# Regulation of GI Function

Of the four GI processes, motility and secretion are the primary regulated functions through the system too rapidly, there will not be enough time for everything in the and absorbed. Secretion is regulated so that the appropriate digestive enzymes can an absorbable form. Digestion in turn depends on motility and secretion.

Scientists used to believe that nutrient absorption was not regulated and that "wha get." Now, however, evidence indicates that some nutrient absorption can be altere term environmental changes.

# The Enteric Nervous System Can Act Independently

The enteric nervous system (ENS) was first recognized more than a century ago, w
that isolated sections of intestine removed from the body created a reflex wave of p
when pressure in the lumen increased. What they observed was the ability of the E
reflex independent of control by the central nervous system (CNS).

In this respect, the ENS is much like the nerve networks of jellyfish and sea anemo
[here]. You might have seen sea anemones being fed at an aquarium. As a piece of
close to the tentacles, they begin to wave, picking up chemical "odors" through the
contacts the tentacles, it is directed toward the mouth, passed from one tentacle to
disappears into the digestive cavity.

This purposeful reflex is accomplished without a brain, eyes, or a nose. The anemo
consists of a nerve network with sensory neurons, interneurons, and efferent neuro
muscles and secretory cells of the anemone's body. The neurons of the Cnidarian n
way that allows them to integrate information and act on it. In the same way that a
food, the human ENS receives stimuli and acts on them. The enteric nervous syste
secretion, and growth of the digestive tract.

Anatomically and functionally, the ENS shares many features with the CNS:

1. *Intrinsic neurons*. The intrinsic neurons of the two nerve plexuses of the dig
   neurons that lie completely within the wall of the gut, just as interneurons
   contained within the CNS. Autonomic neurons that bring signals from the
   system are called extrinsic neurons.

2. *Neurotransmitters and neuromodulators*. ENS neurons release more than 30 neuromodulators, most of which are identical to molecules found in the br neurotransmitters are sometimes called *nonadrenergic, noncholinergic* to dis traditional autonomic neurotransmitters norepinephrine and acetylcholine known GI neurotransmitters and neuromodulators are serotonin, vasoactiv and nitric oxide.
3. *Glial support cells*. The glial cells of neurons within the ENS are more simila brain than to Schwann cells of the peripheral nervous system.
4. *Diffusion barrier*. The capillaries that surround ganglia in the ENS are not v create a diffusion barrier that is similar to the blood-brain barrier of cerebr
5. *Integrating center*. As noted earlier, reflexes that originate in the GI tract ca acted on without neural signals leaving the ENS. For this reason, the neuro is its own integrating center, much like the brain and spinal cord.

It was once thought that if we could explain how the ENS integrates simple behavi system as a model for CNS function. But studying ENS function is difficult because no discrete command center. Instead, in an interesting twist, GI physiologists are a gleaned from studies of the brain and spinal cord to investigate ENS function. The between the enteric and central nervous systems, the endocrine system, and the im to provide scientists with questions to investigate for many years to come.

