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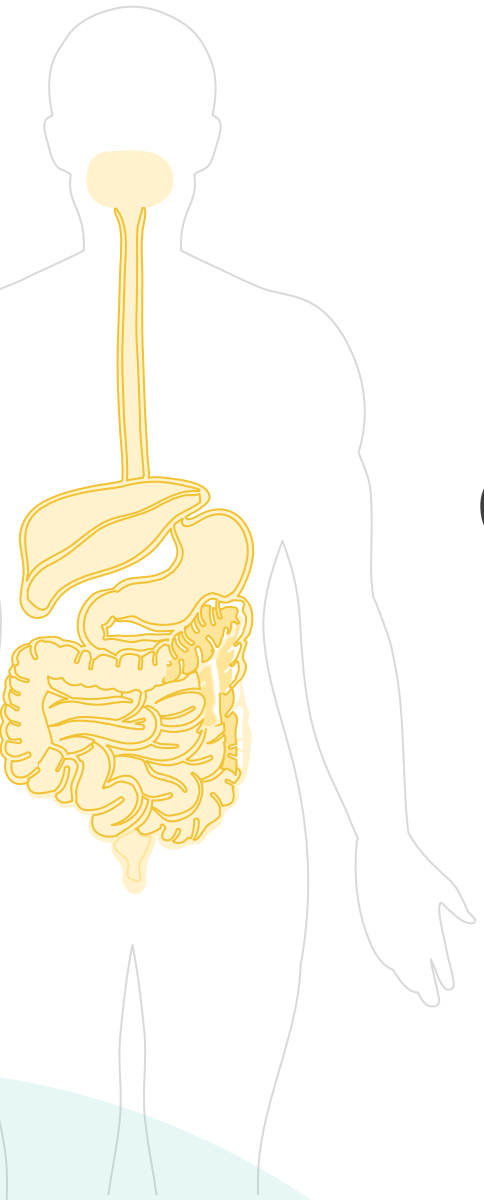


General Principles of GIT Physiology

GNT Physiology

Color Index:

- Main text
- Important
- Female Slides
- Male Slides
- Notes
- Extra

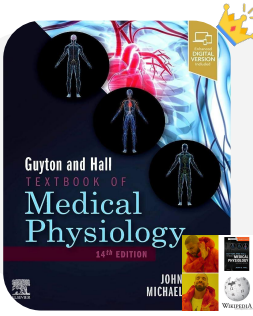
Editing File

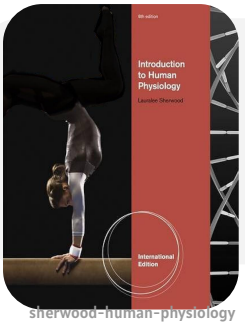
Objectives

- Physiologic Anatomy of the Gastrointestinal Wall
- The General Characteristics of Smooth Muscle
- Smooth muscle cell classifications and types of contraction
- Muscle layers in GI wall
- Electrical Activity of Gastrointestinal Smooth Muscle
- Slow Waves and spike potentials
- Calcium Ions and Muscle Contraction
- Neural Control of Gastrointestinal Function-Enteric Nervous System
- Differences Between the Myenteric and Submucosal Plexuses
- Types of Neurotransmitters Secreted by Enteric Neurons
- Autonomic Control of the Gastrointestinal Tract
- Hormonal Control of Gastrointestinal Motility
- Functional Types of Movements in the GI Tract
- Gastrointestinal Blood Flow-"Splanchnic Circulation"
- Effect of Gut Activity & Metabolic Factors on Gastrointestinal Blood Flow.

Resources

Only GI chapters included





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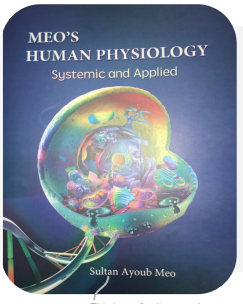


This is prof sultan meo!

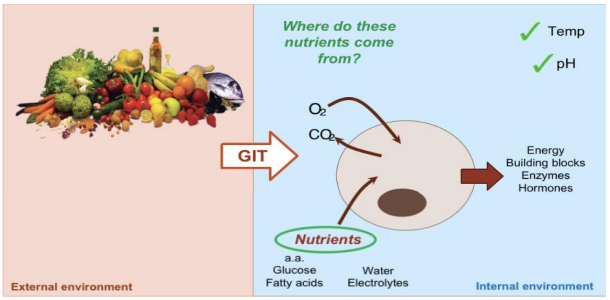
Click here for a helpful channel by the team!

Introduction

Let's start with a story

- The foundations of what we now know about digestion came from a shotgun wound to the abdomen that created a window to the stomach.

1- What is the role of the GI system in maintaining homeostasis?



- This internal environment contains contents which define how the cell will live.
- What essential elements do cells need from the internal environment? O_2, Nutrients, pH, Temperature, waste products

2- What are the challenges facing the GI system while it is trying to do its job?

1-Autodigestion, 2-infection,3-transform Macromolecules to Micromolecules.

3- How do nutrients reach our internal environment?

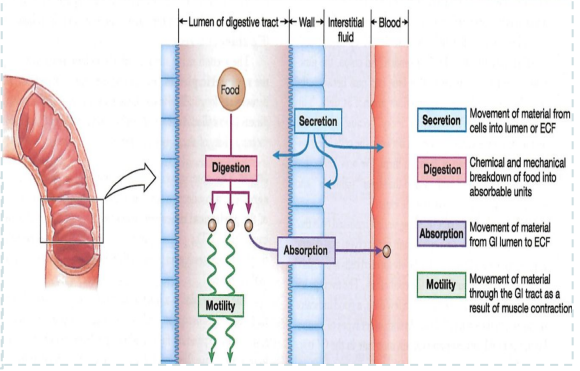
- through the GI system.
- The **main function** of the GI system is **transfer nutrients** from external environment into the internal environment.
- Can our cells utilize nutrients immediately as they are in the food we consume? No. The GI system first need to break down the macromolecule into micromolecule then absorb it from the lumen of GI to blood so it can reach the cell.
  Ex: sugar → monosaccharide, protein → amino acid etc.
- Is it just enough to ingest food to make nutrients available for cells to use?

Protein, meat, carbs, vitamins nutrients, fats. → Ingest → **Macromolecules in food** → **There are 4 basic processes that enable it do its job** → **Micromolecules that cells can use**

The 4 Basic GI Processes:

1 **Motility**: movement of food
The muscular contractions that mixes and moves GI contents forward through the GI tract.

2 **Secretion**:
Along the way, digestive juices are secreted into the GI lumen by exocrine glands.
Importance of secretion: contains enzymes that break down macromolecules, and lubrication, immunity



3 **Digestion**:
As the contents move along the GI tract, complex foodstuff gets broken down into smaller absorbable molecules. It mixes bolus of food with other secretions and makes it more accessible for enzymes and secretion. It's a mechanical and a chemical process

4 **Absorption**:
The small units are transferred from GI lumen into blood or lymph.

Gastrointestinal Processes

Secretion:

Definition: it is an active process in which the GI tract secretes digestive juices (ex: acids, enzymes) which may come from the exocrine glands that are attached to the GI system, or from specialized cells in the GI wall.

Digestive secretions consist of:
Water + electrolytes + specific organic constitutes (enzymes, bile salts, mucus..ect) each region will have its own juice

Digestion:

Three different biochemical categories of foodstuff

Carbohydrates
Main energy source

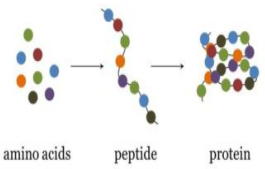
Carbs that we **ingest** are polysaccharides (starch, glycogen, mono-disaccharides)

Carbs that can be **reabsorbed** are monosaccharides (glucose, fructose, galactose)

Digestion will break down polysaccharides into monosaccharides.

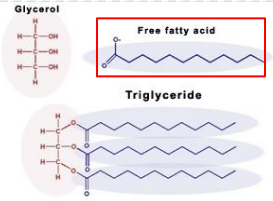
Protein
Imp. for everything

Digestion will break down dietary proteins
↓
small polypeptides
↓
amino acids



Fat
Energy source

Dietary fats is usually triglycerides
↓
Monoglycerides



The end product of triglycerides is = monoglycerides + free fatty acid

Absorption:

Definition: The transfer of small absorbable units form the GI lumen into blood and lymph.

- How and where? It occurs by and in the splanchnic circulation.

Motility:

- The importance of movement of the wall of the GI system is:
  1. Mixing with digestive secretions
  2. Propulsion
  3. Exposure to absorptive surface
- The structure that is responsible for its ability to produce movement is **the smooth muscle cells**.

