CASE 29

A 34-year-old man presents to his primary care physician with the complaint of increased difficulty swallowing both solid and liquid foods. He notices that he sometimes has more difficulty when he is under stress. He often has chest pain and regurgitation and reports difficulty with belching. After a thorough examination, he is diagnosed with achalasia (disorder of the lower esophageal sphincter).

◆ **What part of the gastrointestinal (GI) tract is composed of striated muscle and smooth muscle?**

◆ **What factors are responsible for the tonic contraction of the lower esophageal sphincter (LES) between swallows?**

◆ **What are the major neurotransmitters responsible for regulating contraction and relaxation of the LES?**
ANSWERS TO CASE 29: GI MOTILITY

Summary: A 34-year-old man is diagnosed with achalasia. He has difficulty swallowing solids and liquids.

- **Striated and smooth muscles in GI tract:** Striated muscle found in pharynx, upper third of the esophagus, and external anal sphincter. Smooth muscle found in all areas in between, including the LES.

- **Tone of the LES:** Inherent to the LES smooth muscle and augmented by cholinergic nerves.

- **Neurotransmitters in LES:** Acetylcholine (ACh), vasoactive intestinal peptide (VIP), nitric oxide (NO), adenosine triphosphate (ATP).

**CLINICAL CORRELATION**

Achalasia is a motor disorder of the esophageal smooth muscle in which the LES does not relax normally with swallowing. Patients present with difficulties swallowing both solid and liquid food. They also may experience chest pain and difficulty with belching. The pathophysiology is thought to be a loss of enteric inhibitory nerves. The diagnosis may be confirmed with a barium swallow that shows esophageal dilation and a beaklike narrowing in the terminal portion of the esophagus. Treatment options include medications (nitroglycerin, isosorbide dinitrate, calcium channel blockers), esophageal dilation, and surgery. Other clinical disorders characterized by disordered neuromuscular activity of the GI tract include Hirschsprung disease, which is caused by a developmental lack of inhibitory enteric nerves in the colon; gastroparesis usually resulting from an autonomic neuropathy, often diabetic; ileus caused by trauma or infection; intestinal pseudoobstruction caused by an enteric neuropathy and/or muscle atrophy; and irritable bowel syndrome resulting from altered sensory nerve function and/or altered motility, usually of the colon.

**APPROACH TO GI MOTILITY**

**Objectives**

1. Describe phasic and tonic contractions.
2. Understand the mechanisms of chewing, swallowing, and esophageal motility.
3. Know about gastric motility and small and large intestine motility.
4. Describe regulation of motility.
Definitions

**Segmenting contractions:** Contractions of the small and large intestine (where they are called haustral contractions) that serve to mix and locally circulate intestinal contents.

**Peristaltic contractions:** Contractions occurring in all areas of the gastrointestinal tract that serve to propel intestinal contents, usually forward.

**MMC:** The pattern of contractions in the stomach and small intestine that occurs during the interdigestive state.

DISCUSSION

Digestion and absorption of ingested food and drink require an orderly movement of material through the GI tract. This is accomplished by contractions of the musculature that in part constitutes the walls of the tract. In the esophagus, small intestine, and large intestine, this muscle is arranged in two layers: an outer longitudinal muscle layer and an inner circular layer. In the stomach, an incomplete oblique layer also is present. The muscle in the pharynx, the upper esophageal sphincter (UES), the upper third or so of the esophagus, and the external anal sphincter is visceral striated muscle. The muscle in all other areas is smooth muscle.

The major regulation of contractions of the striated muscle is accomplished by extrinsic special efferent nerves that innervate the muscle cells directly. The major regulation of contractions of the smooth muscle is accomplished by enteric nerves located mainly in the myenteric, or Auerbach, plexus. Activity of these nerves in turn is influenced by extrinsic sympathetic and parasympathetic nerves. Muscles in certain regions also are influenced by endocrine and paracrine mediators.

