

Chapter 2

Control of Digestive System Function

Like any other physiologic process, proper function of the digestive system requires robust mechanisms for control and communication. Maintaining adequate control requires intimate participation from both the nervous and endocrine systems, and the gastrointestinal tract has built-in versions of both. One consequence of the complexity of digestive control systems is that many digestive diseases are associated with dysfunction in these relationships.

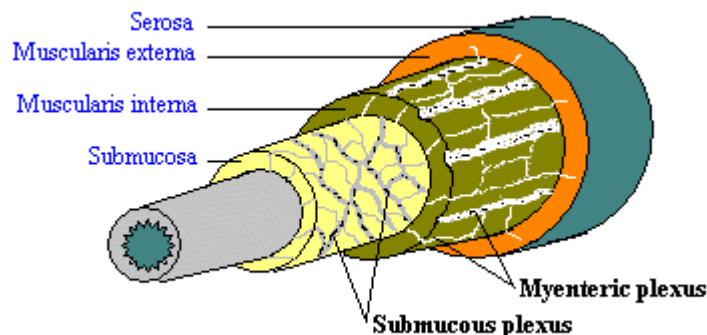
The Enteric Nervous System

The nervous system exerts a profound influence on all digestive processes, namely motility, ion transport associated with secretion and absorption, and gastrointestinal blood flow. Some of this control emanates from connections between the digestive system and central nervous system, but just as importantly, **the digestive system is endowed with its own, local nervous system referred to as the enteric or intrinsic nervous system.** The magnitude and complexity of the enteric nervous system is immense - it contains as many neurons as the spinal cord.

The enteric nervous system, along with the sympathetic and parasympathetic nervous systems, constitute the autonomic nervous system.

The principal components of the enteric nervous system are two networks or plexuses of neurons, both of which are embedded in the wall of the digestive tract and extend from esophagus to anus:

- The **myenteric plexus** is located between the longitudinal and circular layers of muscle in the tunica muscularis and, appropriately, exerts control primarily over digestive tract motility.
- The **submucous plexus**, as its name implies, is buried in the submucosa. Its principal role is in sensing the environment within the lumen, regulating gastrointestinal blood flow and controlling epithelial cell function. In regions where these functions are minimal, such as the esophagus, the submucous plexus is sparse and may actually be missing in sections.



The image below shows part of the myenteric plexus in a section of cat duodenum. Pass your mouse cursor over the image to outline several enteric neurons.

In addition to the two major enteric nerve plexuses, there are minor plexuses beneath the serosa, within the circular smooth muscle and in the mucosa.

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Within enteric plexuses are three types of neurons, most of which are multipolar:

- **Sensory neurons** receive information from sensory receptors in the mucosa and muscle. At least five different sensory receptors have been identified in the mucosa, which respond to mechanical, thermal, osmotic and chemical stimuli. Chemoreceptors sensitive to acid, glucose and amino acids have been demonstrated which, in essence, allows "tasting" of luminal contents. Sensory receptors in muscle respond to stretch and tension. Collectively, enteric sensory neurons compile a comprehensive battery of information on gut contents and the state of the gastrointestinal wall.
- **Motor neurons** within the enteric plexuses control gastrointestinal motility and secretion, and possibly absorption. In performing these functions, motor neurons act directly on a large number of effector cells, including smooth muscle, secretory cells (chief, parietal, mucous, enterocytes, pancreatic exocrine cells) and gastrointestinal endocrine cells.
- **Interneurons** are largely responsible for integrating information from sensory neurons and providing it to ("programming") enteric motor neurons.

Enteric neurons secrete an intimidating array of neurotransmitters. One major neurotransmitter produced by enteric neurons is acetylcholine. In general, neurons that secrete acetylcholine are excitatory, stimulating smooth muscle contraction, increases in intestinal secretions, release of enteric hormones and dilation of blood vessels. Norepinephrine is also used extensively for neurotransmission in the gastrointestinal tract, but it derives from extrinsic sympathetic neurons; the effect of norepinephrine is almost always inhibitory and opposite that of acetylcholine.

