Organization and General Principles of Gastrointestinal Physiology

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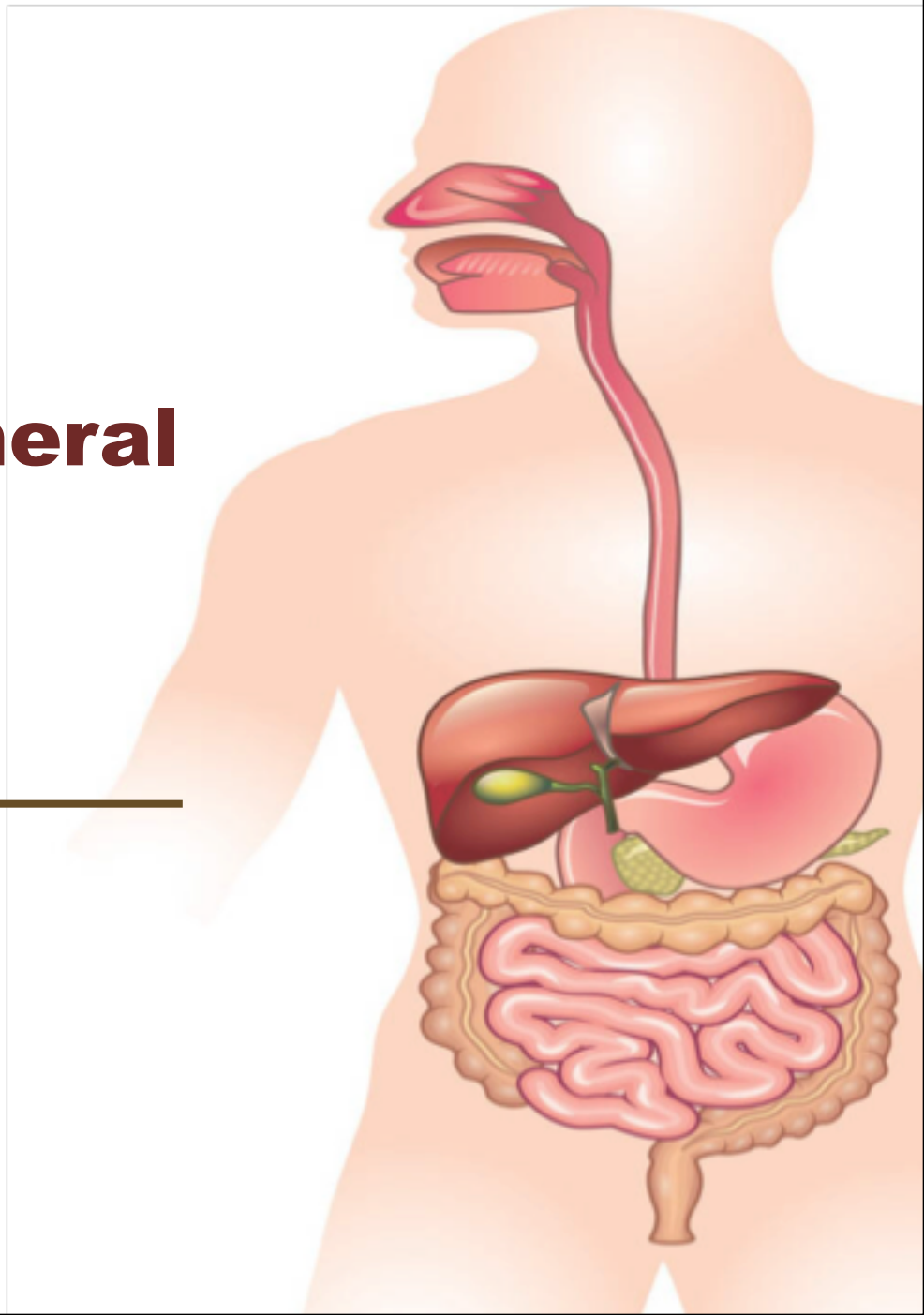


Objectives

- Physiologic anatomy of gastrointestinal wall
- The general characteristics of smooth muscle
- The specific characteristics of smooth muscle
- Control of gastrointestinal function (ENS)
- Types of neurotransmitters secreted by enteric neurons
- Functional types of movements in the gastrointestinal tract
- Gastrointestinal blood flow (Splanchnic circulation)
- Effects of gut activity and metabolic factors on GI blood flow

Introduction

What is the GI system?

What is the importance of the GI system?

What is the GI System?

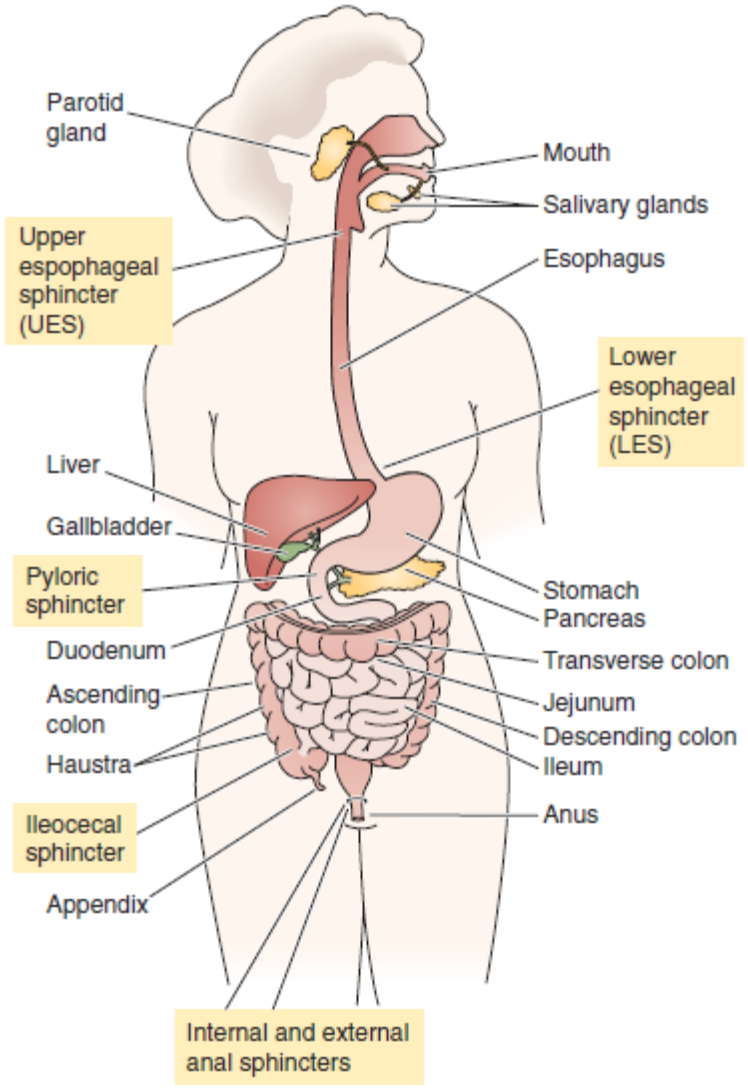


Figure 41-1 The major components of the human digestive system.

- A hollow tube from mouth to anus + accessory glands and organs.
- Hollow organs are separated from each other at key locations by sphincters.

(Medical physiology: a cellular & molecular approach. Edited by Walter Boron and Emile Boulpaep. 2nd Ed.

Functions of the GI System

- The sedentary human body requires ≈ 30 kcal/Kg BW per day.
- This nutrient requirement is acquired through the GI system.
- The food we consume is not in a form that can be directly absorbed by the small intestine.

(Medical physiology: a cellular & molecular approach. Edited by Walter Boron and Emile Boulpaep. 2nd Ed.)

Functions of the GI System

- The GI system processes consumed food mechanically & chemically to facilitate absorption.

Dietary nutrient	Consumed form	Absorbed form
Fat (lipids)	Triglycerides	Fatty acids Monoglycerides
Proteins	Proteins Large peptides	Amino acids
Carbohydrates	Starch Disaccharides Monosaccharides	??

Mouth
Breaks up food particles
Assists in producing spoken language

Salivary glands
Saliva moistens and lubricates food
Amylase digests polysaccharides

Pharynx
Swallows

Esophagus
Transports food

Liver
Breaks down and builds up many biological molecules
Stores vitamins and iron
Destroys old blood cells
Destroys poisons
Bile aids in digestion

Stomach
Stores and churns food
Pepsin digest protein
HCl activates enzymes, breaks up food, kills germs
Mucus protects stomach wall
Limited absorption

Gallbladder
Stores and concentrates bile

Pancreas
Hormones regulate blood glucose levels
Bicarbonates neutralize stomach acid
Trypsin and chymotrypsin digest proteins
Amylase digests polysaccharides
Lipase digests lipids

Small intestine
Completes digestion
Mucus protects gut wall
Absorbs nutrients, most water
Peptidase digests proteins
Sucrases digest sugars
Amylase digests polysaccharides

Large intestine
Reabsorbs some water and ions
Forms and stores feces

Anus
Opening for elimination of feces

Rectum
Stores and expels feces

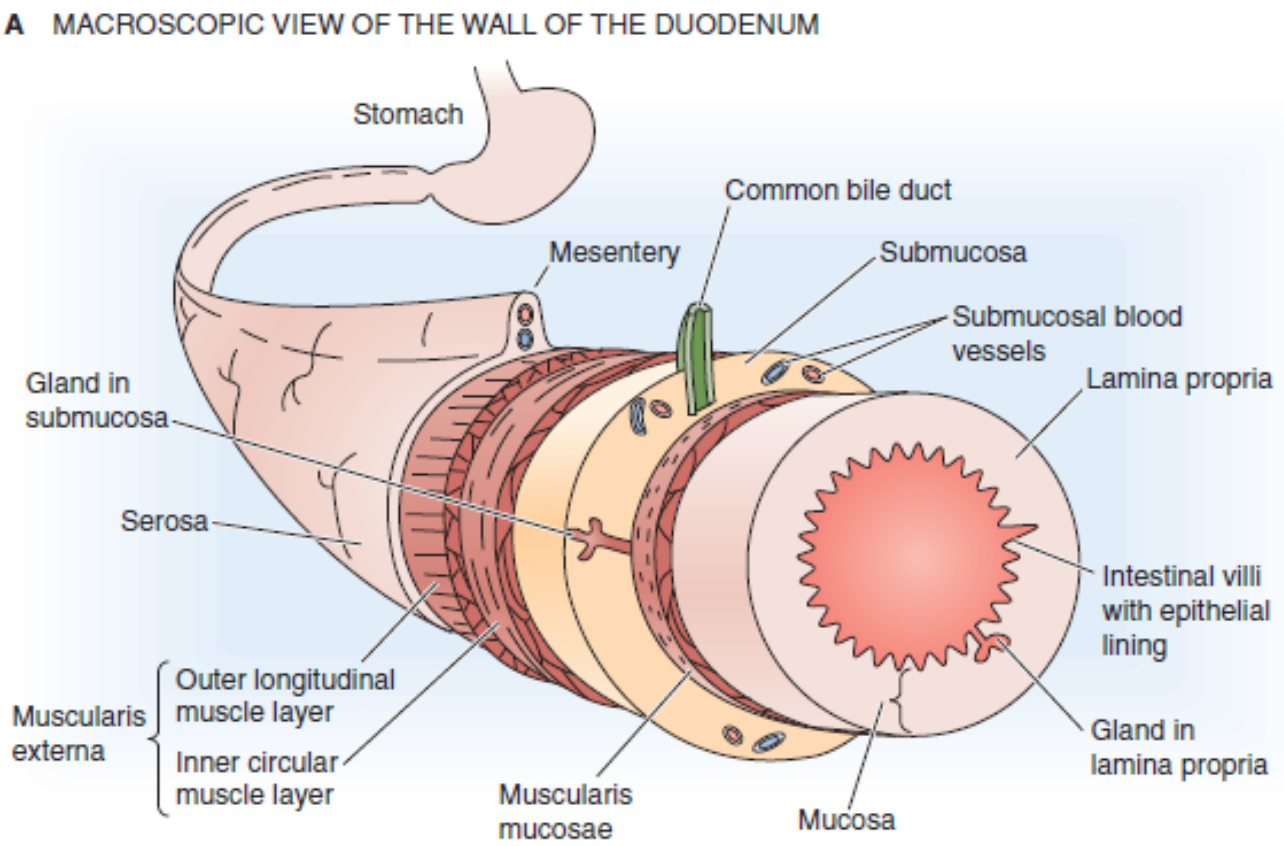
Functions of the GI System

- Excretion of waste material.
  - Non-digested non-absorbed dietary products.
  - Colonic bacteria & their products.
  - Heavy metals (iron & copper).
  - Organic cations & anions (e.g. drugs)
- Regulation of water & electrolyte balance.
- Immunity.

FUNCTIONAL ANATOMY OF THE WALL OF THE GIT

The Wall of the GI tract

The anatomy of the wall varies but there is a common general theme.