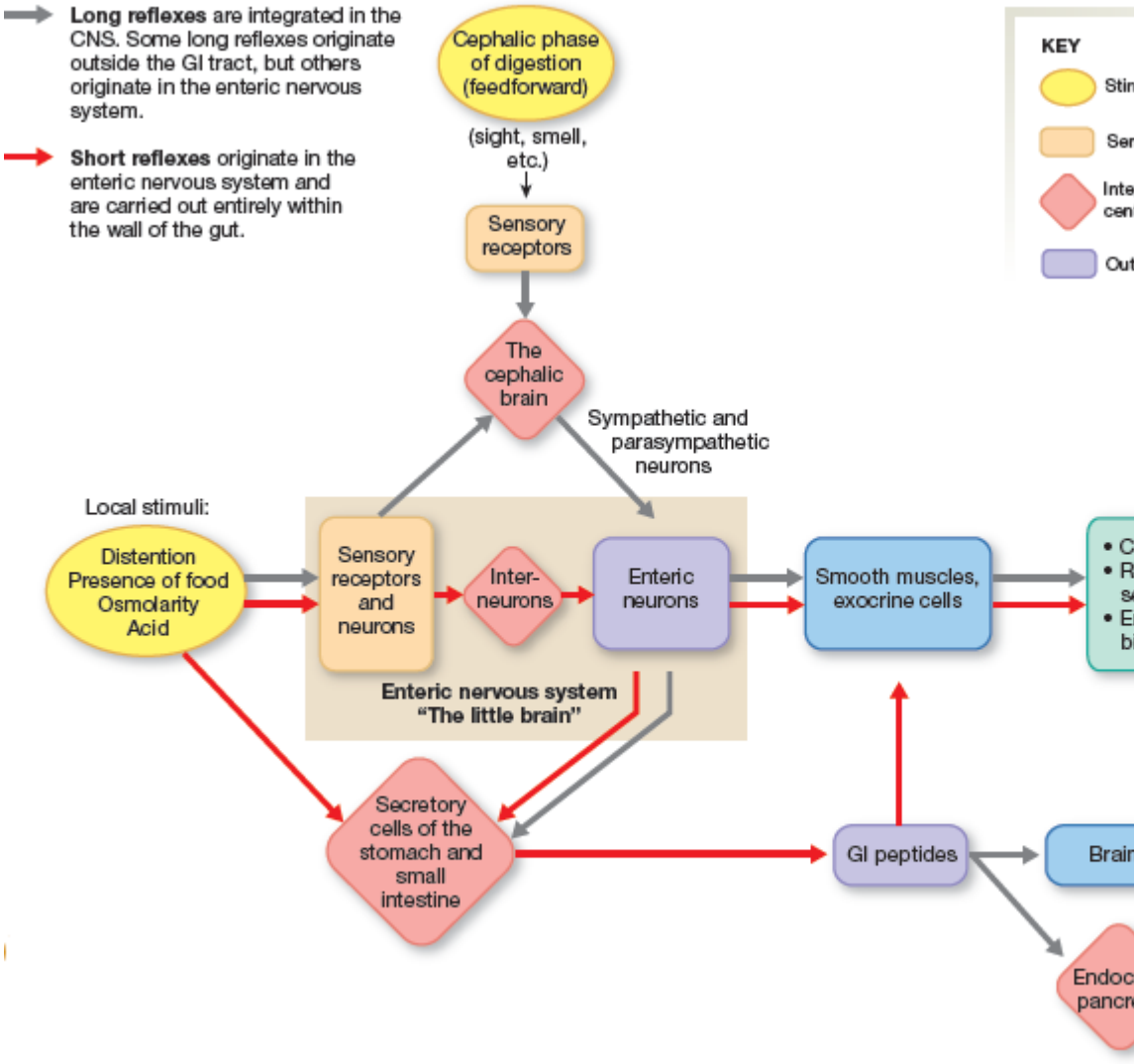
## Short Reflexes Integrate in the Enteric Nervous

The enteric nerve plexuses in the gut wall act as a "little brain," allowing local refle
integrated, and end completely in the GI tract (Fig. 21.5, red arrows). Reflexes th
enteric nervous system and are integrated there without outside input are called **sh**
submucosal plexus contains sensory neurons that receive signals from the lumen o
network integrates this sensory information, then initiates responses. The submuco
secretion by GI epithelial cells. Myenteric plexus neurons in the muscularis externa

FIG. 21.5 **Integration of digestive reflexes**

## Figure Questions

1. Which effectors and responses are controlled by the myenteric plexus and by the submucosal plexus?
2. What type of sensory receptor responds to stretch? to osmolarity? to produ



## Long Reflexes Integrate in the CNS

Although the ENS can work in isolation, it also sends sensory information to the C
from the CNS through autonomic neurons. A classic neural reflex begins with a sti
along a sensory neuron to the CNS, where the stimulus is integrated and acted on.
system, some classic reflexes originate with sensory receptors in the GI tract, but o
the digestive system (Fig. 21.5, gray arrows). No matter where they originate, dig
integrated in the CNS are called **long reflexes**.

Long reflexes that originate outside the digestive system include feedforward reflex
emotional reflexes. These reflexes are called **cephalic reflexes** because they origina
{*cephalicus*, head}. *Feedforward reflexes* begin with stimuli such as the sight, smell, s
food, and they prepare the digestive system for food that the brain is anticipating.
hungry and smell dinner cooking, your mouth waters and your stomach growls.

Emotional reflexes and their influence on the GI tract illustrate another link betwee
digestive system. GI responses to emotions range from traveler's constipation to "b
stomach" to psychologically induced vomiting and diarrhea.

In long reflexes, the smooth muscle and glands of the GI tract are under autonomic
we say that the parasympathetic division is excitatory and enhances GI functions, l
of "rest and digest." Most parasympathetic neurons to the GI tract are found in the
Sympathetic neurons usually inhibit GI function.

## Concept Check

**10.** Excitation of GI function by the parasympathetic division and inhibition by division is an example of what kind of control?

