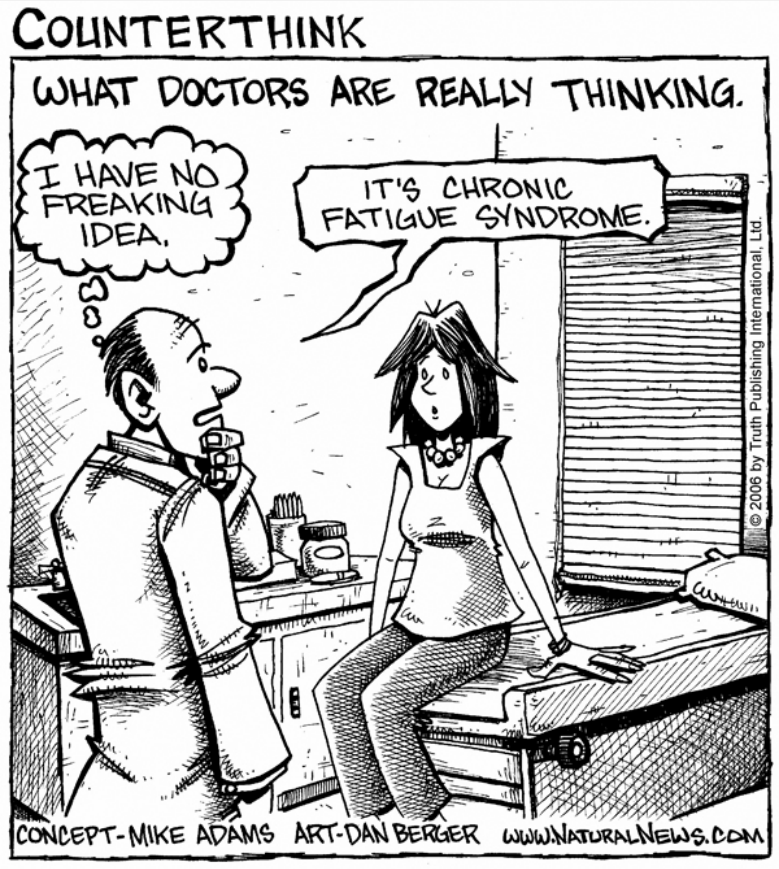
Gastrointestinal Physiology

General Principles of Gastrointestinal Function-Motility, Nervous Control

429 Physiology team



The primary function of alimentary tract is to provides the body with a continual supply of water, electrolytes, and nutrients through:

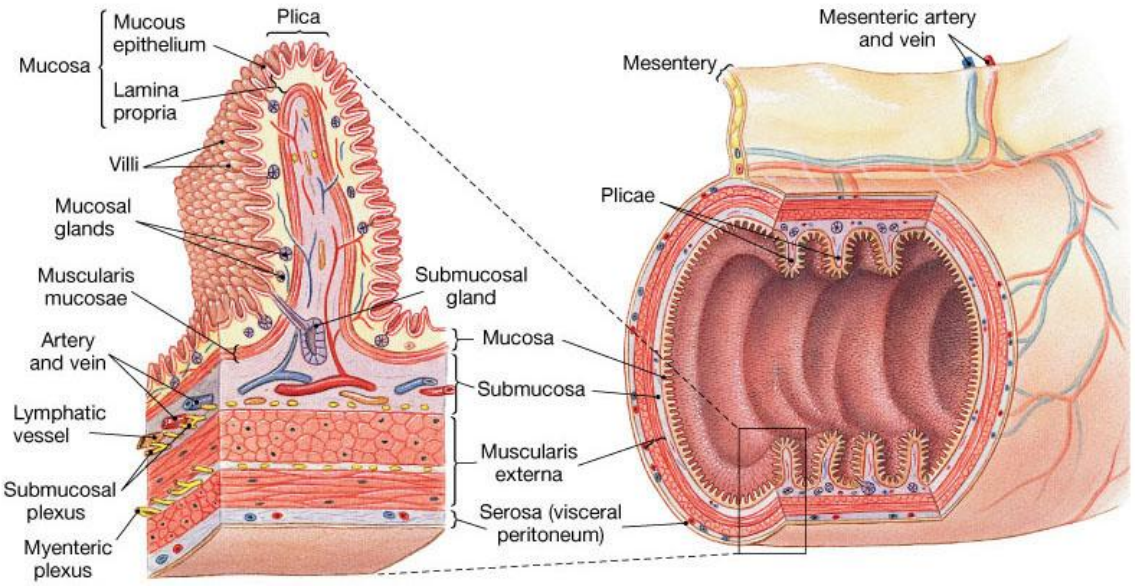
1. **Motility**: movement of food through the alimentary tract from the mouth to the rectum.
2. **Secretion** of digestive juices → glandular organ: salivary gland, liver, gall bladder, pancreas. these organs secrete substances "like HCl" to help in digestion !!
3. **Digestion** of the food → Digestion in stomach mainly !!
4. **Absorption** of water, various electrolytes, and digestive products → absorption mainly in small intestine !!
   not ALL absorbed molecules go into blood , some absorbed into lymph !!

