28

The Cephalic, Oral, and Esophageal Phases of the Integrated Response to a Meal

LEARNING OBJECTIVES

Upon completion of this chapter, you should be able to answer the following questions:

1. What constitutes the functional anatomy of salivary glands, including their secretory elements?
2. What are the cephalic and oral phases (what, why, how it happens) of the response to a meal?
3. What are the general principles of secretion along the gastrointestinal (GI) tract (where do secretions come from, what are the components)?
4. How do the components of secretion vary with the gland or region of the GI tract?
5. What is the correlation between the composition and functions of salivary secretion?
6. How are primary and secondary secretions within salivary glands generated and regulated?
7. What is the sequence of events in swallowing?
8. What are the stimulus and neural pathways generating primary and secondary esophageal peristalsis?
9. What changes in gastric motility take place during swallowing, and what is the significance?
10. What are the major functions of the esophagus and associated structures in terms of protection and propulsion?

This chapter will describe the processes that occur in the gastrointestinal (GI) tract in the early stages of the integrated response to a meal. There are changes in GI tract physiology (1) before food is ingested (the cephalic phase), (2) when ingested food is in the mouth (the oral phase), and (3) when food is transferred from the mouth to the esophagus (the esophageal phase). The responses of the GI tract to the presence of food are mainly associated with preparing the GI tract for digestion and absorption.

Cephalic and Oral Phases

The main feature of the **cephalic phase** is activation of the GI tract in readiness for the meal. The stimuli involved are cognitive and include anticipation or thinking about the consumption of food, olfactory input, visual input (seeing or smelling appetizing food when hungry), and auditory input. The latter may be an unexpected link but was clearly demonstrated in the classic conditioning experiments of Pavlov, in which he paired an auditory stimulus to the presentation of food to dogs; eventually the auditory stimulus alone could stimulate secretion. A real-life analogy is presumably being told that dinner is ready. All these stimuli result in an increase in excitatory parasympathetic neural outflow to the gut. Sensory input (e.g., smell) stimulates sensory nerves that activate parasympathetic outflow from the brainstem. Higher brain sites (e.g., limbic system, hypothalamus, cortex) are also involved in the cognitive components of this response. The response can be both positive and negative; thus, anticipation of palatable food and a person's psychological status, such as anxiety, can alter the cognitive response to a meal. However, the final common pathway is activation of the dorsal motor nucleus in the brainstem, the region where the cell bodies of the vagal preganglionic neurons arise. Activation of the nucleus leads to increased activity in efferent fibers passing to the GI tract in the vagus nerve. In turn the efferent fibers activate the postganglionic motor neurons (referred to as *motor* because their activation results in change of function of an effector cell). Increased parasympathetic outflow enhances salivary secretion, gastric acid secretion, pancreatic enzyme secretion, gallbladder contraction, and relaxation of the sphincter of Oddi (the sphincter between the common bile duct and duodenum). All these responses enhance the ability of the GI tract to receive and digest the incoming food. The salivary response is mediated via the ninth cranial nerve; the remaining responses are mediated via the vagus nerve.

Many of the features of the **oral phase** are indistinguishable from the cephalic phase. The only difference is that food is in contact with the surface of the GI tract. Thus, there are additional stimuli generated from the mouth, both mechanical and chemical **(taste).** However, many of the responses initiated by the presence of food in the oral cavity are identical to those initiated in the cephalic phase, because

the efferent pathway is the same. The responses specifically initiated in the mouth, which consist mainly of the stimulation of salivary secretion, will be discussed next.

The mouth is important for the mechanical disruption of food and for initiation of digestion. Chewing subdivides and mixes the food with the enzymes salivary amylase and lingual lipase and with the glycoprotein mucin, which lubricates food for chewing and swallowing. Minimal absorption occurs in the mouth, although alcohol and some drugs are absorbed from the oral cavity, and this can be clinically important. However, as with the cephalic phase, it is important to realize that stimulation of the oral cavity initiates responses in the more distal GI tract, including increased gastric acid secretion, increased pancreatic enzyme secretion, gallbladder contraction, and relaxation of the sphincter of Oddi, mediated via the efferent vagal pathway.

Properties of Secretion

General Considerations

Secretions in the GI tract come from glands associated with the tract (salivary glands, pancreas, and liver), from glands formed by the gut wall itself (e.g., submucosal glands in esophagus and duodenum), and from the intestinal mucosa itself. The exact nature of the secretory products can vary tremendously, depending on the function of that region of the GI tract. However, these secretions have several characteristics in common. Secretions from the GI tract and associated glands include **water, electrolytes, protein,** and **humoral agents.** Water is essential for generating an aqueous environment for efficient enzyme action. Secretion of electrolytes is important for generation of osmotic gradients to drive the movement of water. Digestive enzymes in secreted fluid catalyze the breakdown of macronutrients in ingested food. Moreover, many additional proteins secreted along the GI tract have specialized functions, some of which are fairly well understood, such as those of mucin and immunoglobulins, and others that are only just beginning to be understood, such as those of trefoil peptides.

Secretion is initiated by multiple signals associated with the meal, including chemical, osmotic, and mechanical components. Secretion is elicited by the action of specific effector substances called **secretagogues** acting on secretory cells. Secretagogues work in one of the three ways that have already been described in Chapter 27—endocrine, paracrine, and neural.

