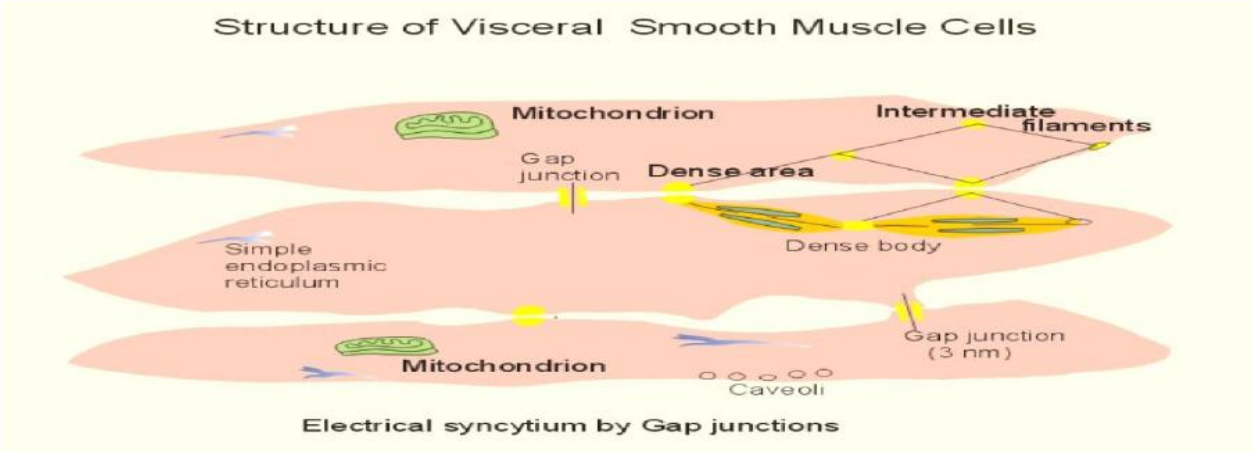
1.Gastrointestinal Smooth Muscle Functions as a Syncytium:

•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.

•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.



2.Electrical Activity of Gastrointestinal Smooth Muscle:

•The smooth muscle of the gastrointestinal tract is excited by almost continual slow, intrinsic (enteric nervous system) electrical activity along the membranes of the muscle fibers.

•This activity has two basic types of electrical waves:

(a) Slow waves (b) Spikes

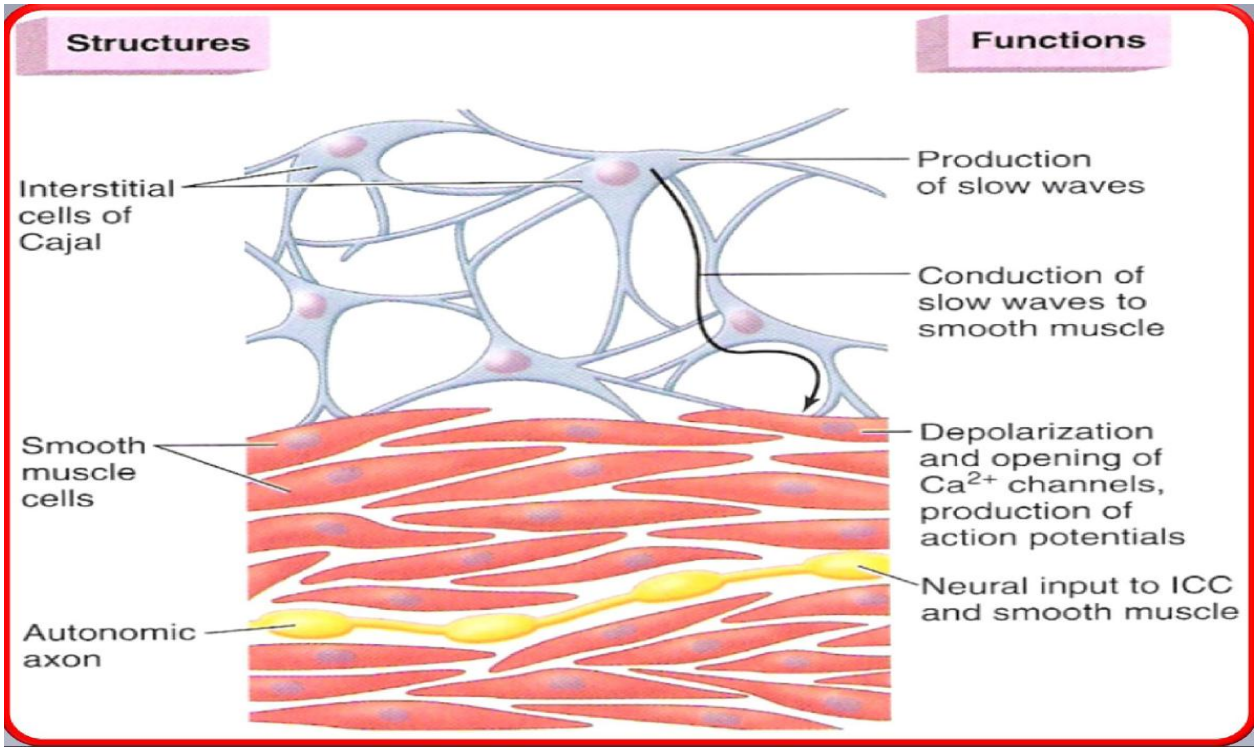
Most gastrointestinal contractions occur rhythmically, and this rhythm is determined mainly by the frequency of so-called "slow waves" of smooth muscle membrane potential.