- circulation of blood through the gastrointestinal organs to carry away the absorbed substances

Layers of Gastrointestinal Wall: from outer surface inward

1. ***serosa***
2. a ***longitudinal muscle layer***
3. a ***circular muscle layer***
4. the ***submucosa***
5. the ***mucosa***.

the wall of GI has almost the same structural layers from the upper 1/3 of esophagus untill the anus (except in the stomach)



Types of smooth muscle:

Unitary type	Multiunit type
Contracts spontaneously in response to stretch	**Contracts in response neural stimulation or hormones**
e.g. stomach and intestine	**e.g. esophagus & gall bladder**
Cells are electrically coupled via gap junctions so they contract as a single unit	

Types of contraction:

Some smooth muscle of the GI exhibits tonic contraction as well as or instead of rhythmical contractions

Phasic contractions (rhythmical)	Tonic contractions
periodic contractions followed by relaxation	**maintained (partial) contraction without relaxation period**
e.g. gastric antrum, small intestine and esophagus	**e.g. orad region of the stomach, lower esoghageal, ileocecal and internal anal sphincter**
associated with slow waves (rhythmical contraction)	**not associated with slow waves (because it's continual contraction not rhythmical)**
	Caused by: **1. repetitive spike potentials** **2. hormones,** **3. continuous entry of Ca ions.**

Main muscle layers:

Longitudinal Smooth Muscles	Circular Smooth Muscles
Contraction of this type increase the diameter of lumen and reduce its length	**Contraction of this type reduces the diameter of the lumen and increases its length**
They are innervated by enteric nervous system (ENS), and mainly by excitatory motor neurons	**They are innervated by ENS, both excitatory and inhibitory motor neurons.** NOTE: Inhibitory neurons causes sphincter (which is tonically contracted) to relax
The Ca influx from outside is important in the activity of this type of muscle.	
	thicker and more powerful
	More gap junctions are available

Specific Characteristics of Smooth Muscle in the Gut:

1. Gastrointestinal Smooth Muscle functions as a **Syncytium** because action potential spreads through **Gap junction**.
2. Electrical Activity of Gastrointestinal Smooth Muscle:

   The smooth muscle of the gastrointestinal tract is excited by almost **continual** slow, intrinsic electrical activity. This activity has electrical waves:

a. *slow waves*

- they are a unique feature of the electrical activity of GI smooth muscle
- They are generated by **interstitial cells of Cajal (ICC)** which are abundant in the myenteric plexues between the longitudinal & circular muscle layers.
- The resting membrane potential shows continuous repeated cycles of depolarization and hyperpolarization (wave pattern) → it is like pacemaker of the heart
- These waves are not action potentials because they don't reach threshold level
- If threshold level is reached (by neural or local factors),spike potential occur.
- Parasympathetic stimulation increases their frequency and amplitude while sympathetic stimulation decrease them → as we said the parasympathetic increase GIT functions → increase threshold of small waves to cause contraction "motility"
- Responsible for rhythmical contractions
- There is **NO Ca influx**
- It is propagated

b. *spikes potential*. "TRUE action potential"

- the normal resting membrane potential is usually about **-50 to -60 mv** (averages about -56 mv)
- action potentials occur on top of slow waves when resting membrane potential reaches threshold (-40 mv)
- It's caused by **Ca influx** (in large numbers) and **Na**
- **It cause CONTRACTION**
- It is not propagated
- It is longer than AP in skeletal muscles

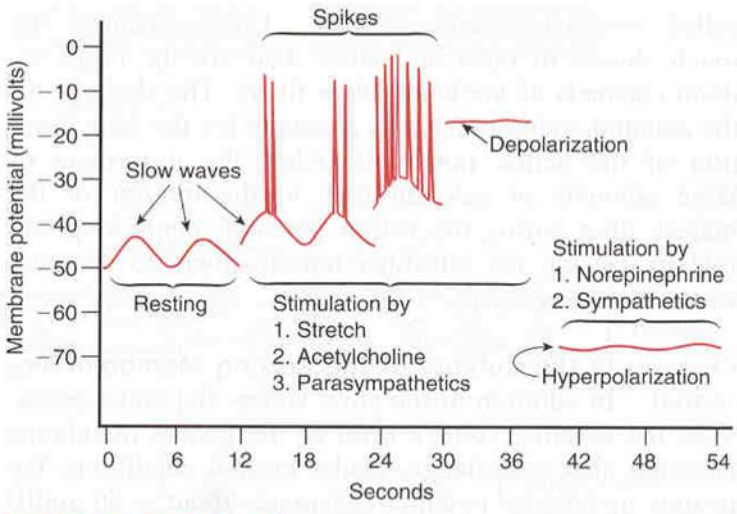


FIGURE 62–3

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

Slow waves	Spike potential
Initiated by interstitial cell of cajal	**Caused by Ca^{+2} & Na^{+} influx**
Don't reach firing level directly	**Reach firing level directly**
It can be propagated	**Can't be propagated**
Don't cause contraction directly	**Cause contraction directly**

Factors that depolarize the membrane (make it more excitable):

1. ***stretching*** of the muscle → e.g . full stomach → inducing contraction and motility
2. stimulation by ***acetylcholine*** → *parasympathtic*
3. stimulation by ***parasympathetic*** *nerves* that secrete acetylcholine " *rest and digest"*
4. stimulation by several *specific gastrointestinal hormones*.

Factors that hyperpolarize the membrane (make less excitable):

1. the effect of ***norepinephrine*** or ***epinephrine***
2. stimulation of the **sympathetic** nerves that secrete mainly norepinephrine " fight and flight : no time for digestion !

Controlling gastric functions :

1. **Neural (Autonomic)**
2. **Hormonal**

Autonomic Control of the Gastrointestinal Tract

1. **Parasympathetic → extrinsic**
2. **Sympathetic → extrinsic**
3. **Enteric Nervous System (ENS) → intrinsic**

extrinsic >> modify GIT functions " systemic"
intrinsic >> coordinate GIT functions " locally"

1. Parasympathetic:

- The *cranial parasympathetic* nerve fibers are almost entirely in the ***vagus nerves***.
- The esophagus, stomach, pancreas and the intestines down through the first half of the large intestine are innervated by *vagus nerves*.
- The distal half of the large intestine and the anus are innervated by the *sacral parasympathetics* (to execute the defecation reflexe)
- postganglionic neurons are located mainly in the myenteric and submucosal plexuses.
- Parasympathetic Stimulation nerves increase entire enteric nervous system activity and gastrointestinal functions.

parasympathetic = rest and digest = Ach
" ALL GIS functions will increase
high vagal activity = hypotension and vasodilatation = relxing sphincter "
lower esophageal sphincter" = reflux occure = lead to VOMITING !!"