Constituents of Secretions

Inorganic secretory components are region or gland specific, depending on the particular conditions required in that part of the GI tract. The inorganic components are electrolytes, including H^+ and HCO_3^-. Two examples of different secretions include acid (HCl) in the stomach, which is important to activate pepsin and start protein digestion, and HCO_3^- in the duodenum, which neutralizes gastric acid and provides optimal conditions for the action of digestive enzymes in the small intestine.

• BOX 28.1 Functions of Saliva and Chewing

Disruption of food to produce smaller particles
Formation of a bolus for swallowing
Initiation of starch and lipid digestion
Facilitation of taste
Production of intraluminal stimuli in the stomach
Regulation of food intake and ingestive behavior
Cleansing of the mouth and selective antibacterial action
Neutralization of refluxed gastric contents
Mucosal growth and protection in the rest of the GI tract
Aid in speech

Organic secretory components are also gland or organ specific and depend on the function of that region of the gut. The organic constituents are enzymes (for digestion), mucin (for lubrication and mucosal protection), and other factors such as growth factors, immunoglobulins, bile acids, and absorptive factors.

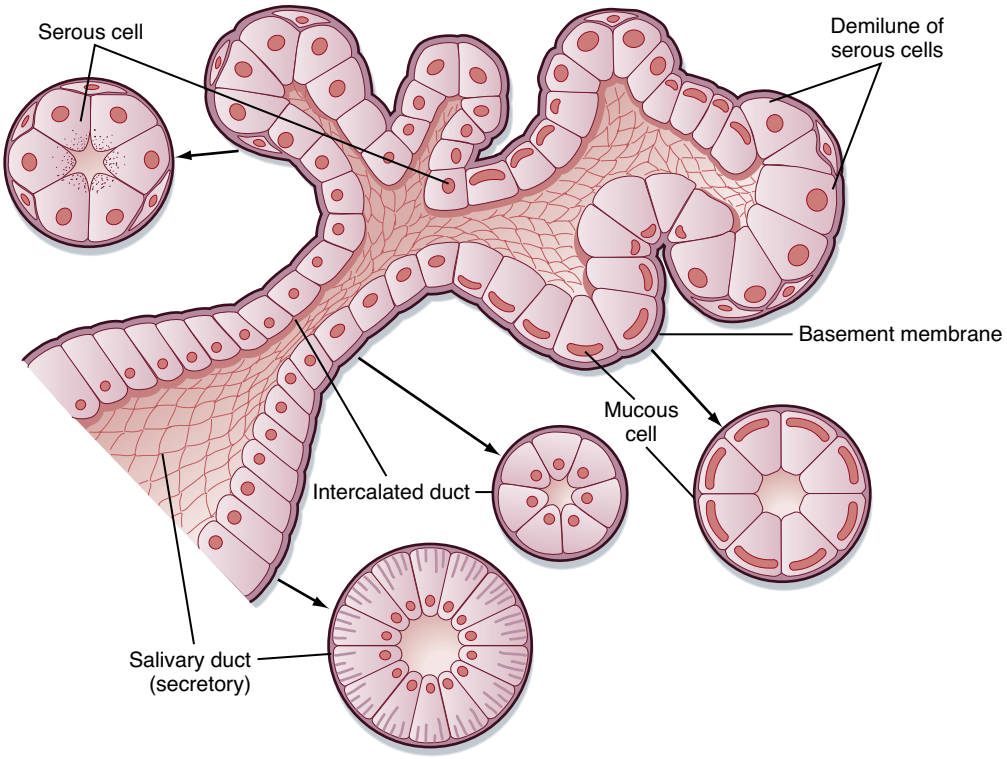
Salivary Secretion

During the cephalic and oral phases of the meal, considerable stimulation of salivary secretion takes place. Saliva has a variety of functions, including those important for the integrative responses to a meal and for other physiological processes (Box 28.1). The main functions of saliva in digestion include lubrication and moistening of food for swallowing, solubilization of material for taste, initiation of carbohydrate digestion, and clearance and neutralization of refluxed gastric secretions in the esophagus. Saliva also has antibacterial actions that are important for overall health of the oral cavity and teeth.

Functional Anatomy of the Salivary Glands

There are three pairs of major salivary glands: parotid, submandibular, and sublingual. In addition, many smaller glands are found on the tongue, lips, and palate. These glands are the typical **tubuloalveolar** structure of glands located in the GI tract (Fig. 28.1). The acinar portion of the gland is classified according to its major secretion: serous ("watery"), mucous, or mixed. The parotid gland produces mainly serous secretion, the sublingual gland secretes mainly mucous, and the submandibular gland produces a mixed secretion.

Cells in the secretory end pieces, or acini, are called *acinar cells* and are characterized by basally located nuclei, abundant rough endoplasmic reticulum, and apically located secretory granules that contain the enzyme amylase and other secreted proteins. There are also mucous cells in the acinus; the granules in these cells are larger and contain the specialized glycoprotein **mucin.** There are three kinds of ducts in the gland that transport secretions from the acinus to the opening in the mouth and also modify the secretion: intercalated ducts drain acinar fluid into larger ducts, the striated ducts, which then empty into even larger excretory ducts. In addition, a single large duct from each gland drains saliva to the mouth. The ductal cells lining the



• **Fig. 28.1** General structure of tubuloalveolar secretory glands (e.g., salivary glands, pancreas) associated with the digestive tract.

striated ducts, in particular, modify the ionic composition and osmolarity of saliva.