# GI Peptides Include Hormones, Neurop and Cytokines

Peptides secreted by cells of the digestive tract may act as hormones or paracrine s GI peptides were first identified and named in other body systems. Because their n do with their function in the gastrointestinal system, learning the terminology can

In the digestive system, GI peptides excite or inhibit motility and secretion. Some p secreted into the lumen, where they combine with receptors on the apical membra epithelium to elicit a response. Others are secreted into the extracellular fluid whe distances to act on neighboring cells.

GI peptides also act outside the GI tract, and some of their most interesting actions example, in experimental studies the GI hormone **cholecystokinin (CCK)** enhan that hunger has been satisfied. However, CCK is also manufactured by neurons an neurotransmitter in the brain, so it is difficult to determine how much of the norma due to CCK from the gut. Another GI peptide, *ghrelin*, is secreted by the stomach a increase food intake.

Researchers have now sequenced more than 30 peptides from the GI mucosa, but widely accepted as hormones. A few peptides have well-defined paracrine effects, long list of candidate hormones. In addition, we know of nonpeptide regulatory m histamine, that function as paracrine signals. Because of the uncertainty associated restrict our focus in this chapter to the major regulatory molecules.

# GI Hormones

GI hormones, like all hormones, are secreted into the blood and transported throu
act on the GI tract, on accessory organs such as the pancreas, and on distant target

The hormones of the gastrointestinal tract occupy an interesting place in the histor
1902, two English physiologists, W. M. Bayliss and E. H. Starling, discovered that a
the small intestine from the stomach caused the release of pancreatic juices even w
pancreas were cut. Because the only communication remaining between intestine a
blood supply that ran between them, Bayliss and Starling postulated the existence
(*humoral*) factor released by the intestine.

When duodenal extracts applied directly to the pancreas stimulated secretion, they
dealing with a chemical produced by the duodenum. They named the substance *se*
proposed that the general name *hormone*, from the Greek word meaning "I excite,"
humoral agents that act at a site distant from their release.

In 1905, J. S. Edkins postulated the existence of a gastric hormone that stimulated g
took more than 30 years for researchers to isolate a relatively pure extract of the ga
was 1964 before the hormone, named *gastrin*, was finally purified.

Why was research on the digestive hormones so slow to develop? A major reason i
secreted by isolated endocrine cells scattered among other cells of the mucosal epi
the only way to obtain these hormones was to make a crude extract of the entire ep
that also liberated digestive enzymes and paracrine molecules made in adjacent cel
was very difficult to tell whether the physiological effect elicited by the extract cam
from more than one hormone, or from a paracrine signal such as histamine.

## GI Hormone Families

The gastrointestinal hormones are usually divided into three families. All the mem
similar amino acid sequences, and in some cases there is overlap in their ability to
sources, targets, and effects of the major GI hormones are summarized in Table 21

Table 21.1 **The GI Hormones**

| | Stimulus for Release | Primary Target(s) | Primary Effect(s) |
|---|---|---|---|
| **Stomach** | | | |
| **Gastrin (G Cells)** | Peptides and amino acids; neural reflexes | ECL cells and parietal cells | Stimulates gastric acid secretion and mucosal growth |
| **Intestine** | | | |
| **Cholecystokinin (CCK)** | Fatty acids and some amino acids | Gallbladder, pancreas, stomach | • Stimulates gallbladder contraction and pancreatic enzyme secretion<br>• Inhibits gastric emptying and acid secretion |
| **Secretin** | Acid in small intestine | Pancreas, stomach | • Stimulates $HCO_3^-$ secretion<br>• Inhibits gastric emptying and acid secretion |

| | Stimulus for Release | Primary Target(s) | Primary Effect(s) |
|---|---|---|---|
| **Motilin** | Fasting: periodic release every 1.5–2 hours | Gastric and intestinal smooth muscle | Stimulates migrating motor complex |
| **Gastric Inhibitory Peptide (GIP)** | Glucose, fatty acids, and amino acids in small intestine | Beta cells of pancreas | • Stimulates insulin release (feedforward mechanism)<br>• Inhibits gastric emptying and acid secretion |
| **Glucagon-Like Peptide-1 (GLP-1)** | Mixed meal that includes carbohydrates or fats in the lumen | Endocrine pancreas | • Stimulates insulin release<br>• Inhibits glucagon release and gastric function |

The *gastrin family* includes the hormones *gastrin* and *cholecystokinin* (CCK), plus se
Their structural similarity means that gastrin and CCK can bind to and activate the

The *secretin family* includes *secretin*; **vasoactive intestinal peptide (VIP)**, a nonadre
neurotransmitter; and **GIP**, a hormone known originally as *gastric inhibitory pepti*

