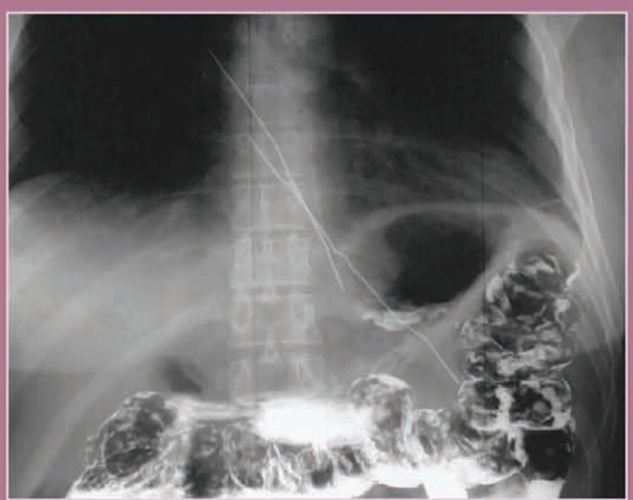
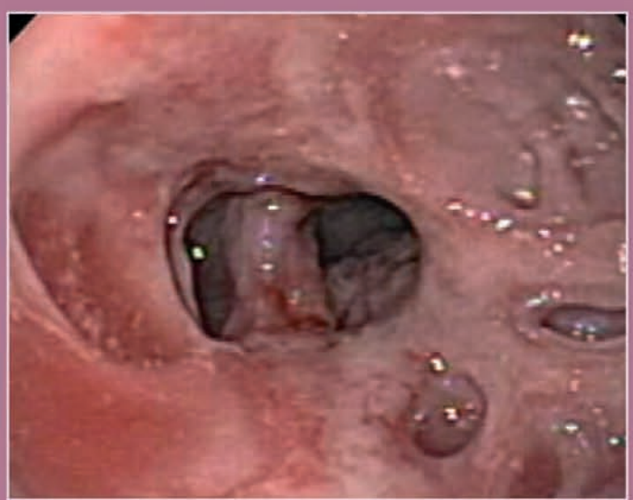
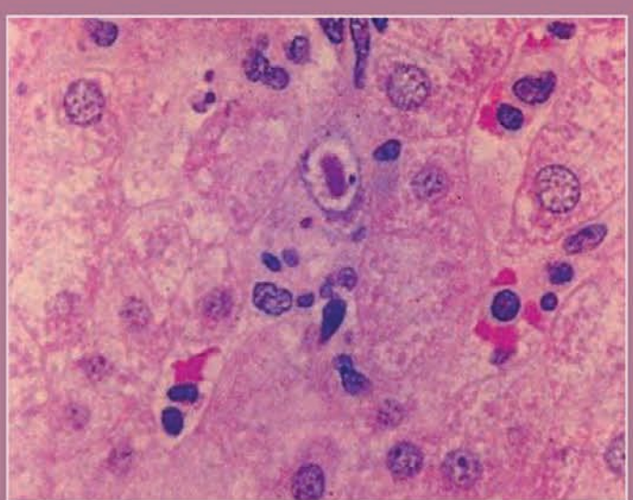
An Atlas of Investigation and Management

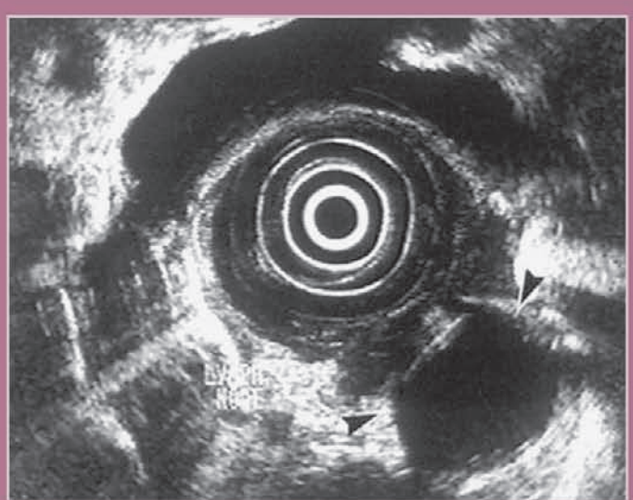
ESOPHAGEAL DISEASES

Michael F Vaezi









CLINICAL PUBLISHING

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ESOPHAGEAL DISEASES

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CLINICAL PUBLISHING
OXFORD

Clinical Publishing
An imprint of Atlas Medical Publishing Ltd
Oxford Centre for Innovation
Mill Street, Oxford OX2 0JX, UK

Tel: +44 1865 811116
Fax: +44 1865 251550
Email: info@clinicalpublishing.co.uk
Web: www.clinicalpublishing.co.uk

Distributed by:
Marston Book Services Ltd
PO Box 269
Abingdon
Oxford OX14 4YN, UK

Tel: +44 1235 465500
Fax: +44 1235 465555
Email: trade.orders@marston.co.uk

First published 2006

A catalogue record for this book is available from the British Library

ISBN 1 904392 55 5
Electronic ISBN 978 1 84692 563 4

Printed in Spain by TG Hostench S.A., Barcelona

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Preface

This Atlas of Esophageal Diseases is intended to provide an overview of the esophagus in health and disease. It is a starting point to familiarize doctors in training, as well as experienced physicians and their staff, with both common and rare diseases which may affect the esophagus. Pattern recognition is often key in establishing the correct diagnosis, and we believe that this atlas provides the basics for such concise and efficient diagnosis.

The atlas is organized to show normal esophageal anatomy and function initially, followed by the role for esophageal testing, and then to review diseases affecting the esophagus from 'A' (achalasia) to 'Z' (Zenker's diverticulum). In each section the reader is provided with tables, figures, and appropriate references. The information provided is in summary and is not intended to be all inclusive. For more detailed information in each area we refer the readers to recent publications and reviews.

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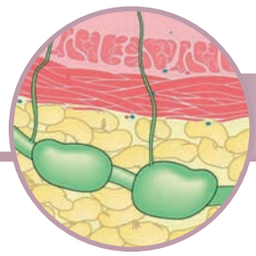
Acknowledgement

We thank Dr Jason Vollweiler for his contributions to this atlas.

Abbreviations

AC alternating current
ACE angiotensin-converting enzyme
ACG American College of Gastroenterology
AGA American Gastroenterological Association
AIDS acquired immunodeficiency syndrome
APC argon plasma coagulator
ASGE American Society of Gastrointestinal Endoscopy
bid twice daily
CMV cytomegalovirus
CT computed tomography
DDx differential diagnosis
DEA distal esophagueal amplitude
DES diffuse esophageal spasm
DGER duodenogastroesophageal reflux
EGD esophagogastroduodenoscopy
EM esophageal manometry
EMR endoscopic mucosal resection
ENT ear, nose, and throat
EUS endoscopic ultrasound
FNA fine-needle aspiration
GEJ gastroesophageal junction
GERD gastroesophageal reflux disease
GI gastrointestinal
GVHD graft-versus-host disease
H2RA histamine receptor antagonist
HGD high grade dysplasia
HIV human immunodeficiency virus
HPV human papilloma virus
HSV herpes simplex virus
IEM ineffective esophageal motility
LES lower esophageal sphincter
LPR laryngopharyngeal reflux
LR reflux laryngitis
MEN multiple endocrine neoplasia
MII multi-channel intraluminal impedance
NE nutcracker esophagus
NERD non-erosive reflux disease
NO nitric oxide
NSAID non-steroidal anti-inflammatory drug
PEG percutaneous gastrostomy (tube)
PET positron emission tomography
po by mouth
PPI proton-pump inhibitor
qac before meals
qd once daily
qhs before sleep
RF radio frequency
SCC squamous cell carcinoma
SCJ squamocolumnar junction
SCM squamocolumnar margin
SIDS sudden infant death syndrome
TBS timed barium swallow
TIPS transhepatic intrajugular portosystemic shunt
TLESR transient lower esophageal sphincter relaxation
TNM tumor, nodes, and metastasis
TPN total parenteral nutrition
UES upper esophageal sphincter
VIP vasoactive intestinal polypeptide