Food Journey Along GIT

1) Mouth & Oropharynx

1. Chop & lubricate food
2. Initiate carb digestion
3. Propels food into the esophagus

Mechanical breakdown of food occurs and the chemical digestion of carbs starts. Oropharynx will propel food into esophagus

2) Salivary glands

1. Lubrication
2. Have enzymes for carb digestion (amylase)

3) Esophagus

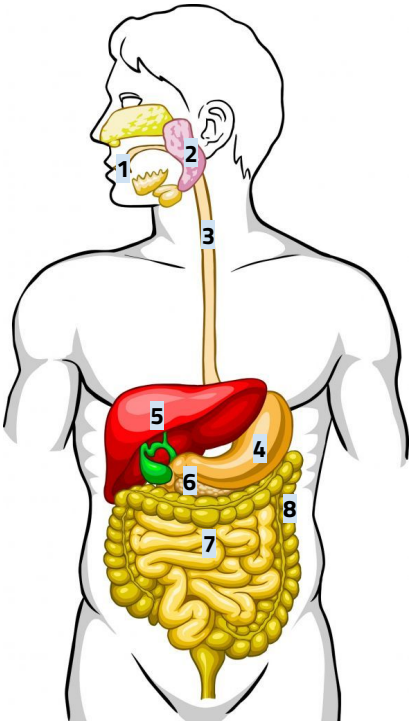
Conducts food to stomach

It's a path that allows food to reach the stomach.

4) Stomach

1. Stores food
2. Initiates protein digestion

When we eat a big meal in bouts which are large. Until the body breaks it down, it will be stored in the stomach.
The stomach continues the process of digestion and breaking down (chemically and mechanically).



5) Liver & Biliary system

Secretes bile for fat digestion

6) Pancreas

Secretes digestive enzymes into duodenum (HCO_3^-)

7) Small Intestines

1. Continues Digestion
2. Primary site of absorption

By the time the bolus of food leaves the stomach and reaches the intestine, it will be called chyme (more liquid).
The intestine will continue digesting whatever had not been digested previously.
It will start absorbing nutrients into the blood.
There will be secretion of digestive enzymes coming from the pancreas as well as bile acids coming from biliary system and liver.

8) Large intestine

1. Reabsorbs fluid & electrolytes
2. Stores fecal matter.

Large Intestine is responsible for reabsorbing electrolytes and fluid that have been secreted into the bolus. Lastly, stores feces until it's time to be excreted

Gastrointestinal Function

Male slides

The alimentary tract provides the body with a continual supply of water, electrolytes & 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

The GI system

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

Digestive Tract

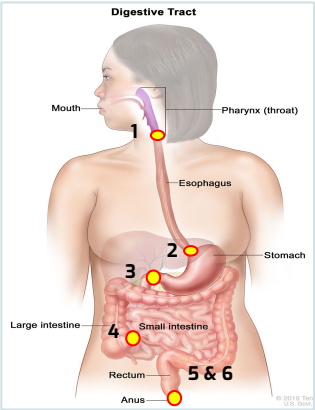
- A hollow tube extending from mouth to anus.
- Each region is modified to serve its function.
- Regions are **separated by** sphincters (to control movement from one region to the other).

Accessory organs

Include:

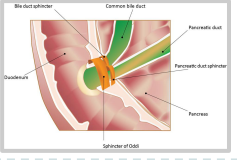
1. Salivary glands (into mouth)
2. Liver and gallbladder (into duodenum & aid in digestion)
3. Pancreas

These add secretions to the digestive tract.



1. **Upper esophageal sphincter (UES) :** Between the pharynx & esophagus
2. **Lower esophageal sphincter (LES):** Between esophagus and stomach
3. **Pyloric sphincter:** Between stomach and duodenum
4. **Ileocecal valve:** Between small intestine and cecum
5. **External and internal anal sphincter:** Between GI system & External env. **Total = 6 sphincters**

In addition of "sphincter of Oddi", that control secretion system coming from Accessory organs into the duodenum.



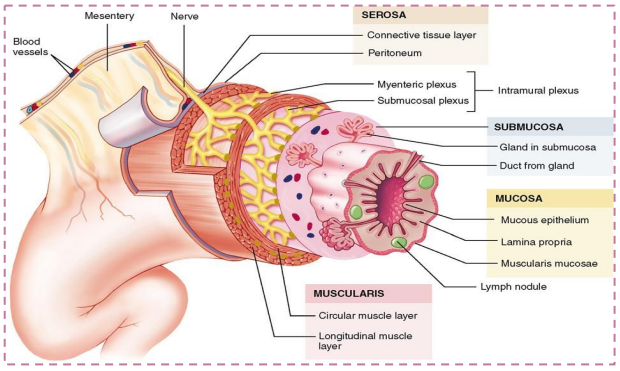
To help U remember, Oddi=Audi 

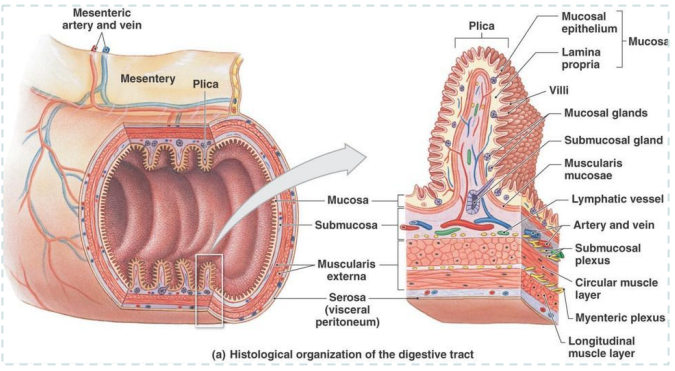
Physiologic Anatomy of the GI wall

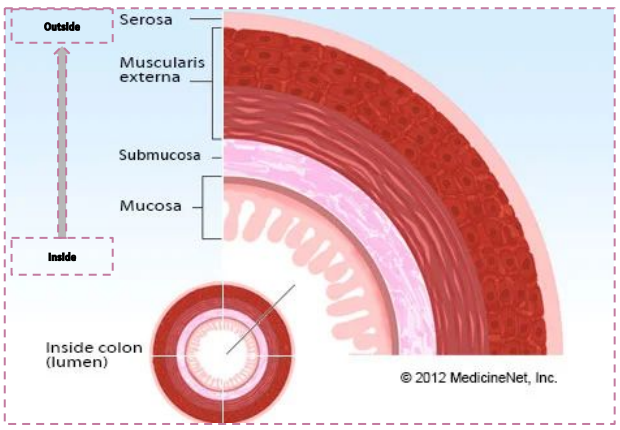
amazing drawing by Sara Alshahrani according to female doctor

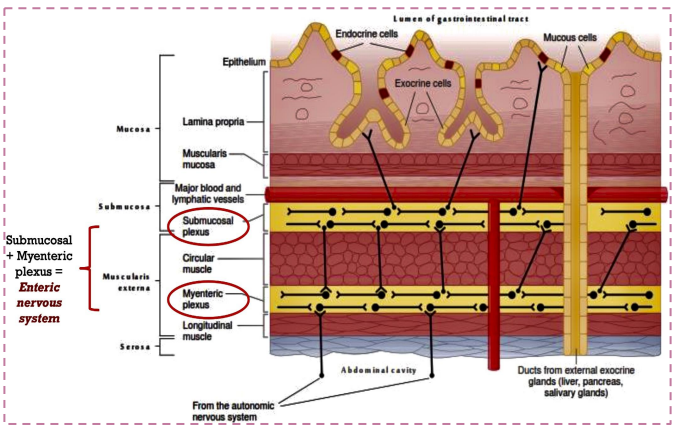
Anatomy of the GI wall:

- **4 main layers/ 5 layers (from outer surface inward):**
  - Serosa
  - Muscularis
    - Longitudinal muscle layer the contraction = shorten of the segment
    - Circular muscles layer the contraction = constrict the lumen and decrease its diameter
  - Submucosa (Denser CT) larger blood vessels, nerves and lymphatics pass through
  - Mucosa (Loose CT) small capillaries, vessel and nerves pass through
- In addition, sparse bundles of smooth muscle fibers, the mucosal muscle lies in the deeper layers of the mucosa.
- Movement is possible in the GIT because of the presence of smooth muscle layer.
- A cross section of the GIT will look the same from the esophagus to anus, because the structure and layers of the wall are the same. All contain 5 layers. However they are different in cells, glands, length etc.