To understand the characteristics of the wall of the GIT, we must talk about the general characteristics of smooth muscles.

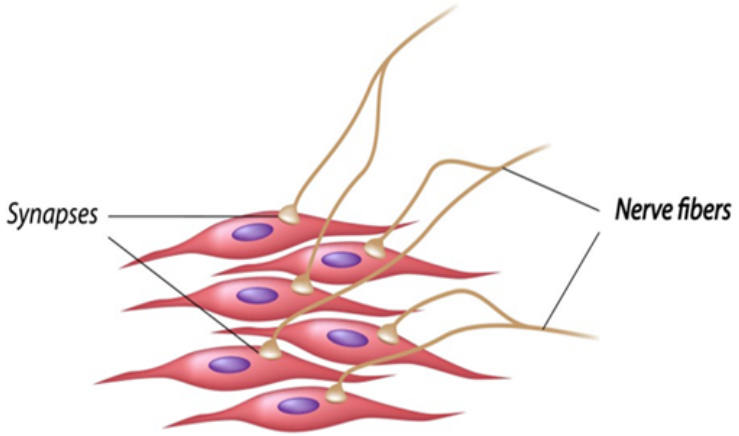
- https://youtu.be/yzQAgfivX74

SMOOTH MUSCLE

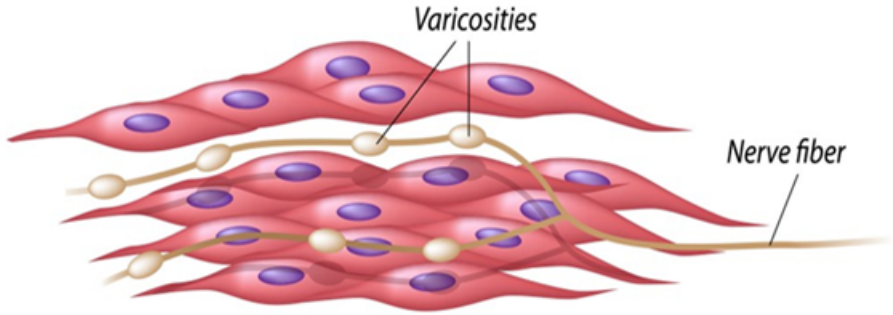
Types of Smooth Muscle

Two major types

- **Multi-unit Smooth Ms**
- **Single-unit Smooth Ms**

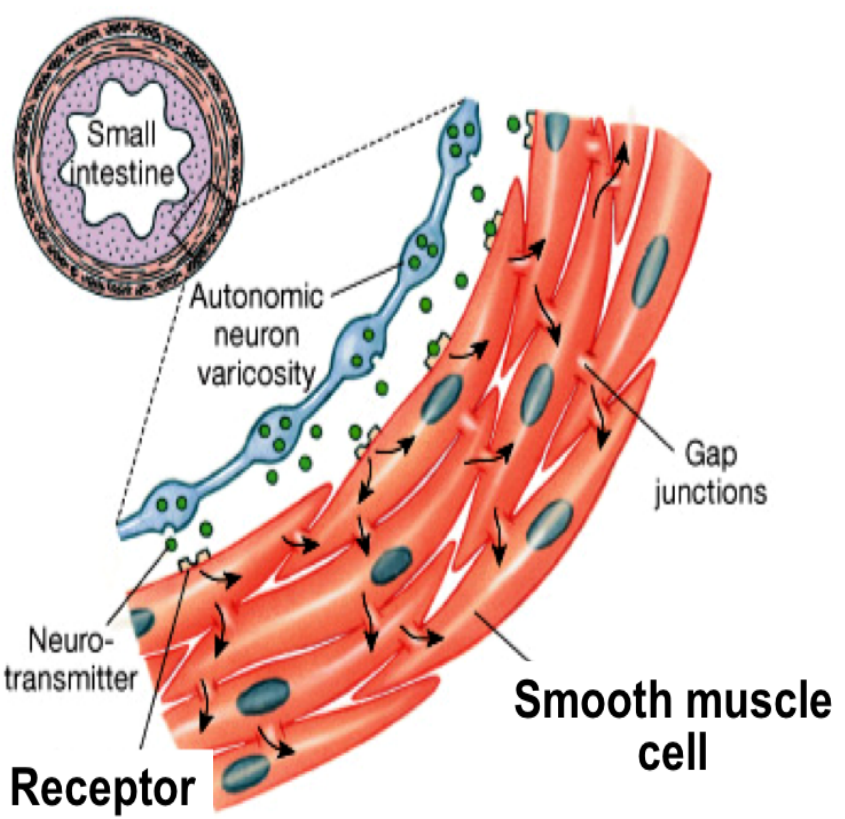


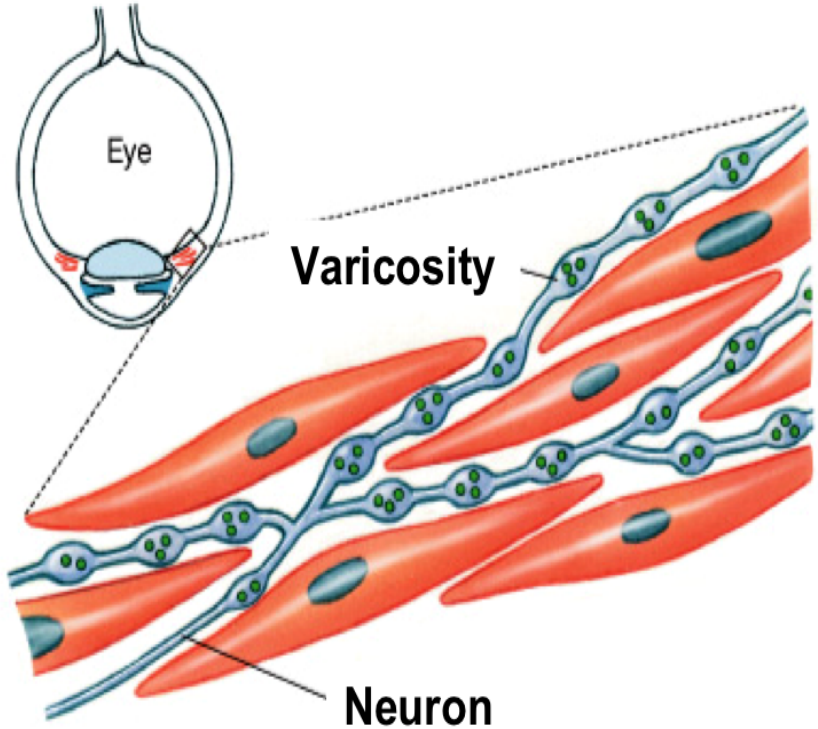
Multiunit Smooth Muscle



Single-unit Smooth Muscle

Examples of the Different Types of Smooth Muscle





Contractile Mechanism of Smooth Muscle

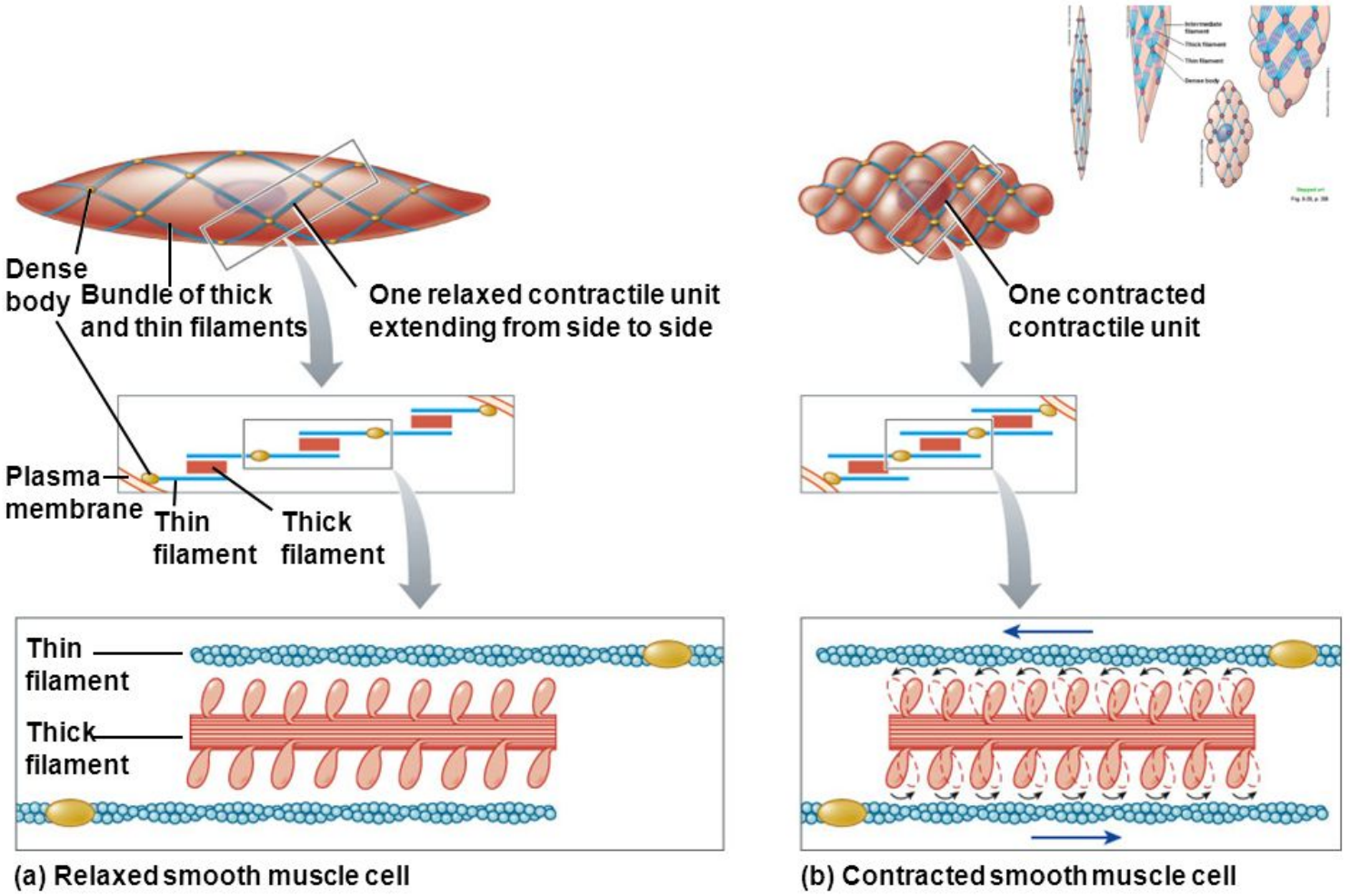
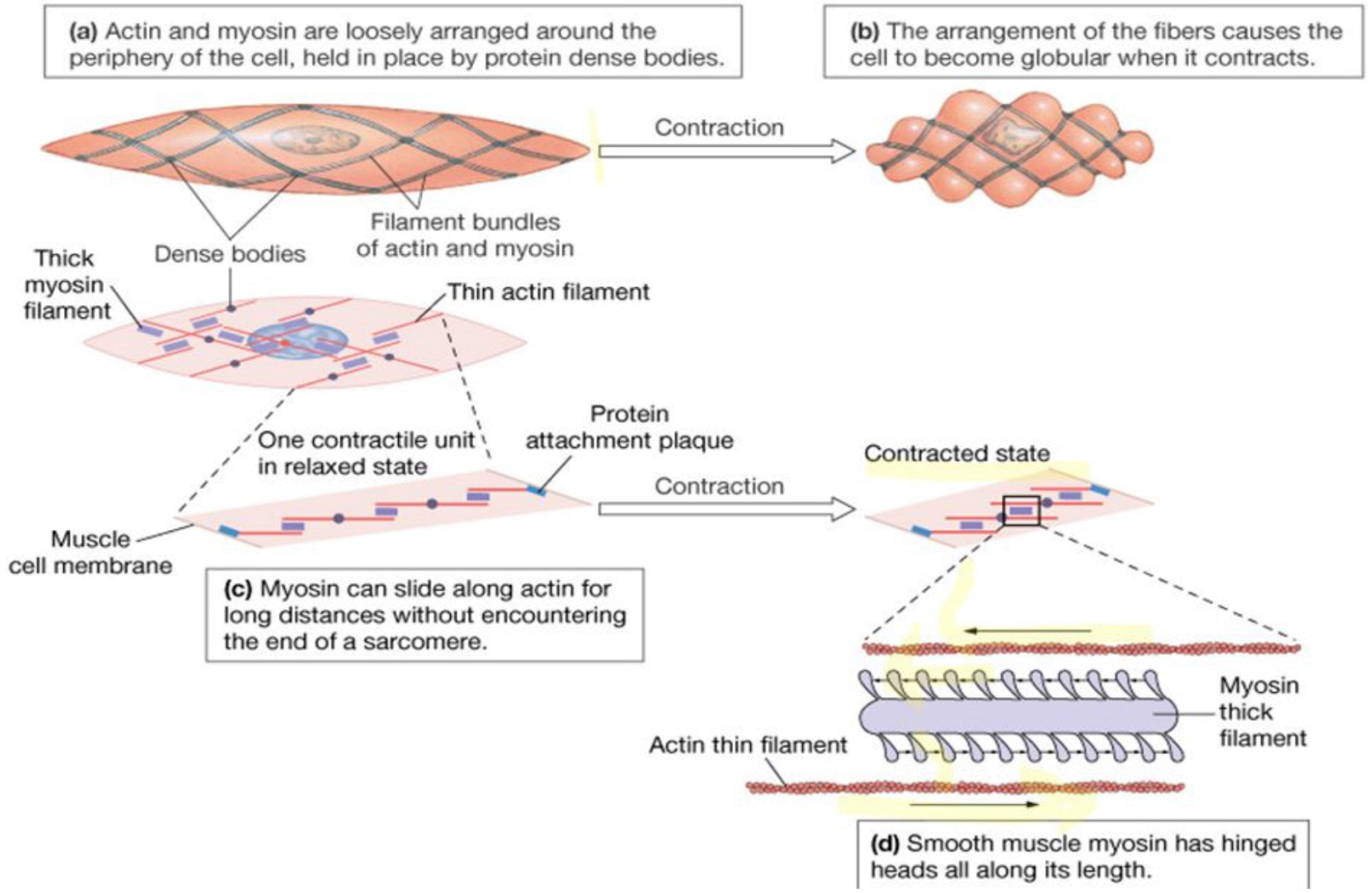
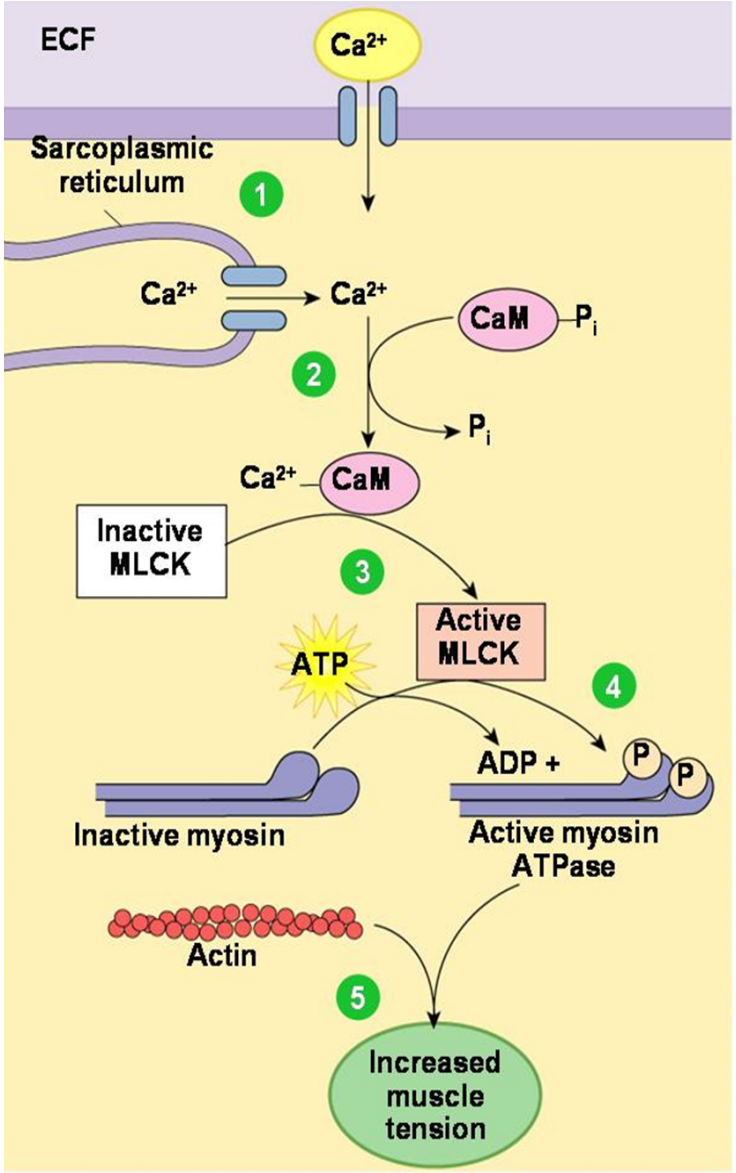