2. Sympathetic:

- The sympathetic fibers to the gastrointestinal tract originate in the spinal cord between segments T-5 and L-2.
- The sympathetics innervate essentially all of the GI tract
- Sympathetic Stimulation *inhibits* activity of the GI.
- Strong stimulation of the sympathetic system can inhibit motor movements

sympathatic = fight and flight = norepinephrine :
there is NO time for relaxing and digestion of food
" ALL GIS FUNCTIONS decrease !!"

3. Enteric Nervous System

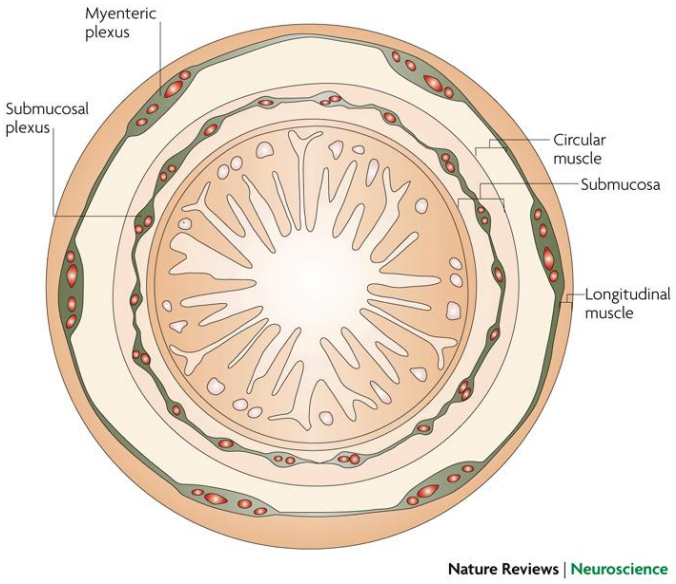
- the nervous system of GI tract.
- It lies entirely in the wall of the gut, from the esophagus to the anus.
- It has as many neurons as spinal cord (about 100 million).
- It control gastrointestinal movements and secretion.
- **The enteric nervous system can function on its own, independently**
- parasympathetic and sympathetic systems **<u>enhance or inhibit</u>** gastrointestinal functions.
- It is composed mainly of two plexuses:
    1. ***myenteric plexus***
    2. ***submucosal plexus*: or *Meissner's plexus:***

it is the Gut mini brain " GIT's small brain !! because , it coordinate GIT functions by reflexes without extrinsic Nervous system !!
ENS is postganglionic fibers of vagus = parasympathetic !!

myenteric plexus	submucosal plexus
controls mainly the gastrointestinal movements	**controls mainly gastrointestinal secretion and local blood flow.**
lying between the longitudinal and circular muscles	**lies in the submucosa**
	controlling function within the inner wall such as intestinal secretion, local absorption, and local contraction of the submucosal muscle and local blood flow
consists mostly of a linear chain of many interconnecting neurons.	
The *myenteric plexus* has *excitatory* and *inhibitory* motor (inhibitory signals are useful for inhibiting some of the intestinal sphincter muscles)	

<u>Myenteric plexus</u> is located in muscular layer → it control muscle contraction ,intensity , rate, conduction

<u>Submucosal plexus</u> is located in submucosa (layer of vessels and glands) → it control secretion and blood flow and the near muscularis mucosa!