Chapter 1

Normal esophageal anatomy and physiology

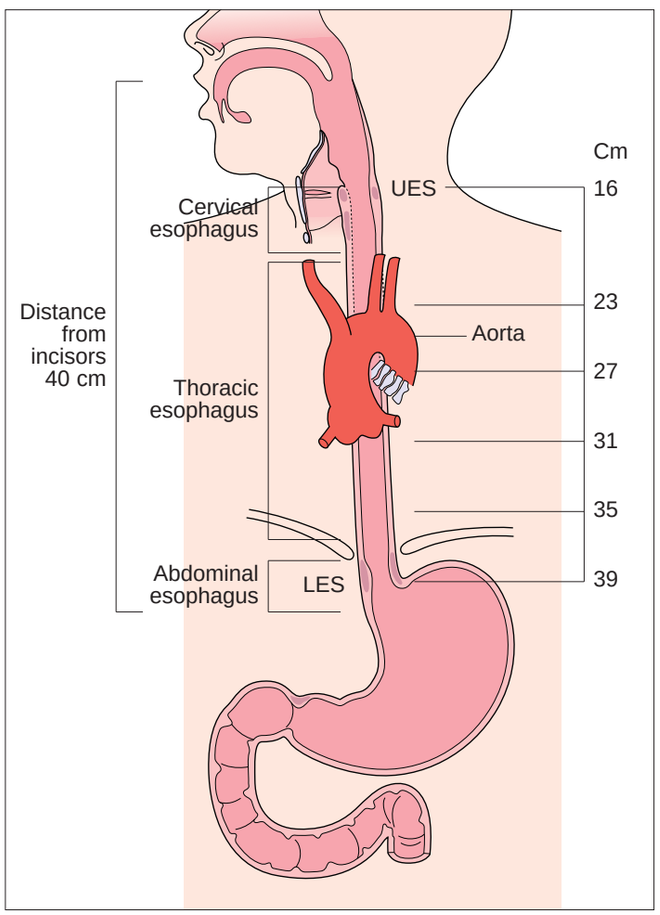
Gross anatomy

The esophagus is a muscular tube connecting the pharynx to the stomach, the proximal margin of which is the upper esophageal sphincter (UES). This is the functional unit that correlates anatomically with the junction of the inferior pharyngeal constrictor and cricopharyngeus muscles. The esophagus extends distally for 18–26 cm within the posterior mediastinum as a hollow muscular tube to the lower esophageal sphincter (LES) (**1.1**), which is a focus of tonically contracted, thickened, circular smooth muscle 2–4 cm long, that lies within the diaphragmatic hiatus.

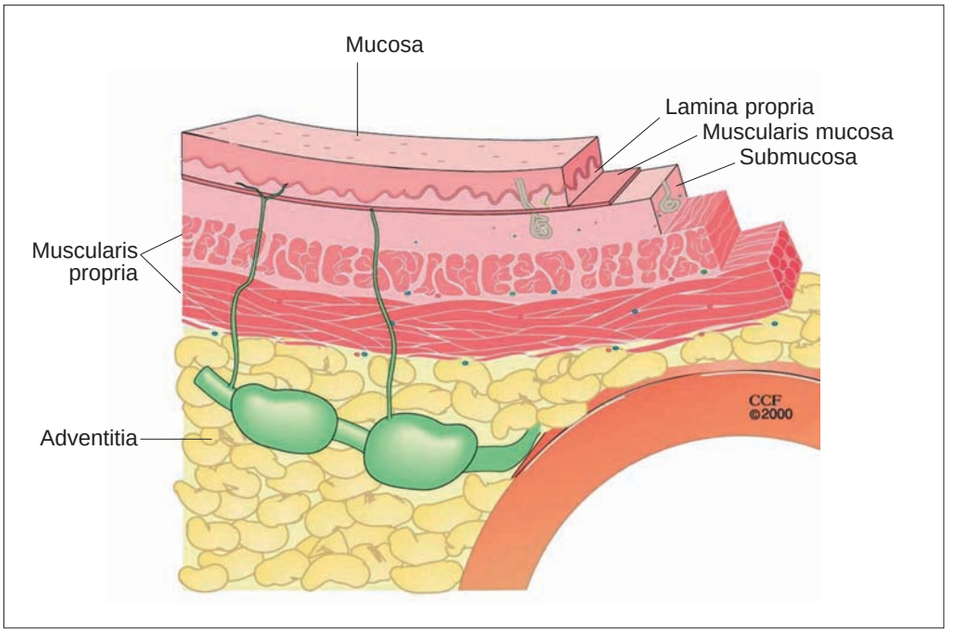
Anatomy of the esophageal wall

The esophageal wall is comprised of four layers: mucosa, submucosa, muscularis propria, and adventitia; it has no serosa, making it unique to the rest of the gastrointestinal (GI) tract. Normal mucosa consists of stratified squamous epithelium, lamina propria, and muscularis mucosa, with lymphatic drainage beginning in the lamina propria (**1.2**).

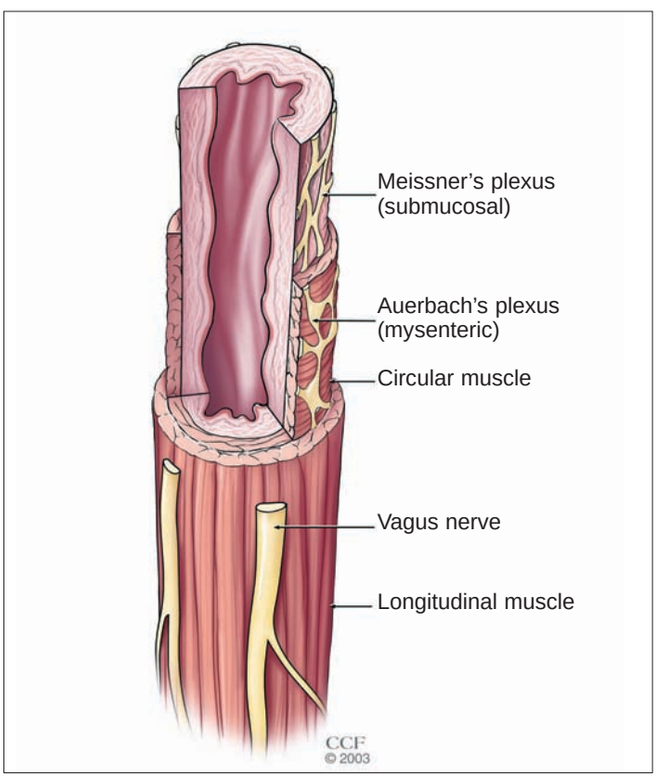
The muscularis propria consists of both skeletal and smooth muscle: the proximal 5–33% is skeletal muscle, the middle 35–40% is mixed, and the distal 50–60% is smooth muscle. Muscles are arranged into inner circular and outer longitudinal layers (**1.3**).



1.1 Schematic view of the esophagus and its relationship to neighboring structures. The proximal margin of the esophagus is the UES. The esophagus then extends for 18–26 cm within the posterior mediastinum as a hollow muscular tube to the LES.