Fig. 8-29, p. 295

SM in relaxed & contracted state



Molecular Basis of Smooth Muscle Contraction



1. Intracellular Ca^{2+} concentrations increase when Ca^{2+} enters cell and is released from sarcoplasmic reticulum.
2. Ca^{2+} binds to calmodulin (CaM).
3. Ca^{2+}–calmodulin activates myosin light chain kinase (MLCK).
4. MLCK phosphorylates light chains in myosin heads and increases myosin ATPase activity.
5. Active myosin crossbridges slide along actin and create muscle tension.

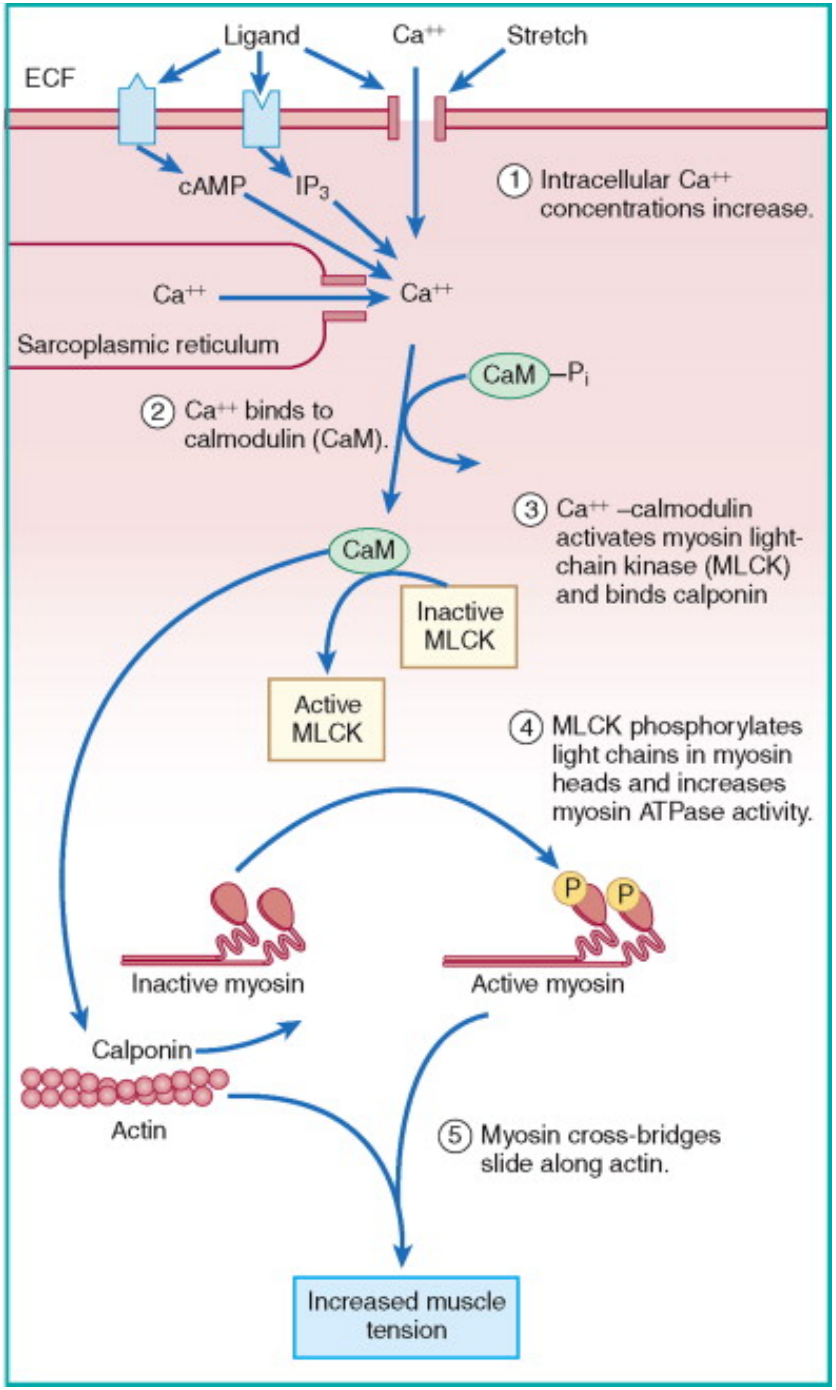
↑ $[Ca^{+2}]_i$

Ca^{+2} binds to calmodulin

Ca-CaM complex activates MLCK

Phosphorylates Myosin head increasing the activity of ATPase

Myosin head attaches to actin causing sliding of the filaments



How Does Smooth Muscle Contraction Stop?

1. A drop in $[Ca^{+2}]_i$ deactivates MLCK.

2. In addition, the phosphorylated myosin heads need to be dephosphorylated (deactivated) by ***Myosin Phosphatase***

Relaxation

Types of Smooth Muscle Contraction

Types of smooth muscle activity pattern

Phasic

Smooth muscle cells contract rhythmically or intermittently.
Contraction followed by relaxation.
e.g. walls of the GI tract.

Tonic

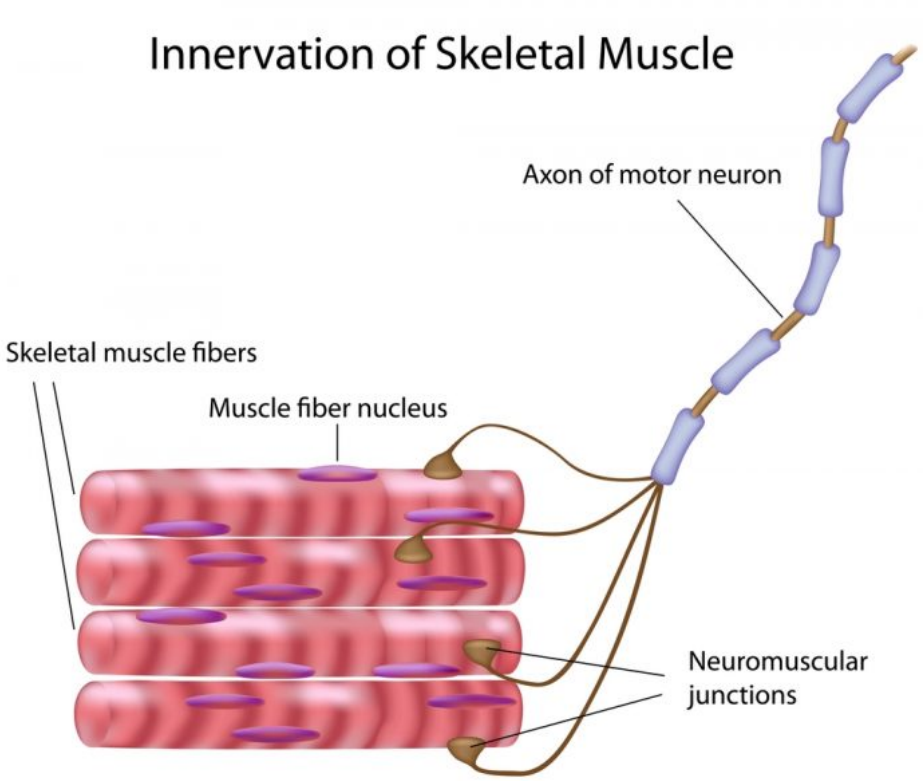
Smooth muscle cells continuously active maintaining a "tone".
Continuous partial contraction.
e.g. vascular & respiratory smooth muscle, sphincters.

