Core Textbook of GASTROENTEROLOGY

Gregory L. Eastwood

Gastroenterology

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The authors and publisher have exerted every effort to ensure that drug selection and dosage set forth in this text are in accord with current recommendations and practice at the time of publication. However, in view of ongoing research, changes in government regulations, and the constant flow of information relating to drug therapy and drug reactions, the reader is urged to check the package insert for each drug for any change in indications and dosage and for added warnings and precautions. This is particularly important when the recommended agent is a new or infrequently employed drug.

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Core Textbook of

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PREFACE

What is the relevance of the basic sciences to clinical medicine? This is a question asked not only by medical students but also by physicians throughout their careers. Thus, although *Core Textbook of Gastroenterology* has been written to address the special needs of medical students, it is appropriate for all physicians who wish to understand clinical gastroenterology in terms of relevant anatomy and pathophysiology.

The emphasis nevertheless is on clinical gastroenterology. What is the reason a patient has difficulty swallowing? What is the physiologic basis for diarrhea? Why do patients become jaundiced? How does the physician evaluate and manage patients with dysphagia, diarrhea, or jaundice? The book is divided into three sections: Section One, Gastrointestinal Disorders, which covers the luminal gastrointestinal tract from esophagus to colon; Section Two, Pancreatic Disorders; and Section Three, Liver and Biliary Disorders. Within each section separate chapters discuss the major clinical disorders. The book is not encyclopedic, but it will provide an understanding of nearly every important aspect of clinical gastroenterology.

The questions at the end of each chapter are intended to highlight important aspects of each chapter and to serve as a teaching aid. The reader is encouraged to review the questions *before* reading the chapter and to try to answer them. After reading the chapter, the questions should be answered again and the correct answers verified in the section at the end of the book.

GREGORY L. EASTWOOD, M.D.

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Section One / Gastrointestinal Disorders

Section One
Gastrointestinal Disorders

1

ESOPHAGEAL DISORDERS

Gregory L. Eastwood

The Normal Esophagus

SWALLOWING

The esophagus is a simple organ. Its sole function is to transport food and secretions from the mouth to the stomach. The act of swallowing is a marvelously coordinated process during which a solid or liquid bolus passes from the mouth to the stomach, irrespective of the force of gravity. Gravity may aid in the passage of the bolus, but a person who has normal swallowing function should be able to swallow a meal whether sitting at the dining room table, hanging by the knees from a trapeze bar, or in a zero-gravity satelliite flying around the earth.

A swallow begins when a bolus is propelled to the back of the mouth and into the pharynx by the tongue. This initiates a series of events, which thereafter become "automatic." First, the upper esophageal sphincter (primarily the cricopharyngeus muscle), which constricts the esophagus just below the pharynx, relaxes and the bolus passes into the upper esophagus. Next, a primary peristaltic contraction propels the bolus down the esophagus. Secondary peristaltic contractions are initiated when the esophagus is distended by the bolus. Finally, when the bolus reaches the mid- to lower esophagus, the lower esophageal sphincter relaxes to allow the bolus to pass into the stomach. The tonic contraction of the lower esophageal sphincter, which relaxes during swallowing, normally presents an effective barrier against the reflux of gastric contents into the esophagus.

The motor response that stimulates a primary peristaltic contraction is initiated in a swallowing center in the medulla near the fourth ventricle, which is mediated by the vagi. The vagi innervate the upper esophagus in its striated muscle portion. If the vagi are cut below this level, peristalsis throughout the smooth muscle portion of the esophagus and function of the lower esophageal sphincter remain intact. This is because innervation to the lower esophagus and to the sphincter is by intramural plexuses or the muscle itself. For the same reason, secondary peristalsis, which arises within the esophagus, does not depend on vagal innervation.

MUSCLE

The musculature of the pharynx, upper esophageal sphincter, and upper third of the esophagus is striated. Striated and smooth muscle intermingle below the upper third until the muscle coat becomes entirely smooth muscle in the lower half of the esophagus, including the lower esophageal sphincter. The distribution of striated versus smooth muscle is clinically relevant. Disorders that primarily affect striated muscle, such as myasthenia gravis or polymyositis, may be associated with difficulty in initiating a swallow, dysfunction of the upper esophageal sphincter, or dysphagia caused by disordered peristalsis of the upper esophagus. On the other hand, smooth muscle disorders, such as progressive systemic sclerosis or achalasia, may affect peristalsis in the mid- and lower esophagus as well as the function of the lower esophageal sphincter. These and other disorders of the esophagus will be discussed in more detail later.

A considerable amount of information has accumulated within the past 15 years about esophageal function in health and disease, particularly in regard to the *lower esophageal sphincter*. Unlike the upper esophageal sphincter, which can be identified anatomically as the cricopharyngeus muscle, the lower esophageal sphincter has defied anatomic description. There is general agreement that an antireflux mechanism exists at the junction of the esophagus and the stomach, manifested as a high-pressure zone when measured manometrically. However, whether that high-pressure zone is a consequence of a pinching effect of the diaphragm, constriction by ligamentous bands, or the sphincteric action of specialized smooth muscle of the lower esophagus has been debated.