1.2 Wall layers and lymphatic drainage of the esophagus. Note the four wall layers: mucosa (stratified squamous epithelium, lamina propria, and muscularis mucosa), submucosa, muscularis propria, and adventitia. There is a rich lymphatic supply, which begins in the lamina propria.



1.3 Cross-sectional anatomy of the esophagus. Note the outer longitudinal layer and inner circular layer of smooth muscle. Auerbach's plexus, which is responsible for peristalsis, is located between the two muscle layers. Meissner's plexus, responsible for sensation, is in the submucosa.

Esophageal innervation

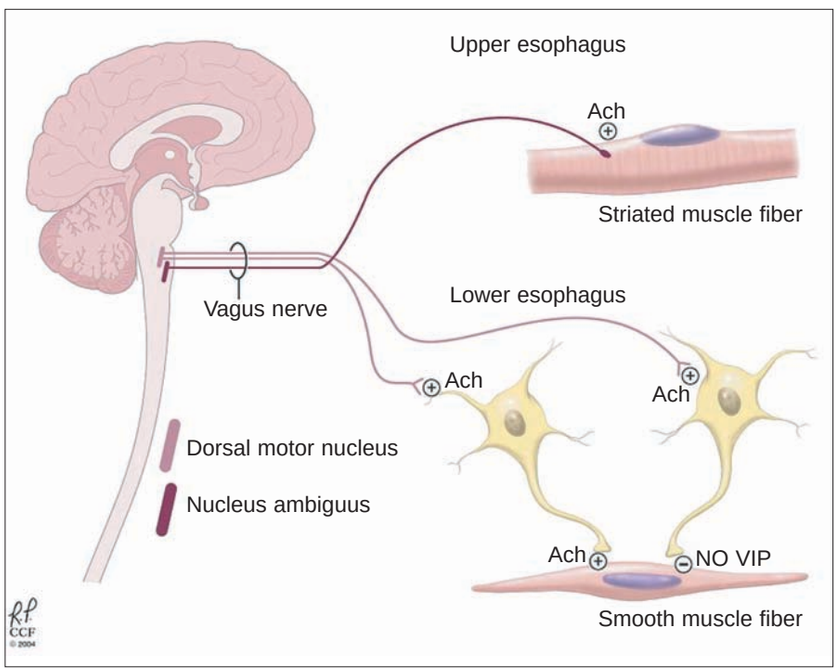
Smooth muscle portions are innervated by the vagus nerve, which controls peristalsis under physiologic conditions. Neural innervation is from the myenteric (Auerbach's) plexus located between the two muscle layers, and from Meissner's plexus located in the submucosal (**1.3**). The myenteric plexus is responsible for esophageal peristalsis, whereas Meissner's complex is the site of afferent sensory input.

There are two main neurotransmitters within the myenteric plexus (**1.4**): (1) acetylcholine produces excitatory stimulation, which mediates contraction of both longitudinal and circular muscle layers, with the largest effect proximally; (2) nitric oxide (NO) causes an inhibitory effect, predominantly on the circular layer, with the greatest effect distally.

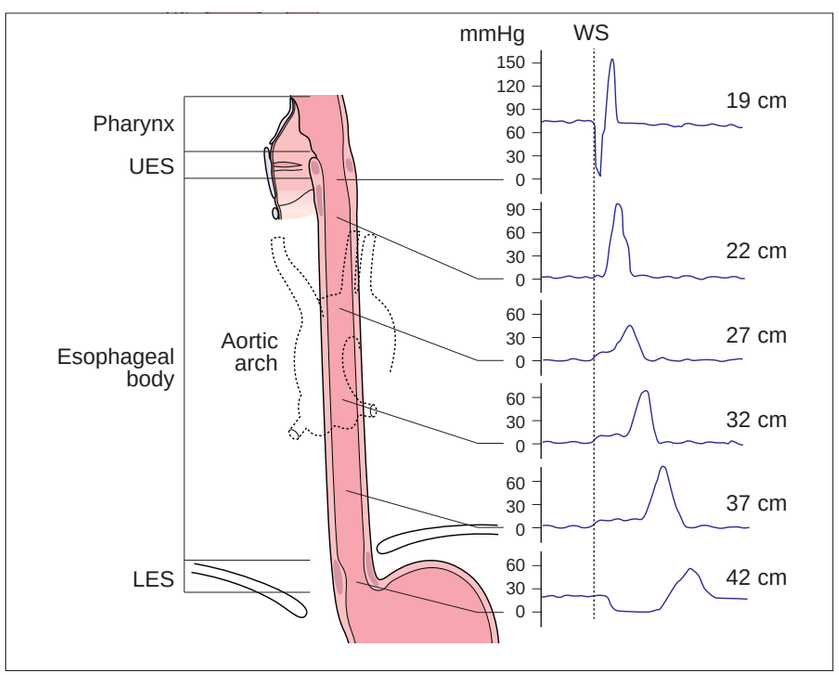
Normal deglutition

The UES, the esophageal body, and the LES act in a coordinated manner to allow swallowing. In the oropharyngeal/voluntary phase of swallowing, the food bolus is propelled into the pharynx from the mouth. This is followed by the esophageal/involuntary phase, during which the bolus is propelled from pharynx to stomach by a rapid sequence of precisely coordinated events (**1.5**), as described

below. The phase begins as the larynx becomes elevated and the epiglottis seals the airway. An immediate pharyngeal contraction then transfers the bolus through the relaxed UES into the esophagus. As the UES closes, progressive circular contraction begins in the upper esophagus and proceeds distally along the esophageal body to propel the bolus through the relaxed LES. Peristaltic pressures ranging from 30–180 mmHg are generated. The LES closes with a prolonged contraction, thus preventing movement of the bolus back into the esophagus. The mechanical effect of peristalsis is a stripping wave that milks the esophagus clean from its proximal to its distal end.



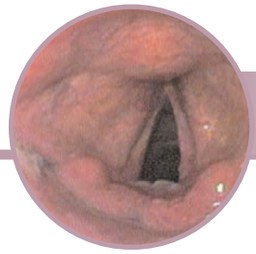
1.4 Innervation of the esophagus. The striated muscle in the proximal one-third of the esophagus is innervated by the somatic efferent cholinergic fibers of the vagus nerve originating from the nucleus ambiguus. In the distal two-thirds, the myenteric plexus is innervated by the pre-ganglionic cholinergic vagus nerve fibers from the dorsal motor nucleus. The myenteric plexus has two types of post-ganglionic neurons: excitatory cholinergic neurons, and inhibitory nitrinergic (NO) and vasoactive intestinal polypeptide- (VIP) containing neurons.



1.5 Normal esophageal peristalsis. The esophageal body and sphincters are intricately coordinated. UES pressure (located at 19 cm) falls quickly at swallow initiation (WS), followed by initiation of esophageal body peristalsis and LES relaxation (located at 42 cm). The peristaltic pressure tends to be lower in the proximal and mid-esophagus, and higher in the distal smooth muscle portion of the esophagus.

Further reading

Goyal RK, Prasad M, Chang HY (2004). Functional anatomy and physiology of swallowing and esophageal motiliy. In *The Esophagus*, DO Castell, JE Richter (eds). Lippincott Williams and Wilkins, New York, pp 1-36.