The enteric nervous system can and does function autonomously, but normal digestive function requires communication links between this intrinsic system and the central nervous system. These links take the form of parasympathetic and sympathetic fibers that connect either the central and enteric nervous systems or connect the central nervous system directly with the digestive tract. Through these cross connections, the gut can provide sensory information to the CNS, and the CNS can affect gastrointestinal function. Connection to the central nervous system also means that signals from outside of the digestive system can be relayed to the digestive system: for instance, the sight of appealing food stimulates secretion in the stomach.

In general, *sympathetic* stimulation causes inhibition of gastrointestinal secretion and motor activity, and contraction of gastrointestinal sphincters and blood vessels. Conversely, parasympathetic stimuli typically stimulate these digestive activities. Some of the prominent communiques enabled by nervous interconnections within the digestive tract have been named as reflexes and serve to illustrate a robust system of control. Examples include the gastrocolic reflex, where distention of the stomach stimulates evacuation of the colon, and the enterogastric reflex, in which distention and irritation of the small intestine results in suppression of secretion and motor activity in the stomach.

Congenital and acquired derangements in the structure or function of the enteric nervous system are well recognized as causes of digestive tract disease. Examples include small intestinal motility disorders, gastric outlet obstructions and megacolon.

The Enteric Endocrine System

The second of the two systems that control digestive function is the endocrine system, which regulates function by secreting hormones. Recall that hormones are chemical messengers secreted into blood that modify the physiology of target cells. A target cell for a particular hormone is a cell that has receptors for that hormone and can thus respond to it.

Digestive function is affected by hormones produced in many endocrine glands, but the most profound control is exerted by hormones produced within the gastrointestinal tract. The gastrointestinal tract is the largest endocrine

organ in the body and the endocrine cells within it are referred to collectively as the *enteric endocrine system*. Three of the best-studied enteric hormones are:

- **Gastrin:** Secreted from the stomach and plays an important role in control of gastric acid secretion.
- **Cholecystokinin:** A small intestinal hormone that stimulates secretion of pancreatic enzymes and bile.
- **Secretin:** Another hormone secreted from small intestinal epithelial cells; stimulates secretion of a bicarbonate-rich fluids from the pancreas and liver.

In contrast to endocrine glands like the anterior pituitary gland, in which essentially all cells produce hormones, the enteric endocrine system is diffuse: single hormone-secreting cells are scattered among other types of epithelial cells in the mucosa of the stomach and small intestine.

For example, most of the epithelial cells in the stomach are dedicated to secreting mucus, hydrochloric acid or a proenzyme called pepsinogen into the lumen of the stomach. Scattered among these secretory epithelial cells are G cells, which are endocrine cells that synthesize and secrete the hormone gastrin. Being a hormone, gastrin is secreted into blood, not into the lumen of the stomach. Similarly, other hormones produced by the enteric endocrine system are synthesized and secreted by cells within the epithelium of the small intestine.

Like all endocrine cells, cells in enteric endocrine system do not simply secrete their hormone continuously, which would not be very useful as a control system. Rather, they secrete hormones in response to fairly specific stimuli and stop secreting their hormone when those stimuli are no longer present. What stimulates the endocrinocytes in the enteric endocrine system? As you might deduce, in most cases these endocrine cells respond to changes in the environment within the lumen of the digestive tube. Because these cells are part of the epithelium, their apical border is in contact with the contents of the lumen, which allows them to continually "taste" or sample the luminal environment and respond appropriately.

To illustrate how control is implemented through the enteric endocrine system, consider the important example of preventing stomach acid from burning the epithelium of the small intestine:

- Acid-laden ingesta flows out of the stomach, into the small intestine.
- Acid in the small intestine stimulates secretion of the hormone secretin from endocrine cells in the intestinal epithelium.
- Secretin stimulates the pancreas to dump a bicarbonate-rich fluid into the lumen of the intestine.
- The bicarbonate neutralizes acid, which removes the stimulus for secretion of additional secretion.

In addition to the hormones listed above, cells in the gastrointestinal tract also secrete a large battery of other peptide regulators that appear to act as paracrine agents or neurotransmitters, affecting such processes as motility, blood flow and growth of the digestive tract.

Further discussion of the physiologic roles of enteric hormones is included in subsequent sections describing digestive organs. Additionally, more detailed descriptions of GI hormones, their receptors and mechanisms of action are to be found in the section on Gastrointestinal Hormones in the Endocrine System text.