There are regions of the GI tract, usually between two organs, where the musculature is in a state of fairly stable contraction to partially or totally occlude the lumen. Such tonic contractile activity is found in the UES, the LES, the ileocecal sphincter, and the internal anal sphincter. The orad, or proximal, portion of the stomach is in a state of tonic contraction, but rather than occluding the lumen, it contracts tonically to shift ingested material into the antrum. The pylorus, rather than acting as a true sphincter to maintain closure of the lumen, contracts tonically and phasically to alter resistance to gastric emptying. The external anal sphincter exhibits little to no tone unless the internal anal sphincter relaxes at a time when the act of defecation is not desired. Although the musculature of the esophagus, antrum, small intestine, and colon exhibits tone, it is characterized mostly by periodic contractions lasting a few seconds, followed by relaxations, often in a cyclical pattern. Thus, these muscles are said to exhibit phasic contractile activity.

The process of digestion begins with the chewing and swallowing of ingested food. Chewing effectively reduces the size of the food and mixes
it with saliva that contains salivary amylase and lingual lipase to begin digestion and mucus to aid in swallowing. Swallowing begins with the voluntary act of manipulating the portion to be swallowed to the oropharynx, using mainly the tongue. The bolus then stimulates receptors in the pharynx to initiate the swallowing reflex. This reflex involves coordinated contractions and relaxations of the striated and smooth muscle that constitute the pharynx and esophagus. The reflex begins with contraction of the pharyngeal muscles to propel the bolus toward the esophagus. Between swallows, the entrance to the esophagus, the UES, is closed to form a barrier between the pharynx, where the pressure is atmospheric, and the intrathoracic esophagus, where the pressure is subatmospheric. With swallowing, the UES relaxes as the bolus approaches to allow easy entry. The UES then regains tone and the muscle of the body of the esophagus contracts in a peristaltic sequence to propel the bolus toward the stomach. The junction between the esophagus and the stomach, the LES, also remains closed between swallows to prevent reflux of gastric contents. During swallowing and before the arrival of the bolus, the LES relaxes to allow passage into the stomach. The LES then regains tone.

Movement of the swallowed bolus into the stomach is facilitated by a decrease in tone of the proximal stomach that is called receptive relaxation with each swallow. Thus, the orad stomach accommodates to maintain a relatively constant pressure as the food is swallowed much faster than it empties into the small intestine. Beginning almost immediately and during the time of gastric emptying of the meal, material moves from the orad stomach into the distal stomach in an orderly fashion. There it is acted on by peristaltic contractions that begin about midstomach and progress toward the pylorus. These contractions usually are not lumen occluding, and they mix contents with gastric secretions as well as propel the contents forward. Indeed, during a single contraction, more material is “retropelled” back into the stomach, causing mixing and mechanical breakdown of the food, than is emptied into the small intestine. Also, this contractile activity, along with tonic and phasic contractions of the pylorus, somehow sieves the material so that only liquids and particles less than about 2 mm³ empty into the small bowel.

The material that enters the small intestine is acted on by phasic contractions of varying strength. Most of the contractions are segmenting and serve to mix contents with secretions of the pancreas and liver and bring the contents into contact with the mucosa, where they can be digested and absorbed further. Some contractions, however, are organized into short peristaltic sequences that serve to propel the contents in a net aboral direction. Thus, meal components, electrolytes, and water that are not absorbed in the small intestine are delivered to the colon.

To access the colon, material must pass through the ileocecal sphincter, a band of muscle that is tonically contracted, but relaxes with ileal distention. Material in the colon is acted on by phasic contractions of long duration
that are called **hastrual contractions**. These contractions serve to bring contents into contact with the mucosa so that electrolytes and water can be absorbed. Net aboral propulsion of the remaining contents is accomplished by infrequent peristaltic contractions called mass movements. Once in the rectum, the contents elicit the rectosphincteric reflex, which is characterized by relaxation of the internal anal sphincter and the sensation of the urge to defecate. Defecation can be prevented, and the reflex accommodated, by contraction of the external anal sphincter. Alternatively, defecation can ensue through **voluntary relaxation of the external anal sphincter** and increases in **intraabdominal pressure**.

