Principles of Digestive Function and Control
Electrical Activity, Nervous Control, Hormonal Control

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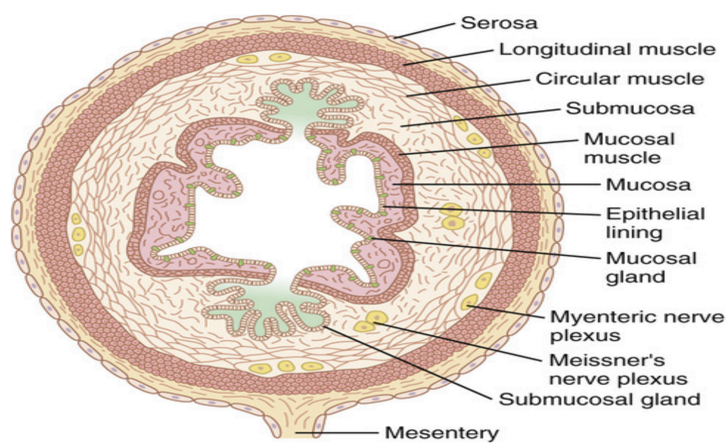
General Principles of Digestive Function

- The GI tract is a “disassembly” line
- The alimentary tract provides the body with a continual supply of water, electrolytes, and nutrients
- Functions of alimentary tract:
    - Movement of food through the alimentary tract
    - Secretion of digestive juices and digestion of the food
    - Absorption of water, various electrolytes, and digestive products
    - Circulation of blood through the gastrointestinal organs to carry away the absorbed substances
    - Control of all these functions by local, nervous, and hormonal systems

Physiologic Anatomy

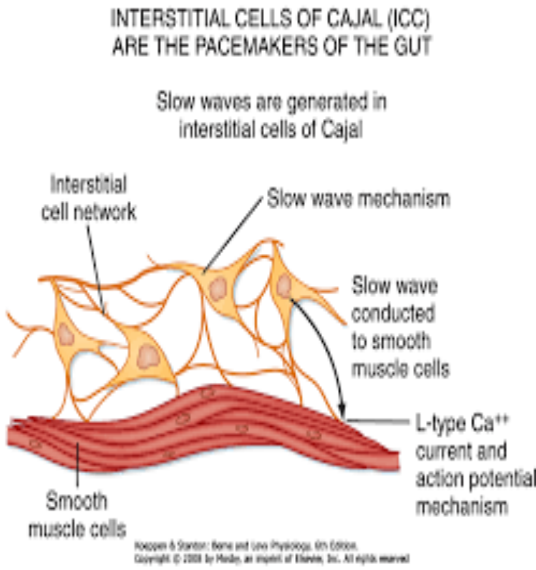
- Typical cross section of the intestinal wall - layers from outer surface inward:
    - The serosa
    - Outer longitudinal muscle layer
    - Inner circular muscle layer
    - The submucosa
    - The mucosa



- The motor functions of the gut are performed by the different layers of smooth muscle.
- The muscle fibers are electrically connected with one another through large numbers of gap junctions that allow low resistance movement of ions from one muscle cell to the next.
- Each muscle layer functions as a syncytium (as one unit)

Electrical Activity

- An action potential is elicited anywhere within the muscle mass, it generally travels in all directions in the muscle.
- Smooth muscle of the gastrointestinal tract is excited by almost continual slow, intrinsic electrical activity
    - Slow waves
    - Spikes
- Most gastrointestinal contractions occur rhythmically.
- This rhythm is determined mainly by the frequency of so called “slow waves” of smooth muscle membrane potential - not action potentials.
- They are slow, rising and falling changes in the Resting Membrane Potential - intensity usually varies between 5 and 15 millivolts
- Frequency ranges in different parts of the human GIT from 3 to 12 per minute
    - The rhythm of contraction of the body of the stomach usually is about 3 per minute.
    - The duodenum about 12 per minute
    - The ileum about 8 to 9 per minute
- Interstitial cells of Cajal are electrical pacemakers for smooth muscle cells.
- These 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.
- The slow waves usually do not by themselves cause muscle contraction in most parts of the gastrointestinal tract, except in the stomach.
- Instead, they mainly excite the appearance of intermittent spike potentials, and the spike potentials in turn actually excite the muscle contraction.



