Atlas of esophageal diseases / editor, Roy C. Orlando ; with 22 contributors.-- 2nd ed.
p. ; cm.
Includes bibliographical references and index.
[DNLM: 1. Esophageal Diseases--Atlases. 2. Esophagus--Atlases. WI 17 A879i1 2002]
RC815.7 .A853 2002
612.3'1--dc21
2001056186

DOI 10.1007/978-1-4613-1093-8

© Copyright 2002 by Springer Science+Business Media New York
Originally published by Current Medicine, Inc. in 2002
All rights reserved. No part of this publication may be reproduced, stored in a retrieval system or transmitted in any form by any means electronic, mechanical, photocopying, recording, or otherwise, without prior written consent of the publisher.
Softcover reprint of the hardcover 2nd edition 2002

Library of Congress Cataloging-in-Publication Data

For more information please call 1 (800) 427-1796 or (215) 574-2266
or e-mail us at inquiry@phl.cursci.com
www.current-science-group.com

Although every effort has been made to ensure that drug doses and other information are presented accurately in this publication, the ultimate responsibility rests with the prescribing physician. Neither the publishers nor the authors can be held responsible for errors or for any consequences arising from the use of information contained herein. Products mentioned in this publication should be used in accordance with the prescribing information prepared by the manufacturers. No claims or endorsements are made for any drug or compound at present under clinical investigation.
Preface

The esophagus is a long, tubular organ designed to actively transmit ingested material from the mouth to the stomach. To do this it is constructed of two bundles of muscle—an inner circular bundle and an outer longitudinal bundle—for peristalsis, and an inner lining of moist stratified squamous epithelium for protection. These structures are remarkable for their capacity to effect safe passage of materials to the stomach whether hot or cold, rough or smooth, hypertonic or hypotonic, acidic or alkaline, or direct chemical irritants (eg, alcohol). When diseased, organ dysfunction becomes clinically manifest by symptoms of dysphagia, chest pain, heartburn, or regurgitation.

This volume of the second edition of Atlas of Esophageal Diseases provides a 12-chapter visual panorama of the esophagus in both health and disease. Beginning with a chapter on esophageal anatomy and physiology, whose content is self-explanatory, this volume takes us through chapters that encompass the role of endoscopy and manometry, pH-monitoring, and Bernstein testing in patient assessment, as well as reviews of gastroesophageal reflux disease, acute esophagitis, endoscopic ultrasonography, esophageal motor disorders, the pharynx, esophageal tumors, noncardiac chest pain, therapeutic endoscopy, and concludes with a chapter detailing surgery of the esophagus. The quality of the chapters in this volume is excellent, and for this I am personally indebted to each of the authors for so generously expending the time and effort necessary to bring this work to fruition.

Roy C. Orlando, MD
Contributors

Matthew S.Z. Bachinski, MD
Staff Physician
Digestive Disease Group PA
Greenwood, South Carolina

Richard S. Bloomfeld, MD
Assistant Professor
Department of Internal Medicine
Wake Forest University Baptist Medical Center
Winston-Salem, North Carolina

Eugene M. Bozymski, MD
Professor
Department of Medicine/Gastroenterology
University of North Carolina School of Medicine
Staff Physician
University of North Carolina Hospital
Chapel Hill, North Carolina

Donald O. Castell, MD
Professor
Department of Medicine
MCP/Hahnemann University
Kimbel Professor and Chairman
Department of Medicine
Graduate Hospital
Philadelphia, Pennsylvania

Ahmet M. Dobrucali, MD
Research Fellow
Department of Medicine
Tulane University Medical School
New Orleans, Louisiana

Gulchin A. Ergun, MD
Associate Professor
Department of Medicine
Baylor College of Medicine
Chief, Digestive Disease Section
Director, Reflux Center
The Methodist Hospital
Houston, Texas

Salima Haque, MBBS, MD
Associate Professor
Department of Pathology
Tulane University Health Sciences Center
Head of Gastrointestinal and Liver Pathology
Tulane University Hospital and Clinic
New Orleans, Louisiana

Bernard M. Jaffe, MD
Professor
Department of Surgery
Tulane University Medical School
New Orleans, Louisiana

Spencer Jenkins, MD
Fellow
Department of Medicine/Gastroenterology
Medical College of Georgia
Augusta, Georgia

Peter J. Kahrilas, MD
Marquart Professor of Medicine
Division of Gastroenterology and Hepatology
Department of Medicine
Northwestern University Medical School
Chief, Division of Gastroenterology and Hepatology
Northwestern Memorial Hospital
Northwestern Medical Faculty Foundation
Chicago, Illinois

Christopher M. Kenney, MD
Fellow
Department of Gastroenterology
University of North Carolina, Chapel Hill
Staff Physician
University of North Carolina Hospitals
Chapel Hill, North Carolina

Michael J. Levy, MD
Instructor
Department of Internal Medicine
Mayo Medical School
Rochester, Minnesota

Todd A. Loehrl, MD
Assistant Professor
Department of Otolaryngology and Communication Sciences
Medical College of Wisconsin
Milwaukee, Wisconsin

Ravinder K. Mittal, MD
San Diego Veterans Affairs Medical Center
San Diego, California

Roy C. Orlando, MD
Professor
Departments of Medicine and Physiology
Tulane University Medical School
New Orleans, Louisiana
Richard I. Rothstein, MD  
Associate Professor  
Department of Medicine/Gastroenterology  
Dartmouth University School of Medicine  
Hanover, New Hampshire  
Chief, Section of Gastroenterology  
Dartmouth-Hitchcock Medical Center  
Lebanon, New Hampshire  

Reza Shaker, MD  
Professor  
Department of Gastroenterology and Hepatology  
Medical College of Wisconsin  
Chief, Division of Gastroenterology and Hepatology  
Director, Digestive Disease Center  
Froedtert Memorial Lutheran Hospital  
Milwaukee, Wisconsin  

Arifa Toor, MD  
Assistant Professor  
Department of Medicine  
Dartmouth Medical School  
Hanover, New Hampshire  
Staff Gastroenterologist  
Dartmouth-Hitchcock Medical Center  
Lebanon, New Hampshire  

Enrique Vazquez-Sequeiros, MD  
Research Fellow  
Department of Gastroenterology  
Mayo Medical School  
Rochester, Minnesota  

Maurits J. Wiersema, MD  
Associate Professor  
Department of Internal Medicine  
Mayo Medical School  
Rochester, Minnesota  

Roy K.H. Wong, MD  
Professor  
Department of Medicine  
Uniformed Service University Health System  
Bethesda, Maryland  
Chief, Gastroenterology Service  
Walter Reed Army Medical Center  
Washington, DC  

Wallace C. Wu, MB, BS  
Professor  
Department of Medicine  
Wake Forest University School of Medicine  
Winston-Salem, North Carolina
Contents

Chapter 1

Esophageal Muscular Anatomy and Physiology

GULCHIN A. ERGUN AND PETER J. KAHRILAS

Oropharyngeal Musculature ........................................ 2
Normal Swallow Sequence ........................................ 4
Neurophysiology of Swallowing ................................ 5
Upper Esophageal Sphincter ....................................... 7
Muscular Anatomy of the Esophagus ......................... 10
Esophageal Physiology and Peristalsis ....................... 13
Lower Esophageal Sphincter ..................................... 18

Chapter 2

The Pharynx

REZA SHAKER AND TODD A. LOEHR

Normal Findings .................................................. 24
Pathologic Findings .............................................. 31

Chapter 3

Esophagogastroscopy and Biopsy

RICHARD S. BLOOMFIELD AND WALLACE C. WU

Equipment and Procedural Techniques ....................... 44
Indications and Contraindications ........................... 46
Normal Endoscopic and Radiologic Anatomy ............... 47
Normal Esophageal Mucosal Histology ..................... 49
Selected Esophageal Lesions .................................. 50

Chapter 4

Endoscopic Ultrasonography

ENRIQUE VAZQUEZ-SEQUEROS, MICHAEL J. LEVY, AND MAURITS J. WIJSEMA

Sample Endoscopes ............................................. 56
Anatomy .......................................................... 57
Indications and Differential Diagnosis ................... 59
Cysts ............................................................... 59
Histoplasmosis .................................................. 60
Subepithelial Lesion (Leiomyoma) ......................... 60
Dysphagia Lusoria ............................................. 61
Portal Hypertension ........................................... 62
Barrett’s Esophagus ........................................... 62
Esophageal Carcinomas ....................................... 63
Endoscopic Ultrasonography for Staging of Non-small Cell Lung Cancer .... 65
Complications ..................................................... 66
Chapter 5

Esophageal Investigative Techniques

DONALD O. CASTELL

Manometry ...................................................... 69
Ambulatory pH Monitoring ........................................ 80
Acid Perfusion Test (Bernstein Test) .................................. 87

Chapter 6

Gastroesophageal Reflux Disease

ROY C. ORLANDO AND AHMET M. DOBRUCALI

Epidemiology ................................................... 93
Pathophysiology and Etiology .................................. 94
Clinical Features ................................................... 101
Complications .................................................. 104
Treatment .................................................... 107

Chapter 7

Acute Esophagitis

MATTHEW S.Z. BACHINSKI, SPENCER JENKINS, AND ROY K.H. WONG

Lye Esophagitis ................................................. 118
HIV .................................................................. 121
AIDS and Clinical Presentation .................................. 121
Cytomegalovirus .................................................. 122
Esophagitis Caused by Herpes Simplex Virus .............. 126
Esophagitis Caused by Candida ................................ 129
Foreign Body Ingestion ........................................ 133
Pill-induced Esophagitis ...................................... 137
Esosinophilic Esophagitis .................................... 140
Esophagitis Caused by Radiation ............................ 141

Chapter 8

Tumors of the Esophagus

SALIMA HAGUE

Epithelial Neoplasms ............................................. 146
Squamous Cell Carcinoma ...................................... 147
Special Types of Squamous Cell Carcinoma .................. 152
Adenocarcinoma ............................................... 155
Mesenchymal Neoplasms ...................................... 159
Chapter 9
Esophageal Motor Diseases
RAVINDER K. MITTAL
Upper Esophageal Dysfunction and Zenker's Diverticulum .................. 164
Achalasia of the Esophagus ........................................... 165
Diffuse Esophageal Spasm ........................................... 168
Nutcracker Esophagus/Hypertensive Lower Esophageal Sphincter .......... 169
Scleroderma .......................................................... 171
Antireflux Mechanisms ............................................. 172
Ultrasonography of Esophageal Motor Disorders .......................... 174

Chapter 10
Evaluation of the Patient with Noncardiac Chest Pain
RICHARD I. ROTHSTEIN AND ARIFA TOOR
Background and Epidemiology ......................................... 182
Characteristics of Esophageal Chest Pain ................................ 184
Mechanisms of Esophageal Chest Pain ................................... 185
Diagnostic Testing ...................................................... 186

Chapter 11
Esophageal Therapeutics
EUGENE M. BOZYMSKI AND CHRISTOPHER M. KENNEY
Upper Gastrointestinal Bleeding ....................................... 198
Esophageal Obstruction ............................................... 208
Esophageal Cancer ..................................................... 214
Esophageal Foreign Bodies ............................................. 217

Chapter 12
Surgery of the Esophagus
BERNARD M. JAFFE
Anatomy ................................................................. 223
Esophageal Perforation ................................................. 224
Esophageal Hernias .................................................... 226
Esophageal Obstruction ............................................... 230

Index ........................................................................ 243
The major function of the esophagus is to transport food from the mouth to the stomach while preventing retrograde movement of gastric contents. It is in essence a hollow muscular tube that is closed at the proximal portion by the upper esophageal sphincter (UES) and by the lower esophageal sphincter (LES) at the bottom. The pharynx and the proximal esophagus contain striated muscle controlled by the swallowing center in the brain stem through the vagus nerves. The lower two thirds of the esophagus contains smooth muscle with peristalsis controlled primarily by an intrinsic neural network located between the longitudinal and circular muscle layers, and is modulated by central mechanisms in the swallowing center. Proximal esophageal function is complex because the oral cavity and pharynx must necessarily serve multiple functions, not only as a food conduit, but also as a respiratory conduit, thereby requiring precise control and efficient coordination of swallowing and respiration.

Swallowing has been traditionally divided into four phases: (1) the preparatory phase, which involves mastication, sizing, shaping, and positioning of the bolus on the tongue with saliva; (2) the oral phase, during which the bolus is propelled from the oral cavity into the pharynx; (3) the pharyngeal phase, during which the bolus is transported from the oral cavity into the pharynx with adequate airway protection; and (4) the esophageal phase, during which the bolus is propelled down the length of the esophagus [1]. This seemingly simple task requires coordination of over 100 muscles that are under voluntary and reflexive control during a period of a few seconds. Dysfunction at the proximal portion may result in poor formation of a bolus with misdirection caused by lingual abnormalities, nasal regurgitation if velopharyngeal closure is poor, incomplete UES opening with impaired hyoid or laryngeal excursion, aspiration with poor laryngeal closure, and choking if hypopharyngeal residue with poor pharyngeal clearance is present.
After the pharyngeal contraction traverses the UES, the peristaltic contraction moves from the proximal striated muscle to the distal smooth muscle of the esophagus at 2 to 4 cm per second. Primary peristalsis is controlled by extrinsic innervation whereas secondary peristalsis is an intramural process [2]. Deglutitive inhibition occurs when a second swallow is initiated during a still-continuing peristaltic contraction and causes rapid and complete inhibition of the contraction induced by the first swallow. Similarly, LES tone is inhibited with swallowing concurrently with deglutitive inhibition.

Physiologic control mechanisms that govern the striated and the smooth muscles of the esophagus are different. The striated muscle esophagus receives excitatory vagal innervation exclusively, and the peristaltic contraction results from sequential activation of motor units in a craniocaudal sequence. Vagal control of the smooth muscle esophagus is more complex, with vagal fibers synapsing directly on myenteric plexus neurons and vagal stimulation can either excite or inhibit esophageal musculature. Finally, two types of effector neurons exist within the esophageal myenteric plexus: (1) excitatory neurons that mediate contraction of both longitudinal and circular muscles through cholinergic receptors [3]; and (2) inhibitory neurons that affect the circular muscle layer through nitric oxide nerves [4,5].

**OROPHARYNGEAL MUSCULATURE**

![Musculature of the pharynx](image)

Musculature of the oral cavity, pharynx, larynx, and proximal esophagus as displayed in a cutaway view. The oral cavity, pharynx, and larynx are all involved in transferring food from the mouth to the esophagus. Within the oral cavity, the lips, teeth, tongue, soft palate, mandible, and floor of the mouth serve functions in chewing and manipulating food to create a bolus that is suitable for transfer to the pharynx. The walls of the oropharynx are composed of the superior, middle, and inferior constrictors posteriorly and the tongue base, which opposes constrictors anteriorly. The superior constrictor arises from the pterygoid hamulus, pterygomandibular raphe, mandible, and tongue, passes posteromedially, and inserts into the posterior median raphe. The middle constrictor arises from the hyoid bone and stylohyoid ligament, passes posteriorly, and also inserts into the posterior median raphe. The inferior constrictor is composed of the thyropharyngeus superiorly and the cricopharyngeus inferiorly. The thyropharyngeus arises from the thyroid cartilage and passes posteromedially to insert into the median raphe. The cricopharyngeus, however, has superior and inferior components that arise from both sides of the cricoid lamina such that the superior fibers course posteromedially to the median raphe and the inferior fibers loop around the esophageal inlet without a median raphe. The cricopharyngeus muscle separates the pharynx from the esophagus.

The pharyngeal walls are supported by attachments to the epiglottic, arytenoid, cuneiform, corniculate, and cricoid cartilages. The larynx and trachea are suspended in the neck between the hyoid bone superiorly and the sternum inferiorly. The laryngeal strap muscles contribute to this suspension and with the intrinsic elasticity of the trachea permit the larynx to be elevated and lowered. The hyoid bone serves as the base for the tongue and is positioned as a fulcrum, crucial in directing forces anteriorly and superiorly toward the larynx and hence esophageal inlet. Laryngeal movement is critical in permitting the swallow response as the laryngeal inlet is closed and physically removed from the bolus path during the course of the swallow. Failure to achieve laryngeal elevation can result in aspiration. (Adapted from Kahrilas [6].)
Figure 1-2. Posterior view of the pharynx showing the oropharyngeal anatomic configuration at rest (A) and during swallow (B). The pharyngeal constrictors are cut at the midline and laid open to reveal the anterior pharyngeal wall. The spaces formed between the lateral insertion of the inferior constrictor and the lateral walls of the thyroid cartilage are the pyriform sinuses. Panel B shows the anatomic configuration during swallow illustrating laryngeal elevation and closure (arrows show the bilateral path taken around the epiglottis by the swallowed material). (Adapted from Kahrilas [6].)
Sequence of a normal swallow. Swallowing can be divided into an oral phase and a subsequent pharyngeal phase. The pharyngeal phase is a complex motor event referred to as the swallow response. The oral phase of the swallowing is highly voluntary and variable, depending on taste and motivation. It is functionally accomplished by (1) manipulation of the bolus by the tongue to contain the food in the mouth until ready to swallow and (2) the propulsion of the bolus by the posterior tongue squeezing the tongue against the palate with the central groove exhibiting centripetal then centrifugal motion [6]. Close to the time that the bolus reaches the posterior tongue, the pharyngeal swallow is triggered. There is then (3) simultaneous apposition of the muscular soft palate to the posterior pharyngeal wall to prevent nasal regurgitation and elevation of the larynx and hyoid bone to close the airway and pull open the upper esophageal sphincter (UES) [7]. This is followed by (4) clearance of any remaining hypopharyngeal residue by the pharyngeal constrictors [7]. After the pharyngeal swallow has been initiated, the sequence of events is involuntary.

A, At 0 seconds, the bolus is in the oral cavity, resting on the tongue, with the laryngeal vestibule open and the UES closed. B, At 0.25 seconds into the swallow the bolus has been pushed back into the valleculae by the posterior tongue, the nasopharynx has been sealed off, and the larynx has begun to elevate. C, By 0.32 seconds the hyoid is maximally elevated, the UES is opened, and the tongue base has been fully retracted against the posterior pharyngeal wall. D, Structures are beginning to return back to the rest position 1.27 seconds after the initiation of the swallow. E, The rest position. (Adapted from Kahrilas et al. [9].)

Progression of a normal swallow imaged by cineradiography. A, Normal preswallow tongue and pharyngeal surface contour are shown before administration of bolus. B, With administration of barium, bolus propulsion begins with the loading phase of the tongue and bolus containment through adaptation of the lingual central groove.

(continued on next page)
C, Bolus is propelled into the pharynx with the tongue central groove exhibiting centripetal then centrifugal motion. D, Nasopharyngeal closure is achieved by soft-palate elevation and apposition to the posterior pharyngeal wall. Airway protection is achieved by laryngeal elevation, vocal cord closure, and arytenoid tilting. Upper esophageal sphincter opening occurs through relaxation of the sphincter and anterior hyoid traction with laryngeal elevation. E, Pharyngeal clearance of ingested contents is achieved by profound shortening of the pharynx, eliminating bolus access to the larynx and the propagating pharyngeal contraction. After the bolus has passed into the proximal esophagus, the epiglottis returns upright, the larynx reopens, and the resting positions are resumed (not shown).

**NEUROPHYSIOLOGY OF SWALLOWING**

![Diagram of swallowing process and related nervous system structures.]

Central nervous system organization of the swallow response. Afferent information from the periphery enters into the solitary tract. This sensory information can initiate deglutition and modify ongoing motor activity within reflexes affecting the esophageal body and sphincters independent of swallowing. Sensory information from the oropharyngeal area enters through the extravagal cranial nerves (trigeminal, facial, hypoglossal, and glossopharyngeal) and vagal nerve pathways. Sensory information from the entire esophagus, including the sphincters, is carried in the vagus nerve with the cell bodies in the nodose ganglion. Sensory information also passes by way of the sympathetics to the spinal cord segments C1 to L3.

The portion of the swallowing center that programs the entire swallowing sequence is located in the solitary tract nucleus and the neighboring reticular substance. The dorsal portion within this center is involved in the initiation of the swallow and the organization of the entire swallowing sequence. The ventral portion appears to serve as a connecting pathway to the various motor neuron pools involved in the swallowing sequence, such as integration of the swallowing sequence with the respiratory center in the medulla.

The motor neurons involved in the efferent output of the swallowing sequence lie mainly in the trigeminal, facial, and hypoglossal nuclei, the nucleus ambiguus of the vagus (for esophageal striated muscle), and the dorsal motor nuclei of the vagus (for esophageal smooth muscle) with some input to striated muscle. (Adapted from Castell [10].)
Sensory field of the superior laryngeal nerve in humans. Electrical stimulation of the superior laryngeal nerve (SLN) elicits the pharyngeal swallow response. The structures innervated by the SLN are relatively distal, supporting the notion that in vivo afferents initiating swallowing probably also travel through the glossopharyngeal nerve. More than likely, reflexive swallows aimed at keeping the pharynx clear of secretions are initiated by stimulation of SLN afferents whereas deglutitive swallows are initiated by proximal stimulation or volition. (Adapted from Kahrilas [6].)

Neuroanatomy of the swallow response. The location of the swallowing center is estimated to be in the reticular substance about 1.5 mm from the midline and 1 to 3 mm dorsal to the inferior olive at a level between the rostral pole of the inferior olive and caudal pole of the facial nucleus. A swallowing center exists bilaterally in each atmosphere, which is capable of independently coordinating swallowing activity, although both sides are extensively interconnected. The swallow center has dominant access to motoneurons and exerts strong inhibitory influence on centers competing for access to these motoneurons. Therefore, an apneic pause of 0.5 to 3.5 seconds occurs to accompany swallowing.
In addition to neurophysiologic electromyographic patterns, deglution can also be described in biomechanical terms. Biomechanical analysis concentrates on the swallowed bolus and how the bolus is manipulated by oropharyngeal structures. Therefore, in biomechanical terms the pharyngeal swallow encompasses several closely coordinated actions: elevation and retraction of the soft palate with the closure of the nasopharynx, upper esophageal sphincter opening, laryngeal closure at the level of the laryngeal vestibule, tongue loading (ramping), tongue pulsion, and pharyngeal clearance. These biomechanical events that comprise the swallow response exhibit systematic variability with the volume of the swallowed bolus.

This figure shows time lines of 1- and 20-mL swallows. The upper unshaded area depicts time relationships among swallow events during 1-mL swallows whereas the shaded area below depicts time relationships during 20-mL swallows. In both cases, time 0 is the end of the swallow, determined by the timing of the UES closure, and all other events are given negative timing values. When viewed in this way, the apparent prolongation of the 20-mL swallow is associated with an earlier mechanical configuration of the pharynx from a respiratory to a swallowing conduit. This earlier configuration is associated with a prolonged tongue loading phase that starts earlier and takes longer [6]. UES opening along with the associated closure of the laryngeal vestibule also commences sooner and persists longer [8]. Propulsive events occur with a very similar time frame, resulting from more vigorous expulsion of a larger boluses. The mechanics and timing of the pharyngeal contraction, important in pharyngeal clearance and in UES closure, on the other hand, is extraordinarily constant among swallow volumes [7]. (Adapted from Kahrilas [12].)

**Figure 1-9.**
Upper esophageal sphincter (UES) imaged by ultrafast CT. The muscular elements of the UES are striated muscle with the cricopharyngeus as well as the adjacent portion of the cervical esophagus and the inferior pharyngeal constrictor contributing to sphincteric function. The cricopharyngeus receives its motor nerve supply through the pharyngeal branch of the vagus. The zone of maximal intraluminal pressure is approximately 1 cm in length axially, and when viewed in cross-section, the closed sphincter has a slitlike configuration with the lamina of the cricoid cartilage anterior and the cricopharyngeus attached in a C configuration making up the lateral and posterior walls.

A. Representative cross-sectional image at the level of the UES as imaged by ultrafast CT. The tracings (B) illustrate the dynamic changes of the bolus cavity during the course of the swallow, ending with luminal closure at time zero. Note how the sphincter is tightly confined between the cricoid cartilage and cervical vertebral. Despite this confinement, the opened sphincter maintains an ovoid rather than a dumbbell configuration. (Panel A from Ergun et al. [13]; with permission.)
Continuous cricopharyngeal electromyography (EMG) recording. These sample data tracings from a dog show the upper esophageal sphincter (UES) intraluminal pressure recorded by sleeve sensor in panel A, the raw EMG recording of the cricopharyngeus in panel B, and the integrated cricopharyngeal EMG activity in panel C while the animal was awake (left) and sedated with pentobarbital (right). The most typical EMG activity pattern of the UES is the brief interval of inhibition followed by a pulse of maximal excitation, regardless of the pre-existing tone or activity pattern of the UES. In the awake state, the swallow is associated with inhibition of the cricopharyngeal EMG followed by a burst of activity corresponding to the passage of the pharyngeal contraction. While sedated, there is no detectable resting cricopharyngeal EMG activity and therefore no detectable cricopharyngeal inhibition at the time of UES relaxation. These findings suggest that the residual UES pressure (approximately 15 mm Hg) in the sedated animal is the result of passive elastic forces in the neck rather than active cricopharyngeal contraction. (Adapted from Jacob et al. [14].)

Movement pattern of the hyoid bone during 1- and 10-mL barium swallows. The upper esophageal sphincter (UES) is tonically closed at rest because of continuous neural excitation. Within 0.2 seconds after a swallow, excitatory discharge to the UES transiently ceases and laryngeal elevation followed by anterior traction of the hyoid work together to pull open the sphincter. Because the only insertion of the sphincteric musculature is anterior to the cartilages of the larynx, the sphincter and larynx are obliged to move in unison during axial laryngeal movement so that the primary mechanism for opening the relaxed UES also serves to produce a uniform conduit for directing the bolus into the esophagus.

The contraction of the suprahyoid and infrahyoid musculature that provides the anterior traction for UES opening also results in the characteristic pattern of hyoid displacement shown in this figure. Each circle represents the hyoid position during a single video frame of the recorded fluoroscopic sequence (1/30th second interval) and the arrows indicate the direction of movement. The open circles indicate frames during which the sphincter was closed, closed circles indicate frames when the sphincter was closed, and the gray circles indicate frames during which the sphincter was variably open, depending on the subject. Both the diameter and duration of sphincter opening increase with increased bolus volume. The increased duration of sphincter opening is related to the persistence of the hyoid excursion, whereas changes in the diameter of the opening are related to increased intrabolus pressure with larger volume swallows. (Adapted from Jacob et al. [11].)
Three-dimensional modeling of the oropharynx during swallowing. This figure shows the reconstructions of nine representative pharyngeal configurations during a 10-mL swallow. In each image the bolus chamber is white, the supraglottic airway is blue, the infraglottic airway is purple, the vertebræ are light brown, the hyoid is orange, the epiglottis is yellow, the arytenoid cartilage is dark green, the cricoid cartilage is red, the tracheal rings are cyan, and the hemisected thyroid cartilage is light green. The times next to the images refer to the upper esophageal sphincter (UES) opening (time, 0.0 seconds). Many mechanical events are encompassed during the act of deglutition. The preswallow configuration (-0.40 seconds) is characterized by the bolus chamber being segregated from the airway by the sealed glossopalatal junction. At the time of velopharyngeal closure (-0.13 seconds) the nasopharynx is sealed from the bolus chamber as the glossopalatal junction opens. The central groove of the tongue blade has deepened and the posterior oral portion of the pharyngeal propulsive chamber is forming. The larynx has begun elevating and the arytenoid cartilage is tilting toward the base of the epiglottis. At the instant of UES opening the laryngeal vestibule has been obliterated by contact of the arytenoid cartilage against the epiglottic base. Note that the UES (at the inferior aspect of the cricoid cartilage) has elevated relative to its preswallow position and that the pharyngeal bolus chamber is fully formed. During lingual bolus propulsion (0.13 seconds) the volume of the bolus chamber is reduced by the centrifugal motion of the tongue surface and bolus expulsion results in full distension of the UES and proximal esophagus. The epiglottis is folded over the arytenoid cartilage and there is maximal pharyngeal shortening. The next four reconstructions—early pharyngeal clearance (0.27 seconds), midpharyngeal clearance (0.40 seconds), late pharyngeal clearance (0.53 seconds), and UES closure (0.67 seconds)—show the caudal progression of the pharyngeal contraction stripping the residua from the oropharynx into the esophagus. Finally, with airway reopening (0.87 seconds) the pharynx commences its return to the respiratory configuration as the larynx descends, the epiglottis flips up, and the velopharyngeal junction reopens. (From Kahrilas et al. [15]; with permission.)
MUSCULAR ANATOMY OF THE ESOPHAGUS

Normal histology of the esophagus. The lining of the esophagus is a partially or nonkeratinized stratified squamous epithelium that overlies the connective tissue of the submucosa and the thick circular and longitudinal muscle layers (not shown). (Courtesy of Dr. Sambastiva Rao, Northwestern University Medical School.)

Cutaway view showing anatomy of the tubular esophagus. The esophagus is a muscular tube that is composed of longitudinal and circular muscle with extensive neural network in between. Auerbach’s plexus (myenteric) lies between the longitudinal and circular muscle layers. Another nerve network, Meissner’s plexus (submucosal), is situated between the muscularis mucosa and the circular muscle layer. Note that there is no serosa to the esophagus and that the lumen is collapsed and empty. In fact, activity of both esophageal sphincters preserves the vacuum of the esophagus; the upper esophageal sphincter acts to exclude air during respiration and the lower esophageal sphincter excludes gastric contents from refluxing back into the esophagus. (Adapted from Kahrilas [6].)

Endoscopic ultrasound of the esophagus. This endosonographic image of the esophageal wall demonstrates the five-layer structure that is seen throughout the gastrointestinal tract. These layers correspond to the mucosa (e,d), submucosa (c), muscularis (b), adventitia (a). Because of balloon filling, the layer structure is not recognizable in all parts of the circumference. (Courtesy of Dr. Arvydas Vanagunas, Northwestern University Medical School.)
Arterial supply of the esophagus. Esophageal circulation is in the form of "shared vasculature" [18]. The vasa propria is derived directly from the aorta, but esophageal vessels are small branches of larger-stem vessels intended to supply other organs, such as the thyroid gland, trachea, and stomach, and are thus secondary vessels. They include tracheoesophageal vessels originating from the inferior thyroid artery, tracheobronchial arteries at the level of the carina, esophageal aortic arteries proper, and cardia vessels derived from the celiac axis (the left gastric and splenic artery). These various vascular sources form a dense, continuous submucosal anastomotic network that further subdivides into minute branches before entering the esophageal wall to provide adequate circulation if the nourishing vessel is ligated.

This Beracryl cast of the arterial tree of the middle and lower esophagus shows the tracheobronchial artery originating from the aorta and giving rise to esophageal arteries. These arteries constitute a fine continuous arterial network with vessel diameters of 130 to 150 μm that surround the lumen of the esophagus shown by an intraesophageal probe. The anastomotic network reflects the shape of the esophagus with larger vessels oriented along a longitudinal axis. (From Liebermann-Meffert et al. [16]; with permission.)

Venous layers of the esophagus. There are three parts of the venous system related to the esophagus: intrinsic veins, associated veins, and extrinsic veins. The two layers of veins in the wall of the esophagus are the superficial venous plexus (located in the lamina propria and muscularis mucosa) and the submucosal plexus (within the circular muscle). In the distal esophagus, venous blood drains first from a superficial mucosal network of small intraepithelial blood vessels into submucosal, longitudinally oriented deep intrinsic veins. Once in the intrinsic veins, blood drains through a system of transverse perforating veins with unidirectional valves into extrinsic serosal and periesophageal veins and ultimately into the left gastric vein inferiorly and the azygos vein superiorly. (Adapted from Kitano et al. [17].)
Direction of flow

**FIGURE 1-18.**
Portal venous blood flow observed with esophageal and gastric varices. *(Adapted from Kitano et al. [17].)*

**FIGURE 1-19.**
Esophageal varices as seen on barium swallow. Portal hypertension results in congestion and dilation with the deep intrinsic veins becoming grossly enlarged, thus displacing the more superficial venous systems. The deep veins eventually occupy a superficial subepithelial location and are identified radiographically and endoscopically as esophageal varices. *(Courtesy of Dr. Frank Miller, Northwestern University Medical School.)*

**FIGURE 1-20.**
Esophageal varices seen endoscopically. The varices appear as slightly bluish dilated vessels *(arrow).*

**FIGURE 1-21.**
Gastroesophageal varices *(arrow)* demonstrated with CT. *(Courtesy of Dr. Frank Miller, Northwestern University Medical School.)*
Normal manometric recording and primary peristalsis. This figure shows a normal manometric tracing using a sleeve sensor. Distance above the center of the sleeve device positioned in the lower esophageal sphincter (LES) is shown on the left with time of contraction onset on the right. At rest, the esophageal body is quiet and there is no motor activity, whereas the upper esophageal sphincter and LES both maintain a contraction that can be measured manometrically and characterized as resting or basal tone. During deglutition the classic coordinated motor pattern of the esophagus, called primary peristalsis, is initiated. With transfer of the bolus into the esophagus, a progressive circular contraction begins in the upper esophagus and proceeds down the esophageal body to propel the bolus through a relaxed LES, which subsequently closes with a prolonged contraction.
Relationship between peristaltic function and esophageal volume clearance. The mechanical equivalent of peristalsis is a stripping wave that clears the esophagus proximally down with the velocity of the stripping wave corresponding to the manometrically recorded contraction such that the point of the inverted V seen fluoroscopically at each manometric sensor occurs simultaneous to the upstroke of the pressure wave. Data defining the relationship between the amplitude of esophageal peristalsis and the efficacy with which the stripping wave empties the esophagus are demonstrated in this figure.

This figure also shows concurrent manometric and video recordings of a 5-mL barium swallow. The tracings of the sequential fluoroscopic images show the distribution of the barium column at the times indicated above the images and by closed arrows on the manometric tracings. Here, a single peristaltic sequence completely cleared the barium from the esophagus. Administration of the barium occurred at 1.0 second, causing some esophageal distension and slightly increasing intraluminal pressure, shown by the open arrows on the manometric record. With onset of peristalsis, luminal closure is achieved as the tail of the barium bolus passes each recording site concurrent with the onset of the manometric pressure wave. LES—lower esophageal sphincter; UES—upper esophageal sphincter. (Adapted from Kahrilas [18].)

Schatzki’s ring on barium esophagram. Esophageal webs and rings are thin esophageal stenoses typically composed of only mucosa. Rings formed at the gastroesophageal junction, as described by Schatzki, are usually silent but become symptomatic when the internal diameter is less than 13 mm. (From McBride and Ergun [19]; with permission.)
Esophageal stenosis. Congenital esophageal anomalies include atresia, stenosis, webs, and duplications. Three variants of congenital esophageal stenosis exist. The most common type is associated with tracheobronchial remnants in the esophageal wall. The second is associated with multiple esophageal webs. The third type, shown here, is fibromuscular stenosis that is unassociated with webs or tracheobronchial remnants. The esophagogram shows evidence of narrowing in the entire length of the esophagus. A, Anteroposterior view; B, oblique view.

Schatzki’s ring viewed endoscopically. Schatzki’s ring viewed endoscopically.

Arteria lusoria. Dysphagia lusoria is caused by extrinsic esophageal compression caused by an aberrant right subclavian artery arising from the descending aorta and passing behind the esophagus (arrows). A, Anterior view; B, oblique view. (From McBride and Ergun [19]; with permission.)
Extrinsic and intrinsic motor innervation of the esophagus. The control mechanisms that govern the striated and smooth musculature of the esophagus are distinct. The extrinsic innervation of the esophagus is through the vagus nerve. The striated muscle receives excitatory vagal innervation exclusively from axons of lower motor neurons with cell bodies in the nucleus ambiguus. Peristaltic contraction of this segment results from sequential activation of motor units in a craniocaudal sequence caused by programming by the medullary swallowing center that is potentiated by stimulation of afferent fibers from the esophagus designed to mimic the effect of a bolus being pushed ahead of a peristaltic contraction. Moreover, vagal motor fibers are inhibited during the pharyngeal phase of swallowing, supporting the concept that deglutitive inhibition has a central origin. Similarly, primary peristalsis of the smooth muscle exists following deviation of the bolus path and curarization of the oropharyngeal and cervical esophagus, suggesting that primary peristalsis in the smooth muscle segment is at least partially governed by the medullary swallowing center. Vagal control of the smooth muscle esophagus is more complex, with vagal innervation provided by the dorsal motor nucleus of the vagus and vagal fibers synapsing on myenteric plexus neurons rather than directly on neuromuscular junctions. There is, however, no vagal activity during secondary peristalsis, supporting the notion that the organization of peristalsis in the smooth muscle is an intramural process.

With respect to the intrinsic control of peristalsis, the entire esophagus has an intramural nerve network (see Fig. 1-13). Interestingly, the function of the myenteric plexus in the striated esophagus is unknown. The morphology and function in the smooth muscle esophagus have yet to be determined; however, there are two main types of effector neurons within the myenteric plexus. Excitatory neurons mediate contraction of both the longitudinal and circular smooth muscle through cholinergic M2 receptors, and inhibitory neurons affect predominantly the circular muscle layer through a nonadrenergic, noncholinergic neurotransmitter (NANC), now believed to be nitric oxide. Cholinergic excitation of the excitatory neurons is nicotinic whereas cholinergic excitation of the NANC can be muscarinic (M1) as well. LES—lower esophageal sphincter. (Adapted from Kahrilas [20].)
Deglutitive inhibition. It has been suggested that swallowing not only induces primary peristalsis, but also triggers a wave of inhibition of the smooth muscle that precedes the arrival of the peristaltic contraction (deglutitive inhibition). This idea was based on in vivo experiments in animals but was never studied in humans in detail because inhibition is difficult to visualize. This figure shows resting pressure and deglutitive pressure waves in the human esophagus with an artificial high pressure zone created originally at 13 cm (A) and then at 8 cm (B) above the lower esophageal sphincter (LES). Note that after swallowing a relaxation of the artificial high pressure zone started simultaneously at 13 cm and 8 cm above the LES. The end of the relaxation coincided with the start of the peristaltic contraction at that level.

This study shows direct evidence that a wave of inhibition precedes a swallow-induced peristaltic contraction in the smooth muscle of the human esophagus. This inhibitory wave was visualized by the appearance, after swallow, of a relaxation of the sustained contraction that was induced by insufflation of a balloon at different levels of the distal esophagus. This relaxation started simultaneously over the entire distal esophageal body but lasted progressively longer in progressively more distal segments. The timing of the relaxation of the artificial high pressure zone strongly suggests that it represents the manometric equivalent of the electrical postdeglutitive smooth muscle membrane hyperpolarization described in animal studies and the esophageal body equivalent of the postdeglutitive LES relaxation. (Adapted from Sifrim [21].)

Anatomy of the gastroesophageal junction highlighting the relationship between the diaphragm and the lower esophageal sphincter (LES). The esophagus, vagal trunks, and esophageal branches of the left gastric vein traverse the diaphragm through the esophageal hiatus. The crural fibers of the diaphragm encircle the esophagus in such a manner that a contraction of the muscle during inspiration constricts the esophagus.

**FIGURE 1-29.**

**FIGURE 1-30.**
Axial hiatus hernia. Most hiatal hernias are classified as axial or sliding. With the axial hiatal hernia there is decreased tethering by the phrenoesophageal ligaments and enlargement of the esophageal hiatus, which allows the gastric cardia to herniate upward into the thorax. The degree of herniation is highly variable. With small hernias only a small amount of the lesser curve and part of the fundus may be apparent, and with large hernias the entire fundus of the stomach may be visible in the thorax.

Paraesophageal hernia. In patients with paraesophageal hiatal hernias the cardioesophageal junction characteristically maintains normal position because the paraesophageal ligaments are normally arranged around most of the esophagus. A break in the continuity of the phrenoesophageal membrane allows the esophageal hiatus to enlarge, allowing a variable portion of the gastric fundus access into the thorax alongside the esophagus. As the hernia enlarges the body of the stomach is also drawn into the hernial sac whereas the pylorus and duodenum remain in the abdominal cavity, still tethered by their normal attachments.

**LOWER ESOPHAGEAL SPHINCTER**

Intrinsic lower esophageal sphincter (LES) pressure. The LES is a 3- to 4-cm segment of tonically contracted smooth muscle with a resting tone that varies from 10 to 30 mm Hg relative to gastric pressure. This positive pressure gradient between the stomach and the esophagus can be considered the driving force for gastroesophageal reflux, with the high pressure zone at the gastroesophageal junction considered a barrier to the prevention of reflux of gastric contents. The high pressure zone has two components: (1) a tonic pressure caused by the LES, which is believed to be caused by a combination of myogenic factors, active tonic neural excitation, and complex interactions of other neural and hormonal factors [22], and (2) superimposed phasic pressure oscillations resulting from contractions of the diaphragmatic crus that encircles the LES [23–26].

This figure shows the contribution of diaphragm contraction (green portion) to basal LES pressure (orange portion). Note that a significant component of LES pressure is contributed by the diaphragm and that augmentation of the LES pressure corresponds temporally and quantitatively with the augmentation of crural electromyographic activity. (Courtesy of Dr. R. Mittal, Charlottesville, VA.)
Extrinsic control of the lower esophageal sphincter (LES). The LES tone is subject to both vagal and adrenergic influences, with vagal stimulation activating both excitatory (cholinergic) and inhibitory (nitric oxide) myenteric neurons. This figure illustrates the extrinsic control of the LES. A, Myelohyoid electromyography (arrow indicates the time of the pharyngeal swallow). B and C, Activity of the vagal inhibitory and excitatory fibers, respectively, to the LES at the time of swallow. D, Intraballoons (bolus) pressure at time of swallow. Note that the excitatory component is selectively activated under basal conditions and the inhibitory component is activated during swallow and mediates LES relaxation. (Adapted from Miolan and Roman [27].)

Epiphenic diverticulum as seen on barium swallow. An esophageal diverticulum is an outpouching of the esophageal wall from the lumen that may contain all portions of the esophageal wall or may lack the muscularis mucosa. Epiphenic diverticula are usually located within 10 cm of the gastroesophageal junction and are thought to be pulsion-type diverticula. These are hypothesized to result from abnormal pulsion forces associated with abnormal esophageal motility and abnormal lower esophageal sphincter relaxation, producing increased intraluminal pressure, thus allowing outpouching to occur.

Endoscopic view of an epiphenic diverticulum. The arrow indicates the opening of the diverticulum. The lumen of the gastroesophageal junction is to the side.
Substances influencing lower esophageal sphincter (LES) pressure. Intra-abdominal pressure, gastric distension, food, and many peptides and drugs affect LES pressure.

**Figure 1-37.**

Transient lower esophageal sphincter (LES) relaxation. Individual gastroesophageal reflux events occur by one of three mechanisms: transient LES relaxations, abdominal strain, or free reflux across a patulous LES [28]. Transient LES relaxations occur in both normal individuals and in patients with gastroesophageal reflux; they are the only potential mechanism for reflux during periods in which the LES is normal. These relaxations are part of the reflex that normally allows for gas venting from the stomach and may be triggered by fundic distension with air [29,30]. This example of transient LES relaxation was recorded in an asymptomatic individual. LES pressure is referenced to gastric pressure. Note that the transient LES relaxation persisted for almost 30 seconds whereas the swallow-induced LES relaxation (Sw) lasted for only 5 seconds. Also note the absence of an electromyographic (EMG) signal from a submental electrode during the transient LES relaxation, signifying the absence of a pharyngeal swallow. (Adapted from Kahrilas and Gupta [31].)
REFERENCES


The pharynx serves as a conduit for both air and food passage and, as such, converts from one function to the other over a thousand times each day. A precise coordination exists between pharyngeal function as a food conduit and as an airway while providing passage of the ingested material through the pharynx and into the esophagus without endangering the safety of the airway. The influence of pharyngeal sensory receptors on the upper gastrointestinal tract as well as on the glottis has been elucidated in recent years. These influences, in the form of several reflexes, exert a stimulatory effect on some parts of the gastrointestinal tract while exerting an inhibitory effect on other parts. These reflexes include the pharyngeal-upper esophageal sphincter contractile reflex, pharyngo-glottal closure reflex, and pharyngo-lower esophageal sphincter and pharyngo-esophageal inhibitory reflexes. On the other hand, closure reflexes of the glottis in response to esophageal distention have been described. These findings confirm the presence of a close and diverse functional relationship between the aerodigestive tract (including the pharynx and glottis) and the upper gastrointestinal tract (including the upper esophageal sphincter, esophageal body, and lower esophageal sphincter).

This chapter provides a pictorial review of these diverse functions to increase the reader’s understanding of the intricate physiologic relationship between the airway and digestive tracts. It concludes with images of benign and malignant abnormalities of the pharyngeal and laryngeal structures.
Schematic drawings of the pharynx from posterior (A) and lateral (B) perspectives. Note the relationships of the valleculae and piriform sinuses to the base of tongue, epiglottis, and larynx. Because the pharynx is part of both the respiratory and alimentary tracts, both the nasopharynx and larynx must be effectively isolated from the pharynx during swallowing. (Adapted from Donner et al. [1].)
Endoscopic view of the regions of the pharynx as seen when traversed transnasally down to the region of the upper esophageal sphincter. A, The nasopharynx at rest as seen from the posterior nares superior constrictor; seen bilaterally, the soft palate is in a resting position located anteriorly. The base of the skull is visible straight ahead. A glimpse of the distal nasopharynx is seen between the skull base and soft palate. B, The soft palate is now elevated toward the tip of the scope, and the superior constrictors are adducted toward the midline. These two events have sealed the nasopharynx during a swallow. The opening of the eustachian tubes is seen bilaterally. C, With the endoscope just entering the proximal region of the nasopharynx, the posterior pharyngeal wall is seen at 6 o'clock, the soft palate and uvula are visible at 12 o'clock, and the lateral pharyngeal wall is seen bilaterally. The lateral diameter of the pharynx is significantly larger than its anteroposterior diameter. D, The tip of the endoscope has advanced further distally. The uvula is seen at 12 o'clock, and the edge of the epiglottis is now visible. E, The tip of the endoscope has advanced beyond the uvula and now is located in the oropharynx. The base of the tongue is at 12 o'clock, and the epiglottis, in resting position, is at the center of the image. The vallecular spaces between the tongue and anterior aspect of the epiglottis are wide open. The posterior wall is at 6 o'clock. The glottal structures are barely visible in the distance just posterior to the epiglottis. F, The tip of the endoscope is now advanced to the level of the epiglottal tip. The vocal cords are visible as the two arms of a “V.” Arytenoids processing are seen at the posterior end of the cords, and the aryepiglottic folds are visible between the arytenoids and the epiglottis. The posterior commissure is located between the arytenoids. The piriform sinuses are seen bilaterally on two sides of the glottis. The area of the opening of the upper esophageal sphincter is seen between the posterior commissure and the posterior pharyngeal wall. G, The tip of the endoscope has advanced distal to the free margin of the epiglottis. The vocal cords are seen partially closed, the arytenoids are adducted, and the aryepiglottic folds and piriform sinuses are seen bilaterally. The area of the opening of the upper esophageal sphincter is visualized between the posterior aspect of the glottis and the posterior pharyngeal wall.
Fluoroscopic view of the pharynx in lateral position during quiet nasal breathing. The mouth is closed, the air column is seen extending into the oral cavity, and the uvula is in resting position without contacting the posterior pharyngeal wall. The air column extends posterior to the uvula into the nasopharynx. The pharyngeal air column is seen extending distally to the level of the vocal cords and beyond into the trachea. Lateral view of the vallecula is observed between the posterior tongue and epiglottis.

**Pharynx during various functions**

Relationship of deglutitive vocal cord kinetics to other events of the oropharyngeal phase of swallowing during 5-mL barium swallows. Bolus transit through the pharynx and across the UES begins and ends while the vocal cords are at maximal adduction.

Swallowing is a highly coordinated physiologic event that involves sequential and overlapping contractions of the facial, cervical, oral, pharyngeal, laryngeal, and esophageal muscular apparatus, and results in transit of ingested material and saliva from the mouth into the stomach. Swallowing can be divided into four consecutive phases representing the anatomic regions traversed by the bolus: preparatory, oral, pharyngeal, and esophageal. From a functional point of view, events that take place during oropharyngeal swallowing contribute to transit of the bolus and protection of the airway. The transit and protective aspects of oropharyngeal swallowing are highly coordinated. Oropharyngeal transit occurs during the full activation of the protective aspect of swallowing. A successful oropharyngeal swallow requires the effective and coordinated actions of the anatomical elements involved in these two functions. TB-O—onset of tongue base movement; SH-O—onset of superior hyoid movement; SM-O—onset of submental myoelectrical activity; UESO—upper esophageal sphincter opening; OT-O—onset of bolus movement from the mouth; PT-O—arrival of bolus into pharynx. (Adapted from Shaker [2].)
Videofluoroscopic recording of 5-ml barium swallow during pharyngeal phase of deglutition demonstrating peristaltic, bolus, and prebolus zones. A, Barium bolus (B) has just entered pharynx. Vestibule (V) is partially closed. Upper border of tracheal air column (T) corresponding to vocal cords is shown. B, C, Barium has progressed into pharynx 0.07 and 0.17 seconds later. The laryngeal vestibule is now completely closed and the larynx is displaced anteriorly. D, The barium bolus has progressed further. Swallowed air is seen traversing ahead of barium, while luminal closure (arrow) follows barium. E, Clearer views of the peristaltic zone resulting in luminal closure (curved arrow), bolus zone filled with liquid barium (B), and prebolus zone (thin arrows). F, Laryngeal vestibule has now reopened. The swallow has ended and the larynx has returned to its original position. LV—laryngeal vestibule. (From Kern et al. [3]; with permission.)

Hypopharynx and glottis viewed by videofluoroscopy, A, and videoendoscopy, B. Although most of the anatomic structures involved in swallowing are visualized by both modalities, the hyoid bone is observed only by the x-ray technique, whereas vocal cords are visualized better by endoscopy; Arrow indicates area of upper esophageal opening. a—arytenoids; e—epiglottis; f—aryepiglottic fold; h—hyoid bone; l—laryngeal vestibule; p—piriform sinus; r—trachea; s—soft palate; v—vocal cord.
Movement of upper esophageal sphincter (UES) during swallowing. As illustrated, both the sensor and UES move orad during swallowing, but the movement is asynchronous. The sensor moves first, probably as a result of elevation of the soft palate. It reaches a maximum orad excursion of approximately 1 cm. The UES segment then begins to rise, reaching a maximum excursion of 2 cm, passing the sensor as the latter descends back to its resting position. Elevation of the UES is caused by laryngeal elevation, which may also be a factor, along with UES relaxation and pharyngeal propulsive force in opening the pharyngoesophageal segment. This asynchronous movement makes positioning of the manometric sensor difficult. Traditional placement in the center of the high-pressure zone results in a period in which the sensor actually descends (relative to UES position) into the cervical esophagus, causing an artifactually prolonged relaxation. An alternative approach to the problem of sphincter segment motion is the use of a water-perfused sleeve catheter assembly, which records the highest pressure along the sleeve's length. The sleeve ensures that axial movement does not result in displacement of the sphincter segment off the recording sensor. (Adapted from Dodds et al. [4].)
Glottal function during esophageal belch. Ventilation of gastric or esophageal gas across the upper esophageal sphincter (UES) into the pharynx may be accompanied by entry of food particles or acid mist into the hypopharynx and may predispose the airway to aspiration. Glottal closure is an integral component of both esophageal and gastric belch reflexes that prevents aspiration of regurgitated material into the airway. The glottal closure mechanism during belching has two tiers of closure: vocal cord closure and aryepiglottic approximation. Glottal and UES functions are closely coordinated during belching; during belching, the UES is pulled open after its relaxation.