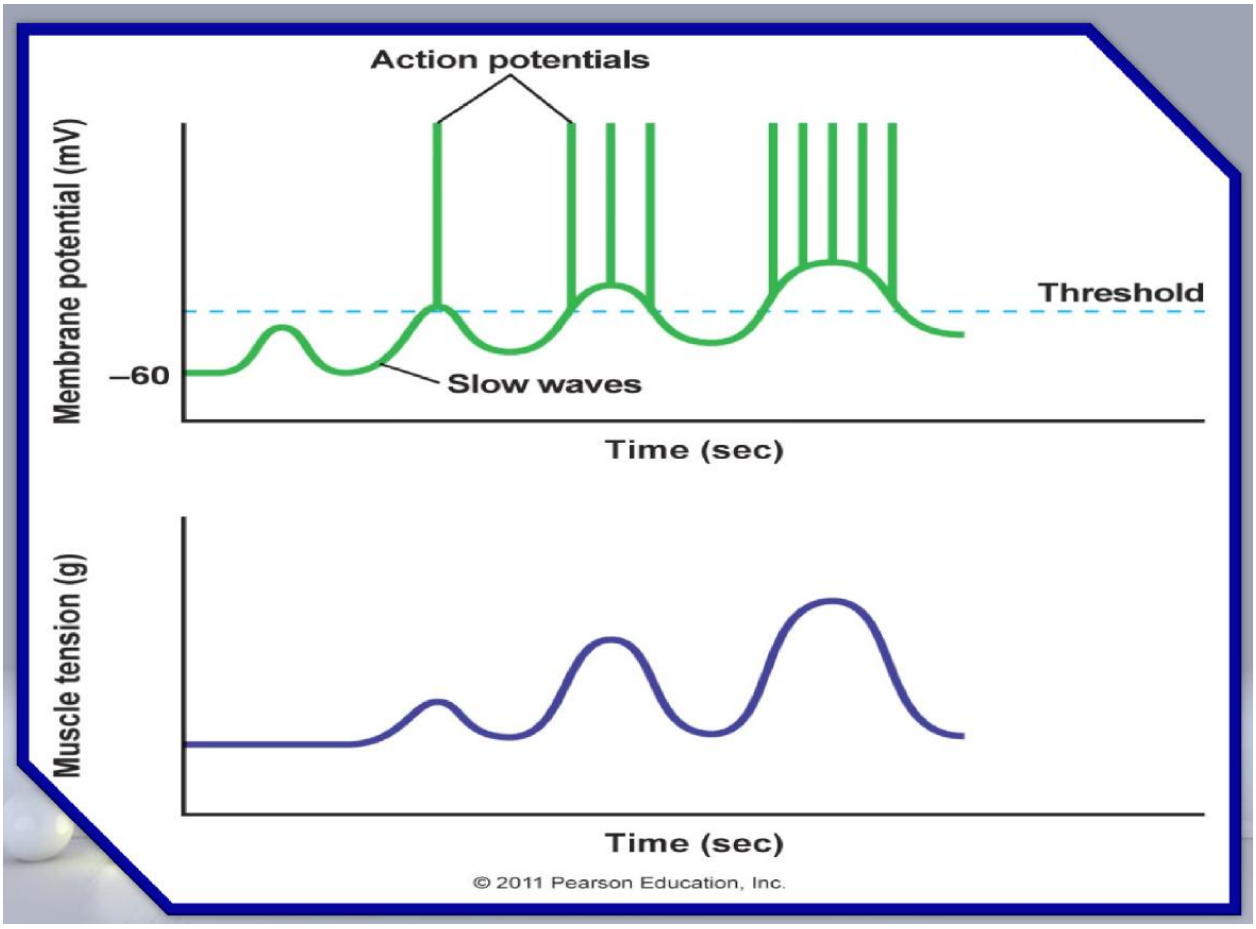
Slow waves (basic electrical rhythm)	Spike potentials
These waves are not action potentials. Instead, they are oscillating (depolarization and repolarization) in the resting membrane potential with unknown cause. * These are slow spontaneous change in RMP (cyclic waves of depolarization & repolarization). * 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. (they don't cause Ca++ entry) * They are generated by interstitial cells of Cajal (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.	* Spikes of action potential are superimposed on the depolarization phase of slow waves followed by contraction. * 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. (because sk.ms depend on Na+ channels only that rapidly open and close) * 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 * 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.