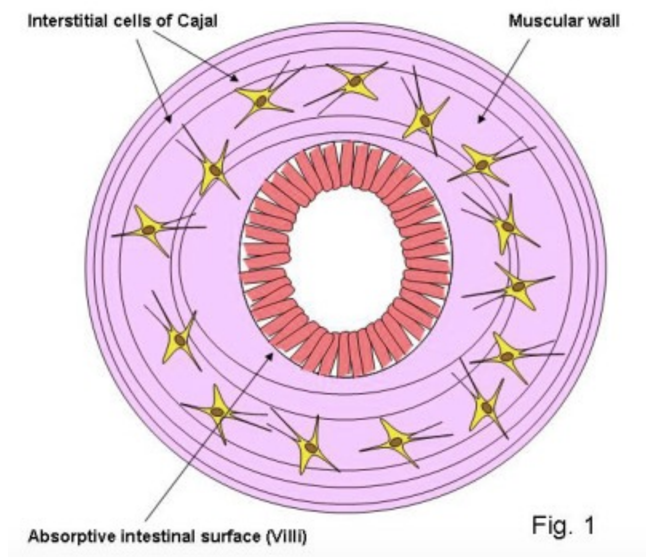


Fig. 1

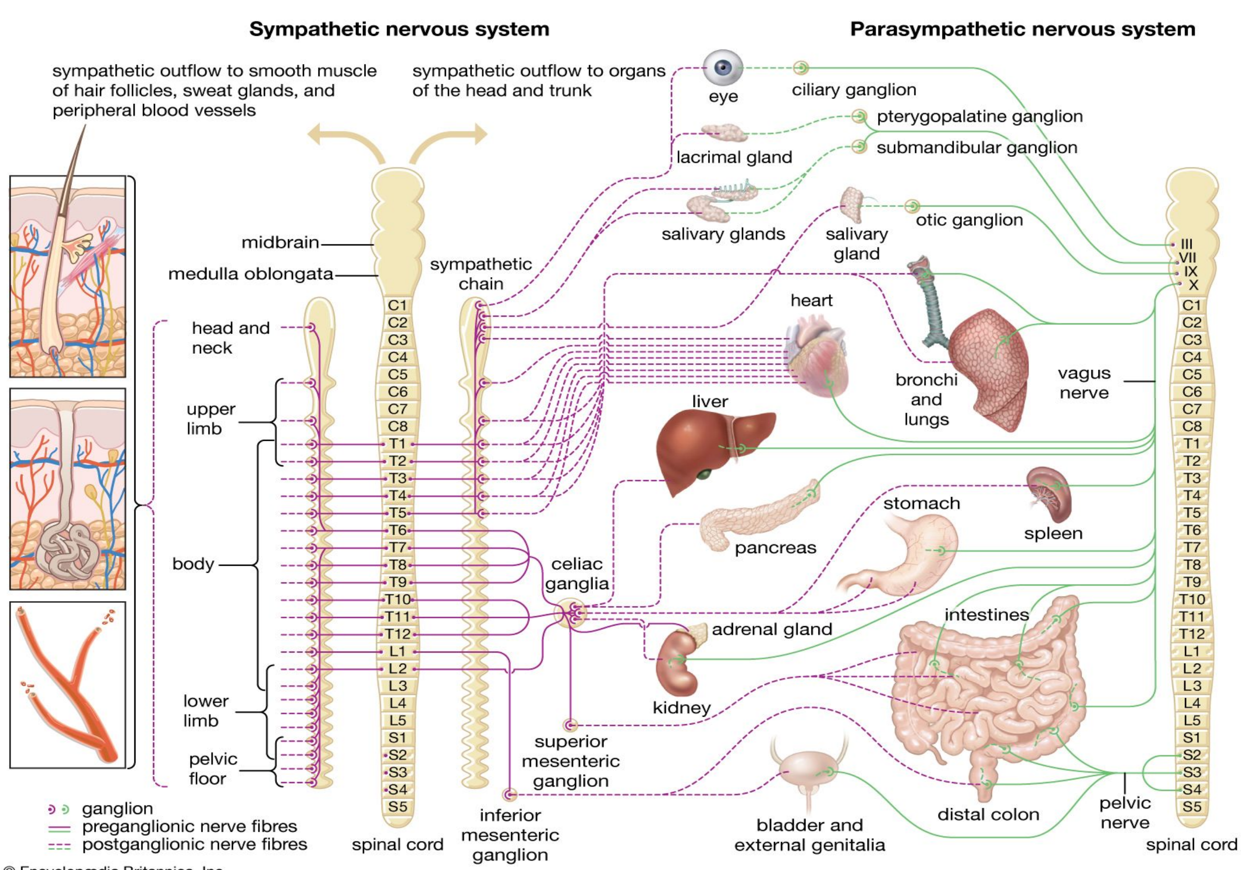
Spiked Potentials
- True action potentials
- They occur automatically when the RMP of the GIT smooth muscle becomes more positive than about -40 millivolts.
- The normal RMP in the smooth muscle fibers of the gut is between - 50 and -60 millivolts.
- Each time the peaks of the slow waves temporarily become more positive than -40 millivolts, spike potentials appear on these peaks.
- The higher the slow wave potential rises, the greater the frequency of the spike potentials - ranging between 1 and 10 spikes / second.
- The spike potentials last 10 to 40 times as long in GIT muscle as that in large nerve fibers, each spike lasting as long as 10 to 20 milliseconds.
- Influx of large numbers of Ca ions to enter along with smaller numbers of Na ions and therefore are called Ca-Na channels.
- Slower to open and close and remain open for long time.
- Long duration of action potentials
- When the potential becomes less negative, the muscle fibers become more excitable.
- When the potential becomes more negative, the fibers become less excitable.
- Factors that depolarize the membrane:
    - Stretching of the muscle
    - Stimulation by acetylcholine
    - Stimulation by parasympathetic nerves that secrete acetylcholine at their endings
    - Stimulation by several specific gastrointestinal hormones.
- Important factors that hyperpolarize the membrane:
    - The effect of norepinephrine or epinephrine on the fiber membrane.
    - Stimulation of the sympathetic nerves that secrete mainly norepinephrine at their endings.