Overwhelming evidence supports the existence of a smooth muscle lower esophageal sphincter. Results of manometric studies have consistently identified a high-pressure zone in normal subjects that ranges from 15 mm Hg to 30 mm Hg. As mentioned earlier, this high-pressure zone relaxes on swallowing to allow passage of the bolus into the stomach. Further, the pressure within the lower esophageal sphincter increases in response to increases in intra-abdominal pressure, and at a rate of increase exceeding that of the intra-abdominal pressure. This means that the normal esophageal sphincter remains competent as an anti-

reflux barrier even after heavy meals, in obesity, or when wearing constricting clothing.

Histologically, there is little to distinguish lower esophageal sphincter from adjacent smooth muscle of the body of the esophagus. Careful morphologic studies in the opossum have indicated that the longitudinal muscle layer of the sphincter and of the esophageal body are similar, but the circular muscle of the sphincter is thicker than the circular muscle of the esophageal body. Electron microscopy has shown that circular muscle fibers of the sphincter have irregular protuberances from their surfaces, whereas smooth surfaces characterize the circular muscle fibers of the esophageal body.

Physiologically and pharmacologically, circular smooth muscle strips from the esophagogastric junction of the opossum behave differently from muscle strips just proximal to the sphincter from the esophageal body or distal to the sphincter from the upper stomach. For example, sphincteric smooth muscle has a lower threshold for isometric contraction to agents such as choline esters, ganglionic stimulants, norepinephrine, and gastrin and develops greater tension with passive stretching than does adjacent smooth muscle above or below the sphincter.

The regulation of lower esophageal sphincter tone is a complex phenomenon. Numerous substances have been identified that either increase or decrease sphincter pressure (Table 1–1). The hormone gastrin increases lower esophageal sphincter pressure but, contrary to the expectation of earlier researchers, who suggested that gastrin was a major regulator of sphincter pressure, subsequent studies indicated that gastrin probably plays only a minor physiologic role. Because incompetence of the lower esophageal sphincter can lead to gastroesophageal reflux symptoms, agents that either decrease sphincter pressure or strengthen the sphincter have obvious clinical importance.

Table 1–1 Agents that Increase and Decrease Lower Esophageal Pressure

Increase Pressure	Decrease Pressure
Gastrin	Secretin
Prostaglandin F2	Cholecystokinin
α-adrenergic agonists (norepinephrine, phenylephrine)	Glucagon
	Prostaglandins E1, E2, A2
Cholinergics (bethanechol, methacholine)	β-adrenergic agonists (isoproterenol)
Anticholinesterases (edrophonium)	α-adrenergic antagonists (phentolamine)
Betazole	Anticholinergics (atropine)
Gastric alkalinization	Theophylline
Metoclopramide	Caffeine
Protein meal	Gastric acidification
	Fat meal
	Smoking
	Ethanol
	Chocolate

MUCOSA

The esophagus is lined by stratified nonkeratinized squamous epithelium (Fig. 1–1). The stratified squamous epithelial lining of the esophagus changes abruptly to the glandular columnar epithelium of the stomach precisely at the location in the mucosa that corresponds to the lower esophageal sphincter in the muscle coat. Thus, the stomach and the remainder of the gastrointestinal tract to the anus are lined by columnar epithelium, which, although it may be convoluted into ridges, villi, glands, and the like, is only one cell thick. In the esophagus, papillae of the lamina propria project into the esophageal epithelium at irregular intervals. The papillae contain nutrient blood vessels and lymphatics and a diffuse infiltration of lymphocytes, macrophages, and fibroblasts. Small esophageal mucous glands, identical in appearance to the cardiac glands of the stomach, are located beneath the epithelium in the upper esophagus and near the esophagogastric junction.

The muscularis mucosae, although present in a patchy fashion in the upper esophagus, gradually becomes a thick layer in the lower esophagus. The longitudinal folds of the mucosa in the lower esophagus are caused by contraction of the muscularis mucosae.

The epithelium of the esophagus undergoes renewal, as is characteristic of the epithelium throughout the gastrointestinal tract. The proliferative zone—that is, the area within the epithelium in which new cells are formed—is the basal layer of polygonal epithelial cells. This layer is applied to the basement membrane overlying the lamina propria in the interpapillary region as well as over the papillary projections. New cells leave the basal layer in a random fashion and migrate toward the esophageal lumen, becoming more squamous in appearance. After a week or more, the cells reach the surface of the epithelium and are sloughed into esophageal lumen.

Dysphagia

Dysphagia means difficulty in swallowing. Clinically the term refers to the inability to initiate swallowing or to the sensation that solids or liquids stick in the esophagus after a swallow has been initiated. Another term, *odynophagia*, is used to describe pain on swallowing. Although odynophagia may accompany dysphagia, such as in esophageal spasm, pain on swallowing and the sensation of food sticking often occur independently. *Globus hystericus* is sometimes confused with dysphagia; this refers to the sensation of a lump in the throat that is usually relieved by swallowing. Globus hystericus is regarded as an emotional disorder. It is actually the converse of dysphagia in that the symptoms are momentarily relieved by swallowing, whereas the symptoms of dysphagia are brought on by swallowing.