Neural Control of GI Function-Enteric Nervous System

- **The sensory nerve endings send afferent fibers to both plexuses of the enteric system and then to:**
    1. **the prevertebral ganglia**
    2. **the spinal cord**
    3. **vagus nerves all the way to the brain stem.**

- **These sensory nerves can be stimulated by**
    1. **irritation of the gut mucosa**
    2. **excessive distention of the gut**
    3. **presence of specific chemical substances in the gut.**

These sensory nerves can elicit local reflexes within the gut wall.

Types of Neurotransmitters Secreted by Enteric Neurons

Excitatory Motor Neurons Evoke Muscle Contraction & Intestinal Secretion:

- **Neurotransmitters of motor neurons:**
  1. **Substance P**
  2. **Ach**
- **Neurotransmitters of secretomotor neurons (releasing of water, electrolytes and mucus from crypts of Lieberkuhn):**
  1. **Ach**
  2. **VIP (vasoactive intestinal peptide)**
  3. **Histamine (neurogenic secretory diarrhea)**

Inhibitory Motor Neurons Suppress Muscle Contraction:

- **Neurotransmitters:**
  1. **NO**
  2. **VIP**

TABLE 8–1. Neurotransmitters and Neuromodulators in the Enteric Nervous System

Substance	Source	Actions
Acetylcholine (ACh)	Cholinergic neurons	Contraction of smooth muscle in wall Relaxation of sphincters ↑ Salivary secretion ↑ Gastric secretion ↑ Pancreatic secretion
Norepinephrine (NE)	Adrenergic neurons	Relaxation of smooth muscle in wall Contraction of sphincters ↑ Salivary secretion
Vasoactive intestinal peptide (VIP)	Neurons of mucosa and smooth muscle	Relaxation of smooth muscle ↑ Intestinal secretion ↑ Pancreatic secretion
Gastrin-releasing peptide (GRP) or bombesin	Neurons of gastric mucosa	↑ Gastrin secretion
Enkephalins (opiates)	Neurons of mucosa and smooth muscle	Contraction of smooth muscle ↓ Intestinal secretion
Neuropeptide Y	Neurons of mucosa and smooth muscle	Relaxation of smooth muscle ↓ Intestinal secretion
Substance P	Cosecreted with ACh	Contraction of smooth muscle ↑ Salivary secretion

Hormonal Control of Gastrointestinal Motility

Hormons secreted by endocrine cells located in pancreas , mucosa and submucosa of stomach , intestine.

Affect on secretory cells , smooth muscles and sphincters of GIT ..

- **Liver has only secretory cells " no endocrine cells"**

Hormone	Site of Secretion	Stimuli for Secretion	Actions
Gastrin	G cells of the stomach	Small peptides and amino acids Distention of the stomach Vagal stimulation (GRP)	↑ Gastric H^+ secretion Stimulates growth of gastric mucosa
Cholecystokinin (CCK)	I cells of the duodenum and jejunum	Small peptides and amino acids Fatty acids	↑ Pancreatic enzyme secretion ↑ Pancreatic HCO_3^- secretion Stimulates contraction of the gallbladder and relaxation of the sphincter of Oddi Stimulates growth of the exocrine pancreas and gallbladder Inhibits gastric emptying
Secretin	S cells of the duodenum	H^+ in the duodenum Fatty acids in the duodenum	↑ Pancreatic HCO_3^- secretion ↑ Biliary HCO_3^- secretion ↓ Gastric H^+ secretion Inhibits trophic effect of gastrin on gastric mucosa
Glucose-Dependent Insulinotropic Peptide (GIP)	K cells of the Duodenum and jejunum	Fatty acids Amino acids Oral glucose	↑ Insulin secretion from pancreatic β cells ↓ Gastric H^+ secretion
Motilin	M cells of the duodenum and jejunum	Fat Acid Nerve	Stimulates: Gastric motility Intestinal motility

Gastrointestinal reflexes

Types of reflexes are essential for G. I control:

1. **reflexes that are integrated entirely within ENS**
   e.g. reflexes that control G.I secretion, peristalsis and mixing contraction.
2. **Reflexes from gut to prevertebral ganglion & then back to GIT.**
   e.g. signals from stomach to cause evacuation of colon.