Muscle Contraction
- Ca influx during spike potential – Ca Calmodulin – MLCK – Contraction
- The slow waves do not cause calcium ions to enter the smooth muscle fiber (only sodium ions)
- No muscle contraction
- During the spike potentials – significant quantities of calcium ions enter the fibers and cause most of the contraction
- Tonic contraction is continuous - lasting several minutes or even hours - increases or decreases in intensity but continues.

Tonic Contraction
- Continuous repetitive spike potentials
    - The greater the frequency, the greater the degree of contraction.
- Hormones or other factors that bring about continuous partial depolarization of the smooth muscle membrane without causing action potentials.
- Continuous entry of calcium ions into the interior of the cell

Enteric Nervous System
- Located in the wall of the gastrointestinal tract starting in the esophagus to the anus
- Controls gastrointestinal movements and secretions
- Controlled by two different nerve plexuses
- Myenteric Plexus or Auerbach's Plexus
    - An outer plexus lying between the circular and longitudinal muscle layers
    - Controls mainly the gastrointestinal movements
- Submucosal Plexus or Meissner's Plexus
    - An inner plexus that lies in the submucosa
    - Controls gastrointestinal secretion and local blood flow
- There are estimated to be **100 million** neurons in the human small intestine alone, making the ENS the largest collection of neurons and glia outside the brain, and by far the largest division of the peripheral nervous system

Dual Innervation
- The extrinsic sympathetic and parasympathetic fibers connect to both the myenteric and submucosal plexuses.
- The enteric nervous system can function on its own and is **independent** of the intrinsic nerves
- Stimulation by parasympathetic and sympathetic systems can greatly increase or decrease GI functions
- Sensory nerve endings start in the GI epithelium or gut wall and send afferent fibers to both plexuses of the enteric system
- Pathway of enteric nervous system
    - Sensory nerves ending in the gut wall >>>
    - Prevertebral ganglia of the sympathetic nervous system >>>
    - To the spinal cord and in the Vagus nerves all the way to the brain stem
- These sensory nerves can elicit local reflexes within the gastrointestinal wall