Composition of Saliva

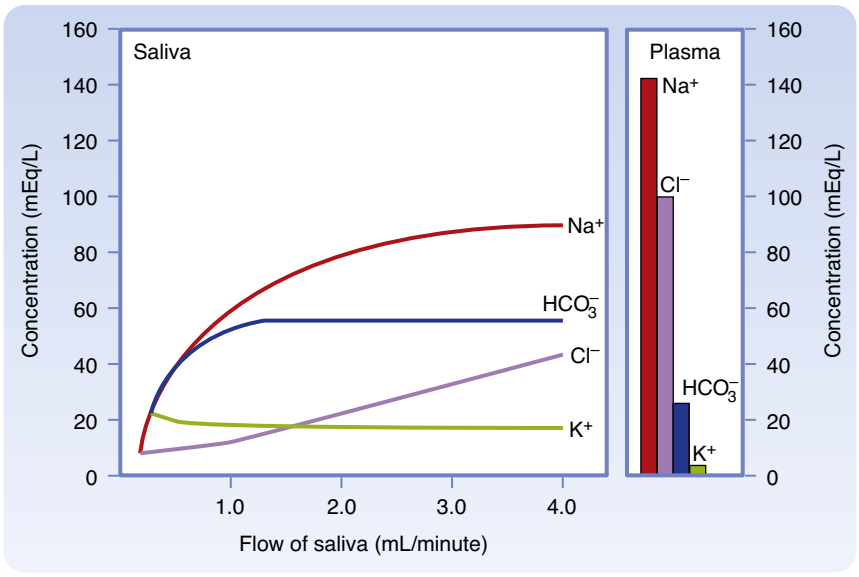
The important properties of saliva are a large flow rate relative to the mass of gland, low osmolarity, high K^+ concentration, and organic constituents, including enzymes (amylase, lipase), mucin, and growth factors. The latter are not important in the integrated response to a meal but are essential for long-term maintenance of the lining of the GI tract.

The inorganic composition is entirely dependent on the stimulus and the rate of salivary flow. In humans, salivary secretion is always hypotonic. The major components are Na^+, K^+, HCO_3^-, Ca^{++}, Mg^{++}, and Cl^-. Fluoride can be secreted in saliva, and fluoride secretion forms the basis of oral fluoride treatment for prevention of dental caries. The concentration of ions varies with the rate of secretion; the flow rate of salivary secretion is stimulated during the postprandial period.

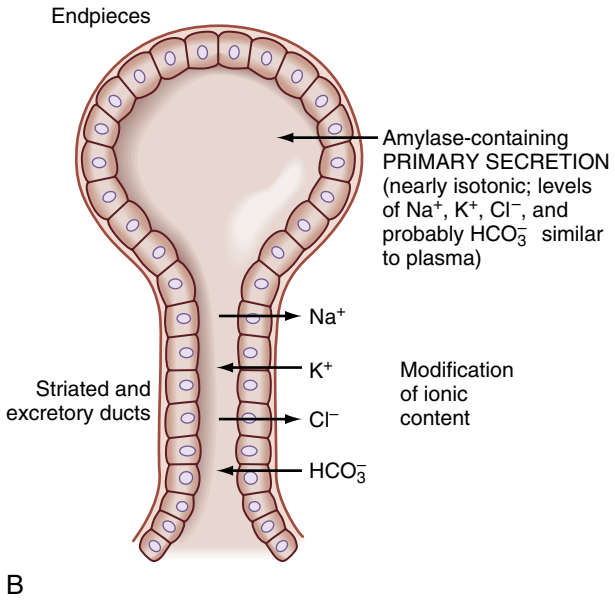
The **primary secretion** is produced by acinar cells in the secretory end pieces (or acini) and is modified by duct cells as saliva passes through the ducts. The primary secretion is isotonic, and the concentration of the major ions is similar to that in plasma. Secretion is driven predominantly by Ca^{++}-dependent signaling, which opens apical Cl^- channels in the acinar cells. Cl^- therefore flows out into the duct lumen and establishes an osmotic and electrical gradient. Because the epithelium of the acinus is relatively leaky, Na^+ and water then follow across the epithelium via the tight junctions (i.e., via **paracellular transport**). Transcellular water movement may also occur, mediated by aquaporin 5 water channels. The amylase content and rate of fluid secretion vary with the type and level of stimulus. As the fluid passes along the ducts, the excretory and striated duct cells modify the ionic composition of the primary secretion to produce the **secondary secretion.** The duct cells reabsorb Na^+ and Cl^- and secrete K^+ and HCO_3^- into the lumen. Na^+ is exchanged for protons, but some of the secreted protons are then reabsorbed in exchange for K^+. HCO_3^- on the other hand is secreted only in exchange for Cl^-, thereby alkalinizing salivary secretion.