A–D, Glottal function during esophageal belch unaccompanied by intragastric pressure increase. Panel A, The glottis immediately before belch; vocal cords are at resting position (arrows). Panel B, Complete vocal cord and arytenoids adduction 0.3 seconds later (arrow), resulting in closure of introitus to trachea before UES opening. Panel C, Triangular opening (arrow) of UES during belching while introitus to trachea is still closed. Panel D, Return of cords to resting position and opening of introitus. (From Shaker [5]; with permission.)

Comparison of upper esophageal sphincter (UES) opening during belching and swallowing. A, Endoscopic view of glottis and hypopharynx at rest. Area of UES opening is shown by arrow. B, Oval UES opening during swallowing. C, Slit-like UES opening during belching. D, Triangular UES opening during belching. Although the shape of the UES opening during belching may vary between slit-like and triangular, its shape during swallowing is oval.
Pharyngoesophageal manometric findings in a patient with Kearns-Sayre syndrome (KSS) complicated by cervical dysphagia compared with an age-matched healthy patient. These findings consist of near absence of peristaltic pressure activity in the pharynx, abnormally low resting upper esophageal sphincter (UES) pressure, and lack of peristalsis in the striated portion of the esophagus. The recordings were obtained using six intraluminal pressure transducers spaced 1.5 cm apart. During resting, the most distal transducer is within the UES; during swallowing (SW), because of orad excursion of the UES, the transducer located immediately above the most distal transducer relocates to the sphincter. This phenomenon is heralded by a hump (arrow) followed by a pressure decline because of UES relaxation. With this arrangement, during swallowing the remaining four transducers record pharyngeal pressure activity from a span of 4.5 cm proximal to the UES. As seen, the patient with KSS generates negligible pharyngeal pressure compared with the control (note differences in scale). (Adapted from Shaker et al. [6].)

Effect of volume and age on duration of pharyngeal peristaltic pressure wave. Although in the young, A, duration of peristaltic pressure wave showed precipitous aboral decrease from sites P1 to P4 (P<0.01), in the elderly, B, this aboral decrease was interrupted at site P4, at which point duration increased significantly instead of decreasing further and became similar to the measurement at site P2. Between-group comparison showed that in the elderly, duration of pharyngeal peristaltic pressure for tested volumes at site P4 was significantly greater than that of the young. (Adapted from Shaker et al. [7].)
FIGURE 2-13.

Lateral and anteroposterior views of the pharynx and the upper esophageal sphincter during swallow of 5 ml barium. A. Barium bolus is still in the oral cavity; the head of the bolus enters over the posterior aspect of the tongue. The pharyngeal cavity is stained with previously swallowed barium sulfate bolus. B. The head of the swallowed barium bolus has reached the area of the upper esophageal sphincter. The tail of the bolus is just exiting the oral cavity. C. The swallowed barium bolus is seen traversing the upper esophageal sphincter and has entered the upper esophagus. The tail of the bolus is still in the pharynx. The upper esophageal sphincter (UES) is wide open without any evidence of cricopharyngeal bar or acha­lasia. A minor posterior indentation by vertebral osteophyte is seen. D. Anteroposterior view of the barium bolus held in the mouth; the vallecula and pyriform sinuses coated with barium during a previous swallow are clearly visible. E. Anteroposterior view of the barium bolus traversing through the UES and entering the proximal esophagus. The UES is wide open.

PATHOLOGIC FINDINGS

FIGURE 2-14.

Modified barium swallow in a patient with cricopharyngeal (CP) achalasia. The term cricopharyngeal achalasia was originally used by radiologists on observation of a prominent pharyngoesophageal segment during swallowing, causing inadequate opening of the pharyngoesophageal junction in patients with cervical dysphagia. A variety of neurogenic causes may result in disordered upper esophageal sphincter (UES) relaxation, or incoordination may develop from primary neurogenic or myogenic cricopharyngeus muscle with pharyngeal peristalsis. Delayed or failed CP muscle opening has been reported in 30% to 50% of patients with brain stem lesions, central degenerative disorders, and posterior cerebellar artery thrombosis, as well as in bulbar paralysis. Primary myogenic CP dysfunction may be caused by loss of elasticity as well as fibrotic changes of the UES caused by several conditions, including gastroesophageal reflux and aging. The primary myogenic abnormality of Zenker's diverticulum first described by Ludlow in the 18th century results from herniation of the pharyngeal mucosa through a weakened area of the posterior pharyngeal wall.

(continued on next page)
Concurrent manometric and radiographic studies show a significantly greater intrabolus pressure in the hypopharynx accompanied by a reduced sagittal and transverse diameter of the sphincter opening. After CP myotomy, the intrabolus hypopharyngeal pressure and maximal area of deglutitive UES opening return to normal.

In secondary CP dysfunction, the pathologic state lies within the suprahypopharyngeal muscles. These patients are incapable of exerting adequate traction force to pull the UES sufficiently open during swallowing and lack normal anterior or superior laryngeal movement. This condition may be seen in elderly patients with a compensated swallowing mechanism. It can also be seen in patients with inflammatory muscular disease, such as inclusion body myositis, in which excitatory impulses to the CP muscle are inhibited during swallowing. Although the UES relaxes, it does not open adequately because of insufficient distraction.

Depending on the severity of the condition, patients with UES dysfunction may present with aspiration pneumonia, swallowing-related cough, choking, repeated swallowing, food sticking in the throat, and weight loss.

A–C, Videofluoroscopic views of a modified barium swallow in a patient with CP achalasia. This patient’s symptoms included a feeling of incomplete swallow, deglutitive cough, and pharyngeal residue. Panel A, During the pharyngeal phase of swallowing, the barium bolus is seen in the pharynx immediately before the upper esophageal sphincter (UES) opens. There is still a trace of barium within the UES and proximal esophagus (arrow). Vestibular penetrations (p) and nasal regurgitation (R) are also present. Panel B, The barium bolus is seen traversing the UES. Incomplete opening of the CP muscle results in a prominent indentation (arrow) with marked narrowing of the UES lumen. However, the barium bolus has filled the proximal esophagus. Nasal regurgitation (R) and vestibular penetration (p) are also present. Panel C, The UES has closed after the pharyngeal phase of swallowing has ended, with a large amount of barium remaining in the hypopharynx (arrow).

D, Complete manometric deglutitive UES relaxation in an elderly patient during UES manometry using a sleeve device. The UES pressure declines sharply to slightly below atmospheric pressure after the onset of UES relaxation (UESR-O). E, UES manometry in a patient with CP achalasia using a sleeve device. Although the UES pressure decreases, it does not reach atmospheric pressure. F, UES manometry utilizing a pneumohydraulic side hole in the patient with CP achalasia. During swallowing, the orad excursion of the UES displaces the side hole of the manometric catheter out of the UES into the proximal esophagus. This results in a spurious recording of UES relaxation. G,H, Examples of electromyographic recordings from the mylohyoid–geniohyoid muscle group (MH), inferior pharyngeal constrictor (IC), and CP muscle for a healthy patient (panel G) and a patient with CP achalasia (panel H) during dry swallow.

(continued on next page)
Note that the MH and IC do not exhibit any tone before swallowing, whereas the CP muscle maintains a basal tone during resting. In the normal control subject, swallowing results in transient inhibition of CP tone, myoelectrical activity of the MH group, and the inferior constrictors. In contrast, swallowing does not lead to inhibition of CP tone in the patient with CP achalasia. CP achalasia is a common cause of dysphagia, resulting in incomplete pharyngeal clearance and aspiration. The disorder may be caused by cerebrovascular accident, pseudobulbar palsy, nasopharyngeal cancer, polyomyelitis, thyroid myopathy, cervical vagotomy, surgical ablation of the pharynx, schizophrenia, polymyositis, dermatomyositis, ocurophtaryngeal syndrome, or amyotrophic lateral sclerosis [8]. The most common cause is cerebrovascular disease [9]. Treatment options include dilation and CP myotomy, both of which have been used to successfully alleviate the dysphagia. (Panels D–F adapted from Shaker et al. [10].)

Zenker’s diverticulum. A, Anteroposterior and B, oblique views of a Zenker’s diverticulum. Note that the barium bolus has been cleared from the pharynx and esophagus after swallowing but remains in the diverticulum. Minimal residue is present in the piri­form sinuses. The most common type of symptomatic esophageal diverticulum is Zenker’s or pharyngoesophageal diverticulum. Zenker’s diverticula occur as a posterior protrusion of the pharyngeal mucosa through Killian’s dehiscence. Killian’s dehiscence is the space between the oblique fibers of the inferior constrictor muscle and the transverse cricopharyngeal muscle fibers [11]. It is a pulsion diverticulum often related to cricopharyngeal muscle dysfunction [12]. Zenker’s diverticula occur throughout adulthood but most commonly present in the seventh and eighth decades of life [13]. Patients most commonly present with symptoms of dysphagia, regurgitation of foul undigested food, halitosis, noisy deglutition, and weight loss. The diagnosis of Zenker’s diverticula is based on history and contrast radiography. Indirect laryngoscopy rarely reveals the sac but may reveal pooling of secretions in the piri­form sinuses. Barium swallow defines the diverticula size and location. Most frequently the sacs protrude on the left side near the posterior midline. Often there is evidence of cricopharyngeal muscle dysfunction associated with the diverticula. Esophagoscopy is hazardous and should be avoided because the diverticulum is easily perforated. Surgical management of Zenker’s diverticula is indicated when the sac is large enough to be symptomatic. Options include an endoscopic approach with incision of the party wall (Dohlman’s procedure) or an external approach with an excision or pexy of the diverticula and cricopharyngeal myotomy [14].

Abnormal upper esophageal sphincter (UES) opening in Zenker’s diverticulum. It has been assumed for many years, based on the radiographic appearance of the pharyngoesophageal segment, that Zenker’s diverticula result from increased pharyngeal pressure due to UES dysfunction. Although early manometric studies using high-compliance water-perfusion systems appeared to confirm this impression, later studies using improved low-compliance technology failed to confirm sphincter dysfunction. Sensor displacement may explain the results of these studies. The figure shows the effect of bolus volume on intrabolus pressure and UES relaxation. Increased intrabolus pressure and failure of UES relaxation is a volume-related phenomenon seen in patients with Zenker’s diverticula, and not in healthy patients. These findings are felt to support the role of UES dysfunction in the pathogenesis of Zenker’s diverticula. (Adapted from Cook et al. [11].)
Supraesophageal reflux disease (SEGERD) denotes gastroesophageal refluxate that reaches the structures above the upper esophageal sphincter. A, Normal larynx. Note the lack of interarytenoid edema, secretions, and erythema. B, Laryngopharyngeal reflux disease. Interarytenoid edema is seen, with thick secretions over the vocal folds and loss of vascular markings. C, Reinke's edema. This condition denotes mucoid, gelatinous fluid in the superficial layer of the lamina propria (Reinke's space). Note the associated interarytenoid edema and erythema, as well as the obliteration of mucosal vascularity by the edema. Reinke's edema is commonly associated with cigarette smoking, voice abuse, and SEGERD; it may also be associated with hypothyroidism. SEGERD has been implicated in the pathogenesis of several otolaryngologic disorders such as chronic posterior laryngitis, laryngeal contact ulcer or granuloma, paroxysmal laryngospasm, vocal cord nodule, Reinke's edema, subglottic stenosis, laryngotracheal stenosis, globus pharyngeus, laryngeal and hypopharyngeal carcinoma, and sudden infant death syndrome [15].

**DIAGNOSIS OF SUPRAESOPHAGEAL COMPLICATIONS OF REFUX DISEASE**

<table>
<thead>
<tr>
<th>SYMPTOMS</th>
<th>PHYSICAL FINDINGS</th>
<th>DIAGNOSTIC TESTING</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic or intermittent hoarseness</td>
<td>Edema of the arytenoids mucosa</td>
<td>Esophageal endoscopy (esophagoscopy)</td>
</tr>
<tr>
<td>Voice fatigue or break</td>
<td>Edema of posterior third of the vocal cords</td>
<td>Barium esophagogram</td>
</tr>
<tr>
<td>Chronic or frequent throat clearing</td>
<td>Pachyderma larynges</td>
<td>Ambulatory 24-hour pharyngoesophageal pH monitoring</td>
</tr>
<tr>
<td>Excessive throat mucus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postnasal drip</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sore throat</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dysphagia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Globus sensation</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Supraesophageal complications of reflux disease (SEGERD). The diagnosis of SEGERD is based upon history, physical examination, and appropriate objective testing methods [15]. Because neoplastic lesions of the larynx, pharynx, or esophagus may produce similar symptoms, they must be excluded. Esophagoscopy provides visualization of the esophageal mucosa and is often performed as an initial investigation for traditional reflux symptoms [16]. The treatment of SEGERD includes the reduction of upper airway acid exposure, lifestyle modifications, acid suppressive therapy, and surgery. Acid suppression may include H2 blockers or proton pump inhibitors when H2 blockers fail. Patients who are intolerant of acid suppression therapy or require long-term therapy may benefit from surgical treatment with Nissen fundoplication [17].
Granuloma of the larynx. These lesions usually occur on the posterior aspect of the vocal folds on the medial surface of the arytenoids. They are associated with supraesophageal reflux disease (SEGERD) and voice abuse [15]. These patients present with hoarseness but frequently have symptoms of SEGERD including globus pharyngeus and throat-clearing. Diagnostic testing for granuloma of the larynx should include videolaryngoscopy and evaluation for SEGERD (see Fig. 2-18). Note the location at the vocal process and the pedunculated nature of the lesion. Vocal fold granulomas should be treated primarily as a medical disease, with surgery reserved for medical failures. Management of granuloma of the larynx should include a trial of antireflux therapy for at least 3 months, even in patients with no symptoms of reflux disease. Close monitoring is advised; if no improvement is noted after 6 to 8 weeks, excisional biopsy should be considered to exclude malignancy. Voice therapy may be considered in patients with evidence of voice abuse. If the lesions recur, treatment options include more aggressive evaluation and management of SEGERD (including Nissen fundoplication) and steroid injection into the base of the lesion after re-excision. Botulinum toxin may also be considered in patients with continued difficulties.

Cervical osteophytes causing obstruction. Cervical osteophytes are commonly seen in middle-aged and elderly patients. They are usually an incidental finding. Even in patients with swallowing disorders, osteophytes are rarely responsible for dysphagia. Symptoms can occur by one of two basic mechanisms: either through narrowing by direct compression or by the impairment of pharyngeal wall movement in the area of osteophytes. Plain film shows bony excrescences along the anterior aspect of many of the cervical spine vertebral bodies consistent with diffuse idiopathic skeletal hyperostosis (Forestier’s arthritis). Note the proximity of the epiglottis to the upper border of the bony mass. Unless videoradiographic study demonstrates greater than 50% narrowing of the lumen, both liquid barium and a barium-impregnated solid bolus usually pass without delay in the absence of some other abnormalities. (From Jones et al. [18]; with permission.)

Cervical osteophytes causing impaired motility. Aside from compromising swallowing by luminal obstruction, osteophytes may cause dysphagia by affecting the motor function of the pharynx. Radiograph from a frame of a video study demonstrates retention in the valleculae and piriform sinuses and some contrast in the larynx. The videoradiographic study demonstrated a pharyngeal propagative wave that stopped abruptly at the level of the osteophyte and that the epiglottis did not tilt fully as it hit the osteophyte posteriorly. The lumen, however, appeared to open adequately during bolus passage. The interrupted peristaltic wave may be caused by fixation of the soft tissue overlying the osteophyte. (From Jones et al. [18]; with permission.)
Leukoplakia and carcinoma in situ. Leukoplakia describes white, plaque-like lesions. It may result from chronic inflammation or represent a malignancy. A, Benign leukoplakia of both vocal cords in a patient presenting with hoarseness. It is typically flat and located on the upper margin of the vocal folds. Even benign disease has a premalignant potential. The biopsies demonstrated epithelial atypia. B, Leukoplakia of the right vocal cord, in a patient with hoarseness. The lesions are more elevated and nodular in appearance than those in panel A. There is also a small red nodule on the left vocal fold. Biopsies revealed bilateral carcinoma-in-situ and areas of invasive carcinoma on the right side. (Courtesy of Haskins Kashima, Baltimore, MD.)

Cancer of the larynx. A, Cancer of the right vocal fold, appearing as a distinct nodular thickening. The entire right vocal fold looks redder than the left, although a white patch on the nodule is evident. Cancer of the larynx can be colored white, red, or (as in this patient) variegated, depending on the degree of keratosis present in a given area. B, Total laryngectomy specimen with supraglottic squamous cell carcinoma. In contrast to patients with hypopharyngeal carcinomas, laryngeal lesions often present initially with hoarseness; pain develops later. Dyspnea and stridor may be associated with obstructive lesions, while dysphagia, odynophagia, and otalgia are associated with invasion of the extralaryngeal structures. At the time of diagnosis, approximately 25% have regional lymph node involvement. Small tumors that do not impair vocal fold mobility can be managed by either surgical laser excision or radiotherapy. The prognosis for small glottic lesions is relatively good. More advanced lesions may be treated with radiation therapy, with salvage total laryngectomy for persistent or recurrent disease, or with primary total laryngectomy. Partial laryngectomy may be an option in some cases, depending on the site or extension of the tumor. (Panel A courtesy of Haskins Kashima, Baltimore, MD.)

Cancer of the pharynx. Endoscopic view of a large mass involving the left pharynx. Notice the mass with a granular mucosal surface protruding from the left aryepiglottic fold as well as the left wall of the pharynx. The white erosion posterior to the mass is the site of a recent biopsy. Note that the left arytenoid process deviated to the right as a result of pressure from the mass. The patient presented with a 6-cm mass on the left side of the neck, representing an involved lymph node. The patient had a long history of esophageal dysphagia and a tight stricture in the distal esophagus that had required dilatation 1 year before he presented with the neck mass. The last esophagoscopy 8 months before had not detected a pharyngeal abnormality.
Cancer of the tongue base. Radiograph of a patient with a cancer of the base of the tongue. There is an extremely large, bulky tumor of the whole of the base of the tongue consistent with cancer. Note that this interferes with the function of the tongue and the epiglottis, which appears somewhat thickened and may be involved. There is retention in the valleculae. (From Jones et al. [18]; with permission.)

Figure 2-26. Cancer of the tongue base. Radiograph of a patient with a cancer of the base of the tongue. There is an extremely large, bulky tumor of the whole of the base of the tongue consistent with cancer. Note that this interferes with the function of the tongue and the epiglottis, which appears somewhat thickened and may be involved. There is retention in the valleculae. (From Jones et al. [18]; with permission.)

Carcinoma of the hypopharynx. This laryngectomy specimen demonstrates a tumor of the right pyriform sinus. Cancers of the head and neck represent the sixth most common cancers in the world. Early detection significantly improves long-term survival; thus, a high index of suspicion is helpful. The majority of these tumors are squamous cell carcinomas and are usually associated with heavy tobacco and alcohol use. Patients with hypopharyngeal carcinomas often present with odynophagia, weight loss, and referred otalgia due to glossopharyngeal nerve involvement. Therefore, any patient with unexplained, persistent otalgia should have a thorough examination of the head and neck. The majority (>50%) of these patients present with cervical metastases on examination. The treatment of the majority of hypopharyngeal lesions consists of laryngopharyngectomy with neck dissection and postoperative radiation therapy. Overall five-year survival rates with combined modality therapy are 35% to 40%.

Figure 2-27. Carcinoma of the epiglottis. A, Radiograph shows obvious thickening of the epiglottis, and the tongue base appears nodular. The extent of tumor involvement is unclear. B, With insufflation by means of phonation, and by coning in on the area of the epiglottis, it is now clear that the valleculae are involved by small nodular masses and that the aryepiglottic folds appear nodular. Oblique views with insufflation help determine whether involvement is unilateral or bilateral. Without insufflation the extent of tumor involvement may be underestimated, as seen in this example, or the tumor may not be evident at all. (From Rubessin et al. [19]; with permission.)
Laryngoceles. A, Endoscopic view of a patient with a left-sided internal laryngocele. Note the swelling of the aryepiglottic fold. B, Computed tomography (CT) scan of a patient with bilateral combined laryngoceles. Note the anatomic distortion and airway compromise secondary to the larger right-sided laryngocele. A laryngocele is an air-filled dilation of the saccule of the laryngeal ventricle. The etiology of laryngoceles is uncertain, although some authors have cited an increase in transglottic pressure [22]. Another cause may be laryngeal carcinoma causing partial obstruction of the laryngeal saccule [23]. Laryngoceles may be classified as internal or combined internal and external [22]. Internal laryngoceles are confined to the larynx and present as cystic swellings of the aryepiglottic fold. Combined laryngoceles result from herniation of the laryngocele through the thyrohyoid membrane. The most common symptoms of laryngoceles include hoarseness, cough, and a foreign-body sensation. Laryngoceles with a large external component may present as a lateral neck mass. Large laryngoceles or infection (laryngopyocele) may result in airway compromise. The evaluation of patients with laryngoceles includes a thorough head and neck exam and CT scan of the neck. Endoscopy should be performed to rule out obstructing carcinomas. Surgical treatment for patients with laryngoceles is recommended; in patients with a combined internal and external laryngocele, an external approach with excision is suggested [24]. An endoscopic marsupialization may be considered in patients with symptomatic internal laryngoceles [25].

Pharyngeal ulcerations in cicatricial (bullous) pemphigoid. A, Severe ulceration of the hypopharynx. A large confluent ulcer is present on the posterior pharynx. In addition, there is a small ulcer of the overlying the right arytenoid. B, Well-demarcated elongated and stellate ulcerations of the oropharynx (the back of the tongue is seen to the right). The presence of gingivitis and conjunctivitis in the patient suggests cicatricial pemphigoid. Although classically thought of as a skin disease, only about 50% of patients with cicatricial pemphigoid actually have skin involvement. Of interest is that the patient presented with dysphagia and videoradiographic studies suggesting pharyngeal paresis. Inflammatory changes can cause pharyngeal weakness that can appear neurogenic in origin. Whether the motor abnormalities seen represent a direct effect of edema or an effect of associated myositis or neural injury is uncertain.
Hyoid penetration
Cricopharyngeal bar
Jet effect

FIGURE 2-30.
Hypopharyngeal (cricopharyngeal) bar. A, Lateral radiograph in a patient with hypopharyngeal bar. There is a prominent horizontal bar protruding from the posterior wall of the pharynx at the level of cervical vertebral bodies 5 and 6. There is a flow phenomenon (jet effect) in the cervical esophagus, produced by the barium “squirting” through the narrowed pharyngoesophageal (PE) segment. B, Pharyngeal paresis with a prominent cricopharyngeus resulting from lack of “push” with a jet phenomenon indicating luminal narrowing. There is also laryngeal penetration during swallowing and subglottic extension into the trachea. As in panel A, there is a hypopharyngeal bar; however, the presence of marked laryngeal penetration suggests that there is pharyngeal dysfunction as well; an impression confirmed on review of the videoradiography, which demonstrated marked pharyngeal paresis. Hypopharyngeal bars are common and often associated with other pharyngeal and esophageal abnormalities. In most patients, the bar is a secondary phenomenon and does not appear to contribute significantly to the patient’s symptoms. The bar in this patient narrows the lumen by about 50% (when compared with the normal esophagus). This is sufficiently tight to cause symptoms without other contributing factors. Whether the hypopharyngeal bar is a significant factor in the production of dysphagia in patients with a neurogenic pharynx may be difficult to determine. It appears that opening of the PE segment is not caused only by relaxation of the upper esophageal sphincter. The PE segment is also “pulled” open by the elevating larynx and “pushed” open by the advancing bolus. Defects in any of these components may produce the radiographic finding of a hypopharyngeal bar. A myotomy may be inappropriate, or at least less likely to be effective, if upper esophageal sphincter relaxation is normal. (From Jones et al. [20]; with permission.)
Pharyngoesophageal interrelationships. An elderly male patient presenting with chronic and solid food dysphagia. The radiograph (taken from an oblique angle) demonstrates the unusual combination of a moderate-sized Zenker’s diverticulum and a midesophageal malignant stricture. Although the specific combination is rare, multiple abnormalities of pharyngeal function or structure are more generally appreciated. At the least, this poses difficulty in determining the contribution of the specific abnormalities to clinical presentation. In this patient, laser therapy of the esophageal cancer successfully eradicated his dysphagia, but the coughing was unaffected and presumably was caused by the diverticulum. The possibility that combined abnormalities of the pharynx and esophagus may be causal relationship should also be considered.

Changes in upper esophageal sphincter (UES) pressure during esophageal stimulation. The UES reacts to various types of stimulation. In this study by Andreollo et al. [21], balloon distention within the proximal esophagus produces an increase in UES pressure. The increase is directly related to the amount of distention. While this observation may theoretically account for the finding of a prominent hypopharyngeal bar in some patients with esophageal dysmotility or obstructing lesion, this remains conjecture. (Adapted from Andreollo et al. [21].)
REFERENCES


Radiology and endoscopy are the two main diagnostic techniques used to evaluate patients with esophageal symptoms. Esophagoscopy has certain advantages including the ability to obtain biopsies and perform therapeutic intervention. In this chapter, endoscopic procedural issues such as sedation and antibiotic prophylaxis are discussed. The indications for diagnostic and therapeutic endoscopy and the complementary role of barium esophagram are also addressed. Examples of selected esophageal lesions such as diverticula, rings, and webs are shown.

Endoscopy of the esophagus with a rigid esophagoscope was first described by Bevan in 1868. Since then the technique has been superseded by fiberoptic endoscopy and later by video endoscopy. Video endoscopy, first introduced in 1983, uses a charge-coupled device to generate electronic images that are then displayed on a monitor. Video endoscopy not only allows for viewing by multiple examiners but also provides better images and storage of data. The images can also be enhanced, modified, and augmented. Ongoing technological improvements will lead to further advancement with smaller endoscopes, larger working channels, and better diagnostic techniques.
Flexible video endoscopy has emerged as the preferred method for examination of the esophagus for many indications. Video endoscopy can provide excellent image quality and allow data storage as well. Additionally, during endoscopy, diagnostic biopsies can be obtained and therapeutic interventions performed.

Patients undergoing endoscopy in the United States are usually premedicated with an intravenous narcotic and a benzodiazepine, with or without topical pharyngeal anesthesia. Studies have shown that many patients can tolerate endoscopy with topical anesthesia alone. The recent development of small caliber endoscopes, which can be passed transorally or transnasally, has the potential to decrease the use of intravenous sedation in the future.
GUIDELINES FOR THE APPROPRIATE USE OF PROPHYLACTIC ANTIBIOTICS FOR ENDOSCOPY

<table>
<thead>
<tr>
<th>PATIENT CONDITION</th>
<th>PROCEDURE CONTEMPLATED</th>
<th>ANTIBIOTIC PROPHYLAXIS</th>
<th>COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prosthetic valve</td>
<td>Stricture dilation, varix sclerosis</td>
<td>Recommended</td>
<td>High-risk conditions for development of infectious complication; procedures are associated with relatively high bacteremia rates</td>
</tr>
<tr>
<td>History of endocarditis</td>
<td>ERCP/obstructed biliary tree</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systemic-pulmonary shunt</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Synthetic vascular graft (&lt; 1 y old)</td>
<td>Other endoscopic procedures, including EGD and colonoscopy (with or without biopsy/polypectomy), variceal ligation</td>
<td>Insufficient data to make firm recommendation; endoscopists may choose on case-by-case basis</td>
<td>While conditions are high risk, procedures are associated with low rates of bacteremia</td>
</tr>
<tr>
<td>Rheumatic valvular dysfunction</td>
<td>Stricture dilation, varix sclerosis</td>
<td>Insufficient data to make firm recommendation; endoscopists may choose on case-by-case basis</td>
<td>Conditions pose lesser risk for infectious complications from endoscopic procedures</td>
</tr>
<tr>
<td>Mitral valve prolapse with insufficiency</td>
<td>ERCP/obstructed biliary tree</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertrophic cardiomyopathy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Most congenital cardiac malformations</td>
<td>Other endoscopic procedures, including EGD and colonoscopy (with or without biopsy/polypectomy), variceal ligation</td>
<td>Not recommended</td>
<td>Procedures are associated with relatively low bacteremia rates</td>
</tr>
<tr>
<td>Other cardiac conditions (including CABG, pacemakers, implantable defibrillators)</td>
<td>All endoscopic procedures</td>
<td>Not recommended</td>
<td>Conditions are low risk for infectious complications from endoscopic procedures</td>
</tr>
<tr>
<td>Obstructed bile duct</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pancreatic pseudocyst</td>
<td>ERCP</td>
<td>Recommended</td>
<td>Prudent, but not substitute for definitive drainage</td>
</tr>
<tr>
<td>Cirrhosis and ascites</td>
<td>Stricture dilation, varix sclerosis</td>
<td>Insufficient data to make firm recommendation; endoscopists may choose on case-by-case basis</td>
<td>Risk for infectious complications related to endoscopic procedures unestablished</td>
</tr>
<tr>
<td>Immunocompromised patient</td>
<td>ERCP/obstructed biliary tree</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Other endoscopic procedures, including EGD and colonoscopy (with or without biopsy/polypectomy), variceal ligation</td>
<td>Not recommended</td>
<td>Procedures are associated with relatively low bacteremia rates</td>
</tr>
<tr>
<td>All patients</td>
<td>Endoscopic feeding tube placement</td>
<td>Prophylaxis recommended</td>
<td>May decrease risk of soft tissue infection</td>
</tr>
<tr>
<td></td>
<td>Any endoscopic procedure</td>
<td>Not recommended</td>
<td>No literature to support infectious risk from endoscopic procedures</td>
</tr>
</tbody>
</table>

FIGURE 3-3.

Guidelines for the appropriate use of prophylactic antibiotics for endoscopy as developed by the American Society of Gastrointestinal Endoscopy [1]. The risk of infective endocarditis or other infectious complications from upper endoscopy is quite low. Nevertheless, transient bacteremia may occur following upper endoscopy with dilation of a stricture or sclerosis of varices. Therefore, antibiotic prophylaxis may be prudent in certain high-risk patients. (Adapted from the American Society of Gastrointestinal Endoscopy [1].)
**DIAGNOSTIC INDICATIONS FOR ESOPHAGOSCOPY**

- Dysphagia and odynophagia
- Certain patients with suspected gastroesophageal reflux disease
- Patients with suspected infectious esophagitis
- Acute or chronic bleeding
- Abnormal results of a radiologic examination
- Surveillance in Barrett’s esophagus
- To evaluate for varices in certain patients with suspected portal hypertension or following endoscopic variceal therapy
- To assess acute injury after caustic ingestion

**THERAPEUTIC INDICATIONS FOR ESOPHAGOSCOPY**

- Dilation of strictures, benign and malignant
- Removal of foreign bodies
- Treatment of bleeding varices
- Treatment of achalasia
- Palliative treatment of malignancy
- Removal of selected polypoid lesions

**CONTRAINDICATIONS FOR ESOPHAGOSCOPY**

- Absolute
  - Lack of patient cooperation
  - Moribund patient
  - Known or suspected perforated viscus
- Relative
  - Unstable cardiovascular or pulmonary status

---

**FIGURE 3-4.** Indications for diagnostic esophagoscopy. Diagnostic esophagoscopy is an appropriate initial evaluation for many patients with esophageal symptoms. It is also an appropriate procedure to further evaluate abnormalities seen on radiologic studies of the esophagus. Not all patients with suspected gastroesophageal reflux disease require endoscopy. Sequential esophagoscopy may be indicated for surveillance of Barrett’s esophagus or to follow up endoscopic variceal therapy.

**FIGURE 3-5.** Indications for therapeutic esophagoscopy. The major advantages of endoscopy over barium esophagram are that biopsies can be obtained and a variety of therapeutic interventions can be performed. Therapeutic capabilities include stricture dilation, removal of foreign bodies, treatment of varices and other bleeding lesions, and treatment of achalasia. Esophageal malignancies can be palliated with dilation, laser therapy, photodynamic therapy, and insertion of metal stents. Endoscopic therapy for the ablation of Barrett’s esophagus and endoscopic interventions for the treatment of gastroesophageal reflux are currently being evaluated.

**FIGURE 3-6.** Contraindications for esophagoscopy. In general, upper endoscopy can be performed safely in almost all patients. It should not, however, be performed in uncooperative or moribund patients. It should also not be performed in patients with a known or suspected perforated viscus. The nonsterile instrument and the air insufflation needed to perform the procedure may aggravate mediastinal or peritoneal contamination. In unstable patients, endoscopy should only be performed if the benefits of endoscopy are judged to outweigh the risks to the patient at that time.
Complications of upper gastrointestinal endoscopy. Such complications are rare. The most common complications are reactions to the sedative medications. Hence, the use of pulse, blood pressure, heart rhythm, and oxygen saturation monitoring is encouraged. Although esophageal perforation can occur with diagnostic endoscopy, it is more likely to result from therapeutic procedures.

### Normal Endoscopic and Radiologic Anatomy

**Figure 3-7.** Normal endoscopic and radiologic anatomy.

**Figure 3-8.** Guiding the endoscope. When performing upper endoscopy, the endoscope should be passed under direct vision. The epiglottis, larynx, and vocal cords are easily identified in this image. At this point, the cricopharyngeus will relax and the esophagus will be seen between the pyriform sinus and the posterior aspect of the larynx. The instrument can then be passed to the esophageal body.

**Figure 3-9.** The normal esophageal body. The normal esophageal body is covered by a smooth intact squamous mucosa. Esophagoscopy can detect inflammatory or neoplastic conditions that affect the esophageal mucosa. Endoscopy can also detect anatomic abnormalities such as webs, rings, strictures, and diverticula. Motor disorders are best detected using other methods.

**Figure 3-10.** The lower esophageal sphincter (LES). The LES is at the junction of the esophagus and stomach. The transition from the squamous mucosa of the esophagus to the columnar epithelium of the stomach is known as the Z-line. Reflux esophagitis can be seen in the distal esophagus just proximal to the Z-line. If the Z-line is located proximal to the esophagogastic junction and there is columnar mucosa in the tubular esophagus, biopsy specimens should be taken to evaluate for Barrett’s esophagus.
Barium esophagram and endoscopy. These procedures are complementary to each other in the diagnosis of esophageal diseases. Barium esophagram can be used to evaluate a variety of esophageal symptoms including dysphagia, odynophagia, and reflux. The accuracy can be increased by use of a double contrast technique. A normal barium esophagram is shown.

**Figure 3-12.** Esophagram of a patient with dysphagia and chest pain. His endoscopy was normal. The esophagram shows changes of diffuse esophageal spasm. Esophageal manometry confirmed the diagnosis.
Comparison of the diagnostic accuracy of radiology with that of endoscopy. Endoscopy is superb for mucosal lesions and has biopsy and therapeutic potential. On the other hand, the role of endoscopy in the diagnosis of motor disorders is limited. For this reason, in patients with dysphagia to both solids and liquids, it may be more appropriate to obtain an esophagram as the initial diagnostic procedure. An esophagram also enables clinicians to rule out oropharyngeal causes of dysphagia that cannot be assessed with endoscopy.

**NORMAL ESOPHAGEAL MUCOSAL HISTOLOGY**

![Image of normal esophageal mucosa](image)

Pinch biopsy of normal squamous mucosa of the esophagus. Pinch biopsies of the esophageal mucosa can be safely obtained with forceps during endoscopic examination. Histopathologic evaluation can help differentiate neoplastic, inflammatory, and infectious conditions of the esophagus. Brush cytology may be a useful adjunct for certain conditions.
Zenker's diverticulum. A Zenker's diverticulum is actually a hypopharyngeal lesion. It is a protrusion of the mucosa between the inferior pharyngeal constrictor and the cricopharyngeus muscle. The pathogenesis of this lesion is controversial, but it appears that pharyngeal and upper esophageal sphincter discoordination may play a role. Many of these are incidentally found, but dysphagia and regurgitation are the most common symptoms. Treatment, if needed, is by surgical methods.

Midesophageal diverticulum. The midesophageal diverticulum is usually small and asymptomatic. Illustrated here, however, is an unusually large mid-esophageal diverticulum. Most of these lesions are associated with an underlying esophageal motility disorder. In most cases treatment is not needed; however, in the patient whose case is illustrated here, surgery was performed because of severe symptoms of dysphagia and regurgitation.

The esophagus of a patient with multiple epiphrenic diverticula and achalasia. This is a known association; the diverticulum is presumably caused by the underlying motility disorder. There may be increased risk to pneumatic dilation in these patients. This patient had a Heller myotomy and multiple diverticulectomy.
Endoscopic view of the esophagus in a patient with a large epiphrenic diverticulum. Two lumens can clearly be seen: one represents the diverticulum and the other the esophageal lumen.

Aperistaltic esophagus. This image is from a patient with a long-standing history of symptoms of gastroesophageal reflux disease. Esophageal manometry showed an aperistaltic esophagus. In addition, he had taken at least eight aspirin a day for many years. Esophagography and endoscopy revealed multiple pseudodiverticula of the lower third of the esophagus. It was postulated that they were formed by repeated damage caused by both acid and aspirin. In addition, the patient's motility disorder probably impaired his esophageal clearance and thus aggravated the situation. In general, the treatment of esophageal pseudodiverticulosis is directed toward the underlying condition.

Lower esophageal mucosal ring. The presence of a lower esophageal mucosal ring is one of the most common causes of dysphagia. It has been proposed that these rings are related to gastroesophageal reflux, but a true ring is not associated with inflammation. A ring's upper surface is covered with esophageal (squamous) epithelium, and its lower surface by gastric (columnar) epithelium. Rings smaller than 13 mm are usually symptomatic and those over 20 mm rarely produce symptoms. Intermittent solid food dysphagia is the main presenting symptom. Treatment consists of dilation, which can be accomplished by passage of a single large-caliber dilator (ie, 17 to 20 mm) through the esophagus to disrupt the ring.
The importance of adequate distension. Adequate examination of the lower esophagus by either radiology or endoscopy is impossible without adequate distension. A common lesion, such as lower esophageal mucosal ring, can be missed by both techniques. The radiologist may also challenge the esophagus with a solid bolus such as a marshmallow or a barium tablet. This patient had intermittent solid food dysphagia for many years. A marshmallow distended the lower esophagus and brought out the lower esophageal mucosal ring. In addition, impaction of the marshmallow reproduced the patient’s symptom. Esophageal dilation rendered this patient asymptomatic.

**Figure 3-22.**

Esophageal webs. These structures are thin membranes of squamous mucosa that occur in the upper or midesophagus. In most patients, no underlying etiology is apparent. This image is from an otherwise healthy elderly patient with dysphagia. Esophageal dilation relieved his symptoms.

**Figure 3-23.**

Multiple esophageal webs. A healthy 32-year-old man presented with solid food dysphagia and was found to have multiple esophageal webs. Multiple webs may be associated with graft-versus-host disease, certain dermatologic disorders, or may be an atypical manifestation of gastroesophageal reflux disease.

**Figure 3-24.**

Atlas of Esophageal Diseases
Multiple esophageal webs. Upper endoscopy confirmed the diagnosis of multiple esophageal webs in this patient. The esophagus was treated with serial dilation over a guidewire. The patient’s symptoms were improved after two sessions.

REFERENCE

Endoscopic evaluation of the esophagus permits a detailed assessment of mucosal abnormalities and, to a lesser extent, motility disorders. However, identification and characterization of deeper structures requires imaging systems that allow penetration through the soft tissue layers. Endoscopic ultrasound is a technology permitting this added perspective. Since the introduction of this technique in the early 1980s, the number and type of instruments available have expanded considerably with improvements in image quality. Today, endoscopic ultrasound is recognized as the most accurate method for locoregional staging of esophageal carcinoma despite improvements in computed tomography, magnetic resonance imaging, and positron-emission tomography. Furthermore, with the addition of endosonography (EUS)-guided fine-needle aspiration biopsy (FNA), periesophageal lymphadenopathy and mass lesions can be biopsied. Collectively, clinical indications for EUS-guided FNA continue to expand due to its ability to provide information not easily obtained through other means.
Mechanical radial echoendoscope. Most endoscopic ultrasound examinations are performed with a radial scanning instrument that provides a transverse image of the esophageal lumen and adjacent structures. The echoendoscope pictured (GF-UM 130; Olympus America, Melville, NY) (13.2 mm wide) has a video optical system (forward oblique view) and an ultrasound transducer operating at 7.5 MHz and 12 MHz located at the tip of the endoscope. A mechanical motor located in the handle of the endoscope allows the ultrasound transducer to rotate, permitting a 360° ultrasound image to be obtained. The ultrasound image is perpendicular to the long axis of the echoendoscope, and depth of penetration ranges from 6 cm to 9 cm. A water-filled latex balloon attached to the ultrasound transducer allows for acoustic coupling. Instillation and suction of air and water can be applied by maneuvering the two buttons located on the handle of the echoendoscope. The ultrasound image can also be frozen and frequency of scanning (7.5 MHz versus 12 MHz) may be switched by using two additional buttons located on the handle of the endoscope. The radial ultrasound echoendoscope features a biopsy channel (2 mm wide) that allows for luminal biopsy with a pediatric forceps.

Electronic linear echoendoscope. To permit ultrasound imaging in the long axis of the endoscope and thereby perform directed fine-needle aspiration biopsy of extraluminal structures, echoendoscopes have been developed with the transducer oriented in a linear or sagittal direction. This echoendoscope (GF-UC30P; Olympus America, Melville, NY) and needle (NA-10J-1; Olympus America, Melville, NY) (11.7 mm wide) also features an optical system that allows for forward oblique viewing and an electronic ultrasound transducer. The ultrasound transducer is located at the tip of the endoscope and operates at 7.5 MHz. The ultrasound images obtained with this equipment (250° scanning field) are oriented along the long axis of the endoscope, instead of perpendicular as occurs with the mechanical radial echoendoscope. These echoendoscopes are provided with biopsy channels ranging in size from 2.8 mm to 3.7 mm in diameter and an elevator. With these instruments, an operator can perform standard biopsies, endosonography (EUS)-guided fine-needle aspiration biopsies, and therapeutic interventions such as EUS-guided pseudocyst drainage with stent placement.

Detailed view of the tip of the linear echoendoscope. As shown in Fig. 4-2, this model features the ultrasound transducer (tip of the scope) with a 22-gauge needle (65 mm long) protruding from the biopsy channel of the echoendoscope.
High-frequency ultrasound mini-probe. When the area of interest for imaging is confined to the esophageal wall, higher resolution imaging is desired. A through-the-scope ultrasound catheter probe (2.4 mm wide) pictured here (UM-2R and UM-3R; Olympus America, Melville, NY) provides high-frequency ultrasound imaging ranging from 12 MHz to 30 MHz. The catheter can be advanced through the biopsy channel of a conventional endoscope, allowing the operator to obtain a detailed image of the gastrointestinal wall and superficial lesions. Adequate acoustic coupling with the gastrointestinal wall is achieved through a water-filled balloon sheath and instillation of water into the lumen.

**ANATOMY**

Rotating motor. The proximal margin of the ultrasound catheter is connected to a portable rotating motor (MH-240; Olympus America, Melville, NY) that allows the ultrasound transducer to spin, giving 360° ultrasound images perpendicular to the long axis of the probe.

**Figure 4-6.**

Esophageal wall layers. Ultrasound imaging allows layers of the intestinal wall to be identified that correlate closely with histology. The radial echoendoscope at 7.5 MHz demonstrates the typical five-layer structure described by Kimmey et al [1]. The first layer (hyper-echoic) correlates with the interface between the luminal fluid and the mucosal surface. The second layer (hypo-echoic) corresponds to the deep mucosa. The third layer (hyper-echoic) represents the submucosal layer and its interface with the muscularis propria. The fourth layer (hypo-echoic) is the remainder of the muscularis propria. This fourth layer may be divided into three different layers (inner and outer muscularis propria and connective tissue in between) when examined with higher frequency probes. The fifth layer in the esophagus has been shown to correspond to the interface arising from the adventitia.
Aortic Arc

Echoendoscopic view of the aortic arch. When the radial echoendoscope is placed in the upper third of the esophagus (20 cm to 30 cm from the incisors), just above the level of the left main bronchus and the pulmonary artery, the spine is posterior and the aortic arch crosses from the posterior to the anterior mediastinum. This level is a site for lymph node metastases for thoracic malignancies. In elderly patients, arteriosclerotic plaque is often found within the aorta.

Echoendoscopic view of the trachea. An air column (hyperchoic with multiple echoes) anterior to the esophageal lumen, which corresponds to the trachea, is seen by advancing the echoendoscope distal to the aortic arch. Careful scanning of this area is extremely important in patients with squamous cell carcinoma of the upper third of the esophagus to assess for tracheal invasion.

Echoendoscopic view of the middle third of the esophagus. More distally, in the middle third of the esophagus (30 cm to 35 cm from the incisors), the azygos vein (AZV) crosses the mediastinum. Anterior to the esophagus, the left atrium (LA) with the pulmonary veins (PV) can be observed. The spine (SP) and aorta (AO) remain in a similar position.

Echoendoscopic view of the lower third of the esophagus. In the distal third of the esophagus (35 cm to 40 cm from the incisors) the right (R) and left (L) pleura appear as echodense interfaces due to the air within the adjacent lung. Small pleural effusions may be detected on the patient’s right side due to its dependent location in the left lateral decubitus position. This region is the most frequent location for esophageal adenocarcinoma. Presence of pleural or aortic invasion should be investigated in these patients.

Echoendoscopic view of the celiac axis. The perigastric and celiac axis regions, located at approximately 45 cm from the incisors, should also be scanned when staging esophageal carcinoma to identify tumor infiltration into the gastric wall and lymphadenopathy. Along the posterior gastric wall the celiac artery origin from the abdominal aorta can be found. The celiac artery divides into the hepatic artery (HA), the splenic artery (SA), and the left gastric artery (not shown). The presence of malignant lymph nodes in this region signifies distant metastases (stage IV disease).
INDICATIONS AND DIFFERENTIAL DIAGNOSIS

INDICATIONS FOR EUS AND EUS-GUIDED FNA IN THE MEDIASTINUM

<table>
<thead>
<tr>
<th>BENIGN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Achalasia</td>
</tr>
<tr>
<td>Duplication cyst</td>
</tr>
<tr>
<td>Mediastinal infection (histoplasmosis, tuberculosis)</td>
</tr>
<tr>
<td>Subepithelial lesion</td>
</tr>
<tr>
<td>External compression</td>
</tr>
<tr>
<td>Portal hypertension</td>
</tr>
<tr>
<td>Barrett's esophagus</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>MALIGNANT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esophageal carcinoma staging</td>
</tr>
<tr>
<td>Re-staging post-adjuvant therapy</td>
</tr>
<tr>
<td>Tumor relapse</td>
</tr>
<tr>
<td>Pseudoachalasia</td>
</tr>
<tr>
<td>NSCLC staging</td>
</tr>
<tr>
<td>Mediastinal malignancy (lymphoma, breast cancer)</td>
</tr>
</tbody>
</table>

**Figure 4-13.**
Indications for endoscopic ultrasound (EUS) and EUS-guided fine-needle aspiration (FNA) in the mediastinum. Endosonography is helpful in diagnosing esophageal disorders as well as in staging thoracic neoplasms. Benign conditions due to intramural mass lesions can be readily discerned by EUS, thereby assisting with therapeutic decisions. Although other cross-sectional imaging methods such as computed tomography will be used when evaluating thoracic neoplasms, EUS provides the advantage of more accurate locoregional staging for esophageal carcinoma. EUS-guided FNA allows the cytologic documentation of imaging abnormalities that may be difficult to biopsy nonsurgically. NSCLC—non-small cell lung cancer

**Figure 4-15.**
Endosonographic view of an esophageal duplication cyst. Esophageal duplication cysts may be difficult to differentiate from subepithelial neoplasms or extrinsic masses. This patient with progressive dysphagia had a questionable mass in the proximal esophagus with normal overlying mucosa. Examination with endosonography demonstrates a cystic mass to the left of the trachea that arises from the esophagus. The mass measures 29 mm, is anechoic, and produces posterior acoustic enhancement (ultrasound is less attenuated when traveling through fluid versus tissue so that structures are brighter behind fluid-filled cavities). The patient underwent resection of a duplication cyst and his symptoms resolved.

**Figure 4-14.**
Differential diagnosis between achalasia and pseudoachalasia. In patients presenting with dysphagia, it is extremely important to differentiate between a malignant versus a benign origin. Standard endoscopy allows for identification of luminal tumors, while esophageal manometry may help identify those patients with a motility disorder (achalasia, scleroderma, etc.). Occasionally, endoscopy and manometry cannot exclude a malignant lesion causing an impaired relaxation of the lower esophageal sphincter (pseudoachalasia). To help differentiate achalasia from pseudoachalasia, high-frequency ultrasound catheters can be used. In those patients with achalasia a thickening of the muscularis propria (MP) (4.4 mm in this case) is frequently seen in the distal esophagus, with no associated mass. Patients with pseudoachalasia will present with a tumor mass and not a diffuse thickening of the muscularis propria. If endoscopic biopsies are unsuccessful at confirming a malignancy, endosonography-guided fine-needle aspiration biopsy can be used to sample the tumor.

*Endoscopic Ultrasonography 59*
Esophageal compression. Granulomatous processes arising in the mediastinum may occasionally involve the esophagus. A patient presented with progressive odynophagia of 3 months' duration. At endoscopy an extrinsic compression was present in the mid to upper esophagus with no luminal or mucosal lesions.

Mediastinal lymphadenopathy. The linear echoendoscope was advanced to the level of the compression, showing a mediastinal lymph node (LN) in the subcarinal space. Endosonography-guided fine-needle aspiration was performed and the material obtained was submitted for cytology and culture.

Histoplasmosis. Cytology smears stained with methenamine silver demonstrated yeast-like organisms consistent with *Histoplasma capsulatum* (arrows). Antifungal therapy was started. The diagnosis was confirmed with cultures and immunodiffusion titers. The patient's symptoms resolved after a 3-month course of oral antifungal therapy.

Leiomyoma. Through identification of esophageal wall layers, submucosal tumors can be distinguished with endosonography. This patient with persistent dysphagia had an external compression versus subepithelial lesion compressing the esophageal lumen in the midthoracic esophagus (arrowhead).
Endosonographic view of leiomyoma. On endosonography an hypoechoic mass occupying 50% of the esophageal circumference with smooth and regular margins is seen. The mass arises from the muscularis propria (MP). These endosonographic findings suggest a gastrointestinal stromal tumor, although malignant degeneration (leiomyosarcoma) is possible. R—right.

Cytopathology of spindle cell neoplasm. An endosonography-guided fine-needle aspiration sample obtained from this mass showed spindle cells with cellular atypia and prominent nucleoli. Surgery was advised and a benign gastrointestinal stromal tumor was resected.

DYSPHAGIA LUSORIA

Aberrant right subclavian artery. The innominate artery typically courses anterior to the esophagus dividing into the right (RT) carotid and subclavian arteries. Occasionally the right subclavian artery originates directly from the aortic arch immediately behind the origin of the left subclavian artery [2]. When this occurs it can cross between the esophagus and the spinal column (80%), run between the esophagus and the trachea (15%), or pass anterior to both trachea and esophagus (5%). This patient had a long history of dysphagia, predominantly to solids, with an extrinsic compression versus subepithelial mass lesion identified at endoscopy. When examined with the radial echoendoscope, the right subclavian artery was seen running posterior to the esophagus. Although this anatomic variant rarely results in symptoms, in this patient surgical correction ameliorated her dysphagia.
Esophageal and gastric varices. In patients with portal hypertension secondary to liver disease and portal or splenic vein thrombosis, esophageal and gastric varices and collateral circulation may be observed (arrows). Varices and collateral vessels are visible as multiple tubular anechoic structures within and adjacent to the wall, respectively. Presence of esophageal perforating vessels communicating with the collateral circulation after endoscopic band ligation may predict bleeding relapse. AZV—azygos vein.