Control of Smooth Muscle Contraction

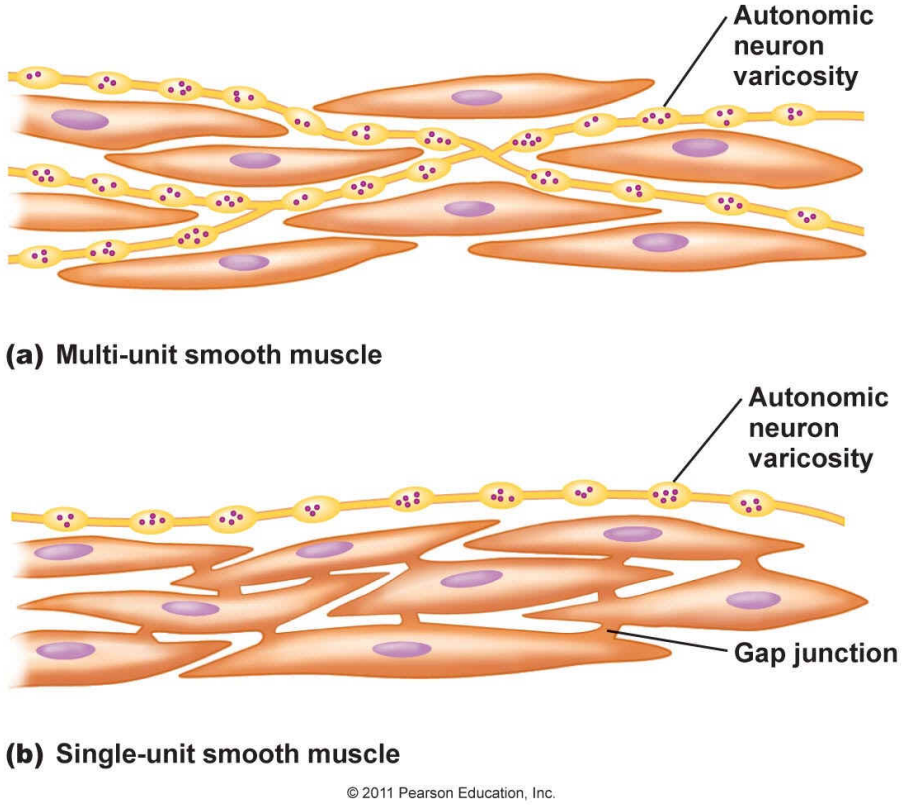
- Unlike skeletal muscle, smooth muscle can be stimulated to contract by many types of signals;
  - Nervous signals.
  - Hormonal signals.
  - Mechanical signals (e.g. stretch).
  - Pacemaker activity.

Nervous Control of Smooth Muscle Contraction

- Somatic neuron.
- Branching end feet.
- Ach.



- Autonomic neuron.
- Axons have multiple varicosities.
- Ach & NA.



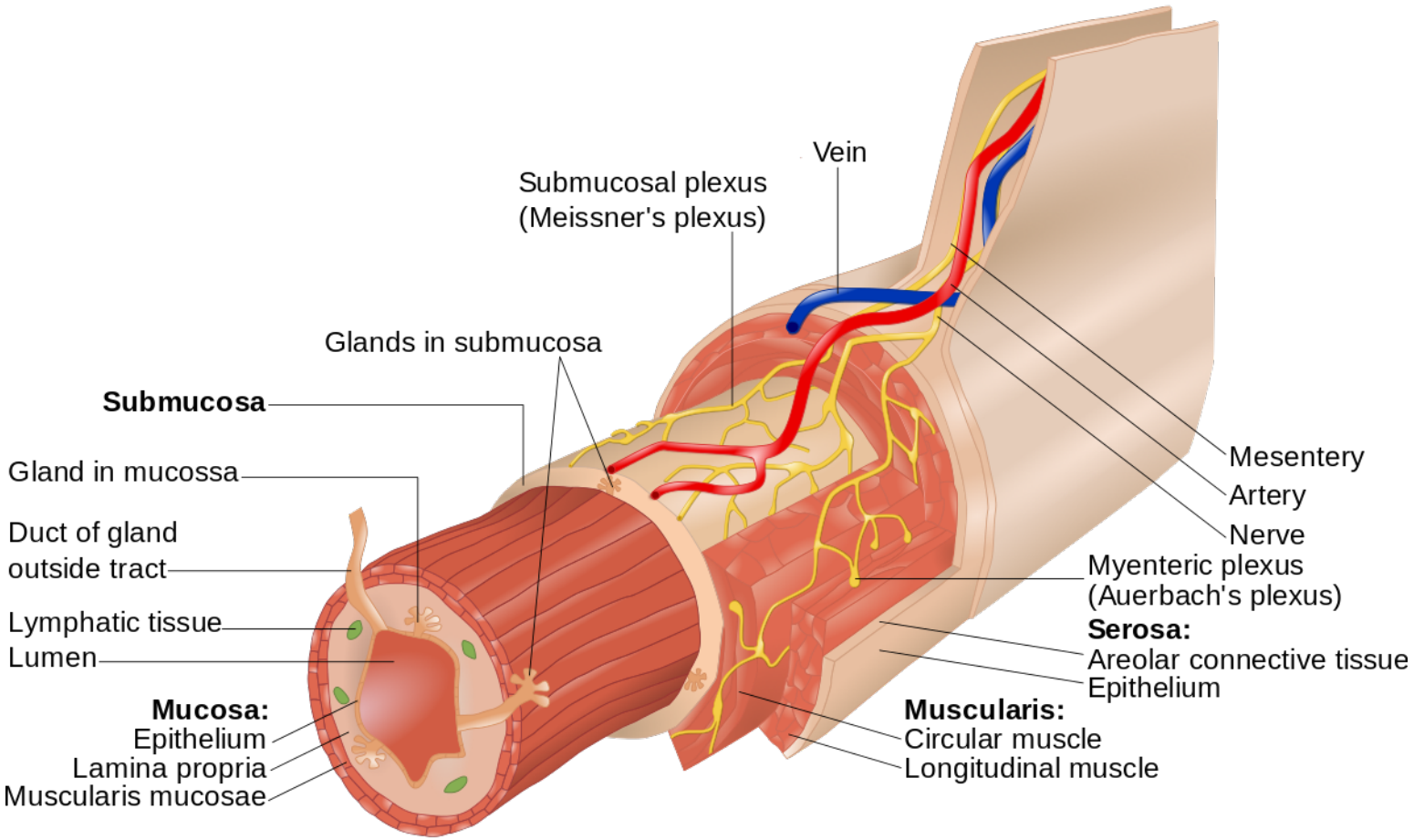
Control of Smooth Muscle Contraction

- In smooth muscle contraction can happen in the absence of an action potential.

Now that we discussed the general characteristics of smooth muscles, lets go back to GI smooth muscles.

GASTROINTESTINAL MOTILITY

GI Smooth Muscle



Each muscle layer functions as a syncytium.
A few connections exist between circular & longitudinal muscle layers.

Electrical Activity of GI Smooth Muscle

- What is the Resting membrane potential for smooth muscle cells? And at what level is the threshold?

Two basic types of electrical waves are seen in the GIT

Slow waves

Rhythmic oscillations in RMP of 5-15mv with variable frequency depending on region.
Stomach = 3/min
Duodenum = 12/min
Ileum = 8-9/min

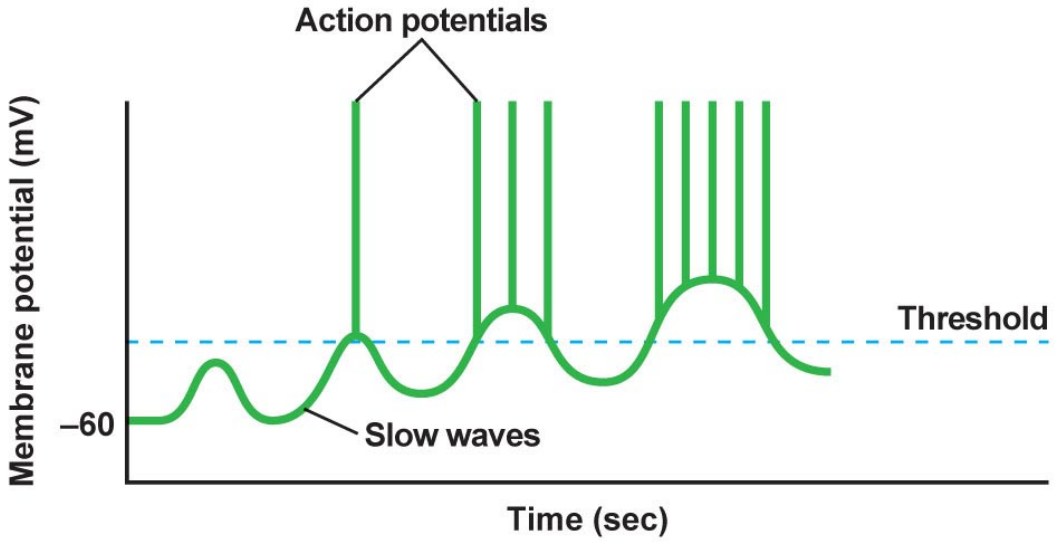
Spike potentials

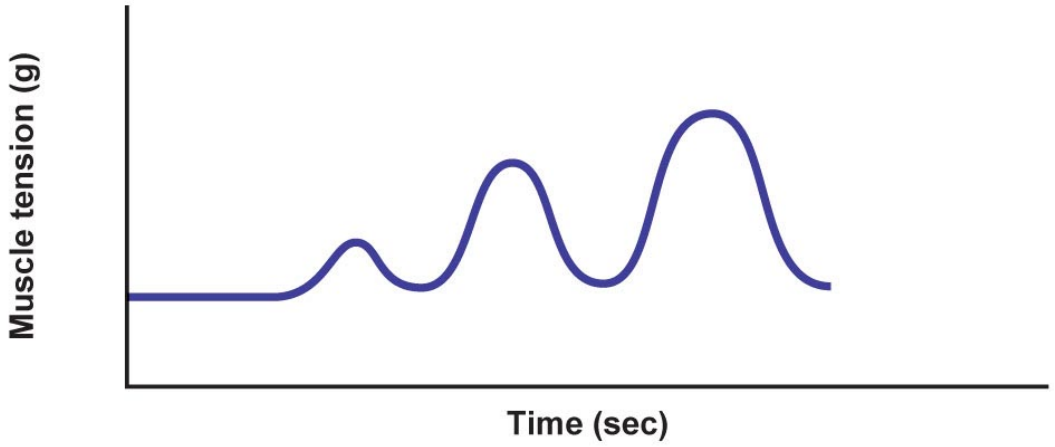
Are true action potentials. The frequency of spike potentials depends on the extent of increase in slow wave potential above the level of threshold.

Slow Waves vs Spike Potential

What do you notice from the graph?

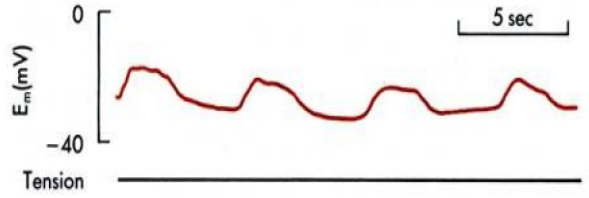
And what is the cause of;
Slow waves.
Spike potentials.



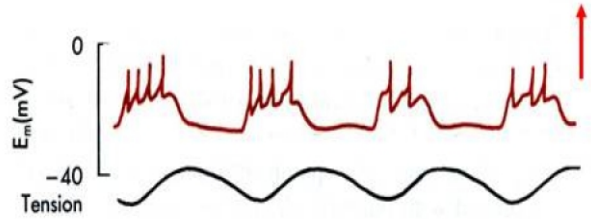


What Happens if the RMP is Changed?

Smooth muscle is excitable tissue, and shows electrical activity



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

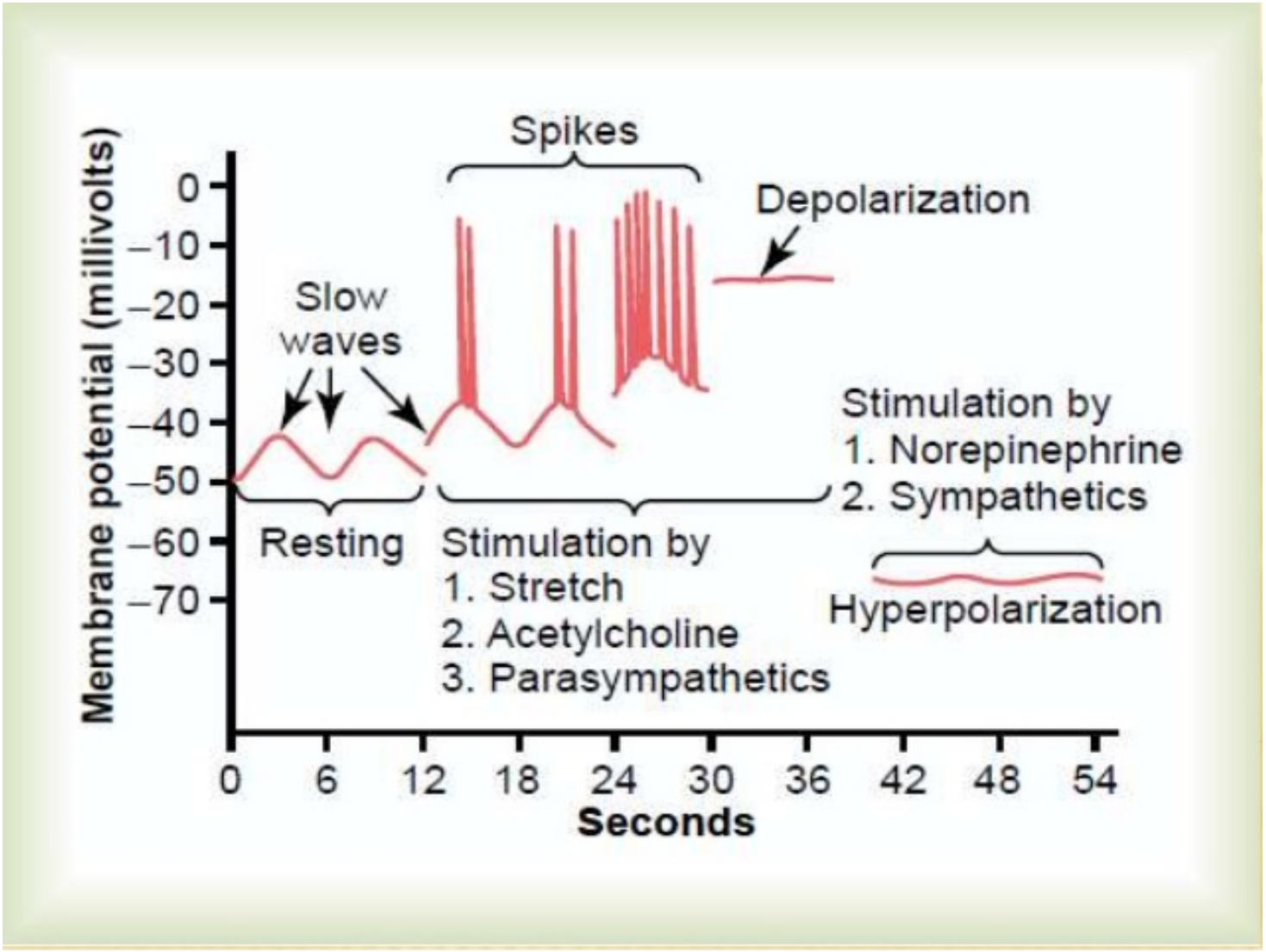


With ***parasympathetic*** **input**, the membrane at the plateau of the slow wave depolarizes all the way to threshold; action potentials occur "on top of" the slow wave, and these set off contractions. The contraction / tension follows slightly after the electrical response.