At rest, final salivary secretion is hypotonic and slightly alkaline. The alkalinity of saliva is important in restricting microbial growth in the mouth, as well as in neutralizing refluxed gastric acid once the saliva is swallowed. When salivary secretion is stimulated, there is a small decrease in the K^+ concentration (but it always remains above plasma concentrations), the Na^+ concentration increases toward plasma levels, and Cl^- and HCO_3^- concentrations increase, thus the secreted fluid becomes even more alkaline (Fig. 28.2). Note that HCO_3^- secretion can be directly stimulated by the action of secretagogues on duct cells. The duct epithelium is relatively tight and lacks expression of aquaporin, and therefore water cannot follow the ions rapidly enough to maintain isotonicity at moderate or high flow rates during stimulated salivary secretion. Thus, with an increase in secretion rate, there is less time for ionic modification by the duct cells, and the resulting saliva more closely resembles the primary secretion and therefore plasma. However, $[HCO_3^-]$ remains high because secretion from duct cells and possibly acinar cells is stimulated (Fig. 28.2).

The organic constituents of saliva—proteins and glycoproteins—are synthesized, stored, and secreted by the acinar



A



B

• **Fig. 28.2 A,** The composition of salivary secretion as a function of the salivary flow rate compared with the concentration of ions in plasma. Saliva is hypotonic to plasma at all flow rates. [HCO_3^-] in saliva exceeds that in plasma except at very low flow rates. **B,** Schematic representation of the two-stage model of salivary secretion. The primary secretion containing amylase and electrolytes is produced in the acinar cell. The concentration of electrolytes in plasma is similar to that in the primary secretion, but it is modified as it passes through ducts that absorb Na^+ and Cl^- and secrete K^+ and HCO_3^-.

cells. The major products are amylase (an enzyme that initiates starch digestion), lipase (important for lipid digestion), glycoprotein (mucin, which forms mucus when hydrated), and lysozyme (attacks bacterial cell walls to limit colonization of bacteria in the mouth). Although salivary amylase begins the process of digestion of carbohydrates, it is not required in healthy adults because of the excess of pancreatic amylase. Similarly, the importance of lingual lipase is unclear.

Metabolism and Blood Flow of Salivary Glands

The salivary glands produce a prodigious flow of saliva. The maximal rate of saliva production in humans is about 1 mL/min/g of gland; thus, at this rate, the glands are producing their own weight in saliva each minute. Salivary glands have a high rate of metabolism and high blood flow; both are proportional to the rate of saliva formation. Blood flow to maximally secreting salivary glands is approximately 10 times that of an equal mass of actively contracting skeletal muscle. Stimulation of the parasympathetic nerves to salivary glands increases blood flow by dilating the vasculature of the glands. Vasoactive intestinal polypeptide (VIP) and acetylcholine are released from parasympathetic nerve terminals in the salivary glands and are vasodilatory during secretion.

Regulation of Salivary Secretion

Control of salivary secretion is exclusively neural. Salivary secretion is stimulated by both the sympathetic and parasympathetic subdivisions of the autonomic nervous system. Primary physiological control of the salivary glands during the response to a meal is via the parasympathetic nervous system. Acinar cells and duct cells are innervated by parasympathetic nerve endings. Parasympathetic stimulation increases synthesis and secretion of salivary amylase and mucins, enhances the transport activities of the ductular epithelium, greatly increases blood flow to the glands, and stimulates glandular metabolism and growth.

If the parasympathetic supply is interrupted, salivation is severely impaired and the salivary glands atrophy.

Sympathetic fibers to the salivary glands stem from the superior cervical ganglion. Preganglionic parasympathetic fibers travel via branches of the facial and glossopharyngeal nerves (cranial nerves VII and IX, respectively). These fibers form synapses with postganglionic neurons in ganglia in or near the salivary glands.

Ionic Mechanisms of Salivary Secretion

Ion Transport in Acinar Cells

Fig. 28.3 shows a simplified view of the mechanisms of ion secretion by serous acinar cells. The basolateral membrane of the cell contains **Na^+, K^+-ATPase** and an **Na^+-K^+-$2Cl^-$ symporter.** The concentration gradient for Na^+ across the basolateral membrane, which is dependent on Na^+,K^+-ATPase, provides the driving force for entry of Na^+, K^+, and Cl^- into the cell. Cl^- and HCO_3^- leave the acinar cell and enter the lumen via an anion channel located in the apical membrane of the acinar cell. This secretion of anions drives the entry of Na^+ and thus water into the acinar lumen across the relatively leaky tight junctions.