Endosonographic view obtained from the gastric cavity of the patient shown in Figure 4-23. Multiple collaterals can be seen in the perigastric space (arrows).

Barrett’s esophagus. The endoscopic ultrasound examination of a patient with Barrett’s esophagus and high-grade dysplasia on endoscopic biopsies is shown. The first two layers of the esophagus (interface with mucosa and deep mucosa) showed a hypoechoic thickening (yellow arrows), clearly abnormal if compared with the normal esophageal mucosa shown in Figure 4-6. This mucosal thickening may be related to the presence of glandular epithelia replacing the normal squamous mucosa. The submucosal layer (SM) was intact, suggesting that if malignant degeneration were already present in the Barrett’s columnar metaplasia, the lesion would be stage T1. Surgical pathology of this patient confirmed the presence of Barrett’s esophagus with segments of high grade dysplasia, but no focus of adenocarcinoma was identified. MP—muscularis propria.
ESOPHAGEAL CARCINOMAS

**Figure 4-26.** Pathologic T1 (pT1) esophageal carcinoma. Endosonography (EUS) is 80% to 90% accurate when determining depth of tumor invasion in esophageal carcinoma. On EUS an hypoechoic tumor infiltrates the mucosa and submucosa (7.5 MHz, radial echoendoscope). The deeper margin of the submucosa, represented by a hyperechoic white line (arrowheads), is preserved, defining the lesion as a T1 carcinoma (up to but not completely through the submucosa). The left atrium (LA) and pulmonary vein (LPV) are anterior.

**Figure 4-27.** High-frequency view of pathologic T1 (pT1) esophageal carcinoma. To better determine the depth of penetration of the tumor, ultrasound imaging at higher frequencies (12 MHz) and magnified imaging (4 cm range) were used. This view shows the T1 lesion in Figure 4-26 with a half-screen display. The tumor extended into the submucosa but the deeper margin of the submucosa was not infiltrated by tumor. The azygos vein (AZV) and thoracic duct (TD) can also be identified in the posterior mediastinum in this patient, adjacent to the tumor.

**Figure 4-28.** High-frequency view of pathologic T2 (pT2) esophageal carcinoma. Adenocarcinoma of the mid esophagus (TU) examined with endosonography. The tumor was scanned with a dedicated radial echoendoscope, and in a magnified view obtained at high frequency (12 MHz) the tumor was seen infiltrating into the diaphragm (arrows). These ultrasound findings are suggestive of pT2 esophageal carcinoma (into but not completely through the muscularis propria), based on endosonographic criteria.

**Figure 4-29.** Pathologic T3 (pT3) esophageal carcinoma. Endosonographic image of an adenocarcinoma located at the distal third of the esophagus. The tumor shows irregular borders and tumoral pseudopodia infiltrating the adventitia and mediastinal fat. Space is present between the deeper extent of the tumor and the right pleura. Based on these endosonographic findings, a diagnosis of T3 (invasion through the esophageal wall but no involvement of adjacent structures) was rendered.

**Figure 4-30.** Pathologic T4 (pT4) esophageal carcinoma. A stenosing adenocarcinoma of the gastroesophageal junction was examined with endosonography. The tumor was scanned with a dedicated radial echoendoscope, and in a magnified view obtained at high frequency (12 MHz) the tumor was seen infiltrating into the diaphragm (arrows). These ultrasound findings support the diagnosis of T4 (invasion of adjacent structures), based on the presence of diaphragmatic invasion by tumor.

**Figure 4-31.** Adenocarcinoma of the mid esophagus. The tumor extended through 360° of the esophageal circumference. The tumor invaded the patient's right pleura (arrows), represented as a white hyperechoic line. The hyperechoic line is continuous in healthy people. However, when the tumor invades the pleural space the hyperechoic line becomes discontinuous and is frequently associated with a pleural effusion (arrows), as seen in this patient. These endosonographic findings defined a T4 stage, based on invasion of the right pleura.

*Endoscopic Ultrasonography*
Pathologic N0 (pN0) esophageal carcinoma. This view shows a squamous cell carcinoma of the esophagus. On withdrawal of the echoendoscope a lymph node (LN) was visualized in the subcarinal space, anterior to the azygos vein (AZV), spine, and aorta. This lymph node had irregular borders and mixed echogenicity, was oblong, and measured less than 10 mm wide. These findings were suggestive of benign nature and the tumor was classified as N0 stage.

Pathologic N1 (pN1) esophageal carcinoma. This view of a patient with an adenocarcinoma of the distal esophagus showed a lymph node (LN) in the right periesophageal space posterior to the left atrium and anterior to the right pleura, azygos vein (AZV), aorta, and spine. The lymph node was hypoechoic, had smooth borders, and measured 9 x 12 mm. These findings were suggestive of malignant involvement, therefore classifying the lesion as an N1 tumor.

Pathologic M1b esophageal carcinoma. Ultrasound view of the lesion in Figure 4-35 obtained with a linear echoendoscope. The echo characteristics of the liver lesion are similar to those described with the radial echoendoscope, and a hypoechoic ring surrounding the hepatic lesion is also present, reinforcing the impression of malignant involvement.

Pathologic M1a esophageal carcinoma. Examination of the celiac axis area is mandatory when evaluating patients with esophageal carcinoma. The celiac artery is observed when the echoendoscope is placed in the stomach approximately 45 cm from the incisors. Presence of lymph nodes between the hepatic (HA) and splenic artery (SA), less than 2 cm from the aorta, as shown in this patient (LN1 and LN2), with malignant echo features (round, hypoechoic, smooth borders, and width greater than 10 mm) are suggestive of stage M1a (stage IVa).

Liver metastasis. Due to the worrisome nature of the lesion found in the liver (Fig. 4-35), a fine-needle aspiration was performed under real-time endosonographic guidance with the linear echoendoscope. The needle tip can be observed in the center of the lesion. Gentle to and fro movements within the lesion were performed and a cytologic sample was obtained, providing a diagnosis of metastatic adenocarcinoma to the liver (stage M1b, stage IVb).
Endoscopic view of esophageal carcinoma following chemoradiation. A patient with a histologically-proven esophageal adenocarcinoma staged as a T3N1 lesion by computed tomography and endosonography (EUS) underwent neoadjuvant therapy (chemotherapy and radiation therapy) prior to surgical resection. After completion of the neoadjuvant treatment and prior to surgical resection, the patient was re-evaluated by endoscopy and EUS to assess response to adjuvant therapy. The endoscopic image of the luminal tumor following treatment shows friability and stenosis with minimal intraluminal tumor growth.

Endosonographic view of esophageal carcinoma following chemoradiation. On endosonography (EUS) a hypoechoic mass infiltrating the full circumference of the esophagus is observed. This mass extends into the adventitia and mediastinal fat, suggesting that the tumor did not improve with therapy. However, the deeper extent of the tumor is more hypoechoic than the primary mass (arrowheads). These hypoechoic areas correlate with peritumoral inflammation and desmoplastic reaction secondary to chemoradiation therapy, and may be responsible for the low accuracy of EUS when restaging patients with previous adjuvant therapy. Accuracy for T and N stage after chemoradiation has been reported at 43% and 37%, respectively. These results compare poorly with the 85% (T stage) and 77% (N stage) reported for nonirradiated patients [3–5].

Esophageal carcinoma relapse at the surgical anastomosis. A patient with a resected adenocarcinoma of the esophagus was referred for dysphagia 16 months after completion of surgery. Upper endoscopy was unremarkable with no luminal lesions. Computed tomography showed mild thickening at the level of the anastomosis, consistent with a postoperative state. Endosonography (EUS) examination with the radial echoendoscope showed thickening of the anastomosis (14.2 mm). This thickening was hypoechoic in nature and irregularly bordered, suspicious for tumor relapse. Tumor relapse at the level of the anastomosis was confirmed by EUS-guided fine-needle aspiration. The sensitivity and specificity of EUS for detection of tumor relapse at the anastomosis has been shown to be 92% and 96%, respectively [6,7].

AO—aorta; AZ—azygos vein.

ENDOSCOPIC ULTRASONOGRAPHY FOR STAGING OF NON-SMALL CELL LUNG CANCER

Computed tomography (CT) scan of a patient with non-small cell lung cancer (NSCLC). Preoperative lymph node staging of NSCLC can be challenging. Bronchoscopy-guided transtracheal fine-needle aspiration (FNA), CT-guided biopsy, and mediastinoscopy can be used to obtain lymph node staging. Patients with malignant mediastinal lymph nodes are typically not considered for surgical resection. In recent years, endosonography (EUS) and EUS-guided biopsy of mediastinal lymph nodes have shown promising results for the preoperative lymph node staging of patients with NSCLC (accuracy: 96%) [8]. CT scan of a patient with NSCLC identifies several subcarinal lymph nodes (arrowheads). Bronchoscopy-guided FNA of the lymph nodes was negative for malignancy.
Endosonography (EUS) and EUS-guided fine-needle aspiration (FNA) for non-small cell lung cancer. On EUS, the linear endoscope is able to localize the subcarinal lymph nodes (LN) and guide FNA.

**COMPLICATIONS**

### COMPLICATIONS INHERENT TO EUS AND EUS-GUIDED FNA

<table>
<thead>
<tr>
<th>EUS</th>
<th>EUS-GUIDED FNA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perforation (cervical, duodenal)</td>
<td>Perforation (cervical, duodenal)</td>
</tr>
<tr>
<td>Bleeding</td>
<td>Infection</td>
</tr>
</tbody>
</table>

Cytology for non-small cell lung cancer. The aspirated material is sprayed onto glass slides using an air-filled syringe with residual material saved for a cell block. Diff-Quick (Harleco, Gibbstown, New Jersey) staining is used for an on-site adequacy assessment and Papanicolaou stain is employed for final cytologic study. A loosely cohesive cluster of cells with a high nuclear/cytoplasmic ratio, irregular contours, and hyperchromasia are consistent with metastatic adenocarcinoma. Mature lymphocytes and red blood cells are visible in the background.

EUS are similar to those of standard upper endoscopy. Perforation of the gut wall has been associated more frequently with EUS and occurs at two sites: cervical esophagus (during the echoendoscope intubation, with a frequency of 0.03%) and duodenum (when advancing the echoendoscope from the first to the second portion of the duodenum) [9]. Previously, the risk for esophageal perforation was thought to be increased if the patient presented with an esophageal tumor requiring dilation to allow echoendoscope passage. Using equipment with a more blunt tip than currently available instruments, a perforation rate of 24% was identified [10]. More recent reports using newer instruments suggest that EUS in the setting of esophageal tumors is safe if caution is used when dilating and passing the echoendoscope [11, 12]. When performing EUS-guided FNA there is also an added risk of infection when sampling cystic lesions (14% if no antibiotic prophylaxis is administered) [13]. Self-limited bleeding can be seen with EUS-guided FNA (1.3%) [14]. However, it should be noted that complications arising from EUS and EUS-guided FNA are rare, and the majority of them are minor.
Esophageal perforation: pneumomediastinum. A patient who presented with a stenotic adenocarcinoma of the distal esophagus (not traversable with the endoscope) is shown. Dilation of the tumor stenosis was performed with a balloon dilator to allow instrument passage, reaching a maximum diameter of 15 mm. Endosonographic examination was performed with the radial echoendoscope immediately after balloon dilation, showing the presence of air (arrowheads) in the mediastinum surrounding the esophageal tumor. A diagnosis of esophageal perforation and pneumomediastinum was made, and the patient was referred for surgery. Surgical pathology confirmed the presence of a 4-mm perforation at the level of the tumor.

**REFERENCE**

MANOMETRY

Historical perspective

The first manometric studies were performed in 1883 by Kronecker and Meltzer, who used air-filled balloons and an external pressure transducer. Water-filled balloons were first used by Ingelfinger and Abbot in 1940. Because of their inaccuracy and delayed assessment of rapid pressure changes in the esophagus, these methods were later found not to be clinically useful and were abandoned. Studies using water-filled catheters first began in the 1950s and initiated development of the basic knowledge of the physiology and pathophysiology of esophageal motility. The lower esophageal sphincter (LES) was first identified manometrically by Fyke et al. in 1956. Small intraluminal solid-state transducers were introduced in the 1970s.

The devices for measurement of esophageal pressures remain either a water-filled catheter connected to external transducers or a catheter assembly containing small direct intraluminal transducers. Although very slow infusion rates are sufficient (<1.0 mL/min) to record tonic sphincter squeeze, a more vigorous infusion rate within the catheter is required to record accurately the transient high pressures produced during intraesophageal peristaltic activity. Even the best infusion system is incapable of recording the extremely rapid pressure changes (>1000 mm Hg/sec) in the pharynx.

Accurate recording of sphincter pressure and esophageal peristaltic pressure can also be obtained with small direct intraluminal transducers. A comparison of this technique with the best infusion techniques reveals excellent correlation. Increasing numbers of clinical motility laboratories are equipped with this methodology; the resulting lack of dependence on infusion pumps and fluid-filled systems and the ability to record pharyngeal pressures accurately are considered assets. Either system, however, is satisfactory for quantitative clinical studies of esophageal function when properly applied.
Pioneering work with prolonged pH monitoring was first performed by Spencer in 1967 and developed into a clinically applicable technique by Johnson and DeMeester in the mid-1970s. The latter investigators documented that intraesophageal pH could be measured over a 24-hour cycle by using an indwelling pH probe positioned 5 cm above the LES and a standard laboratory physiograph. Reflux was defined as intraesophageal pH below 4; the duration of the reflux episode was the time interval until the pH returned to greater than 4. The value pH 4 was chosen because (1) it is unequivocally distinct from the usual esophageal pH (approximately 7.0) (2) the proteolytic enzyme pepsin is essentially inactive above pH 4 and (3) patients with symptomatic reflux show good association between an intraesophageal pH of 4 and onset and resolution of their symptoms.

Multichannel intraluminal impedance (MII) is a rapidly evolving technique that allows the measurement of bolus movement within the esophagus in either direction independent of pH and without the use of radiation. By the use of multiple metallic rings separated by 2-centimeter intervals, changes in the electrical circuit within the esophageal lumen are recorded with MII. This technique holds the promise of introducing two important advances in esophageal function testing recording esophageal transit of various bolus types and detecting gastroesophageal reflux. With the latter technique, adding a pH sensor to the catheter permits accurate testing of both acid and nonacid reflux.

Clinical application of esophageal manometric studies

The major value of an esophageal manometry laboratory in clinical practice is in the diagnosis of esophageal (or pharyngeal and upper esophageal sphincter [UES]) motility dysfunction. These conditions can be placed in two types: those in which the motility defect is a primary condition involving only the esophagus and those in which an esophageal abnormality is a secondary aspect of a more generalized disease. The physician using an esophageal manometric laboratory for diagnostic help should recognize these distinctions and note particularly the potential esophageal motility disorders associated with various systemic diseases.

Disease entities in which motility changes are essentially pathognomonic include scleroderma and achalasia. The important manometric feature of sclerodermatous involvement of the esophagus is the marked abnormality in the smooth muscle portion of this organ (ie, lower two thirds) with relative normality of the striated muscle segment (ie, upper third). Achalasia is defined by specific manometric criteria characterized primarily by a poorly relaxing, hypertensive LES and total absence of esophageal peristalsis.

For the clinician the paramount problem is definition of the real value of esophageal manometry for a more precise diagnosis of patients with symptoms potentially of esophageal or pharyngeal origin.

**SUGGESTED CLINICAL USES OF ESOPHAGEAL MOTILITY TESTING**

**Stationary manometry**
- Evaluation of patients with dysphagia
- Primary esophageal motility disorders (eg, achalasia)
- Secondary esophageal motility disorders (eg, scleroderma)
- Upper esophageal sphincter/pharyngeal manometry for pharyngeal dysphagia
- Evaluation of patients with possible gastroesophageal reflux disease
- Identify high-risk patients (lower esophageal sphincter pressure < 10 mm Hg)
- Evaluate defective peristalsis (particularly before fundoplication)
- Exclude scleroderma
- Assist in placement of pH probe

**Ambulatory manometry**
- Most commonly used in combination with 24-hour pH monitoring
- Primarily a research tool
- Probably beneficial for unexplained chest pain
- Possibly beneficial
  - Nonobstructive dysphagia
  - Gastroesophageal reflux disease

**Evaluation of patients with noncardiac chest pain**
- Primary esophageal motility disorders
- Pain response to provocative testing
- Exclude generalized gastrointestinal tract disease
- Scleroderma
- Chronic idiopathic intestinal pseudo-obstruction
- Exclude esophageal etiology for suspected eating disorder

**Figure 5-1.**

Suggested clinical uses of esophageal motility testing. Controversy over the value of esophageal motility testing exists. In some situations esophageal manometry may be particularly helpful, specifically to exclude achalasia or as a preoperative assessment of esophageal motility prior to antireflux surgery. In contrast, the use of esophageal manometry in patients with unexplained chest pain appears to be of limited clinical use.
A, Schematic representation of a transverse section of a standard infused catheter modified for construction of the 6-cm long Dent sleeve. The section is cut at the level of the midsleeve position showing the location of the single-site recording orifice at this level. B, Lower esophageal sphincter pressure trace from the sleeve illustrated in panel A and the midsleeve side hole as the catheter device is pulled through the sphincter. The solid triangles at the base of the figure indicate each 5-mm catheter movement. Note that the sleeve records pressure uniformly over a distance of 4 to 5 cm and that the pressure is similar to the maximal pressure recorded by the single side hole at the midsleeve position. (Adapted from Dent et al. [1].)

**Figure 5-2.**

---

**Figure 5-3.**

Manometric recording of the “pull through” of a solid-state transducer across the normal lower esophageal sphincter (LES). The upper tracing shows progressive increases in pressure as the catheter is slowly withdrawn across the LES. Maximal average pressure was obtained just distal to the pressure inversion point (arrow) before the transducer moved into the esophagus (right side of the graph). Phasic variations in pressure result from respiration. Note that the average intragastric pressure measured before initiation of the pull through is identified on each portion of the graph by a horizontal dotted line. Esophageal pressure is lower than the intragastric pressure, reflecting negative intrathoracic pressure. The lower tracing is recorded from a transducer spaced 3 cm distal to the transducer recording the upper tracing and is shown to begin to enter the high-pressure zone of the LES as the proximal transducer moves into the esophageal body.

---

**Figure 5-4.**

Manometric tracing with two recording sites: one in the distal esophageal body (top tracing) and the second in the high-pressure zone of the lower esophageal sphincter (LES) (bottom tracing). Two water swallows are shown, illustrating normal relaxation of the LES. Note that the average resting tone of the LES is approximately 35 mm Hg greater than the gastric baseline pressure (horizontal dotted line) and that during relaxation the pressure falls close to the gastric baseline. Residual pressure, defined as the difference between gastric pressure and the nadir of the relaxation pressure, should not exceed 8 mm Hg in normal patients.

---

*Esophageal Investigative Techniques* 71
Range of normal values for stationary esophageal manometry. UES—upper esophageal sphincter.

### Manometric Tracing

Manometric tracing within the esophageal body. Recording sites are located at 3 cm (bottom tracing), 8 cm (middle tracing), and 13 cm (top tracing) above the lower esophageal sphincter (LES). A series of four water swallows is illustrated, demonstrating the sequential contraction pattern of typical peristalsis in the distal esophagus. Amplitudes in the distal two recording sites vary between approximately 60 and 150 mm Hg and represent a typical average pressure of approximately 100 mm Hg.
Proximal esophageal peristaltic activity of a series of four swallows. Recording sites are located 1 cm (top tracing), 6 cm (middle tracing), and 11 cm (bottom tracing) below the upper esophageal sphincter (UES). Following the four wet swallows a peristaltic wave is initiated in the proximal esophagus transmitted into the mid-esophagus. Note the more rapid upstroke and shorter duration of the skeletal muscle contraction shown at the proximal recording site and the slower uptake and broader duration shown at the distal recording site. The pressure trough, frequently seen in the transition area between skeletal and smooth muscle, is identified by the nearly flat line at the middle recording site.

Manometric tracing of a slow pull through of the circumferential solid state transducer across the upper esophageal sphincter (UES) (bottom tracing). Note the progressive rise in average resting pressure as the catheter is advanced in 0.5-cm increments. The average maximal UES pressure is 80 mm Hg, approximately the normal average pressure. Note that the middle transducer (spaced 3 cm above the distal transducer) records a tail of the UES pressure as it moves into the pharynx and that the proximal transducer (5 cm above the distal transducer) records pharyngeal pressure.

Manometric recording of three wet swallows with recording sites at the upper esophageal sphincter (UES) (bottom tracing) and 3 cm (middle tracing) and 5 cm (top tracing) above the UES. This figure demonstrates the ideal technique to record actual relaxation of the UES. Here, the distal circumferential transducer has been placed just proximal to the UES to allow it to be captured by the sphincter during elevation at the beginning of the swallow (identified by the initial pressure rise in the distal recording site). This is followed by the relaxation and subsequent contraction of the sphincter, which in turn is followed by return of pressure as the UES descends once more to a position below the transducer. This produces the characteristic "M" configuration on the manometric recording. The proximal and middle transducers demonstrate peristaltic pressures in the pharynx and normal coordination of this event with the relaxation phase of the UES. Note that UES residual pressure (nadir of relaxation) is often negative to the esophageal baseline pressure measured before movement of the transducer across the UES and is demonstrated by the horizontal dotted line.
### A. CLASSIFICATION OF PRIMARY ESOPHAGEAL MOTILITY ABNORMALITIES

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Motility findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Achalasia (the true disorder)</td>
<td>Absent distal peristalsis</td>
</tr>
<tr>
<td></td>
<td>Incomplete LES relaxation (residual pressure &gt; mm Hg)</td>
</tr>
<tr>
<td></td>
<td>Elevated resting LES pressure (&gt; 45 mm Hg)</td>
</tr>
<tr>
<td></td>
<td>Increased baseline esophageal pressure</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Abnormal motility patterns</th>
<th>Motility findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>(nonspecific esophageal dysmotility)*</td>
<td>Simultaneous contractions (&gt;20% wet swallows)</td>
</tr>
<tr>
<td></td>
<td>Intermittent peristalsis</td>
</tr>
<tr>
<td></td>
<td>Repetitive contractions (≥3 peaks)</td>
</tr>
<tr>
<td></td>
<td>Prolonged duration contractions (&gt; 6 sec)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hypercontracting esophagus</th>
<th>Motility findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertensive peristalsis</td>
<td>Increased distal peristaltic amplitude (&gt; 180 mm Hg)</td>
</tr>
<tr>
<td></td>
<td>Increased distal peristaltic duration (&gt; 6 sec)</td>
</tr>
<tr>
<td>Hypertensive LES</td>
<td>Resting LES pressure &gt; 45 mm Hg</td>
</tr>
<tr>
<td></td>
<td>May be incomplete LES relaxation (residual pressure &gt; 8 mm Hg)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hypocontracting esophagus</th>
<th>Motility findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ineffective motility†</td>
<td>Increased nontransmitted peristalsis (≥ 30%)</td>
</tr>
<tr>
<td></td>
<td>Low distal peristaltic amplitude (&lt; 30 mm Hg)</td>
</tr>
<tr>
<td>Hypotensive LES †</td>
<td>Resting LES pressure (&lt; 10 mm Hg)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Others</th>
<th>Motility findings</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Retrograde contractions</td>
</tr>
<tr>
<td></td>
<td>Triple-peaked contractions</td>
</tr>
<tr>
<td></td>
<td>Isolated incomplete LES relaxation (&gt; 8 mm Hg)</td>
</tr>
</tbody>
</table>

*Defined as exceeding two standard deviations from mean of normal values.
†May be "secondary" to gastroesophageal reflux disease.

### B. CLASSIFICATION OF SECONDARY ESOPHAGEAL MOTILITY ABNORMALITIES

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Motility findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systemic sclerosis</td>
<td>Loss of distal (smooth muscle) peristals</td>
</tr>
<tr>
<td></td>
<td>Weak LES pressure (&lt; 10 mm Hg)</td>
</tr>
<tr>
<td>Chagas' disease</td>
<td>Normal proximal esophagus and UES (striated muscle)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>Identical to idiopathic achalasia (see above)</td>
</tr>
<tr>
<td>Chronic idiopathic intestinal pseudo-obstruction</td>
<td>A variety of motility abnormalities of the esophageal body</td>
</tr>
<tr>
<td>Chronic gastroesophageal reflux disease</td>
<td>Loss of distal esophageal motility</td>
</tr>
<tr>
<td></td>
<td>Ineffective motility</td>
</tr>
<tr>
<td></td>
<td>Hypotensive LES</td>
</tr>
</tbody>
</table>

Classification of esophageal motility abnormalities. Traditionally, esophageal motility abnormalities have been divided into primary (occurring without associated diseases), representing abnormalities limited to the esophagus (A), or secondary, defined as esophageal involvement in a patient with an associated systemic disease (B). LES—low esophageal sphincter; UES—upper esophageal sphincter.
Achalasia

Figure 5-11.
Manometric tracing of a pull through into the lower esophageal sphincter (LES) in a patient with achalasia. Note the high resting LES pressure of approximately 54 mm Hg. During water swallows (right side of tracing) relaxation is incomplete, with a residual pressure of approximately 20 mm Hg. The bottom tracing shows the trailing transducer moving into the LES.

Figure 5-12.
Manometric tracing of a patient with achalasia. The transducers are placed at 3 cm (bottom tracing), 8 cm (middle tracing), and 13 cm (top tracing) above the lower esophageal sphincter. Note that a pressure change is identified with each of the water swallows but a peristaltic wave front is completely absent. In fact, the pressure changes noted at each recording site are identical, or mirror images. These waves represent pressure transmitted throughout the dilated, nonpropulsive esophagus, and have also been termed hyperbaric waves. This is a typical pattern of esophageal body motility in a patient with achalasia.

Diffuse esophageal spasm

Figure 5-13.
Manometric tracing of a patient with diffuse esophageal spasm (DES). Recording sites are located at 3 cm (bottom tracing), 8 cm (middle tracing), and 13 cm (top tracing) above the lower esophageal sphincter. Variations in manometric responses (as shown in this patient) are quite typical of DES. On the left a spontaneously occurring simultaneous contraction is shown. This is followed by a swallow-induced peristaltic wave that appears normal. The final water swallow (on the right) shows simultaneous and repetitive contractions, which are typical of DES. This entity is characterized by increased numbers of simultaneous contractions after wet swallows (20% or more), but with intermittent normal peristaltic responses, as illustrated in this figure.
Hypercontracting esophagus

Manometric recording from a patient with hypertensive peristalsis (nutcracker esophagus). Recording sites are located at 3 cm (bottom tracing), 8 cm (middle tracing), and 13 cm (top tracing) above the lower esophageal sphincter. The two responses to water swallows show a normally progressive peristaltic wave of excessive amplitude (approximately 240 mm Hg) at the distal two recording sites. Nutcracker esophagus is defined by average peristaltic responses at these two recording sites, exceeding 180 mm Hg.

Ineffective esophageal motility

Manometric tracing from a patient showing findings previously classified as nonspecific esophageal dysmotility, characterized by essentially nontransmitted contractions following a series of three swallows with only very low amplitude (approximately 20 mm Hg) contractions seen at the distal site. Recording sites are 3 cm (bottom tracing), 8 cm (middle tracing), and 13 cm (top tracing) above the lower esophageal sphincter. This tracing illustrates one of the typical features of what has previously been classified as nonspecific dysmotility, and is better classified as ineffective esophageal motility.
Diabetes mellitus

**FIGURE 5-17.**
Manometric tracing from a patient with diabetes mellitus. Recording sites are located at 3 cm (bottom tracing), 8 cm (middle tracing), and 13 cm (top tracing) above the lower esophageal sphincter. On this tracing a series of water swallows shows peristaltic sequences of low amplitude. Abnormal motility (as shown in this tracing) is common in patients with diabetes mellitus and includes a spectrum from ineffective peristalsis of low amplitude (as shown here) to exaggerated nonperistaltic contractions resembling diffuse esophageal spasm. Interestingly, these patients are often asymptomatic for esophageal symptoms despite quite marked motility abnormalities.

Chronic idiopathic intestinal pseudo-obstruction

**FIGURE 5-18.**
Manometric recording from a patient with chronic idiopathic intestinal pseudo-obstruction (CIIP). This tracing demonstrates the degree of unusual motility that may be seen in the esophagus in patients with CIIP showing spontaneous activity of the esophageal body. The proximal tip is 32 cm from the teeth, the two middle tips are both 37 cm from the teeth, and the distal tip is 42 cm from the teeth. The distal tip is located in the upper portion of the lower esophageal sphincter (LES). Most of the pressure variations are related to respiration. Rates of spontaneous contractions vary at 5 cm and 10 cm above the LES. The patient has not swallowed during this interval, as shown by the flat record from the swallow marker. (*Adapted from Schuffler et al.* [2].)
Hypertensive resting upper esophageal sphincter pressure

Manometric tracing of a patient with a hypertensive resting upper esophageal sphincter (UES) pressure. The distal circumferential transducer is slowly pulled across the UES to identify maximal resting pressure, here reaching approximately 260 mm Hg (normal upper value approximately 115 mm Hg). The middle transducer, located 3 cm proximally, moves out of the UES high-pressure zone and into the pharynx as the distal transducer is drawn into the sphincter. The proximal transducer (5 cm above the distal transducer) records pharyngeal pressures.

Zenker's diverticulum

Manometric tracing of pharyngeal and upper esophageal sphincter (UES) function during swallowing in a patient with Zenker's diverticulum. Recording sites are at the UES (bottom tracing) and 3 cm (middle tracing) and 5 cm (top tracing) above the UES. Although the pharyngeal contraction sequence is peristaltic and properly coordinated with UES relaxation, relaxation is defective, as indicated by a residual pressure of approximately 15 mm Hg. This abnormal relaxation is associated with defective opening of the UES segment seen radiographically in these patients and results in the large intrabolus pressure seen preceding the pharyngeal clearing pressure in the middle recording site (arrow).

Oculopharyngeal muscular dystrophy

Manometric tracing from a patient with oculopharyngeal muscular dystrophy. The recording sites are located in the upper esophageal sphincter (UES) (bottom tracing), hypopharynx, 3 cm proximally (middle tracing), and oropharynx, 5 cm proximally (top tracing). During the single wet swallow illustrated, the UES demonstrates defective relaxation, characterized by a residual pressure of approximately 20 mm Hg above the proximal esophageal baseline (dotted horizontal line) and with a very short duration of relaxation of approximately 0.3 seconds. In addition, the pharyngeal contraction is weak (maximal pressure approximately 55 mm Hg) and is not coordinated with the inadequate UES relaxation. This combination of pharyngeal weakness and poor relaxation of the UES is typical of the manometric abnormality in these patients as their dysphagia becomes more progressive. This represents a true example of cricopharyngeal achalasia. Such patients have been shown to respond well to a cricopharyngeal myotomy.
Pharyngeal paresis

Figure 5-22.
Manometric tracing from a patient with pharyngeal paresis secondary to severe neuromuscular disease. Recording sites are located in the upper esophageal sphincter (UES) (bottom tracing) and 3 cm (middle tracing) and 5 cm (top tracing) above the sphincter. During the swallow shown in the tracing, elevation and relaxation of the UES are normal, but there is almost complete absence of pharyngeal contraction with the exception of a weak (20 mm Hg) contraction in the hypopharynx.

Oropharyngeal dysphagia

Figure 5-23.
Manometric tracing from a patient with severe oropharyngeal dysphagia and marked manometric abnormalities showing both pharyngeal spasm and incomplete upper esophageal sphincter (UES) relaxation. Recording sites are located in the UES (bottom tracing) and at 3 cm (middle tracing) and 5 cm (upper tracing) above the sphincter. Note the early and discoordinated repetitive (spastic) contractions in the oropharynx (top tracing) and the early contraction in the hypopharynx (middle tracing). Relaxation is very short and incomplete in the UES, showing a residual pressure of approximately 40 mm Hg.

Stroke

Figure 5-24.
Manometric tracing from a patient following a stroke with brain-stem involvement. Recording sites are located at the UES (bottom tracing), at 3 cm (middle tracing), and at 5 cm (upper tracing) above the sphincter. The most striking abnormality involves the simultaneous and broad contraction pattern in the pharyngeal recordings with marked incoordination between the pharynx and the relaxation of the UES.
Johnson and DeMeester [3] developed a scoring system based on six variables to characterize the patterns of reflux. They introduced the concept of *physiologic reflux*, which is defined as a pattern seen in asymptomatic volunteers and characterized by rapidly cleared reflux episodes occurring primarily postprandially in the upright position, with rarer reflux episodes while recumbent (see Fig. 5-24). They also called attention to the importance of nocturnal (recumbent) reflux episodes as a risk factor for esophagitis and the associated prolonged clearance of acid during recumbent reflux.

This series of pH tracings shows a 3-minute interval, during which a single reflux episode was recorded during a 24-hour, 5-channel pH monitoring. In this example reflux spreads rapidly throughout the esophagus. Clearing of refluxate is stepwise. Note that at 15 cm above the lower esophageal sphincter the fall in pH does not pass the threshold of pH below 4 whereas the curve shows the same overall pattern as in the distal esophagus. This observation by Weusten et al. [4] illustrates the importance of accurate placement of the pH probe when testing duration of acid exposure in the esophagus and also suggests that a pH cut off above 4.0 might be preferable to identify proximal reflux. (Adapted from Weusten et al. [4]).
Relationship between total percentage of time with pH below 4 comparing the 24-hour study with the 16-hour interval of the same study from 4 PM through 8 AM in the same patients. The excellent correlation ($r=0.98$) indicates that a total recording time of 16 hours can provide information similar to that of a full 24-hour study, particularly if the period studied includes the overnight recumbent phase and an equal portion of upright recording, as was performed in the study shown in the figure. (Adapted from Dobhan et al. [5].)

**Figure 5-28.**

Dual electrode pH recording showing distal acid exposure 5 cm above the lower esophageal sphincter (LES) (heavy line) and proximal pH 20 cm above the LES (narrow line) in a normal individual studied postprandially. Note the occasional brief episodes of distal reflux shown in this patient over a 45-minute period following the evening meal (not shown).

**Figure 5-29.**
Dual electrode pH recording showing esophageal (top tracing) and gastric (bottom tracing) pH in a patient with abnormal upright reflux. During the 24-hour period illustrated in the figure, this patient shows repeated episodes of reflux while awake and in the upright position, many associated with symptoms. In contrast, while in a recumbent position during sleep the patient shows a total absence of reflux. This is a frequent pattern seen in the patient who has reflux only when upright.

Dual electrode pH recording on the computer screen showing esophageal (top tracing) and gastric (bottom tracing) pH for 2 hours in a patient with severe recumbent gastroesophageal reflux. Note the abrupt drop in pH followed by prolonged recovery, itself followed by additional episodes of reflux. This tracing demonstrates the markedly prolonged esophageal acid exposure time due to prolonged acid clearance that occurs in patients with recumbent reflux.

Reflex patterns occurring in healthy controls, upright refluxers, supine refluxers, and combined refluxers shown as mean percentage of time pH below 4 during the 24-hour study in these patient groups.*—mean values significantly greater ($p < 0.05$) than those found in the control group. (Adapted from Johnson and DeMeester [3].)
This graph shows the relative prevalence and severity of endoscopic esophagitis compared to the reflux patterns identified during pH monitoring as shown in Figure 5-32. The prevalence of reflux and its severity increase with the total duration of acid exposure and, particularly, with the percentage of time of abnormal pH with the patient supine. (Adapted from Johnson and DeMeester [3]).

Figure 5-34.
Triple electrode pH recording with the proximally placed electrode (top line) 20 cm above the lower esophageal sphincter (LES), middle electrode (heavy line) positioned 5 cm above the lower esophageal sphincter, and the distal electrode (bottom line) 15 cm below the LES in the gastric fundus. This tracing demonstrates a typical pattern of distal reflux with the intraesophageal pH falling to the level of the intragastric pH. During the distal acid reflux, proximal acid exposure is also present. Note that proximal reflux occurs later and clears sooner than distal reflux. This tracing demonstrates severe reflux in a patient in the upright position.
Data illustrated on this figure document the rough correlation found between the severity of esophagitis and the total percentage of time pH is less than 4 in the distal esophagus during ambulatory monitoring. Normal acid exposure was found for normal controls and symptomatic patients without evidence of esophagitis. Although considerable overlap of values is noted, there is a definite trend toward greater amounts of acid exposure as the grade of esophagitis progresses from 1 through 3. E₀—absence of macroscopic or microscopic esophagitis; E₁—microscopic esophagitis with or without mucosal hyperemia or edema; E₂—nonconfluent esophageal erosions; E₃—confluent erosions with or without erosions or Barrett's esophagus. (Adapted from Mattioli et al. [6].)

Double electrode pH recording with electrodes in the distal esophagus (top tracing) and gastric fundus (bottom tracing). During this 1-hour interval the patient had four episodes of typical chest pain, each precisely related to a reflux event. A strong symptom association of this kind is extremely helpful to confirm the diagnosis of reflux-related symptoms.
Double electrode pH recording with the fainter line indicating distal esophageal pH and the heavier line gastric pH. The patient is taking omeprazole, 20 mg b.i.d. Intragastric pH remains above 4 throughout the 22 hours and 30 minutes of recording with the exception of brief drops in pH during meal periods (indicated by letter M) produced by acidic contents of ingested material. This pH tracing demonstrates the type of total control of intragastric pH that can be achieved with omeprazole, 20 mg b.i.d.

In contrast to the prolonged ambulatory pH study demonstrated in Figure 5-37, this dual electrode study of distal esophageal pH (top tracing) and intragastric pH (bottom tracing) while the patient is taking omeprazole, 20 mg b.i.d., demonstrates total lack of control of gastric acid and of reflux. Note that the intragastric pH remains below 4 throughout the study with the exception of the brief period of neutralization following the evening meal (indicated by letter M). Similarly, repeated and frequent esophageal acidification is noted, in particular, showing long periods of slowly cleared acid during the sleeping recumbent period, identified by the letter "S," followed by the broken line above the tracing itself.

O—time omeprazole taken.

In this figure a classic example of alkaline reflux is seen. There is an abrupt rise in the intragastric pH from the usual baseline level of approximately pH 1.5 to a peak of approximately 8.0. The patient has noted the onset of symptoms with the event marker identified by the letter S above the tracing. Simultaneously, with the abrupt rise in intragastric pH, the esophageal pH rises from its normal level of 6.0 to 7.0 to approximately 8.0 and then gradually recovers as the wave of alkalinity clears. This is an example of duodenogastric esophageal reflux.
The studies illustrated in this figure show double esophageal pH recording in the distal esophagus (upper line) and in the gastric fundus (lower line). The experiment shown includes recording of baseline values, showing the usual level of pH as seen in the esophagus and stomach. This was followed by having this normal volunteer dissolve a neutral lozenge in the mouth to stimulate saliva. Note the rise in distal esophageal pH to a value of approximately 7.5 pH units, with the repeated increases in intragastric pH to a peak value in the same range. In the absence of the lozenge the recovery shows return of the esophageal and gastric pH levels to their usual value. This experiment demonstrates the potential for a false-negative study simulating alkaline reflux, produced by increased salivary flow. (Adapted from DeVault et al. [7].)

The studies illustrated in these graphs were performed with the direct recording bilirubin probe (Bilitec, Synectics, Inc., Irving, TX) compared with a pH electrode, both placed in the distal esophagus. A group of healthy controls and patients with gastroesophageal reflux disease or Barrett’s esophagus is included. The data, presented as a logarithmic transformation of all values, indicate a poor relationship between percentage of time with pH above 7 and bilirubin absorbance (A), but a strong correlation was seen between percentage of time with pH below 4 and bilirubin absorbance (B). These data show that duodenogastric esophageal reflux containing bile is much more likely to be nonalkaline than to have a pH above 7 (actual alkaline level). (Adapted from Champion et al. [8].)
The effect of omeprazole treatment (20 mg b.i.d.) on distal esophageal acid exposure (A) (percentage of time pH < 4) and distal esophageal bilirubin absorption (B), measured by the Bilitec (Synectics, Inc., Irving, TX) probe in a group of patients demonstrating duodenogastric esophageal reflux in a primarily acid environment. The suppression of bile reflux coincidental with the suppression of gastric acid suggests that most bile reflux occurs as total gastric reflux mixed with acid. The improvement in bile reflux while on omeprazole therapy is most likely explained by a dramatic decrease in total gastric fluid volume. (Adapted from Champion et al. [8].)

\[\text{Figure 5-42.}\]

Acid Perfusion Test (Bernstein Test)

Following its introduction in 1958 by Bernstein and Baker, esophageal acid perfusion was widely accepted and used as a clinical test to identify symptoms resulting from gastroesophageal reflux. The patient sits upright in a chair with a nasogastric tube placed 30 cm from the nares. Normal saline solution is infused for 15 minutes followed by 0.1 sodium hydrochloride solution for 30 minutes or until symptoms are produced. Solutions are infused at a rate of 100 to 120 drops (6 mL to 7.5 mL) per minute in such a manner that changes in solutions can be made unknown to the subject. The test is considered positive when the patient’s symptom is twice reproduced during acid perfusion and relieved by saline solution.

The initial report found that 19 of 22 patients with gastroesophageal reflux had a positive test whereas 20 of 21 controls had a negative test resulting in study sensitivity of 85% and specificity of 95%. Over the last 20 years subsequent studies have continued to find a high degree of clinical correlation, with an overall sensitivity of 79% and specificity of 82%. Patients with reflux usually become symptomatic early in the course of the acid infusion, frequently within 7 to 15 minutes, whereas false-positive studies are characterized by symptoms appearing later. This modification may increase the specificity of the acid perfusion test to near 100%, but will also decrease its sensitivity.

The acid perfusion test only shows the sensitivity of the distal esophagus to acid. It is not a test for esophagitis and does not actually measure acid reflux. This test is designed to deliberately produce a symptom (ie, pain) through esophageal acid stimulation that the patient can compare with symptoms he or she experiences spontaneously. Therefore, the test is most useful in patients with multiple or atypical symptoms. If results of the acid perfusion test are positive, particularly early in the perfusion, one can be certain that the symptoms are esophageal in origin. A negative test, does not eliminate an esophageal source. This test may, however, have been made relatively obsolete by ambulatory pH monitoring, now advocated as an endogenous Bernstein test.

The data illustrated here compare Bernstein’s acid-infusion test with spontaneous reflux symptoms noted during ambulatory intraesophageal pH monitoring in 61 patients. The comparison of a positive or negative Bernstein test is made with the symptom index recorded as a percentage of reflux symptoms that were specifically associated with a fall in intraesophageal pH below 4.0. These data indicate that the Bernstein test shows rather poor association with the spontaneous relationship between acid reflux and symptoms, even in those patients at the extremes (ie, having a low or high symptom index). Studies of this kind reinforce the suggestion that ambulatory pH monitoring may have made the Bernstein test obsolete, replacing it with an endogenous test of reflux and associated symptoms. (Adapted from Wiener et al. [9].)
Acid and nonacid reflux. A. Acid reflux episode recorded with combined multichannel intraluminal impedance (MII) and pH (six impedance channels and one distal esophageal pH channel). A sequential drop in impedance, proceeding from distal to proximal esophagus, is typical of a reflux episode. pH, at the bottom of the tracing, falls below 4.0.

(continued on next page)
FIGURE 5-44. CONTINUED

B. Nonacid reflux episode recorded with combined MII and pH (six impedance channels and one distal esophageal pH channel). pH, at the bottom of the tracing, remains above 4.0. (Adapted from Srinivasan et al. [10] and Vela et al. [11].)

REFERENCE

Gastroesophageal reflux (GER) is a process in which gastric contents move spontaneously into the esophagus. This process in itself is for the most part benign in that it occurs in everyone, many times a day and without producing symptoms or signs of tissue injury [1]. However, GER can also be associated with symptoms and signs of tissue damage, and, under these circumstances, the resulting pathology is encompassed under the umbrella term of gastroesophageal reflux disease (GERD).

Predictably, the esophagus is the organ most commonly damaged by exposure to refluxed gastric contents. When damage occurs, it is typically heralded by the development of heartburn. The prevalence of heartburn in the United States is reported as high as 44% of adults, and approximately 10% of adults have heartburn daily. Furthermore, gross damage to the esophageal epithelium can be observed visually on upper endoscopy in some with heartburn; in others, damage is only evident histologically in biopsies of the esophageal epithelium. Those with gross damage shown on endoscopy or acute inflammation on biopsy are said to have reflux esophagitis, and those without endoscopically visible lesions and only non-inflammatory changes on biopsy are said to have symptomatic reflux. GERD also encompasses reflux damage to the oropharynx, larynx, or lower airway, resulting in asthma, laryngitis, or chronic cough. Damage to these tissues often occurs without concomitant esophageal damage.

The etiology of reflux damage to the esophagus is at present unclear. However, it is clear that the disease develops through the acquisition of one or more defects in the esophageal antireflux barriers, luminal clearance mechanisms, or mechanisms for tissue resistance. Such defects result in reflux damage to the esophagus by enabling contact between the esophageal epithelium and gastric (hydrochloric) acid and pepsin suf-
ciently long for acid and pepsin to damage the epithelium [1]. What constitutes sufficient time to cause disease, however, varies greatly among individuals because up to 50% of patients with heartburn and nonerosive disease have normal pH monitoring. The natural history of reflux esophagitis is also poorly understood, but it appears that between 15% and 20% of patients with nonerosive disease may progress to erosive disease over a period of 3 or more years and 5% to 20% of patients with erosive esophagitis may go on to develop a complication in the form of either an esophageal stricture, ulcer, or Barrett’s esophagus [2].

Barrett’s esophagus is important because it is through this lesion that patients with reflux disease are placed at increased risk for the development of esophageal adenocarcinoma [1]. Although reflux disease is a chronic condition and carries considerable morbidity and alteration in the quality of life, it is rarely the direct cause of death.

The treatment of reflux damage to the esophagus is initially medical. Medical therapy has two components lifestyle modification and pharmacotherapy. These therapies are designed to either reduce the noxious quality of the refluxate or increase the strength of one or more of the esophageal defenses. In some instances, reflux disease is severe enough to warrant surgery for control of symptoms or prevention of relapse [1]. Recently, the options for the treatment of GERD have been expanded by the availability of two novel endoscopic antireflux procedures, the EndoCinch (Bard, Murray Hill, NJ) and Stretta (Curon Medical, Sunnyvale, CA), both of which have been approved by the United States Food and Drug Administration.

---

**Figure 6-1.**

The relationship between gastroesophageal reflux (GER) and gastroesophageal reflux disease (GERD). A, GER may be either physiologic or pathologic. When it is pathologic, it is known as GERD. GERD encompasses both nonerosive and erosive pathology resulting from GER, with the erosive pathology being further subdivided into “symptomatic reflux” and “reflux esophagitis” based on the absence or presence of endoscopically detectable inflammation and necrosis, respectively. Notably, the frequency and severity of heartburn does not distinguish between symptomatic reflux and reflux esophagitis, yet the distinction is of clinical importance because only those with reflux esophagitis are at significant risk of complications such as hemorrhage, stricture, or Barrett’s esophagus.

(continued on next page)
B. The nonesophageal complications of GERD include damage to the oropharynx, larynx, and bronchopulmonary system; these give rise to sore throat, hoarseness, and dyspnea or chronic cough, respectively. Damage to each of these areas may also be accompanied by signs of damage and result in complications such as tooth loss, laryngeal stricture, asthma, apnea, pneumonia, and sudden death in infants.

**Epidemiology**

![Figure 6-2](image_url)

Prevalence of heartburn in adult Americans. Heartburn is the primary symptom complex associated with gastroesophageal reflux disease. Its prevalence is depicted in terms of subjects who admit to having heartburn at least once monthly, weekly, or daily [3–5]. There is approximately a three to one male to female predominance, and heartburn is reportedly more common in white Americans than in black Americans [2].

![Figure 6-3](image_url)

Incidence of heartburn in northeast Scotland. The most detailed data available on the incidence of heartburn are reported for a population from northeast Scotland. As depicted, the incidence of symptomatic reflux is very low through the fourth decade of life. In the fifth decade of life, the incidence increases, and it continues to escalate until very late in life. (Adapted from Brunnen et al. [6].)
Pathophysiology and etiology. The initial cause of reflux esophagitis is unknown. However, the key pathogenetic mechanisms involve the ability of noxious gastric contents, especially hydrochloric acid (HCl) and pepsin, to access the esophagus and remain within the lumen long enough to produce damage to the epithelial lining. Because gastric acid and pepsin secretion are normal in patients with gastroesophageal reflux disease (GERD) and bile salts are present in noncytotoxic amounts in gastric juice, the likely cause of GERD involves one or more defects in the esophageal defense against refluxed acid-pepsin. This may include defects in the antireflux barrier (lower esophageal sphincter [LES], diaphragm), which controls the frequency of gastric contents entering the esophagus; the luminal clearance mechanisms (esophageal peristalsis, salivary and esophageal submucosal gland bicarbonate secretion), which control the duration of contact between gastric contents and esophageal epithelium; and the esophageal epithelium, which determines whether the time of contact between epithelium and gastric contents results in injury.

(Adapted from Orlando [1].)
Antireflux mechanisms. Three mechanisms are shown to account for most (acidic) reflux events in healthy control subjects and patients with gastroesophageal reflux disease (GERD): 1) transient lower esophageal sphincter (LES) relaxations, 2) intra-abdominal pressure transients, and 3) spontaneous free reflux. Transient LES relaxations, which are reflex, non-swallow-associated relaxations of the LES, account for almost all reflux events in healthy controls and the large majority (approximately 75%) of events in patients with nonerosive disease. Transient LES relaxations are also common in patients with erosive esophagitis, but less so than in nonerosive reflux disease due to increased frequencies of both spontaneous free reflux across an incompetent LES (< 4 mm Hg LES pressure) and intra-abdominal pressure transients producing stress reflux across a weak LES (< 10 mm Hg LES pressure). (Adapted from Dodds et al. [7].)

Antireflux mechanisms. The mechanisms for reflux in ambulatory patients with gastroesophageal reflux disease (GERD) differ considerably in the presence or absence of a hiatal hernia. The mechanisms for reflux in GERD patients without a hiatal hernia (A) are predominantly caused by transient lower esophageal sphincter relaxation (TLESR) and, to a much lesser extent swallow-associated prolonged lower esophageal sphincter relaxation (SAPLESR). In patients with GERD who also have a hiatal hernia (B), the mechanisms for reflux events are more evenly divided among TLESR, low LES pressure (LESP), and strain, with smaller but significant numbers of events also occurring with normal duration swallows (ie, swallow-associated normal duration LES relaxations [SANLESR]). This results in patients with a hiatal hernia having less than 50% of the total reflux events each day being caused by TLESR. (Adapted from Margot et al. [8].)