Factors that cause the RMP to become less negative (stretch, Ach, some GI hormones)

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

Norepinephrine & Epinephrine.


Spikes
Depolarization
Slow waves
Stimulation by
1. Norepinephrine
2. Sympathetics
Membrane potential (millivolts)
0
−10
−20
−30
−40
−50
−60
−70
Resting
Stimulation by
1. Stretch
2. Acetylcholine
3. Parasympathetics
Hyperpolarization
0
6
12
18
24
30
36
42
48
54
Seconds

Control of GI Function

- Neural control;
  - Enteric nervous system (ENS).
  - Autonomic nervous system.
- Hormonal control.
- GI contents.

Neural Control of GI Function "The Enteric Nervous System"

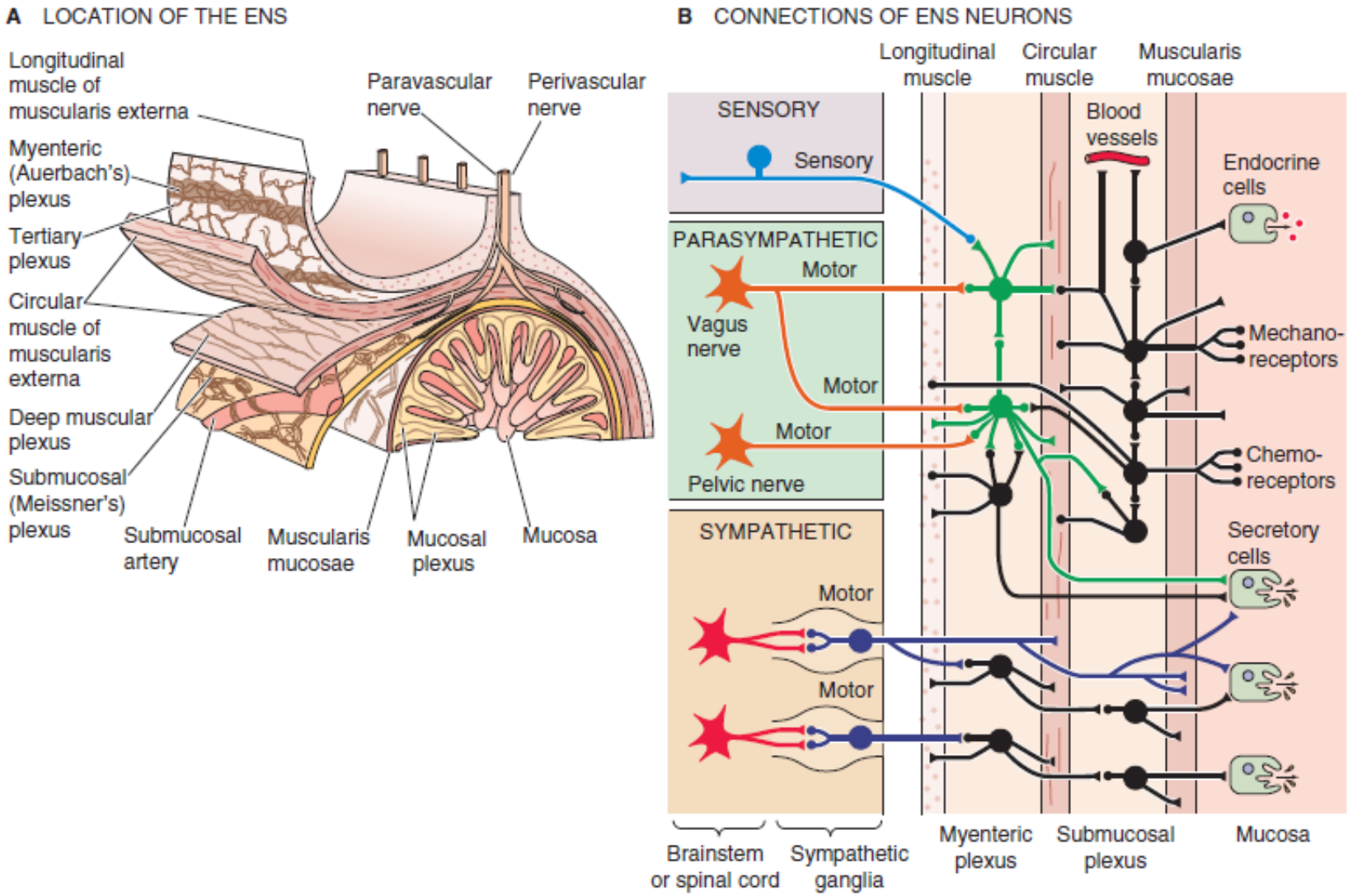
- The GIT has a nervous system of it own → "***Enteric nervous system***".

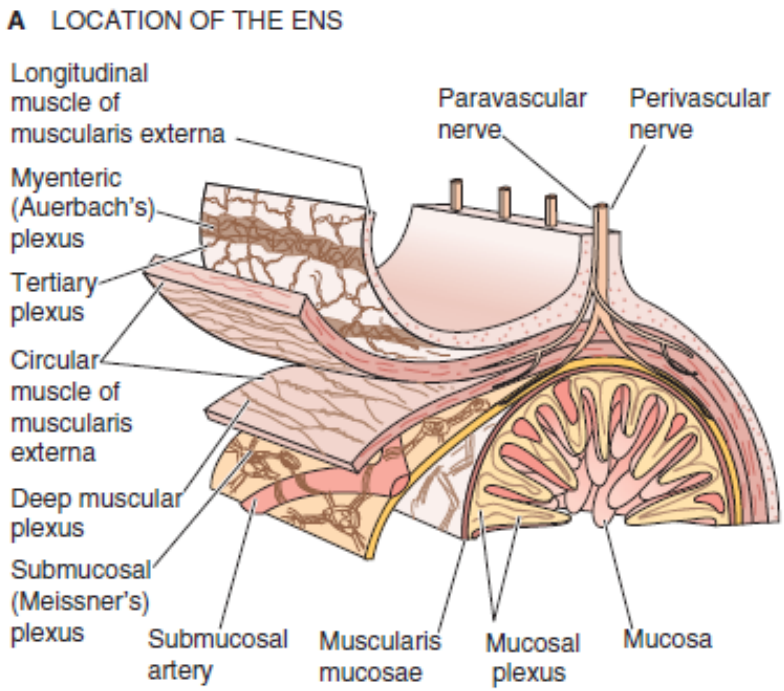
- Its function is largely independent of the extrinsic nervous system → "***mini-brain***".

Composed of 2 main plexuses

- **Myenteric "Auerbach's" Plexus**
- **Submucosal "Meissner's" Plexus**

“The Enteric Nervous System”





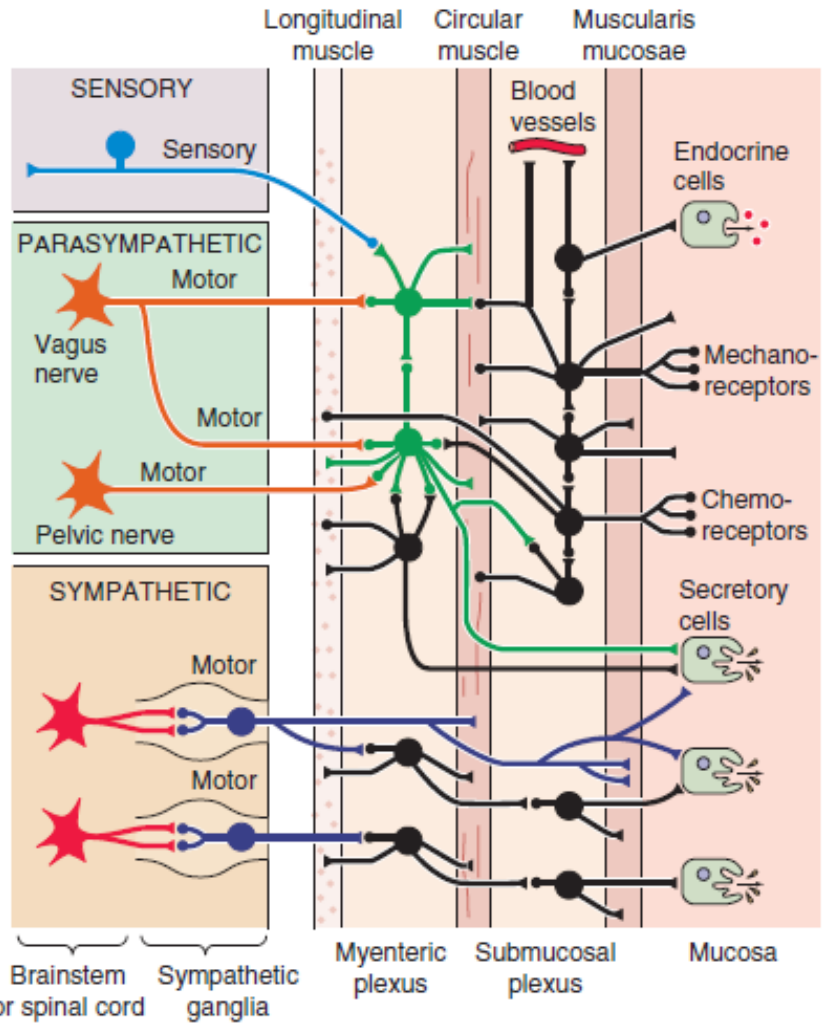


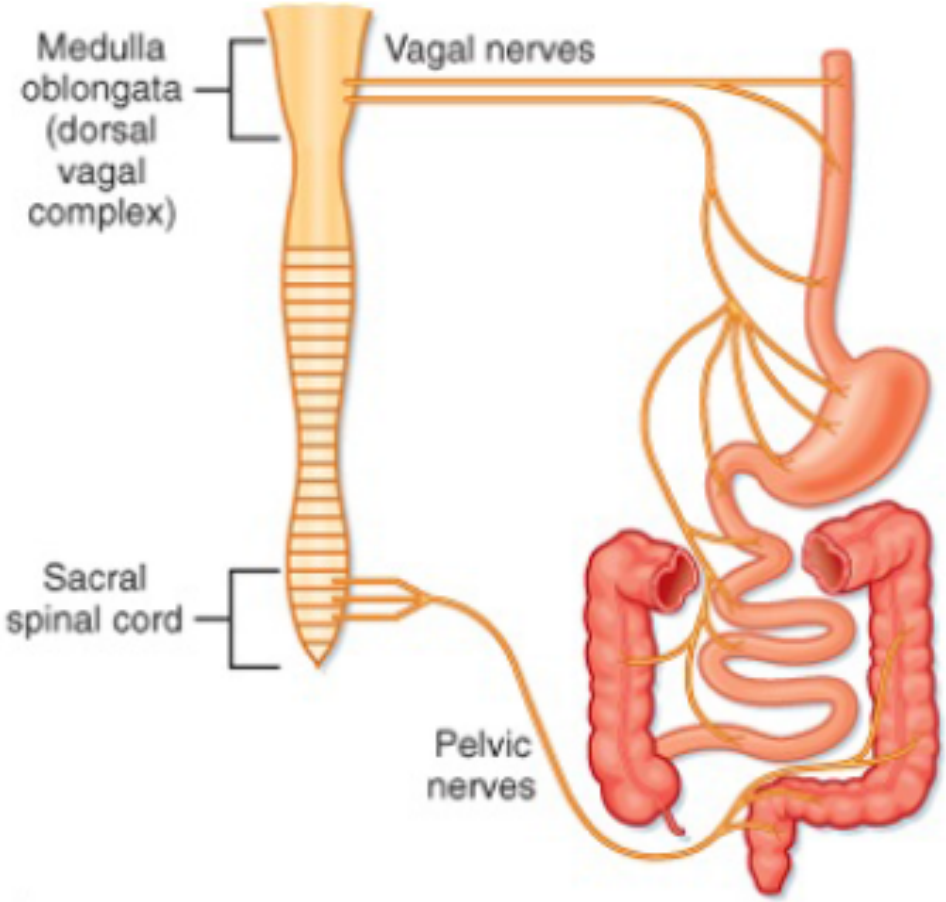
Figure 41-3 Schematic representation of the ENS. **A,** The submucosal (or Meissner's) plexus is located between the muscularis mucosae and the circular muscle of the muscularis externa. The myenteric (or Auerbach's) plexus is located between the circular and longitudinal layers of the muscularis externa. In addition to these two plexuses that have ganglia, three others—mucosal, deep muscular, and tertiary plexus—are also present. **B,** The ENS consists of sensory neurons, interneurons, and motor neurons. Some sensory signals travel centrally from the ENS. Both the parasympathetic and the sympathetic divisions of the ANS modulate the ENS. This figure illustrates some of the typical circuitry of ENS neurons.