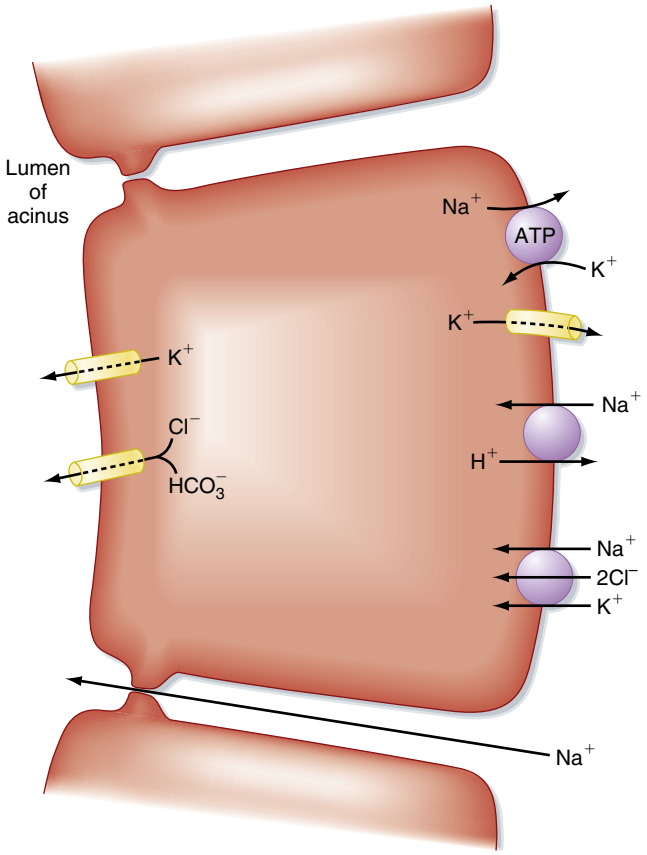
Acinar cell fluid secretion is strongly enhanced in response to elevations in intracellular [Ca^{++}] as a result of activation of the muscarinic receptor for acetylcholine.

Ion Transport in Ductular Cells

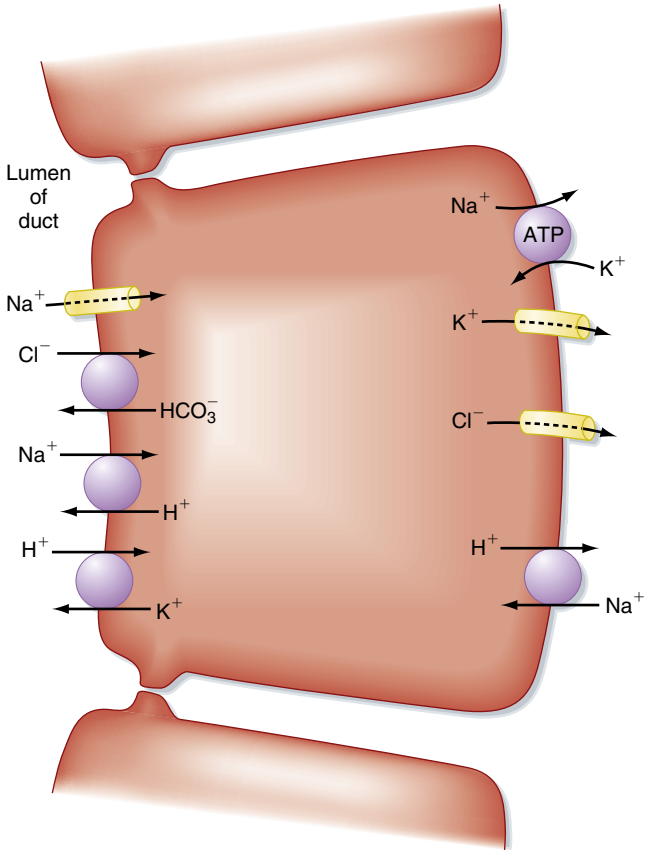
Fig. 28.4 shows a simplified model of ion transport processes in epithelial cells of the excretory and striated ducts. Na^+,K^+-ATPase located in the basolateral membrane maintains the electrochemical gradients for Na^+ and K^+ that drive most of the other ionic transport processes of the cell. In the apical membrane the parallel operation of the Na^+/H^+ antiporter, the Cl^-/HCO_3^- antiporter, and the H^+/K^+ antiporter results in absorption of Na^+ and Cl^- from the lumen and secretion of K^+ and HCO_3^- into the lumen. The relative impermeability of the ductular epithelium to water prevents the ducts from absorbing too much water by osmosis.

Swallowing

Swallowing can be initiated voluntarily, but thereafter it is almost entirely under reflex control. The **swallowing reflex**



• **Fig. 28.3** Ionic transport mechanism involved in the secretion of amylase and electrolytes in salivary acinar cells.



• **Fig. 28.4** Ionic transport mechanism involved in secretion and absorption in epithelial cells of the striated and excretory duct of the salivary gland.

is a rigidly ordered sequence of events that propel food from the mouth to the pharynx and from there to the stomach. This reflex also inhibits respiration and prevents entrance of food into the trachea during swallowing. The afferent limb of the swallowing reflex begins when touch receptors, most notably those near the opening of the pharynx, are stimulated. Sensory impulses from these receptors are transmitted to an area in the medulla and lower pons called the *swallowing center*. Motor impulses travel from the swallowing center to the musculature of the pharynx and upper esophagus via various cranial nerves and to the remainder of the esophagus by vagal motor neurons.