Esophageal luminal acid clearance mechanisms. Esophageal luminal acid clearance mechanisms act to minimize the time that refluxed gastric acid remains in contact with the esophageal epithelium. It consists of the four processes listed here. Two of the processes—esophageal peristalsis (both primary caused by swallowing and secondary caused by distension) and gravity—act to clear the refluxed bolus from the lumen. The other two processes—swallowed saliva and secretions from esophageal submucosal glands (both rich in bicarbonate)—act to dilute and neutralize residual acid within the lumen and unstirred water layer adjacent to the epithelium surface. On average, it takes a healthy subject about 3 to 5 minutes to clear acid from the esophagus after a single bout of reflux.
Esophageal luminal acid clearance mechanisms. The interactivity between mechanisms for volume clearance and acid clearance in a healthy subject is illustrated. Gravity is negated because the subject is supine. After injection of 15 mL of hydrochloric acid (pH 2.0) into the esophagus, peristalsis initiated by dry swallows (DS) is shown to clear the bolus with one to two swallows. Bolus clearance, however, does not raise the esophageal pH to a normal level. Additional swallows are performed that incrementally raise the luminal pH back to normal; this occurs because of the requirement for swallowed saliva to neutralize the residual luminal acid after bolus clearance. Confirmation of the latter concept is presented by the absence of incremental increases in esophageal pH if salivary secretions are suctioned from the mouth before swallows (data not shown). (Adapted from Helm et al. [9].)

Esophageal luminal acid clearance. An increase in frequency of failed peristaltic sequences after swallows is present in patients with mild to severe esophagitis. By delaying bolus (and so acid) clearance, this increases acid contact time and the risk of damage to the esophageal epithelium. (Adapted from Kahrilas [10].)
Esophageal luminal acid clearance. Although the presence of a hiatal hernia alone is not enough for the development of reflux disease, there is an association between a hiatal hernia and erosive esophagitis. This association likely results from the ability of hernias both to increase the frequency of reflux through distortion of the relationship between the lower esophageal sphincter (LES) and diaphragm, impairing the gastroesophageal junction's high-pressure zone (see Fig. 6-6), and to delay esophageal luminal acid clearance by producing "early retrograde reflux" (ie, reflux early during the swallow-initiated relaxation phase of the LES). The data also indicate that this latter phenomenon is more typical of hernias that do not reduce during swallows to their normal position, so-called "non-reducing" hernias [11]. (Adapted from Sloan et al. [11].)

![Figure 6-12.](image)

Hiatal hernia. An example of a moderate-sized sliding hiatal hernia (arrows) is demonstrated on this barium esophagogram. This figure illustrates the distorted anatomy of the gastroesophageal junction in the presence of the hernia. (From Eisenberg [12]; with permission.)

![Figure 6-13.](image)

Bile salt concentrations in various forms of reflux esophagitis. There is uniform acceptance of the fact that gastric acid and pepsin, although secreted in normal amounts, play the primary role for the development of reflux esophagitis (data not shown). There continues, however, to be debate about the role that refluxed bile salts play in esophageal injury and its complications. The data in this figure illustrate that the concentration of bile salts present in stomach and refluxed into the esophagus increases with increasing severity of disease. The predominant bile acids detected were the primary bile acids—cholic, taurocholic, and glycocholic acid—with significantly greater proportions of secondary bile acids—deoxycholic and taurodeoxycholic acid—present in patients with erosive esophagitis, Barrett's esophagus, and stricture. It should be noted, however, that the maximum concentrations of the bile salts reported fall well below the 5 mM concentrations shown to be cytotoxic to esophageal epithelium. (Adapted from Nehra et al. [13].)
POTENTIAL COMPONENTS OF TISSUE RESISTANCE AGAINST ACID INJURY IN THE ESOPHAGUS

Pre-epithelial defenses
Mucus layer
Unstirred water layer
Surface bicarbonate ion concentration
Epithelial defenses
Physical barriers
Cell membranes
Intercellular junctional complex
Tight junctions
Intercellular glycoconjugates or mucin
Functional components
Cellular defense against acidification
Apical membrane Na+ channel regulation
Intracellular pH regulation
Intracellular buffering
Basic proteins
Bicarbonate ions
Phosphates
Epithelial repair (basal layers only)
Epithelial restitution
Cell replication
Postepithelial defenses
Blood flow
Delivery of beneficial substances
Oxygen
Metabolic substrates (nutrients)
Bicarbonate ions (extracellular buffering)
Removal of noxious agents
CO2
H+
Metabolic byproducts
Cellular debris

Potential components of tissue resistance against acid injury in the esophagus. Tissue resistance is a multifaceted process that is designed to protect the esophageal epithelium from injury by noxious luminal elements. Those designed to protect against luminal acidity are depicted here and in Figure 6-11. (Adapted from Orlando [14].)
Tissue resistance. Tissue resistance can be envisioned as comprising structural and functional defenses. Structural barriers limit the rate of diffusion of luminal acid (H⁺) into and between the esophageal epithelial cells; these include the cell membrane and intercellular junctional complex, respectively. Functional defenses include both intracellular and extracellular buffers and processes for the extrusion of H⁺ from the cytosol (eg, basolateral membrane NaH⁺/H⁺ exchanger and Na⁺-dependent Cl⁻/HCO₃⁻ exchanger). CA—carbonic anhydrase; ICS—intercellular space. (Adapted from Orlando [1].)

Tissue resistance. A number of factors that can alter the ability of the esophageal epithelium to defend itself against refluxed gastric acid are depicted here. Among the most common factors are smoking; alcohol; hot (temperature) beverages; foods such as pizza; salt and spices that produce hypertonic luminal environments; and medications that produce topical irritation, including tetracycline or doxycycline, potassium chloride, vitamin C, quinine, and nonsteroidal anti-inflammatory drugs.
Figure 6-17.
Conditions and activities reported to be associated with gastroesophageal reflux disease.

Figure 6-18.
*Helicobacter pylori.* One important pathogenetic factor in duodenal (and gastric) ulcer disease is chronic infection with *H. pylori.* This figure illustrates that unlike duodenal ulcer disease, the prevalence of *H. pylori* infection in reflux esophagitis is similar to that of healthy control subjects. This supports the lack of causality for *H. pylori* infection in patients with reflux disease. Also, patients with Barrett's esophagus, particularly when infected with CAG A+ strains (data not shown), generally have lower frequencies of infection with *H. pylori* than healthy subjects. The observation raises the question as to whether infection with *H. pylori*, by damaging gastric mucosa and raising gastric pH, may serve a protective role against reflux disease and its complications. (Adapted from Newton et al. [15].)

Figure 6-19.
The protective role of *Helicobacter pylori.* The possibility that infection with *H. pylori* may serve a protective role against the development of reflux esophagitis has support in the observation that the incidence of endoscopic esophagitis occurred twice as much over a 3-year period in patients with duodenal ulcer in whom *H. pylori* was successfully eradicated (closed circles) as those in whom *H. pylori* infection persisted (open circles). (Adapted from Labenz et al. [16].)
Characteristics of heartburn. Heartburn is a symptom complex characterized by substernal (burning) pain radiating toward the mouth, which is worsened by meals and recumbency and ameliorated by antacid ingestion. When typical, recurrent heartburn is adequate for the diagnosis of gastroesophageal reflux disease (GERD). Acid regurgitation, the spontaneous eructation of bitter material in the esophagus and mouth, and water brash, the spontaneous appearance of a bland or salty fluid in the mouth, are also common symptoms of GERD. Odynophagia, however, is very uncommon in those with GERD and usually reflects mucosal destruction from pills (doxycycline or tetracycline, nonsteroidal antiinflammatory agents, vitamin C, quinine) or infectious agents (Herpes simplex virus, cytomegalovirus, Candida albicans, HIV).

Esophageal pathology in gastroesophageal reflux disease. Reflux-induced damage to the esophageal epithelium exhibits a broad spectrum of pathology, ranging from noninflammatory to inflammatory changes and from normal epithelial (squamous) repair to aberrant repair in the form of Barrett’s esophagus. The newest addition to these changes is the presence of dilated intercellular spaces, a lesion initially identified on electron microscopy but one that may also be appreciated on light microscopy (see Fig. 6-23). (Adapted from Orlando [17].)
Histopathology. The histopathologic changes of reflux damage to the esophageal epithelium most commonly noted on esophageal biopsy are basal cell hyperplasia and elongation of the rete pegs (arrows) [18]. These features have a high sensitivity but relatively low specificity for disease, the latter because of the presence of these features in 20% of healthy subjects in the lower 2.5 cm of esophagus [19]. (From Lewin [18]; with permission.)

Histopathology of gastroesophageal reflux disease (GERD). Dilated intercellular spaces are another important feature of early reflux damage to the esophageal epithelium. This abnormality, which reflects an increase in paracellular permeability, has been noted in both patients with nonerosive and erosive esophagitis using transmission electron photomicroscopy. A, Control subject. B, Erosive GERD. C, Nonerosive GERD. Original magnification, × 3000. (From Tobey et al. [20]; with permission.)

Histopathology. Acute inflammation on esophageal biopsy is generally observed accompanying cell necrosis in patients with erosive esophagitis. The lesion is characterized by the presence of edema, polymorphonuclear or eosinophilic leukocyte infiltration, and vascular congestion and extravasation. These changes, however, are not pathognomonic for reflux-induced injury. In particular, the presence of more than 20 eosinophils per high-power field should raise the specter of eosinophilic or allergic esophagitis [10,21]. (From Mitros [22]; with permission.)
Endoscopic view of erosive esophagitis. The endoscopic hallmark of reflux esophagitis is the presence of one or more erosions within the distal esophagus [23]. Shown here is grade III esophagitis with confluent erosions involving the entire circumference of the distal esophagus. The endoscopic presence of erosions, however, is an insensitive indicator of reflux disease because the lesions are identified in fewer than 50% of subjects with heartburn severe enough to undergo the procedure. (From Tytgat et al. [23]; with permission.)

**ENDOSCOPIC GRADING SYSTEM FOR REFUX ESOPHAGITIS**

<table>
<thead>
<tr>
<th>CLASSIFICATION</th>
<th>GRADE</th>
<th>CHARACTERISTICS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Savary-Miller classification</td>
<td>I</td>
<td>Single lesion (erosive or exudative) involving only one longitudinal fold</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>Multiple lesions (erosive or exudative) involving more than one longitudinal fold but not circumferential</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>Circumferential (erosive or exudative) lesions</td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td>Chronic lesions: ulcer, stricture, or short esophagus ± lesions of grades I to III</td>
</tr>
<tr>
<td></td>
<td>V</td>
<td>Barrett’s epithelium ± lesion of grade I through IV</td>
</tr>
<tr>
<td>Los Angeles classification</td>
<td>A</td>
<td>One or more mucosal breaks (erosions) confined to the folds, each no longer than 5 mm</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>At least one mucosal break more than 5 mm long confined to the mucosal folds but not continuous between the tops of the mucosal folds</td>
</tr>
<tr>
<td></td>
<td>C</td>
<td>At least one mucosal break continuous between the tops of two or more mucosal folds but not circumferential</td>
</tr>
<tr>
<td></td>
<td>D</td>
<td>Circumferential mucosal break</td>
</tr>
<tr>
<td>Hetzel (Hetzel-Dent) classification</td>
<td>0</td>
<td>Normally appearing mucosa</td>
</tr>
<tr>
<td></td>
<td>I</td>
<td>Mucosal edema, hyperemia, or friability</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>Erosions that involve &lt; 10% of the lower 5 cm of the esophagus</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>Erosions that involve 10% to 50% of the distal esophagus</td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td>Deep ulceration or erosions that involve &gt; 50% of the distal esophagus</td>
</tr>
</tbody>
</table>

Endoscopic grading systems for reflux esophagitis. The grading system lacks standardization. The table lists the criteria used for three of the most commonly cited classifications in the literature. The Savary-Miller is the oldest and most widely used classification in the United States [24]; it grades erosions as single (I), multiple (II), and circumferential (III) and then uses more advanced grades for complications, with IV for ulcer and stricture and V for Barrett’s esophagus. The Los Angeles and Hetzel classifications also grade erosions but, unlike the Savary-Miller classification, they do not have grades for complications of esophagitis.

The Los Angeles classification grades erosion length and extent more importantly than number. Erosions with maximum length of less than 5 mm are denoted as grade A; erosions with at least one whose length is greater than 5 mm denoted as grade B; erosions that form a lesion that connects the tops of two folds denoted as grade C; and erosions that are completely circumferential denoted as grade D [25]. The Hetzel (or Hetzel-Dent) classification is the only classification that gives a grade (other than 0) for more subtle (and subjective) endoscopic findings, mucosal edema, friability, and hyperemia being reported as grade I; erosions whose area covers less than 10% of the distal (5 cm) esophagus reported as grade II; erosions that cover 10% to 50% of the distal esophagus are reported as grade III; and erosions that cover more than 50% of the distal esophagus or deep ulceration are reported as grade IV [26].
Esophageal strictures. A barium esophagogram demonstrates the presence of a high-grade, smooth-walled distal esophageal stricture that resulted from reflux esophagitis [1]. Patients with this complication of reflux disease usually note amelioration of heartburn as they develop the symptom of dysphagia. The dysphagia is for solids and not liquids (unless their is solid food impaction first), indicating the presence of a lumen-narrowing lesion. The absence of anorexia and weight loss and slow rate of progression of dysphagia are good indications that the lesion is a benign peptic process. The presence of anorexia and weight loss and rapid progression of dysphagia raises the likelihood that the lesion is malignant and most likely an adenocarcinoma arising in a Barrett’s esophagus (see Fig. 6-29). (From Stewart et al. [27]; with permission.)
Barrett's esophagus. Three types of columnar epithelium have been identified within the lower esophagus: 1) junctional epithelium, which is similar to the epithelium that lines the gastric cardia; 2) atrophic fundic epithelium, which is similar to the epithelium that lines the gastric fundus; and 3) specialized columnar epithelium, which has the appearance of small intestine with a villiform surface, microvilli, and Paneth cells, and contains highly characteristic goblet cells that stain positive (blue) for acidic mucins with Alcian blue, pH 2.5. However, only the presence of specialized columnar epithelium (shown here) is diagnostic of Barrett's esophagus [29]. Furthermore, specialized columnar epithelium, unlike junctional and atrophic fundic epithelia, represents true metaplasia with the inherent potential for malignant degeneration. The figure depicts Barrett's epithelium with prominent surface mucous and (blue staining) goblet cells and mucous glands in the lamina propria (original magnification × 200). (From Lewin [18]; with permission.)

Barrett's esophagus. The prevalence of Barrett's esophagus as detected on endoscopy is shown to increase with age. This adds support for Barrett's esophagus' being an acquired lesion. In absolute numbers the frequency of (long segment) Barrett's esophagus in adult populations is estimated to be about 1% of autopsies and all patients having endoscopy. For patients with gastroesophageal reflux disease patients undergoing endoscopy, the frequency rises to approximately 10% to 15% [1]. (Adapted from Cameron [31].)

Rising incidence of adenocarcinoma of the esophagus. Barrett's esophagus carries with it the risk for development of adenocarcinoma of the esophagus. As shown here, adenocarcinoma of the esophagus is a cancer with one of the greatest increases in incidence over the last 30 years. The reason for this increase is unknown, but it is principally confined to those of European ancestry. White men are at the highest risk, particularly those who are overweight, consume excess alcohol, and smoke.

Another major risk factor for the development of adenocarcinoma of the esophagus is the length of Barrett's metaplasia within the esophagus [33]. The incidence of cancer's developing in the esophagus of patients with Barrett's esophagus has been estimated to be from one in 52 patient years to one in 441 patient years, with the best overall estimate for the United States being one in 200 patient years or 0.5% of patients per year. This incidence, although very low, still represents a relative increase in risk of esophageal cancer (representing 2.2% of all cancers in the United States in 1998) that is 30 to 125 times that of the general population [1]. (Adapted from Pera et al. [32].)
Frequency of cancer in patients based on frequency, severity, and duration of heartburn. In 1999, Lagergren et al. [34] published an article linking the risk of developing esophageal adenocarcinoma in (Swedish) patients to heartburn. As shown here, the relative risk of this cancer's developing increases with heartburn frequency, severity, and duration, with a maximal risk exceeding 40 times that of the general (non-heartburn) population. (Adapted from Lagergren et al. [34].)

Incidence of cancer based on the frequency of heartburn or in Barrett's esophagus. As shown in Figure 6-28, the relative risk of developing esophageal adenocarcinoma in patients with heartburn is high. However, the low absolute incidence of esophageal adenocarcinoma in the United States (approximately 6000 cases per year) and the high frequency of heartburn (estimates range from 13 million to more than 60 million) calculates to a relatively low absolute risk of esophageal cancer for any given patient with heartburn. Note that the cancer risk in Barrett's esophagus at one in 200 patients per year is much greater irrespective of the presence or absence of heartburn. (Adapted from [3].)

Tests for diagnostic assessment of gastroesophageal reflux disease (GERD), its mechanisms, and its consequences. Testing falls into four categories, depending on the information desired. For example, there are tests that can document reflux, assess symptoms, assess esophageal damage, or the assess the pathophysiology of GERD. GI—gastrointestinal; PPI—proton pump inhibitor [1]. (Adapted from Orlando [1].)
MODIFICATION OF LIFESTYLE TO LESSEN REFLUX ESOPHAGITIS

- Elevate the head of the bed 6 inches
- Stop smoking
- Stop consuming excessive alcohol
- Reduce fat in diet
- Reduce size of meals
- Avoid eating at bedtime
- Lose weight (if overweight)
- Avoid wearing tight-fitting clothes
- Avoid certain foods
  - Chocolate
  - Carminatives (eg, spearmint, peppermint)
  - Coffee (eg, caffeinated and decaffeinated)
  - Tea
  - Cola beverages
  - Tomato juice
  - Citrus juices
- Avoid certain drugs, when possible
  - Anticholinergics
  - Theophylline
  - Diazepam
  - Narcotics
  - Calcium channel blockers
  - β-Adrenergic agonists (isoproterenol)
  - Progesterone (some contraceptives)
  - α-Adrenergic antagonists (phentolamine)

**Figure 6-36.** Modifications of lifestyle to lessen reflux esophagitis. Lifestyle modifications are indicated for all patients with reflux disease. Many of the recommended strategies do not only improve reflux disease but also reduce the risk of some other illnesses (eg, a low-fat diet reduces the risk of colon cancer and heart disease). Moreover, most of these strategies come at little or no cost. The benefit of reducing or stopping medications that may promote reflux needs to be balanced against the necessity for treatment of other conditions. Most of the medications, although they do lower esophageal sphincter (LES) pressure, do so only modestly and may not adversely influence LES relaxation. (Adapted from Orlando [35].)
### Management of Gastroesophageal Reflux Disease by Pharmacotherapy

<table>
<thead>
<tr>
<th>Conventional Drugs</th>
<th>Dosage</th>
<th>Mechanisms of Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antacid: liquid (Mylanta II*, Maalox TCT; HCl neutralization, capacity, 25 mEq/5 mL)†</td>
<td>15 mL QID 1 hour after meals and at bedtime</td>
<td>Buffer HCl</td>
</tr>
<tr>
<td>Gaviscon§ (AI hydroxide, Mg trisilicate, NaHCO₃, aliginic acid)</td>
<td>Two to four tablets QID after meals and at bedtime</td>
<td>Decrease reflux by viscous mechanical barrier; buffer HCl in esophagus</td>
</tr>
<tr>
<td>H₂-receptor antagonists</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cimetidine</td>
<td>800 mg BID</td>
<td>Decrease HCl secretion and gastric volume by inhibiting H₂ receptor</td>
</tr>
<tr>
<td>Ranitidine</td>
<td>150 mg QID/300 mg BID</td>
<td>Decrease HCl secretion and gastric volume by inhibiting H₂ receptor</td>
</tr>
<tr>
<td>Famotidine</td>
<td>20 mg QID</td>
<td>Decrease HCl secretion and gastric volume by inhibiting H₂ receptor</td>
</tr>
<tr>
<td>Nizatidine</td>
<td>150 mg BID</td>
<td>Decrease HCl secretion and gastric volume by inhibiting H₂ receptor</td>
</tr>
<tr>
<td>Prokinetics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bethanechol</td>
<td>25 mg QID 1/2 hour before meals and at bedtime</td>
<td>Increase LESP</td>
</tr>
<tr>
<td>Increase esophageal acid clearance</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metoclopramide</td>
<td>10 mg QID</td>
<td>Increase LESP</td>
</tr>
<tr>
<td>Cisapride (withdrawn from market)</td>
<td>10 mg TID of QID 1/2 hour before meals and at bedtime</td>
<td>Increase LESP; increase gastric emptying</td>
</tr>
<tr>
<td>Mucosal protectant</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sucralfate</td>
<td>1 g QID 1 hour after meals and at bedtime</td>
<td>Increase tissue resistance</td>
</tr>
<tr>
<td>Buffer HCl in esophagus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bind pepsin and bile salts</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inhibitors of H₂-K⁺-ATPase</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Omeprazole</td>
<td>20 mg/d</td>
<td>Decrease HCl secretion and gastric volume</td>
</tr>
<tr>
<td>Lansoprazole</td>
<td>30 mg/d</td>
<td>Decrease HCl secretion and gastric volume</td>
</tr>
<tr>
<td>Rabeprazole</td>
<td>20 mg/d</td>
<td>Decrease HCl secretion and gastric volume</td>
</tr>
<tr>
<td>Pantoprazole</td>
<td>40 mg/d (PO or IV)</td>
<td>Decrease HCl secretion and gastric volume</td>
</tr>
<tr>
<td>Esomeprazole</td>
<td>20 to 40 mg/d</td>
<td>Decrease HCl secretion and gastric volume</td>
</tr>
</tbody>
</table>

†Novartis, Summit, NJ.
‡Patients with reflux are generally not known to be hypersecretors of gastric acid. Therefore, therapeutic doses of antacids are based on the capacity to buffer basal HCl secretion of approximately 1 to 7 mEq/hour (mean, 2 mEq/hour) and peak meal-stimulated HCl secretion of approximately 10 to 60 mEq/hour (mean, 30 mEq/hour).
§SmithKline Beecham, Pittsburgh, PA.

Management of gastroesophageal reflux disease by pharmacotherapy. The medications used in the treatment of reflux esophagitis are listed. These include antacids that act by buffering gastric acid, either within the esophageal lumen or stomach; H₂-receptor antagonists, or proton pump inhibitors that inhibit gastric acid secretion, thereby making the refluxate less noxious to the esophageal epithelium; prokinetics that increase smooth muscle contractility, thereby increasing lower esophageal sphincter pressure, amplitudes of esophageal peristaltic contractions, and the rate of gastric emptying; and mucosal protectants, which act on the epithelium to reduce the damaging action of acid and pepsin. ATPase—adenosine triphosphatase; BID—twice a day; IV—intravenous; LESP—lower esophageal sphincter pressure; QID—four times a day; PO—per oral; TID—three times a day. (Adapted from Orlando [1].)
Physiology of parietal cell acid secretion. One of the most effective means of treating patients with gastroesophageal reflux disease is to inhibit gastric acid secretion. This can be effectively achieved by the administration of either H₂-receptor antagonists (H₂RAs) or proton pump inhibitors (PPis). The H₂RAs act by blocking the histamine-2 receptor on the basolateral cell membrane. The PPis block the apical membrane proton pumps. Because the proton pump is the final common pathway for acid secretion, the PPis are more powerful acid suppressants than are the H₂RAs. Note that anticholinergic agents can reduce gastric acid secretion by blocking the basolateral membrane acetylcholine receptor, but they are poorly tolerated because of other systemic anticholinergic effects (e.g., they produce dry mouth, diplopia, tachycardia and urinary retention). CCK₈—cholecystokinin beta receptor; ECL—enterochromaffin-like; H₂—histamine-2 receptor; M₃—muscarinic cholinergic receptor type 3.

Relationship of gastric acid secretion to healing of erosive esophagitis. There is a strong and almost direct relationship between the duration of inhibition of gastric acid secretion and the healing of erosive esophagitis. The same is true of reflux symptoms such as heartburn. This is the case because reduction in acid secretion is paralleled by reduction in acidity of the refluxate. This observation also explains why proton pump inhibitors are overall more effective than are histamine-2 receptor antagonists (H₂RAs) in managing patients with reflux disease. Nonetheless, about 50% of patients with heartburn can have symptoms effectively controlled by the H₂RAs, although healing rates in those with erosive disease is much lower (Adapted from Wilkinson et al. [36].)

Pharmacotherapy and acid inhibition. The duration of action of various pharmacologic agents used in the treatment of reflux disease to control gastric acidity (pH > 4). The duration of control of acidity for the different agents parallels their success in healing patients with erosive esophagitis. ANT—antacid 450 mmol seven times daily; C4B—cimetidine, 400 mg at bedtime; C4Q—cimetidine, 400 mg four times daily; C8N—cimetidine, 800 mg at bedtime; F40—famotidine, 40 mg at bedtime; O20—omeprazole, 20 mg/day; O30—omeprazole, 30 mg/day; O60—omeprazole, 60 mg/day; R3N—ranitidine, 300 mg at bed time; R150—ranitidine, 150 mg twice daily. (Adapted from Wilkinson et al. [36].)
Relapse rates after healing erosive esophagitis. Symptoms and signs of erosive esophagitis can be readily controlled with an 8- to 12-week course of proton pump inhibitors. This figure, however, shows that after their cessation, the relapse rate is exceedingly high—about 50% at 3 months and 80% at 6 months. This observation supports the need for maintenance therapy in most patients with erosive disease. (Adapted from Hetzel et al. [37].)

The percentages of patients in remission remaining in the five different treatment groups during 12 months (cisapride 10 mg three times a day, ranitidine 150 mg three times a day, omeprazole 20 mg once a day) \( (n = 35 \text{ for each treatment group}) \). Currently, six medications are approved by the Food and Drug Administration for maintenance in reflux disease: two H₂-receptor antagonists (ranitidine 150 mg twice a day [BID], famotidine 40 mg/d), and four proton pump inhibitors (PPIs; lansoprazole 15 mg/d, omeprazole 20 mg/d, rabeprazole 20 mg/d, and esomeprazole 20 mg/d). Notably, one of the most important predictors of success with maintenance therapy is the initial grade of esophagitis—the higher the grade, the lower the success rate over time. Additionally, maintenance is significantly less effective for PPIs when given on weekends only or every other day. (Adapted from Wigneri et al. [38].)

Long-term therapy with proton pump inhibitors (PPIs). The potency of PPIs in inhibiting gastric acid secretion results in almost all patients developing hypergastrinemia while taking therapy. The hypergastrinemia is caused by the increase in antral pH (pH > 3.0) from therapy stimulating the release of gastrin from the gastric antral G cells. Because hypergastrinemia produces an increase in parietal cell mass, when therapy is stopped and gastrin levels return to normal within a few weeks, there is a rebound hyperacidity that may last for at least 2 months. Hypergastrinemia also has importance in that it has been linked to the risk of certain tumors in humans (see Fig. 6-44). (Adapted from Brunner et al. [39].)
Long-term risks of acid suppression. Long-term risks, which include acid suppression, particularly with maintenance proton pump inhibitor (PPI) therapy, are related to their ability to produce hypochlorhydria and hypergastrinemia. As illustrated, hypochlorhydria, which is responsible for the hypergastrinemia, can directly lead to impaired absorption of iron and vitamin B₁₂ and a worsening of *Helicobacter pylori* gastritis. Although *H. pylori*-induced gastritis is a forerunner to gastric atrophy, this sequence has not been unequivocally proven to be accelerated by concomitant treatment with PPIs. Hypochlorhydria also leads to bacterial overgrowth, which increases production of gastric nitrosamines, a known carcinogen and risk factor for gastric adenocarcinoma. Hypergastrinemia is shown to result in benign gastric fundic polyps and enterochromaffin cell hyperplasia. It also causes carcinoid tumors in rats and, although carcinoid tumors have been reported in hypergastrinemic patients with pernicious anemia and Zollinger-Ellison syndrome, it has not been reported for humans using PPIs for up to 10 years [40]. Another risk of chronic hypergastrinemia (for a duration of approximately 15 years) is that of colon cancer. To date, however, no reports have documented a link between colon cancer and chronic PPI therapy [41,42].
Surgical management. Patients who are successfully controlled with acid suppressant therapy but do not desire to remain on medications lifelong are candidates for antireflux surgery. The most commonly performed surgical procedures for gastroesophageal reflux disease are the Hill gastropexy (A), Belsey (partial) fundoplication (B), and Nissen (complete) fundoplication (C) [28]. The Nissen procedure is the most popular and can be performed either as an open procedure or using the laparoscopic approach. The laparoscopic Nissen procedure has an initial failure rate of approximately 10% and an approximate 1% breakdown of the wrap each year. The procedure itself carries little mortality risk, but morbidity rates, including esophageal perforations, wound infections, splenic tears, postoperative dysphagia, and gas bloat, occur in about 10% of patients. The cost of a successful Nissen procedure is estimated to be equivalent in cost to 10 years of chronic proton pump inhibitor (PPI) therapy, but this analysis will change in favor of PPI therapy after a generic version is available in 2002. (Adapted from Pope [43].)

Endoscopic therapy of reflux disease. The Food and Drug Administration has approved two novel endoscopic techniques for the treatment of gastroesophageal reflux disease, the EndoCinch (A) procedure and the Stretta procedure (B). The EndoCinch procedure permits the endoscopist to create a gastroplication just below the esophagogastric junction using an overtube and sewing attachment, and this plication serves as a barrier to reflux [44,45]. The Stretta procedure, through the use of thermocouples attached to a balloon and catheter system positioned at the esophagogastric junction, permits the delivery of high-frequency energy to the lower esophageal sphincter and cardia of the stomach. This injury within the sphincter region controls reflux by producing collagen deposition, remodeling, and reduced compliance of the esophagogastric junction [46,47]. Although these procedures have been met with initial enthusiasm and some success in reducing the reliance on chronic acid suppressant medications, neither one is free of serious side effects, and their data have not established their durability. These procedures are also not indicated in patients with hiatal hernias or erosive esophagitis, and they should currently be considered experimental.
Alarm symptoms
Weight loss
Dysphagia
GI bleeding

Yes
Early endoscopy to rule out cancer and/or control bleeding

No
Empric therapy
Lifestyle modification
Antacids taken as necessary for heartburn
Acid suppressant therapy with OTC $H_2$RA PRN

Unsuccessful
Treat with $H_2$RA BID 2 weeks

Unsuccessful
Treat with PPI QD 2 weeks

Unsuccessful
Treat with PPI BID 2 weeks

Endoscopy and 24-h pH monitoring on treatment

Unsuccessful
Negative pH monitoring with endoscopic lesion
Rule out pill-induced esophagitis
Rule out infectious esophagitis
Rule out eosinophilic esophagitis

Negative pH monitoring without endoscopic lesion
Rule out esophageal motor disorders
Rule out visceral hypersensitivity syndrome
Rule out eosinophilic esophagitis

Positive pH monitoring with or without endoscopic lesion
Rule out Zollinger-Ellison syndrome
Increase PPI dosage
Consider antireflux procedures

If successful, one attempt to taper off medication after a period of 8 to 12 weeks is desirable. If unsuccessful in controlling symptoms on BID PPI therapy, upper endoscopy and 24-hour pH monitoring are desirable for diagnosis. The pH monitoring is valuable in establishing whether acid suppression has translated into effective control of esophageal acidity. If acid contact time in the esophagus is normal and endoscopy does not show lesions, consider the diagnosis of esophageal motor disease, visceral hypersensitivity, or noneosophageal causes of chest discomfort. If endoscopy shows esophagitis, consider pill-induced or infectious causes. If the patient’s acid contact time is abnormal, consider lack of compliance, problems with absorption of medications, or Zollinger-Ellison syndrome. OTC—over the counter, PRN—as required.
EFFECTS OF THERAPY ON THE NEED FOR SUBSEQUENT DILATATION IN PATIENTS WHO HAVE ESOPHAGITIS WITH STRICTURE AT THE END OF 6 MONTHS OF THERAPY

<table>
<thead>
<tr>
<th></th>
<th>Omeprazole (n = 17)</th>
<th>H₂RA (n = 15)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients needing follow-up dilatations, %</td>
<td>41</td>
<td>73</td>
<td>0.07</td>
</tr>
<tr>
<td>Dilatation sessions, n</td>
<td>0.6 ± 0.9 SD</td>
<td>2.1 ± 1.5</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Dilatation sessions, total</td>
<td>11</td>
<td>31</td>
<td></td>
</tr>
</tbody>
</table>

Effects of therapy on the need for subsequent dilatation in patients who have esophagitis with stricture at the end of 6 months of therapy. The proton pump inhibitor omeprazole is shown to be more effective than an H₂-receptor antagonist (H₂RA) in reducing the number of dilatations for control of dysphagia in patients with acid-peptic esophageal strictures. Patients with strictures likely benefit from acid suppressant therapy because their lumen-narrowing properties are partly the result of inflammation produced by continuing acid reflux. SD—standard deviation. (Adapted from Marks [48].)

MEAN LENGTH AT BASELINE DURING EACH VISIT AND CHANGE FROM BASELINE OF BARRETT’S EPITHELIUM

<table>
<thead>
<tr>
<th>Treatment Month</th>
<th>Patients, N</th>
<th>Baseline, Mean (SD)</th>
<th>Visit, Mean (SD)</th>
<th>Change* from Baseline, Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>27</td>
<td>5.6 (2.3)</td>
<td>5.3 (2.2)</td>
<td>-0.3 (1.4)</td>
</tr>
<tr>
<td>12</td>
<td>27</td>
<td>5.7 (2.3)</td>
<td>5.9 (2.2)</td>
<td>-0.8 (1.4)</td>
</tr>
<tr>
<td>18</td>
<td>24</td>
<td>5.8 (2.3)</td>
<td>5.7 (2.2)</td>
<td>-0.1 (1.3)</td>
</tr>
<tr>
<td>24</td>
<td>20</td>
<td>5.9 (2.4)</td>
<td>5.4 (2.4)</td>
<td>-0.5 (1.4)</td>
</tr>
<tr>
<td>30</td>
<td>18</td>
<td>5.7 (2.4)</td>
<td>5.4 (1.9)</td>
<td>-0.3 (1.8)</td>
</tr>
<tr>
<td>36</td>
<td>8</td>
<td>4.8 (1.7)</td>
<td>4.8 (2.0)</td>
<td>0.0 (1.8)</td>
</tr>
<tr>
<td>Final</td>
<td>27</td>
<td>5.7 (2.3)</td>
<td>5.3 (2.3)</td>
<td>-0.4 (1.7)</td>
</tr>
</tbody>
</table>

*No statistically significant changes from baseline at P < 0.05.

Mean length at baseline during each visit and change from baseline of Barrett’s epithelium. Although proton pump inhibitors (PPIs) can effectively control gastric acidity and heal esophageal inflammatory lesions, they have little or no ability to produce regression of Barrett’s esophagus, even with years of continuous high-dose therapy. In this study, 3 years of continuous therapy produced no change in the length of Barrett’s esophagus, but small (clinically insignificant) islands of squamous epithelium appeared within the columnar-lined segment. It is also important to recognize that maintenance therapy with PPIs provides no protection against the development of adenocarcinoma in patients with Barrett’s esophagus. SD—standard deviation. (Adapted from Sampliner [49].)
Evolution toward cancer. If dysplasia is found to be high grade and it is verified by a pathologist skilled in the art, it is recommended that an esophagectomy is performed because up to one third of patients with high-grade dysplasia have already harbored a cancer in the specimen.

Alternatively, there have been a number of approaches developed in an attempt to avoid the need for future esophagectomy, the latter carrying a mortality rate of approximately 5% to 8% and a morbidity rate of approximately 25%. Mucosectomy and ablation therapy are among the approaches. Ablation therapy has been done with heat and laser light, the latter with and without the administration of a photosensitizing agent such as 5-aminolevulinic acid or photofrin. After ablation, high-dose proton pump inhibitors are used to control gastric acidity so the wounded areas heal with squamous epithelium. Although there have been reported successes with this approach, particularly with photodynamic therapy, there are considerable downsides, including mediastinitis, atrial fibrillation, skin photosensitivity, perforation, pleurisy, and high rates (up to 58%) of stricture formation. Furthermore, there are moderate frequencies of islands of Barrett’s epithelium found buried under the new squamous linings. This indicates that ablation therapy cannot guarantee a cure of Barrett’s esophagus and may limit the ability for surveillance (by biopsy) of any remaining tissue [1, 51].

**REFERENCES**

With the spread of the AIDS epidemic and the more general use of immunosuppressive agents for cancer chemotherapy and autoimmune disease, acute infectious esophagitis is a more frequent finding. Less commonly, other forms of acute esophageal injury result from toxins, radiation, or from foreign-body penetration of the esophagus. This chapter systematically reviews the endoscopic, radiographic, and histologic findings in addition to discussing the epidemiology, pathogenesis, and treatment of these entities.
Epidemiology. Chemical ingestion remains an important problem in the United States despite improved packaging, child-proof containers, and labeling. Approximately 5000 ingestions of caustic material occur per year. In the 1950s the concentration of lye in drain cleaners was greater than 50%; by the 1970s, it was reduced to 25% to 26%, and at present most lye products contain less than 10% NaOH. Hence, acute injuries have become less devastating although long-term esophageal stricture formation is still common. Crystalline solid preparations generally cause oral, pharyngeal, and laryngeal injury because of difficulty swallowing solid particles and local pain. Liquid products can be more readily swallowed and therefore cause more extensive esophageal injury.

Pathology. The acute and chronic sequelae of ingestion of caustic matter relate to the severity of esophageal injury and are histologically proportional to the depth of tissue necrosis. Experimentally, three phases of caustic injury occur: (1) liquefactive necrosis (0 to 5 days), (2) reparative phase (5 days to months), and (3) scar retraction (2 weeks to months).

Clinical presentation. Patients may present with uncomplicated ingestion manifested by acute oral burns, pain, and dysphagia. This is followed by a latent phase without esophageal symptoms. A final retractive phase occurs when 10% to 30% of patients have scar and stricture formation, usually within 2 to 8 weeks. Complications include acute dysphagia, acute respiratory compromise, laryngeal edema, tracheitis and pneumonitis, esophageal perforation, septicemia, mediastinitis, peritonitis, empyema, hemorrhage, and death.
Algorithm for the treatment of ingestion of caustic material. Endoscopy is not generally part of the acute evaluation. Initially, neutralization of ingested chemicals should be attempted. Patients should be stabilized by protecting the airway, and resuscitated hemodynamically as appropriate. After the patient is stable and surgery has been ruled out, patients should undergo a gentle and careful upper endoscopy to determine the severity of the injury. There are four common esophagogastroduodenoscopy (EGD) findings: (1) no injury, (2) gastric only, (3) longitudinal, linear esophageal injury, and (4) circumferential esophageal injury with risk of stricture.

Endoscopic view of caustic injury. This endoscopic photograph demonstrates a desquamated esophageal epithelium from the middle to the distal esophagus. The likelihood of stricture formation in this patient with circumferential injury is high.

Grading of burns. In general there is little indication for biopsy of lye-induced esophagitis, but if performed, there is a grading system based on the level of invasion. (Adapted from Fenoglio-Preiser et al. [1].)
Radiology. Radiologic studies are used during the initial evaluation and resuscitation. Chest radiographs to evaluate for pneumonitis and abdominal films to look for free air signifying hollow viscus perforation should be done. Esophagogram with water-soluble contrast is reserved for patients with suspected perforation.

This series of radiographs are from a patient who had four separate barium swallows over a 5-week period following lye ingestion. They demonstrate the progression from acute lye injury to esophageal mucosal repair followed by scarring and stricture formation. In panel A and panel B, taken October 19, proximal esophageal ulceration is seen without evidence of narrowing. In panel C and panel D, taken October 26, there is increased ulcerative changes seen best in the midesophagus. There is some evidence of early narrowing. In panel E and panel F, taken November 6, midesophageal stricture with proximal dilation is also seen. Note in panel G, taken November 17, the long middle to distal esophageal stricture diagnostic for lye stricture. To date no good evidence shows that steroids or antibiotics alter the long-term outcome from lye ingestion except antibiotics in cases of infection. Supportive care and watchful anticipation of possible complication remain the most important aspects of care. Early careful bougienage may be necessary to maintain patency of the esophageal lumen and to prevent future esophagectomy.
Epidemiology and pathophysiology. HIV-1 is a 100-nm, single-stranded, diploid RNA retrovirus that preferentially infects CD-4 surface antigen-presenting lymphocytes. Patients with HIV infection can be subject to acute esophageal symptoms at two points during their infection: first following acute seroconversion and later when the immune status becomes compromised. This second illness may be associated with an unrecognized cause, such as cytomegalovirus (CMV) and herpes simplex virus (HSV), but is currently termed HIV-associated idiopathic esophageal ulceration. HIV-positive patients with esophageal ulcers should have biopsies done for tissue culture, histopathology, and special stains to exclude other causes of esophagitis. Electron microscopy of esophageal biopsies has shown viral particles of similar morphology to those of retroviruses. In one study, polymerase chain reaction to the HIV genome was positive in 80% of tissue from HIV-associated idiopathic ulcers. Esophageal biopsies in HIV patients without esophageal ulcer, however, have revealed HIV virus, raising the question of whether it was an active invasion or simply a "carrier" status. About a third of patients with AIDS and esophageal symptoms have been found to harbor HSV, CMV, and Candida.

**Figure 7-8.**

Signs and symptoms of HIV. Seroconverters have acute onset of flu-like illness lasting 2 to 14 days, characterized by fever, diarrhea, rash, and dysphagia or odynophagia. Patients with chronic HIV present with acute/subacute dysphagia and odynophagia indistinguishable from other infections.
The endoscopic characteristics of an esophageal ulcer caused by HIV. Ulcers are variable, ranging from small, superficial shallow aphthous ulcers (0.5 to 1.0 cm) to large, deep ulcers with undermining borders (1 to 5 cm). To be considered as an ulcer caused by HIV other causes of esophageal ulceration must be excluded. Panel A demonstrates a large, 2-cm ulceration with some hemorrhage in the midesophagus. Panel B and panel C demonstrate large 6-cm chronic ulcers with deep undermining edges and nodularity within the ulcer base. Idiopathic HIV-associated ulcers have been treated with intravenous corticosteroid therapy. In one study, 23 of 24 patients (95.8%) improved. Relapses were common after discontinuation of therapy. To maintain remission, long-term therapy was required. Trials of sucralfate four times daily mixed with dexamethasone (0.5) mg given as a slurry have been promising. These results must be tempered by the risk of additional long-term immunosuppressive therapy.

**Cytomegalovirus**

### Epidemiology

Signs and symptoms of cytomegalovirus (CMV). CMV is a ubiquitous herpesvirus, with approximately 80% of the world's population seropositive. It is the most common viral infection of the esophagus after herpes simplex 1, and is almost exclusively found in the immunocompromised host. Normally, seroconversion occurs during preschool or teenaged years, with latent infections reactivating in the immunocompromised host. About 1% of AIDS patients developed esophagitis caused by CMV.

This figure shows clinical presentation of CMV. Asymptomatic patients shedding viral particles must be differentiated from symptomatic patients with active organ involvement. Both the humoral and the cellular components of immunity are required to prevent reactivation. As with herpes simplex virus (HSV), cytomegalovirus (CMV) may coexist with other viral (eg, HSV) or fungal organisms. Patients present with gradual onset of nausea, vomiting, fever, epigastric pain (ie, retrosternal pain is less common than with HSV), diarrhea, and weight loss. If untreated, patients may progress to unrelenting dysphagia, secondary to severe esophagitis.
Esophageal tissue invasion by pathogens. The hallmark of active esophagitis caused by cytomegalovirus (CMV) is submucosal injury with ulceration. Cytopathic effects are seen in the glandular epithelium as opposed to the squamous epithelium in HSV, and are present in both endothelial cells and fibroblasts of the granulation tissue. A role for vasculitis caused by CMV has also been implicated.

This figure shows sites of tissue invasion of the esophagus by pathogens. Biopsies with the greatest yield for CMV should be obtained from the ulcer crater (site 1). Biopsies for HSV should be obtained adjacent to the ulcer or on a vesicle (site 2). Candida is best diagnosed by biopsies obtained from an active ulcer (site 3). Appropriate biopsy from the ulcer crater reveals large cells in the subepithelial layer with amphophilic intranuclear inclusions, a halo surrounding the nucleus, and multiple small cytoplasmic inclusions (not seen with HSV). Analysis of tissue samples can rapidly detect CMV by using special techniques such as rapid Giemsa staining or fluorescent antibody staining. Giemsa staining can be done from a touch prep whereas fluorescent antibody staining can be performed on either touch prep or frozen sample. Tissue histology is better than cytologic brushings or tissue culture for the diagnosis, and special techniques, such as rapid Giemsa and fluorescent antibody staining, increase both the sensitivity and specificity of diagnosis.

**Acute Esophagitis**
Double-contrast radiographic views of the esophagus. A–C, Radiographs showing a large longitudinally-oriented ulcer in the middle to distal two thirds of the esophagus. The ulcer is shown outlined in double contrast with some barium in the ulcer base. Arrowheads identify the extent of the ulceration. (Courtesy of Dr. Arunas E. Gasparitis, Chicago, IL.)

Esophagogram. A–B, Esophagogram taken during the late phases of infection reveals large deep ulceration (large arrowhead) with raised borders secondary to edema. The small arrowhead identifies the edematous border. Esophagogastroduodenoscopy with biopsy of the ulcer crater is required for diagnosis. Brushings of this area are not helpful. Findings early in the course include mucosal erythema and superficial erosions with geographic, serpiginous, nonraised borders. (Courtesy of Dr. Arunas E. Gasparitis, Chicago, IL.)

Endoscopy

Midcourse lesions. This figure shows typical midcourse lesions with shallow ulcers 0.5 to 10 cm in which complete denudation of the esophagus is unusual. These ulcers may be indistinguishable from herpes simplex virus ulceration, and biopsy is required. Cytomegalovirus infections of the esophagus is typically most prominent in the mid to distal esophagus.

Large ulcerations typical of the late course of infection caused by cytomegalovirus (CMV). These ovoid or elongated ulcers may extend for several centimeters. Herpes simplex virus ulcers are rarely more than several centimeters in length and the presence of one or more giant ulcers is suggestive of CMV esophagitis. Large ulcers may become hemorrhagic.
Esophageal fistula. The rare complication of formation of a fistula between the esophagus and left main-stem bronchus in a patient with chronic infection caused by cytomegalovirus (CMV). Other complications of CMV include superinfection (viral, bacterial, fungal), stricture, hemorrhage, and perforation (rare). (From Fenoglio-Preiser et al. [1]; with permission.)

**PREVENTION AND TREATMENT OF ESOPHAGITIS CAUSED BY CMV**

<table>
<thead>
<tr>
<th>DRUG FORMULATION</th>
<th>PREVENTION OF CMV INFECTION*</th>
<th>TREATMENT OF ESTABLISHED CMV DISEASE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acyclovir, for IV use (500 mg/10 mL vial, admixed to final concentration &lt;7 mg/mL)</td>
<td>For seropositive patients or recipients of organs from seropositive donors: 500 mg/m² BSA IV every 8 hours</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Ganciclovir, for IV use (500 mg/10 mL vial, admixed to final concentration &lt; 10 mg/mL)</td>
<td>For seropositive patients or recipients of organs from seropositive donors: 5 mg/kg every 12 hours IV for 5 days, then once daily as maintenance therapy</td>
<td>5 mg/kg every 12 hours IV for 2 weeks, then once daily for maintenance (if indicated)</td>
</tr>
<tr>
<td>Foscarnet, for IV use (12 g/500 mL)</td>
<td>Not applicable</td>
<td>60 mg/kg every 8 hours (or 90 mg/kg every 12 hours) IV for 2 weeks, then 90–120 mg/kg daily for maintenance (if indicated)</td>
</tr>
<tr>
<td>Epidemiologic methods</td>
<td>For seronegative patients. Transfusion of CMV seronegative blood products. Organ transplants from CMV seronegative donors. Leukofiltration of CMV seropositive blood products.</td>
<td>Not applicable</td>
</tr>
</tbody>
</table>

*For patients at risk.
1 Adjust dose for renal function.
2 Marrow transplantation patients; trials of prophylactic ganciclovir for patients infected with HIV have not been completed.
3 Use of oral ganciclovir formulations are under current study.
4 Induction therapy should be extended if the patient has not completely responded and other etiologies are excluded.

**FIGURE 7-20.** Prevention and treatment of esophagitis caused by cytomegalovirus (CMV). Therapy for CMV can be given as prevention of disease in patients known to be immunocompromised or a therapy against established disease proven by tissue biopsy. Current therapy includes ganciclovir and acyclovir for prophylaxis and ganciclovir and foscarnet for treatment of established disease. In AIDS patients with biopsy-proven CMV esophageal ulceration, both ganciclovir and foscarnet therapy have been associated with endoscopically documented ulcer healing in some patients in 2 weeks or less. (Adapted from Baehr and McDonald [2].)
ESOPHAGITIS CAUSED BY HERPES SIMPLEX VIRUS

Epidemiology

Infectious esophagitis

Predisposing factors

Syndromes not related to immunodeficiency

General debilitation

Drug therapy

Old age

Abnormal esophageal motility

Immunodeficiency syndrome

HIV

Cancer

Chemotherapy

Organ transplantation

Alcoholism

Radiotherapy

Congenital immunodeficiency

Diabetes mellitus

Infectious esophagitis. Herpes simplex virus is a large, enveloped, double-stranded DNA virus with humans as the only reservoir. Infection occurs most commonly as a reactivation of a silent infection rather than as an exogenous infection. Esophagitis can occur with both HSV type 1 and type 2. The likelihood is that reactivation will occur and then the severity of disease will be inversely related to the immunocompetence of the patient.

Several factors predispose patients to infectious esophagitis. None of these is specific for herpetic infection, but they share a common theme. The common finding is a compromised immune system. At present, with the AIDS epidemic, infectious esophagitis is seen most frequently in these patients; however, because of underreporting of AIDS cases, misdiagnosis of infectious esophagitis, and empiric therapy for complications of infectious esophagitis, the actual number of cases per year is not available.

Clinical presentation. Eighty percent of patients present with painful or difficult swallowing. Of these, 30% have oral lesions at the time of diagnosis. Unlike esophagitis caused by Candida, where 25% of patients will be asymptomatic, virtually all patients with esophagitis caused by herpes simplex virus have symptoms.
performed. Early lesions are vesicular, occurring in the midesophagus, and are rarely seen because few endoscopies are performed at this stage, when the vesicles are fragile and easily ruptured. Midway in the course of the disease sharply demarcated small ulcers with raised margins are noted (A). The mucosa surrounding the ulcers is often erythematous and edematous. In the late necrotic phase of the disease process, diffuse esophagitis is noted with confluent esophageal ulcers (B).

The location of the biopsy site is essential to accurately diagnose esophagitis caused by HSV accurately. Because the virus is active only in epithelial cells, biopsies should be directed at the ulcer edge and not into the crater, which will only yield necrotic debris. (A, Courtesy of Dr. S. Kadakia, Brooke Army Medical Center; B, courtesy of Dr. K. Yamamoto, Madigan Army Medical Center.)

Complications of esophagitis caused by herpes simplex virus

<table>
<thead>
<tr>
<th>COMPLICATIONS FROM HERPES SIMPLEX VIRUS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mucosal necrosis</td>
</tr>
<tr>
<td>Mucosal superinfection</td>
</tr>
<tr>
<td>Hemorrhage</td>
</tr>
<tr>
<td>Stricture</td>
</tr>
<tr>
<td>Tracheoesophageal fistula</td>
</tr>
<tr>
<td>Dissemination</td>
</tr>
</tbody>
</table>

Herpetic infection of the esophagus in immunocompromised patients is generally limited to the mucosa. There can be dramatic complications, such as hemorrhage and fistulization to the trachea. Superinfection can occur with other viruses or bacteria.