Enteric Nervous System

- The myenteric plexus consists mainly of a linear chain of countless interconnecting neurons that extend the entire length of the gastrointestinal tract
- When the plexus is stimulated, its main effects are
  - Increased tone of the gut wall
  - Increased intensity of the contractions
  - Slight increase of rate of the contractions
  - Increased velocity of conduction of excitatory waves along the gut wall, causing more rapid movement of the gut peristaltic waves
- The submucosal plexus is mainly concerned with controlling function within the inner wall
- Local intestinal secretion, local absorption, and local contraction of the submucosal muscle
- Neurotransmitters:

  (1) Ach (2) NE (3)ATP (4) 5 – HT (5) dopamine (6) cholecystokinin, (7) substance P (8) VIP (9) somatostatin (10) bombesin, (11) metenkephalin (12) leuenkephalin
- Inhibitory transmitter - vasoactive intestinal polypeptide (VIP) - pyloric sphincter, sphincter of the ileocecal valve

Autonomic Control - Parasympathetic

- The cranial parasympathetic nerve fibers
  - Mouth and pharyngeal regions of the alimentary tract, esophagus, stomach, and pancreas and somewhat less to the intestines down through the first half of the large intestine
- The sacral parasympathetics originate in the 2nd, 3rd & 4th sacral segments of the spinal cord and pass through the pelvic nerves to the distal half of the large intestine and all the way to the anus.
- The sigmoidal, rectal, and anal regions are considerably better supplied with parasympathetic fibers than are the other intestinal areas - defecation reflexes

Sympathetic Innervation

- Spinal cord between segments T-5 and L-2.
- Pre ganglionic - sympathetic chains - celiac ganglion and various mesenteric ganglia – post ganglionic
- Innervate essentially all of the gastrointestinal tract – inhibitory
  - to a slight extent by direct effect of secreted NE to inhibit intestinal tract smooth muscle
  - to a major extent by an inhibitory effect of NE on the neurons of the entire enteric nervous system

Afferent Sensory Nerve Fibers

- Sensory nerves can be stimulated by
  - irritation of the gut mucosa
  - excessive distention of the gut
  - presence of specific chemical substances in the gut.

Gastrointestinal Reflexes

- Reflexes that are integrated entirely within the gut wall enteric nervous system – secretion, peristalsis, mixing contractions, local inhibitory effects
- Reflexes from the gut to the prevertebral sympathetic ganglia and then back to the GIT
  - Signals from the stomach to cause evacuation of the colon (the gastrocolic reflex)
  - Signals from the colon and small intestine to inhibit stomach motility and stomach secretion (the enterogastric reflexes)
  - Reflexes from the colon to inhibit emptying of ileal contents into the colon (the colonoileal reflex)
- Reflexes from the gut to the spinal cord or brain stem and then back to the gastrointestinal tract

- ◦ 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
  - ◦ Pain reflexes that cause general inhibition of the entire gastrointestinal tract
  - ◦ 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