Chapter 2

Esophageal testing

Endoscopy

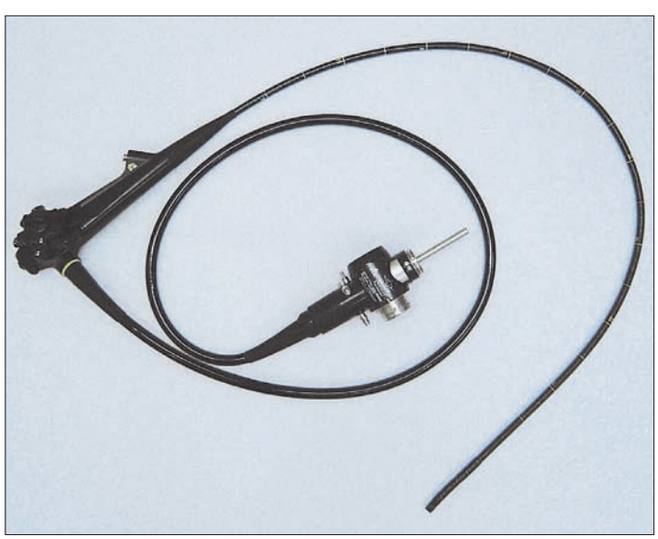
Indications

Endoscopy is the technique of choice to detect structural abnormalities of the esophagus and to evaluate the mucosa. The most common indications include dysphagia, symptoms of gastroesophageal reflux disease (GERD), and gastrointestinal (GI) bleeding.

Equipment

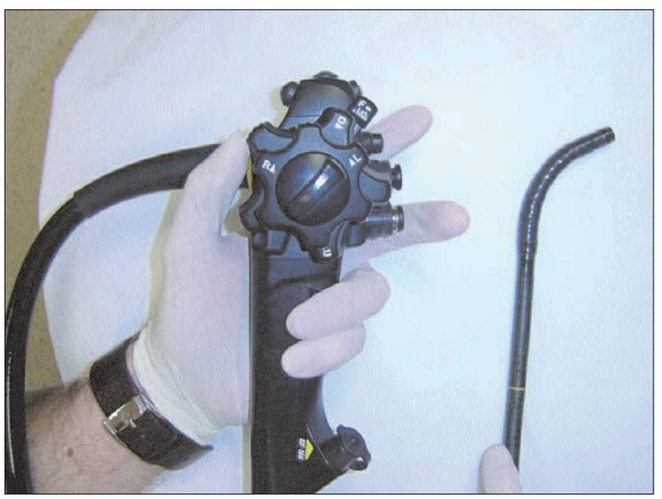
Endoscopy allows direct visualization of the esophageal mucosa and detect structural abnormalities**.** Endoscopes use fiberoptic technology to capture and transmit the image from the distal end of the endoscope (**2.1**). Four-way tip deflection is permitted by the use of two control knobs, one with up/down movement and the other with right/left movement (**2.2**–**2.4**). Endoscopes are equipped with internal channels for air, water, suction, and instruments (**2.5**, **2.6**). The separate instrument channel allows the passage of biopsy forceps and other instruments used for treatment of upper GI disorders. Visualization is improved when air is used to insufflate the esophagus and stomach, which are normally compressed.

Both small and large scopes are available (**2.7**, **2.8**): the 'therapeutic' endoscope contains a larger instrument channel that permits passage of 'jumbo' biopsy forceps and larger coagulation devices, whereas 'pediatric' endoscopes may be as small as 4 mm and allow transnasal or transoral endoscopy without sedation.



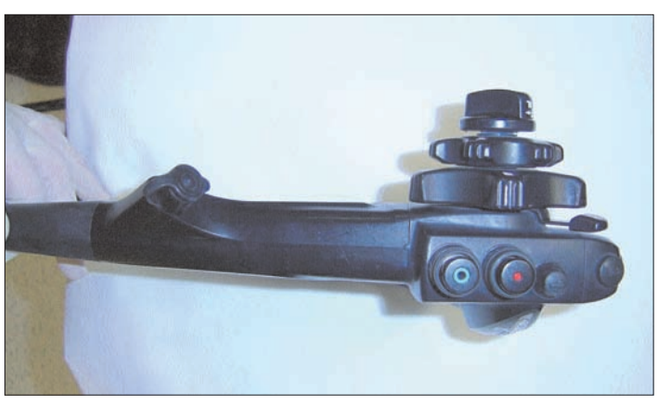
2.1 The typical forward-viewing endoscope used for examination of the upper GI tract in an adult. Standard endoscopes range from 8–11 mm in diameter, and are from 100–160 cm in length. Controls allow for manipulation of viewing direction, air insufflation, suction, water spray, and taking still photos or video.

2.2 Side view close up. The two control knobs allow for four-way tip deflection. The outer/smaller dial is for right/left movement and the inner/larger dial for up/down movement. The biopsy channel allows for insertion of multiple instruments including biopsy forceps, brushes, electrocautery probes, snares, and sclerotherapy needles.



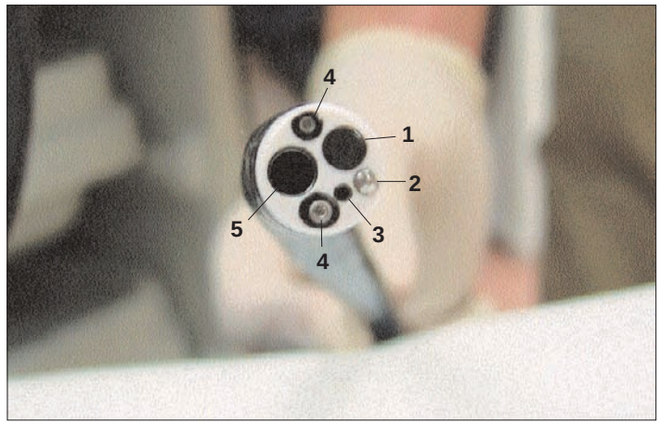
2.3 Rotating the inner dial up with the thumb causes the tip of the endoscope to deflect downward.

2.4 Rotating the inner dial down in the opposite direction causes the tip to deflect upward. Note the degree of deflection is not as great as when deflected downward.



2.5 Front view of the endoscopic controls. The two buttons allow for suction, water spray, and air insufflation. The forefinger is used to press the top button for suction. The second finger is usually employed to cover the second button resulting in air insufflation. Pressing this button will result in water spray.

2.6 End view of the endoscope. Note the three channels for suction, insufflation, and instruments. Two light sources are also present. (1: video camera lens; 2: water flush nozzle for lens cleaning; 3: auxillary water channel; 4: light; 5: instrument channel.)



2.7 Upper GI endoscopes come in a variety of sizes. The small caliber endoscope (right), or 'pediatric' endoscope, has a diameter of 5–6 mm. It is ideal for use in children, but is also useful in adults with strictures or narrowings that the standard caliber endoscope cannot pass. These smaller instruments do have disadvantages, including decreased durability, poorer image quality, and smaller biopsy sizes. The larger 'therapeutic' scope (left) allows the passage of larger tools and more effective suction.