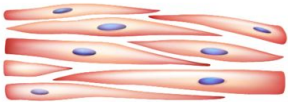
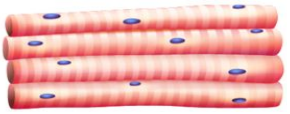
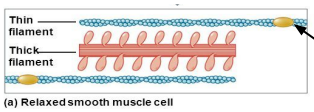
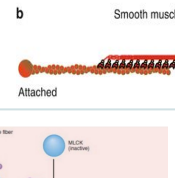
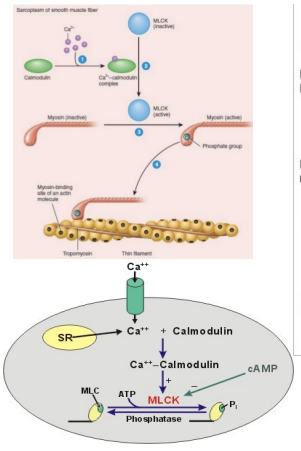
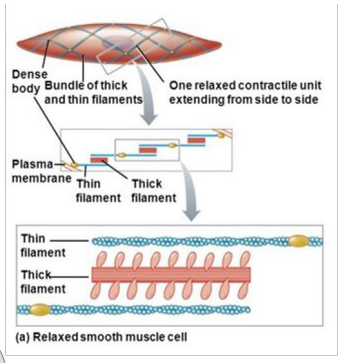
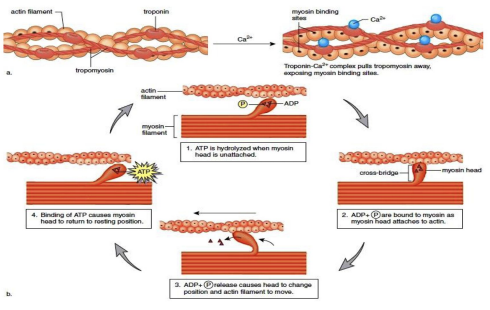
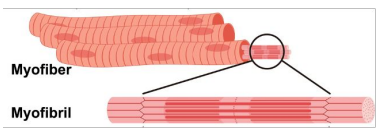








Characteristics of Smooth & Skeletal Muscle

Smooth muscles	Skeletal muscle
	
Spindle shaped, Non-striated	Cylindrical muscle fibers, Striated
Single nucleus	Multinucleated
Smaller and shorter	Long
Involuntary	Voluntary
Contractile units arranged **diagonally**	Contractile units arranged **parallel** to long axis of fiber
 **Dense bodies** actin لتثبيت	**Z-lines** actin لتثبيت
Cross bridges are present along the entire length of the thick filament	Bare portion in the center of the thick filament.
Side-polar myosin arrangement. Cross bridge is covering the whole thick filament (myosin)	Bipolar myosin arrangement (no cross bridge in the middle)
Ca^{+2} induces a **chemical** change in **myosin** (**thick** filament)	Ca+2 induces a **physical** (mechanical) change in **actin** (**thin** filament)
Contraction: thin filaments surrounding the thick filament will move into opposite directions	**Contraction:** both thin filaments surrounding thick filament will move in the same direction
	
 	 

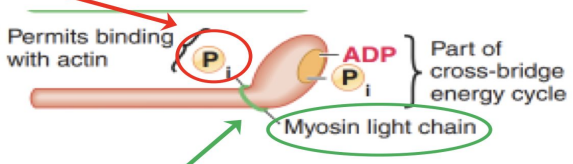
Contraction of Smooth Muscles

- Contraction is brought about by sliding of the **thin** filament **over** the **thick** filament.
- Myosin attaches to actin by its actin-binding site and then the power stroke causes sliding of the actin filament over myosin.
- The thin filament of smooth muscle **does not** have troponin.
- Tropomyosin **does not** block actin-binding site.

What stops myosin from binding to actin at rest?

The myosin head can interact with actin only when the MLC is ***phosphorylated***

The **thick filaments** are composed of myosin, and the **thin filaments** are predominantly actin.



At the neck region of the myosin head → a lightweight protein is attached = Myosin light chain (MLC)

Myosin is prevented from binding to actin at rest by myosin light chain (MLC). When MLC is phosphorylated, myosin will form a cross bridge with actin and a **contraction** will occur

↑ $[Ca^{+2}]_i$

↓

Ca^{+2} binds to calmodulin

↓

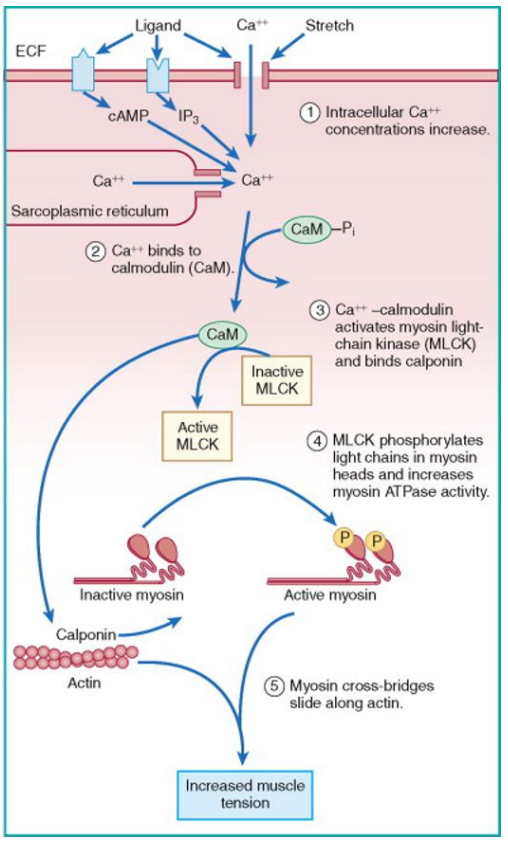
Ca-CaM complex activates MLCK (Myosin light-chain kinase)

↓

Phosphorylates myosin head increasing the activity of ATPase

↓

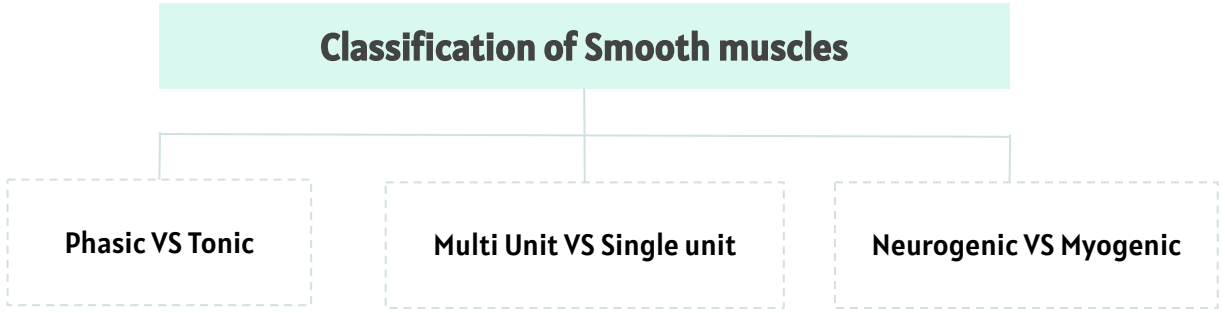
Myosin head attaches to actin causing sliding of the filaments



Smooth muscle cells use cross-bridge cycling between actin and myosin to develop force, and calcium ions (Ca^{+2}) serve to initiate contraction. Thus, contractile activity in smooth muscle is determined primarily by the phosphorylation state of the light chain of myosin

Classification of Smooth muscles

Smooth muscles can be classified in many ways depending on the timing and means of increasing cytosolic Ca^{+2}



A smooth muscle of one organ may be multi unit, phasic and neurogenic While another organ it might be single-unit, tonic and myogenic. it can be classified by the 3 classifications at the same time.

Phasic VS Tonic

(depending on its contractile activity and how its cytosolic Ca^{+2} increases)

Phasic

- Contracts in bursts "intermittently"
- Contraction → Relaxation
  a cycle of a contraction followed by a relaxation
- Contraction triggered by an action potential which increase [Ca^{+2}]
  When an AP reaches cell, it will open Ca^{+2} channels. Ca^{+2} will flow from ECF to ICF, and some will come from Sarcoplasmic reticulum -> trigger contraction process.
- Associated with slow wave

Examples:

1. GI tract Most of GI tract is phasic
2. Gastric antrum
3. Small intestine
4. Esophagus

Tonic

- Muscle is usually partially contracted at all times.
- Continuous partial contraction = (Tone)
  they only relax when there's an inhibitory signal coming from NS
- **Causes of tonic contractions:**
  1. Repetitive spike potentials
  2. Hormones
  3. Continuous entry of Ca^{+2} ions
- Not associated with slow wave unlike phasic (often lasting several minutes or hours).
- This type has a **low RMP** (close to +ve than -ve) at which some **voltage gated Ca^{+2}** channels are open → entry of Ca^{+2}→ partial contraction
- **Examples:**

1. Blood vessels are always at a certain tone. This plays a role in BP regulation
2. Airways
3. Orad region of stomach (Orad = upper part of stomach)
4. Lower esophageal, ileocecal, internal anal **sphincters**

Focus its LOWER esophageal sphincter because the upper is made of skeletal muscle NOT smooth muscle

Classification of Smooth muscles cont.

Single unit vs. Multi-unit

Based on how they get excited

Multi Unit

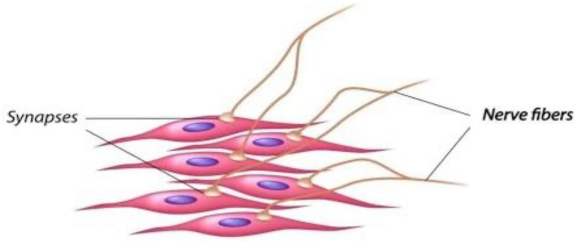
- Composed of discrete, separate smooth muscle fibers.
- Each fiber **operates independently.**
- Each is innervated by a single-nerve ending.

- **Does not** contract in response to stretch or **without** neural input (such as in esophagus & gallbladder) activated by hormones and neurotransmitters.