Hormonal Control - Gastrin

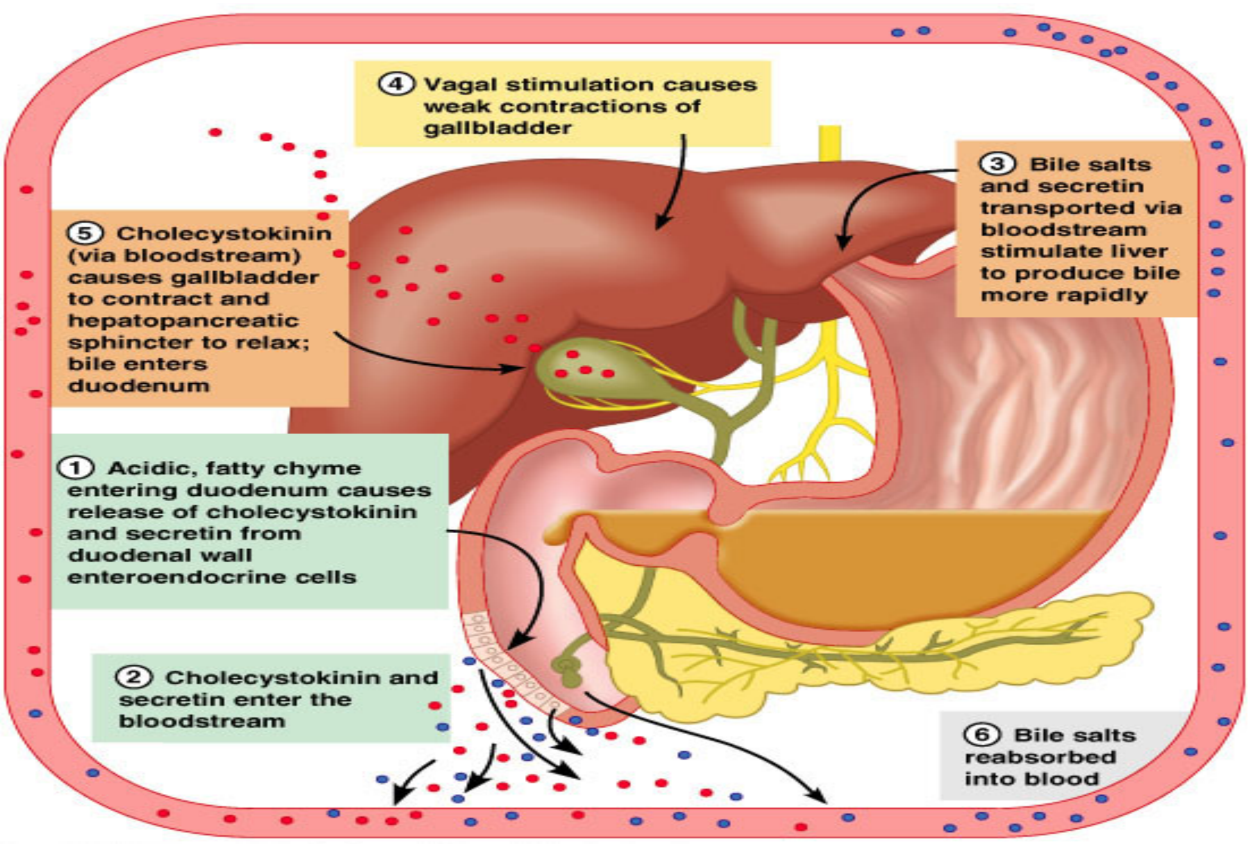
- Gastrin is secreted by the "G" cells of the antrum of the stomach in response to stimuli associated with ingestion of a meal, such as
  - distention of the stomach,
  - the products of proteins,
  - gastrin releasing peptide, which is released by the nerves of the gastric mucosa during vagal stimulation.
    - stimulation of gastric acid secretion and
    - stimulation of growth of the gastric mucosa

Hormonal Control - CCK

- Cholecystokinin (CCK) is secreted by "I" cells in the mucosa of the duodenum and jejunum mainly in response to digestive products of fat, fatty acids, and monoglycerides in the intestinal contents.
- This hormone strongly contracts the gallbladder, expelling bile into the small intestine where the bile in turn plays important roles in emulsifying fatty substances, allowing them to be digested and absorbed.
- Cholecystokinin also inhibits stomach contraction moderately which gives adequate time for digestion of the fats in the upper intestinal tract.

Regulation of Bile

- Fat in duodenum >>>> Liberates Enzyme CCK >>>>Tells Gallbladder to Contract >>>> Contraction Releases Bile >>>>Bile in Duodenum Emulsifies F



Hormonal Control - Secretin

- Secretin is secreted by the "S" cells in the mucosa of the duodenum in response to acidic gastric juice emptying into the duodenum from the pylorus of the stomach.
- Secretin has a mild effect on motility of the GIT and acts to promote pancreatic secretion of bicarbonate which in turn helps to neutralize the acid in the small intestine
- Gastric inhibitory peptide is secreted by the mucosa of the upper small intestine, mainly in response to fatty acids and amino acids but to a lesser extent in response to carbohydrate.
    - It has a mild effect in decreasing motor activity of the stomach and therefore slows emptying of gastric contents into the duodenum when the upper small intestine is already overloaded with food products.