During interdigestive periods when no nutrients are in the stomach or small intestine, contractions of the stomach and small intestine occur, but their pattern of occurrence changes to one that has been referred to as the **migrating motor complex** (MMC). This complex consists of three phases, and the transition from the digestive to the MMC pattern can begin with any of the phases. **Phase 1** is a period of time lasting 20 to 60 minutes during which no gastric contractions occur. This is followed by a 10- to 30-minute period of intermittent peristaltic contractions of variable amplitude (**phase 2**). This is followed by a period of 5 to 10 minutes of strong peristaltic contractions (**phase 3**) that begin in the orad stomach and sweep the length of the stomach, pushing the contents through a relaxed pylorus into the small intestine. As each peristaltic contraction approaches the duodenum, the duodenum relaxes to accommodate the material being emptied from the stomach. The timing of the various phases of the complex is almost identical in the duodenum and the stomach. However, each phase occurs at progressively more distal sites of the small intestine, with a lag in time giving the impression of a slow migration of the phases toward the colon. Phases 2 and 3 move undigested material toward the colon, reaching the distal ileum about the time the cycle is repeating in the stomach. The MMC pattern recurs until ingestion of the next nutrients.

The **act of swallowing** is under **neural regulation**. Sensory nerves from the **pharynx and esophagus** project to regions of the medulla referred to collectively as the **swallowing center**. This “center” then **initiates a sequence of motor events** consisting of (1) **sequential activation of vagal nerves** innervating striated muscle of the **pharynx**, causing a **peristaltic contraction**, (2) **inhibition of vagal nerves** innervating the **UES**, causing relaxation, (3) **activation of vagal nerves** innervating visceral striated muscle of the **esophagus**, causing a **peristaltic contraction**, and (4) **activation of vagal nerves innervating the enteric nerves** in smooth muscle regions of the **esophagus and stomach**. Activation of the enteric nerves leads to a continuation of the peristaltic contraction in the body of the esophagus and to relaxation of the **LES** and orad region of the stomach. The **excitatory neurotransmitter** released by the vagal nerves innervating the **striated muscle and enteric nerves** is **acetylcholine**. The excitatory and inhibitory neurotransmitters released by the enteric nerves innervating the smooth muscle are less well characterized.
There is evidence for ACh and the tachykinins serving as excitatory transmitters and for nitric oxide, VIP, and ATP, serving as inhibitory transmitters.

Contractions of the distal stomach, the small intestine, and the large intestine are regulated by inhibitory and excitatory enteric nerves that modulate intrinsic electrical activities of the smooth muscle cells. The enteric nerves and/or muscles are influenced by excitatory and inhibitory extrinsic nerves and hormones. Also in this region, smooth muscle cells and associated interstitial cells of Cajal generate omnipresent cyclical membrane depolarizations and repolarizations that are called slow waves. In the antrum, their frequency is about 3 cycles per minute (cpm). In the small intestine, the frequency is about 12 cpm in the duodenum and decreases to about 8 cpm in the ileum. Frequencies in the colon are more complex but also usually are about 3 cpm. Although frequencies at two adjacent sites in any area will be the same, there will be a phase lag so that there appears to be a wave of depolarization spreading aborally. Slow waves themselves do not initiate significant contractions. However, the electrical events leading to contraction (spike or action potentials) occur only during the depolarization phase of a slow wave. Thus, slow waves ensure that contractions are phasic, set the maximum frequency of contraction, and help establish the peristaltic nature of contraction, especially in the stomach.