Gastric action potential is long duration than in nerve fibers because it depend on Ca channel that is slow in open and in close

Gastric action potential depends in contraction on Ca unlike nerve fibers which depends on Na channel

slow wave doesn’t cause calcium influx, it depend on Na only therefore no muscle contraction except in stomach.


Structures
Functions
Interstitial cells of Cajal
Production of slow waves
Conduction of slow waves to smooth muscle
Smooth muscle cells
Depolarization and opening of Ca^{2+} channels, production of action potentials
Neural input to ICC and smooth muscle
Autonomic axon


Action potentials
Membrane potential (mV)
Threshold
–60
Slow waves
Time (sec)
Muscle tension (g)
Time (sec)
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3. Changes in Voltage of the Resting Membrane Potential.

- The resting membrane potential averages about (-56) millivolts, 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
  - Resting potential goes up and down (not fixed) is slow wave
  - Slow wave is resting potential and is less negative (-50) than normal resting potential (-70)

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.

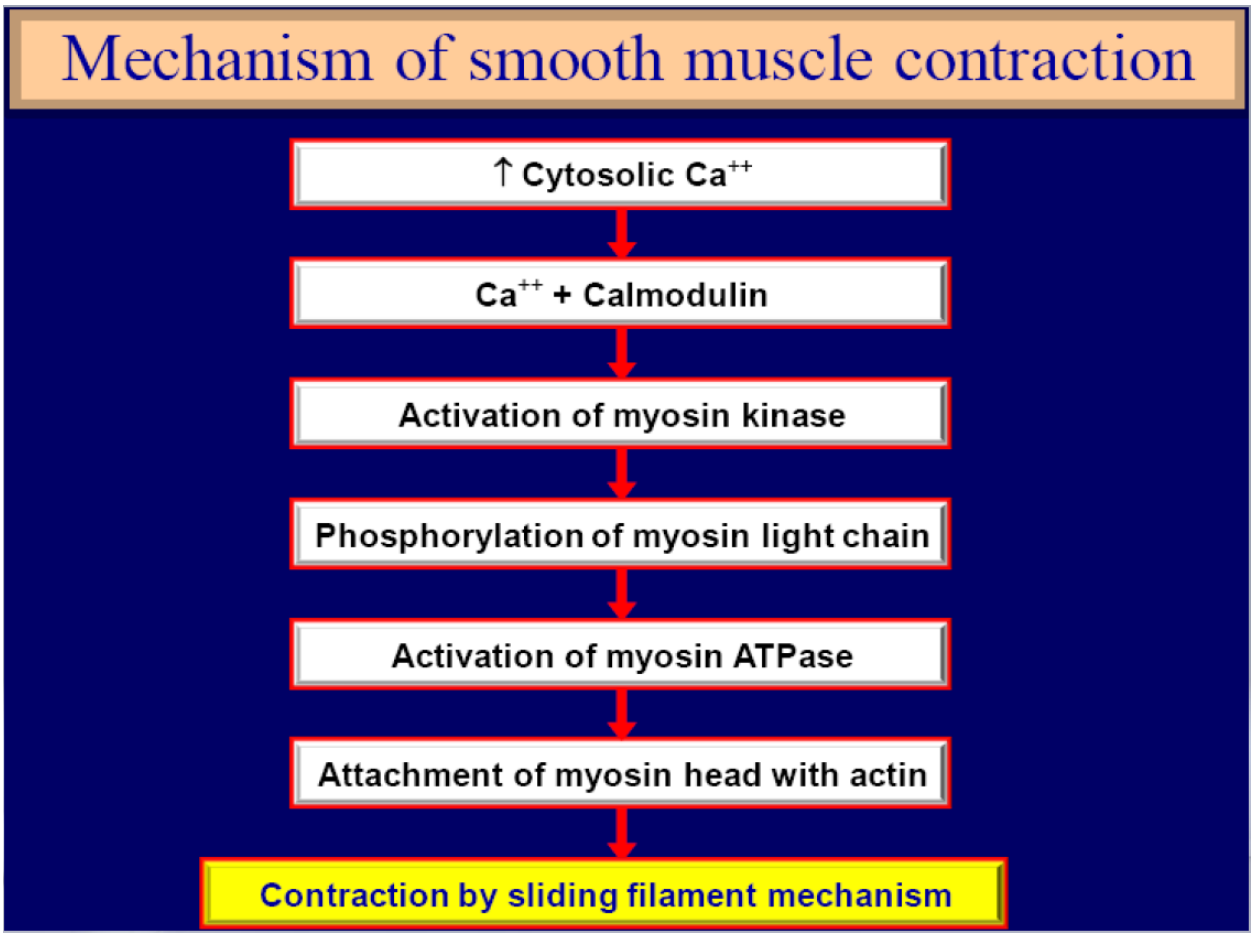
4. Calcium Ions and Muscle Contraction.

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.

Only to understand



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. (Ca++ entry is continuous not excessive, if excessive then it will alter membrane potential)

Control of GIS functions

I- Neural control

* Autonomic (extrinsic) nervous system → sympathetic / Parasympathetic

* The enteric nervous system

II- Hormonal control

Autonomic Nervous System(extrinsic)	Enteric Nervous System (intrinsic)