Examples:

-Ciliary muscle and iris of the eye (accomodation)

-Piloerector muscle (goose bumps قشعريرة)

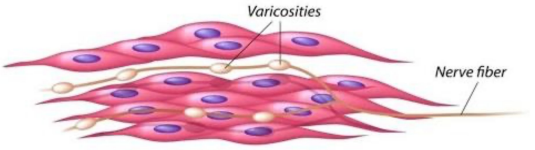


Multiunit Smooth Muscle

Single (Unitary)

- Composed of many smooth muscle fibers that become excited and **contract as a single unit.**
- Cells are connected by **gap junction**
- Function as a **syncytium.**
- Contracts spontaneously in the absence of neural or hormonal influence but in response to **stretch** (such as in stomach and intestine).
- The smooth muscles are connected to each other by gap junctions. So when a stimulus arrives it doesn't have to arrive at each muscle, it's enough for it to arrive at one then the signal will spread to the rest of the muscle through gap junctions.

Examples: Uterus, GI tract.



Single-unit Smooth Muscle

Myogenic vs. Neurogenic

Female slides

Based on how contraction is initiated

Neurogenic

- Contraction is initiated in response to nerve "signals" stimulation.

Myogenic

- Self-excitable
- Contraction is initiated intrinsically within the muscle **without** external nervous stimulus.

They are specialized cells that act as **pacemakers** and generate an AP regardless of external innervation.

Types of Smooth Muscles in GI

The General Characteristics of Smooth Muscle in the Gut

	Longitudinal	Circular
Characteristics	• Thinner and weaker than circular • Contraction **shortens** the segment of the intestine and expands the lumen • The **Ca^{+2} influx from outside is important in the activity** of this type of muscle. because the intracellular Ca^{++} storage is insufficient • Contraction shortens the distance that the food has to travel	• Thicker and more powerful than longitudinal • Contraction **reduces** the **diameter** of the lumen and increases its length. • **Intracellular release of Ca^{+2}** is more important. • More gap junctions are available. • Contraction pushes food forward or backward
Contains	**Excitatory** motor neurons	**Excitatory & inhibitory** motor neurons because they sometimes need to relax
Innervated by	**Enteric Nervous System (ENS)**	

Important

The Specific Characteristics of Smooth Muscle in the Gut

Gastrointestinal Smooth Muscle Functions as a Syncytium

Numbers are not important
Individual smooth muscle fibers
Length: 200 to 500 µm
Diameter : 2 to 10 µm

Arranged in bundles of ≤ 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**, that is when an action potential is elicited within the muscle mass, it generally travels in all directions in the muscle.

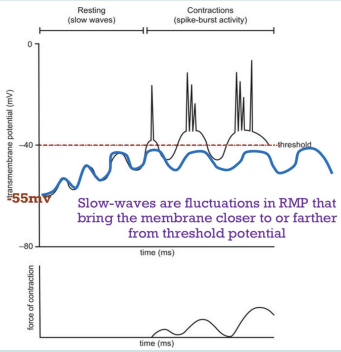
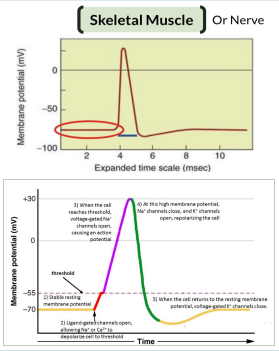
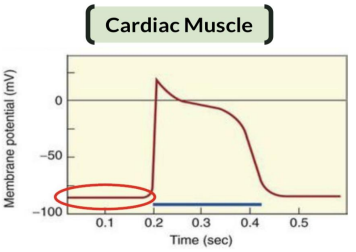
Electrical Activity of Gastrointestinal Smooth Muscle

The smooth muscle of the GIT is excited by almost **continual slow, intrinsic electrical activity** along the membranes of the muscle fibers.

The activity is divided into two types of electrical waves :

- **Slow Waves** (Resting)
- **Spikes** (Action potentials)

Electrical Activity of Different Muscles Types

	Smooth muscle	Skeletal muscle/Nerve	Cardiac muscle
RMP value	**-50mV** to -60mV (More +ve)	-70mV	-90mV
RMP behavior	NOT stable (Fluctuating)	Stable (Linear)	Stable (Linear)
Feature	Threshold: -40mV RMP is characterised by spontaneous gradual alternating (Fluctuations): Hyperpolarization (Far from threshold) & Depolarization (Close to threshold) swings in the potential these fluctuations are called Slow wave potentials (no contraction occurs) If the depolarization of slow waves reaches the threshold, spike potential appears (real AP) → causes contraction. -Why does this fluctuating happen? Because GIT smooth muscles don't have to be contracted all the time (e.g. during fasting)	AP is generated by stimulus, which increases RMP to threshold level AP produced by Na+ influx	AP is generated by stimulus, which increases RMP to threshold level AP produced by Na+ influx While plateau is caused by Ca+2
Graphs			

Guyton

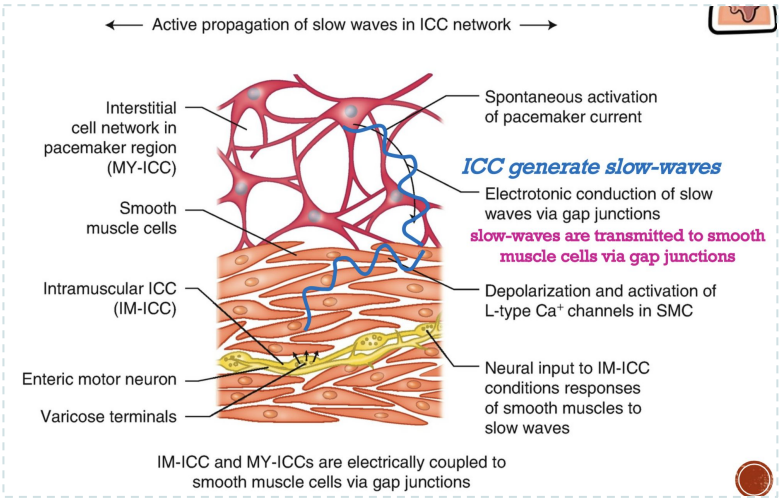
The slow waves usually do not by themselves cause muscle contraction in most parts of the gastrointestinal tract, except perhaps in the stomach. Instead, they mainly excite the appearance of intermittent spike potentials, and the spike potentials in turn actually excite the muscle contraction.

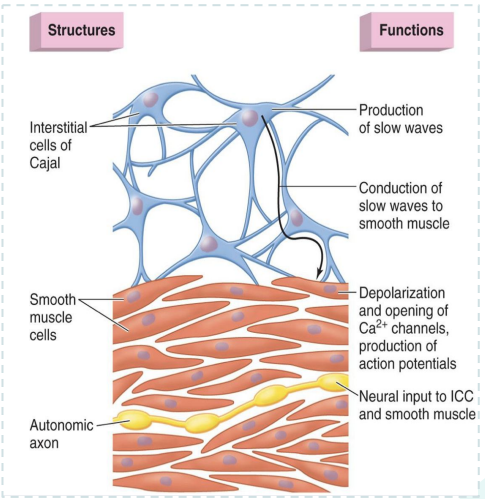
Electrical Activity: Slow Waves

Slow waves	
Definition	• Most GI contractions occur **rhythmically**, determined mainly by the frequency of slow waves of smooth muscle membrane potential. • These waves are **not action potentials.** • **They are oscillating depolarization and repolarization in the resting membrane potential with unknown cause.**
Intestinsity	• The Intestinsity of slow wave varies between 5-15mV

Frequency	• The **frequency of slow wave varies from one organ to the other in GIT**:
	  ○ **Stomach = 3/min** which is why gastric emptying is considered slow when compared to the rest of GIT
	  ○ **Duodenum = 12/min**
	  ○ **Ilium = 8-9/min**

RMP	• RMP is NOT stable. It is characterized by **spontaneous alternating hyperpolarizing and depolarizing swings** in potential slow wave potential. • The level of RMP in smooth muscle can be modified by several factor:. 1- If it becomes less negative = depolarized muscle is more excitable. 2- If it becomes more negative = hyperpolarized muscle becomes less excitable.
Features	• **No Ca entry** (only Na) • Slow waves are not AP. They can not generate contractions. • Slow waves can generate an AP that will generate a contraction. • **IMPORTANT:** The ion that is responsible for the slow wave is Na+ influx **not** Ca^{+2}
Threshold	• When the slow wave potential reaches threshold → true action potential is generated on the peak of slow wave = **spike potential.** • Every action potential will have a depolarization followed by repolarization.
Origin:	• They may originate in the **interstitial cells of Cajal (ICC)** • **Interstitial cells of Cajal (ICC):** a specialized, non-contractile cell that can undergo cyclical changes in membrane potential. • **ICC is the pacemakers** of the gut. • ICC are abundant in the myenteric plexuses. • These ICCs form a network with each other and are interposed between the smooth muscle layers, with synaptic-like contacts to smooth muscle cells. • When we disconnect the GI system from CNS, the GI can work normally since it has its own pacemaker.