AT THE CELLULAR LEVEL

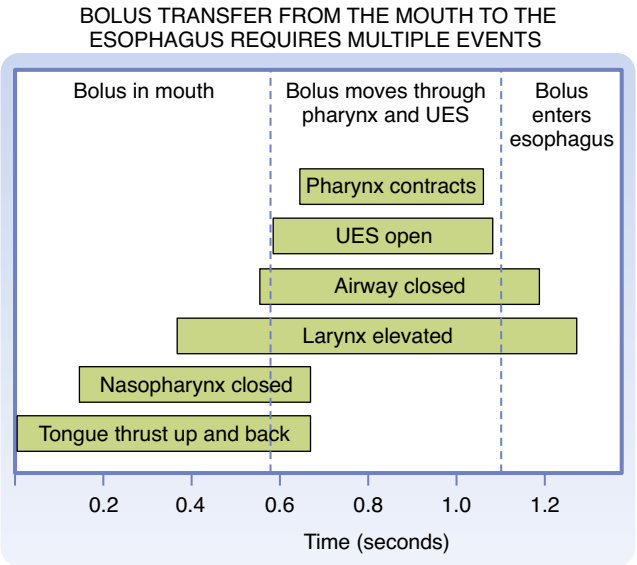
The acinar cells and duct cells of the salivary glands respond to both cholinergic and adrenergic agonists. Nerves stimulate the release of acetylcholine, norepinephrine, substance P, and vasoactive intestinal polypeptide (VIP) by salivary glands, and these hormones increase the secretion of amylase and the flow of saliva. These neurotransmitters act mainly by elevating the intracellular concentration of cyclic adenosine monophosphate (cAMP) and by increasing the concentration of Ca^{++} in the cytosol. Acetylcholine and substance P, acting on muscarinic and tachykinin receptors, respectively, increase the cytosolic concentration of Ca^{++} in serous acinar cells. In contrast, norepinephrine, acting on β receptors, and VIP, binding to its receptor, elevate the cAMP concentration in acinar cells. Agonists that elevate the cAMP concentration in serous acinar cells elicit a secretion that is rich in amylase; agonists that mobilize Ca^{++} elicit a secretion that is more voluminous but has a lower concentration of amylase. Ca^{++}-mobilizing agonists may also elevate the concentration of cyclic guanosine monophosphate (cGMP), which may mediate the trophic effects evoked by these agonists.

IN THE CLINIC

People with **dysphagia** have difficulty in swallowing, often with accompanying pain (odynophagia). Swallowing is a complex process, involving coordination of voluntary and involuntary reflex control of many different muscle groups in the oral cavity (tongue and jaw muscles), the pharynx, and the esophagus. Dysphagia occurs when there is a defect in the neural control or coordination of any or all of these structures. If serious, dysphagia can result in difficulty in swallowing even liquids (including a patient's own saliva) and a patient may not be able to maintain adequate nutrition. Dysphagia is most common in the elderly population and can be associated with a stroke or head injury, or neurodegenerative diseases such as Parkinson's disease, amyotrophic lateral sclerosis (ALS), or cognitive decline. Some treatments for cancers in the head, neck, or esophagus can cause dysphagia. Treatment options for dysphagia are limited, and involve physical therapy to help patients change behavior, muscle strength, and posture.

The timing of events in swallowing is shown in Fig. 28.5. The voluntary phase of swallowing is initiated when the tip of the tongue separates a bolus of food from the mass of food in the mouth. First the tip of the tongue and later the more posterior portions of the tongue press against the hard palate. The action of the tongue moves the bolus upward and then backward into the mouth. The bolus is forced into the pharynx, where it stimulates the touch receptors that initiate the swallowing reflex. The pharyngeal phase of swallowing involves the following sequence of events, which occur in less than 1 second:

1. The soft palate is pulled upward and the palatopharyngeal folds move inward toward one another; these movements prevent reflux of food into the nasopharynx and open a narrow passage through which food moves into the pharynx.
2. The vocal cords are pulled together, and the larynx is moved forward and upward against the epiglottis; these actions prevent food from entering the trachea and help open the upper esophageal sphincter (UES).
3. The UES relaxes to receive the bolus of food.



• **Fig. 28.5** Timing of motor events in the pharynx and UES during a swallow. *UES*, Upper esophageal sphincter.

IN THE CLINIC

The ability to measure and monitor a wide range of molecular components that are indicative of overall health is useful in diagnosis and monitoring. Saliva is easy to access, and collection of it is noninvasive. It is used to identify individuals with disease (presence of biomarkers) and to monitor the progress of affected individuals under treatment. In endocrinology, levels of steroids can be measured in the free form rather than as the free and bound form, as in plasma (e.g., the stress hormone cortisol and the sex hormones estradiol, progesterone, and testosterone). Viral infections such as human immunodeficiency virus (HIV), herpes, hepatitis C, SARS-CoV-2, and Epstein-Barr virus infection can be detected by polymerase chain reaction (PCR) techniques. Bacterial infections, such as *Helicobacter pylori,* can likewise be detected in saliva, and saliva is also used for monitoring drug levels.

4. The superior constrictor muscles of the pharynx then contract strongly to force the bolus deeply into the pharynx.

A peristaltic wave is initiated with contraction of the pharyngeal superior constrictor muscles, and the wave moves toward the esophagus. This wave forces the bolus of food through the relaxed UES. During the pharyngeal stage of swallowing, respiration is also reflexively inhibited. After the bolus of food passes the UES, a reflex action causes the sphincter to constrict.