A- Sympathetic control The sympathetic fibers to the gastrointestinal tract originate in the spinal cord between segments T-5 and L-2. The sympathetics innervate essentially all of the GI tract via postganglionic adrenergic fibers whose cell bodies are located in prevertebral and paravertebral ganglia. **Functions:** 1.Inhibits the motor activity. 2.Contracts the sphincters. 3.Causes vasoconstriction of splanchnic(GIT) blood vessels. 4.Secretion is not necessary inhibited, may be moderately increased. e.g salivary gland secretion is increased by sympathetic 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). •The enteric nervous system is composed mainly of two plexuses: (1) An outer plexus lying between the longitudinal and circular muscle layers, called the myenteric plexus; controls mainly the gastrointestinal movements. (2) An inner plexus, called the submucosal plexus or Meissner's plexus, that 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

B- **Parasympathetic control**

- Via preganglionic cholinergic fibers of vagus and pelvic nerves
- The esophagus, stomach, pancreas and the intestines down through the first half of the large intestine are innervated by vagus nerves.(all GIT until colon)
- 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).
- They terminate on the ganglionic cells of the intramural (submucosal and myenteric) plexuses.

Functions:

a- Increases motility.
b- Relaxation of sphincters.
c- Causes vasodilatation of blood vessels.
d- Stimulates of secretion.

The *postganglionic neurons* of the gastrointestinal parasympathetic system are located mainly in the myenteric and submucosal plexuses. Stimulation of these parasympathetic nerves causes general increase in activity of the entire enteric nervous system

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

The myenteric plexus :

•Consists mostly of a linear chain of many interconnecting neurons.

•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 (VIP))

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

Parasympathetic is excitatory and sympathetic is inhibitory except in sphincter.