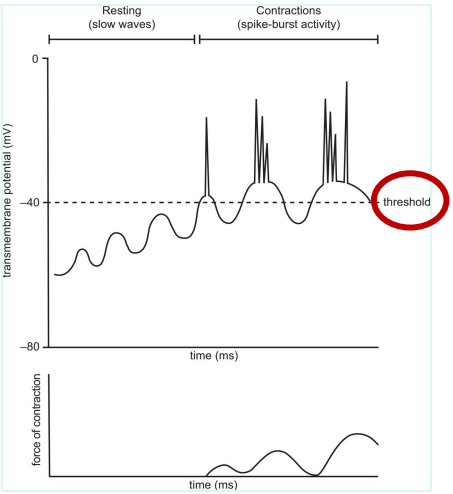
Important

Electrical Activity: Spike Potential

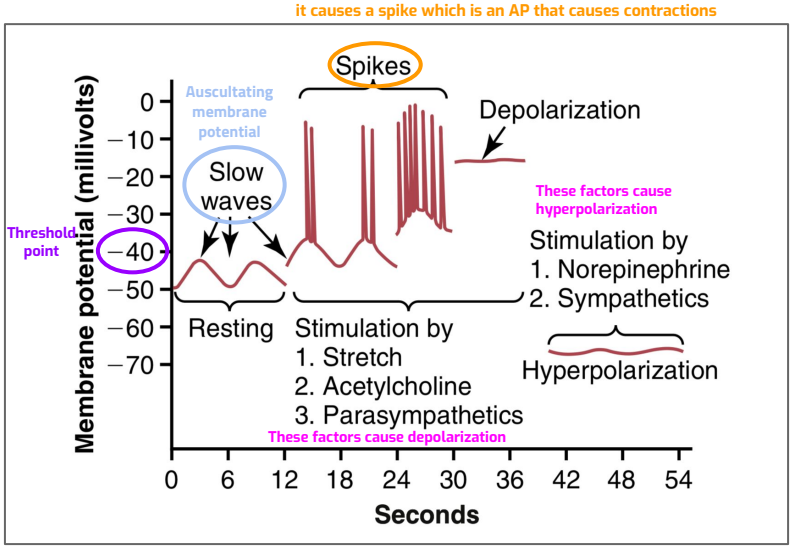
- Spike potential are **true action potentials.**
- They occur automatically when the resting membrane potential of the gut smooth muscle is more positive (<-40mV)
- **Threshold:** <-40mV
- **Normal RMP in smooth muscles:** between -50 and -60 mV
- The resting membrane potential averages about -56 mV

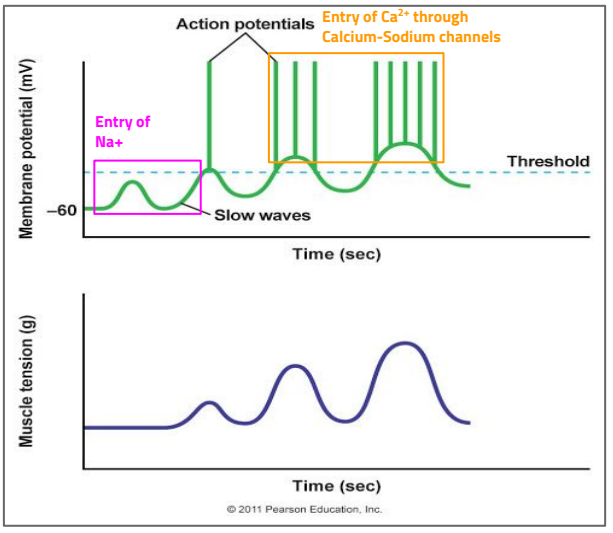
  RMP= resting membrane potential
- **The higher the slow wave potential rises, the greater the frequency of the spike potential, ranging between 1 - 10 pikes per second.**

- They last **10 - 40 times** as long in gastrointestinal muscle as the action potentials in large nerve fibers, each garoeintenal spike lasting as long as **10 - 20 msec.**
- **Increases in the spikes' frequency → increase in the strength of contraction.** الدكتور قالها بالحرف ودي اجيبها
- **More rises in the slow wave ->increase in the frequency of the spikes.** تكملة للملاحظة الي فوق



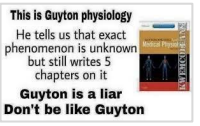
When the slow waves reach the threshold, it causes a spike which is an AP that causes contractions





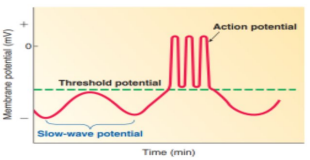
Guyton

The precise cause of the slow waves is not completely understood, although they appear to be caused by complex interactions among the smooth muscle cells and specialized cells, called the interstitial cells of Cajal, which are believed to act as electrical pacemakers for smooth muscle cells. 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. The interstitial cells of Cajal undergo cyclic changes in membrane potential due to unique ion channels that periodically open and produce inward (pacemaker) currents that may generate slow wave activity.

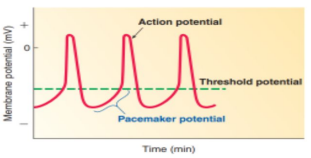


Female slides

The AP of the smooth muscle is similar to the AP pacemaker of cardiac muscle "SA node". The difference it that the SA node is unstable but it's regular. It always reaches the threshold, unlike muscle contraction. Significance: we don't need the GIT to work while we're asleep, unlike the cardiac muscle. we need our heart to pump through out our whole life.



Slow-Wave potential



Pacemaker potential

Smooth Muscle Electrical Activity

- In GI smooth muscle fibers, 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.**
- These channels are **much slower** to open and close than the rapid Na channels of large nerve fibers.

Ca++ ions & Muscle Contraction:

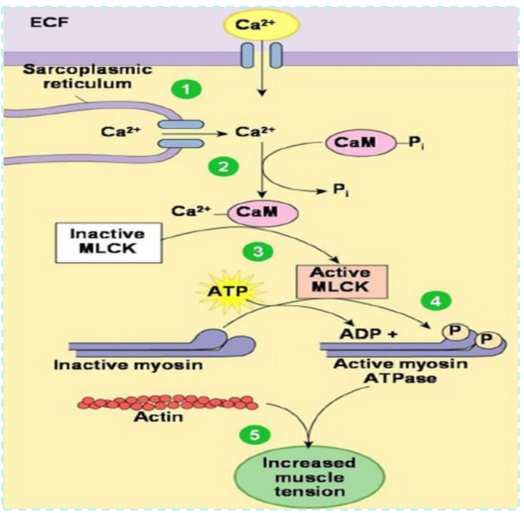
- **Smooth muscle contraction occurs in response to entry of calcium ions into the muscle fiber.**
- **The slow waves** do not cause calcium ions to enter the smooth muscle fiber **(only sodium ions).**
- Therefore, the **slow waves** by themselves usually **cause no muscle contraction** (except in the stomach). Instead, it is during the spike potentials, generated at the peaks of the slow waves, that significant quantities of calcium ions do enter the fibers and cause most of the contraction.

Tonic Contraction of Some GI Smooth Muscle:

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

They don't depend on slow wave because a slow wave may and may not generate an AP. They are controlled by: repetitive spike potentials, hormones and continuous entry of Ca++ ions.

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. Activate myosin crossbridges slide along actin and create muscle tension.



Smooth muscle electrical activity cont.

Important

Factors that <u>hyperpolarize</u> the membrane potential

- **1-** The effect of **norepinephrine** or **epinephrine** on the fiber membrane
- **2-** Stimulation of the **sympathetic** nerves that secrete mainly **norepinephrine** at their endings. Sympathetic stimulation decrease number of spike potentials

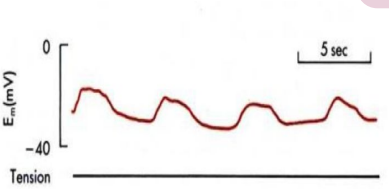
Important

Factors that <u>depolarize</u> the membrane potential

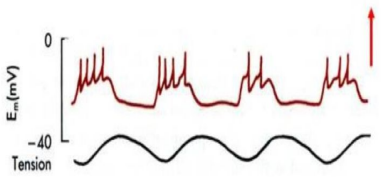
- **1- Stretching** of the muscle
- **3-** Stimulation by several specific gastrointestinal **hormones**
- **2-** Stimulation by **acetylcholine** released from the endings of **parasympathetic** nerve it is considered as an excitatory NS for the GI

Female slides

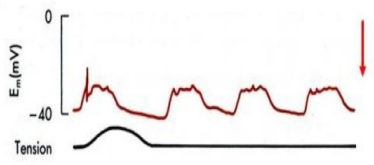
Slow or myogenic wave (oscillating depolarization and repolarization; "basic electrical rhythm") **fail to induce contraction because E_m is below threshold**

