Gastrointestinal Physiology

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• A basic understanding of the overall organization of the gastrointestinal system. An understanding of how the different gastrointestinal organs are regulated and coordinated with each other

• Overview; enteric nervous system
• Textbook:
  ◦ Syllabus-primary source
  ◦ Endoscopy videos: The DAVE Project (Digital Atlas of Video Education)
Gastrointestinal Organs

- Oral cavity
- Salivary glands
- Esophagus
- Stomach
- Liver

- Gallbladder
- Pancreas
- Small intestine
- Large intestine
- Rectum and anus
Physiological Processes

- Muscular contraction/Motility
- Nervous
- Endocrine system
- Exocrine system
- Epithelial transport
- Biochemical biosynthesis & detoxification
Pathology

- Oncology
- Infectious Disease
- Nutrition
- Metabolism
- Motility/neurobiology
- Vascular
- Endocrine
- Immunology/autoimmune diseases
<table>
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<tr>
<th>Description</th>
<th>Value</th>
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<tbody>
<tr>
<td>Ingested</td>
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<td>Endogenous secretions</td>
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<td>Salivary glands</td>
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<td>Stomach</td>
<td>2500</td>
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<tr>
<td>Bile</td>
<td>500</td>
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<td>Pancreas</td>
<td>1500</td>
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<td>Intestine</td>
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<tr>
<td>Total input</td>
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<td>Reabsorbed</td>
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<td>Jejunum</td>
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<tr>
<td>Ileum</td>
<td>2000</td>
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<tr>
<td>Colon</td>
<td>1300</td>
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<td>Balance in stool</td>
<td>200</td>
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*Moore, EW. Physiology of Intestinal Water and Electrolyte Absorption, 1976*
Integrative Functions

Enteric Nervous System
Gastrointestinal Hormones
GI Motility and Nervous System Control

Enteric NS controls:

- GI motility and movement of lumenal contents
- Secretion of digestive enzymes and fluids
- Absorption of digestive products, water and electrolytes
- Circulation of blood and the removal of absorbed substances
Typical cross-section of the gut
Cellular organization of GI smooth muscle

A MULTIUNIT

Electrical isolation of cells allows finer motor control.

Smooth muscle cell

Varicosities (synaptic contacts)

B UNITARY

Autonomic neurons

Gap junctions permit coordinated contraction.
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 physiological conditions of the intestine.
The gastric action potential

Figure 27–13 ■ The gastric action potential.
A. Gastric antrum

B. Small intestine

C. Colon
In addition to intrinsic muscle cell activity, the GI tract is endowed with…

A nervous system of its own
Myenteric and submucosal plexuses

100,000,000 neurons!
Descending input to both plexuses
Relation between enteric and sympathetic and parasympathetic nervous systems
Overall control by sympathetic nervous system

Fig. 9.1 Diagram to illustrate the principal noradrenergic pathways to the small intestine and their connections. The chemical coding of neurons applies to the guinea-pig small intestine: it might be different in other regions or species. The pathways and functions of the neurons, however, appear to be the same in all mammals. Separate noradrenergic neurons supply inhibitory inputs to the myenteric ganglia and to the submucous ganglia and excitatory inputs to intestinal arteries and arterioles. The noradrenergic nerves thus inhibit motility and water and electrolyte secretion and reduce blood flow. Noradrenergic neurons receive excitatory cholinergic inputs from the spinal cord. Motility-inhibiting and secretion-inhibiting but not vasoconstrictor neurons receive excitatory inputs from sensory neuronal pathways that originate in the intestine. See text for further details.
Enteric sensation sends inputs to higher centers and feedback input to enteric nervous system.
Importance of enteric nervous system for peristalsis
Excitatory, cholinergic motor neurons activate circular muscle contraction

![Diagram of excitatory cholinergic motor neuron](image)

**Fig. 7.5** The excitatory cholinergic motor neuron to the circular muscle of the guinea-pig small intestine. From physiological studies it is deduced that these neurons supply the band of circular muscle below the myenteric ganglia in which the cell bodies are found. They are S neurons, that is, they receive fast synaptic inputs and they probably have Dogiel type I morphology.
Fig. 2/3 The neuromuscular unit in the intestine. This drawing shows the way in which an individual myenteric neuron supplies the circular muscle of the intestine and is deduced from microscopic and physiological studies (see text). Each neuron supplies a bundle of smooth muscle cells via its branching process. The smooth muscle cells within the bundle are electrically coupled, so that when the neuron is active, it affects all the cells. Moreover, there is a polynervous innervation of the unit by both excitatory and inhibitory neurons, so the response of the muscle is a summation of the individual effects of many neurons. The muscle bundles are also connected to their neighbours electrically, but electrical signals pass between bundles with considerable decrement.
Excitatory junction potentials are very slow

Fig. 7.4: Excitatory junction potentials (e.j.p.s) recorded with intracellular microelectrodes from intestinal smooth muscle cells. These transient potential changes are the consequences of stimulating a group of enteric cholinergic motor neurons with single pulses. The left hand record is of a single e.j.p., which did not initiate an action potential. Larger e.j.p.s, such as that the right hand record, initiate regenerative action potentials in the muscle. The e.j.p.s are blocked by antagonists of muscarinic receptors for acetylcholine. (Reproduced
Enteric inhibitory neurons oppose depolarization, contraction

**Fig. 7.9** Transmission from enteric inhibitory motor neurons to the muscle of the intestine, recorded with intracellular microelectrodes. A single pulse (a) gives an inhibitory junction potential (i.j.p.). Successive i.j.p.s have similar amplitudes (b) or, if the frequency of stimulation is sufficiently great, hyperpolarization can be maintained (c). Stimuli were applied at the arrows (a, b) and at the negative deflections (c). In each case one or more action potentials follow the membrane repolarization. (Reproduced from Furness 1970b.)
There are many putative neurotransmitter substances.
Role of NO as inhibitor of GI contractility

nitric oxide synthase (NOS)
L-arginine $\rightarrow$ nitric oxide (NO) $\Rightarrow$ $\uparrow$guanylate cyclase $\Rightarrow$ $\uparrow$cGMP $\Rightarrow$ $\downarrow$contraction
$\downarrow$
L-citrulline

- Nitric oxide synthase (NOS) in enteric neurons
- non-adrenergic, non-cholinergic inhibitory transmission responds to inhibitors of NOS
- NOS system may work in parallel with VIP
Enteric NOS-containing neurons

NOS often colocalized w/ VIP or NPY
Inhibitory neurons project downstream to relax circular muscle in advance of intraluminal content.
Propulsion generated by coordinated contractions of smooth muscles

**Figure 27–3** Peristaltic propulsion is a stereotyped behavior pattern consisting of a propulsive segment and a receiving segment. Contraction of the longitudinal muscle and inhibition of the circular muscle occur in the receiving segment. In the propulsive segment, the longitudinal muscle is relaxed while the circular muscle contracts.
Distension causes reflexive upstream contraction
Diseases arising from deficient enteric neurons

• *Adynamic Ileus*
  stress response

• *Chaga’s Disease (Trypanosoma Cruzi)*
  megacolon and megaesophagus.

• *Paraneoplastic syndromes*

• *Hirschsprung’s disease*
  congenital megacolon, agangliosis
Normal Abdominal X-ray
Adynamic Ileus
Hirschsprung’s Disease

Fig. 1 - (A) Barium contrasted radiography from the esophagus showing a slightly enlarged organ. (B) Barium contrasted radiography from the large intestine presenting a very large rectum-sigmoid segment filled with fecal mass.