Myenteric vs Submucosal Plexus

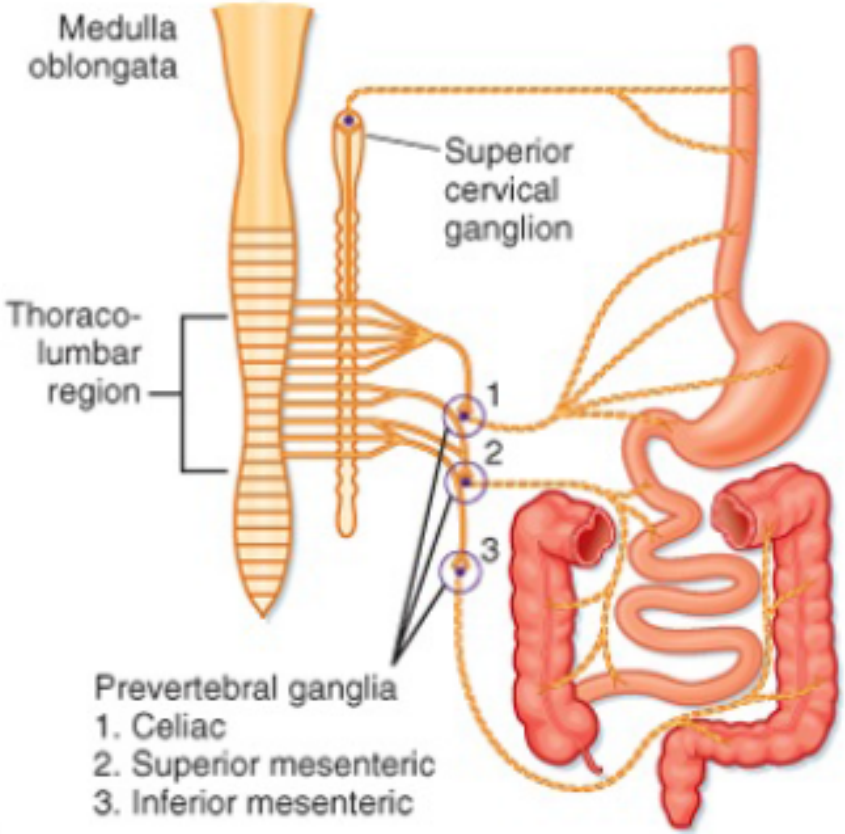
Myenteric plexus	Submucosal plexus
• Located in the muscle layer between longitudinal & circular muscle layers. • Controls GI movement. • Found throughout the GIT.	• Located in the submucosa. • Controls GI secretion & local blood flow. • Only in the small & large intestine.

Autonomic Control of GIT

Parasympathetic



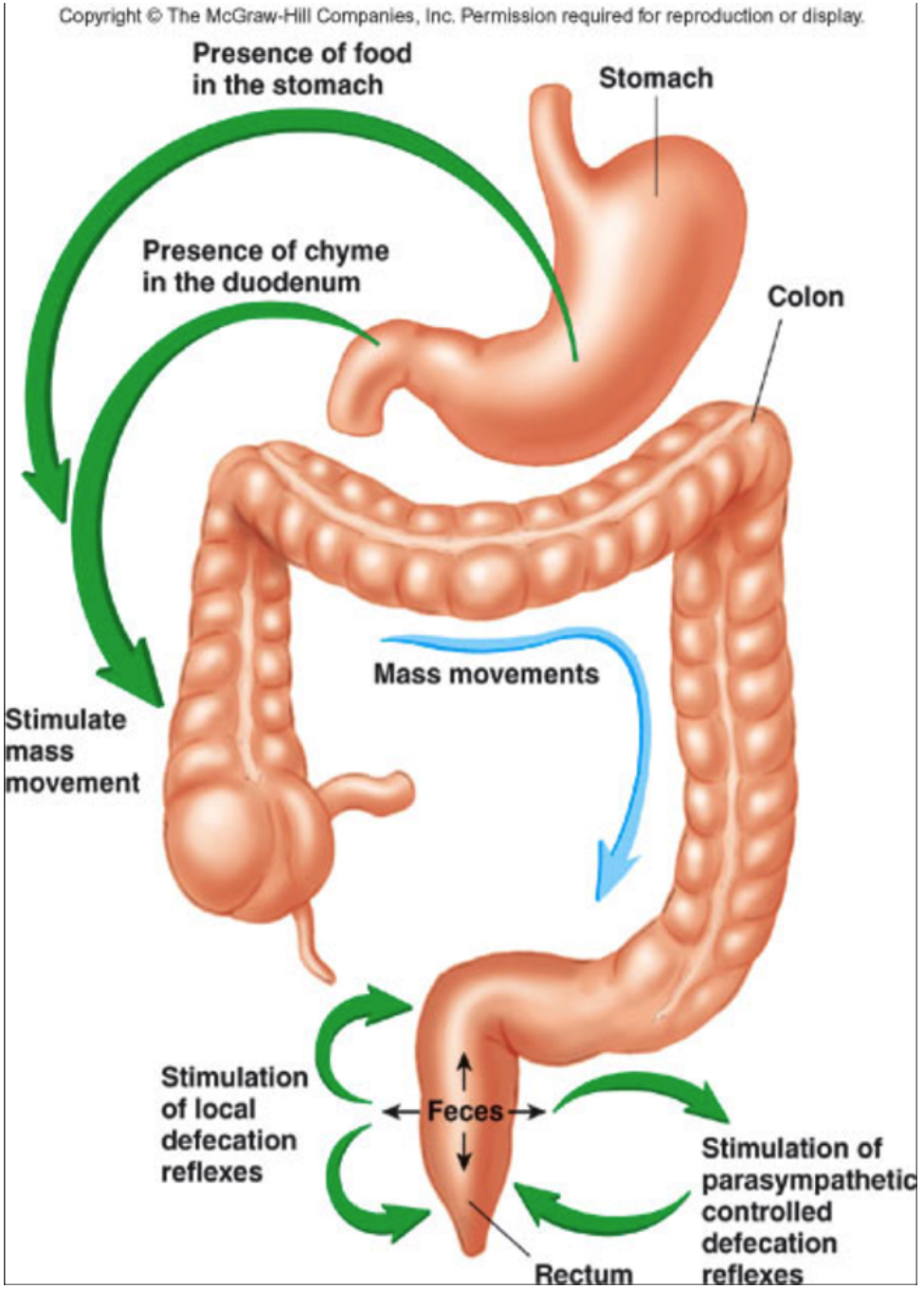
Sympathetic



GI Reflexes

3 types of reflexes

Integrated within the ENS	Integrated at Sympathetic ganglia	Integrated at spinal cord/brain stem
Control local effects; GI secretion Peristalsis Mixing movement	Gastro-colic reflex Entero-gastric reflex Colono-ileal reflex	Pain reflexes Defecation reflex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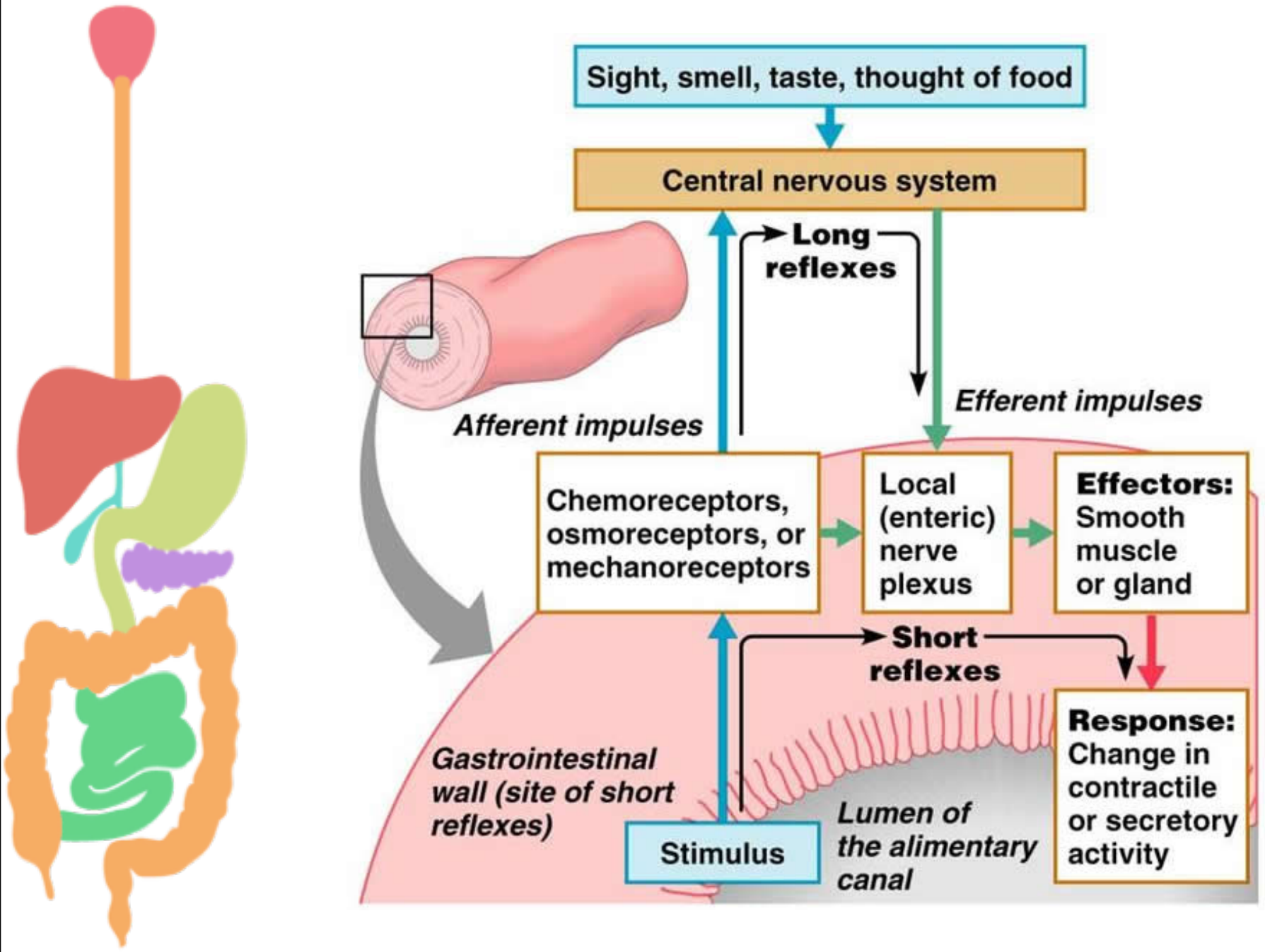
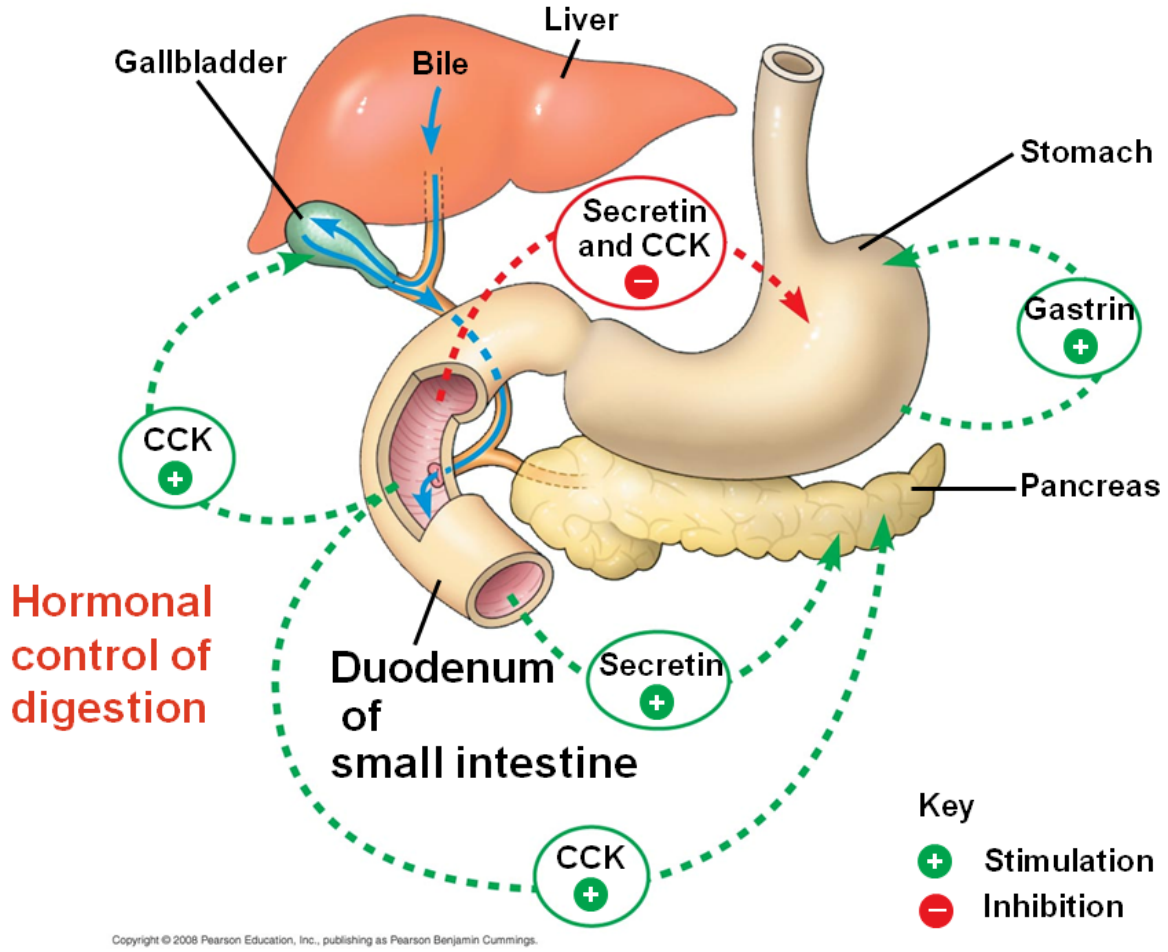
Presence of food in the stomach
Stomach
Presence of chyme in the duodenum
Colon
Mass movements
Stimulate mass movement
Stimulation of local defecation reflexes
Feces
Stimulation of parasympathetic controlled defecation reflexes
Rectum