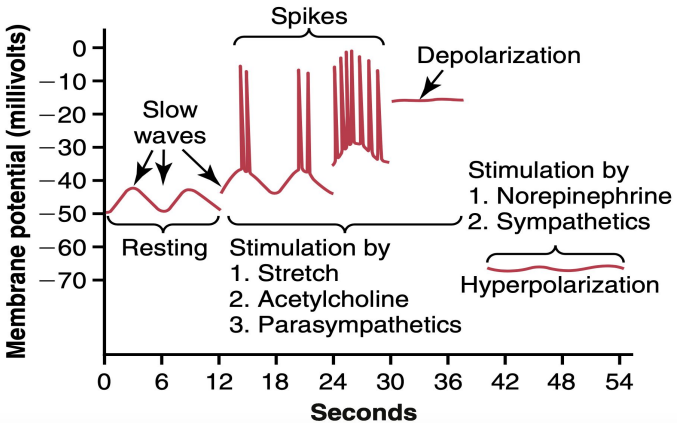


with Parasympathetic input, the membrane at the plateau of the slow wave depolarizes all the way to threshold; **action potentials occur "on top of" the slow wave, and these set off contractions. the contraction /tension follows slightly after the electrical response**



If resting potential is shifted to more negative values (from sympathetic input) spikes and contractions **will not occur**





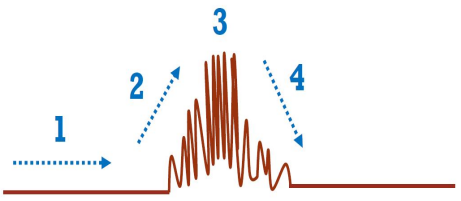
- **The level of RMP in smooth muscle can be modified by several factors, it averages about -56mV.** which is less negative than other cells making it easily excitable
- **If it becomes less negative = depolarized → muscle is more excitable.**
- **If it becomes more negative= hyperpolarized → muscle becomes less excitable.**

Migratory motor complex (MMC)

Please be familiar with the abbreviation

Important

- Rhythmic **contractions** of the small intestine **during** the **fasting** state.
- To clear intestine from it's contents.
- Allows particles > 2mm to pass from stomach to duodenum.
- Starts at the **stomach** and moves down **to** terminal **ileum.**
- At intervals of **90 - 120** min.
- **Motilin** is thought to play a role in their generation.



4 Main Phases

1
Prolonged quiescent period

2
Period of increasing AP and contractility

3
Period of peak electrical & mechanical activity

4
Period of declining activity

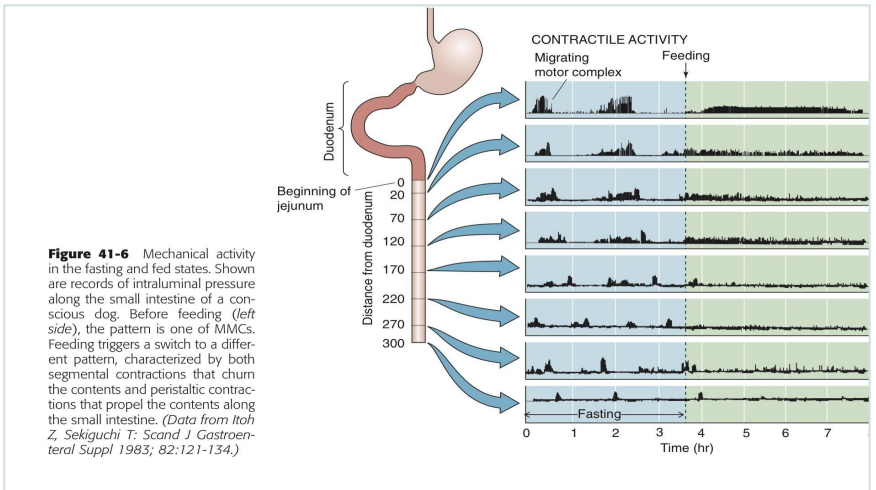


Figure 41-6 Mechanical activity in the fasting and fed states. Shown are records of intraluminal pressure along the small intestine of a conscious dog. Before feeding (*left side*), the pattern is one of MMCs. Feeding triggers a switch to a different pattern, characterized by both segmental contractions that churn the contents and peristaltic contractions that propel the contents along the small intestine. *(Data from Itoh Z, Sekiguchi T: Scand J Gastroenteral Suppl 1983; 82:121-134.)*

Migratory motor complexes
Disappear upon feeding

Control of the GIT system

1 Neural

2 Hormonal

External

-Sympathetic Innervation
(Thoracolumbar Outflow)
-Parasympathetic Innervation
(Craniosacral Outflow)

Local
Brain of gut

Embedded in the wall of the GIT (Enteric Nervous System)

Connections of the Enteric nervous system (ENS):

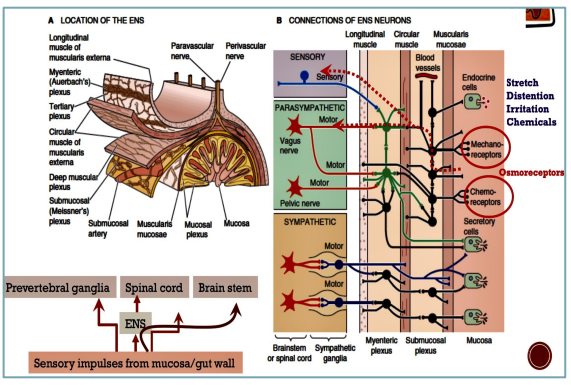
Autonomic Output Connections

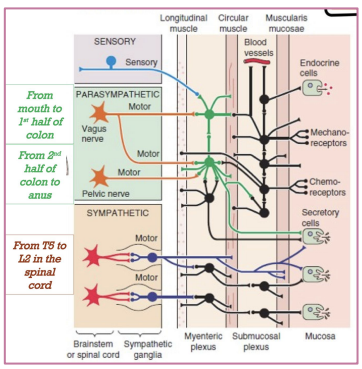
- **Sympathetic Innervation (Thoracolumbar outflow)**: the sympathetic fibers originate in the spinal cord between segments T5 and L2. The sympathetic **innervate all GIT and Secret norepinephrine mainly.**
- Its stimulation **inhibits activity** of the GI system.
- strong Stimulation of SNS can Inhibit motor movements of the gut so greatly that this literally can block movement of food through the GI tract.

- **Parasympathetic Innervation (Cranial and Sacral outflow):**
- **Vagus nerves(cranial division)** innervate 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 **detection reflex**).
- Its stimulation **Increase in activity** of the entire enteric nervous system.

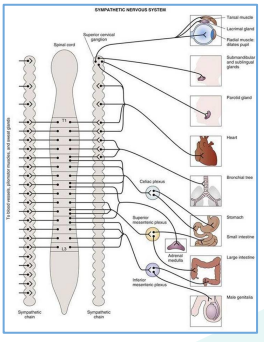
Sensory Input Connections

1. **Stimulus:** Stretch,Distention ,Irritation ,Chemicals.
2. **Receptors stimulated**
3. **Signal Relayed**
4. **Signal Transmitted**: Prevertebral ganglia ,Spinal Cord, Brainstem
5. **Type of signal transmitted**: Inhibitory or Excitatory.

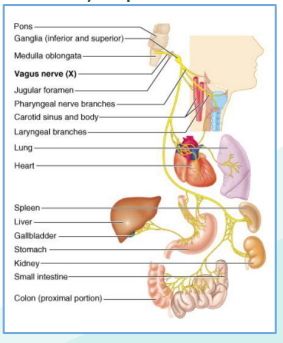




Sympathetic



Parasympathetic



Control of the GIT system cont..

Enteric Nervous System:

- Enteric Nervous System (ENS) is the nervous system of GI tract.
- **It's a part of autonomic nervous system as sympathetic and parasympathetic.**
- 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).

Neural Control of Gastrointestinal Function-Enteric Nervous System

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 brainstem.

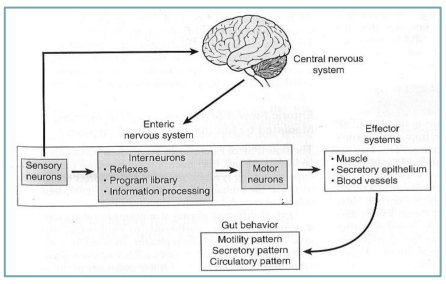
These sensory nerves can elicit local reflexes within the gut wall

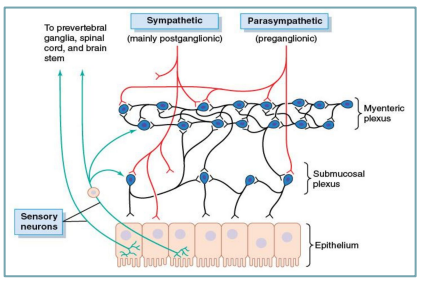
Important

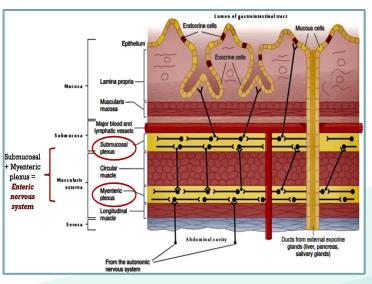
Components of the enteric nervous system

It is composed mainly of two plexuses (interconnected)

The Myenteric (Auerbach's) Plexuses	The Submucosal (Meissner's) Plexuses
• An outer plexus • It lies in between the longitudinal and circular muscle layers. • **Control mainly the gastrointestinal movements (motility)** • Consists mainly of a linear chain of many interconnecting neurons. • When stimulated, its principal effect is to: 1. Increase tonic contraction 2. Increase intensity and rate of the **rhythmical** contractions. 3. Increase velocity of conduction of excitatory waves along the gut wall. • The myenteric plexus has **excitatory and inhibitory** motor neurons.	• An inner plexus • It lies in the submucosa beneath the circular muscle layer • **Controls mainly GI secretion and local blood flow** • Controls : (1) Local intestinal secretion, (2) Local absorption (3) Local contraction of the submucosal muscle that causes various degrees of enfolding of the gastrointestinal mucosa.