Histology

Immunohistologic staining for herpes simplex virus (HSV). Pathologists should be notified that esophagitis caused by HSV is suspected so that immunohistologic staining can be performed. A, HSV invades only the squamous epithelium, causing necrosis of the esophageal mucosa. Findings include multinucleated giant cells and ballooning degeneration of the squamous epithelial cells. Immunohistologic staining clearly identifies cells containing HSV. B, Characteristic findings of ballooning degeneration, ground glass nuclei, eosinophilic intranuclear inclusions, and herpetic giant cells (arrowhead). Special stains (Papanicolaou's stain) demonstrate multinucleated cells (arrowhead); this makes changes associated with HSV more evident.

Viral culture can be used to augment histopathology in diagnosing herpetic esophagitis. Viral culture is more sensitive than endoscopic inspection and microscopic examination. HSV can be rapidly grown in diploid fibroblasts or rabbit kidney cells. Cytopathic changes in culture occur rapidly and are evident within 24 to 96 hours after inoculation. (B, Courtesy of Dr. P. McNally, Eisenhower Army Medical Center.)
Double contrast esophagram. This radiograph can be normal or diagnostic. Disease is often midesophageal with discrete, superficial, stellate ulcers. Advanced disease may have plaques, cobblestoning, or even a shaggy ulcerative appearance similar to that seen in infection caused by Candida. This figure shows a double-contrast esophagram demonstrating numerous oval mucosal elevations representing a thin, lucent ring of edema surrounding the herpetic ulcers. Note the similarity between the appearance of this radiograph and Figure 7-32A. (From Fenoglio-Preiser et al. [1]; with permission.)

Ulcers. Multiple discrete, punctate ulcers are distributed throughout the proximal and middle third of the thoracic esophagus.

### Prevention and Treatment of Esophagitis Caused by Herpes Simplex Virus (HSV)

<table>
<thead>
<tr>
<th>Drug Formulation</th>
<th>Prevention of HSV Infection*</th>
<th>Treatment of Established HSV Infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acyclovir, capsules (200 mg)</td>
<td>200–400 mg orally 4–5 times daily, or 800 mg orally twice daily</td>
<td>900–400 mg orally 5 times daily for 2 weeks</td>
</tr>
<tr>
<td>Acyclovir, for IV use (500 mg/10 mL vial, admixed to final concentration &lt;7 mg/mL)</td>
<td>250 mg/m² every 12 hours IV</td>
<td>250 mg/m² every 8 hours IV for 2 weeks¹</td>
</tr>
<tr>
<td>Foscarnet, for intravenous use (12 g/500 mL)²</td>
<td>Not applicable</td>
<td>60 mg/kg every 8 hours (or 90 mg/kg every 12 hours) IV for 2 weeks, then 90–120 mg/kg daily for maintenance (if indicated)§</td>
</tr>
</tbody>
</table>

*For patients at risk.

¹Intravenous acyclovir therapy can be converted to oral route for completion of induction therapy in responders.

²For treatment of HSV resistant to acyclovir.

§Induction therapy should be extended if the patient has not completely responded and other etiologies are excluded.

Prevention and treatment of esophagitis caused by herpes simplex virus. Current therapeutic strategies are based on the severity of disease and immune status of the patient. Clinical decisions must be made to determine if a patient is at significant risk to merit the use of prophylaxis. Options include supportive care, acyclovir, or foscarnet. (Adapted from Baehr and McDonald [2].)
ESOPHAGITIS CAUSED BY CANDIDA

Signs and symptoms of esophageal Candida. Although Candida is a normal component of the oral flora, esophageal candidal infection occurs most commonly in the immunocompromised host. Candidiasis is the most common type of infectious esophagitis in patients with HIV involvement, but is also seen in other illnesses, such as progressive systemic sclerosis, diabetes mellitus, following caustic ingestion, after solid-organ or bone-marrow transplantation, esophageal motility disorders, or in esophageal obstruction. Compromise of the host's immune function predisposes the patient to candidal infection. Suppressed lymphocyte function leads to superficial mucosal infection whereas suppressed granulocyte function may permit deep mucosal invasion and disseminated infection. Typical infections progress from colonization to epithelial infection, and then to deeper tissue invasion.

Patients may present with a spectrum of complaints related to the gastrointestinal system. Unlike in esophagitis caused by herpes simplex virus wherein virtually all patients are symptomatic, as many as 25% of patients with esophageal candidiasis are asymptomatic, particularly immunocompetent hosts. Studies indicate that patients with AIDS who have esophageal symptoms and oral candidiasis have a positive predictive value of 71% to 100% for candidal esophagitis.

Candidiasis and AIDS. The magnitude of the AIDS epidemic and its multiple complications have, to some extent, driven the diagnostic evaluation and management of acute esophageal symptoms in patients with AIDS. Patients presenting with dysphagia or odynophagia and positive results of an oral examination revealing candidiasis should receive empiric treatment with systemic antifungal medication. More invasive diagnostic procedures should be performed in patients who fail to respond to empiric antifungal therapy or have more severe symptoms suggesting an alternative diagnosis. Blind esophageal brushing of the esophagus can be obtained by passing a sheathed brush orally through a nasogastric tube. Sheathed tubes prevent contamination. This technique has a sensitivity of 88% and specificity of nearly 100% when compared with endoscopically-obtained specimens. Blind smears can be used but will not diagnose Kaposi's sarcoma, pill-induced injury, esophageal injury caused by gastroesophageal reflux disease or infections caused by human immunodeficiency virus, herpes simplex virus, or cytomegalovirus, which can also occur in this setting. (From Pounder et al. [3]; with permission.)
Early findings in acute esophagitis caused by *Candida*. A–C, Normal or tiny nodular lesions with a granular appearance in the upper half of the esophagus. Radiologic evaluation of esophagitis caused by *Candida* may be less diagnostic in the early stages because it resembles other causes of esophagitis.

**Figure 7-31.**
Histologic specimen with large numbers of pseudohyphae (arrowhead) in the esophageal mucosa on periodic acid-Schiff staining. Specimens can be obtained either from blind esophageal brushing or through endoscopically guided brushings. Silver stain can also be used and may aid in the diagnosis of candidal infection.

**Figure 7-32.**
Early findings in acute esophagitis caused by *Candida*. A–C, Normal or tiny nodular lesions with a granular appearance in the upper half of the esophagus. Radiologic evaluation of esophagitis caused by *Candida* may be less diagnostic in the early stages because it resembles other causes of esophagitis.

**Figure 7-33.**
Classic findings in acute esophagitis caused by *Candida*. A–B, Discrete plaque-like lesions, oriented longitudinally, produce linear or irregular filling defects with distinct margins (arrowhead).
Coalescing plaques. A–B. Severe findings in acute esophagitis caused by Candida include coalescing plaques. Pseudomembranes may produce a grossly irregular or shaggy pattern.

**Endoscopic Findings**

Endoscopic grading of esophageal candidiasis. (Adapted from Kodsi et al. [4].)

Early findings of esophagitis caused by Candida with plaques not yet becoming confluent. As the infection worsens, there is associated hyperemia. Brushing and biopsy are diagnostic and help to rule out secondary causes of esophagitis. Generally plaques caused by Candida will not wash off. Biopsy should be obtained using hematoxylin and eosin stain as well as stains for fungus (silver and periodic acid-Schiff). A, Grade 1; B, grade 2. (A, Courtesy of Dr. A. Tsuchida, Madigan Army Medical Center; B, courtesy of Dr. K. Yamamoto, Madigan Army Medical Center.)

Disease progression. Panel A (grade 2-3) and panel B (grade 3-4) represent the progression of esophageal disease caused by candidiasis. (B, Courtesy of Dr. M. Lyons, Madigan Army Medical Center.)
Grade 4 esophagitis caused by Candida with distal ulceration and hemorrhage. (Courtesy of Dr. M. Lyons, Madigan Army Medical Center.)

Figure 7-38.

A-B, A nearly healed case of severe esophagitis caused by Candida, showing a healing ulcer in the foreground.

Figure 7-39.

<table>
<thead>
<tr>
<th>DRUG FORMULATION</th>
<th>NO OR MINIMAL LYMPHOCYTE DEFECTS AND NORMAL GRANULOCYTES</th>
<th>DECREASED LYMPHOCYTE FUNCTION BUT NORMAL GRANULOCYTES</th>
<th>DECREASED GRANULOCYTE FUNCTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral, nonabsorbable drugs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nystatin suspension</td>
<td>1–3 MU orally, 4 times daily</td>
<td>Not applicable</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Amphotericin B lozenge</td>
<td>1–2 lozenges or 1 mL suspension, 4 times daily</td>
<td>Not applicable</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Micronazole oral gel</td>
<td>10 mL orally, 4 times daily</td>
<td>Not applicable</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Clotrimazole troches</td>
<td>10 mg troche, dissolved in mouth 5 times daily</td>
<td>Not applicable</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Clotrimazole vaginal tablets</td>
<td>100 mg tablet, dissolved in mouth 3 times daily</td>
<td>100 mg tablet, dissolved in mouth 3–5 times daily</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Oral, absorbable drugs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ketoconazole tablets</td>
<td>900 mg orally, once daily</td>
<td>400–800 mg orally, once daily</td>
<td>400–800 mg orally, once daily</td>
</tr>
<tr>
<td>Fluconazole capsules</td>
<td>50 mg orally, once daily</td>
<td>100 mg orally, once daily</td>
<td>100–200 mg orally, once daily</td>
</tr>
<tr>
<td>Fluocytosine capsules</td>
<td>Not applicable</td>
<td>Not applicable</td>
<td>50–150 mg kg⁻¹ day⁻¹, at 6 hr intervals</td>
</tr>
<tr>
<td>Intravenous drugs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amphotericin B for IV use</td>
<td>Not applicable</td>
<td>0.3 mg kg⁻¹ day⁻¹, intravenously</td>
<td>0.5 mg kg⁻¹ day⁻¹, intravenously</td>
</tr>
<tr>
<td>Fluconazole for IV use</td>
<td>100 mg intravenously, once daily</td>
<td>100 mg intravenously, once daily</td>
<td>100–200 mg intravenously, once daily</td>
</tr>
</tbody>
</table>

*Not available in the USA.
†Not for use as a single agent. See text for discussion of the use of this drug.
‡When oral route is not available.
§The therapy of choice under each column is given in bold.

Figure 7-40.

Treatment of esophagitis caused by Candida. (Adapted from Baehr and McDonald [2].)
Incidence of impaction. Several important factors are related to foreign body impaction. This figure demonstrates the bimodal incidence of impaction with age. Children account for the first peak with impaction of small objects, such as coins, which are easily found and swallowed by curious unsuspecting children. The second peak occurs in the fifth to sixth decade, when pathologic stricture or B-ring causes impaction of common foods at narrowed areas. Poor dentition and the inability of elderly patients to masticate food increases the likelihood of impaction, especially if underlying pathology is present. Other risk factors for impaction include age less than 10 years and greater than 50 years; underlying disease; ring, web; stricture; tumor; motility disorder; oral disease; poor dentition; dentures; and mental impairment. The magnitude of the problem of foreign body ingestion in the United States remains unclear. Each year 1500 to 2750 persons die from foreign body ingestion. Of the objects that are ingested, 80% to 90% pass into the stomach and do not require therapeutic intervention. (Adapted from Giordano et al. [5].)

Physical abnormalities contributing to impaction. When considering all age groups, most foreign body impactions occur in patients without attendant esophageal pathology, such as web, ring, or stricture. In the older patient, however, clinicians must consider these lesions and determine if underlying pathology is present. This figure indicates common areas of abnormality at which impactions are likely to occur.
Sites of possible impaction. A, Locations where normal anatomic structures can cause physiologic narrowing of the esophagus and increase the likelihood of foreign body impaction (the anatomic relationship between the cardio-pulmonary system and the esophagus is noted in Figure 7-42). B, A radiograph of the normal esophagus demonstrates the compressive effect of the arch of the aorta (closed arrow), left mainstem bronchus (arrowhead), and spinal processes on the esophagus (open arrow). (From Fenoglio-Preiser et al. [1]; with permission.)

Radiology and foreign body impaction. Taking plain radiographic films of the neck when evaluating foreign body impaction is important. Panel A and panel B show a coin in a child’s esophagus, with the coin seen head on in the anteroposterior projection. (From Yoshida et al. [7]; with permission.)
Algorithmic approach to a patient with food impaction. Diagnostic evaluation should precede with a complete history and physical examination. The patient is usually able to give specifics concerning the size, consistency, and time of foreign body ingestion. A past history of gastroesophageal reflux disease, dysphagia, loss of teeth, or change in dentures are clues concerning the etiology. Posteroanterior and lateral chest radiographs, as well as neck radiographs with radiographic technique to emphasize soft tissues, are important to assess impaction in the hypopharynx and cervical esophagus as well as airway compromise. Barium swallow is generally not indicated in suspected foreign body impaction because aspiration may occur and the barium may prevent endoscopic visualization. Additionally, other objects should not be swallowed to try to "drive" the impacted object into the stomach.

This figure shows an algorithmic approach to a patient with food impaction. The first consideration when approaching the patient would be the nature of the ingested object. Sharp objects should be considered for removal. Toxic or caustic objects should also be considered for early removal. Location, as determined by radiology studies, is also important. All objects stuck in the esophagus should be considered for removal if adequate resources are available. (Adapted from Cotton et al. [8].)
Various objects causing impaction. Food, particularly meat and small pieces of bone, are common causes of impaction. A, A chicken bone within the esophageal lumen and mild trauma in the esophagus proximal to the impacted bone. B, Squamous cell carcinoma of the esophagus as the underlying abnormality causing narrowing of the esophagus. C, Subsequent impaction of a theophylline pill that required removal endoscopically with forceps. (A, Courtesy of Dr. P. McNally, Eisenhower Army Medical Center; B, courtesy of Dr. K. Yamamoto, Madigan Army Medical Center.)
Factors associated with esophageal clearance

Location of pill injury. Pill-induced esophageal injury occurs when the caustic contents of pills remain in contact with the esophagus long enough to produce mucosal damage. Anyone who ingests caustic pills is susceptible to pill-induced esophageal injury because the moderate delay in transit through the esophagus is a common event even with normal esophageal motility. Although delays in transit are necessary for pill-induced injury, they alone are not sufficient because the content of the pill must be inherently caustic. Doxycycline and ascorbic acid produce pH levels below 3.0 when dissolved and can cause local burns. Other agents, such as nonsteroidal anti-inflammatory drugs and doxycycline, may produce injury by causing local toxic accumulation within the esophageal mucosa. Cardiac and vascular medications, including antihypertensives and antiarrhythmics, can be very caustic. Quinidine alone has been reported in 13 cases of pill-induced injury; seven of 13 patients later developed strictures, making quinidine a particularly injurious substance. Alendronate sodium (Fosamax) is an oral aminobiphosphonate that inhibits bone osteoclast activity and is used to treat osteoporosis in postmenopausal women. It can cause significant esophageal injury. The package insert advises how to administer the drug to maximize esophageal clearance. These factors include consuming 6 oz to 8 oz water with the pill and remaining upright for 30 minutes after taking the pill. Contraindications for Fosamax include abnormalities of the esophagus that delay esophageal emptying and the inability to stand or sit upright for 30 minutes after ingestion of the pill. Risks of pill-induced injury include structural abnormalities, hiatal hernia, stricture, tumor, supine position, old age, abnormal esophageal motility, minimal liquid taken with medications, type of pill, concurrent ingestion of alcohol, and underlying gastroesophageal reflux disease. Factors associated with esophageal clearance include body position during and following pill ingestion (easily modified), saliva production, esophageal motility, structural abnormalities, and volume of water consumed (easily modified).

Clinical presentation

Clinical presentation. Patients typically have no prior history of esophageal disease and present with sudden onset of retrosternal pain, exacerbated by swallowing. Pain may be mild or so severe that swallowing may be impossible. Typically, the pain increases over the first 72-hour pill ingestion and gradually subsides. Patients with pre-existing esophageal problems, such as gastroesophageal reflux disease, frequently present with worsening symptoms of heartburn, regurgitation, and dysphagia. In more severe esophageal injury patients may present with odynophagia. Patients with severe or persistent esophageal symptoms and an appropriate (continued on next page)
History of pill ingestion should undergo endoscopy. Findings, often including esophagitis, hiatal hernia, Schatzki's B-ring, or stricture, are almost all most commonly found in the distal esophagus. Most pill-induced lesions occur in the endoscopically normal esophagus and are located between the junction of the proximal and middle esophagus. The lesions associated with pill-induced esophageal injury vary with the agent ingested and the duration of injury.

The type of pill and duration of esophageal contact may influence the injury. Punctate ulcers with well-circumscribed borders may be noted with antibiotics, such as doxycycline and erythromycin. A shallow plaque-like ulcer with a thin membrane can also be noted, resulting from lower toxic concentrations or shorter duration of injury. Raised, plaque-like membranes can be seen with quinidine-induced esophageal injury. Pill-induced lesions may be single or multiple, with remnants of pills sometimes noted within the ulcer crater. Fosamax typically causes a circumscribed ulceration covered by a thick, loosely adherent exudate. Histology confirms a leukofibrinous exudate similar to pseudomembranous colitis.

A. A discrete tetracycline-induced ulcer with normal surrounding mucosa. B. Aggressive plaque-like, membranous ulceration, secondary to doxycycline with adjacent ulcers on each side of the esophagus. Friability and bleeding is noted following intubation of the endoscope. C. Large, deep ulcer and smaller more discrete ulceration secondary to erythromycin. D. Classic pill-induced "kissing ulcerations." (A, courtesy of Dr. T. Peller, Madigan Army Medical Center; B, courtesy of Dr. K. Yamamoto, Madigan Army Medical Center.)

Pill fragments visible in ulcer bases on endoscopy. In this case, an ibuprofen (Motrin) tablet is seen in the esophagus with adjacent ulceration.
Radiographic findings

A raised membrane in the proximal third of the esophagus. This finding is classic for quinidine-induced esophageal injury, which may be mistaken endoscopically for esophagitis caused by *Candida* because of the whitish membranous plaques. Stricture formation can occur, as shown in Figure 7-52B, which shows a more severe, long-term esophageal injury. This single contrast spot film of the proximal third of the esophagus shows a high-grade smooth stricture at the level of the aortic arch (an area of physiologic narrowing).

**Therapy**

**THERAPY FOR PILL-INDUCED ESOPHAGITIS**

- Discontinue use of nonsteroidal anti-inflammatory drugs
- Acid blockade
- Sucralfate
- Local analgesia
- Supportive care

**Prevention of Pill-Induced Injury**

- Taking a large volume of liquid with pills
- No pills less than 1 hour before bed
- Upright posture during and following pill ingestion
- Ingestion of liquid forms of medicines when available

**Figure 7-54.** Therapy. Pill-induced esophagitis can cause intense pain, but this is generally short-lived (1–3 days). Therapy is supportive with medicine to decrease pain and prevent further injury. A mixture of lidocaine, Mylanta (Johnson & Johnson–Merck Consumer Pharmaceuticals, Ft. Washington, PA), and Benadryl (Warner-Lambert, Groton, CT) in equal parts can decrease pain. Discontinuing injurious agents and decreasing acid, particularly in patients with reflux disease, is also helpful.

**Prophylactic interventions**

**Figure 7-55.** Prevention. There are four easily modified actions that will decrease the risk of pill-induced esophageal injury. Esophageal clearance can be improved simply by ingesting more liquid with pills and taking pills in an upright position. These simple measures will generally prevent pill-induced esophageal injury.
**EOSINOPHILIC ESOPHAGITIS**

**Epidemiology and clinical presentation**

Histologic view of esophageal eosinophilia. Isolated eosinophilic esophagitis is an uncommon clinical entity seen more commonly in a pediatric population. Patients present with dysphagia or chest pain. Patients usually appear healthy and are young, with a male predominance. There is usually no weight loss or any severe systemic symptoms. Patients may have a history of allergies and peripheral eosinophilia.

Esophageal eosinophilia is defined as greater than 20 eosinophils per high power field, and is nicely demonstrated in the histogram. Proximal esophageal involvement is often greater than distal. In contrast, eosinophilic infiltration of the esophagus that can occur in gastroesophageal reflux disease usually involves the distal esophagus with typically less than 5 eosinophils per high power field. Involvement of deeper layers of the esophagus in eosinophilic esophagitis may be associated with manometric abnormalities such as diffuse esophageal spasm and “nutcracker esophagus.”

**Endoscopy and pathophysiology**

Endoscopic appearance of eosinophilic esophagitis. The endoscopic appearance can be normal or can include a variety of appearances such as mucosal whitening, erythema, granularity, superficial ulcers, vertical furrowing, or rings. The exact pathophysiologic mechanism for eosinophilic esophagitis is not known. It has been associated with food and drug allergies as well as asthma and sinusitis. This entity must be distinguished from gastroesophageal reflux disease (GERD) in which eosinophils can be seen, although typically fewer in number and more distal in location. Unlike patients with eosinophilic esophagitis, patients with GERD tend to respond to standard anti-reflux therapy, and if they develop strictures they tend to be more distal in location. Also, isolated eosinophilic esophagitis must be distinguished from eosinophilic gastroenteritis with esophageal involvement. These patients generally have more systemic symptoms and have eosinophils in other areas of the gastrointestinal tract such as the stomach and small intestine.

**Radiology**

Radiologic appearance of eosinophilic esophagitis. Segmental strictureing in the proximal esophagus is often identified as shown in this barium study. Conservative care with careful esophageal dilation when needed may be beneficial. However, in resistant cases, corticosteroids have been reported to be very effective and cause a prompt clinical response. (Courtesy of James Rick, MD, Walter Reed Army Medical Center.)
ESOPHAGITIS CAUSED BY RADIATION

Pathophysiology

The deleterious effect of radiation to the gastrointestinal tract has been reported since 1897. In general, the incidence of radiation-induced injury to the esophagus ranges between 1% to 25%, with serious damage reported in 1% to 5% of patients. This incidence may be increasing because chemotherapeutic agents, such as adriamycin, potentiate radiation damage. Additionally, a recall phenomenon has been observed with adriamycin because subsequent doses without additional radiation produce endoscopic and radiographic findings, which are indistinguishable from those seen with radiation-induced esophagitis.

Incidence and severity of radiation-induced esophageal injury are directly proportional to the radiation dose administered and to the total surface area of esophagus that is irradiated. Radiation acutely damages cells by inhibiting mitosis in the epithelial germinal layer, thus predisposing to esophageal ulceration and sloughing. Endothelial cells of submucosal arterioles are particularly radiosensitive. Although capillary dilation, edema, and leukocyte infiltration are early morphologic changes, with time endothelial proliferation results in ischemia and fibrosis of the submucosa and lamina propria with damage to smooth muscle fibers and neural elements.

Histology

Radiation injury to the esophagus. A patient 10 years after radiation therapy showing epithelial hyperplasia as well as fibrosis (arrowhead) throughout the submucosa and esophageal wall. B, A higher magnification of the esophageal wall showing extensive fibrosis (small arrowhead) interlaced between muscle bundles (large arrowhead).
Clinical effects of radiation dosage

**EFFECT OF RADIATION DOSAGE ON THE ESOPHAGUS**

- > 30 Gy Nonspecific or none*
- > 40 Gy Retrosternal burning and esophagitis
- > 50 Gy Severe esophagitis
- > 60 Gy Stricture and fistulas

* All can be worsened by chemotherapy.

Methods to decrease radiation injury

**PREVENTING RADIATION-INDUCED ESOPHAGITIS**

- Specialized ports
- Shielding
- Dose hyperfragmentation
- Alternate-day schedule

Clinical presentations

**FIGURE 7-61.**
Dose-dependent injury. The magnitude of injury to the esophagus secondary to radiation therapy is directly proportional to the dose of radiation delivered. As the dose increases, esophagitis, stricturing, and fistula formation can occur.

**FIGURE 7-62.**
Prevention. The esophagus is relatively fixed in location. To minimize radiation injury to the esophagus, radiation oncologists have tried several methods to decrease radiation intensity delivered to the esophagus.

**FIGURE 7-63.**
Esophagitis induced by combined radiation and chemotherapy (doxorubicin). Patients often present to the gastroenterologist during the third to fifth week of radiation therapy, although the natural history of the radiation injury may be altered with the coadministration of chemotherapeutic agents. Retrosternal burning, dysphagia, or odynophagia are typical symptoms that may be persistent and require supportive care to maintain hydration and nutrition. Additionally, patients must be considered for the possibility of superinfection with organisms such as *Candida*. A, Barium esophagram performed 10 days after the onset of symptoms demonstrates a dilated esophagus with thickened folds. Peristaltic activity was diminished at fluoroscopy. B, Esophagram 16 days after the onset of symptoms demonstrates a narrowed esophagus with markedly irregular mucosa and formation of a stricture in the distal half. No peristalsis was evident at fluoroscopy. C, High-grade stenosis involving about 9 cm of the distal esophagus with significant obstruction was found on follow-up examination 2 months after the onset of symptoms. The lumen of the stricture is irregular. The transition from the proximal esophagus, although abrupt, appears benign and is characterized by concentric narrowing. *(From Boal et al. [9]; with permission.)*
Complications of radiation-induced esophagitis. At a radiation dose of less than 30 Gy, patients have self-limited, asymptomatic esophagitis. At dosages above 30 Gy, there may be progression to fibrosis and scarring of the esophagus. Strictures are typically smooth and elongated with thickened walls. Neural elements of the esophageal wall are frequently damaged. Esophageal peristalsis may be absent proximal to the stricture. Other complications include ulceration, pseudopolyp formation, mucosal bridging, and fistulization to the tracheal or bronchia apparatus, mediastinum, or aorta. The findings noted at endoscopy vary with the duration of time that the patient has received radiation therapy. The endoscopic findings include a spectrum of injury from acute esophagitis to circumferential ulceration with stricture formation, as demonstrated both radiographically (A) and endoscopically (B) in this figure. (From Wilcox [10]; with permission.)

Therapy

Therapeutic options in radiation esophagitis that can markedly improve patients' quality of life. The three that tend to impact the most are acid blockade, prokinetic agents, and repeated dilations. Radiation causes small vessel anteriolitis and nerve damage, which leads to dismotility of the esophagus. Prokinetic agents may improve the function of the esophagus while strong acid blockade can decrease reflux symptoms. Repeated dilations can have very satisfying results, allowing very ill patients to swallow and eat during the last months of their lives.

References


Chapter 8

Tumors of the Esophagus

Tumors of the esophagus may be broadly classified as either benign or malignant. Benign neoplasms are uncommon and are rarely of any clinical significance. They are usually found incidentally and are symptomatic only when large. Leiomyomas are the most frequently occurring type of benign neoplasm, followed by fibrovascular polyps [1]. Squamous papillomas, granular cell tumors, lipomas, neurofibromas, and inflammatory fibroid polyps are all uncommon types.

Malignant tumors of the esophagus are mostly carcinomas (a majority of these tumors are squamous cell carcinoma) and are still highly lethal. Worldwide, esophageal carcinoma is the ninth most common malignancy, but the prevalence varies widely from one geographic area to another [2,3]. There is a high prevalence of squamous cell carcinomas in China and Iran within the so-called "Asian esophageal cancer belt," extending from the south shore of the Caspian Sea in the west to North China in the east. Other pockets of high incidence areas are southeastern Africa and northwestern France, as well as areas in Finland and Iceland. In the United States esophageal carcinoma is relatively uncommon, accounting for approximately 5% to 7% of all gastrointestinal malignancies and 1.5% to 2% of all cancers. The incidences of squamous cell carcinoma are approximately equal in men and women in Asia and Africa, whereas in the United States and western Europe, the disease is much more common in blacks than in whites [4]. The incidence among black men is higher than any other ethnic group, and the death rate for blacks is three times higher than in whites. In Asia it is considered a disease of rural areas whereas in the Western hemisphere it is the disease of urban areas associated with poor social economic status. This difference is probably due to environmental factors as well as genetic makeup.

The incidence of adenocarcinomas of the esophagus and gastric cardia, once rare, has increased in recent years and they are rapidly becoming common types of gastrointestinal carcinoma in the industrialized countries of the Western hemic...
sphere. In the United States and western Europe prior to 1970, adenocarcinomas constituted less than 8% of all esophageal carcinomas. By 1990 the number had risen to 34% [5,6]. Nearly 50% of all newly diagnosed cases and 80% of all carcinomas in the lower esophagus are adenocarcinomas [6,7]. Most (95%) cases are reported in whites, with a male-to-female ratio of 5:1.

Clinically, in its early stages, esophageal carcinoma may be asymptomatic and difficult to diagnose; however, in more advanced stages it may present with progressive dysphagia, anorexia, and weight loss. Flexible fiberoptic endoscopy with direct vision biopsy and brush cytology is a powerful diagnostic tool and can provide positive diagnosis 95% to 99% of the time.

The overall prognosis for esophageal carcinoma is poor; 30% to 40% of patients have advanced disease at the time of presentation. The single most important morphologic prognostic indicator is stage (depth of tumor infiltration through the esophageal wall, lymph node involvement, and distant metastasis). TNM classification as defined by the American Joint Committee on Cancer and the International Union Against Cancer is the most widely used staging system.

Radiation is the most common form of treatment for carcinomas of the upper esophagus, while surgery is usually performed for the lower third. Other forms of treatment in use include combined chemotherapy and radiation with or without surgery.

### Epithelial Neoplasms

**Benign tumor**

Squamous papillomas are rarely found in the esophagus. They are usually identified incidentally, the most common site being the mid-esophagus. Some of them may be associated with human papillomavirus (HPV) infection. Macroscopic appearance varies from single to multiple sessile nodules or polyps. In this illustration, multiple nodules can be seen on the mucosal surface of the esophagus in a patient with papillomatosis. Squamous papillomatosis is usually seen in young children and may be numerous. (From Lewin et al. [8]; with permission.)

**Figure 8-1.**

A, Microscopic appearance of squamous papilloma. The mucosal surface is irregular, with hyperplasia and hyperkeratosis of squamous epithelium. It is associated with upward elongation of papillae (connective tissue core), thus giving the mucosa a papillary configuration. B, Higher magnification of the squamous papilloma showing a thickened epithelium thrown up into papillary folds containing a central fibrovascular core. (A, From Oota and Sobin [9]; with permission; B, from Lewin et al. [8]; with permission.)
Malignant tumors of the esophagus. The great majority of malignant tumors of the esophagus are carcinomas. Among these, squamous cell carcinoma is the most common primary neoplasm, followed by adenocarcinoma. Other malignant tumors are uncommon. Primary lymphoma is very rare in the esophagus but several cases have been reported in the AIDS setting. Kaposi’s sarcoma has also been reported in patients with AIDS. Tumor metastatic to the esophagus is infrequent. More commonly, the esophagus is involved by direct spread from tumors arising in contiguous organs, such as lung, stomach, thyroid, and larynx.

### SQUAMOUS CELL CARCINOMA

Trends in age-adjusted incidence rates for esophageal carcinoma among males by race and cell type, 1974–1976 to 1992–1994. Epidemiologic features of esophageal carcinoma in the U.S. and western Europe have changed significantly over the past 20 years. The incidence of esophageal adenocarcinoma in the U.S. has risen dramatically during this time period, especially among white males, whereas the incidence of squamous cell carcinoma has declined. Among white males, the steadily increasing incidence of esophageal adenocarcinoma overtook the incidence of squamous cell carcinoma around 1990. Among white females the incidence of adenocarcinoma has risen slightly, while the rate of squamous cell carcinoma has remained the same. Among black males the incidence of squamous cell carcinoma remains high; the incidence of adenocarcinoma is low but the rate is rising. ( Adapted from Devesa et al [6].)
Squamous cell carcinoma is the most common malignant neoplasm of the esophagus and constitutes 90% to 95% of all esophageal carcinomas. It commonly affects males, with the peak age of onset between 50 and 70 years. Smoking tobacco and excessive alcohol consumption are the two most important risk factors. Human papillomavirus infection and a variety of dietary triggers have also been suggested as risk factors. Among the predisposing conditions and attendant associations are celiac sprue, prior irradiation, tylosis palmaris et plantaris, Plummer-Vinson syndrome, achalasia, and stricture resulting from the ingestion of lye.

Squamous cell carcinoma may occur anywhere in the esophagus but is most commonly found in the middle- and secondly, in the lower-third portions. Macroscopic appearance of advanced esophageal carcinomas vary from exophytic mass to ulcerated, infiltrating lesion, to a combination of all these. A, In this figure the squamous cell carcinoma is shown to be grossly exophytic, fungating, and partially ulcerated, involving the distal esophagus. The tumor had extensively involved the esophageal wall, spreading into the periesophageal soft tissue. B, An exophytic and infiltrating squamous cell carcinoma causing annular constriction of the esophagus. The tumor showed massive circumferential infiltration of the esophageal wall, resulting in obstruction of the lumen.

C, Squamous cell carcinoma may also present as a large excavating esophageal ulcer, as seen in this figure. The carcinoma had infiltrated into the periesophageal soft tissue. Note the tumor nodules in the surrounding periesophageal soft tissue. The esophagus has a rich lymphatic supply, which accounts for the frequent lymphatic spread to surrounding lymph nodes. Metastasis to distant organs is also common, especially to the liver, lungs, pleura, and adrenals. Occasionally the tumor extends directly into the mediastinum. D, The infiltrating squamous carcinoma showed only focal surface ulceration, although the tumor had extensively spread along the submucosa underneath of the intact esophageal mucosa. This type of submucosal extension is common in all types of esophageal carcinoma. The tumor may also spread into the submucosa of the stomach through the submucosal lymphatics. (B, Courtesy of Beth Israel Hospital, Boston; C and D, from Ming [10]; with permission.)
Microscopic features of esophageal squamous cell carcinoma range from well-differentiated to poorly differentiated squamous cell carcinomas. The well-differentiated tumors contain squamous nests, pearls, intercellular bridges, and individual cell keratinization. Moderately differentiated squamous cell tumors have features such that they may be considered to be between well- and poorly differentiated carcinomas. Undifferentiated squamous cell carcinomas have no special differentiating features and do not make keratin. The tumor cells may have pleomorphic nuclei and scanty cytoplasm with many mitotic figures.

A. Histologic appearance of well-differentiated squamous cell carcinoma of the esophagus infiltrating the submucosa. The tumor is producing abundant keratin, manifested in the form of squamous pearls, and is evoking an intense inflammatory reaction around itself. Note the dysplastic squamous epithelium on the surface. B. Higher magnification of the tumor shown in panel A, showing keratin nests and pearls in greater detail.

A. Histologic appearance of invasive, moderately differentiated squamous cell carcinoma of the esophagus. Note the presence of keratin pearls in the superficial portion of the tumor and the less well-differentiated nonkeratinizing squamous cells at the lower infiltrating margin. B. Higher magnification of an island of a moderately differentiated squamous cell carcinoma from the view in panel A, showing individual cell keratinization. Note the presence of inflammatory cells in the background.
A. Histologic appearance of undifferentiated squamous cell carcinoma diffusely infiltrating the esophagus. B. The tumor has no differentiating features and is composed of sheets of single, large cells with pleomorphic nuclei and scanty cytoplasm. The overlying squamous epithelium had a focus of in situ carcinoma, making the diagnosis easier. C. A few islands of poorly differentiated squamous cell carcinoma. Immunohistochemical stains such as cytokeratin, vimentin, or leukocyte common antigen may be necessary to identify undifferentiated carcinoma from lymphoma and sarcoma. D. The sheets of undifferentiated carcinoma cells showing strong positive staining for cytokeratin.

Squamous cell carcinoma: intraesophageal spread. Esophageal carcinomas have a unique way of infiltrating within the esophagus. Carcinoma in situ extends and breaks off from the surface epithelium into the lamina propria to become intramucosal carcinoma. The tumor then penetrates the muscularis mucosae and enters the submucosa. The submucosa is made up of loose connective tissue, rich in lymphatics and blood vessels. As a result, once the carcinoma reaches the submucosa it expands circumferentially and also invades the lymphovascular channels. Lymphatic spread of malignant cells in the submucosa commonly produces satellite nodules several centimeters away from the main tumor mass. This spread can take place in both directions but is usually more cephalad. Carcinomas confined to lamina propria and submucosa are called superficial carcinomas. Once the tumor reaches the muscularis propria, it infiltrates along the direction of the muscle fibers. In the inner circular muscle layer the tumor grows down perpendicularly, while in the outer longitudinal muscle layer it follows the direction of muscle fibers and grows peripherally as shown. Once the carcinoma enters the adventitia, it can extend in any direction and usually evokes a tissue reaction in the form of dense stromal fibrosis (desmoplasia).
ESOPHAGEAL TNM PATHOLOGIC STAGING

Classification
Primary tumor (T) class
- Tis: Carcinoma in situ
- T1: Invades lamina propria or submucosa
- T2: Invades muscularis propria
- T3: Invades adventitia
- T4: Invades adjacent structures

Nodal (N) class
- N0: No regional node metastases
- N1: Regional node metastases

Distant metastases (M) class
- M0: No distant metastases
- M1: Distant metastases

Stage grouping
- 0: Tis N0 M0
- I: T1 N0 M0
- IIA: T2–T3, N0 M0
- IIB: T1–T2, N1 M0
- III: T3 or T4 N1 M0
- IV: AnyT AnyN M1

Accurate staging of esophageal cancer is important for therapeutic management and evaluation of treatment. This table illustrates the staging scheme developed by the American Joint Committee on Cancer in cooperation with the TNM Committee of the International Union Against Cancer. The classification given here applies to all esophageal carcinomas. The pathologic stage is based on examination of the resected esophagectomy specimen. The clinical staging is based on clinical examination before treatment is given and includes physical examination, endoscopy, imaging, and endoscopic ultrasonography. Computed tomography and endoscopic ultrasound scanning are particularly useful in the evaluation of the depth of invasion and of the status of the lymph nodes. (Adapted from the American Joint Committee on Cancer [11].)

ESOPHAGEAL CARCINOMA: PATTERN OF LYMPHATIC SPREAD

Carcinoma of cervical esophagus
- Cervical and superior mediastinal lymph nodes

Carcinoma of upper and middle thoracic esophagus
- Mediastinal lymph nodes
- Superior gastric lymph nodes

Carcinoma of lower esophagus
- Lower mediastinal lymph nodes
- Superior gastric lymph nodes
- Lymph nodes around celiac and splenic arteries

Figure 8-11.
Esophageal carcinoma: pathologic TNM staging. Pathologic staging is based on gross and histologic examination of the resected esophagus and associated lymph nodes. PT in the American Joint Committee on Cancer classification of esophageal carcinoma is based only on the depth of primary tumor invasion, regardless of the histologic type, size of the tumor, or region of involvement. Tis—carcinoma in situ; T1—tumor invades lamina propria or submucosa; T2—tumor invades muscularis propria; T3—tumor invades adventitia; T4—tumor invades adjacent structures in the mediastinum. This classification applies to all carcinomas.

Figure 8-12.
Esophageal carcinoma: pattern of lymphatic spread. Lymphatic involvement is present in 42%–67% of patients at time of diagnosis and is usually bidirectional to many sites.
ESOPHAGEAL CARCINOMA: DIRECT SPREAD

- Trachea and bronchi
- Aorta
- Pleural cavity
- Lungs
- Thyroid
- Pericardium
- Major vessels and nerves

ESOPHAGEAL CARCINOMA: SITES OF NODAL METASTASIS

<table>
<thead>
<tr>
<th>Site</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver</td>
<td>50%</td>
</tr>
<tr>
<td>Lungs</td>
<td></td>
</tr>
<tr>
<td>Adrenal gland</td>
<td>10%</td>
</tr>
<tr>
<td>Kidney</td>
<td>10%</td>
</tr>
<tr>
<td>Pleura</td>
<td>5%</td>
</tr>
<tr>
<td>Bone</td>
<td>8%</td>
</tr>
<tr>
<td>Stomach</td>
<td>8%</td>
</tr>
</tbody>
</table>

SPECIAL TYPES OF SQUAMOUS CELL CARCINOMA

Basaloid carcinoma

Basaloid carcinoma. A, Basaloid carcinoma, or basaloid variant of squamous cell carcinoma, arising in the distal portion of the esophagus as an infiltrating, annular, constricting neoplasm. The tumor had infiltrated through the esophageal wall into the main bronchus, resulting in the production of an esophagobronchial fistula. The cotton swab is going through the tract of the fistula. This is a rare, highly malignant, esophageal tumor usually occurring in the distal part of the esophagus. Note that the macroscopic appearance is similar to that of conventional squamous cell carcinoma of the esophagus. B, Microscopically, it presents as islands of infiltrating, poorly differentiated carcinoma, often exhibiting differentiation toward pseudoglandular structures resembling adenoid cystic carcinoma. Many of the infiltrating islands of tumor have central necrosis, giving them a pseudoglandular appearance.

(continued on next page)
Verrucous carcinoma

Verrucous carcinoma showing papillary architecture. A. This appearance is similar to that of verrucous carcinoma in other organs. Each papillary frond is made up of well-differentiated squamous cells surrounding a delicate fibrovascular core. Marked acanthosis and parakeratosis are present with blunt pegs extend into the submucosa of the esophagus. B. Higher magnification of the deeper end of tumor showing broad blunt pegs of squamous epithelium with central necrosis. Dysplasia is minimal and is confined to the basal layer. Macroscopic appearance is either that of a polypoid or an exophytic papillary mass. Verrucous carcinoma is a rare tumor, which grows slowly. It is less aggressive than the usual squamous cell carcinoma and does not appear to metastasize. The tumor may invade locally. (From Oota and Sobin [9]; with permission.)

Spindle cell variant (carcinosarcoma) of squamous cell carcinoma

Spindle cell carcinoma in the lower esophagus, presenting as a large polypoid mass. The surface of the tumor is partially ulcerated and necrotic. The tumor did not have a well-defined pedicle and showed extensive infiltration of the submucosa. This is a rare neoplasm, which usually presents as a large polypoid mass occurring in the middle and distal portions of the esophagus.
A. Microscopic appearance of the spindle cell variant of squamous cell carcinoma, showing small foci of squamous cell carcinoma and large interlacing bundles of malignant spindle cells. B. Higher magnified view of the spindle cell component, showing sarcoma-like cells and mitosis. C. Spindle cell carcinoma composed of large pleomorphic elongated cells and bizarre giant cells, which resemble malignant fibrous histiocytoma. Superficially invasive squamous cell carcinoma is present in the upper portion of the picture. The epithelial component of this neoplasm may be meager, confined only to a few in situ and superficially invasive areas. Mesenchymal differentiation toward bone, cartilage, or muscle may be present in the tumor. (From Lewin et al. [8]; with permission.)

Superficial esophageal carcinoma is defined as carcinoma limited to the epithelium (Tis), invading the lamina propria or superficially the submucosa (T1). It is a potentially curable disease despite the fact that many cases will have lymph node metastasis as well as lymphovascular invasion at time of resection [12]. A recent study found lymph node metastasis in approximately 34% of patients with superficial esophageal carcinoma, lymphatic invasion in 46%, and venous invasion in 3% [13]. Superficial carcinomas may be the spreading type and tend to be multifocal [13]. Complete resection with clear resection margins is important for cure.

Advanced esophageal carcinoma resected for cure: prognosis. Esophageal carcinoma is a highly lethal disease, and most advanced cases are not resectable. Even in those that are resectable, the prognosis is poor. Various biologic prognostic indicators are being studied to predict response to therapy and survival. So far, DNA ploidy, overexpression of p53 protein, cyclin D1, epidermal growth factor receptor and Ki-67 labeling index appear promising [3,12].
Small cell carcinoma of the esophagus growing in a diffuse infiltrative pattern. This very rare, very aggressive neoplasm is composed of small cells with scanty cytoplasm and hyperchromatic nuclei. It has a predominance among women, in whom it usually occurs in the lower and then in the mid-esophagus. Histologically, such neoplasms are identical to small cell undifferentiated (oat cell) carcinoma of the lung. Macroscopically, the tumor usually presents as an exophytic, fungating mass and rarely may occur in multiple foci. Histologically, the tumor has a diffuse growth pattern; it is made up of anaplastic small cells with round to oval hyperchromatic nuclei and scanty cytoplasm. The tumor cells may form rosettes and glands. Squamous pearls and, at times, foci of squamous carcinoma, may also be present. This tumor may be associated with production of ectopic hormones, such as calcitonin and adrenocorticotropic hormone.

Adenocarcinomas of the esophagus usually involve the lower third of the esophagus, but more rarely may be seen in the mid- or upper esophagus. They commonly arise from metaplastic columnar epithelium (ie, Barrett’s esophagus), as shown in this illustration. Note the irregular gastroesophageal junction (small arrow) and the nodular tumor mass (large arrow). Adenocarcinomas may also arise from heterotopic gastric mucosa or from the submucosal glands. It is one of the most significant complications of Barrett’s esophagus of the “specialized cell” type (columnar with goblet cells). In Barrett’s esophagus, the normal squamous epithelium of the esophagus is replaced by glandular-type epithelium as a consequence of long-standing gastroesophageal reflux disease. It is usually seen in men between the ages of 40 and 60, but also has been reported in children. The incidence appears to be increasing. (From Lewin et al. [8]; with permission.)

An exophytic, ulcerated adenocarcinoma arising in Barrett’s esophagus. The gross appearance of adenocarcinomas is very similar to that of squamous cell carcinomas of the esophagus, varying from plaques to large, fungating, ulcerated masses. When arising in Barrett’s epithelium, these tumors may be multiple. Endoscopically and grossly, they may be flat or may resemble an ulcerated Barrett’s mucosa, which is not easily recognizable as a tumor; however, they may also appear as a large exophytic, fungating mass. (From Lewin et al. [8]; with permission.)
A. Histologic appearance of Barrett’s esophagus with dysplasia. Note the hyperplastic squamous epithelium on the side. B. High-power view, showing the characteristic goblet cells intermixed with columnar cells as seen in metaplastic Barrett’s esophagus. Adenocarcinoma arising in Barrett’s esophagus is always preceded or accompanied by dysplasia. In the literature the presence of high grade dysplasia seen in association with adenocarcinoma has been reported from 68% to 100% of cases.

The histologic appearance of adenocarcinoma varies widely from the well-differentiated intestinal type to diffuse, poorly differentiated carcinoma, to carcinomas with signet-ring cell features. The spectrum of histologic features seen in adenocarcinoma arising in Barrett’s esophagus. C. Well-differentiated adenocarcinoma, intestinal type; D. moderately differentiated adenocarcinoma showing extensive intramural spread. The metaplastic columnar epithelium on the surface had many foci of high grade dysplasia; E, higher magnification of the view of the carcinoma seen in panel D; F–G, poorly differentiated adenocarcinoma with some cells containing mucin vacuoles; H, mucinous carcinoma; I, signet-ring cell carcinoma.

(continued on next page)
The histologic appearance and tumor grade do not appear to correlate with survival rates. These carcinomas are all very similar to squamous cell carcinomas in their biologic behavior and prognosis. (H and I, from Lewin et al. [8]; with permission.)

**DYSPLASIA IN BARRETT’S ESOPHAGUS: HISTOLOGIC CRITERIA**

<table>
<thead>
<tr>
<th>HIGH-GRADE DYSPLASIA</th>
<th>LOW-GRADE DYSPLASIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crypt architecture</td>
<td>Crypt architecture is preserved</td>
</tr>
<tr>
<td>Distorted, marked branching</td>
<td></td>
</tr>
<tr>
<td>Lateral budding</td>
<td></td>
</tr>
<tr>
<td>Back-to-back glands</td>
<td></td>
</tr>
<tr>
<td>Nuclei</td>
<td>Nuclei</td>
</tr>
<tr>
<td>Stratified to apical surface</td>
<td>Stratified near base, not the apex</td>
</tr>
<tr>
<td>Loss of polarity</td>
<td>Enlarged</td>
</tr>
<tr>
<td>Hyperchromatic</td>
<td>Hyperchromatic</td>
</tr>
<tr>
<td>Variable size and shape</td>
<td>Crowded</td>
</tr>
<tr>
<td>Abnormality extends to mucosal surface</td>
<td>Abnormality extends to mucosal surface</td>
</tr>
</tbody>
</table>

Dysplasia in Barrett’s esophagus: histologic criteria. Barrett’s esophagus is associated with an increased risk of adenocarcinoma. Dysplasia usually precedes adenocarcinoma, but may also be associated with adenocarcinoma. Thus, it can be used as a marker for detecting patients at high risk for developing carcinoma. Dysplasia is usually classified as high grade, low grade, and indefinite for dysplasia. The diagnosis of dysplasia is based on both architectural and cytological abnormalities, as shown in this table. The diagnosis may be made difficult by inflammatory/reactive changes as well as interobserver variation. Ancillary techniques for better detection of dysplasia are being researched. Among these, DNA content flow cytometry may come to play an important role.
Primary malignant melanoma of the esophagus presenting as a large, polypoid mass. A few cases of primary malignant melanoma of the esophagus have been reported. It is important to document the intraepithelial component of the neoplasm in the adjacent squamous mucosa in order to exclude it from metastatic melanoma. Primary tumors may also be associated with pigmentation (melanosis) of the uninvolved mucosa. Although primary melanomas can involve any part of the esophagus, they tend to occur more commonly in the lower third. Prognosis for the patient with this finding is extremely poor (From Morson and Dawson [14]; with permission.)

Microscopic appearance of the intraepithelial component (junctional activity) necessary for diagnosis of primary malignant melanoma, as seen in the esophageal mucosa adjacent to the focus of the malignant melanoma. A, Proliferation of melanocytes in the basal layer of the squamous mucosa. B, The melanocytes are pigmented and extend upward, toward the surface of the mucosa. (From Lewin et al. [8]; with permission.)
A, Malignant melanoma arising in the esophageal mucosa and infiltrating deep into the submucosa. The tumor is composed of large, malignant, epithelioid cells with prominent nuclei and nucleoli. Note the presence of melanocytic nests in the squamous mucosa. Immunohistochemical staining with S-100 protein, vimentin, and monoclonal antibody such as HMB-45 are helpful in confirming diagnosis.

HMB-45 is a more specific, but less sensitive, marker. B, Higher magnification of panel A showing the tumor cells to be large with increased nuclear-cytoplasmic ratio, pleomorphic nuclei, and prominent nucleoli. Many pigment-laden macrophages are also present. (From Lewin et al. [8]; with permission.)

**FIGURE 8-28.**

Fibrovascular polyps are fairly common benign tumors; they are found more often in men, in whom they typically appear in the upper third portion of the esophagus. Endoscopically, they may present as sessile or pedunculated masses. They do, however, often grow to a much larger size and have long stalks. As shown in this figure, the fibrovascular polyp has assumed a large sausage-shaped configuration, causing nearly complete obstruction. (From Ming [10]; with permission.)
The bulk of the tumor is made up of loose, edematous, and at times, myxoid connective tissue with dilated blood vessels and scattered mononuclear cells. Strands of spindle cells and islands of adipose tissue may also be present. (Courtesy of R. E. Petras, MD.)