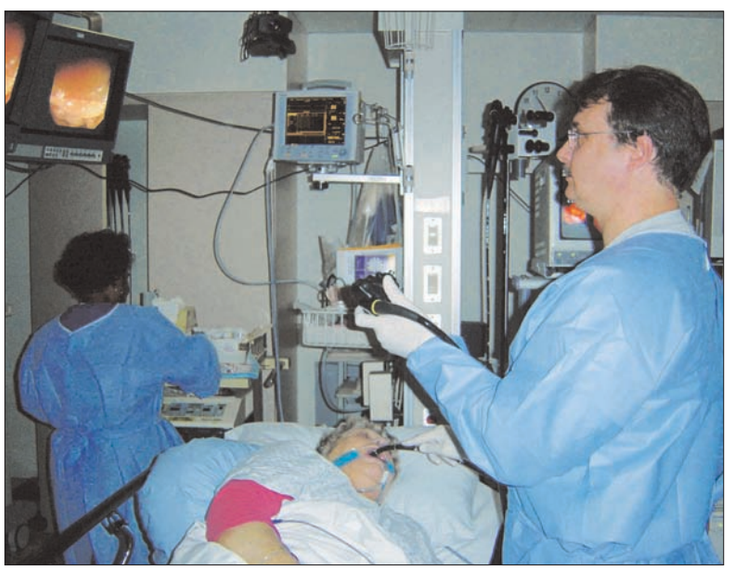
2.8 End view of instrument channel of different size endoscopes. Note the decrease in size of the channel from the therapeutic endoscope (left) to the small caliber endoscope (right).

Technique

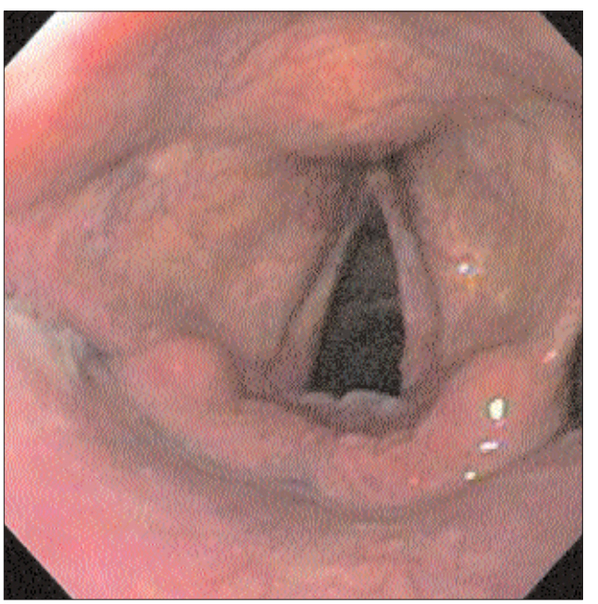
In the United States, upper GI endoscopy is routinely performed under conscious sedation. Local anesthetic is sprayed on the posterior pharynx and intravenous sedation administered while the patient is in the left lateral decubitus position (**2.9**). The endoscope is inserted into the posterior pharynx where the pharynx and larynx can be examined for abnormalities (**2.10**). The endoscope is then advanced under direct vision into the tonically closed upper esophageal sphincter. The patient is asked to swallow to relax the upper esophageal sphincter (UES) and the endoscope is advanced to the proximal esophagus, where the mucosa should normally be smooth and light pink (**2.11**, **2.12**).

The area of the gastroesophageal junction (GEJ) is carefully examined to identify specific landmarks (**2.13**), and is defined by the proximal margin of the gastric folds. The squamocolumnar junction (SCJ) can be recognized by the irregular Z-line demarcating the interface between the light pink esophageal squamous mucosa and the red columnar mucosa gastric mucosa (**2.14**).

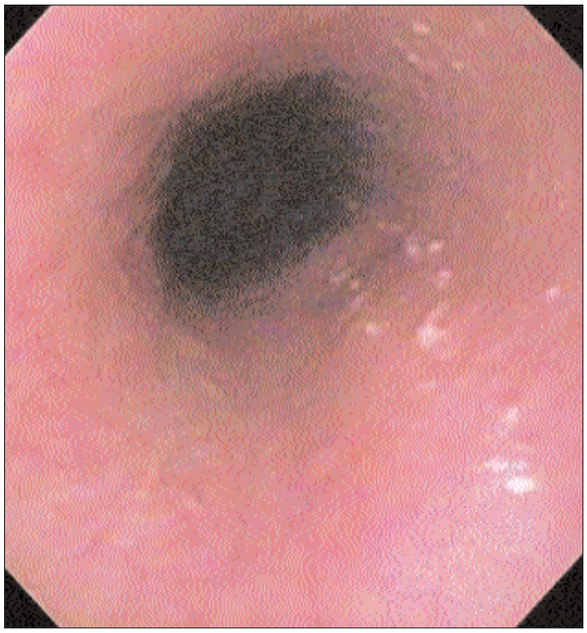
The diaphragmatic hiatus can be identified by diaphragmatic contraction noted during patient respiration. The SCJ, the GEJ, and the diaphragmatic hiatus are normally located at the same level, unless pathology is present. In patients with Barrett's esophagus, the SCJ is more proximal in the esophagus than the GEJ, whereas in patients with hiatal hernia, the GEJ is more proximal than the diaphragmatic indentation. While in the stomach, the endoscope is 'retroflexed' to look back at the GEJ; this yields a better view of the gastric side of the junction (**2.15**).



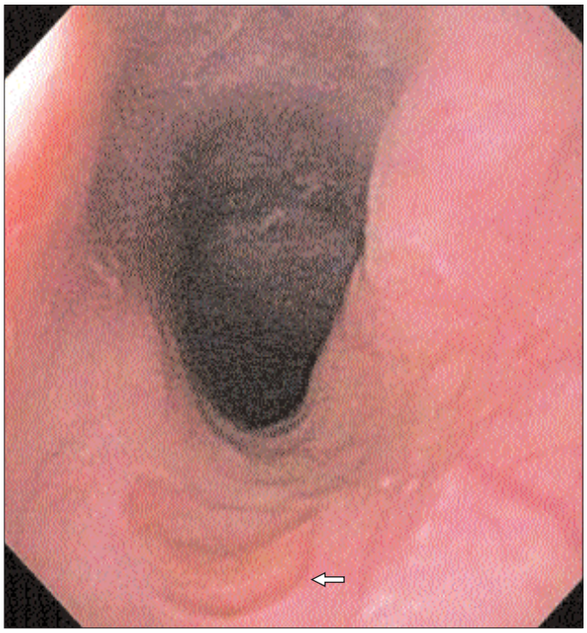
2.9 The patient is placed in left lateral decubitus position for proper positioning. The endoscopist stands directly in front of the patient's mouth with the view screens located directly opposite. (Courtesy of John J Vargo, MD, Cleveland Clinic, Ohio, USA.)



2.10 An endoscopic view of normal appearing vocal cords. This landmark is identified as an endoscopic exam begins, after the endoscope is passed through the incisors and over the tongue. Patients with extraesophageal reflux disease can present with symptoms, such as hoarseness, which can be caused by exposure of the vocal cords to gastric acid. Findings suggestive of reflux disease may include erythema, edema, granulomas, ulcerations, and laryngeal carcinoma.