Smooth muscle electrical activity cont.

Types of Neurotransmitters Secreted by Enteric Neurons

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

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

- **Neurotransmitters of motor neurons:** (increase motility)
  - Substance P
  - Ach
- **Neurotransmitters of secretomotor neurons:** (from glands)
  (releasing of water, electrolytes and mucus from crypts of Lieberkuhn)
  - Ach
  - Vasoactive intestinal peptides (VIP)
  - Histamine

2. Inhibitory Motor Neurons:
Suppress Muscles contraction

(decrease motility and secretion)

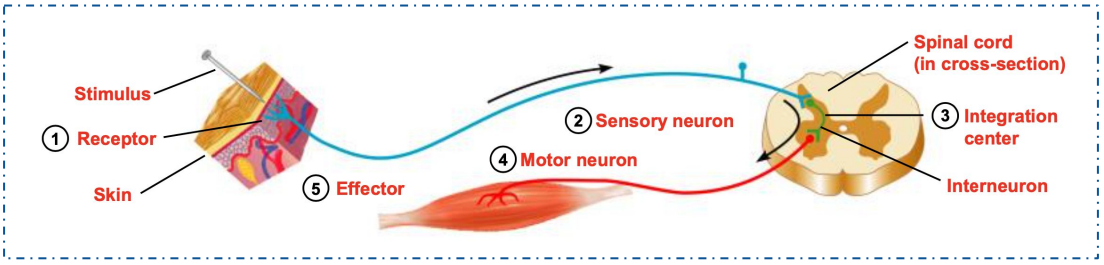
- Adenosine tri-peptide (ATP)
- Nitric oxide (NO)
- VIP

Notice that VIP has dual action
A. Released near glands → Gland activation
B. Released near muscle → Muscle inhibition

Male slides

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
  a. Irritation of the gut mucosa
  b. Excessive distention of the gut
  c. Presence of specific chemical substances in the gut.
- Signals transmitted through the fibers can then 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 brain medulla, which in turn initiates vagal reflex signals **(vagovagal reflexes).**



GI reflex

1- Short Reflexes

Reflexes that are integrated entirely within the gut wall (enteric nervous system):

- GI Movement: Peristalsis/Mixing
- GI Secretions
- Inhibitory Effects

2- Long GI reflexes:

A- Prevertebral sympathetic ganglia:

Important

- Reflexes **from** the gut **to** the **prevertebral sympathetic ganglia** and then **back to** the GIT
- A way for organs to communicate with each other
- These reflexes transmit signals long distances to other areas of the GI tract, such as:

Gastrocolic Reflex:	Enterogastric Reflex:	Colonoileal Reflex:
Signals from stomach causes evacuation of colon (increase motility of the colon) When eating breakfast: Stomach Tells the Colon to **start emptying**, so it's ready for the upcoming bolus of food	**Signals from intestine inhibit emptying of stomach (inhibit gastric motility & secretions)** When you are full: Intestine Tells the Stomach to **stop emptying**, so it can reabsorb the bolus of food	**Signals from colon inhibit emptying of ileal contents** When you want to defecate: Colon Tells the Ilium to **stop emptying**, so it can eject feces into anus without interruptions

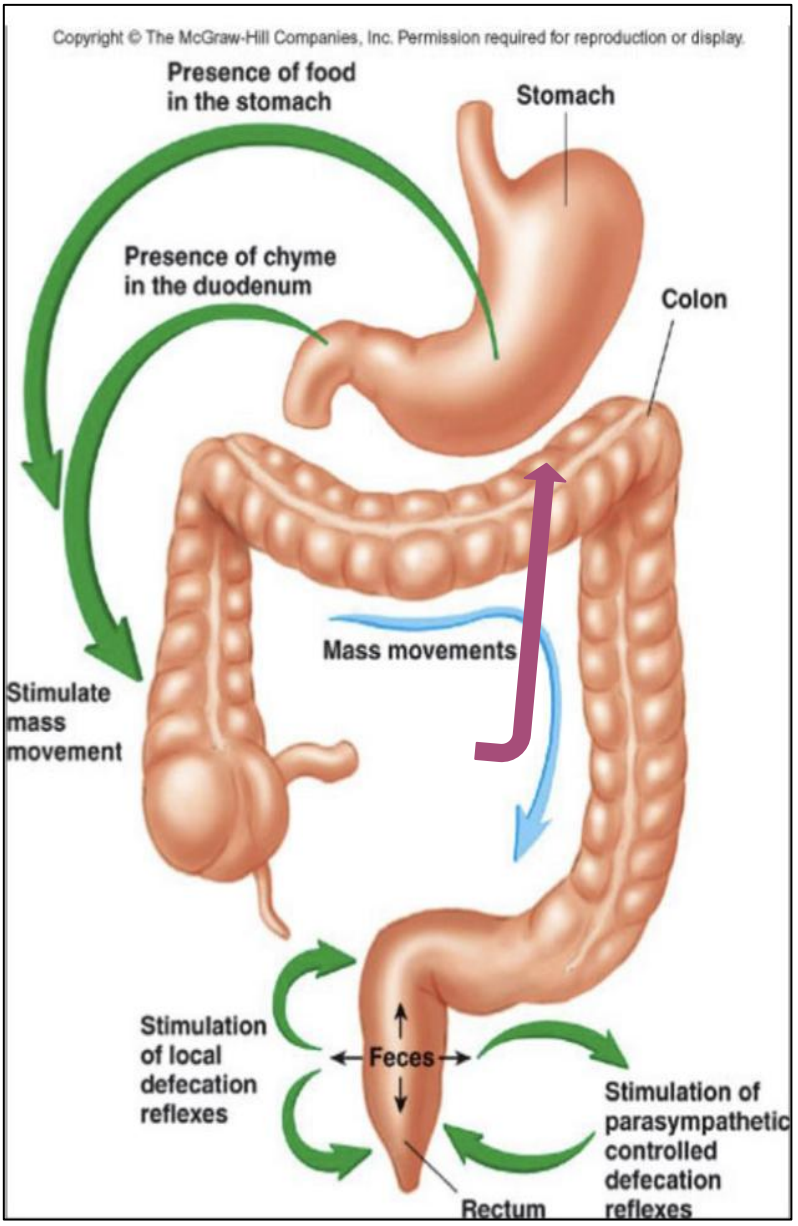
B- Spinal Cord & Brain Stem

Important

Reflexes **from** the gut **to** the **spinal cord or brain stem** and then **back to** the GIT, such as:

Gastric control:	Pain reflexes:	Defecation reflexes:
Reflexes **from** the stomach & duodenum **to** the brain stem and **back to** the stomach (by way of the vagus nerves) to **control gastric motor and secretory activity.**	**Pain reflexes** that cause general **inhibition** of the entire **GI** tract after the area of pain.	**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 **innervated by: pelvic nerves (sacral division of parasympathetic)**

GI reflex cont..



Gastrocolic reflex

Signals from stomach causes evacuation of food

signals from stomach to colon and large intestine to get rid of the the storaged feces because there's a new day and a new food will arrive

Will be discussed in colon physiology lecture later

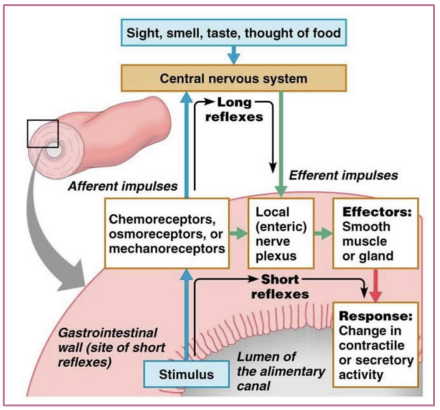
Enterogastric reflex

Signals from intestine inhibit emptying of stomach

stimulates mass movements after a meal. Will be discussed in detail in stomach secretion lecture