Regulation by enteric nerves is critical for normal motility of smooth muscle regions of the GI tract. This is best exemplified, as in this case, by the consequences of their being absent or damaged. Although the neurotransmitters involved have not been identified precisely, the ones mentioned above play major roles. In addition, serotonin (5-hydroxytryptamine [5-HT]) appears to be involved in many of the enteric nerve reflexes that control motility. A few of the GI hormones appear to play physiologic roles in regulating motility. CCK relaxes the orad stomach, relaxes the sphincter of Oddi, and contracts the gallbladder. Gastrin and other digestive hormones may play a role in the gastrocolic reflex, which is the increase in colonic motility often seen upon the initial ingestion of a meal. Finally, motilin may be the hormone that initiates the migrating motor complex seen in the fasting state.

**COMPREHENSION QUESTIONS**

[29.1] During the ingestion and digestion of a meal, peristaltic contractions are the primary type of contractions occurring in which of the following regions of the GI tract?

A. Esophagus  
B. Proximal stomach  
C. Jejunum  
D. Ileum  
E. Colon
Which of the following regions of the GI tract are the most depend-ent on extrinsic nerves for regulation?
A. Lower esophagus and distal stomach
B. Lower esophagus and proximal stomach
C. Small intestine and large intestine
D. Upper esophagus and distal stomach
E. Upper esophagus and external anal sphincter

Esophageal manometry is performed on a patient who is experiencing difficulty swallowing. Between swallows, pressures above atmospheric pressure are recorded in the UES and LES and pressures below atmospheric pressure are recorded in the thoracic esophageal body. Upon swallowing, the UES relaxes and a normal peristaltic contraction occurs in the upper esophagus. The peristaltic contraction occurring in the lower esophagus is slightly abnormal, but there is no relaxation of the LES. The defect in this patient most likely lies in which of the following structures?
A. Extrinsic nerves innervating the esophagus
B. Intrinsic nerves of the esophagus
C. Smooth muscle of the esophagus
D. Striated muscle of the esophagus
E. Swallowing center

Answers

A. Peristaltic contractions are the primary, if not the only, contrac-tions of the esophagus that result in the rapid transfer of material from the mouth to the stomach. The proximal stomach undergoes mainly receptive relaxation and tonic contraction during the ingestion and digestion of a meal. In both the small and the large intestine, segmenting (phasic) contractions are most numerous.

E. The upper esophagus and the external anal sphincters are composed of striated muscle that has no intrinsic activity and depends on extrinsic innervation to regulate its contractions. The lower esophagus, distal stomach, small intestine, and colon are composed of smooth muscle and are innervated by enteric nerves that impart a high degree of independence from extrinsic nerves. The proximal stomach is intermediate in its dependence, with receptive relaxation being impaired by vagotomy.

B. Normal resting pressures in the UES and LES and normal peristalsis in the upper esophagus with swallowing indicate that the muscle, extrinsic nerves, and swallowing center are intact. The slightly abnormal peristaltic contractions of the lower esophagus and especially the lack of relaxation of the LES upon swallowing indicate a defect in the intrinsic nerves.
PHYSIOLOGY PEARLS

❖ Contractions of the pharynx, UES, and striated portion of the esophagus are coordinated by a central nervous system (CNS) center and are mediated by direct vagal innervation of the muscle. Events in the smooth muscle portion of the esophagus, LES, and orad stomach are coordinated by both central and enteric nerves acting on the muscle.

❖ Tonic contraction of the orad stomach is regulated by enteric and extrinsic nerve reflexes and by CCK. Antral contractions are regulated by slow waves and enteric neural reflexes. Tonic and phasic contractions of the pylorus are regulated by enteric neural reflexes.

❖ Segmenting and peristaltic contractions of the small intestine and segmenting (hastral) contractions and mass movements of the colon are regulated by slow waves, enteric and extrinsic nerve reflexes, and perhaps GI hormones.

❖ In smooth muscle areas of the GI tract, enteric nerves are vital for normal motility. Their lack or damage can result in achalasia, pseudobstruction, Hirschsprung disease, and other motility disorders.

REFERENCES