Sight, smell, taste, thought of food
Central nervous system
Long reflexes
Afferent impulses
Efferent impulses
Chemoreceptors, osmoreceptors, or mechanoreceptors
Local (enteric) nerve plexus
Effectors: Smooth muscle or gland
Short reflexes
Response: Change in contractile or secretory activity
Gastrointestinal wall (site of short reflexes)
Lumen of the alimentary canal
Stimulus

Hormonal Control of GI Function

https://www.sciencelearn.org.nz/resources/1836-hormonal-control-of-digestion



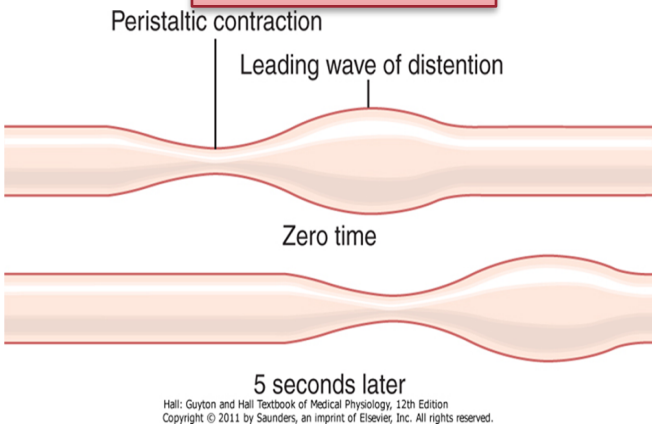
Types of Movement in the GIT

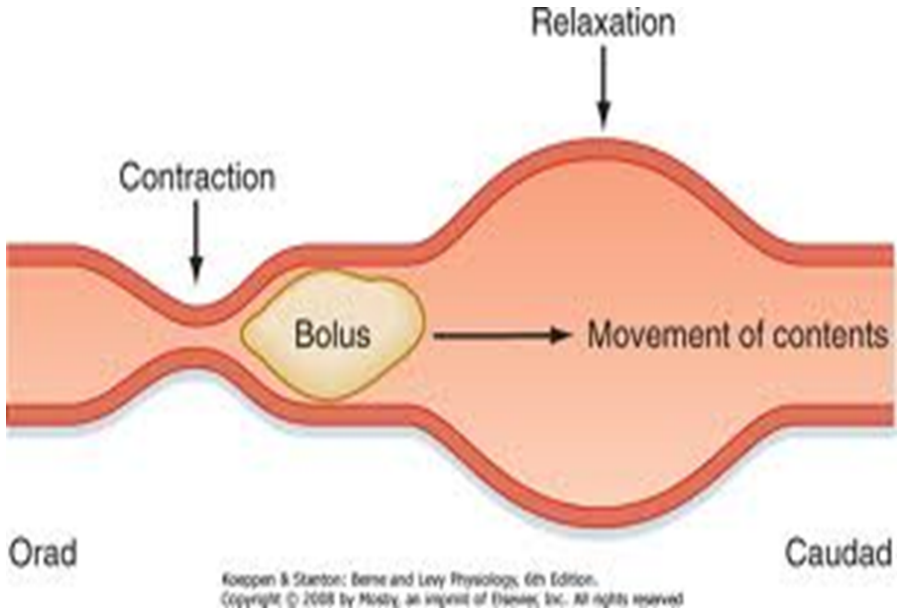
Motor activity of the GIT

Propulsive movement "Peristalsis"	Mixing movement "Segmentation"
Progressive wave of contraction & relaxation. Move GI content in a caudal direction. ***"Law of the Gut"*** Distension of bowel → contraction of circular muscle & relaxation of longitudinal ms in upstream segment + the opposite in the downstream segment.	Non-propulsive segmental contractions. Cause mixing and chopping of intestinal content. Due to contraction of circular muscle + relaxation of receiving segment.

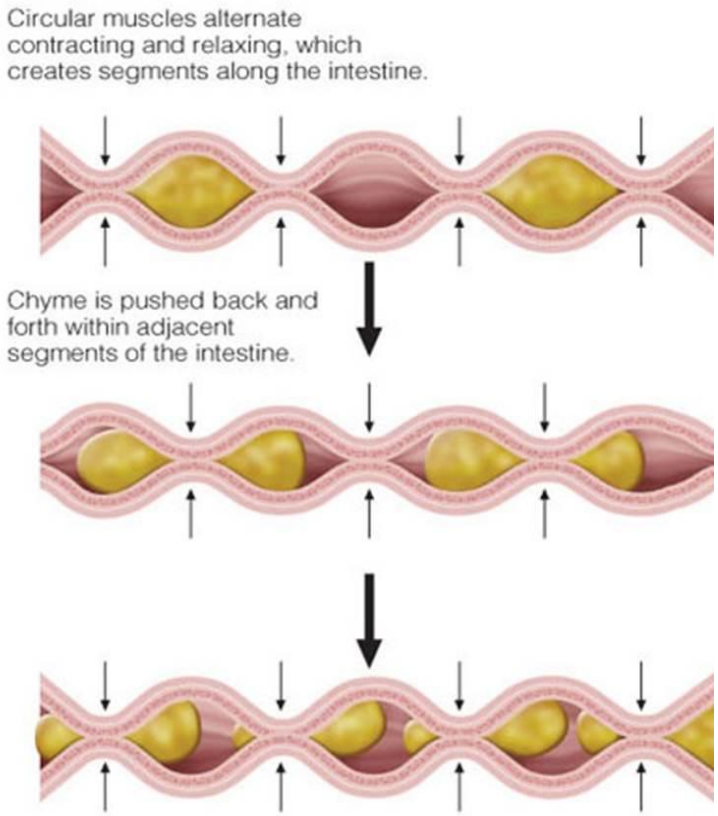
Types of Movement in the GIT

Peristalsis



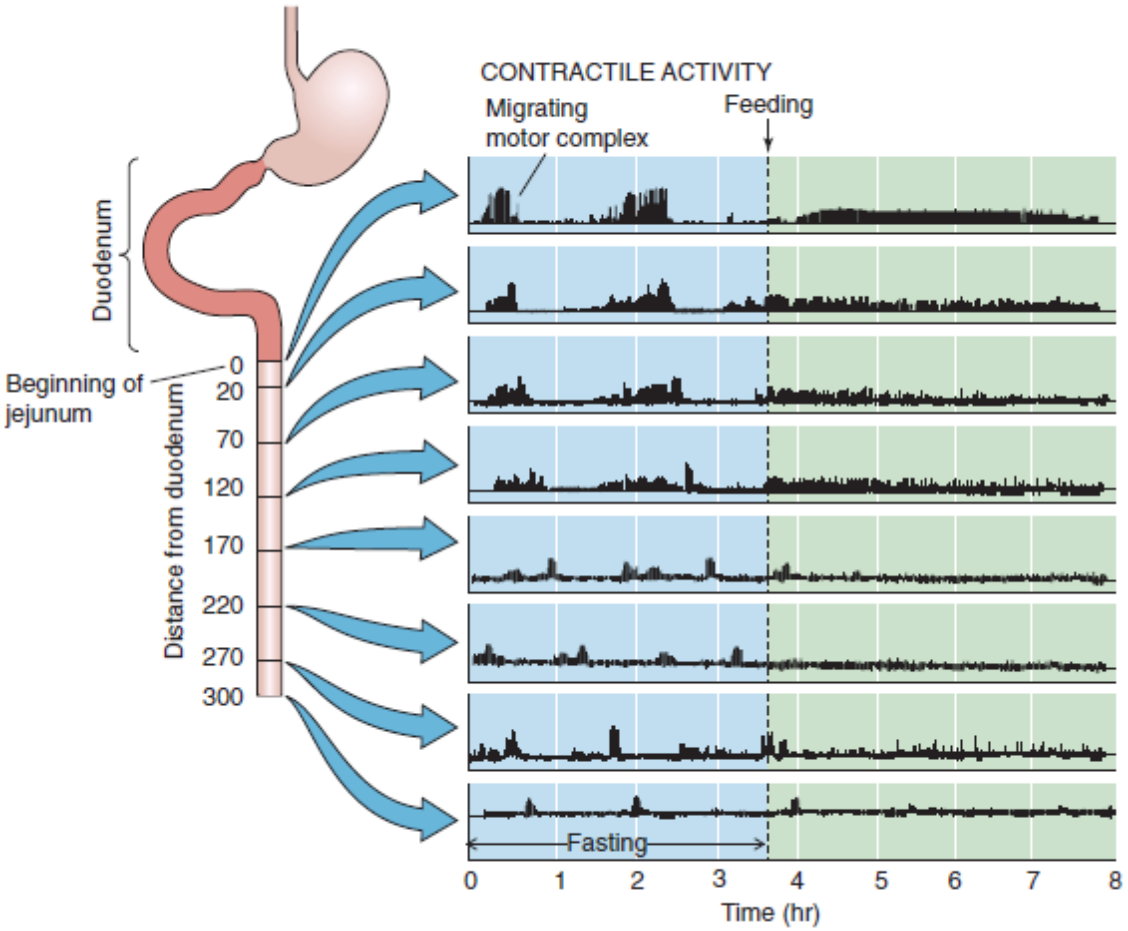


Segmentation



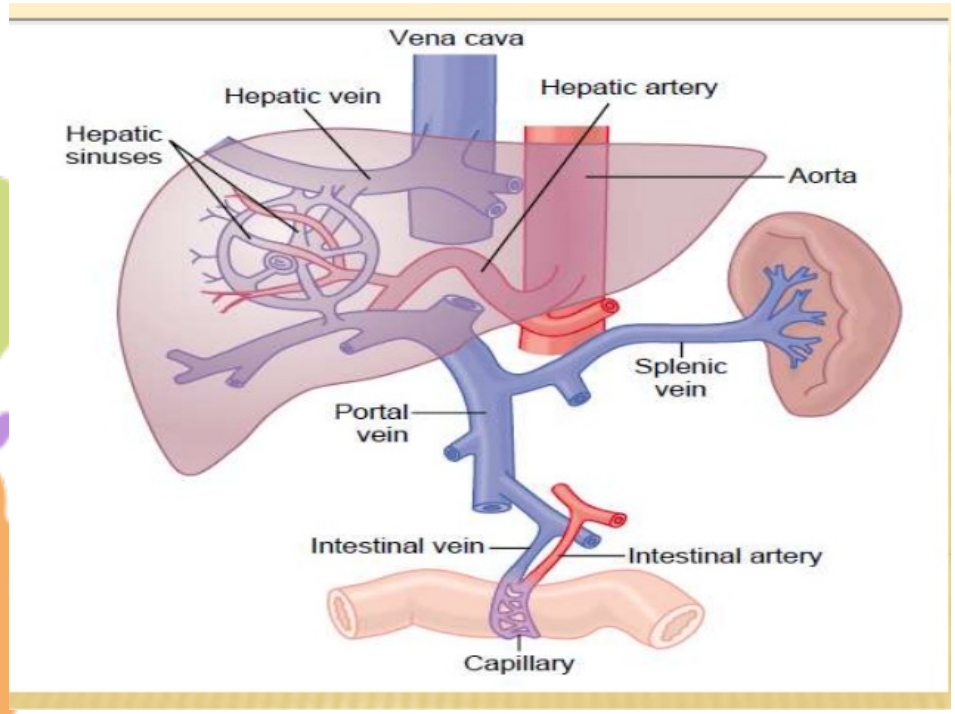
Does the Bowel Move in the Fasting State?