Hormonal Control - Motilin

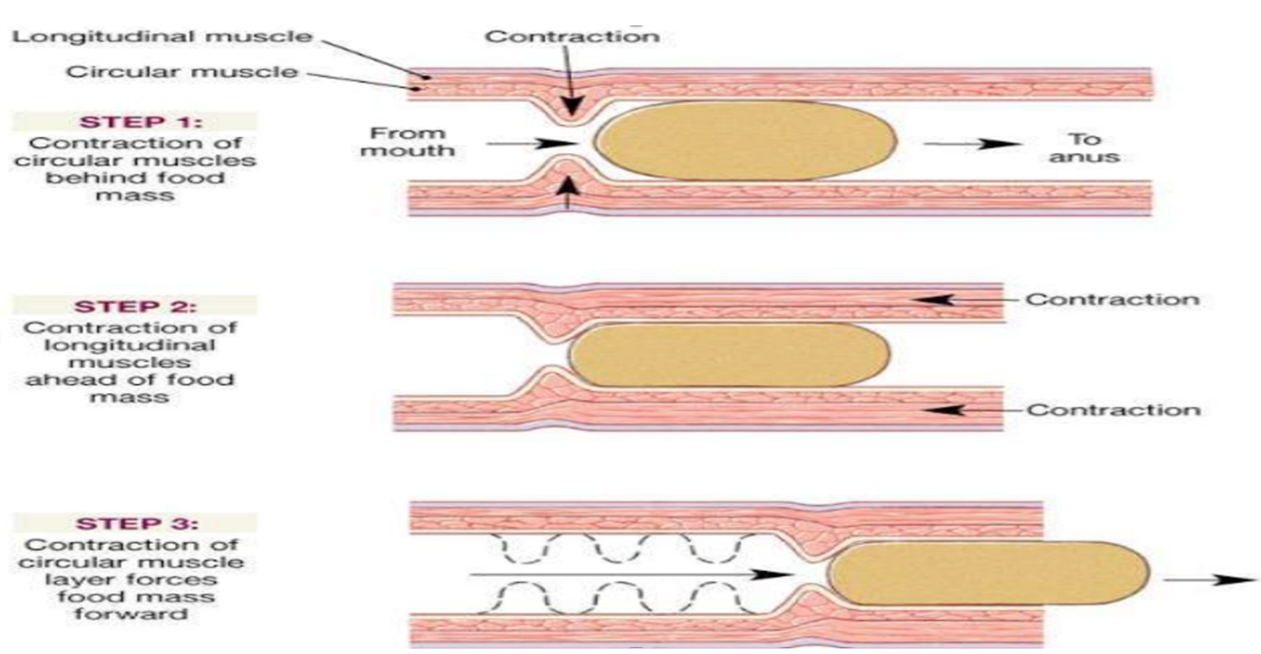
- Motilin is secreted by the upper duodenum during fasting, and the only known function of this hormone is to increase gastrointestinal motility.
- Motilin is released cyclically and stimulates waves of gastrointestinal motility called interdigestive myoelectric complexes that move through the stomach and small intestine every 90 minutes in a fasted person.

Movements in the Gastrointestinal Tract

- The basic propulsive movement of the GIT is peristalsis
- A contractile ring appears around the gut and then moves forward
    - Any material in front of the contractile ring is moved forward
- Stimulation at any point in the gut can cause a contractile ring to appear in the circular muscle, and this ring then spreads along the gut tube.
- Peristalsis also occurs in the bile ducts, glandular ducts, ureters, and many other smooth muscle tubes of the body