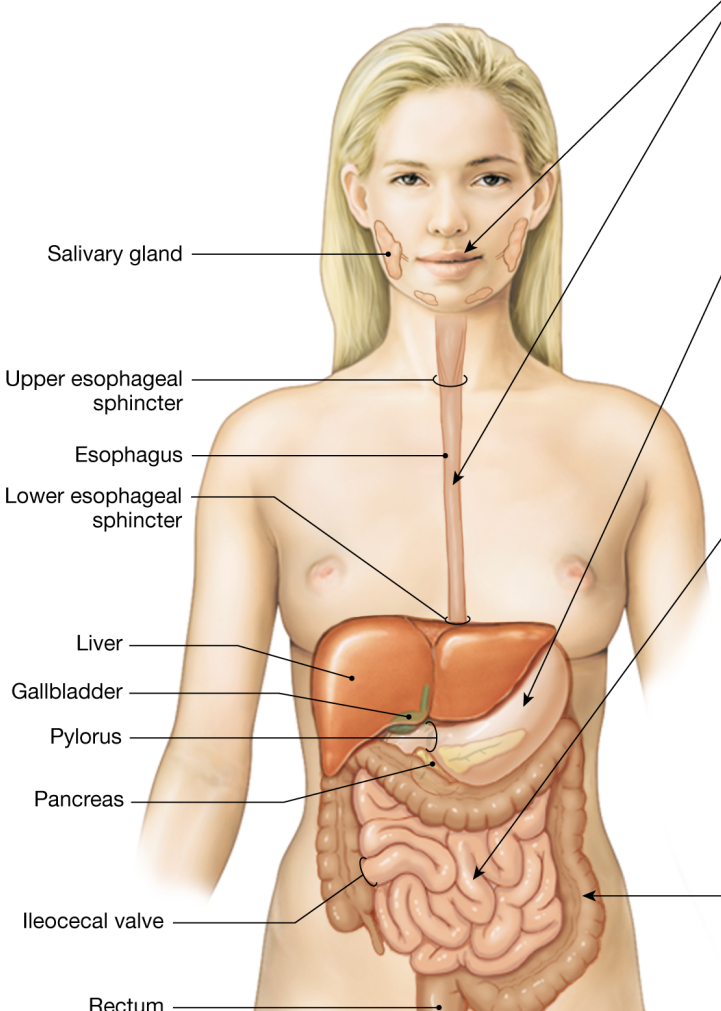
gastric acid secretion in early experiments. Subsequent studies, however, indicated in lower physiological doses does not block acid secretion. Researchers proposed a same initials—**glucose-dependent insulinotropic peptide**—that more accurately de action: it stimulates insulin release in response to glucose in the intestinal lumen. H part *gastric inhibitory peptide* has remained the preferred name.

Another member of the secretin family is the hormone **glucagon-like peptide-1** (G act together as feedforward signals for insulin release, as you will learn when you s pancreas [Chapter 22].

The third family of peptides contains those that do not fit into the other two familie member of this group is the hormone **motilin**. Increases in motilin secretion are as migrating motor complex.

In the remainder of this chapter, we integrate motility, secretion, digestion, and abs food passing through the GI tract. Figure 21.6 is a summary of the main events th section of the GI tract. Food processing traditionally is divided into three phases: a gastric phase, and an intestinal phase.

FIG. 21.6 **Overview of digestive function**




| Oral Cavity and Esophagus | |
|---|---|
| **Secretion** | Saliva (salivary glands) |
| **Digestion** | Carbohydrates |
| **Absorption** | None |
| **Motility** | Chewing. Swallowing. |

| Stomach | |
|---|---|
| **Secretion** | HCl (parietal cells). Pep (chief cells). Mucus and cells). Gastrin (G cells). |
| **Digestion** | Proteins. Fats (minimal |
| **Absorption** | Lipid-soluble substanc |
| **Motility** | Peristaltic mixing and p |

| Small Intestine | |
|---|---|
| **Secretion** | Enzymes (enterocytes) Hormones: CCK, secre cells). Enzymes and bic Bile (liver, stored in gall |
| **Digestion** | Polypeptides. Carbohy |
| **Absorption** | Amino acids and small Fatty acids, monoglyce bases. Water. Ions, mir |
| **Motility** | Mixing and propulsion Some peristalsis. |

| Large Intestine | |
|---|---|
| **Secretion** | Mucus (goblet cells) |
| **Digestion** | None (except by bacte |
| **Absorption** | Ions, minerals, vitamins molecules made by gu |
| **Motility** | Segmental mixing. Mas |