**Stromal and smooth muscle tumor**

Leiomyomas. These are the most commonly seen benign tumors of the esophagus, representing 60%–70% of all benign esophageal neoplasms. They may occur at any age, but the peak incidence of occurrence is between 30 and 59 years of age [1]. They occur more often in men, with a male:female ratio of 1.93:1. Although they can be found anywhere in the esophagus, they have a predilection for the lower-third portion. A majority of leiomyomas are located intramurally, arising from the smooth muscle of the wall of the esophagus. Dysphagia is the most common symptom followed by pain, but approximately 15% are asymptomatic and are found incidentally [1]. Leiomyomas tend to be slow-growing tumors and are smaller in size than their malignant counterparts. Leiomyosarcomas (LMS) are rare in the esophagus. A majority of them are found in patients over the age of 50 years, with a peak age of occurrence between 50 and 69 years. They are slightly more common in men, with a male:female ratio of 1.55:1. Leiomyosarcomas also arise from the smooth muscle wall of the esophagus and may be located intramurally; more commonly, they present as intraluminal polypoid tumors. LMS may have an infiltrative growth pattern and at times may present as an extraluminal mass in the mediastinum. In addition to dysphagia and pain, patients with LMS may complain of weight loss. The prognosis is poor, with a 20% 5-year survival rate [1]. A, Large multinodular esophageal leiomyoma. The lesion is submucosal with an intact surface epithelium. Larger leiomyomas tend to be multilobular and may have surface ulceration. B, C, Nodular leiomyoma with a smooth outer surface. Cut surface appears to be grayish-tan and whorled. Macroscopically, the leiomyoma appears as a well-circumscribed rubbery mass. Most leiomyomas are intraluminal and intramural but, rarely, may present as a mediastinal mass. D, Histologic appearance of esophageal leiomyoma with smooth muscle cells arranged in interfacing bundles. Note the lack of mitosis and bland appearance of the neoplasm. Microscopic features of leiomyoma include spindle-shaped smooth muscle cells with cigar-shaped nuclei arranged in herringbone, stori-form, or palisading patterns with rare or no mitosis. (A, From Ming [10]: with permission.)
A tumor infiltrating submucosa

Squamous epithelium

Submucosa

Leiomyosarcoma forming large extraluminal mass in mediastinum

Muscularis propria

**Figure 8-32.**

Histopathologic features of esophageal leiomyosarcomas similar to benign leiomyomas. The most important criteria for malignancy is two or more mitoses per high-power field [1]. Other features that may be found include hypercellularity, increased and irregular cell and nuclear size and shape, and necrosis. Most leiomyosarcomas arise de novo rather than from malignant transformation of an existing leiomyoma. The main differential diagnosis of this malignant tumor is the spindle-cell variant of squamous cell carcinoma. Therefore, before a diagnosis of leiomyosarcoma is made, the entire tumor should be thoroughly searched for evidence of epithelial (squamous cell) differentiation.

A. Low magnification view of esophageal leiomyosarcoma infiltrating through the esophagus to form an extraluminal mass.

B. Higher magnification of same tumor. Note the hypercellularity and many mitotic figures present in the leiomyosarcoma.

**REFERENCES**

The orderly propulsion of a bolus following its ingestion is caused by a set of coordinated activities in the muscles of the esophagus. This organized motility is caused by a number of complex events that take place in the brain stem, extrinsic and intrinsic nerves, and muscles of the esophagus. From a simplistic point of view, after mastication and organization of the bolus in the mouth, the cheek, tongue, and muscles of the floor of the mouth propel the bolus back into the pharynx. The stimulation of the receptors in the pharynx by the bolus results in afferent impulses that travel along the fifth, seventh, ninth, and tenth cranial nerves into the brain stem. In the medulla oblongata these nerve impulses are coordinated, and programmed efferent impulses travel along the vagus nerve and coordinate motor events in the esophagus.

The esophagus in humans is guarded by upper and lower esophageal sphincters. The body of the esophagus is 20 to 25 cm in length and made up of skeletal muscle in the upper third, a mixture of skeletal and smooth muscle in the middle third, and only smooth muscle in the lower third. Esophageal enteric nervous system is present in the wall of the esophagus. Efferents from the brain stem connect with the esophageal enteric nervous system and coordinate the motor events in the esophagus. These motor events result in relaxation of the upper and lower esophageal sphincters as well as a peristaltic contraction along the length of the esophagus. Peristaltic contraction in the smooth muscle esophagus and relaxation of the lower esophageal sphincter can also be coordinated by the esophageal enteric nervous system in the absence of central connections.

The motor abnormalities of the esophagus are the result of either systemic disorders affecting the muscles of the esophagus or a loss of central or peripheral control of esophageal motility.
peristalsis and its sphincters. A number of systemic diseases, such as scleroderma, diabetes mellitus, dermatomyositis, and the neurologic conditions affecting the brain stem or vagus nerve, can affect the esophageal motility (secondary motor disorders). The etiology of the primary motor disorders of the esophagus is not known; however, the pattern of contraction abnormalities in the esophagus are well described and can be easily identified through the technique of intraluminal pressure measurement (ie, manometry). The primary or idiopathic motor disorders of the esophagus are categorized into upper esophageal sphincter dysfunction and Zenker’s diverticulum, achalasia of the lower esophageal sphincter and esophagus, diffuse esophageal spasm, nutcracker esophagus or hypertensive esophageal peristalsis, isolated hypertensive lower esophageal sphincter, and gastroesophageal reflux disease.

**UPPER ESOPHAGEAL DYSFUNCTION AND ZENKER’S DIVERTICULUM**

**FIGURE 9-1.**
Radiologic appearance of cricopharyngeal bar. The indentations (arrow) seen in the barium swallow, usually occurring at the level of cervical vertebra 4 or 5, represent either a nonrelaxing or a noncompliant upper esophageal sphincter. The patient usually has oropharyngeal dysphagia; however, asymptomatic individuals can have this radiologic finding.

**FIGURE 9-2.**
Zenker’s diverticulum. Radiograph of a 70-year-old patient with oropharyngeal dysphagia, coughing, choking spells, and recurrent pneumonia. Note the outpouching of the pharynx above the level of the cricopharyngeus (arrow). This outpouching is located in the posterior wall of the pharynx. Zenker’s diverticulum is a true pulsion diverticulum and is the result of increased intrapharyngeal pressures during swallowing as a result of a noncompliant or nonrelaxing upper esophageal sphincter. There may be penetration of the barium into the laryngeal inlet and spilling into the tracheobronchial tree. The treatment of this condition in the setting of severe symptoms is usually cricopharyngeal myotomy.
Endoscopic view from a patient with achalasia of the lower esophageal sphincter (LES). Note that the region of the LES is tightly closed. Usually a small amount of pressure is needed before the endoscope pops into the stomach. Above the LES there is a wide-mouth diverticulum known as the epiphrenic diverticulum.

Barium swallow in a patient with achalasia of the esophagus. This study shows a dilated esophagus in a patient with achalasia of the lower esophageal sphincter (A). The gastroesophageal junction does not open, resulting in a classical bird's beak appearance at the distal end of the esophagus (B). The serrated margin (arrow) in the midesophagus is referred to by radiologists as tertiary contractions.

Lateral radiograph from a barium swallow in a patient with achalasia of the esophagus. There is lack of an opening of the gastroesophageal junction; however, unlike the esophagus in Figure 9-4B, the esophagus is not dilated. Irregular margins of the distal esophagus are the result of tertiary contractions. An air-fluid level is seen in the proximal esophagus. This case demonstrates that not all patients with achalasia of the esophagus have dilated, tortuous, and sigmoid esophagus.
A-B. Barium swallows of a patient with secondary achalasia. The barium swallows in this figure represent the appearance of the esophagus in a patient with adenocarcinoma of the gastroesophageal junction, which can produce a motility disorder identical to primary or idiopathic achalasia. The gastroesophageal junction shows a bird’s beak appearance, and on multiple spot films there was no evidence of an opening of the esophagogastric region. Case reports of metastatic tumor from prostate, breast, lymphoma, lung carcinoma, hepatocellular carcinoma, colon carcinoma, esophageal lymphangioma, and pleural mesothelioma causing secondary achalasia have been described.

Figure 9-7.
Manometric tracing from a patient with achalasia of the esophagus. Simultaneous pressure measurements were made in the stomach, lower esophageal sphincter (LES), at three sites in the distal esophagus (5 cm apart), and at the pharynx. The subject was asked to swallow 5 mL of water for each of the three wet swallows (WS) shown in the tracing. Each swallow results in a pharyngeal contraction followed by a simultaneous pressure wave throughout the distal esophagus. The LES pressure is high (> 40 mm Hg), and there is incomplete relaxation of the LES in response to each of the swallows.

Figure 9-8.
Simultaneous pressure recording and fluoroscopy during barium swallow in a patient with achalasia of the esophagus. The esophageal pressures were measured at seven sites spaced 3 cm apart along the length of the esophagus. Note that the swallow resulted in a simultaneous pressure wave throughout the length of the esophagus. This simultaneous pressure wave is not caused by a simultaneous esophageal contraction. Rather, it is caused by an isobaric fluid pressure wave generated between an esophageal contraction at the top end of the esophagus and a closed lower esophageal sphincter region (LES) at the bottom. UES—upper esophageal sphincter. (Adapted from Massey et al. [5].)
Epiphrenic diverticulum in a patient with achalasia of the esophagus. The diverticulum just above the region of the esophagogastric junction can be seen, albeit infrequently, in patients with classical achalasia; it is more common in patients with rigorous achalasia. The latter have hypertensive esophageal peristalsis. The diverticulum is caused by a large increase in the intraesophageal pressure during propulsion of the bolus.

**Figure 9-9.**

Pneumatic dilation of the lower esophageal sphincter using a Rigiflex Balloon (Microvasive, Boston Scientific, Watertown, MA) in a patient with achalasia of the esophagus. This radiograph was taken at the time of maximal balloon inflation. Note the symmetrical appearance along the whole extent of the balloon and the absence of a waist. A waist on the balloon usually indicates inadequate dilation.

**Figure 9-10.**

Algorithm for treatment of esophageal achalasia. Achalasia of the esophagus can be treated either medically or surgically. Smooth muscle relaxants, nitrate, and calcium channel blockers reduce laser esophageal sphincter pressure and improve dysphagia symptom. Injection of botulinum toxin can also reduce sphincter pressure and improve esophageal emptying; however, standard therapy for achalasia is pneumatic dilation. Patients with recalcitrant symptoms, despite medical therapy, require surgical myotomy.
Barium swallow study in a patient with diffuse esophageal spasm. Note the corkscrew or rosary-bead appearance along the length of the distal esophagus.

Manometric appearance of diffuse esophageal spasm. This manometric tracing is from a patient with diffuse esophageal spasm. Pressure measurements are made simultaneously in the stomach, lower esophageal sphincter (LES), and three sites spaced 5 cm apart in the distal esophagus and pharynx. Two swallows are shown in this trace. Each swallow results in a simultaneous pressure wave between the 7- and 12-cm sites. The esophageal contractions are prolonged and have a double-peaked and triple-peaked appearance. The contraction amplitudes are high. The normal contraction amplitudes are between 50 and 180 mm Hg and duration is less than 6 seconds. In this subject the contraction amplitudes were as high as 370 mm Hg and contraction durations were prolonged.

Simultaneous manometry and fluoroscopy of barium swallow in a patient with diffuse esophageal spasm. The genesis of simultaneous pressure waves in a patient with diffuse esophageal spasm is different than in a patient with achalasia. The simultaneous pressure waves in a patient with achalasia are the result of fluid pressure built up between a proximal esophageal contraction and a distal closed lower esophageal sphincter (LES). On the other hand, in a patient with diffuse esophageal spasm, true simultaneous contraction does exist in the distal esophagus, which results in compartmentalization of the esophageal lumen. The barium flows in a to-and-fro fashion, resulting in impairment of the esophagus transit. DS—dry swallow; UES—upper esophageal sphincter.

(Adapted from Massey et al. [5].)
Algorithm for the treatment of esophageal spasm. Infrequent symptoms caused by esophageal spasm are best treated by reassurance. Frequent symptoms require medical therapy with antireflux agents or smooth muscle relaxants. Surgical therapy is reserved for most symptomatic patients who are resistant to medical therapy.

**Figure 9-15.**

Nutcracker esophagus. This manometric tracing was obtained from a patient with noncardiac chest pain. The pressures were measured simultaneously in the stomach, lower esophageal sphincter (LES), and three sites in the distal esophagus, spaced 5 cm apart. Note that the esophageal contractions are high in amplitude and have multiple peaks. Contraction durations are prolonged. In contrast with the diffuse esophageal spasm, these contractions are peristaltic. The LES does not relax completely in response to swallow. In 30% to 50% of patients there is dysfunction of the LES, either in the form of a hypertensive or a partially relaxing LES. Even though a significant number of patients with noncardiac chest pain have this abnormality, there is a lack of temporal association between the chest pain and abnormal esophageal contractions. The prolonged ambulatory motility studies reveal that only 10% to 20% of chest pain events occur in close temporal association with abnormal esophageal contractions in the esophagus. Fifteen percent to 20% of pain events occur in association with acid reflux and the etiology of the remainder remains obscure [9]. Treatment of this disorder with calcium channel blockers and other smooth muscle relaxants results in decreased contraction amplitude without a major improvement in the frequency of chest pain [10]. WS—wet swallow.
Radiograph of esophageal diverticulum. This is an example of an esophageal pulsion diverticulum (arrow). The pulsion diverticulum is seen in the setting of esophageal motility disorders, such as hypertensive esophageal peristalsis, diffuse esophageal spasm, or achalasia of the esophagus.

**Figure 9-18.**
Esophageal manometric tracing of a patient with hypertensive lower esophageal sphincter (LES) pressure. Normally the LES pressure is less than 35 mm of mercury. This patient complained of symptoms of moderate dysphagia for solids and liquids for longer than 5 years. The LES pressures were greater than 35 mm of mercury. Complete relaxation of the LES pressure in response to swallowing was present. The mechanism of dysphagia in a patient with complete relaxation of the LES is not clear. It is, however, most likely related to the poor compliance or opening mechanism of the region of the LES, resulting in poor transit.
SCLERODERMA

Radiographic view of scleroderma of the esophagus, stomach, and duodenum. This picture was taken one-half hour after patient swallowed barium. Note that barium is still present in the esophagus. There is also retained barium in the stomach. The duodenum is enlarged and the small intestine is dilated. Scleroderma is a connective tissue disorder characterized by replacement of the smooth muscles with fibrous tissue. There is loss of peristalsis and dilation of the esophagus. The lower esophageal sphincter is usually very weak, which can result in severe reflux disease and reflux-related esophageal stricture.

Radiographic view of scleroderma of the esophagus. In addition, the patient has esophagitis caused by candidal infection.

Manometric tracing from a patient with severe involvement of scleroderma. The pressures are measured simultaneously in the stomach, lower esophageal sphincter (LES), and three sites in the esophagus and pharynx spaced 5 cm apart. Three wet swallows (WS) are shown on this tracing. Note that the LES pressures are low (5–7 mm Hg). In response to WS there is a small-amplitude, simultaneous pressure wave along the entire length of the distal esophagus. These pressure waves most likely represent the isobaric pressure wave, as described in achalasia of the esophagus.
Illustration of esophageal function in a woman with scleroderma and severe esophageal motor impairment. The esophageal motor function was assessed by three separate techniques: radionuclide scintigraphy (A), barium swallow (B), and esophagography (C). There was complete retention of the radionuclide material in the esophagus after four swallows. The fluoroscopic study showed similar retention of the barium associated with absent peristalsis, and the manometric study showed absence of peristalsis and esophageal contractions in the distal esophagus. The sensitivity and specificity of the three tests used to assess esophageal motor function are similar. (Panels A and B from Klein et al. [11]; with permission.)

ANTIREFLUX MECHANISMS

Anatomy of the two lower esophageal sphincters. Anatomic relationship between the lower esophageal sphincter (LES) and crural diaphragm based on electrophysiologic measurements. The length of the LES is approximately 4.4 cm and of the crural diaphragm is 1.8 cm. The crural diaphragm encircles the proximal half of the LES. Approximately 2.5 cm of the lower esophageal sphincter is intra-abdominal in location. The squamocolumnar junction is usually located either in the middle or at the proximal end at the LES. (Adapted from Heine [12].)
An esophageal manometric pressure tracing shows the contribution of lower esophageal sphincter (LES) and crural diaphragm to the esophagogastric junction pressure. A tonic component measures as end-expiratory pressure is due to the contraction of the smooth muscles of the LES. With each inspiration there is an increase in LES pressure, which is due to contraction of the crural diaphragm.

E—esophagus; S—stomach; DEA—diaphragm electrical activity; EKG—electrocardiogram.

**Figure 9-24.**

A spontaneous, transient, lower esophageal sphincter (LES) relaxation. The onset of relaxation is indicated by the arrow. Relaxation occurred in the absence of swallow as manifested by the absence of pharyngeal pressure wave. The LES relaxation is complete to the level of intragastric pressure (indicated by the horizontal line) and is sustained for longer than 20 seconds. Transient LES relaxation is associated with inhibition of the crural diaphragm as indicated by the loss of inspiratory increase in LES pressure and diaphragmatic electromyography (DEMG). Note the esophageal contractions at the onset of LES relaxation. Reflux (drop in esophageal pH) occurs after complete LES relaxation has been achieved, and is associated with an increase in intraesophageal pressure (common cavity, marked by an asterisk). A secondary peristaltic clearance response can be seen at the end of LES relaxation. Transient LES relaxation is the major mechanism of gastroesophageal reflux in normal controls as well as patients with reflux disease. Transient LES relaxation is a neural reflex that is controlled through the brain stem and is mediated through the vagus nerve. (See Chapter 6 for further discussion of gastroesophageal reflux.)
Ultrasound images of the lower esophageal sphincter (LES) in a normal subject (A) and in a patient with achalasia of the esophagus (B). These ultrasound images were obtained using a high-frequency intraluminal ultrasound probe (USP). The USP is 6.2 Fr in diameter and contained a 20-MHz transducer. Different layers of the esophagus can be identified using this USP. The ones that are easily identifiable in these figures are the mucosa (MUC), the circular muscle (CM), and the longitudinal muscle (LM). Note excessive thickening of the CM in panel B.

Ultrasound images of the esophagus in a normal subject (A) and in a patient with achalasia of the esophagus (B) using a high-frequency intraluminal catheter-based ultrasound probe. The esophagus is 5 cm above the lower esophageal sphincter in the normal subject. The three layers that can be identified include the mucosa (MUC), the circular muscle (CM), and the longitudinal muscle (LM). Note that the mucosa is tightly wrapped around the ultrasound probe (USP) in a normal situation. In the patient with achalasia of the esophagus there is wide separation of the mucosa from the USP. This wide separation is caused by the accumulation of the fluid in an aperistaltic esophagus. SP—spine.

Ultrasound images of the normal distal esophagus using high-frequency intraluminal ultrasonography. These images were obtained using an IVUS system (Diasonic, Milpitas, California). This catheter is 6.2 Fr in diameter and contains a 20-MHz transducer. The transducer rotates 360 degrees and provides images of the seven different layers of the esophagus. This figure represents the image of a distal esophagus obtained in a normal subject showing the correlation of the different layers with the ultrasonographic images. Seven different layers of the esophagus (mucosa, submucosa, muscularis mucosa, circular muscle [CM], septum, longitudinal muscle [LM], and adventitia) can be seen on these images. There is excellent correlation between different ultrasonographic images (A) to the histologic images obtained on an autopsy specimen (B). The muscularis propria (CM and LM layers) appear darker than the mucosa and submucosa on these images. T—transducer. (From Miller et al. [13]; with permission.)
Ultrasoundographic and histologic images in a patient with scleroderma. Note the increase in the echogenicity of the circular muscle (CM) as well as longitudinal muscle (LM) layers compared to the normal esophagus. There appears to be an excellent direct correlation between the increase in the echogenicity and the extent of fibrous matter in scleroderma. CM is usually more involved than LM. In addition to histologic correlation, there was also direct correlation between the 24 pH scores and the severity of abnormality detected by the ultrasonographic technique. T—transducer. (From Miller et al. [13]; with permission.)

Correlation between changes in the thickness of the circular, longitudinal and total muscle thickness with the intraluminal pressure during an esophageal contraction. Pressure and ultrasound images were recorded simultaneously during a swallow-induced esophageal contraction. The ultrasound images were analyzed every 250 milliseconds. There is a close temporal correlation between increase in the thickness of both muscle layers, A, and changes in esophageal pressure, B. The peak pressure corresponds to the peak thickness of the circular, longitudinal, and total muscle.
**Figure 9-31.**
Sustained esophageal contraction (SEC) prior to episode of heartburn and chest pain. The vertical line indicates the onset of heartburn and chest pain; note the acid reflux event prior to the onset of heartburn. There is a sustained increase in muscle thickness (SEC) before the onset of heartburn and chest pain. The onset of SEC occurred approximately 20 seconds before the onset of heartburn. It is suggested that SEC rather than acid reflux is the cause of heartburn event [14].

**Figure 9-32.**
An example of a heartburn episode associated with sustained esophageal contraction (SEC) during acid perfusion of the esophagus (Bernstein test). During sustained acid infusion there were two episodes of heartburn experienced by this individual, with a brief period of relief from heartburn in between. Note that both instances of heartburn symptoms were associated with sustained increase in the muscle thickness (SEC). The first heartburn symptom occurred 3 minutes after the onset of acid infusion into the esophagus and 20 seconds after the onset of SEC [15].
Ultrasound image analysis of esophageal muscle thickness during a negative and a positive edrophonium (Tensilon) test. A, B, Changes in esophageal muscle thickness after injection of Tensilon in two patients with symptoms of esophageal chest pain. The patient in panel A had no chest pain; the patient in panel B had chest pain following injection of Tensilon. The horizontal dashed line denotes baseline muscle thickness; note the difference in the changes in esophageal muscle thickness. Peaks in muscle thickness are voluntary 5 ml water swallows which were performed every 60 seconds following the injection of Tensilon. There is no sustained increase in esophageal muscle thickness in the patients who had no chest pain after edrophonium injection (panel A). In contrast, the patient who had chest pain 72 seconds after injection of edrophonium demonstrated a sustained increase in the esophageal muscle thickness preceding the onset of pain (panel B) [15].

REFERENCES


Noncardiac chest pain (NCCP) is a common and important clinical problem. The most common esophageal cause of NCCP is gastroesophageal reflux disease (GERD); other esophageal etiologies include abnormal esophageal motility, altered nociception, or an "irritable esophagus." With many similarities in the presenting symptoms of cardiac and noncardiac chest pain, certain historic features may suggest an esophageal cause; however, it is important first to determine a possible cardiac cause. If results of studies are negative for a cardiac cause of pain, the diagnostic work-up should be directed at identification of gastrointestinal disease. The presence of dyspepsia, dysphagia, or frequent heartburn symptoms in association with chest pain should prompt endoscopy. For chest pain without these associated symptoms, specific testing for GERD (acid-perfusion test, ambulatory pH monitoring) or esophageal motor disorders (esophageal manometry, ambulatory manometry) should be undertaken. Specialized provocative testing for altered esophageal sensitivity (edrophonium, balloon distention) may reveal the esophagus to be involved in the production of an individual's symptom of chest pain.

### BACKGROUND AND EPIDEMIOLOGY

As many as 30% of coronary arteriograms performed in the evaluation of chest pain demonstrate normal or insignificant coronary anatomy to explain the symptoms, suggesting alternative noncoronary causes. These patients with NCCP with normal coronary anatomy have an excellent prognosis, with follow-up in studies of up to 10 years demonstrating a less than 1% death rate from cardiac disease [1–3]. Despite reasonable exclusion of coronary artery disease and explanation to the patient of this, patients with NCCP continue to have chest pain that compromises their lifestyle, with a possible inability to work; they persist with visits to physicians' offices and emer-
gery departments for further evaluation of their chest pain symptoms [4–6].

The sources for chest pain symptoms in these patients include noncoronary cardiac disease, pulmonary disease, musculoskeletal disorders, panic disorder, and disorders of the esophagus or other gastrointestinal organs. Studies of patients with angina-like pain, excluding those with evidence of cardiac disease, revealed esophageal causes for symptoms in 50% [7–14]. Thus, esophageal disease is a common cause for production of symptoms in patients with NCCP; gastroenterologists are often responsible for the evaluation of this group of patients.

**CHARACTERISTICS OF ESOPHAGEAL CHEST PAIN**

Patients with NCCP may present with the same angina-like symptoms as those found to have coronary artery disease. Patients presenting to emergency departments are often anxious about possible cardiac disease, and may share with those patients who are found to have coronary ischemic pain symptoms of fear and autonomic discharge (diaphoresis, pallor, dizziness, tremor). In patients with NCCP referred to an esophageal laboratory after cardiac disease has been excluded, symptoms of heartburn and regurgitation were seen in the majority, while almost half had experienced dysphagia along with their chest pain symptoms, and only 11% had no esophageal symptoms other than their chest pain [15]. However, these esophageal symptoms are not isolated to patients with chest pain in whom cardiac disease is ruled out, for they were found to be present in about half of patients with chest pain who had proven coronary disease [16]. Although certain characteristics of the pain history may prompt investigation into possible esophageal causes, it is reasonably necessary to exclude cardiac disease as the first evaluation.

**MECHANISMS OF ESOPHAGEAL CHEST PAIN**

The specific mechanisms producing esophageal chest pain are not well understood. Acid reflux may stimulate chemoreceptors and trigger the sensation of heartburn or chest pain, but data from patients with abnormal total reflux time and esophagitis suggest that only about 20% of reflux events produce symptoms [17].

Esophageal motor disorders may cause myoischemia [18] or distention and result in symptom production. The use of 24-hour high-frequency intraluminal ultrasonography of the esophagus recently demonstrated a strong temporal correlation between sustained esophageal muscle contraction and both spontaneous and provoked esophageal chest pain [19]. Ingestion of cold liquids, stimulating thermoreceptors, may induce aperistalsis with esophageal distention and resultant chest discomfort [20]. Dysfunction of the belch reflex may also result in acute esophageal distention and discomfort [21]. Studies of esophageal balloon distention as a provocative test show that smaller inflation volumes produce chest pain sensa-

**GERD, ESOPHAGEAL MOTILITY DISORDERS, AND CHEST PAIN**

In patients with NCCP, 24-hour pH monitoring shows abnormal reflux in about half [7,15,27,28]. GERD may also produce symptoms in patients with proven obstructive coronary disease, and combined ambulatory Holter and pH monitoring can help to elucidate the cause. In one such study, abnormal reflux parameters were identified in 39% of patients, with half experiencing chest pain coinciding with identifiable reflux events [29].

Although upper gastrointestinal endoscopy and biopsy may identify patients with reflux esophagitis, the majority of symptomatic patients with NCCP have normal findings. Barium radiography and esophageal scintigraphy may demonstrate gastroesophageal reflux to be present in a given patient, but do not necessarily correlate to symptoms. The acid-perfusion (Bernstein) test has good specificity, but a poor sensitivity; it has been supplanted in most centers by ambulatory pH monitoring. Prolonged pH monitoring has excellent sensitivity and specificity and permits the correlation between chest pain and acid reflux episodes, even when total reflux exposure may not be excessive [15,30].

Recent studies suggest a role for empiric acid inhibition to diagnose GERD in patients with frequent NCCP in place of traditional invasive testing for GERD. A one-week course of high-dose omeprazole identified GERD as a cause of chest pain with a sensitivity of 78% and specificity of 86%. An economic analysis showed cost savings of $573 per patient over traditional testing and a 59% reduction in the number of diagnostic procedures performed [31]. These results add to the findings of previous investigators who had demonstrated improvement in chest pain symptoms in 81% of GERD-positive NCCP patients receiving high-dose omeprazole versus 6% improvement from placebo [32]. Treatment of acid-related symptoms with omeprazole in patients with proven obstructive coronary artery disease being optimally managed with antianginal therapy was similarly effective in relieving chest pain symptoms, improving 65% of those who had at least some of their symptoms related to GERD [33].
Historically, esophageal spasm was described in association with noncardiac chest pain. The disorder called nutcracker esophagus, consisting of high-amplitude peristaltic contractions which may be of prolonged duration, was subsequently identified to be the most common esophageal motility disorder (EMD) identified in patients with NCCP, accounting for about half of EMDs when present [9,34]. Although some of the motor disorders may directly relate to causation of pain, through mechanisms of spasm or distention (eg, achalasia, diffuse spasm), most investigators now consider the EMDs to be an epiphenomenon found in chronic patients with chest pain or as a response to stress [35,36]. Furthering this concept is a recent report showing that patients with nutcracker esophagus may have a hypersensitive and stiff esophagus when measured by balloon distention and impedance planimetry [37].

**Prolonged ambulatory esophageal testing and provocative testing**

The esophagus is likely the source of a patient’s chest pain if the usual discomfort is shown to occur during an abnormal esophageal event that could cause the pain, such as acid reflux, abnormal motility, or both. Comparison of stationary and ambulatory esophageal studies in patients with NCCP shows that patients with acid-related chest pain most often have normal baseline esophageal manometry, whereas abnormal baseline manometry is more likely associated with an abnormal motility episode during spontaneous pain [11,12]. In patients undergoing combined 24-hour pH and motility testing, an esophageal cause for NCCP symptoms is found in 10% to 47% [38]. Gastroesophageal reflux accounts for the majority (about 70%) of these symptoms, whereas abnormal motility events account for the minority.

Esophageal provocative testing has evolved as a method to reproduce esophageal chest pain while patients are in the laboratory; the procedure is similar to performing cardiac stress tests to bring out symptoms or findings of ischemic heart disease. Historically, ergonovine maleate and bethanecol had been used as esophageal provocative tests; however, they are nonspecific stimulants and may produce chest pain from coronary artery disease. Also, their use is limited by significant side effects (eg, coronary spasm, headache, nausea, pain at injection site, sweating) [39,40].

The most frequently used esophageal provocative test is administration of the cholinesterase inhibitor edrophonium. The test is believed specific for the esophagus, producing strong esophageal contractions without affecting esophageal blood flow [41], has few side effects, and provokes chest pain only in 20% to 30% of patients with NCCP [42,43].

Intraesophageal balloon distention often reproduces chest pain in patients with NCCP (60%), but produces chest discomfort in only 20% of asymptomatic volunteers; patients are found to have their pain stimulated by lower inflation volumes of esophageal distention [22,23].

The addition of balloon distention to acid-perfusion and edrophonium testing provides an increased identification of the esophagus as the likely source of the NCCP [44,45]. Although helpful in the search for an esophageal cause of chest pain, prolonged esophageal ambulatory studies and provocative tests are limited by variable diagnostic yield, the lack of standard criteria, and the intermittent nature of chest pain.

**Evaluation of patients with NCCP**

Following a search for a coronary ischemic cause of chest pain, a thoughtful review of its differential diagnosis and a stepwise evaluation should be undertaken. The differential diagnosis includes, but is not limited to, cardiac causes (eg, mitral valve prolapse, microvascular angina, pericarditis), pulmonary causes (eg, pleurisy, parenchymal diseases), musculoskeletal causes (eg, costochondritis, myofascial syndromes), gastrointestinal diseases (eg, peptic ulcer disease, gallbladder disease, esophageal tumor or infection), panic disorder, and the esophageal disorders of reflux, dysmotility, and abnormal nociception. In many patients with NCCP, cardiac, esophageal, musculoskeletal, and psychiatric problems may overlap, suggesting a common abnormality, such as a smooth muscle disorder or abnormal visceral nociception, but much remains to be determined in the study of the interrelationships of these disorders and their treatments [46–50].
Major developments in the history of noncardiac chest pain (NCCP). The early descriptions of patients with chest pain refer to the interplay of emotional issues or possible altered pain perception with disordered function of the esophagus [51–55]. Following the development of esophageal manometric recording, esophageal motor disorders were specifically defined and found in association with symptoms in patients with NCCP [9,56,57]. Studies using provocative or prolonged ambulatory esophageal events permitted a correlation of symptoms with defined esophageal events. More recently, an overlap concept has emerged, linking the “irritable esophagus” with “sensitive heart” (microvascular angina) and panic disorder, as associated causes of chronic chest pain.

Coronary versus noncoronary chest pain. Coronary arteriography demonstrates abnormal anatomy in about 70% of patients with chest pain. The remaining patients have their symptoms arising from diverse origins, including esophageal, cardiac, pulmonary, psychiatric, musculoskeletal, and other causes. In patients with noncardiac chest pain (NCCP) referred for esophageal testing, about 50% are found to have an associated esophageal cause [7,27,58,59]. EMD—esophageal motor disorder; GERD—gastroesophageal reflux disease.
Prevalence of noncardiac chest pain in patients presenting to the emergency room. In a multicenter trial, 10,689 patients who presented with chest pain or symptoms suggestive of acute myocardial ischemia were followed for one month. Ultimately 17% met the criteria for acute myocardial ischemia, while 21% had other cardiac problems. The remaining 55% had noncardiac causes of their chest pain, emphasizing the high prevalence of this disorder.

Prognosis. Prognosis in patients with angina-like symptoms and normal coronary anatomy at cardiac catheterization is excellent. In a 10-year follow-up study, the incidence of cardiac death was 0.6% [1]. This was confirmed in a study of over 4000 patients with noncardiac chest pain (NCCP) observed for 7 years with a mortality rate less than 1% from cardiac causes [3]. The importance of searching for a cardiac cause before reassuring the patient of the benign nature of esophageal NCCP was emphasized in a small study in which 8 of 8 patients (100%) with "definite" esophageal pain were alive at a 4-year follow-up, whereas 2 of 8 patients (25%) with "probable" esophageal pain had died [61].

Follow-up of functional status of patients with unexplained chest pain and normal coronary arteriograms in 57 patients who had been told that their hearts were normal, the source of their chest pain was noncardiac, and that no limitation was needed on physical activity. They were evaluated at a follow-up interval of 16 to 7.7 months [4]. Large numbers of these patients still described their activities to be limited by chest pain, were unable to work, and continued to believe the heart was the source of their chest discomfort. There was a significant reduction in patient use of medical facilities compared with rates of use before the cardiac catheterizations. A similar decrease in chest pain hospitalizations was found in another group of patients with noncardiac chest pain (NCCP), the majority of whom demonstrated persistence of symptoms. An improved functional status was found in those patients with a defined or presumed esophageal cause of symptoms [62]. The overall decline in hospitalizations suggests an ability for esophageal testing to reduce overall health care costs for patients with NCCP who are reassured about the noncardiac etiology of their symptoms, although a significant number of the tested patients did not remember or understand the explained results of their esophageal investigations and continued to believe themselves to be disabled by cardiac disease. (Adapted from Ockene et al. [4].)
Characteristics of esophageal chest pain. Consecutive patients presenting with chest pain on an emergency basis were interviewed before they were fully investigated; features tending to favor a cardiac or esophageal source were identified [16,63]. Although 83% of the esophageal group described having associated symptoms of heartburn, regurgitation, dysphagia, and vomiting, a finding confirmed by Hewson et al. [15], these symptoms were also experienced by 46% of patients with chest pain ultimately ascribed to a cardiac source. Although the chest pain of esophageal origin is often described as nonexertional, exercise-induced gastroesophageal reflux does occur with reproduction of angina-like chest pain in patients with normal coronary anatomy [28].

**Figure 10-6.**
Characteristics of esophageal chest pain.

<table>
<thead>
<tr>
<th>Classic Symptoms of Angina Pectoris Versus Those Arising from Esophageal Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esophageal chest pain usually:</td>
</tr>
<tr>
<td>Produces pressure-like squeezing or burning</td>
</tr>
<tr>
<td>Can radiate to neck, jaw, back, or arms</td>
</tr>
<tr>
<td>May persist minutes to hours</td>
</tr>
<tr>
<td>May be sharp and severe</td>
</tr>
<tr>
<td>Resolves or abates often spontaneously when treated with antacids or nitrates</td>
</tr>
</tbody>
</table>

Features in the history that help to distinguish esophageal pain from cardiac pain:

- Atypical response to exercise
- Pain that continued as a background ache
- Retrosternal pain without lateral radiation
- Pain that disturbed sleep
- Presence of certain esophageal symptoms (e.g., heartburn, regurgitation, dysphagia)

**Figure 10-7.**
Prediction of cardiac versus noncardiac causes of chest pain by history. Interviews were conducted prior to diagnostic coronary angiography with 248 patients with chest pain. Cardiologists classified 185 patients as having typical anginal pain, while 63 patients were believed to have noncoronary chest pain. Interestingly, 26% of the patients with typical anginal pain had normal coronary angiography while 25% of patients deemed noncardiac had abnormal angiograms. Thus the cardiologist was incorrect 25% of the time in each group using history alone. These data suggest that history alone is not an accurate predictor of the source of chest pain, and exclusion of a cardiac source should always precede the search for an esophageal etiology [64].
Mechanisms of esophageal chest pain. Sensation from the esophagus travels to the central nervous system (CNS) by pathways of the sympathetic and parasympathetic systems, and involves stimulation of esophageal chemoreceptors, mechanoreceptors, thermoreceptors, and nociceptors [65]. The specific mechanisms producing esophageal chest pain are not well understood. Investigation has centered on the evaluation of esophageal sensitivity to chemical and mechanical stimuli; the finding that multiple stimuli may produce identical symptoms in some individuals with chest pain has led to the acceptance of the concept of an *irritable esophagus* [66,67]. Although acid sensitivity from gastroesophageal reflux is believed to be a source of noncardiac chest pain (NCCP), the relationship between acid reflux and symptoms is not well understood. Motility disturbances found at the time of stationary esophageal testing are most often asymptomatic; motility changes documented at prolonged monitoring are also often not symptomatic. Some have suggested that these changes in motility should be viewed as an epiphenomenon of chronic chest pain [35], rather than causative of symptoms. In patients with NCCP simultaneously monitored for acid reflux and dysmotility, many patients are discovered to have multiple causes to explain their symptoms [38,72], suggesting esophageal sensitivity to various stimuli is capable of producing identical chest pain symptoms (the *irritable esophagus*, previously mentioned) [67,73].

**Figure 10.8.** Mechanisms of esophageal chest pain. Sensation from the esophagus travels to the central nervous system (CNS) by pathways of the sympathetic and parasympathetic systems, and involves stimulation of esophageal chemoreceptors, mechanoreceptors, thermoreceptors, and nociceptors [65]. The specific mechanisms producing esophageal chest pain are not well understood. Investigation has centered on the evaluation of esophageal sensitivity to chemical and mechanical stimuli; the finding that multiple stimuli may produce identical symptoms in some individuals with chest pain has led to the acceptance of the concept of an *irritable esophagus* [66,67]. Although acid sensitivity from gastroesophageal reflux is believed to be a source of noncardiac chest pain (NCCP), the relationship between acid reflux and symptoms is not well understood. Motility disturbances found at the time of stationary esophageal testing are most often asymptomatic; motility changes documented at prolonged monitoring are also often not symptomatic. Some have suggested that these changes in motility should be viewed as an epiphenomenon of chronic chest pain [35], rather than causative of symptoms. In patients with NCCP simultaneously monitored for acid reflux and dysmotility, many patients are discovered to have multiple causes to explain their symptoms [38,72], suggesting esophageal sensitivity to various stimuli is capable of producing identical chest pain symptoms (the *irritable esophagus*, previously mentioned) [67,73].

**Figure 10.9.** Mechanisms of esophageal chest pain: issues. Acid reflux may induce esophageal motility changes with possible chest symptoms, but it also may provoke bronchial or cardiac reflexes involved in pain sensation from the chest. Patients with noncardiac chest pain (NCCP) often have documented esophageal motility disorders, but the relationship between abnormal contraction patterns and pain symptoms is not well understood. Motility disturbances found at the time of stationary esophageal testing are most often asymptomatic; motility changes documented at prolonged monitoring are also often not symptomatic. Some have suggested that these changes in motility should be viewed as an epiphenomenon of chronic chest pain [35], rather than causative of symptoms. In patients with NCCP simultaneously monitored for acid reflux and dysmotility, many patients are discovered to have multiple causes to explain their symptoms [38,72], suggesting esophageal sensitivity to various stimuli is capable of producing identical chest pain symptoms (the *irritable esophagus*, previously mentioned) [67,73].

**Figure 10.10.** Psychologic factors in noncardiac chest pain (NCCP). This figure shows the results of the average score for values (plus or minus the standard error of the mean) on the Millon Behavioral Health Inventory scales of gastrointestinal susceptibility and somatic anxiety for five study groups: irritable bowel syndrome (IBS); nutcracker esophagus (NC); structural esophageal abnormalities—rings or esophagitis (SA); hospital healthy controls (HC); and nonhospital healthy controls (NHC). Subjects in the NC and IBS groups scored significantly higher \( (P < 0.05) \) on both scales than did all other subject groups. This pattern suggests that these patients react to psychologic stress with frequent and severe gastrointestinal symptoms and display hypochondriacal tendencies and unusual amounts of fear about bodily dysfunction.

Patients with gastroesophageal reflux disease whose symptoms correlate poorly with acid-reflux events differ significantly in their psychosocial profiles from those with good symptom–reflux association, showing more trait anxiety and hysteria, and having less adequate social support structures; these factors may be important in the etiology of their symptoms and in their management [74]. Unlike patients with IBS, patients with NCCP are less likely to have been sexually or physically abused; however, those who had been abused had significantly altered pain perception, higher levels of functional disability, and greater number of psychiatric disorders [75]. (Adapted from Richter [25].)
Diagnostic testing to determine the relationship of gastroesophageal reflux disease (GERD) to noncardiac chest pain (NCCP). GERD is the most commonly identified esophageal cause of NCCP and data from 24-hour ambulatory pH monitoring show abnormal acid reflux in about half of patients [7,15,27,28]. GERD is also one of the most treatable causes of NCCP; therefore, diagnosing it as the cause of NCCP is of the utmost importance. Upper gastrointestinal endoscopy and barium radiography are often not sufficiently sensitive to identify GERD as the cause of chest pain, but they are useful in detecting structural complications related to GERD. The two diagnostic modalities that are widely available and sufficiently sensitive are 24-hour ambulatory pH monitoring and empiric acid blockade. While esophageal scintiscanning and the acid perfusion test have been used in identifying GERD, they are not widely available and continue to be used as research tools.

Acid-perfusion (Bernstein) test. As originally described by Bernstein and Baker [76], a patient is seated upright with a nasogastric tube placed into the midesophagus and, with the patient blinded to the administration, normal saline solution and dilute hydrochloric acid (0.1 N HCl) are alternatively infused into the esophageal lumen. A positive test result is one in which acid infusion produces the patient's usual chest pain, whereas infusion of saline does not and in fact may relieve the symptoms provoked by the acid. The cause of pain from acid perfusion of the esophagus has been attributed to triggered chemoreceptors, induction of dysmotility, or acid sensitivity of normal and inflamed mucosa.
Sensitivity and specificity measurements for the acid-perfusion test in patients with gastroesophageal reflux (GER). \textit{(Adapted from Richter [77].)}

Sensitivity and specificity of the acid perfusion test in patients with noncardiac chest pain (NCCP). Experience with acid-perfusion testing in patients with NCCP has revealed good specificity but poor sensitivity, especially when compared with prolonged ambulatory monitoring [78]. \textit{AP+}—positive result from acid perfusion test. \textit{(Adapted from Bruley des Varannes [66].)}

Ambulatory esophageal pH monitoring can reveal correlation of symptoms and acid-reflux events. Small, compact devices are in use for continuous intraesophageal recording from 2-mm flexible pH probes placed transnasally with the distal recording tip at 5 cm above the lower esophageal sphincter. Downloading of the stored recorded data permits a correlation of symptoms and reflux events (pH dropping to 4 or less). Parameters of total esophageal acid exposure time, total number of reflux events, duration of reflux episodes, upright versus supine acid reflux, and relationship to meal intake are determined. A symptom index can be calculated by dividing the total number of chest pain episodes into the number of them associated with acid reflux. A positive symptom score may be found in some patients in whom the other reflux parameters were normal; this helps to direct therapy.

Evaluation of the Patient with Noncardiac Chest Pain 187
An esophageal test was defined as definitely identifying the esophagus as a cause of chest pain if provocative testing replicated the patient’s usual chest pain or the patient’s spontaneous chest pain correlated with episodes of acid reflux (positive symptom index) during 24-hour pH monitoring. Abnormal stationary manometry or acid-reflux parameters without associated chest pain only suggested the esophagus as a possible cause of the symptoms. Esophageal pH monitoring with symptom index was significantly superior \( (P < 0.001) \) to traditional esophageal tests in definitively identifying the esophagus as a cause of chest pain symptoms. +APT—positive acid perfusion test; +E—positive edrophonium test; +GER—abnormal acid-reflux parameters; +SI—positive symptom index. (Adapted from Richter [79].)

**Figure 10-16.**
Comparison between the diagnostic yield of traditional esophageal tests and 24-hour esophageal monitoring in 100 consecutive patients with noncardiac chest pain (NCCP).

**Figure 10-17.**
Economic and clinical value of the proton pump inhibitor test in patients with noncardiac chest pain (NCCP). In a cross-over design, 39 patients with frequent NCCP were randomized to receive high-dose omeprazole (40 mg a.m., 20 mg p.m.) or placebo for 1 week. Using 24-hour pH probe monitoring as the gold standard, the sensitivity of the omeprazole test was found to be 78% and the specificity 86%. Economic analysis showed an average cost savings of $573 per patient and a 59% reduction in number of procedures performed when empiric high-dose omeprazole use was compared with standard evaluation on NCCP [31]. These results add to the findings of previous investigators who had demonstrated improvement in chest pain symptoms in 81% of gastroesophageal reflux disease-positive NCCP patients receiving high-dose omeprazole versus 6% improvement from placebo [32].

**Figure 10-18.**
Reflux-associated chest pain is also common in patients with demonstrated obstructive coronary artery disease. As demonstrated in this figure, prolonged esophageal pH monitoring combined with simultaneous (Holter) cardiac monitoring defined the percentage of pain episodes attributed to acid reflux or myocardial ischemia in 30 patients with 164 episodes of chest pain [33]. Of these patients, 20 (67%) had at least one episode of chest pain related to an acid-reflux event, and nearly 75% of patients had improvement in chest pain with the use of acid-suppressive therapy. (Adapted from Singh et al [33].)
Esophageal motility disorders in noncardiac chest pain. LES—lower esophageal sphincter; LESP—lower esophageal sphincter pressure. (Adapted from Spechler et al. [81].)

Although some of the motor disorders may directly relate to causation of pain through mechanisms of spasm and distention, most investigators now consider the esophageal motility disorders to be an epiphenomenon found in patients with chronic chest pain or as a response to stress [35,36]. Contributing to this changing view are data that demonstrate that pain is most often not present during stationary manometry when abnormal motor events are recorded; it is the minority of patients undergoing ambulatory motor studies who have a motility disorder during an episode of pain [11]. The findings that successful resolution of chest pain symptoms may occur in the absence of any significant change in the underlying esophageal motor abnormalities [84], and that esophageal motility disorders may be treated with little effect on chest pain symptoms [85] have encouraged questions about the etiologic role of motor disorders in NCCP. Of further interest is the finding that 35% of patients with nutcracker esophagus were shown to have evidence of gastroesophageal reflux disease and that acid-suppressive therapy improved symptoms in 83% [80]. An alternative mechanism of pain in patients with nutcracker esophagus was suggested by a recent report that demonstrated a hypersensitive and stiff esophagus as measured by balloon distention and impedance planimetry [37]. DES—diffuse esophageal spasm; LES—hypertensive lower esophageal sphincter; NEMD—nonspecific esophageal motility disorders. (Adapted from Richter [83].)
Provocative testing attempts to reproduce esophageal chest pain while patients are undergoing stationary evaluations. Provocative testing can increase the yield of esophageal causes over baseline testing, as seen in Figure 10-22. Issues in the interpretation of provocative testing include that the provoked chest pain may not be the same as spontaneous chest pain and a baseline dysmotility does not predict positive provocative tests. Historically, ergonovine maleate and bethanecol were used as esophageal provocative agents; however, they are limited in their usefulness due to significant side effects (e.g., coronary spasm, headache, nausea, pain at the injection site, sweating) [39,40]. The most frequently used esophageal provocative test is parenteral administration of edrophonium, a cholinesterase inhibitor, which produces increased esophageal contraction amplitude and duration in normals and patients with noncardiac chest pain (NCCP). A positive test result is one in which reproduction of the patient's usual chest discomfort occurs while the patient swallows water, within minutes of the edrophonium intravenous injection, but not following injection of a saline placebo. The edrophonium challenge test is believed to be specific for the esophagus, produces few side effects, and provokes chest pain in 20% to 30% of patients with NCCP [42,43]. The interaction between patient and test administrator may influence the results of edrophonium provocative testing in patients with NCCP, demonstrating the powerful influence of coaching on the outcome of the study [86].

**Figure 10-21.**

Result of edrophonium testing in a patient with noncardiac chest pain. Edrophonium given as 80 mcg/kg body weight intravenously. Although an increase in amplitude and duration of esophageal contractions may be seen in anyone following administration of edrophonium, the reproduction of the patients' usual chest pain makes this a positive test. Recently, Swedish investigators demonstrated that strong esophageal contractions and not a decrease in esophageal blood flow seemed to be the cause of chest pain provoked by edrophonium chloride administration [41]. Panel A equals baseline; panel B equals edrophonium. P—proximal; M—middle; D—distal.

**Figure 10-22.**

Result of edrophonium testing in a patient with noncardiac chest pain. Edrophonium given as 80 mcg/kg body weight intravenously. Although an increase in amplitude and duration of esophageal contractions may be seen in anyone following administration of edrophonium, the reproduction of the patients' usual chest pain makes this a positive test. Recently, Swedish investigators demonstrated that strong esophageal contractions and not a decrease in esophageal blood flow seemed to be the cause of chest pain provoked by edrophonium chloride administration [41]. Panel A equals baseline; panel B equals edrophonium. P—proximal; M—middle; D—distal.
Manometry without provocative tests
Normal or negative, not esophageal 72%
Abnormal manometry, probably esophageal 28%

Manometry with provocative tests
Normal or negative, not esophageal 52%
Definitely esophageal 27%

Diagnosis
Nonesophageal—655 patients
(72%)
Probably esophageal—255 patients (28%)

Diagnosis
Nonesophageal—475 patients
(52%)
Definitely esophageal—243 patients (27%)

Diagnostic yield of esophageal testing in 910 consecutive patients with noncardiac chest pain [9]. Manometry alone identified the esophagus as a "probable" cause of chest pain, based on abnormal stationary motility patterns, in 28% of patients. Acid-perfusion and edrophonium (Tensilon [T]) provocative testing definitely reproduced esophageal chest pain in 27%, and thus increased the overall yield of esophageal causes to 48%. B—Bernstein's test. (Adapted from Richter [77].)

Response to intraesophageal balloon distention in 30 noncardiac chest pain (NCCP) patients and 30 controls. In all, 60% of patients with NCCP experienced pain with balloon distention compared with only 20% of controls developing chest pain with this provocative test [22]. The patients with NCCP developed pain at smaller distention volumes than controls, suggesting a lower pain threshold to esophageal distention, or altered nociception. This heightened visceral awareness is similar to that seen in patients with irritable bowel syndrome in whom distention of the rectosigmoid colon by balloon inflation provoked abdominal pain at smaller balloon volumes than those volumes that produced pain in healthy controls [87]. (Adapted from Richter [77].)

A—B, Repeated esophageal balloon distension: effect on esophageal sensitivity. Pain-sensation scores varied directly with balloon volume, and mean pain scores were significantly higher for the chest pain group. In the controls and dysphagia group, pain-sensation scores were not significantly different between the first, second, or third distention at a given volume. In the chest pain group, however, pain-sensation scores increased significantly following repeated balloon distension using the same volume, suggesting a conditioning phenomenon associated with a visceral sensory abnormality. (Adapted from Paterson [23].)
Chest pain response to provocative testing [41]. Intraesophageal acid perfusion produced chest pain in 5 of 50 patients (10%) whereas intravenous edrophonium produced pain in 8 of 50 patients (16%). Overall, with one patient positively responding to both acid perfusion and edrophonium, these two tests identified an esophageal cause in 12 of 50 patients (24%). A positive result of a balloon distention test occurred in 11 of these patients as well as identifying an additional 13 patients, increasing the diagnostic yield of esophageal causes to 48% (24 of 50 patients). (Adapted from Barish [44].)