Peristalsis

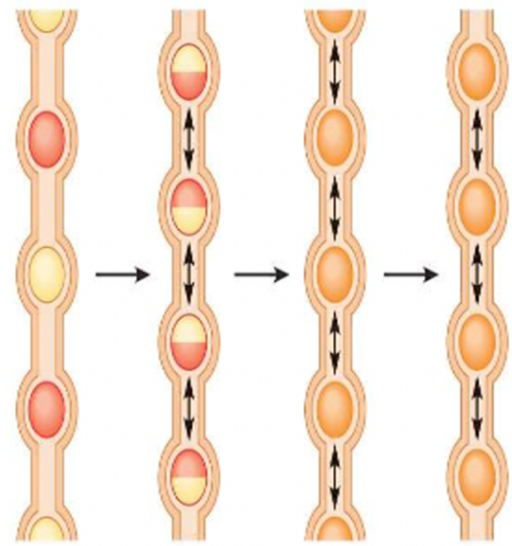
- The usual stimulus for intestinal peristalsis is distention of the gut
    - If a large amount of food collects at any point in the gut, the stretching of the gut wall stimulates the enteric nervous system to contract the gut wall 2 to 3 cm behind this point, and a contractile ring appears that initiates a peristaltic movement
    - Chemical or physical irritation of the epithelial lining of gut
    - Strong parasympathetic nervous signals
- Peristalsis occurs only weakly or not at all in any portion of the GIT that has congenital absence of the myenteric plexus.
- Also, it is greatly depressed or completely blocked in the entire gut when a person is treated with atropine to paralyze the cholinergic nerve endings of the myenteric plexus.
- Peristalsis normally dies out rapidly in the oral direction while continuing for a considerable distance toward the anus



Law of the Gut

- A law stating that a stimulus within the intestine (that is, the presence of food) initiates a band of constriction on the proximal side and relaxation on the distal side and results in a peristaltic wave.
- “Peristaltic contractions travels from a point of stimulation in both directions, but contraction in oral direction disappears and persists in anal direction” Startling - 1901

Segmentation



- Mixing movements differ in different parts of the alimentary tract. In some areas, the peristaltic contractions themselves cause most of the mixing
- When forward progression of the intestinal contents is blocked by a sphincter, so that a peristaltic wave can then only churn the intestinal contents, rather than propelling them forward
- Local intermittent constrictive contractions occur every few centimeters in the gut wall. These constrictions usually last only 5 to 30 seconds
- New constrictions occur at other points in the gut, and chop and shear the contents first here and then there.

Splanchnic Circulation

- All the blood that courses through the gut, spleen, and pancreas
    - Portal vein
    - Liver
    - Millions of minute liver sinusoids
    - Hepatic veins
    - Vena cava of the general circulation
- This allows the reticuloendothelial cells that line the liver sinusoids to remove bacteria and other particulate matter that might enter the blood from the gastrointestinal tract
- The nonfat, water-soluble nutrients absorbed from the gut (such as carbohydrates and proteins) are transported in the portal venous blood
- Fats absorbed from the intestinal tract are absorbed into the intestinal lymphatics and then conducted to the systemic circulating blood by way of the thoracic duct, bypassing the liver.
- Blood supply - celiac artery, superior mesenteric and inferior mesenteric arteries
- During active absorption of nutrients, blood flow increased as much as eightfold.
- Likewise, blood flow in the muscle layers of the intestinal wall increases with increased motor activity in the gut.
- Sympathetic stimulation, by contrast, has a direct effect on essentially all the gastrointestinal tract to cause intense vasoconstriction of the arterioles with greatly decreased blood flow.
- After a few minutes of this vasoconstriction, the flow often returns almost to normal by means of a mechanism called “autoregulatory escape”.
- The local metabolic vasodilator mechanisms that are elicited by ischemia become prepotent over the sympathetic vasoconstriction
    - Redilate the arterioles return of blood flow to the gastrointestinal glands and muscle.
- Sympathetic vasoconstriction allows shut-off of gastrointestinal and other splanchnic blood flow for short periods of time during heavy exercise, when increased flow is needed by the skeletal muscle and heart.
- In circulatory shock, when all the body’s vital tissues are in danger of cellular death for lack of blood flow (especially the brain and the heart) sympathetic stimulation can decrease splanchnic blood flow to very little for many hours.

Splanchnic Circulation

- Sympathetic stimulation also causes strong vasoconstriction of the large volume intestinal and mesenteric veins.
  - This decreases the volume of these veins, thereby displacing large amounts of blood into other parts of the circulation.
- In hemorrhagic shock or other states of low blood volume, this mechanism can provide as much as 200 to 400 milliliters of extra blood to sustain the general circulation.