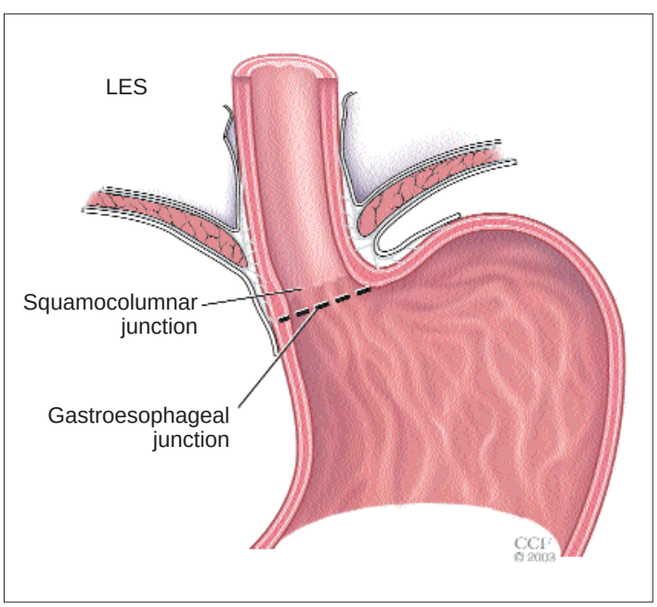


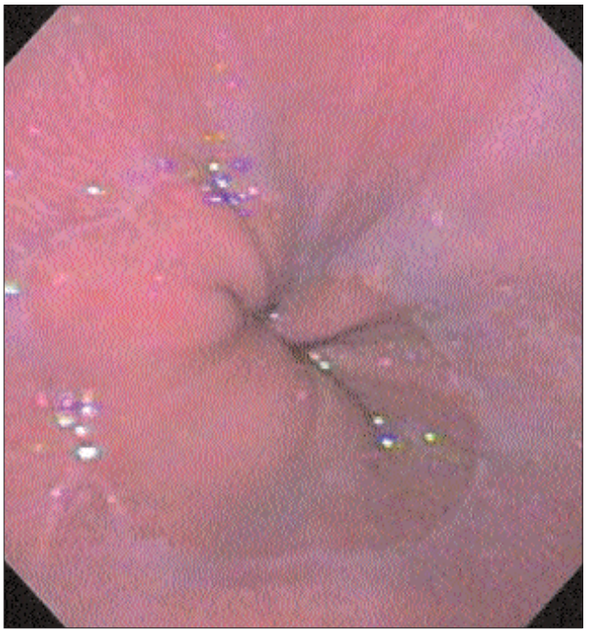
2.11 Endoscopic appearance of the mid-esophagus during a normal examination. The squamous mucosa is pale and pink, without ulceration or inflammation. The lumen is of uniform caliber, and expands uniformly with air insufflation. Landmarks seen as the esophagus is traversed include pulsation of left atrium and aorta along with indentation from left mainstem bronchus.



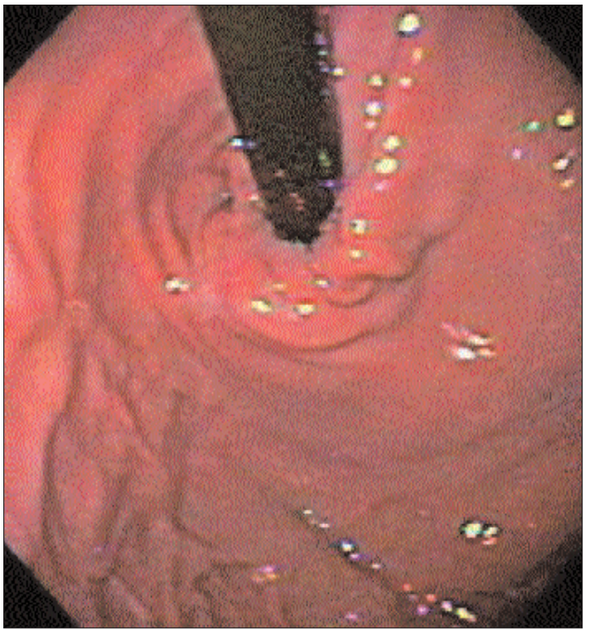
2.12 An esophageal inlet patch (arrow) is an area of heterotropic gastric epithelium found in the cervical esophagus. Note the darker red gastric mucosa, in contrast to the pale, pink esophageal mucosa. This is a common finding on upper endoscopy, and does not cause any symptoms in the patient. Inlet patches do not undergo malignant transformation, and usually no further follow-up is warranted.

2.13 Schematic diagram of the composition of the normal gastroesophageal junction. Note the relationship of the squamocolumnar junction to the diaphragm, which comprises the LES. The LES is the most important barrier protecting the esophagus from the regurgitation of gastric contents.





2.14 An endoscopic view of a normal SCJ. The more proximal pale pink esophageal squamous mucosa meets the darker red gastric mucosa. The junction is irregular, and is called the 'Z-line'. The location of the transition point more than 2 cm above the diaphragm signifies hiatal hernia. This junction is usually found at 38–40 cm from the incisor teeth in adults.



2.15 Gastric cardia on endoscopic retroflexion. Abnormalities to be noted include hiatal hernia, ulcers, gastric varices, and Mallory–Weiss tears.

Endoscopic ultrasound

Indications

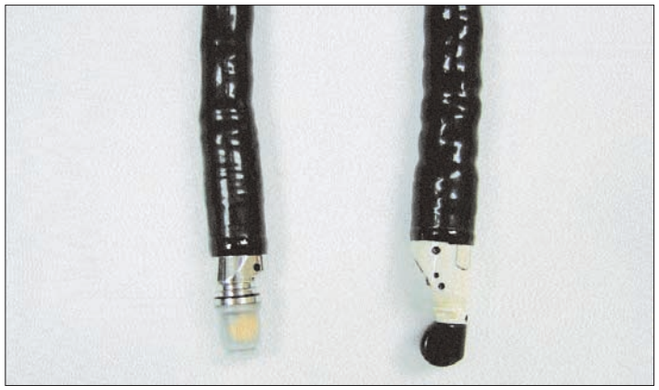
Endoscopic ultrasound (EUS) provides images of the distinct layers of the esophageal wall and periluminal structures (such as lymph nodes). The primary indications for esophageal EUS are staging of esophageal cancer and evaluation of submucosal esophageal lesions.

Equipment

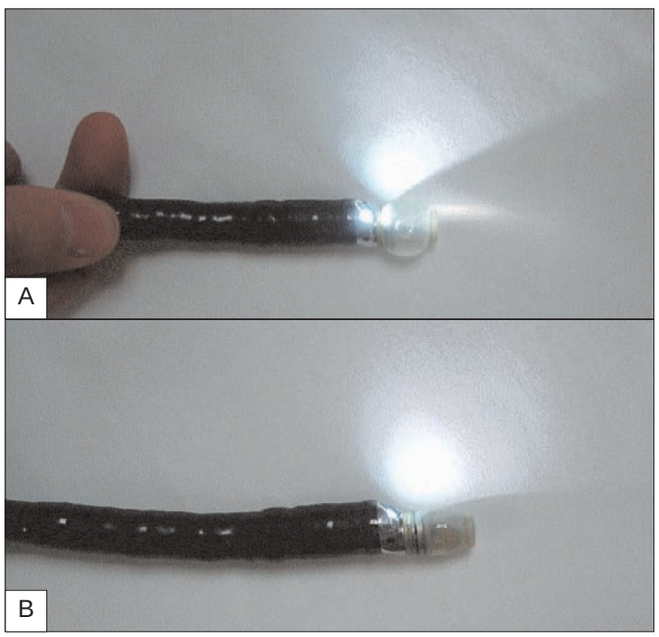
An endoscope is used that has ultrasound transmission and reception capability at the tip of the instrument (**2.16**, **2.17**). Linear echoendoscopes scan in the same plane as the long axis of the endoscope, whereas radial echoendoscopes have a rotating mechanical ultrasound probe that scans in a circle at 90 degrees to the long axis of the endoscope.