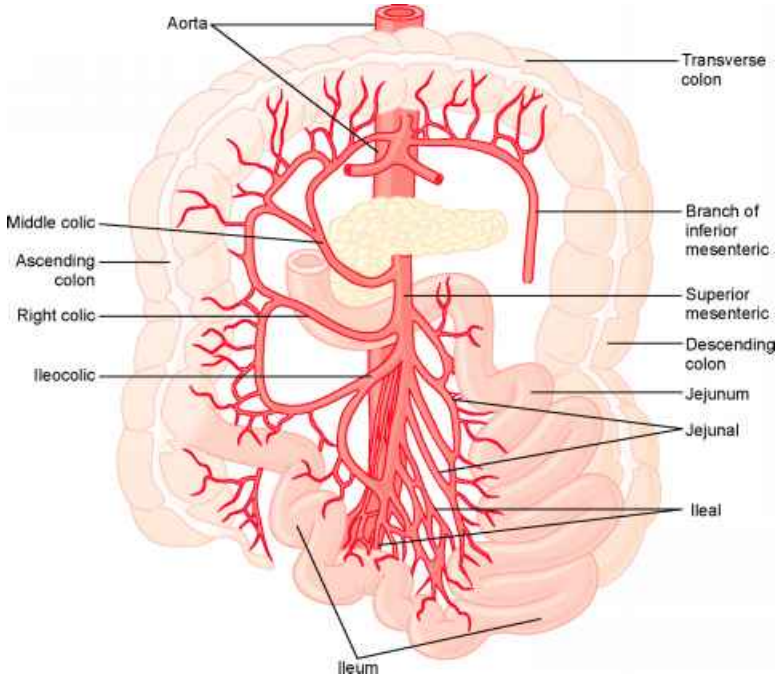
- Migrating motor complexes (MMC).
- Every 90-120min.
- 4 phases.



What hormone is implicated and what is the purpose of it?

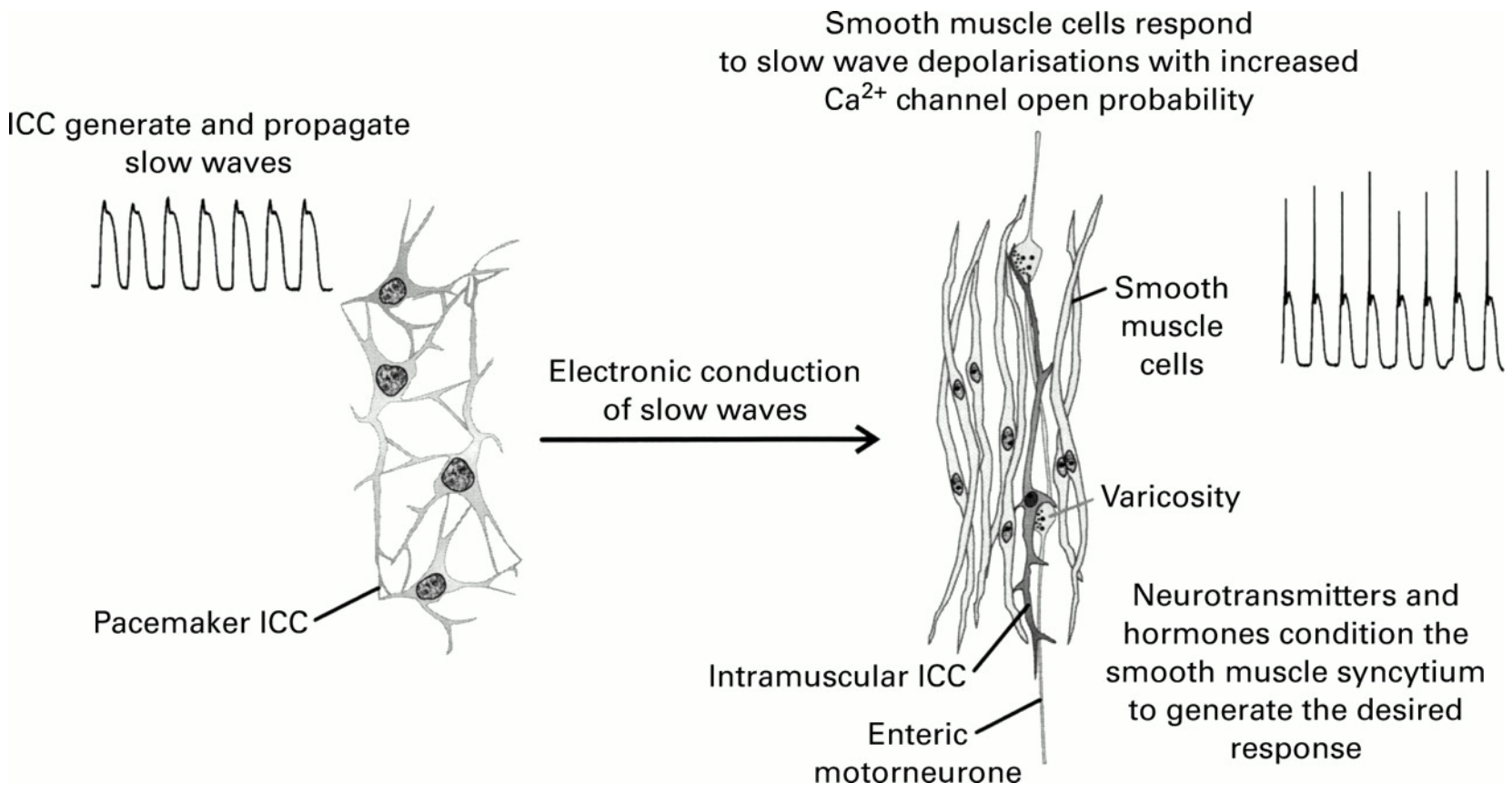
Splanchnic Circulation

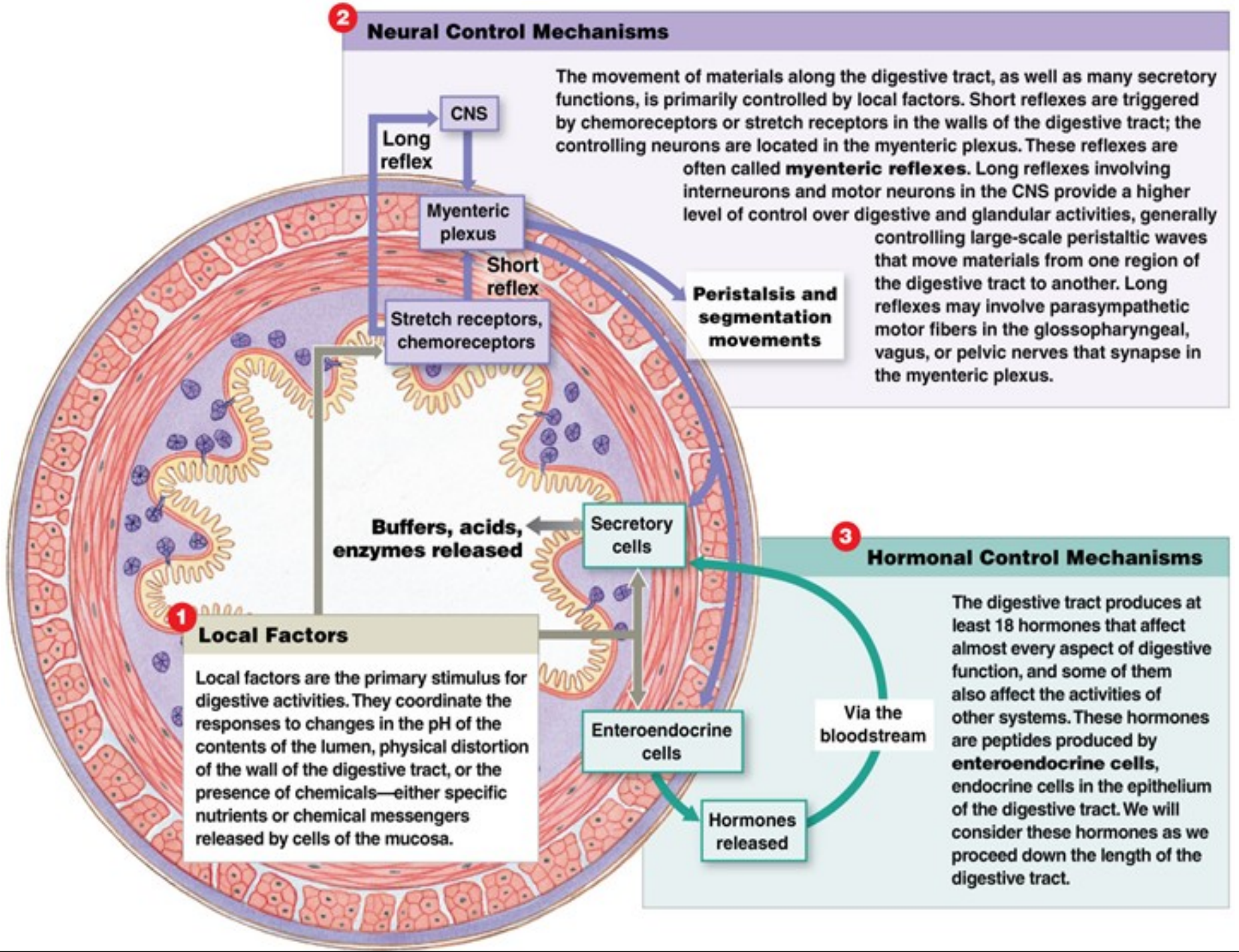




Read from Guyton & Hall Textbook of Medical Physiology. Chapter 62. 12th ed.

Thank you


ICC generate and propagate slow waves
Pacemaker ICC
Electronic conduction of slow waves
Smooth muscle cells respond to slow wave depolarisations with increased Ca^{2+} channel open probability
Smooth muscle cells
Varicosity
Intramuscular ICC
Enteric motorneurone
Neurotransmitters and hormones condition the smooth muscle syncytium to generate the desired response


2
Neural Control Mechanisms
The movement of materials along the digestive tract, as well as many secretory functions, is primarily controlled by local factors. Short reflexes are triggered by chemoreceptors or stretch receptors in the walls of the digestive tract; the controlling neurons are located in the myenteric plexus. These reflexes are often called myenteric reflexes. Long reflexes involving interneurons and motor neurons in the CNS provide a higher level of control over digestive and glandular activities, generally controlling large-scale peristaltic waves that move materials from one region of the digestive tract to another. Long reflexes may involve parasympathetic motor fibers in the glossopharyngeal, vagus, or pelvic nerves that synapse in the myenteric plexus.
CNS
Long reflex
Myenteric plexus
Short reflex
Stretch receptors, chemoreceptors
Peristalsis and segmentation movements
Buffers, acids, enzymes released
Secretory cells
1
Local Factors
Local factors are the primary stimulus for digestive activities. They coordinate the responses to changes in the pH of the contents of the lumen, physical distortion of the wall of the digestive tract, or the presence of chemicals—either specific nutrients or chemical messengers released by cells of the mucosa.
Enteroendocrine cells
Hormones released
Via the bloodstream
3
Hormonal Control Mechanisms
The digestive tract produces at least 18 hormones that affect almost every aspect of digestive function, and some of them also affect the activities of other systems. These hormones are peptides produced by enteroendocrine cells, endocrine cells in the epithelium of the digestive tract. We will consider these hormones as we proceed down the length of the digestive tract.