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

VIP inhibits muscle contraction and excites gland secretion

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

Afferent *Sensory* Nerve Fibers from the Gut

- **Many afferent sensory nerve fibers innervate the gut. Some of them have their cell bodies in the enteric nervous system 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, or (3) presence of specific chemical substances in the gut.**
- **Signals transmitted through the fibers can then cause *excitation* or *inhibition* of intestinal movements or intestinal 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 gastrointestinal tract into the brain medulla, which in turn initiates vagal reflex signals (vagovagal reflexes).**

Gastrointestinal Reflexes

- **The anatomical arrangement of the enteric nervous system and its connections with the sympathetic and parasympathetic systems support three types of gastrointestinal reflexes that are essential to gastrointestinal control. They are the following:**
  1- ***Reflexes that are integrated entirely within the gut wall enteric nervous system.***
  2- ***Reflexes from the gut to the prevertebral sympathetic ganglia and then back to the gastrointestinal tract.***

  These reflexes transmit signals long distances to other areas of the gastrointestinal tract, such as signals from the stomach to the colon (the *gastrocolic reflex*), signals from the colon and small intestine to inhibit stomach motility and stomach secretion (the *enterogastric reflexes*), and reflexes from the colon to inhibit emptying of ileal contents into the colon (the *colonoileal reflex*).
  3- ***Reflexes from the gut to the spinal cord or brain stem and then back to the gastrointestinal tract.***

  These include: (1) reflexes from the stomach and duodenum to the brain stem and back to the stomach—by way of the vagus nerves—to control gastric motor and secretory activity; (2) pain reflexes that cause general inhibition of the entire gastrointestinal tract; and (3) 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 (the defecation reflexes).

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

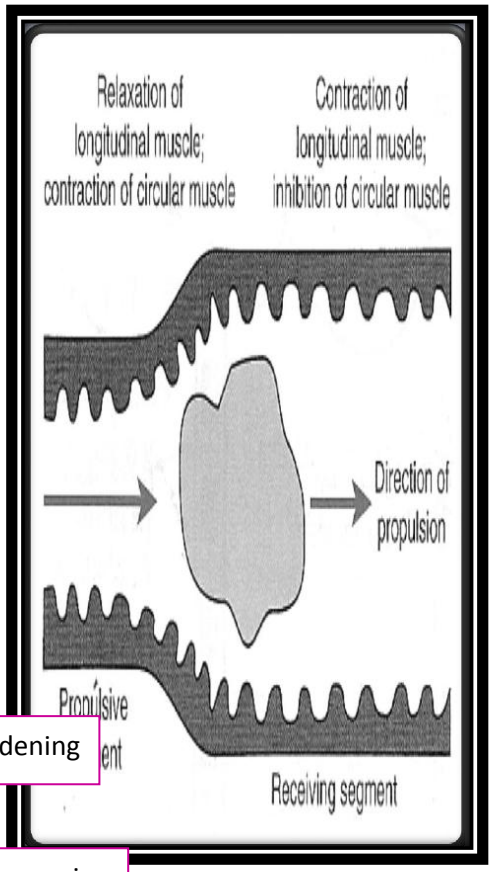
* Endocrine cells are located the pancreas, in the mucosa and submucosa of the stomach and intestine.
* They produce hormones that act on the secretory cells located in the wall of GIT, in the pancreas or in the liver to alter the rate or composition of their secretion.
* Other hormones act on smooth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

At the end of the GIT block it should be easy

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.) } Lumen widening

Propulsive segment ---contraction (circular M.)
----relaxation (longitudinal M.) } Lumen narrowing