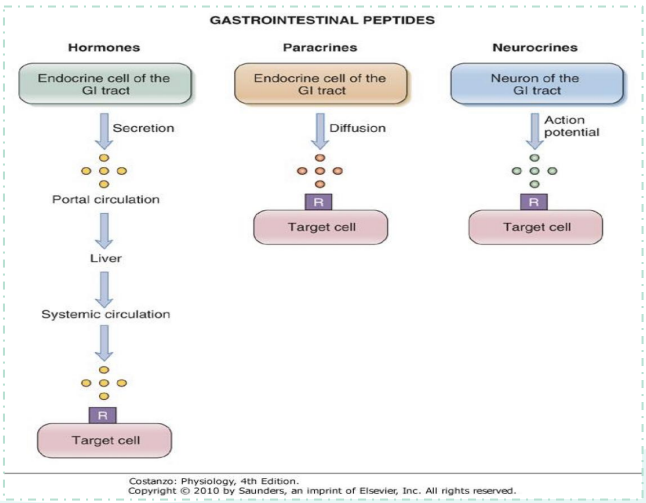
Colonileal reflex

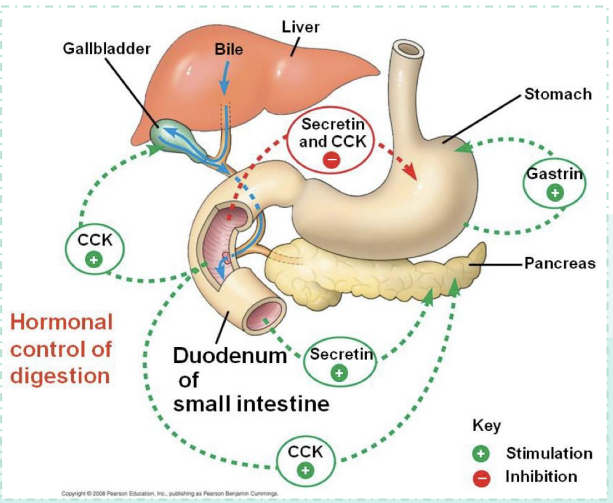
Signals from colon inhibit emptying of ileal contents



Hormonal control

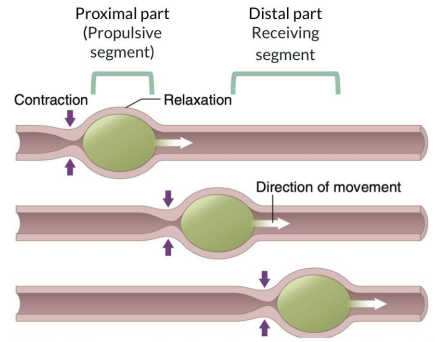
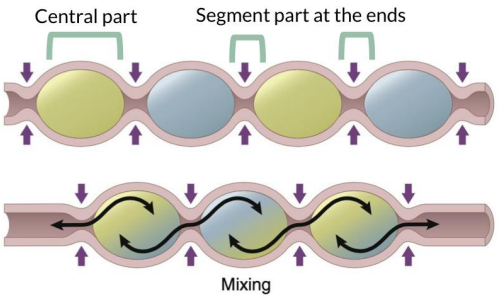
Hormone	Site of secretion	Stimuli for secretion	Actions	
			Stimulates:	Inhibits:
Gastrin(M)	**G** cells of the: - Antrum - Duodenum - Jejunum	(Acid inhibit its release) - Protein - Distention of the stomach - Vagal stimulation - (GRP)	- Gastric H^+ secretion - Growth of gastric mucosa	-
Cholecystokinin (CKK)	**I** cells of the: - Duodenum - Jejunum - Ileum	- Protein - Fatty acids - Acids	- Pancreatic enzyme secretion - Pancreatic HCO^-_3 secretion - Gallbladder contraction - Growth of the exocrine pancreas - Relaxation of sphincter of Oddi	Gastric emptying
Secretin	**S** cells of the: - Duodenum - Jejunum p - Ileum	- Acids & fat in the duodenum	- Pepsin secretion - Pancreatic HCO^-_3 secretion - Biliary HCO^-_3 - Growth of the exocrine pancreas	Gastric H^+ secretion
Glucose-Dependent Insulinotropic Peptide (GIP)	**K** cells of the: - Duodenum - Jejunum	- Protein - Fatty acids - Oral glucose	- Insulin secretion from pancreatic β cells	
Motilin	**M** cells of the: - Duodenum - Jejunum	- Fat - Acid - Nerve	- Gastric motility - Intestinal motility	-





GI movement

Important

Propulsive "Peristalsis"	Mixing "Segmentation"
• Moves food forward along the tract. • **Usual stimulus is distention.** • Distension→stimulates the proximal portion to contract and the distal portion to relax • Organizes propulsion of material over variable distances within the GI lumen. • Other stimuli that can initiate peristalsis include chemical or physical irritation of the epithelial lining in the gut. • Myenteric plexus is important. • Atropine (cholinergic blocker) depresses propulsion. (ADR: constipation) • **Propulsive segment:** (contracts) 1.contraction (circular M.) 2.relaxation (longitudinal M.) • **Receiving segment:** (relaxs) 1.contraction (longitudinal M.) 2.relaxation (circular M.) • **propagated** , rhythmical.	• **Provides mixing of intestinal contents with digestive juices.** • Segment of bowel contracts at both ends. • A second contraction occurs in the center of the segment • **Blend different juices with the chime.** • **Bring products of digestion in contact with absorptive surfaces** • Segmental contractions are responsible for mixing. • Alternate segments contract, and there is little or no net forward movement. • Contraction happens at the middle of chyme • **It's not propagated**
 A. **Peristalsis contractions** (esophagus, stomach, small intestine)	 B. **Segmentation contractions** (small and large intestines)

Peristaltic reflex & the Law of the Gut:

Orad=upper part = mouth direction
Caudad=lower part= Anal direction

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 **Orade side** of the distended segment, pushing the intestinal contents in the **anal direction (Caudad direction)** for 5 to 10 cm before dying out.

Control of the GI blood flow

1) Neural:

Parasympathetic stimulation:
↑ Local blood flow
↑ Glandular secretion

Sympathetic stimulation:
Intense vasoconstriction of the arterioles
↓ Local blood flow (greatly)

The local metabolic vasodilator mechanisms override the sympathetic effects, returning the normal blood flow to GI muscle and glands

2) Gut activity & metabolic factors:

Possible causes of the increased blood flow during gut activity

- Most of the peptide hormones

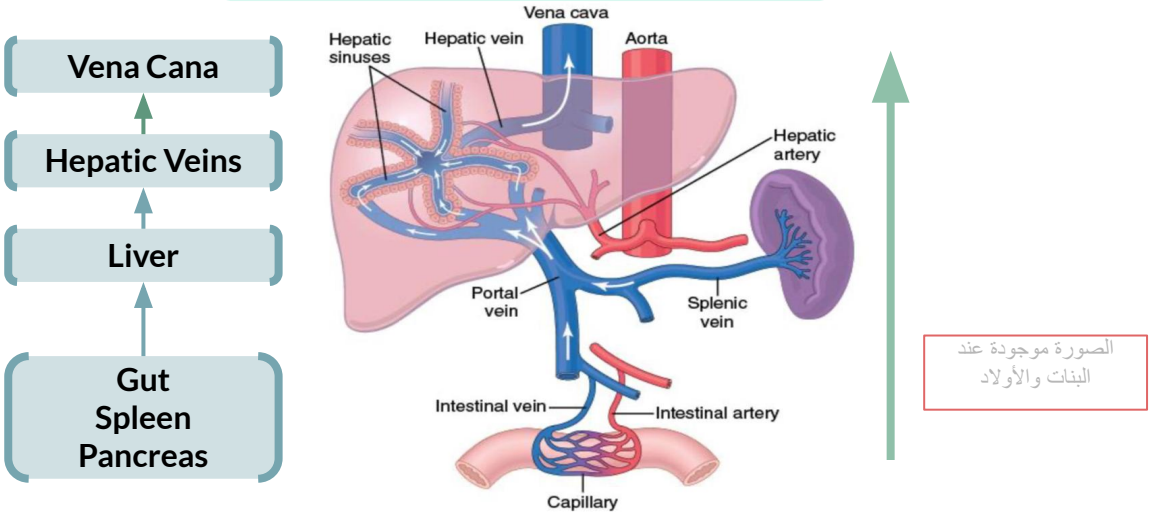
1) CCK 2) VIP 3) Gastrin 4) Secretin

- Some of the GI glands release into the gut wall two kinins (vasodilators):

1) Kallidin 2) Bradykinin 3) kinins

- ↓ O2 conc. in the gut wall → ↑ intestinal blood flow at least 50 - 100%.

The Splanchnic Circulation



الصورة موجودة عند البنات والأولاد

- **Splanchnic circulation** includes the blood flow through the gut, 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.

TEST YOURSELF !

MCQ:

Q1) which one of the following is not considered as one of the accessory organs?

A) gallbladder | B) spleen | C)liver | D)pancreas

Q2) What is the frequency of slow-wave potential in the ileum?

A) 3 | B) 6 | C) 9 | D) 12

Q3) Which one of the following increase blood flow during GI activity?

A) CCK | B) bradykinin | C) decrease O2 concentration | D) all

Q4) Which of the following is an example of tonic contraction

A) GI tract | B) Gastric antrum | C) small intestine | D) blood vessels

Answers: Q1:B | Q2:C | Q3:D | Q4:D

SAQ:

Q1) List three factors that cause increase blood flow during GI activity.

- Gastrin
- Bradykinin
- Decrease oxygen concentration

Q2) Briefly explain the mechanism of the Contraction of Smooth Muscles.

1- ↑ $[Ca^{+2}]$
2- Ca^{+2} binds to calmodulin
3- Ca-CaM complex activates MLCK (Myosin light-chain kinase)
4- Phosphorylates myosin head increasing the activity of ATPase
5- Myosin head attaches to actin causing sliding of the filaments

PHYSIOLOGY

GNT Block

Team 443

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