Technique

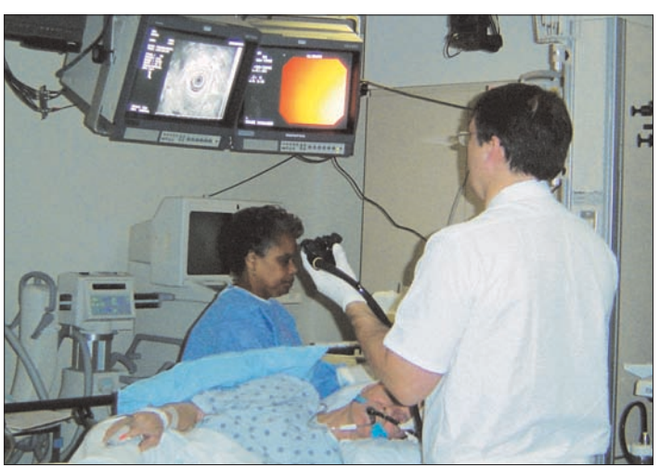
The echoendoscope is inserted using a similar technique to a regular endoscope. Two video screens are used: one displays a standard endoscopic image, and the other the ultrasound image (**2.18**). The endosonographic layers of the esophagus can then be delineated as five alternating hyperechoic and hypoechoic bands that correspond to the histologic layers (*Table 2.1*, **2.19**). Structures adjacent to the esophagus including the aorta, spine, left lobe of the liver, left atrium, lungs, and lymph nodes can also be visualized (**2.20**–**2.23**). With a linear instrument, fine-needle aspiration (FNA) can be performed of adjacent lymph nodes. This is critical for accurately staging esophageal cancer.



2.16 View of echoendoscopes. The radial echoendoscope (left) has a rotating mechanical ultrasound probe that scans in a circle 90 degrees to the long axis of the scope. The linear echoendoscope (right) scans in the long axis of the scope.



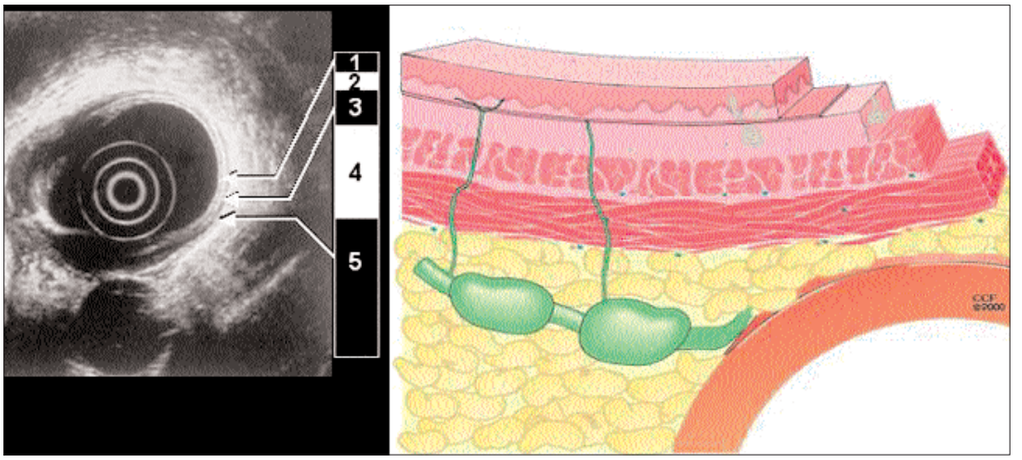
2.17 Balloon insufflation. A small latex balloon is placed over the ultrasound transmitter. With the balloon filled with water (**A**), better acoustic coupling can be achieved between the probe and the esophageal wall. This results in an improved ultrasound image. Note the light source is on which will provide an oblique endoscopic view.



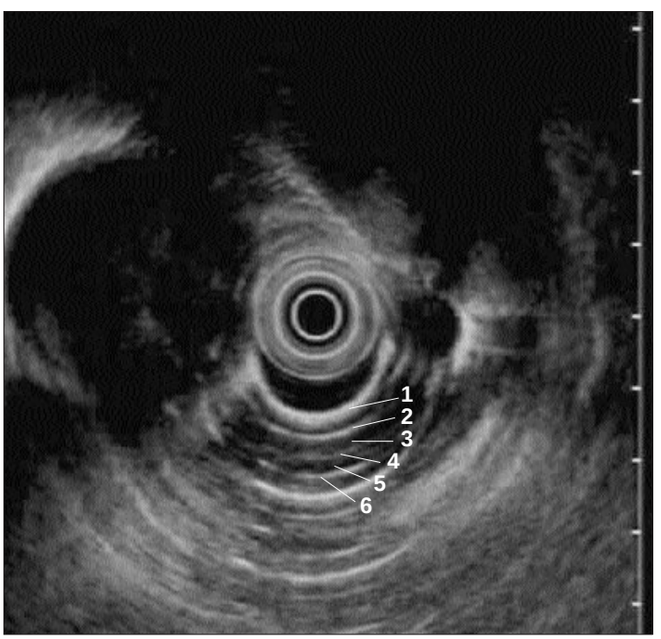
2.18 Two video screens are utilized: one screen shows the standard endoscopic image and the other the ultrasound image. (Courtesy of John J Vargo, MD, Cleveland Clinic, Ohio, USA.)

Table 2.1 Endosonographic appearance of esophageal wall layers

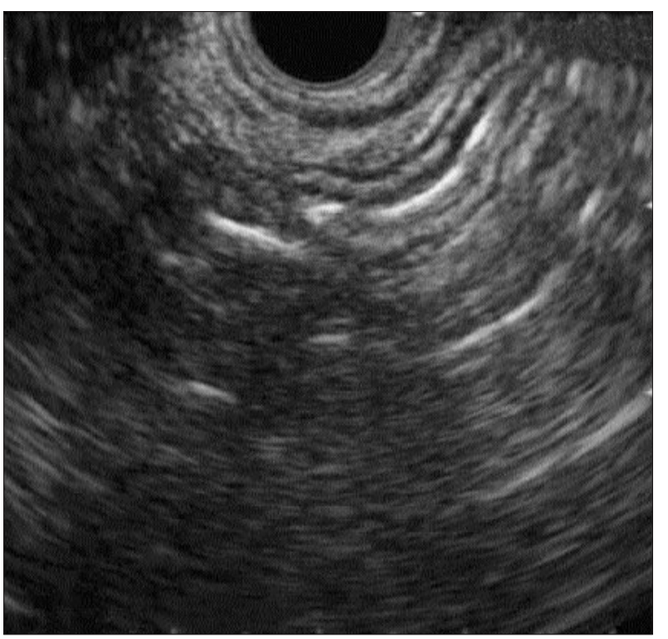
Esophageal wall layer	*Endosonographic appearance*
Superficial mucosa	Hyperechoic
Deep mucosa	Hypoechoic
Submucosa	Hyperechoic
Muscularis propria	Hypoechoic
Adventitia	Hyperechoic



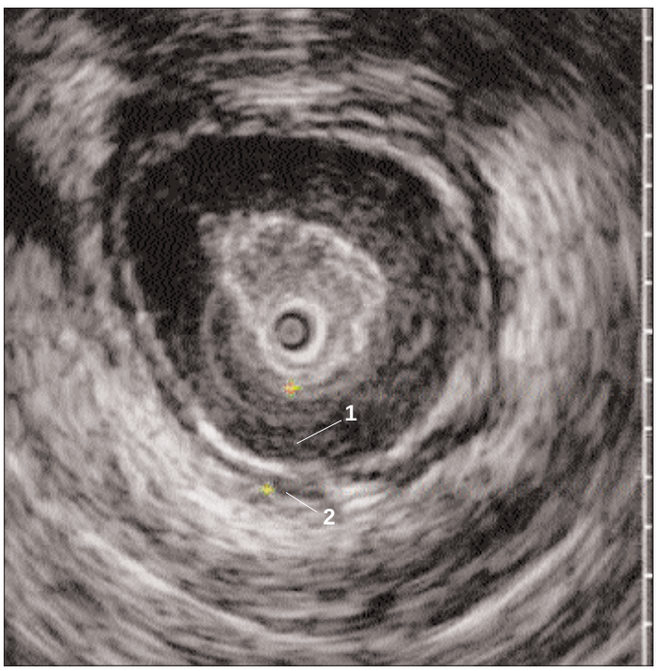
2.19 Schematic view of the esophageal wall and associated endoscopic ultrasound view. The endosonographic layers of the esophagus can be delineated as five alternating hyperechoic and hypoechoic bands that correspond to the histologic layers. The innermost layer is hyperechoic and corresponds to the interface between the ultrasound waves and the superficial mucosa. The second layer is hypoechoic and corresponds to the deep mucosa. The third layer is hyperechoic and corresponds to the submucosa. The fourth layer represents muscularis propria and is depicted as a hypoechoic band. The fifth layer is hyperechoic and represents the adventitia in the esophagus.