"like when you eat and feel you have to empty your colon Know !! :) to recieve new food !!"

3. **Reflexes from gut to brain & spinal cord, then back to GIT.**

e.g. reflexes from stomach to brain stem to stomach to control gastric motor & secretory activity.

Reflex : GIT >> afferent >> Center
Center >> efferent >> GIT

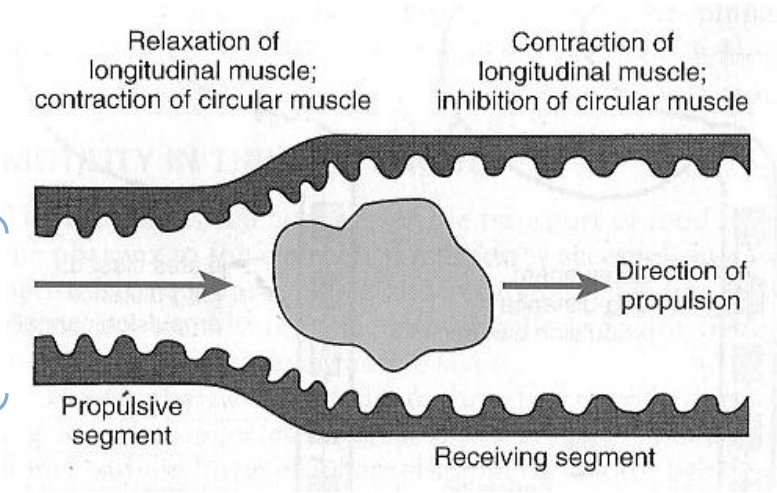
center : one of these three
1- brain and spinal cord
2- prevertebral ganglia " sympathetic "
3- ENS " myentric or submucosa plexus"

Types of Movements in the Gastrointestinal Tract

1. *ropulsive movements*

- Usual stimulus is distention.
- chemical or physical irritation of the epithelial lining in the gut may also stimulate it.
- Myenteric plexus is important
- Atropine (cholinergic blocker) depresses propulsion.

Propulsive segment
contraction (circular M.)
relaxation (longitudinal



Receiving segment:
contraction (longitudinal M.)
relaxation (circular M.)

2. Mixing movements (segmentation)

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

Further Reading

Gastrointestinal Blood Flow-"Splanchnic Circulation"

- **Splanchnic circulation includes the blood flow through the gut itself plus blood flows through the spleen, pancreas, and liver. The design of this system is such that all the blood that courses through the gut, spleen, and pancreas then flows immediately into the liver by way of the *portal vein*. In the liver, the blood passes through millions of minute *liver sinusoids* and finally leaves the liver by way of *hepatic veins* that empty into the vena cava of the general circulation.**

Effect of Gut Activity and Metabolic Factors on Gastrointestinal Blood Flow

- **Possible Causes of the Increased Blood Flow During Gastrointestinal Activity**

1. **Most of the peptide hormones, including *cholecystokinin*, *vasoactive intestinal peptide*, *gastrin*, and *secretin*.**
2. **Some of the GI glands release into the gut wall two kinins, *kallidin* and *bradykinin***
3. ***Decreased oxygen concentration* in the gut wall can increase intestinal blood flow at least 50 to 100 per cent.**

Nervous Control of Gastrointestinal Blood Flow

- **Stimulation of the parasympathetic nerves going to the *stomach* and *lower colon* increases local blood flow at the same time that it increases glandular secretion.**
- **Sympathetic stimulation, by contrast, has a direct effect on essentially all the gastrointestinal tract to cause intense vasoconstriction of the arterioles with greatly decreased blood flow. But the local metabolic vasodilator mechanisms override the sympathetic vasoconstiction effects, returning the normal blood flow to GI muscle and glands.**