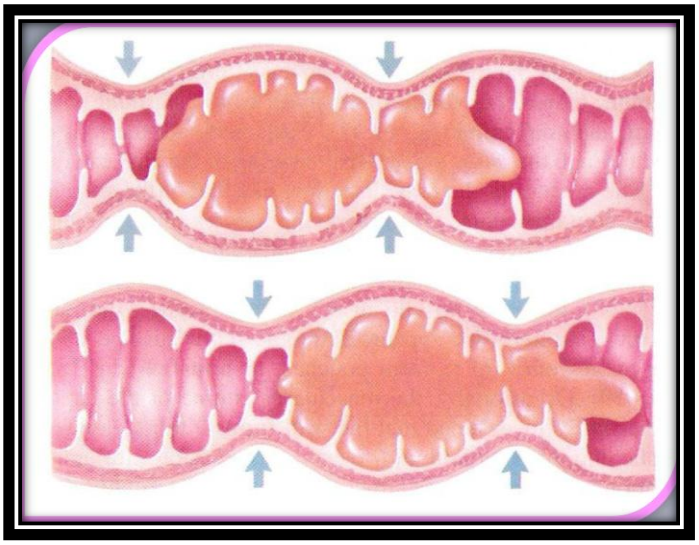
Peristaltic Reflex and the "Law of the Gut." When a segment of the intestinal tract is excited by distention and thereby initiates peristalsis, the contractile ring causing the peristalsis normally begins on the orad side of the distended segment and moves toward the distended segment, pushing the intestinal 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

(contraction rings at different levels at the same time---- segments)

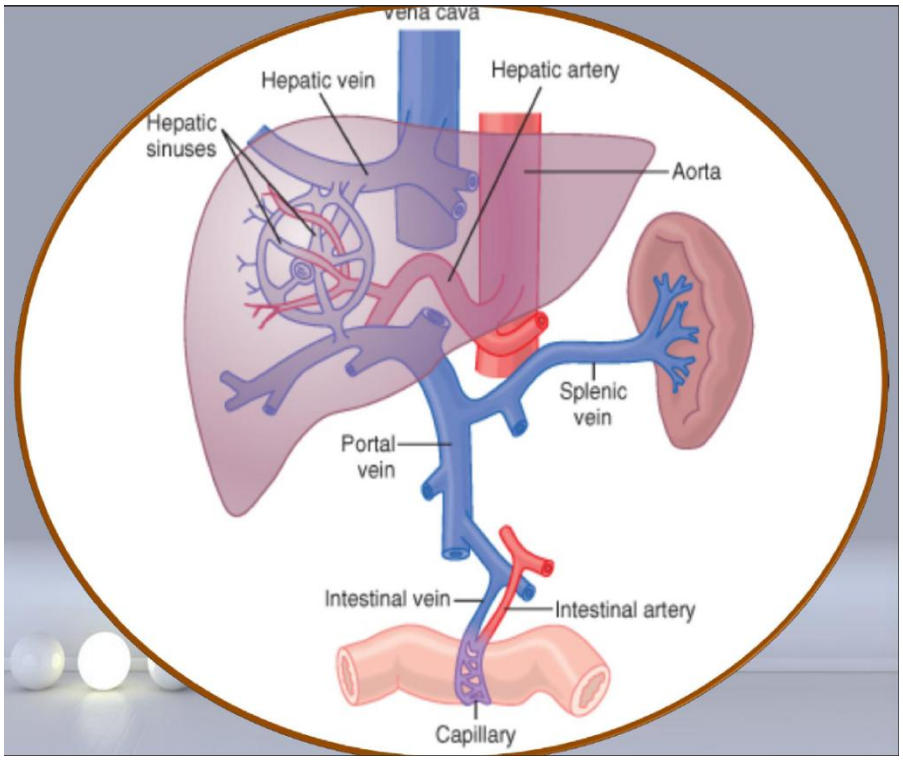


Gastrointestinal Blood Flow-"Splanchnic Circulation"

•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 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.

Summary

- Unitary type is contracted in respond to stretch because it has a lot of gap junctions

-Multiunit type is contracted by neural input

-interstitial cell of cajal is pacemaker .

-Gastro colic reflex : ask colon to increase contraction

-Gastroemtic reflex : small intestine send to sympathetic to tell the stomach to stop motility and secretion.

-Propulsive depend on myentric plexus

-Mixing movements: Blend different juices with the chyme

Bring products of digestion in contact with absorptive surfaces

Questions

1. stimulation of the sympathetic system

A. increase in activity of the entire enteric nervous system.

B. inhibit motor movements of the gut

C. increase activity of the GI

2. Movements in the Gastrointestinal Tract

A. contraction (longitudinal M.) in Propulsive segment

B. contraction (circular M.) in Receiving segment-

C. relaxation (circular M.) in Propulsive segment

D. relaxation (longitudinal M.) in Propulsive segment