A. EVALUATION OF 281 PATIENTS WITH NONCARDIAC CHEST PAIN

<table>
<thead>
<tr>
<th>FIRST AUTHOR, YR</th>
<th>NO. OF PATIENTS TESTED</th>
<th>ACID ABNORMAL MOTILITY</th>
<th>BOTH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Janssens, 1986</td>
<td>60</td>
<td>7</td>
<td>13</td>
</tr>
<tr>
<td>Peters, 1988</td>
<td>94</td>
<td>21</td>
<td>17</td>
</tr>
<tr>
<td>Soffer, 1989</td>
<td>20</td>
<td>20</td>
<td>5</td>
</tr>
<tr>
<td>Hewson, 1990</td>
<td>45</td>
<td>24</td>
<td>11</td>
</tr>
<tr>
<td>Ghillebert, 1990</td>
<td>50</td>
<td>26</td>
<td>8</td>
</tr>
<tr>
<td>Humeau, 1990</td>
<td>45</td>
<td>20</td>
<td>ND</td>
</tr>
<tr>
<td>Nevens, 1991</td>
<td>37</td>
<td>11</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>281</td>
<td>18%</td>
<td>10%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PROVOCATION TEST, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACID</td>
</tr>
<tr>
<td>EDROPHONIUM</td>
</tr>
<tr>
<td>BALLOON</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>OVERALL ASSESSMENT, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACID SENSITIVITY</td>
</tr>
<tr>
<td>MECHANOSENSITIVITY</td>
</tr>
<tr>
<td>IRRITABLE ESOPHAGUS</td>
</tr>
</tbody>
</table>

Esophageal causes of chest pain may coexist in patients with demonstrated cardiac disease. Esophageal motility disorders and gastroesophageal reflux disease have been documented in from 10% to 67% of patients with abnormal coronary arteriograms and angina-like chest pain [33,88,89]. In patients with microvascular angina and atypical chest pain, esophageal disorders can be documented in 23% to 75% [46,90,91]. A recent report suggests that esophageal hypersensitivity rather than esophageal dysmotility was an important factor in development of chest pain in patients with syndrome X, and that acid suppression could ameliorate pain in a substantial proportion of patients for whom abnormal acid sensitivity was the main culprit [49]. From 52% to 86% of patients with chest pain and documented mitral valve prolapse are shown to have esophageal disorders as evidenced by routine and provocative testing [92–94]. Interestingly, gastroesophageal reflux may lower the anginal threshold in some patients [95]; some investigators have shown esophageal acid perfusion to induce electrocardiographic changes of myocardial ischemia, or to reduce coronary blood flow via a neural reflex [50,96], although two other reports do not support this finding [33,97].

A, B. Identical esophageal noncardiac chest pain (NCCP) may be induced by a variety of stimuli: the irritable esophagus concept. Some patients experience their usual chest pain when (1) induced by acid reflux; (2) at a time of abnormal motor activity with no accompanying reflux; (3) following edrophonium challenge; or (4) during intraesophageal balloon distention. This sensitivity to a variety of stimuli producing identical chest symptoms has been termed irritable esophagus [67,73], a concept also applied to hypersensitivity of the esophagus to stimuli not producing symptoms in healthy controls. Details from long-term monitoring studies of 281 patients with NCCP show an acid-sensitive esophagus in 20%, a mechanosensitive esophagus in 14%, and an irritable esophagus in 24% [24].

Atlas of Esophageal Diseases
B. CRITERIA FOR PATIENTS WITH CHEST PAIN OF ESOPHAGEAL ORIGIN

<table>
<thead>
<tr>
<th>PATIENT GROUP</th>
<th>CHARACTERISTIC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acid-sensitive esophagus</td>
<td>Spontaneous pain episodes related to acid reflux (with or without accompanying motor disorders)</td>
</tr>
<tr>
<td>Mechanosensitive esophagus</td>
<td>With or without positive result of acid perfusion test</td>
</tr>
<tr>
<td>Irritable esophagus</td>
<td>Spontaneous pain episodes related to motility disturbances without reflux</td>
</tr>
</tbody>
</table>

This heightened sensitivity to various stimuli is also noted in patients with irritable bowel syndrome [98] and suggests that an altered nociception contributes to increased symptom-reporting. (Adapted from Janssens [24].)

Emerging overlap concept of altered pain sensitivity. Patients with panic disorders score high in measures of anxiety and hypochondriasis, and panic attack symptoms overlap with those of chest pain of esophageal origin and microvascular angina having fear of dying, shortness of breath, choking or smothering sensation, palpitations, chest pain or discomfort, sweating, faintness, dizziness, and nausea, among others. Patients with microvascular angina have been shown to have frequent demonstrable esophageal motility disorders and heightened visceral awareness of acid exposure and esophageal distension. Abnormal nociception may link esophageal with coronary smooth muscle sensitivity; patients with microvascular angina frequently have their pain provoked during injection of intracoronary contrast media and, as has been pointed out, patients with chest pain of esophageal origin may have heightened sensitivity to esophageal distension with balloon provocation. Investigators have shown a co-occurrence that is common between panic disorder symptoms and mitral valve prolapse. This is not likely cause and effect, but rather a heightened sensitivity in the susceptible patient. A generalized disorder of smooth muscle sensitivity gives rise to the “irritable person,” manifesting itself with symptoms referable to the esophagus, the bowel, the heart, or other organ systems. These various symptoms arise as physiologic responses to stress. A comprehensive approach to diagnosis and treatment in the patient with atypical chest pain is mandatory. GERD—gastroesophageal reflux disease; EMD—esophageal motility disorders.
Diagnostic and therapeutic approach to the patient with unexplained chest pain. The evaluation should always begin with a detailed history and physical examination. Because cardiac etiologies are associated with a much worse prognosis and cannot always be easily identified by history alone, a thorough exclusion of cardiac disease is recommended in consultation with a cardiologist. Testing may include a chest x-ray, an electrocardiogram, an exercise stress test, a cardiac catheterization with or without ergonovine stimulation, and more specific testing for microvascular angina. If there are symptoms suggestive of biliary colic an abdominal ultrasound would be in order. If there is dysphagia or ulcer-like dyspepsia, barium radiography or upper gastrointestinal endoscopy should be done. If the patient clearly describes chest pain with associated heartburn or regurgitation, the likelihood of gastroesophageal reflux disease (GERD) causing the chest pain is high and an empiric trial of high-dose proton pump inhibitor (PPI) should be considered. If specific clues to the etiology of pain are not present in the history or if a trial of PPI is unsuccessful, prolonged pH monitoring should be undertaken and GERD treated if present. If this is normal, further testing for esophageal motility disorders should be undertaken with esophageal manometry with provocative testing (edrophonium, intrasophageal balloon distention). If this is normal or positive only with provocation consideration should be given to treatment with low dose tricyclic antidepressants or trazodone [45, 78, 100]. If a spastic motility disorder is found, treatment with a calcium channel blocker, nitrates, or botulinum toxin injection to the lower esophageal sphincter (LES) should be considered [101–103].

REFERENCES

Evaluation of the Patient with Noncardiac Chest Pain


The advances in therapeutic endoscopy over the last several decades have been impressive and rapid. Progress in endoscopic therapy is expected to continue and esophageal disease will be the target of much of that therapy. The esophagus, being a long, relatively narrow, tubular structure, is particularly suited to endoscopic study and therapies. It is subject to numerous pathologic processes which tend to provoke symptoms that lead the patient to a physician and often then to a gastroenterologist. For example, the proximity of the squamous mucosa of the distal esophagus to the stomach renders it susceptible and vulnerable to acid-peptic injury, which may result in a symptomatic peptic stricture. Also, the collateral circulation that develops in the setting of portal hypertension may result in esophageal varices, which frequently can present with life-threatening hemorrhage. Malignant disease of the esophagus usually presents late, and the gastroenterologist is often involved in the palliation of patients with these tumors.

The first therapeutic procedures involving the esophagus were dilations of esophageal strictures with various forms of “bougies” (eg, wax candles, whalebones, etc.) and have been performed for centuries. In the 20th century, surgery had been the standard approach to the majority of esophageal disorders (with the notable exception of strictures). Although the first flexible fiberoptic endoscopy was done in 1957, only in the last several decades has therapeutic endoscopy directed toward the esophagus become more widely practiced. This of course was due in large part to advances in the endoscope itself and also the technology one was able to bring to the esophagus with accessories through the biopsy channel. Endoscopic techniques and accessories for dealing with esophageal disease have continued to develop and evolve so that many disorders involving the esophagus can be primarily treated most effectively and safely by the physician through the endoscope.
Through-the-scope balloon dilators and endoscopically placed wires for the guided dilator technique are relatively new and have just flourished since the mid-1980s. Likewise, sclerotherapy, which is now being challenged and replaced in large part by rubber band ligation of varices, has only been generally practiced since the early 1980s. Current new techniques that are exciting include expandable metal stents for the palliation of esophageal malignancy, local injection of botulinum toxin for achalasia, and alcohol injection, photodynamic laser therapy, and argon plasma coagulation for cancer and precancerous lesions.

New methods will continue to develop as expertise with current techniques accumulates and technology evolves. This chapter provides an overview of currently applied techniques of therapeutic endoscopy involving the esophagus. Emphasis is placed on practical considerations as well as on newer techniques that appear to represent significant advances in the treatment of esophageal disorders.

### UPPER GASTROINTESTINAL BLEEDING

#### Mallory-Weiss tears

**Precipitating factors for Mallory-Weiss tears**

- Nausea and vomiting
- Retching
- Coughing
- Excessive straining (Valsalva maneuver)
- Epileptic convulsions
- Hiccoughs under anesthesia
- Blunt abdominal trauma
- Closed chest massage
- Endoscopy

**Figure 11-2.** Endoscopic view of Mallory-Weiss (MW) tears. A, MW tear with adherent clot. B, MW tear with adherent clot and second tear on opposite wall. C, Healing MW tear. MW tears account for approximately 5% of upper gastrointestinal bleeds [1-3]. Most bleeding spontaneously resolves prior to endoscopy. Treatment should be directed at endoscopic control of bleeding if needed and prevention of further nausea, vomiting, and esophageal trauma.

**Figure 11-1.** Precipitating factors for Mallory-Weiss tears. These were first described in 1929 by Mallory and Weiss in alcoholic patients with retching and vomiting followed by often massive, rarely fatal upper gastrointestinal bleeding. These tears are short, linear mucosal lacerations occurring at the gastroesophageal junction, often in association with hiatal hernia, usually following an initial traumatic episode of retching and nonbloody emesis. If a tear involves a vessel, bleeding may be seen and can be severe. Precipitating factors resulting in Mallory-Weiss tears involve processes that rapidly increase intra-abdominal pressure such as retching [1-3].

Endoscopic treatment of active bleeding should include epinephrine injection and gentle tamponade with several 1 sec pulses of bipolar heater probe [4]. No evidence suggests the need for endoscopic hemostasis of MW tears with stigmata of recent bleed, unless the patient has already rebled from this same lesion [5]. Rebleeding occurs in less than 20% of patients [4,6].

---

198 Atlas of Esophageal Diseases
CAUSES OF ESOPHAGEAL ULCERATIONS

Gastroesophageal reflux disease
Infectious agents
  Cytomegalovirus
  Herpes simplex virus
  Human immunodeficiency virus
  Candida
Inflammatory disorders
  Crohn's disease
  Behçet's disease
  Vasculitis
Irradiation
Ischemia
Pill-induced
Graft-versus-host disease
Caustic substance ingestion
Post-sclerotherapy
Post-esophageal variceal band ligation
Dermatologic diseases
  Epidermolysis bullosa dystrophica
  Pemphigus vulgaris
Idiopathic

FIGURE 11-3.
Causes of esophageal ulcerations.

FIGURE 11-4.
Endoscopic views of esophageal ulcerations. Esophageal ulcerations result from direct mucosal injury, viral infection, and systemic disease, and they account for approximately 8% of upper gastrointestinal bleeds. Treatment is directed towards the underlying disease, withdrawal of the offending agent, acid suppression, and endoscopic hemostasias if isolated bleeding lesions are present. A, Erosive esophagitis. B, Cytomegalovirus esophagitis. C, Herpes simplex virus esophagitis. D, Human immunodeficiency virus-associated idiopathic ulceration.

(continued on next page)
MEDICATIONS ASSOCIATED WITH PILL-INDUCED ESOPHAGITIS

NSAIDs (including acetylsalicylic acid)
Tetracyclines (including doxycycline)
Quinidine
Emepronium
Papain
Bisphosphonates (alendronate)
Potassium chloride and citrate
Isotretinoin
Theophyllines
Oxybutynin
Captopril
Ascorbic acid
Iron preparations
Penicillins
Sodium valproate
Cromolyn sodium
Clindamycin
Chloral hydrate


FIGURE 11-4. (CONTINUED)

FIGURE 11-5.
Medications associated with pill-induced esophagitis [7].
Pathogenesis of esophageal varices. Esophageal (and gastric) varices are enlarged veins that are part of the extensive collateral circulation that can develop in the setting of portal hypertension (A). In normal individuals, almost 100% of portal venous flow (approximately 1 L/min) is recoverable in the hepatic vein, whereas in the patient with cirrhosis up to 87% may be directed into collateral flow. Although varices can develop in many areas, they are most problematic in the esophagus (and proximal stomach), wherein life-threatening hemorrhage may occur. Increased portal venous pressure is most commonly secondary to cirrhosis from a variety of causes, but can be caused by noncirrhotic liver disease or from extrahepatic causes. Systemic vasodilation with decreased vascular resistance and the formation of a hyperdynamic circulation may also play a role in the development of portal hypertension and subsequent varices. It has been estimated that this increased flow is responsible for 40% of the increase, and that resistance to flow is responsible for 60% of the increase in portal pressure in cirrhosis. B, Active hemorrhage from a distal esophageal varix with a sclerotherapy injector at the 7-o’clock position. (A adapted from Waye [8].)

Factors involved in variceal hemorrhage. The lifetime risk for bleeding from esophageal varices has been estimated at 10% to 67%, with the probable risk being from 30% to 40%. Multiple factors have been proposed to identify varices at higher risk for hemorrhage. A portal pressure of at least 12 mmHg appears to be necessary for the development of varices and for significant hemorrhage. Higher pressures, however, do not correlate with greater bleeding risk. Variceal size appears to have some predictive value, and perhaps wall thickness does as well, particularly in how they contribute to wall tension (τj). Wall tension in larger varices will be greater than in smaller varices with the same intravariceal pressure (p). Wall tension also varies inversely with the thickness of the variceal wall (W). A. These relationships are demonstrated in the modification of Laplace’s law [9,10].

(continued on next page)
B-D, "Red color" signs also appear to portend a greater risk of bleeding; when seen on large varices they are particularly worrisome. They represent "varices on varices" and probably correspond histologically with dilated intraepithelial venules. Also note the fibrin-platelet plugs (panels C and D) which identify the site of recent hemorrhage and provide useful information to the endoscopist.

**Figure 11-8.** Options in acute variceal hemorrhage. Endoscopic therapy is useful in the management of acute variceal hemorrhage. Other options include medical treatment, first tamponade with a Sengstaken-Blakemore tube or a Minnesota tube (pictured), placement of an intrahepatic shunt (i.e., transjugular-intrahepatic portosystemic shunt) placed by vascular interventional radiology, or surgical intervention. Vasoactive drugs such as octreotide, vasopressin, nitroglycerin, and terlipressin are effective in the acute setting in decreasing bleeding by lowering portal pressures. Some gastroenterologists feel that concurrent use of vasoactive drugs during endoscopic treatment of acute bleeding improves visualization and outcome, although this has not been proven. Despite all these options, the 1-year survival rate after initial hemorrhage has changed little over the last 50 years, and remains about 40%.

**Figure 11-9.** Endoscopic sclerotherapy. This technique has been used in previous years as an effective treatment for acute variceal hemorrhage and for prophylaxis for recurrent hemorrhage after the initial bleeding episode has stopped. Both paravariceal and intravariceal injection techniques have been recommended. Regardless of the location of the external puncture, the depth of needle penetration may be difficult to control and may range from intravariceal to submucosal, or into the muscular layer, the latter perhaps predisposing to deeper ulceration (A). The preferred technique is for injections of 1 mL to 2 mL of sclerosant into the varix starting as distally in the esophagus as possible (near or just below the esophageal-gastric junction) and in a circumferential route. Injections are then repeated 2 cm to 5 cm more proximally (B). The total volume of sclerosant should not exceed 20 mL per session, above which rate the incidence of complications may increase. No particular sclerosant has emerged as consistently superior; sodium tetradecyl, ethanolamine oleate, absolute ethanol, and sodium morrhuate are agents available in the United States. (Adapted from Waye [8].)
Endoscopic variceal band ligation (EVL). Endoscopic variceal band ligation is the preferred method to treat varices. The equipment is readily available and easily used with most endoscopes. This figure demonstrates the technique for preparing the multi-band ligator (ie, six-shooter) for EVL. The handle has two positions that control rotation. The firing position (A) allows the handle to be rotated in the forward direction only. The two-way position (B) allows the handle to rotate in both directions. Prior to introducing the endoscope, keep the handle in the two-way position. C, Insert the multi-band ligator handle into the endoscope accessory channel. This may vary for different brands of endoscopes. D, Introduce the loading catheter through the white seal in the multi-band ligator handle and advance, in short increments, until it exits the tip of the endoscope (inset). E, Attach the trigger cord to the hook on the end of the loading catheter, leaving approximately 2 cm of trigger cord between the knot and the hook. Withdraw the loading catheter and trigger cord up through the endoscope and out through the multi-band ligator handle. F, Attach the Opti-Vu (Wilson-Cook Medical, Winston-Salem, NC) barrel to the tip of the endoscope, ensuring the barrel is advanced onto the tip as far as possible. G, H, With the endoscope tip straight, place the trigger cord into the slot on the spool of the multi-band ligator handle and pull down until the knot is seated in the hole of the slot.

(continued on next page)
FIGURE 11-10. (CONTINUED)

I. With the multi-band ligator handle in the two-way position, slowly rotate the handle clockwise to wind the trigger cord onto the handle spool until it is taut. Check the endoscopic view. To maximize visualization, the operator may alter the position of the trigger cord by rotating the Opti-Vu barrel. (Adapted from [12].)

---

Endoscopic variceal band ligation. Given the somewhat limited view of the endoscopic field with the band ligator adapter in place, the clinician should initially survey the involved region of the esophagus without the adapter and then plan the sites and order of banding. Targeting should be similar to that for sclerotherapy, that is, initially low, near the gastroesophageal junction, and circumferential, then banding more proximally.

A. With the multi-band ligator handle in the two-way position, introduce the endoscope into the esophagus. B. After intubation, place the handle in the firing position. C, D. Visualize the selected varix and aspirate it into the Opti-Vu (Wilson-Cook Medical, Winston-Salem, NC) barrel.

(continued on next page)
FIGURE 11-11. (CONTINUED)

E. Maintain suction and deploy the band by rotating the multi-band ligator handle clockwise until band release is "felt," indicating deployment. F. Release the suction button of the endoscope, insufflate air, then withdraw the scope slightly to release the ligated varix. Repeat the ligation process as needed. More than one ligation band for each varix may be needed to control acute bleeding. If more bands are required, remove the endoscope and attach a new multi-band ligator. An average of three to four ligation sessions may be required to obliterate varices. (Adapted from [12].)

FIGURE 11-12.
Endoscopic variceal band ligation. A–D, Endoscopic views of variceal band ligation that correspond to the sequence of steps discussed in Figure 11-11.
Comparison of the efficacy of endoscopic variceal band ligation (EVL) and esophageal sclerotherapy (ES). EVL has been compared with ES in two randomized, controlled trials [13,14]. The survival rates compare the two treatment modalities stratified according to severity of liver disease, rated by Child-Pugh class [13]. In patients with less severe liver disease (classes A and B, upper lines in graph), treatment with banding was associated with improved survival. The efficacy in cessation of active bleeding, length of hospital stay, and transfusion requirement for the initial bleeding was comparable in both groups. The incidence of nonbleeding complications (e.g., pneumonia, esophageal ulceration, stricture formation) was lower in the EVL group and probably contributes to the improved survival. Complete obliteration of varices occurs more quickly with EVL (average one to two fewer sessions). Some groups have advocated combination ligation and sclerotherapy at the same session, reporting even more rapid variceal eradication [15]. (Adapted from Stiegman et al. [13].)
Complications of endoscopic treatment of varices. The overall complication rate from sclerotherapy is from 10% to 20%. Local complications include stricture formation (3% to 5%) and perforation (rare, <1%). The incidence of esophageal ulceration approaches 100% and should not be considered a complication unless it leads to stricture, perforation, or persistent dysphagia. A deep sclerotherapy-induced ulcer 1 week after injection (A) and 4 weeks after injection (B) with substantial healing (this patient developed a symptomatic stricture). Banding has been reported to cause less severe ulceration because the muscularis propria may not be injured, which may occur with deeper injections [16].

C. Histologic sections of the banded mucosa and submucosa. D. The same ulcer healing at 7 days with an intact muscularis. Other related complications of sclerotherapy include pulmonary complications (eg, pneumonitis, pleural effusion, and aspiration), transient bacteremia (5% to 50% of cases), and bleeding from collateral vessels [15,17]. Very rare complications include infarcts of the spinal artery and distal large vessel thrombosis. (C and D, from Stiegman et al. [16]; with permission.)
SYMPTOMS ASSOCIATED WITH ESOPHAGEAL DISORDERS

ACID-PEPTIC STRICTURES
Heartburn—long standing
Dysphagia—solids > liquids

OTHER BENIGN STRICTURES
Stable symptoms
Absence of reflux symptoms
Solids > liquids
History of radiation treatment
History of esophageal surgery
Corrosive substance ingestion

MALIGNANT STRICTURES
Progressively worsening dysphagia
Tobacco-alcohol history
Older age
Weight loss
Dysphagia—solids > liquids
Odynophagia
Remote history of corrosive ingestion

ACHALASIA OR OTHER MOTILITY DISORDER
Solid and liquid dysphagia at the onset and intermittent weight loss
Regurgitation
Aspiration and pulmonary symptoms
Chest pain
Widened mediastinum on chest radiography
Air-fluid level on chest radiography; absent gastric air bubble

The patient’s history in esophageal disorders. In general, the history is most important in the evaluation of patients with esophageal disease. Dysphagia is the symptom which most often prompts the patient with a stricture to seek treatment from a physician. The history provides more significant information than the physical examination regarding the type of stricture present. For example, long-standing reflux symptoms with dysphagia for solid foods suggests a benign, peptic stricture. Progressive dysphagia with weight loss and history of tobacco and alcohol use is more suggestive of an esophageal malignancy. Interestingly, patients with esophageal cancer often only recall a relatively short (2 months or shorter) duration of dysphagia. Odynophagia may be an earlier symptom in some patients. Schatzki’s ring is the most common cause of dysphagia with the severity of symptoms based on both the diameter of the ring and on the size of the ingested bolus. Initially dysphagia is intermittent in these patients and is marked by increasingly frequent episodes of solid food (usually meat and/or bread) impaction that either eventually pass or are intentionally regurgitated by the patient. Food impactions that require endoscopic removal may occur.

Use of contrast radiography in preparation for therapeutic esophageal endoscopy. Contrast radiography is an important part of the work-up of a patient with dysphagia and provides the best measure of lumen caliber. In addition to defining the location of the lesion and probable cause, it also helps clarify the best therapeutic approach, including the method of dilation, the need for fluoroscopic guidance, the need for biopsies or brushings, and aids in follow-up examinations. Barium esophagram may also identify a motility disorder as the cause of the dysphagia. Esophagrams demonstrating peptic stricture (A), Schatzki’s ring (B).
Peptic strictures

Endoscopic appearance of benign strictures. Acid-septic strictures and Schatzki’s rings are the most common strictures requiring dilation. Although in most instances endoscopic examination allows obvious distinction between the two, variation in air insufflation and the differences in magnification over short distances between the lower esophageal sphincter and the endoscope can make the assessment of the lower esophagus difficult in some patients. A subtle peptic stricture may be missed endoscopically, or, more precisely, may be confused with a Schatzki’s ring. Contrast radiology can be a more sensitive technique for demonstrating subtle rings and strictures and for calibrating the lumen more precisely. A–C, Endoscopic photographs of several Schatzki’s rings.

(continued on next page)
Types of dilators: Hurst/Maloney. Mercury-filled rubber bougies, first used by Hurst in 1915, have a blunt tip. Mercury is used for the inner core because it provides an optimal balance between rigidity and flexibility, although its weight is helpful as well. Tungsten is being used to replace the mercury in some dilators. Maloney was the first to describe the tapered tip version of this type of bougie, which has become popular. No studies compare the safety and efficacy of the two. Some clinicians, however, believe that the Maloney version is easier for patients to swallow and is better suited for introducing the dilator into smaller strictures. On the other hand, because of its smaller tip, the Maloney model has a greater chance of becoming misdirected (e.g., into a small esophageal diverticulum or becoming coiled in a large hiatal hernia sac). Some believe that the Hurst dilator is the dilator of choice for therapy of a Schatzki ring because it provides more of a "bursting" effect rather than a stretching of the ring. Both types of dilators are shown in the figure.

**Figure 11-18.** (Continued)

D–G, peptic strictures. Note the esophageal pseudodiverticula proximal to the peptic stricture in panels F and G. Their presence increases the risk of unguided dilatation of the esophagus and mandates the use of a guidewire technique. H. Tight anastomotic stricture (suture at 10 o'clock) and "watermelon esophagus" viewed endoscopically. The watermelon seeds and kernel of corn provide a reference for the pinhole quality of this stricture.

**Figure 11-19.**
Types of dilators: Hurst/Maloney. Mercury-filled rubber bougies, first used by Hurst in 1915, have a blunt tip. Mercury is used for the inner core because it provides an optimal balance between rigidity and flexibility, although its weight is helpful as well. Tungsten is being used to replace the mercury in some dilators. Maloney was the first to describe the tapered tip version of this type of bougie, which has become popular. No studies compare the safety and efficacy of the two. Some clinicians, however, believe that the Maloney version is easier for patients to swallow and is better suited for introducing the dilator into smaller strictures. On the other hand, because of its smaller tip, the Maloney model has a greater chance of becoming misdirected (e.g., into a small esophageal diverticulum or becoming coiled in a large hiatal hernia sac). Some believe that the Hurst dilator is the dilator of choice for therapy of a Schatzki ring because it provides more of a "bursting" effect rather than a stretching of the ring. Both types of dilators are shown in the figure.

**Figure 11-20.**
Types of dilators (wire-guided): Savary/Eder-Puestow. Management of esophageal strictures improved in 1955 when Puestow developed a guide-wire technique involving the passage of a steel wire beyond the stenosis with subsequent passage of successively larger metal olives over the wire with the assistance of a carrier device. In 1980, Savary and Coll developed a flexible, tapered polyvinyl dilator with a hollow central core that permitted direct passage of the dilator over a guidewire. By the middle and late 1980s, Savary dilators had largely replaced Eder-Puestow dilators as the instruments of choice when dilation over a guidewire is required, because of their ease of passage and the fact that by necessity they must follow the guidewire. A range of Savary dilators is shown.
Types of dilators: balloons. Balloon dilators are an additional option for the endoscopist approaching an esophageal stricture. They may be placed over a guidewire or through the scope (TTS). Theoretically, balloons have the advantage of being safer because of the radial application of force, and elimination of the shearing effect of rigid dilators. Moreover, dilation can be performed under direct visualization using the TTS balloon. Recent balloon innovations facilitating their use include longer balloons that avoid the tendency for slippage with inflation, and high-pressure balloons that should provide a truer diameter for the dilation of more resistant strictures. In the limited number of randomized studies comparing Savary-type dilators with balloon dilators, they appeared equally safe. Efficacy, as assessed by symptom improvement and luminal patency, has been variably reported in the literature favoring either technique [18–20].

A. Range of available balloons and an inflation gun. B–E, A peptic stricture before and after balloon dilation, thus demonstrating the direct visualization that is possible with the TTS technique.

Pneumatic balloon dilators for achalasia. Dilation of the lower esophageal sphincter with a pneumatic balloon is generally the therapy chosen for achalasia. Successful dilation entails rupturing of some of the circular muscular layer of the esophagus [21]. The newer polyethylene balloons are currently the most readily available and range in size from 30 to 40 mm; they are passed over a guidewire. There are different recommendations regarding the technique of pneumatic dilatation for achalasia. There does not appear to be an increased risk associated with longer periods of inflation (up to 1 to 2 minutes), although we prefer a shorter duration (5 to 10 seconds). Risk of perforation increases with performing the initial dilation with larger balloons, and a 30-mm balloon should always be used as the first dilator [22]. The range of pneumatic dilator balloons and a manometer for insufflation are pictured.
Pneumatic balloon dilators for achalasia. To perform a pneumatic dilation, the balloon is positioned fluoroscopically so that it straddles the lower esophageal sphincter near the level of the diaphragm. The balloon is then inflated, creating an hour-glass appearance under fluoroscopic visualization until either one or both sides of the waist of the hour-glass are obliterated. Typically, this requires 9 to 15 psi. We also prefer to obtain a contrast study as soon as the patient is alert enough to swallow, to rule out a perforation (risk = 0.6%-11%). This can usually be done within minutes of completing the dilation. If a noncontained perforation occurs, early detection with prompt surgical repair is required. Many perforations after pneumatic dilation are contained and can be managed conservatively with intravenous antibiotics, nasogastric decompression, and thoracic surgery consultation [23].

Intrasphincteric injection of botulinum toxin for the treatment of achalasia. A temporary modality useful in the treatment of achalasia is the endoscopic injection of botulinum toxin in the region of the lower esophageal sphincter (LES). The toxin binds presynaptically and prevents release of acetylcholine, thus causing local paresis and hypotonia of the LES. The complications appear to be minimal; however, the effects tend to be relatively short-lived. In the only placebo-controlled trial, the treatment group had improved symptom scores at 1 week, lower LES pressures, and improved esophageal emptying (measured by scintigraphy) compared with the placebo group. Ultimately, all patients were treated and the response rate after the initial injection was 90% with 66% still in remission at 6 months [24]. The tendency for botulinum toxin’s effects to wane with time requiring repeated injections makes it a less than ideal treatment for the younger patient. Its primary use will probably be in the elderly patient who is at high surgical risk if perforation occurs following pneumatic dilation. Laparoscopic myotomy is a good alternative in many patients with achalasia. (Adapted from Paricha et al. [24].)
Risk of bacteremia in therapeutic esophageal endoscopy. Incidence of bacteremia associated with therapeutic gastrointestinal procedures involving the esophagus is relatively high compared with simple diagnostic upper endoscopy. Thus, it is rational to use antibiotic prophylaxis in higher risk procedures in susceptible individuals, even though only a handful of endoscopically related cases of endocarditis have been reported. The table demonstrates the range of bacteremia measured by surveillance blood cultures obtained after a surgical procedure in several pooled studies [25]. Current recommendations by the American Heart Association and the American Society for Gastrointestinal Endoscopy identify a prosthetic heart valve, previous endocarditis, and surgically created systemic-pulmonic shunts as high-risk lesions that require prophylaxis [26]. Lower risk lesions for which prophylaxis may be given include hypertrophic cardiomyopathy, most congenital lesions, acquired valvular dysfunction, and mitral valve prolapse with a murmur. Prophylaxis is not generally warranted in other settings unless accompanied by a significant immune deficiency. The recommended regimen for intravenous prophylaxis is ampicillin (2 g) and gentamycin (1.5 mg/kg up to 80 mg maximum dose) with vancomycin substituted for penicillin allergic patients or oral amoxicillin as an alternative for low-risk patients.

Dilation techniques: Hurst/Maloney type. If the stricture is well-defined radiographically, or, if it has been recently dilated, a nonendoscopically guided dilation can be performed, and, in most cases, no sedation is required. The patient sits upright, the posterior pharynx is anesthetized, and the neck is flexed forward. The patient is asked to swallow and the bougie is advanced with the strong hand. With the index and middle finger of the guide hand placed on the hard palate, the dilator is passed between the two fingers through the stricture. The tactile feel of the dilation is important and the amount of resistance should be noted. A “pop” or “give” is often felt. The “rule of threes” remains a useful guideline. This states that the clinician should not attempt to pass more than three successively larger dilators than the first size that met resistance. If, however, there is a considerable amount of blood on any dilator, the procedure should generally be immediately terminated. Even if the patient has been sedated for endoscopy, it is preferable to have the patient sitting upright because this position appears to facilitate correct passage of the dilator (compared with a higher rate of misdirected passage demonstrated by fluoroscopy when the patient remains in the left lateral decubitus position [27]).

Dilation techniques: guidewire technique. In a Savary dilation, the first step is placement of the guidewire beyond the stricture. This may be done endoscopically or with fluoroscopy. In either case, the patient is usually in the left lateral decubitus position. With endoscopic placement, if the stenosis is traversible with the endoscope, the wire is passed under direct visualization into the antrum and the endoscope is withdrawn while the assistant advances, or exchanges, the wire in corresponding increments. If the endoscope cannot be advanced beyond the stricture, then wire placement should be guided by fluoroscopy. Impregnated markings on the guidewire aid in maintaining a stationary wire position, which is essential throughout the procedure. The rule of threes is applied, as successively larger dilators are passed. The dilator should be passed gently, holding it much like a pencil and advancing with movement of the wrist. After passage of the final dilator, the wire and dilator are removed together as a single unit.
Palliative options in the treatment of esophageal cancer.

**Figure 11-28.**

Palliative options in the treatment of esophageal cancer.

**Figure 11-29.**

Prosthetic devices and stents. Endoscopically placed stents have not emerged as a superior method of palliation; however, they appear to be as effective as other treatments. Their role in treating malignant tracheoesophageal fistulas is well established; indeed they are the treatment of choice. With the development of the newer, metallic, self-expandable stents, the use of esophageal prostheses may become more common. A variety of stents is available in different lengths and diameters. A, Atkinson stents and insertion rod. B–C, Expandable metal stent with a silicon-coated membrane is depicted, partially deployed and still contained within the sheath (panel B) and fully expanded (panel C). The membrane helps to prevent tumor ingrowth and allows adequate treatment of a fistula.
Placement of a rigid prosthetic stent. Before stent placement, the tumor margins should be precisely measured during endoscopy and the lumen should be dilated up to 15 mm to 17 mm (several sessions are generally required). A, Measuring the tumor and correctly marking the pusher tube. B–C, Placement of the prosthesis. A smaller Savary dilator passed over a guidewire is advanced beyond the stricture and acts as a guide for the prosthesis that is advanced with a pusher tube. With the use of fluoroscopic guidance and the pre-marked pusher tube, the stent is positioned with the proximal and distal flange approximately three cm beyond the tumor margins. Before insertion of the prosthesis, a thin string is tied through a small hole to the end of the proximal flange to allow for withdrawal if necessary during the insertion. After successful placement, the string is removed [28]. (Adapted from Fleischer et al. [28].)
Expandable metallic stents. Self-expanding metallic stents are relatively new and may increase the use of stenting to palliate patients with esophageal cancer. They have several advantages over traditional stents. Their small pre-expansion diameter requires less dilation before stent placement and permits easier placement. Their post-expansion diameter is generally larger than rigid stents and, therefore, should provide more effective relief of dysphagia and longer stent patency. In one prospective, randomized trial to date comparing expandable stents with rigid stents, the expandable metal stents were more cost-effective and had fewer complications [29]. In these models, tumor ingrowth through the mesh was a problem, although some more recent models are coated with synthetic membranes designed to prevent this. If tumor ingrowth or overgrowth at the margins occurs, then it is often treatable with laser or additional stent placement. Although metal stents are easier to place after expansion, they are difficult to reposition, and, therefore, should only be placed by experienced physicians. A–B. Endoscopic views of an esophageal tumor before and after stent placement. C. Radiograph demonstrating the expanded stent in the esophagus.

Endoscopic palliation of malignant disease: laser therapy. Endoscopically delivered laser therapy can be used in the palliation of esophageal cancer. With experienced operators, luminal patency is generally achieved in 90% of appropriately selected patients in two to three sessions. Functional improvement, however, is less, typically ranging from 70% to 80%. Selection of suitable lesions to treat with laser is determined by the exophytic appearance on endoscopy, distal location, and a straight segment of the esophagus; the total length of the lesion should be less than 6 cm. Argon plasma coagulation (APC) has also been studied in palliative tumor therapy, stent in-growth, and Barrett's esophagus with early studies suggesting potential benefit. Data are limited, but APC may prove to be a very valuable tool for the palliation of esophageal cancer and treatment of Barrett's esophagus with dysplasia in the near future.

Endoscopic laser treatment of esophageal cancer. This procedure can generally be done with intravenous conscious sedation rather than general anesthesia. Two strategies for laser application exist. The initially developed method involves application of the laser beam with concentric destruction of tumor proceeding from the lumen to the wall, proximally to distally as much as possible during a single session (A).
Progression to the distal portion of the tumor may be limited by the formation of edema with this method. The second, and more preferred, technique involves application of laser distal to proximal (B). If feasible, a guidewire is first placed distal to the lesion into the stomach; several Savary dilators are passed to facilitate maneuverability of the scope during the treatment. This latter method generally requires fewer treatment sessions. An exophytic tumor obstructing the esophagus (C) and a patent lumen (D) established after laser treatment.

**FIGURE 11-34.**

Esophageal foreign bodies. In the last several decades, endoscopy has become the method of choice in the management of esophageal foreign bodies, although a trial of sublingual nitroglycerin and intravenous glucagon is warranted. At times this will allow the offending bolus to pass. The most common location of the impaction is the distal esophagus at the level of the diaphragm; however, compressions at the level of the cricopharyngeus, aortic arch, and left main-stem bronchus may also be the site of impaction. It is also helpful to identify foreign bodies as sharp or dull, pointed or blunt, and toxic or nontoxic (eg, batteries). Also, food-related impactions should be distinguished. If the foreign body is known, in vitro simulation may be helpful in choosing the right accessory for use during the procedure.
Esophageal foreign bodies. A variety of devices that may assist the endoscopist in the retrieval of esophageal foreign bodies exist. For sharp and pointed objects, attention must be given to protection of the mucosa on withdrawal. Occasionally, the object must be pushed into the stomach and reoriented before removal. The hood adapter or the overtube can provide protection for sharp tipped objects. Coins cannot be adequately grasped with the routine forceps and require alligator forceps or coin retrieval forceps. An awareness of the resistance of the upper esophageal sphincter and a firm grasp on the object are required because aspiration of a partially removed foreign body can occur. Pictured are a snare, tripod, several forceps, banding adaptor, and the hood adaptor (the hood covers the sharp object as the hood is drawn through the lower esophageal sphincter).

Esophageal foreign bodies: food impactions. In the adult population, the most commonly encountered esophageal “foreign body” is impacted food. Techniques for removal include: gentle forward pressure with the scope only if there is lumen visualized; forceful targeted flushing of the bolus with water; piecemeal removal with the forceps using the overtube (if retrieval is attempted early on, the bolus tends to be easier to remove in a single or larger clumps); suction using a simultaneously passed nasogastric (NG) tube with endoscopically directed placement of the NG tube over the bolus before applying suction; and use of the endoscopic variceal band ligator adaptor to generate a larger suction force than possible with the scope alone (also used with the overtube). If one can ascertain the direction of the lumen and advance the scope under direct vision (much like advancing a sigmoidoscope over stool in the colon) into the stomach, the food sometimes follows. Definitive dilation should generally not be carried out in this acute setting, but, rather, the patient should be reexamined at a later date and appropriate therapy undertaken at that time. A, A meat bolus lodged in the esophagus; B, it is gently pushed into the stomach with the tip of the endoscope.

REFERENCES


Chapter 12
Surgery of the Esophagus

Surgical Anatomy of the Esophagus

The esophagus courses from the pharynx to the stomach and is divided arbitrarily into four segments. The pharyngoesophagus is that segment which intervenes between the laryngopharynx and the upper border of the cricopharyngeus muscle. This latter structure represents the esophageal introitus. The cervical esophagus begins at the inferior border of the first thoracic vertebral body and extends caudally for 5 to 6 cm. The thoracic esophagus spans the posterior mediastinum. It includes the bronchoaortic constriction and the superior and inferior dilations above and below. A second constriction is present at the diaphragm. The abdominal esophagus extends for 1 to 6 cm below the diaphragm and ends at the esophagogastric junction. This segment of the esophagus includes the lower esophageal sphincter. The arterial supply and venous and lymphatic drainage (see Figs. 12-1 and 12-2) are critical to successful surgery of the esophagus.

Esophageal Perforation and Hiatal Hernias

Two major types of esophageal defects are perforation (see Figs. 12-3 to 12-5) and hernias (see Figs. 12-6 to 12-13). Of the four major etiologies of esophageal perforation (see Fig. 12-3), the most common are spontaneous and iatrogenic causes. Esophageal perforation continues to carry significant rates of morbidity and mortality.

Esophageal, or hiatal, hernias occur as sliding or para-esophageal hernias. Sliding hiatal, or type I, hernias do not create symptoms and do not warrant therapy. On the other hand, gastroesophageal reflux occurs primarily in patients with hiatal hernias. Operative therapy for gastroesophageal reflux is indicated for reflux esophagitis (ie, not merely reflux) when medical treatment has failed or when the patient is noncompliant.
Paraesophageal, or type II, hiatal hernias differ significantly from the sliding variety. As displayed in Figure 12-7, the following occurs in paraesophageal hernias: the esophagogastric junction remains in the normal location; a true peritoneal hernial sac is present; structures other than the stomach (eg, spleen, splenic flexure, omentum, etc.) can herniate above the diaphragm; there is an associated incidence of gastric volvulus; compression at the hiatus can cause ischemic necrosis of the herniated viscera. In further contrast with sliding hernias, all paraesophageal hernias require repair whether they are symptomatic or not. Paraesophageal hernia repairs require anatomic correction of the specific abnormalities involved. This mandates resection of the stomach and all herniated viscera, excision of the hernial sac in its entirety, and anatomic closure of the defect in the hiatus, both anterior and posterior to the esophagus. This final component is the most difficult because the muscular crura are severely attenuated. By anchoring the posterior position of the crural closure to the arcuate ligament, however, successful repair can consistently be accomplished. Rates of recurrence average 10% to 15%, significantly higher than those for repairs of sliding hiatal hernias.

Some controversy exists about the need for simultaneous Nissen fundoplication during paraesophageal hernia repair. One argument offered by proponents is that some patients have gastroesophageal reflux preoperatively, which warrants operative correction. The absence or presence of reflux should be assessed before repair is undertaken and fundoplication should be performed only in patients with complications such as esophagitis. Some surgeons further argue that the Nissen procedures are protective if the repair fails and the patient develops a sliding hiatal hernia [1]. Fundoplication should not be performed prophylactically; however, rather, the focus should be on meticulous care to prevent recurrent herniation.

**ESOPHAGEAL OBSTRUCTION**

Dysphagia is the characteristic symptom of esophageal obstruction. The obstruction can be functional in origin, as in achalasia and esophageal diverticular diseases, or mechanical, as a result of fibrous stricture or malignant luminal occlusion. Aggressive therapy is indicated under both circumstances, because unless the obstruction is relieved, the patient cannot eat nor clear salivary secretions.

**Achalasia**

Techniques for diagnosing achalasia are described elsewhere in this volume. For most patients, hydrostatic balloon dilation is appropriate initial therapy. Surgery (Heller myotomy) is reserved for those patients in whom dysphagia recurs after two dilations, those who wish immediate definitive therapy, and those who have a hiatal hernia with or without a history of reflux esophagitis. Myotomy provides excellent results in curing achalasia (see Figs. 12-14 and 12-15). In the series of 468 patients reported by Okike et al. [2], the operative mortality rate was 0.2%; only 1% of patients had mucosal perforation. More recently, the Heller myotomy procedure has been added to the list of procedures that have been successfully performed laparoscopically [3].

**Esophageal diverticula**

Esophageal diverticula (see Figs. 12-17 and 12-18) occur as Zenker’s diverticula, traction diverticula, or epiphrenic diverticulum. Pharyngoesophageal, or Zenker’s, diverticula are the most common types. Because they are caused by a muscular abnormality, myotomy plays a major role in their treatment. Novel endoscopic approaches for treatment of a Zenker’s diverticulum have also emerged using electrocautery laser and stapling devices for division of the wall between the cervical esophagus and diverticulum [4]. Traction diverticula occur in the middle third of the esophagus and result from adhesion to inflammatory lymph nodes at the carina. These lesions usually do not cause dysphagia, but when they do, they are best treated by excision with staple closure of the defect with or without oversewing with sutures. Myotomy is not necessary.

Like Zenker’s diverticula, epiphrenic diverticula are caused by muscular hyperplasia, and treatment requires myotomy.

**Benign esophageal strictures**

Reflux esophagitis is the most common cause of esophageal strictures (see Fig. 12-19). Fibrosis following caustic ingestion is another cause. Alkaline material, such as lye, causes esophageal mucosal necrosis and induces a severe inflammatory response. The end results of this process may be fibrosis and luminal obliteration. Ingested acid generally affects the stomach far more than it does the esophagus. Consequently, gastric, rather than esophageal, obstruction generally occurs.

Both these lesions, reflux-induced and caustic ingestion-induced strictures, are associated with an increased incidence of carcinoma. In reflux disease, malignancy may occur in areas of Barrett’s esophagus or in gastric mucosal esophageal metaplasia. In patients with Barrett’s esophagus, endoscopic surveillance with mucosal biopsy is indicated to identify the premalignant state, or high-grade dysplasia, in areas of the intestinal type of adenomatous metaplasia.

The goal of treatment for benign esophageal strictures is to provide an adequate lumen through which food and salivary secretions readily pass. This may be accomplished by strictureplasty (see Fig. 12-20) or by resection and reanastomosis.

**Esophageal carcinoma**

The incidence of esophageal carcinoma is increased in patients with a history of caustic ingestion, Barrett’s esophagus, achalasia, and combined heavy smoking and drinking. Ingested nitrosamines have also been incriminated in the pathogenesis of esophageal malignancy.

The predominant symptoms of esophageal carcinoma relate to luminal obstruction. Virtually all patients describe dysphagia, but weight loss, regurgitation, cough, and chest pain are also common manifestations. The only successful treatment of esophageal carcinoma is surgical excision.
Physical examination of affected patients is generally normal, and any findings (cervical lymphadenopathy, Horner's syndrome, vocal cord paralysis, or hepatomegaly) attest to the presence of extensive disease.

ANATOMY

A. Arterial supply of the esophagus. The tenuous nature of the arterial supply accounts for some of the technical problems with esophageal surgery. As shown, the arteries are derived from multiple sources, including the left gastric and the innominate arteries. The major vascular supply, however, comes directly from the aorta.

B. Venous drainage of the esophagus. Venous drainage parallels the arterial supply. Major vessels include the inferior thyroid and azygous, hemiazygous, and coronary veins. The proximal esophagus drains into the systemic circulation whereas the distal esophagus drains through the portal system. (Adapted from Rothberg et al. [5].)
Lymphatic drainage. Lymphatic drainage of the esophagus is pertinent to the treatment of esophageal carcinoma. Lymph flow is bidirectional at the level of the bifurcation of the trachea. In addition to the paraesophageal nodes, lesions distal to that anatomic juncture drain distally, including into the celiac nodes, whereas proximal lesions drain cephalad to the cervical nodes. (Adapted from Liebermann-Meffert [6].)

Causes of esophageal perforation. Spontaneous perforation of the distal esophagus, or Boerhaave's syndrome, is the most common cause. The frequency of iatrogenic perforation, however, is increasing as exploration of the esophagus with instruments becomes more common. Postsurgical perforation, or leakage following esophageal resection, occurs with an incidence of approximately 5%. Perforation in areas of malignancy and peptic esophagitis is rare, even in the presence of ulceration.

Early recognition of perforation is critical to successful therapy. The predominant symptoms include chest pain, nausea, vomiting (occasionally with hematemesis), and shortness of breath. Physical findings include fever, tachycardia, cervical crepitus, mediastinal crunch, decreased breath sounds over the left chest, and abdominal tenderness and guarding.
Radiographic diagnosis of esophageal perforation. Chest radiography may reveal air with or without fluid in the left pleural space. There may also be free air under the diaphragm if the perforation is low. The diagnosis is confirmed by Gastrografin (Squibb, Princeton, NJ) swallow, which demonstrates extravasation from the esophageal lumen. (From Skinner [7]; with permission.)

 Repair of esophageal perforation. The principles of therapy include operative closure of the perforation buttressing with a patch of pleura and/or intercostal muscle. A. Esophageal closure and selection of the buttressing flap; B, wrapping the closure. Pleural drainage with two large-bore chest tubes and gastrostomy are also performed.

Perforation of the esophagus mandates surgical correction to prevent or minimize the severity of mediastinitis. For example, if the esophagus cannot be closed because of a tumor or if the diagnosis of perforation is made after 24 hours or more, cervical esphagostomy should be performed to divert the saliva from the perforation. Despite advances in operative management and antibiotic therapy, esophageal perforation carries a significant mortality rate (10% to 15% with prompt management; 50% if treatment is delayed longer than 24 hours). (Adapted from Skinner [8].)
The anatomy of the esophageal hiatus. The esophageal hiatus is a complex and highly variable structure; this accounts for some of the developmental problems resulting in hiatal hernias. Most commonly, the right crus of the diaphragm constitutes both limbs of the hiatal ring. Almost 40% of the time, however, the ring includes components from both right and left crura (A). Finally, a variety of patterns and configurations exist in the remaining patients (B–F). No relationship exists between the crural pattern of derivation of the hiatus and the development of hiatal hernias. On the other hand, this variability adds to the complexity of repair of the hiatus, when indicated. (Adapted from Gray et al. [9].)
Types of hiatal hernia. In a type I, or axial or sliding hiatal hernia, the endoabdominal fascia relaxes, allowing a portion of the gastric fundus to slide through the hiatus into the mediastinum (A). The phrenoesophageal membrane remains intact and there is no hernial sac. In a type II, or paraesophageal hernia, the esophagogastric junction is at the normal site and there is a true hernial sac (B). (Adapted from Gray et al. [10].)

Surgical treatment of gastroesophageal reflux. Various operative procedures have been derived to treat gastroesophageal reflux and to relieve reflux esophagitis. Each attempts to recreate the esophagogastric angle of His, but varies in technical details. The most commonly used procedure is the transabdominal Nissen fundoplication. The Nissen procedure creates a 360-degree wrap of gastric fundus around the esophagus. This is facilitated by division of the short gastric vessels. Gastric wall is passed behind the esophagus to permit the wrap. To prevent "slipping" of the wrap, the esophageal wall is incorporated in the repair (A). Once completed (B), the procedure recreates the angle of His and works equally well if the esophagogastric junction is above or below the diaphragm. (Adapted from Skinner [11].)
Results of Nissen fundoplication 10 years after surgery. The results of transabdominal fundoplication for gastroesophageal reflux are excellent [1]. The most frequent postoperative side effects are change in mastication (food is chewed more completely), excessive flatus, and difficulty in belching. When the operation is performed using at least a 40-Fr bougie, dysphagia is a rare complication. For patients with simultaneous duodenal ulcer disease, a parietal cell vagotomy can readily be added without any increase in morbidity.

Laparoscopic Nissen procedure. Rather than a single incision, the laparoscopic procedure is carried out through four or five 1-cm ports. A critical component of the procedure is closure of the esophageal hiatus. Hospitalization and recuperation times are considerably shorter than after the open procedure. So far, the success rates of the open and laparoscopic procedures appear to be comparable. (Adapted from Hinder [12].)
Technique of the Hill repair of reflux esophagitis. This procedure has two major goals: (1) maintaining the gastroesophageal junction below the diaphragm by anchoring the superior margin of the gastrohepatic ligament to the arcuate ligament, the strong band of fascia which crosses in front of the aorta; and (2) “calibrating” the cardia by narrowing it at the base of the esophagus to increase the lower esophageal sphincter pressure by 40 to 50 mm Hg. A. Suture placement in the stomach and crus; B, completed procedure. Although this procedure is effective, it is technically demanding and suitable only for surgeons with considerable experience in its use. (Adapted from Skinner [13].)