IN THE CLINIC

Gastroesophageal reflux disease (GERD) is commonly referred to as *heartburn* or *indigestion* and is a common cause of noncardiac chest pain. It is primarily a condition of the lower esophageal sphincter (LES) and occurs when the LES allows the acidic contents of the stomach to reflux back into the distal part of the esophagus. This is thought to be caused by transient relaxations of the LES that occur independently of a swallow. This is not an uncommon event, even in healthy individuals, and only a small percentage of reflex events are symptomatic. This region of the esophagus, unlike the stomach, does not have a robust system to protect the mucosal lining. Acid will activate pain fibers resulting in discomfort and pain and in the long term, continual reflux can result in damage to the esophageal mucosa. GERD can be treated by therapies that reduce gastric acid secretion, for example, H_2 receptor antagonists (e.g., ranitidine [Zantac]) or by proton pump inhibitors (e.g., omeprazole [Prilosec]). In GERD patients refractory to treatment, antireflex surgery called fundoplication may be used, which involves reinforcement of the LES by wrapping the upper part of the stomach around it, but the use of this surgery is controversial.

Esophageal Phase

The **esophagus,** the **UES,** and the **lower esophageal sphincter (LES)** serve two main functions (Fig. 28.6). First, they propel food from the mouth to the stomach. Second, the sphincters protect the airway during swallowing and protect the esophagus from acidic gastric secretions.

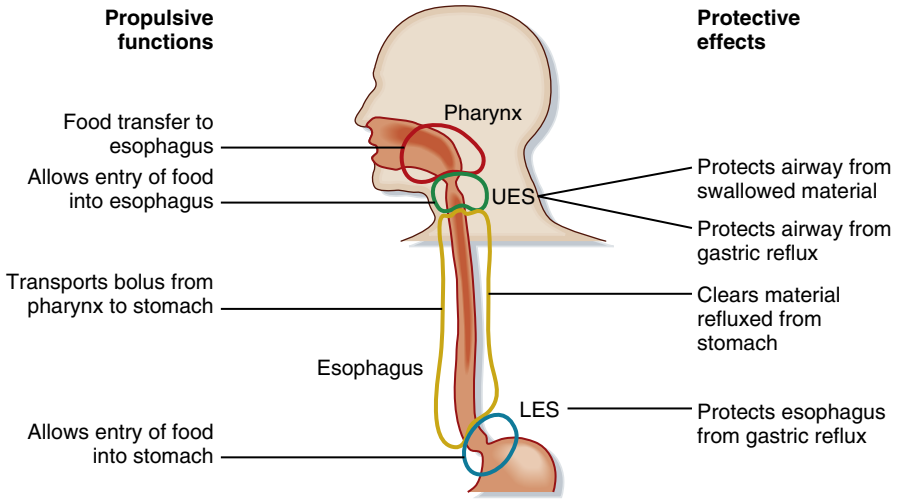
The stimuli that initiate the changes in smooth muscle activity that result in these **propulsive** and **protective functions** are mechanical and consist of pharyngeal stimulation during swallowing and distention of the esophageal wall itself. The pathways are exclusively neural and involve both extrinsic and intrinsic reflexes. Mechanosensitive afferents in both the extrinsic (vagus) nerves and intrinsic neural pathways respond to esophageal distention. These pathways include activated reflex pathways via the brainstem (extrinsic, vagus) or solely intrinsic pathways. The striated muscle is regulated from the nucleus ambiguus in the brainstem, and the smooth muscle is regulated by parasympathetic outflow via the vagus nerve. The changes in function resulting from mechanical stimuli and activation of reflex pathways are peristalsis of striated and smooth muscle, relaxation of the LES, and relaxation of the proximal portion of the stomach.

Functional Anatomy of the Esophagus and Associated Structures

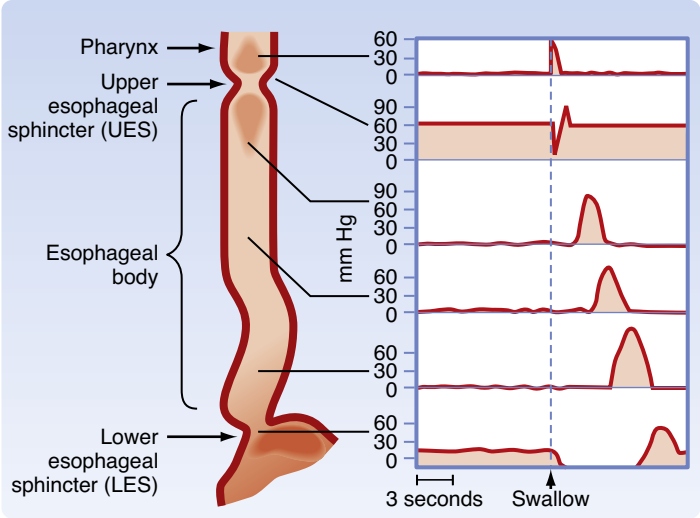
The esophagus, like the rest of the GI tract, has two muscle layers—circular and longitudinal—but the esophagus is one of two places in the gut where striated muscle occurs, the other being the external anal sphincter. The type of muscle (striated or smooth) in the esophagus varies along its length. The UES and LES are formed by thickening of striated or circular smooth muscle, respectively.

Motor Activity During the Esophageal Phase

The UES, esophagus, and LES act in a coordinated manner to propel material from the pharynx to the stomach. At the end of a swallow, a bolus passes through the UES, and the presence of the bolus, via stimulation of mechanoreceptors and reflex pathways, initiates a peristaltic wave (alternating



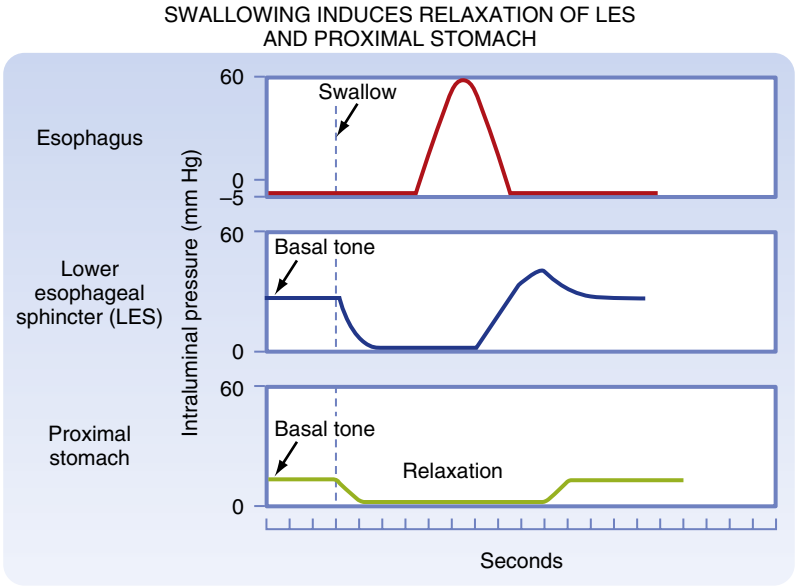
• **Fig. 28.6** The esophagus and associated sphincters have multiple functions involved in movement of food from the mouth to the stomach and also in protection of the airway and esophagus. *LES*, Lower esophageal sphincter; *UES*, upper esophageal sphincter.



• **Fig. 28.7** Changes in pressure in the different regions of the pharynx, esophagus, and associated sphincters initiated during a swallow. The pressure trace is a diagrammatic representation from that obtained during manometry in an awake human. Stimulation of the pharynx by the presence of a bolus initiates a decrease in pressure (= opening) of the UES and a peristaltic wave of contraction along the esophagus. Stimulation of the pharynx also relaxes the smooth muscle of the LES to prepare for entry of food.

contraction and relaxation of the muscle) along the esophagus that is called **primary peristalsis** (Fig. 28.7). This wave moves down the esophagus slowly (3–5 cm/s). Distention of the esophagus by the moving bolus initiates another wave called **secondary peristalsis.** Frequently, repetitive secondary peristalsis is required to clear the esophagus of the bolus. Stimulation of the pharynx by the swallowed bolus also produces reflex relaxation of the LES and the most proximal region of the stomach. Thus, when the bolus reaches the LES, it is already relaxed to allow passage of the bolus into the stomach. Similarly, the portion of the stomach that receives the bolus is relaxed. In addition, esophageal distention produces further receptive relaxation of the stomach. The proximal part of the stomach relaxes at the same time as the LES; this occurs with each swallow, and its function is to allow the stomach to accommodate large volumes with a minimal rise in intragastric pressure. This process is called **receptive relaxation** (Fig. 28.8).

The LES also has important protective functions. It is involved in preventing acid reflux from the stomach back into the esophagus. An insufficient tonic contraction of the LES is associated with reflux disease, a gradual erosion of the esophageal mucosa, which is not as well protected as the gastric and duodenal mucosa. There is also some evidence that peristalsis in the absence of swallowing (secondary peristalsis) is important for clearing refluxed gastric contents.



• **Fig. 28.8** Swallowing in the form of pharyngeal stimulation induces neural reflex relaxation of the LES and the proximal part of the stomach to allow entry of food.

Key Concepts

1. The cephalic and oral phases of the meal share many characteristics and prepare the remainder of the GI tract for the meal; these responses are neurally mediated, predominantly by the efferent vagus nerve.
2. Salivary secretion has important functions and, together with chewing of the food, allows the formation of a bolus that can be swallowed and passed along the esophagus to the stomach.
3. The ionic composition of salivary secretion varies with the flow rate, which is stimulated during a meal. The primary secretion comes from cells in the acini and is modified by epithelial cells as it passes through the ducts.
4. Regulation of salivary secretion is exclusively neural; parasympathetic innervation is most important in the response to food.
5. The swallowing reflex is a rigidly ordered sequence of events that propel food from the mouth to the pharynx and from there to the stomach.
6. The major function of the esophagus is to propel food from the mouth to the stomach. The esophagus has sphincters at either end that are involved in protective functions important in swallowing and preserving the integrity of the esophageal mucosa.
7. Esophageal peristalsis (primary) is stimulated by mechanical stimulation of the pharynx, and secondary peristalsis is stimulated by distention of the esophageal wall.
8. Esophageal function and the associated sphincters are regulated by extrinsic and intrinsic neural pathways.