Technique of the Belsey Mark IV repair of reflux esophagitis. This transthoracic procedure creates the equivalent of a 270-degree gastroesophageal wrap. This is accomplished using two rows of sutures. The initial layer sutures the upper cardia to the lower esophagus for three quarters of their combined circumference (A); this recreates the equivalent of the angle of His. The second row passes through the more distal gastric cardia and the undersurface of the diaphragm to ensure that the newly created valve is maintained within the abdomen (B). The hiatus is also narrowed to its normal size using posterior crural sutures. By careful placement of sutures the vagi can readily be spared, avoiding the need for pyloroplasty or pyloromyotomy. (Adapted from Skinner [14].)
ESOPHAGEAL OBSTRUCTION

Achalasia

Heller myotomy as therapy for achalasia. A. It is vital that both circular and longitudinal muscles are completely divided and that the mucosa bulges freely. The myotomy must be carried either to the aortic arch or high enough on the esophagus to include all thickened smooth muscle. The distal extent of the gastric component is controversial. There is no question that extending the myotomy for 1 to 2 cm into the stomach lowers the rate of recurrent achalasia. This incision also greatly increases the risk of reflux, however. B. Some surgeons advocate long myotomy and the routine addition of the Belsey Mark IV antireflux operation. I am not a proponent of this combined procedure. If properly performed, a myotomy carried just onto the gastric side of the gastroesophageal junction relieves the characteristic obstructive symptoms without rendering the lower esophageal sphincter incompetent and inducing reflux as a new problem. In performing the Heller myotomy the surgeon must avoid two pitfalls: injury to the vagus nerves and incision through the mucosa into the esophageal lumen. (Adapted from Skinner [16].)
Diverticula

Zenker's diverticulum

**Symptoms of Zenker's diverticulum, %**

<table>
<thead>
<tr>
<th>Symptom</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oropharyngeal dysphagia</td>
<td>98</td>
</tr>
<tr>
<td>Regurgitation of undigested food</td>
<td>85</td>
</tr>
<tr>
<td>Episodes of aspiration</td>
<td>61</td>
</tr>
<tr>
<td>Weight loss</td>
<td>36</td>
</tr>
<tr>
<td>Noisy deglutition</td>
<td>20</td>
</tr>
<tr>
<td>Halitosis</td>
<td>25</td>
</tr>
<tr>
<td>Hoarseness</td>
<td>13</td>
</tr>
</tbody>
</table>

Symptoms of Zenker's diverticulum. The constellation of Zenker's diverticulum is so characteristic that the diagnosis can generally be made on clinical grounds alone. Virtually all patients have dysphagia, more from the hypertrophic muscle than the pouch itself. Regurgitation and aspiration are secondary to esophageal obstruction. Although only one fourth of patients have halitosis, it is quite characteristic. This manifestation is due to stasis of food within the diverticula. *(Adapted from Duranceau [17].)*

Surgical treatment of Zenker's diverticula. Pharyngoesophageal or Zenker's diverticula are caused by inflammation and fibrosis of the cricopharyngeus muscle, resulting in increased upper esophageal sphincter and intrapharyngeal pressures. Attempts by the hypopharynx to overcome resistance at the esophageal introitus causes extrusion of esophageal mucosa posteriorly just above the cricopharyngeus muscle. Diverticula tend to protrude to the left side of the neck twice as frequently as to the right. Regardless of their size, these diverticula are rarely palpable on physical examination. Endoscopy is contraindicated because of the risk of perforation. After the diagnosis has been confirmed by barium swallow, surgery is indicated. Zenker's diverticula are best approached by a left cervical incision along the anterior border of the sternocleidomastoid muscle. The sac should be isolated and dissected back to its origin. Myotomy of the cricopharyngeus muscle should be performed for 2 to 3 cm up onto the hypopharynx and caudally to the level of the thoracic inlet. After the myotomy has been completed, diverticula of 2 cm or less in diameter disappear spontaneously with no further therapy. Larger sacs should be suspended vertically by suturing the dome of the sac to the pharyngeal wall. The alternative approach, suturing the diverticulum to the prevertebral fascia, is associated with a significantly higher rate of infection. Only rarely is the sac so large that resection (rather than suspension) is indicated. This can safely be accomplished using either a staple or suture closure of the mucosal defect. *(Adapted from Duranceau [18].)*
Surgical treatment of epiphrenic diverticula. Epiphrenic diverticula result from motor disorders at the lower esophageal sphincter. Elevated intraluminal pressure caused by muscular hyperplasia and contraction extrudes the mucosa between longitudinal muscle fibers. The most common location is on the right side of the supradiaphragmatic esophagus, just posterior to the vagus nerve. Because of the associated motor disorder, the predominant symptom is dysphagia. Repair requires myotomy as a vital component of the procedure.

The approach is through a left thoracotomy. After the esophagus is detached by dissection from the mediastinal tissues it is rotated 90 degrees to provide access to the right side of the organ. The sac is isolated and cleared of attenuated muscle fibers. The sac should be excised back to normal tissue (A) and the esophagus closed in two layers (B), taking care to protect the adjacent vagus nerves (C). After the diverticulectomy has been completed, the esophagus is allowed to return to its normal position and a myotomy is performed, as it is for achalasia. The results of diverticulectomy plus myotomy for epiphrenic diverticulum are quite good. Dysphagia is cured in 75% to 80% of patients, whereas symptoms improve in the remainder. The complication rate is low, and less than 5% of candidates develop reflux or perforation following operation. (Adapted from Skinner [19].)
Benign strictures

Benign esophageal stricture. Benign strictures most commonly result from long-standing reflux esophagitis. Most younger patients have a long history of symptomatic reflux; the stricture, therefore, represents a failure of pharmacologic management. In contrast, strictures may be the first manifestation of reflux esophagitis in the elderly. Prevention is the key to the management of esophageal strictures. When strictures develop despite appropriate conservative therapy, attempts should be made to dilate them, accepting some risk of perforation. Operative repair is indicated only for patients with nondilatable fibrous strictures.

Although strictures are easy to identify on barium swallow, the distinction between benign and malignant may be quite subtle. Shouldering and irregularity of adjacent mucosa, which are characteristic of cancer, also commonly occur with benign strictures. Computed tomographic scanning often provides important diagnostic information, as does endoscopic ultrasonography. Because the treatment of malignant strictures is so different from that of the benign variety, every attempt must be made (by endoscopy and multiple biopsies) to identify cancer preoperatively. If a malignancy is initially identified during operative stricture repair, any chance of curing the patient is lost.

![Image of stricturoplasty](Image)

**Figure 12-19.**

Stricturoplasty. Distal strictures can readily be treated by making a full-thickness longitudinal incision through the strictured esophagus onto the very proximal stomach. This assures adequate luminal volume. The defect is closed by suturing the serosal surface of the stomach over the defect as a patch. The use of the gastric wall accomplishes two objectives: it bridges the defect without compromising the luminal diameter and recreates the angle of His, thus preventing gastroesophageal reflux.
Inherent

Technique Anastomoses

Upper limit of

Disadvantages

<table>
<thead>
<tr>
<th>Organ</th>
<th>Technique</th>
<th>Anatomoses</th>
<th>Inherent possible morbidity</th>
<th>Upper limit of usefulness</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stomach</td>
<td></td>
<td>1</td>
<td>+</td>
<td>Cervical esophagus and pharynx</td>
<td>Bulky, Reflux risk</td>
</tr>
<tr>
<td>Greater curvature tube</td>
<td></td>
<td>1</td>
<td>+</td>
<td>Cervical esophagus and pharynx</td>
<td>Reflux risk</td>
</tr>
<tr>
<td>Reversed gastric tube</td>
<td></td>
<td>1</td>
<td>+++</td>
<td>Cervical esophagus and pharynx</td>
<td>Long suture line; limited blood supply</td>
</tr>
<tr>
<td>Nonreversed gastric tube</td>
<td></td>
<td>1</td>
<td>++</td>
<td>Lower cervical esophagus</td>
<td>Long suture line</td>
</tr>
<tr>
<td>Right colon</td>
<td></td>
<td>3</td>
<td>+++</td>
<td>Lower cervical esophagus</td>
<td>Thin-walled; bulky; short pedicle</td>
</tr>
<tr>
<td>Left colon</td>
<td></td>
<td>3</td>
<td>+++</td>
<td>Most versatile organ or use at any level; lower third to pharynx</td>
<td>Extensive operation; redundancy over time</td>
</tr>
<tr>
<td>Jejunum</td>
<td>(Roux-en-Y loop)</td>
<td>2</td>
<td>+</td>
<td>Lower third</td>
<td>Limited graft length without revision of pedicle or bowel</td>
</tr>
<tr>
<td>Jejunum</td>
<td>(Interposition)</td>
<td>3</td>
<td>+</td>
<td>Lower third</td>
<td></td>
</tr>
<tr>
<td>Free graft</td>
<td>(2 microvascular)</td>
<td>5</td>
<td>+++</td>
<td>Pharynx and cervical esophagus</td>
<td>Microvascular anastomoses required</td>
</tr>
</tbody>
</table>

Types of esophageal replacement. Resection of the strictured area leaves a gap, usually of at least several centimeters, between the cut ends of the stomach and esophagus. The various techniques developed to bridge this deficit can be divided into two broad approaches: partial bypass of the esophagus using a thoracic upper anastomosis and total esophageal bypass with a cervical anastomosis. Thoracic bypasses are significantly simpler to perform but they subject the patient to the considerable risks of an intrapleural esophageal anastomosis. Cervical conduits are more complex to create and run a higher risk of ischemia. Leakage from the cervical esophagus, however, is far less mortal and significantly easier to control than an intrathoracic leak.

A number of organs have been used. The stomach can be mobilized directly and sutured to the cervical esophagus or constructed as a tube. Both right and left colon can be used, as can the jejunum. Free flaps of jejunum sutured using microsurgical techniques are effective and can be used to bridge gaps within the chest.

Although all these techniques are useful in specific circumstances, I prefer to use the stomach for intrathoracic anastomoses. The gastric blood supply is so extensive that ischemia is extremely rare, even when the left gastric and gastroepiploic arteries are divided. Anastomoses between the cut end of the thoracic esophagus and a newly created orifice in the anterior gastric wall (the proximal gastric suture line is closed) are relatively easy to perform. They also permit simultaneous creation of a Nissen wrap using the remaining gastric cardia; this procedure requires two separate incisions. The abdominal component permits mobilization of the stomach and performance of either pyloroplasty or pyloromyotomy, necessary because the vagi are invariably divided during esophagectomy. Feeding jejunostomy should also be performed. The resection, reanastomosis, and antireflux procedure are accomplished via thoracotomy. When total esophageal bypass is required, I prefer to use right colon passed through a substernal tunnel (see Figs. 12-22 and 12-23). (Adapted from Hiebert and Bredenberg [20].)
Technique of right colon bypass. **A**, By carefully preserving the marginal artery of Drummond, a viable bypass can be constructed based on the middle colic artery and vein. **B**, The colon is divided and passed behind the stomach through the lesser sac into the anterior or posterior mediastinum. Intestinal continuity is restored by ileo-transverse colostomy. *(Adapted from Clowes et al. [21].)*

**Figure 12-22.**

Position of the substernal colon bypass. The right colon usually provides adequate length to reach the distal cervical esophagus. Whenever possible, I prefer to anastomose the cervical esophagus to the very distal ileum because it ensures a better size match. Although this bypass uses isoperistaltic colon, emptying the segment is accomplished predominantly by gravity. Colon bypasses are durable procedures that are associated with low anastomotic stricture rates and surprisingly few symptoms. *(Adapted from Skinner [22].)*

**Figure 12-23.**

<table>
<thead>
<tr>
<th>Type of Tumor</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Squamous cell carcinoma</td>
<td>820</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>177</td>
</tr>
<tr>
<td>Mucoepidermoid carcinoma</td>
<td>19</td>
</tr>
<tr>
<td>Anaplastic (small-cell) carcinoma</td>
<td>16</td>
</tr>
<tr>
<td>Leiomyosarcoma</td>
<td>4</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>2</td>
</tr>
<tr>
<td>Melanoma</td>
<td>2</td>
</tr>
<tr>
<td>Carcinosarcoma</td>
<td>1</td>
</tr>
<tr>
<td>Unclassified</td>
<td>7</td>
</tr>
</tbody>
</table>

FUNCTIONAL GRADES OF DYSPHAGIA

<table>
<thead>
<tr>
<th>Grade</th>
<th>Definition</th>
<th>Incidence at diagnosis, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Eats normally</td>
<td>11</td>
</tr>
<tr>
<td>II</td>
<td>Requires liquids with meals</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>Able to take semisolids but unable to take any solid food</td>
<td>30</td>
</tr>
<tr>
<td>IV</td>
<td>Able to take liquids only</td>
<td>40</td>
</tr>
<tr>
<td>V</td>
<td>Unable to take liquids, but able to swallow saliva</td>
<td>7</td>
</tr>
<tr>
<td>VI</td>
<td>Unable to swallow saliva</td>
<td>12</td>
</tr>
</tbody>
</table>

Classification of dysphagia. Takita et al. [25] have characterized the grades of dysphagia. Symptoms range from normal ability to eat (grade I) to unable to swallow saliva (VI). Seventy percent of patients fall into grades III and IV and are unable to tolerate solid foods. (Adapted from Peters and DeMeester [26].)
Barium study in esophageal carcinoma. The diagnosis of esophageal carcinoma can usually be made by barium swallow. The characteristic abnormalities include shouldering and irregularity of esophageal involvement because of submucosal invasion in both directions from the intraluminal mass. Endoscopy, biopsy, and computed tomographic scanning of the chest and upper abdomen are other essential components of the work-up. If the lesion is at the level of the carina or higher, bronchoscopy should also be performed to rule out invasion of the respiratory tree. Staging of esophageal malignancy is performed at the time of operation (see Figs. 12-28 and 12-29). (From Casson [27]; with permission.)

Invasion of esophageal carcinoma. In staging of esophageal malignancies the T descriptor is based on the depth to which the invasion of T1 lesions is confined to the mucosa or submucosa, T2 to the muscularis, T3 to the adventitia, and T4 to invasion into surrounding structures. Endoscopic ultrasound can accurately determine the depth of malignant invasion. (Adapted from DeMeester et al. [28].)
A–B, Lymph node involvement. Identification of lymph node involvement is best characterized by mapping of the cervical, mediastinal, and subdiaphragmatic areas. This information is useful in predicting survival rates as well as in directing radiation therapy. (Adapted from Casson [29].)

**Figure 12-29.**

**Figure 12-30.**

Staging of esophageal carcinoma. The final staging is based on the T and N descriptors plus information as to the presence or absence of distant metastases. (Adapted from Orringer [30].)
Algorithm for therapeutic decisions in esophageal carcinoma. This algorithm is quite pessimistic because of the aggressiveness of esophageal carcinoma. Overall, rates of survival are poor, even with surgical resection. Palliation and a good quality of life plays a vital role in the treatment of this disease. (Adapted from Peters and DeMeester [31].)

Survival by stage of carcinoma. As expected, survival rates can be predicted based on the stage of malignancy. Following resection in 444 patients, median survival times were 27 months for stage I, 19 months for stage II, 7 months for stage III, and 4 months for stage IV. (Adapted from Fok and Wong [32].)
Role of lymph node status in survival from esophageal carcinoma. Positive lymph nodes have enormous negative implications for survival. In 44 patients treated with preoperative radiation and chemotherapy positive lymph nodes were associated with a highly significant ($P < 0.005$) decrease in survival as compared with cohorts with no positive nodes. (Adapted from Vogel et al. [33].)

Curative resection for esophageal carcinoma. In a series of 507 patients, curative resection was associated with a 5-year survival rate of 33% and a median survival time of 23 months. In contrast, the results for patients who underwent palliative resection were 6% and 7 months, respectively. (Adapted from Fok and Wong [32].)

Downstaging of tumor size. Because patients resected for cure fare significantly better than those operated on for palliation, preoperative radiation plus chemotherapy has been used to downstage patients by shrinking primary lesions and by sterilizing the node-bearing areas. Preoperative radiation and chemotherapy administered to 44 patients resulted in disappearance of tumor in 14 patients (A) and only residual microscopic tumor in 15 others (B). In contrast, gross carcinoma remained following therapy in 15 patients. (Adapted from Vogel et al. [33].)
**LYMPH NODE STATUS**

<table>
<thead>
<tr>
<th>GROUP</th>
<th>NO. OF PATIENTS</th>
<th>POSITIVE NODES</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adjuvant pharmacotherapy and surgery</td>
<td>44</td>
<td>10</td>
<td>23*</td>
</tr>
<tr>
<td>Surgery only</td>
<td>54</td>
<td>26</td>
<td>48</td>
</tr>
<tr>
<td>Downstage</td>
<td></td>
<td>1</td>
<td>18</td>
</tr>
<tr>
<td>No tumor</td>
<td>14</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Microscopic tumor</td>
<td>15</td>
<td>1</td>
<td>6.6</td>
</tr>
<tr>
<td>Gross tumor</td>
<td>15</td>
<td>9</td>
<td>60</td>
</tr>
</tbody>
</table>

*P=0.02.

**FIGURE 12-37.** Survival rates following preoperative radiation and chemotherapy. Preoperative adjuvant therapy improved 5-year survival rates from 11% (operation alone) to 36% (operation plus preoperative radiation and chemotherapy). Among the latter group of patients there was a good correlation between tumor regression and survival. Overall, 18 of 29 patients (62%) whose specimens contained either no tumors or only microscopic tumors were still alive at last reporting. *(Adapted from Vogel et al. [33].)*

**REFERENCES**


A
Abdominal esophagus, anatomy of, 221
Achalasia, 74, 75, 165–167
balloon dilation in, 167, 211–212, 222, 231
barium studies in, 165, 166, 209
botulinum toxin injection in, 167, 212
cricopharyngeal, 31–33, 79
differentiated from pseudoachalasia, 59
and epiphrenic diverticula, 50, 165, 167
manometry in, 70, 74, 75, 166
myotomy in, 167, 222, 230–231
symptoms associated with, 208
ultrasonography in, 59, 174
Acid exposure and clearance time in GER, 81, 83, 84, 94
and healing of esophagitis, 109
mechanisms of acid clearance in, 95–97
and severity of esophagitis, 84, 85, 96
and tissue resistance to acid injury, 98–99
Acid perfusion test, 88
in chest pain, 176, 180, 186–187
compared to symptoms during pH monitoring, 88
sensitivity and specificity of, 88, 187
Acyclovir
in cytomegalovirus esophagitis, 125
in herpes simplex esophagitis, 128
Adenocarcinoma of esophagus, 63, 64, 155–157, 236
achalasia in, 166
in Barrett's esophagus, 105, 114, 115, 155–157
in heartburn, 106
histologic appearance in, 156–157
incidence of, 105, 106, 145–146, 147
sites of, 155
Adriamycin, and radiation-induced esophageal injury, 141, 142
AIDS and HIV infection. See HIV infection and AIDS
Airways
gastroesophageal reflux affecting, 34, 35, 91, 93
pharynx function in, 23
protection in swallowing, 5
Alcohol use
carcinoma of esophagus in, 148, 222, 236
Mallory-Weiss tears in, 198
tissue resistance to esophageal acid injury in, 99
Alendronate sodium, esophageal injury from, 137, 138
Alkaline reflux, 86, 87, 88
Amphotericin B in Candida esophagitis, 132
Ampicillin prophylaxis in endoscopy, 213
Anesthesia in endoscopy, 44
Angina, 183, 184
microvascular, 182, 192
Antacids in GER, 108, 109
Antibiotics
in endoscopy, prophylactic use of, 45, 66, 213
esophageal injury from, 137, 138, 200
Anti-inflammatory drugs, pill-induced esophagitis from, 137, 139, 200
Antireflux surgery, 112, 221, 222, 227–230
in Barrett's esophagus, 115
Arteria lusoria, 15
Arterial supply of esophagus, 11, 221, 223
Arytenoid cartilage, 9
Ascorbic acid, esophageal injury from, 137
Aspiration, fine-needle,
complications in, 66
in histoplasmosis, 60
in leiomyoma, 61
in lung cancer, 65, 66
Aspirin, pseudodiverticulosis from, 51
Atkinson stent, 214
Auerbach plexus, 10
excitatory and inhibitory neurons in, 2, 16, 19
in reflux esophagitis, 104
in Schatzki's ring, 14, 208
in spasm of esophagus, 48, 168
in varices of esophagus, 12
video recording of, 14
Barrett's esophagus, 92, 104–105, 222
antireflux surgery in, 115
carcinoma in, 155–157
incidence of, 105, 236
prevention of, 114–115
risk for, 92, 157, 222
surveillance for, 115
columnar epithelium in, 104–105, 114
dysplasia in, 115, 156–157
dysplasia in, 162, 104, 105, 115
histologic appearance in, 156–157
pH monitoring in, 87
prevalence of, 105
proton pump inhibitor therapy in, 114
short segment, 104
Basaloid carcinoma of esophagus, 152–153
Belching, 29
Belsey antireflux procedures, 112, 229–230
Bernstein test. See Acid perfusion test
Bethanechol
in assessment of chest pain, 181, 190
in management of gastroesophageal reflux, 108
Bile acids in reflux esophagitis, 94, 97
Bilirubin absorption, 2, 16
Bilitec probe, 87, 88
Biomechanics of swallowing, 7
Biopsy, 43, 55, 59
in Candida esophagitis, 129, 130, 131
in cytomegalovirus esophagitis, 123
in herpes simplex esophagitis, 127
in histoplasmosis, 60
in HIV infection and esophageal ulceration, 121
in leiomyoma, 61
in lung cancer, 65–66
normal histology of esophagus in, 49
Bird's beak appearance in achalasia, 165, 166
Bleeding, upper gastrointestinal, 198–207
Boerhaave's syndrome, 224
Botulinum toxin in achalasia, 167, 212
Bronchoscopy in lung cancer, 65
Bronchus
echoendoscopic view of, 58
and esophageal fistula in cytomegalovirus esophagitis, 125
Candida esophagitis, 129–132
herpes simplex esophagitis compared to,
126, 128, 129
in HIV infection and AIDS, 121, 129
pill-induced esophagitis compared to, 139
Carcinoma
of epiglottis, 37
of esophagus, 145, 147–157, 236–241
adenocarcinoma. See Adenocarcinoma
of esophagus
advanced, 154
barium studies in, 237
in Barrett’s esophagus. See Barrett’s
esophagus, carcinoma in
basaloid, 152–153
in caustic injury, 222, 236
chemotherapy in, 65, 146, 240, 241
diagnosis of, 146
endoscopic ultrasonography in, 63–65, 67
foreign body impaction in, 136
incidence of, 105, 106, 145–146, 147, 236
infiltrating, 148, 150
in situ, 150
keratin pearls in, 149
lymph node involvement in, 151, 238,
240, 241
macroscopic appearance of, 148
metastatic. See Metastasis, of esophageal
carcinoma
microscopic features of, 149
obstruction of esophagus in, 222
prognosis in, 146, 154
radiation therapy in. See Radiation therapy,
in esophageal carcinoma
in reflux esophagitis, 222
risk factors for, 92, 148, 157, 222, 236
sites of, 155, 236
small cell, 155
spindle cell variant, 153–154
squamous cell, 64, 136, 145, 147–154, 236
staging of, 146, 151, 237, 238
submucosal extension of, 63, 148, 149,
150, 237
superficial, 150, 154
surgery in. See Surgery, in carcinoma of
esophagus
survival rates in, 239, 240, 241
symptoms in, 146, 223, 236
treatment decisions in, 239
undifferentiated, 150
 verrucous, 153
 well-differentiated, 149
 of gastroesophageal junction, 63, 166
 of hypopharynx, 37
 of vocal fold, 36
Carcinosarcoma of esophagus, 153–154
Caustic injury of esophagus, 118–120, 137, 222
Celiac axis, 58, 64
Central nervous system in swallowing response, 5, 6
Cerebrovascular disorders, 80
Cervical esophagus
anatomy of, 221
carcinoma of, 151, 236
in resection and reanastomosis
 procedures, 234, 235
Cervical osteophytes, 35
Chagas’ disease, 74
Chemical esophagitis, 118–120
Chemotherapy
in esophageal carcinoma, 65, 146, 240, 241
esophagitis from, 141, 142
Chest pain, 179–194
acid perfusion test in, 176, 180, 186–187
in altered esophageal sensitivity, 179, 180, 185
diagnostic tests in, 191, 192–193
associated symptoms in, 179, 180, 184, 185
balloon distention test in, 181, 191
barium studies in, 48
characteristics of, 180, 184
in coronary artery disease, 179–184
and gastroesophageal reflux, 188, 192
diagnostic testing in, 176–180, 181, 186–194
differential diagnosis in, 181
edrophonium test in, 181, 190–192
and ultrasonography, 177
in esoinophilic esophagitis, 140
epidemiology of, 179, 180, 182, 183
follow-up on functional status in, 183
in gastroesophageal reflux. See
Gastroesophageal reflux, chest pain in
and heartburn. See Heartburn
historical descriptions of, 182
history of patient in, 184
in irritable esophagus, 179, 180, 182, 185
diagnostic tests in, 192, 193
mechanisms of, 180, 181, 185
in motility disorders of esophagus. See
Motility disorders, chest pain in
in nutcracker esophagus, 169, 181, 189
pH monitoring in, 85, 180, 181, 186, 187, 188
prognosis in, 183
provocative testing in, 181, 190–192
psychological factors in,
ultrasonography in, 176, 177
Children
esoinophilic esophagitis in, 140
foreign body ingestion in, 133, 134
Cholinergic receptors, 2, 16, 19
Cimetidine in GER, 108, 109
Cirrhosis, 201
Cisapride in GER, 108, 110
Clotrimazole in Candida esophagitis, 132
Colon bypass technique, 234–235
Congenital disorders of esophagus, 15
Constrictor muscles, 2–3
Coronary arteriography in chest pain, 182, 183
Coronary artery disease, chest pain in, 179–184
with reflux-associated chest pain, 188, 192
Cricoid cartilage, 9
Cricopharyngeal bar, 39, 40, 164
Cricopharyngeus muscle, 2, 7, 31–33
achalasia of, 31–33, 79
 electromyography of, 8, 32–33
in Zenker’s diverticula, 31, 33, 231
Cysts, esophageal duplication, 59
Cytomegalovirus esophagitis, 122–125
in HIV infection and AIDS, 121, 125
ulceration of esophagus in, 123, 124, 199
D
Deglutitive inhibition, 2, 16, 17
Desmoplasia, 150
Diabetes mellitus, manometry in, 74, 77
Diaphragm
anatomy in hiatal hernia, 226
relationship with lower esophageal
sphincter, 17, 18
Dilation procedures, 208–213
in achalasia, 167, 211–212, 222, 231
in esophageal webs, 52, 53
laser therapy in, 217
in lower esophageal mucosal ring, 51, 52
in lye ingestion, 120
in radiation-induced esophagitis, 143
in reflux esophagitis, 114
stent placement in, 215
Diverticula, 50
epiphrenic, 19, 50, 51
and achalasia, 50, 165, 167
myotomy in, 222, 232
and intramural pseudodiverticulosis, 50
midesophageal, 50
pulsion, 170
surgery in, 33, 164, 222, 231–232
traction, 222
Zenker’s. See Zenker’s diverticula
Doxorubicin, and radiation-induced
esophageal injury, 141, 142
Doxycycline, esophageal injury from, 137, 138
Duodenogastric esophageal reflux, 86, 87, 88
Duplication cyst, esophageal, 59
Dysphagia, 208–209, 222
barium studies in, 48, 49, 208–209
in Candida esophagitis, 129
in carcinoma of esophagus, 236
in caustic injury of esophagus, 118
cervical, 30, 31
in cytomegalovirus esophagitis, 122
in esoinophilic esophagitis, 140
in epiphrenic diverticula, 232
glottis in, 28
grades of, 236
in herpes simplex esophagitis, 126
in HIV infection and AIDS, 121
sphincter, 15, 61
in mucosal ring of lower esophagus, 51, 52
oropharyngeal, 80, 164, 231
in osteophytes, 35
in pill-induced esophagitis, 137
in reflux esophagitis, 104
in webs, esophageal, 52
in Zenker’s diverticula, 50, 164, 231
Dysplasia in Barrett’s esophagus, 115, 156–157

E
Eder-Puestow dilator, 210
Edrophonium test in chest pain, 181, 190–192
and ultrasonography, 177
Electromyography of cricopharyngeus muscle, 8, 32–33
EndoCinch procedure, 92, 112
Endoscopy, 43–52, 197–218
in achalasia, 165, 211–212
anatomy in, 10, 47, 57–58
antibiotic prophylaxis in, 45, 213
in Barrett’s esophagus, 62, 104, 105, 115
in bleeding, upper gastrointestinal, 198–207
in cancer of esophagus, 214–217
in Candida esophagitis, 131–132
in caustic injury of esophagus, 119
complications of, 47, 66–67
bacteremia in, 213
in variceal bleeding, 206, 207
contraindications to, 46
in cytomegalovirus esophagitis, 124, 199
in eosinophilic esophagitis, 140
in epiphrenic diverticula, 19, 51
equipment in, 44, 56–57
in foreign bodies, esophageal, 217–218
in gastroesophageal reflux, 102, 104, 105, 115
and esophagitis, 47, 102
in therapy, 92, 112, 115
guidance of endoscope in, 47
in herpes simplex esophagitis, 127, 199
historical development of, 197–198
indications for, 46, 49, 59
lower esophageal sphincter in, 47
in Mallory-Weiss tears, 198
in obstruction of esophagus, 208–213
of pharynx, 25
in pill-induced esophagitis, 138, 200
premedication in, 44
in radiation-induced esophagitis, 143, 200
in Schatzki’s ring, 15
in ulceration of esophagus, 199–200
in HIV infection and AIDS, 122, 199
ultrasonography in. See Ultrasonography in varices, esophageal and gastric, 12, 62,
201–207
video technique, 27, 43, 44
Eosinophilic esophagitis, 140
Epiglottis, 9, 24
carcinoma of, 37
doscopic view of, 25
Epiphrenic diverticula, 19, 50, 51
and achalasia, 50, 165, 167
myotomy in, 222, 232
Epithelial neoplasms of esophagus, 146–147
Ergonovine maleate test in chest pain, 181, 190
Erythromycin, esophageal injury from, 138
Esomeprazole in GER, 108, 110
Esophagitis, 117–143
Candida, 121, 126, 128, 129–132, 139
cytomegalovirus, 121, 122–125, 199
eosinophilic, 140
in foreign body ingestion, 133–136
herpes simplex, 121, 124, 126–128, 129, 199
in HIV infection and AIDS, 121–122, 125,
126, 129, 199
in lye ingestion, 118–120
pill-induced, 137–139, 200
radiation-induced, 141–143, 200
reflux, 84, 85, 91–92
acid exposure time in, 84, 85, 96
antireflux surgery in, 221, 222, 227–230
bile salt concentrations in, 94, 97
complications of, 104–106
drug therapy in, 108–111, 114
endoscopy in, 47, 84, 103
etiology of, 91–92, 94
grading system in, 103
lifestyle factors in, 107
management strategy in, 113
natural history of, 92
protective role of Helicobacter pylori in, 100
risk for carcinoma in, 222
stricture formation in, 104, 114, 222, 233

F
Facial nerve in swallow response, 5
Famotidine in GER, 108, 109, 110
Fibrosis in radiation-induced esophagitis, 141, 143
Fistula formation in cytomegalovirus esophagitis, 125
in radiation-induced esophagitis, 142
Fluconazole in Candida esophagitis, 132
Flucytosine in Candida esophagitis, 132
Food affecting LES pressure, 20
impaction of, 136, 217, 218
algorithmic approach to, 135
incidence of, 133
removal techniques in, 218
Foreign body ingestion, 133–136, 217–218
Forestier’s arthritis, 35
Foscarnet in cytomegalovirus esophagitis, 125
in herpes simplex esophagitis, 128
Fundoplication
Belsey procedure, 112
Nissen procedure, 112, 222, 227–228

G
Ganciclovir in cytomegalovirus esophagitis, 125
Gastrin levels, proton pump inhibitors affecting, 110, 111
Gastritis in Helicobacter pylori infections, 111
Gastroesophageal junction adenocarcinoma of, 63, 166
anatomy of, 17
as barrier to gastric reflux, 18
Gastroesophageal reflux, 91–115
acid exposure and clearance time in. See Acid exposure and clearance time in GER
acid perfusion test in, 88, 186–187
antireflux surgery in, 112, 221, 222, 227–230
in Barrett’s esophagus, 115
Barrett’s esophagus in, 104–105, 114–115
barriers to, 18, 91, 94–95, 172–173
chest pain in, 179, 180
and coronary artery disease, 188, 192
diagnostic tests in, 186–188
mechanisms of, 180, 185
medical therapy in, 180, 186, 188
pH monitoring in, 85, 180, 181, 186, 187–188
clinical features in, 101
complications of, 91, 93, 104–106
conditions and activities associated with, 100
diagnostic tests in, 106
in chest pain, 186–188
endoscopic therapy in, 92, 112, 115
epidemiology of, 93
esophageal pathology in, 91, 92, 101
esophagitis in
pill-induced, 137
reflux. See Esophagitis, reflux
free spontaneous, 95
heartburn in. See Heartburn
in hiatal hernia, 95, 97
histopathology in, 102
laryngopharyngeal disorders in, 91, 93
lifestyle factors in, 107
medical therapy in, 92, 108–111, 114
in chest pain, 180, 186, 188
multichannel intraluminal impedance in,
70, 89–90
pathophysiology in, 94–100
pH monitoring in, 70, 81–90, 92
in chest pain, 85, 180, 181, 186, 187–188
physiologic, 81, 92
protective role of Helicobacter pylori in, 100
pseudodiverticulosis in, 51
in recumbent position, 81, 83
in scleroderma, 77
stricture formation in, 104, 114, 222, 233
supersophageal complications of, 34, 35
swallow-associated prolonged LES
relaxation in, 95
symptomatic, 91, 92
tissue resistance to acid injury in, 98–99
in transient LES relaxation, 20, 95, 173
in upright position, 83, 84
Gentamycin prophylaxis in endoscopy, 213
GER. See Gastroesophageal reflux
Glossopharyngeal nerve in swallow response, 5
Glottis, 23, 27
in belching, 29
in dysphagia, 28
Granuloma of larynx, 35
Gravity in esophageal acid clearance mechanisms, 95–96

H
Heart, chest pain in disorders of, 179–184,
188, 192
Heartburn, 91, 92
characteristics of, 101, 180
epidemiology of, 93
management strategies in, 113
mechanisms of, 180
risk of esophageal adenocarcinoma in, 106
in sustained esophageal contraction, 176
ultrasonography in, 176
Helicobacter pylori infections gastritis in, 111
protective role in reflux esophagitis, 100
Heller myotomy in achalasia, 222, 230–231
Hemorrhage, upper gastrointestinal, 198–207
Hernia, hiatal. See Hiatal hernia
Herpes simplex esophagitis, 126–128, 199
Candida esophagitis compared to, 126, 128,
129
cytomegalovirus esophagitis compared to, 124
in HIV infection and AIDS, 121, 126
ulceration of esophagus in, 128, 199
Hetzel classification of reflux esophagitis, 103
Hiatal hernia, 221–222, 226–230
gastroesophageal reflux in, 95, 97
surgery in, 221–222, 226–230
type I (axial or sliding), 18, 97, 221, 222, 227
type II (paraesophageal), 18, 221, 222, 227
Hill repair, 112, 229
Histamine H2-receptor antagonists in GER,
108, 109, 113, 114
Histoplasmosis, 60
Historical aspects
of endoscopic therapy, 197–198
of manometry, 69
Jet effect in cricopharyngeal

Intestinal pseudo-obstruction, chronic

Hypercontracting esophagus,

Liver metastasis of esophageal carcinoma, 64

Hypoglossal nerve in swallow response, 5

Hypocontracting esophagus, 74, 76

Hypochlorhydria from proton pump inhibitors, 110, 111

Hypopharyngeal bar, 39, 40, 164

Killian’s dehiscence, 33

Ketoconazole in

Keratin pearls in esophageal carcinoma, 149

Keams-Sayre syndrome, 246

Laryngocele, 38

Laundered esophagus, 138

Intestinal pseudo-obstruction, chronic idiopathic, 74, 78

Irritable esophagus, chest pain, 179, 180, 182, 185
diagnostic tests in, 192–193

Jejunum in esophageal replacement procedures, 234

Jet effect in cricopharyngeal bar, 39

Kearns-Sayre syndrome, 30

Keratin pearls in esophageal carcinoma, 149

Ketoconazole in Candida esophagitis, 132

Killian’s dehiscence, 33

Lansoprazole in GER, 108, 110

Laparoscopy

Heller myotomy in, 222

Nissen fundoplication in, 112, 228

Laryngeal nerve, superior, 6

Laryngoecele, 38

Larynx

cancer of, 36

caucic injury of, 118
gastroesophageal reflux affecting, 34, 35, 91, 93
granuloma of, 35
movement in swallowing, 2, 3, 4, 9
muscles of, 2

Laser therapy

in Barrett’s esophagus, 115
in esophageal cancer, 216–217

Leiomyoma of esophagus, 60–61, 145, 160

Leiomyosarcoma of esophagus, 160, 161

LES. See Lower esophageal sphincter

Leukoplakia, 36

Lifestyle factors in reflux esophagitis, 107

Liver metastasis of esophageal carcinoma, 64

Los Angeles classification of reflux esophagitis, 103

Lower esophageal sphincter, 1, 2, 18–20

in achalasia, 75, 165–167

in antireflux mechanism, 18, 94–95, 172–173
diagnostic appearance of, 47
hypertensive, 74, 76, 170
hypotensive, 74

manometry of, 69, 71, 74, 75, 173

in hypertensive LES, 76, 170
normal values in, 13, 72
pressure of, 18, 71

de glutamamic inhibition, 17

normal values in, 13, 72

substances affecting, 20

relationship with diaphragm, 17, 18

swallow-associated prolonged relaxation of, 95

transient relaxation of, 20, 173
gastroesophageal reflux in, 20, 95, 173

Lung cancer, endoscopic ultrasonography in, 65–66

Lye esophagitis, 118–120

Lymph nodes, 224

in esophageal carcinoma, 151, 238, 240, 241

in lung cancer, 65–66

Lymphoma of esophagus, 147

Malory-Weiss tears, 198

Maloney dilator, 210, 213

Manometry, 13, 14, 69–80

in achalasia, 70, 74, 75, 166

in chest pain, 181, 189, 191

clinical applications of, 70

and concurrent video recording of barium swallow, 14

historical aspects of, 69

in hypercontracting esophagus, 74, 76
indications for, 70

in Kearns-Sayre syndrome, 30

mirror images in, 75

normal values in, 13, 72

in nutcracker esophagus, 74, 76, 169

pharyngeal. See Pharynx, manometry of recording sites in, 28, 72, 73

in scleroderma, 70, 74, 77, 171

sensor sleeve in, 28, 71

in spasm of esophagus, 74, 75, 168

in Zenker’s diverticula, 33, 79

Meissner’s plexus, 10

Melanoma of esophagus, 158–159

Metastasis

of esophageal carcinoma, 148, 150, 151, 238

direct spread in, 152
to liver, 64

sites of, 152
to esophagus, 147

Metoclopramide in GER, 108

Miconazole in

Mallory-Weiss tears, 198

in Zenker’s diverticula, 33, 79

in esophageal cancer, 216–217

gastroesophageal reflux affecting, 34, 35, 91, 93

muscles of, 2

and heart disorders, 192

historical descriptions of, 182

mechanisms of, 180, 181, 185

in nutcracker esophagus, 169, 181, 189

classification of, 74, 164

and epiphrenic diverticula, 50, 165, 167

and gastroesophageal reflux, 74, 172–173, 176–177

in hypertensive LES, 74, 170

inffective esophageal motility, 74, 76

manometry in. See Manometry

and midesophageal diverticula, 50

in nutcracker esophagus, 74, 76, 169

and pseudodiverticulosis, 51

in radiation-induced esophagitis, 143

in scleroderma, 70, 74, 77, 171–172

in spasm of esophagus, 74, 75, 168, 169

ultrasonography in, 174–177

in Zenker’s diverticulum, 79, 164

Motor innervation of esophagus, 16, 163

Mucosa

in Barrett’s esophagus, 62

biopsy of, 49

in carcinoma of esophagus, 63, 237

diagnostic applications of, 10, 57

at Z-line, 47

Multichannel intraluminal impedance, 70, 89–90

Muscular dystrophy, oculopharyngeal, 79

Muscularis

adventitia, 10, 57

propria, 57

in carcinoma of esophagus, 237

Myenteric plexus, 10

excitatory and inhibitory neurons in, 2, 16, 19

Myotomy

in achalasia, 167, 222, 230–231

in epiphrenic diverticula, 222, 232

in Zenker’s diverticula, 222, 231

Nasopharynx

endoscopic view of, 25

in swallowing, 5, 7, 9

Neurons in myenteric plexus, excitatory and inhibitory, 2, 16, 19

Nissen fundoplication, 112, 222, 227–238

laparoscopic, 112, 228

Nitric oxide, 2, 16, 19

Nizatidine in GER, 108

Nutcracker esophagus, 169

chest pain in, 169, 181, 189

manometry in, 74, 76, 169

Nystatin in Candida esophagitis, 132

Obstruction of esophagus, 208–213

surgery in, 222–223, 230–241

Oculopharyngeal muscular dystrophy, 79

Omeprazole in GER, 108, 109, 110, 114

and chest pain, 180, 188

pH monitoring in, 86, 88

Oral cavity

caucic injury of, 118

gastroesophageal reflux affecting, 91, 93

muscles of, 2–3

in swallowing sequence, 4, 5, 9

Osteophytes, cervical, 35

Pain

in chest. See Chest pain

in pill-induced esophagitis, 137, 139
Pneumomediastinum in esophageal polyps, 118, 120

Portal plaque, 58

Pneumonitis in caustic ingestion, 118, 119, 120, 222

Paresis, pharyngeal, 38, 39, 80

Pemphigoid, pharyngeal ulceration in, 38, 94, 97

Peptic strictures, 209–211

Perforation of esophagus, 221, 224–225

in balloon dilation for achalasia, 211, 212

in endoscopy, 66, 67, 207

Percutaneous gastronomy, 58

Peristalsis, 163

acid clearance in, 95–96

anatomy and physiology in, 1, 2
disorders of. See Motility disorders

and esophageal volume clearance, 14

hypertensive, 74, 76

manometry in, See Manometry.

pharyngeal pressure wave in, 30

primary, 2, 13, 16

secondary, 2, 16

pH monitoring, 70, 81–90

in chest pain, 85, 180, 181, 186, 187–188

normal values in, 81

symptom association in, 85, 187, 188

Pharyngoesophageal diverticula, See Zenker’s
diverticula

Pharynx, 23–40

anatomy of, 24–26
cancer of, 36

causative injury of, 118

endoscopic view of, 25

fluoroscopic view of, 26

gastroesophageal reflux affecting, 34, 35, 91, 93

manometry of, 80

in Kears-Sayre syndrome, 30

normal values in, 72, 73

problems in, 28

muscles of, 1, 2–3

paresis of, 38, 39, 80

peristaltic pressure wave of, 30

respiratory function of, 23, 24

in swallowing, 1–2, 4, 5, 26–31

biomechanics of, 7

three-dimensional model of, 9

ulceration of, 38

Photodynamic therapy in Barrett’s esophagus, 115

Pill-induced esophagitis, 137–139, 200

Plaque, 130, 131

in Candida esophagitis, 130, 131

in pill-induced injury, 138

Pneumomediastinum in esophageal perforation, 67

Pneumonitis in caustic ingestion, 118, 120

Polyps of esophagus, fibrovascular, 159–160

Portal hypertension, 12, 62, 201

Prosthetic devices, esophageal, 214–216

Proton pump inhibitors in GER, 108, 109, 110, 111

and Barrett’s esophagus, 114

and chest pain, 188

compared to antireflux surgery, 112

and incidence of stricture dilation, 114

in stepped approach to management, 113

Pseudoachalasia, 59

Pseudodiverticulosis, 50, 51, 210

Pseudo-obstruction of intestines, chronic idiopathic, 74, 78

Psychological factors in chest pain, 180, 182, 185, 193

Q

Quinidine, esophageal injury from, 137, 139

R

Rabeprazole in GER, 108, 110

Radiation therapy

in esophageal carcinoma, 146

combined with chemotherapy, 65, 146, 240, 241

endoscopic ultrasonography after, 65

esophagitis from, 141, 142

esophagitis from, 141–143, 200

Ranitidine in GER, 108, 109, 110

Reflux

acid gastroesophageal, See

Gastroesophageal reflux

alkaline, 86, 87, 88

Reinke’s edema, 34

Rings, esophageal

lower mucosal, 51, 52

Schatzki’s, 14, 15, 208, 209

Saliva, 87, 95–96

Savary dilator, 210, 213, 215, 217

Savary-Miller classification of reflux esophagitis, 103

Scar formation in caustic ingestion, 118, 120

Schatzki’s ring, 14, 15, 208, 209

Scleroderma, 171–172

manometry in, 70, 74, 77, 171

ultrasonography in, 77, 175

Sclerotherapy, endoscopic, in variceal hemorrhage, 202, 206, 207

Sedation in endoscopy, 44

Sengstaken-Blakemore tube, 202

Sliding hiatal hernia, 18, 221, 222, 227

Small cell carcinoma of esophagus, 155

Smoking

carcinoma of esophagus in, 148, 222, 236

tissue resistance to esophageal acid injury in, 99

Smooth muscle, 1, 2, 16

Spasm of esophagus, 168, 169

barium studies in, 48, 168

chest pain in, 181, 189

manometry in, 74, 75, 168

Spindle cell carcinoma of esophagus, 153–154

Squamous cell carcinoma of esophagus, 145,

147–154, 236

endoscopic ultrasonography in, 64

foreign body impaction in, 136

Staging

of esophageal carcinoma, 146, 151, 237, 238

of lung cancer, 65–66

Stenosis of esophagus, congenital, 15

Stents, esophageal, 214–216

Stomach

burns in caustic ingestion, 119

in esophageal replacement procedures, 234

pH monitoring, 84, 85–87

Stretta procedure, 92, 112

Striated muscle, 1, 2, 7, 16

Stricture formation

benign, 222, 233–235

endoscopic appearance in, 209

symptoms associated with, 208

bypass procedures in, 234–235

in caustic ingestion, 118, 119, 120, 222

in endoscopic treatment of varices, 207

in esoinophilic esophagitis, 140

malignant, 208, 209

Zenker’s diverticula with, 40

pill-induced, 137, 139

in radiation-induced esophagitis, 142, 143

in reflux esophagitis, 104, 114, 222, 233

symptoms associated with, 208

Stricturoplasty, 222, 233

Stroke, manometry in, 80

Subclavian artery, aberrant right, 15, 61

Submucosa

in Barrett’s esophagus, 62

in carcinoma of esophagus, 148, 149, 150, 237

endoscopic ultrasonography of, 63

staging of involvement, 237

endoscopic ultrasonography of, 10, 57, 63

Submucosal plexus, 10

Sucralfate in GER, 108

Supraesophageal reflux disease, 34, 35

Surgery, 221–241

in achalasia, 222, 230–231

anatomy in, 221, 223–224

in benign strictures, 222, 233–235

in carcinoma of esophagus, 146, 222, 236–241

in advanced disease, 154

with chemotherapy and radiation therapy, 65, 146, 240, 241

relapse in, 65

in diverticula, 33, 164, 222, 231–232

in gastroesophageal reflux, 112, 221, 222, 227–230

and Barrett’s esophagus, 115

in hiatal hernia, 221–222, 226–230

in obstruction of esophagus, 222–223, 230–241

in perforation of esophagus, 225

replacement of esophagus in, 234–235

Swallowing response, 4, 5–6

Swallowing, 1–9

deglutitive inhibition, 2, 16, 17

in esophageal acid clearance mechanisms, 95–96

manometry in, 13, 14

pharynx in, 1–2, 4, 5, 26–31

biomechanics of, 7

three-dimensional model of, 9

phases of, 1–2, 4–5, 26

Swallowing center, 5, 6

Syndrome X, 192

T

Tetracycline, esophageal injury from, 138

Theophylline pill impaction, 136

Thoracic esophagus

anatomy of, 221

carcinoma of, 151, 236

in resection and reanastomosis procedures, 234
Thyropharyngeus muscle, 2
TNM staging of esophageal carcinoma, 151, 238
Tongue
cancer of, 37
in swallowing sequence, 4, 5, 9
Trachea, echoendoscopic view of, 58
Trauma
in caustic ingestion, 118–120
pill-induced, 137–139
radiation-induced, 141–143
Trigeminal nerve in swallow response, 5
Tumors
of epiglottis, 37
of esophagus, 145–161
carcinoma. See Carcinoma, of esophagus epithelial, 146–147
histopathology in, 236
incidence of, 145–146, 147
laser therapy in, 216–217
leiomyoma, 60–61, 145, 160
melanoma, malignant, 158–159
palliative treatment in, 214–217
papilloma, squamous, 145, 146
polyps, fibrovascular, 159–160
prosthetic devices and stents in, 214–216
types of, 145, 236
and Zenker's diverticula, 40
of hypopharynx, 37
of larynx, 35, 36
of pharynx, 36
of tongue, 37

UES. See Upper esophageal sphincter
Ulceration
of esophagus, 199–200
bleeding in, upper gastrointestinal, 199–200
in Candida infection, 132
in caustic ingestion, 120
in cytomegalovirus infection, 123, 124, 199
in endoscopic treatment of varices, 207
in herpes simplex virus infection, 128, 199
in HIV infection and AIDS, 121, 122, 199
pill-induced, 138, 200
in squamous cell carcinoma, 148
of pharynx, 38
Ultrasoundography, 10, 55–67
in achalasia, 59, 174
in aspiration procedures, fine-needle, 55, 59
in Barrett's esophagus, 62
in carcinoma of esophagus, 63–65, 67
in cysts, 59
in dysphagia lusoria, 61
in histoplasmosis, 60
in leiomyoma, 60–61
in lung cancer, 65–66
in motility disorders, 59, 77, 174–177
in scleroderma, 77, 175
in varices, 62
Upper esophageal sphincter, 1, 2, 7–9
in belching and swallowing, 29
hypertensive resting pressure, 78
in Kearns-Sayre syndrome, 30
manometry of, 13, 72, 73, 78
normal values in, 13, 72
sensor placement and movement in, 28
nonrelaxing or noncompliant, 164
response to balloon distention of esophagus, 40
in Zenker's diverticula, 33, 50, 79, 164, 231

V
Vagus nerve, 2, 5, 16
Varices, esophageal and gastric, 12, 62, 201–207
Venous drainage of esophagus, 11, 221, 223
Verrucous carcinoma of esophagus, 153
Video endoscopy, 27, 43, 44
Vocal cords, 25, 26
in belching, 29
leukoplakia of, 36

W
Webs, esophageal, 52–53

Z
Zenker's diverticula, 31, 50
barium studies in, 33
and cancer of esophagus, 40
dysphagia in, 50, 164, 231
manometry in, 33, 79
surgery in, 33, 164, 222, 231
symptoms in, 33, 164, 231
Z-line, 47