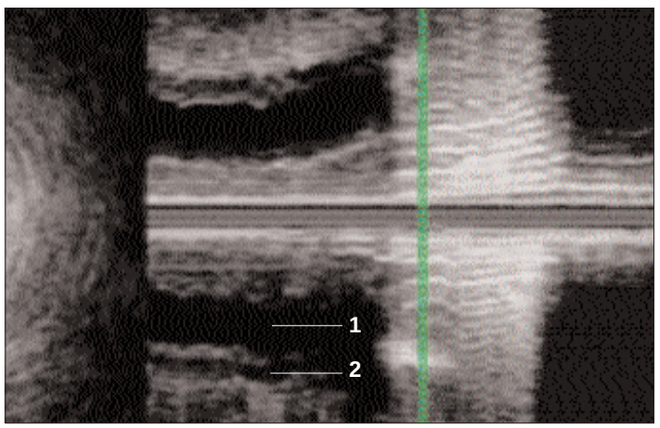
2.20 Normal endoscopic ultrasound, radial. (1: mucosa and muscularis mucosa; 2: submucosa; 3: inner circular smooth muscle; 4: intermuscular connective tissue; 5: outer longitudinal muscle; 6: adventitia.)



2.21 Normal endoscopic ultrasound, linear. (Courtesy of John J Vargo, MD, Cleveland Clinic, Ohio, USA.)



2.22 Endoscopic ultrasound of the LES. An echo-endoprobe with higher frequency (higher detail, less penetration) can allow detailed visualization of the musculature of the LES. Note the hypoechoic inner circular and outer longitudinal layers separated by a thin band of hyperechoic material (1: inner circular smooth muscle; 2: outer longitudinal smooth muscle).



2.23 3-D Endoscopic ultrasound of the LES. Here the ultrasound image is reconstructed to a longitudinal view. Again note the two layers of the muscularis propria (1: inner circular smooth muscle; 2: outer longitudinal smooth muscle).

Barium swallow

Introduction

Contrast studies enable radiographic examination of the esophagus and can be done alone, in combination with oropharyngeal evaluation, or as a part of an upper GI series. The following techniques are used for routine examination:

- Double contrast.
- Full-column.
- Mucosal relief.
- Fluoroscopic observation.

Indications

Indications for a barium swallow include:

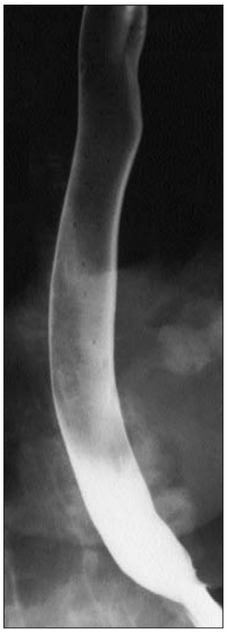
- Dysphagia.
- Odynophagia.
- GERD.
- Esophageal strictures.
- Esophageal motility disorders.
- Esophageal function testing.

Double contrast

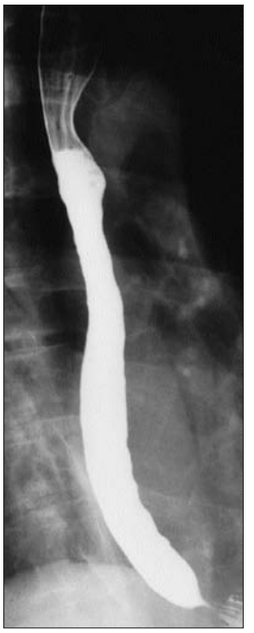
This can be achieved by coating the esophagus with dense barium and subsequently distending it with gas (**2.24**). Double contrast is a good test for evaluating the esophageal mucosal surface to detect small neoplasms, esophagitis, and diverticulosis. In some cases the gastroesophageal junction may not adequately distend, resulting in poor detection of hiatal hernias, lower esophageal mucosal rings, and peptic strictures.

Full-column

This involves rapid filling of the esophagus with barium (**2.25**) while patient is in prone position and is a good test for evaluating esophageal motility. It is also a useful technique to visualize hiatal hernias, lower esophageal mucosal rings, and peptic strictures (see figures from the appropriate sections), but may not detect small neoplasms, mild esophagitis, and esophageal varices.



2.24 Double contrast barium swallow. Double contrast barium swallow is performed by coating the esophagus with a dense barium and distending it with gas. This allows simultaneous examination of the distended esophagus and its mucosal surface.



2.25 Full-column barium swallow, obtained by rapid filling of the esophagus with barium while the patient is in the prone position. Esophageal motility may be assessed with fluoroscopy in the prone position by observing multiple swallows of barium. It is a good test to visualize hiatal hernias, lower esophageal mucosal rings, and peptic strictures. However, it may not detect small neoplasms, mild esophagitis, and esophageal varices.

Mucosal relief

Imaging of the collapsed esophagus coated with dense barium allows good visualization of smooth, longitudinal esophageal folds. Irregularity of the thickening of these folds can be due to small neoplasms, esophagitis, and esophageal varices. Lesions that require esophageal distension are not seen well.

Fluoroscopic observation

Fluoroscopic observation provides a motion recording of esophageal function and motility with each barium swallow, which facilitates evaluation of esophageal and oropharyngeal functional disorders.

Esophageal manometry

Introduction

Manometry can be used as a diagnostic test to evaluate esophageal motor function.

It measures intraluminal pressures and coordination of the pressure activity of the three functional regions of the esophagus: the lower esophageal sphincter (LES), esophageal body, and UES. The manometry probe consists of a 4 mm polyvinyl catheter containing several small caliber lumens that are perfused with water from a low compliance perfusion device (**2.26**). When a catheter port is occluded by an esophageal contraction, water pressure builds within the catheter exerting a force, which is conveyed to an external transducer. The electrical signals from the transducers are transmitted to a computer, which produces a graphic record.

Indications

Indications for manometry are presented in *Table 2.2*, and include:

- Evaluation of dysphagia in patients without evidence of mechanical obstruction, such as strictures, or in whom achalasia is suspected.
- Defining the location of the LES for placement of intraluminal devices, such as a pH probe, which requires positioning relative to LES.
- Pre-operative evaluation for anti-reflux surgery in patients suspected of having esophageal motility disorder such as achalasia.
- Other possible indications are:
  - Evaluation of dysphagia in patients treated for achalasia or have undergone anti-reflux surgery.
  - Routine pre-operative assessment of esophageal peristalsis prior to anti-reflux surgery.

Manometry is *not* indicated for making or confirming the diagnosis of GERD, or as the initial test for non-cardiac chest pain.

Technique

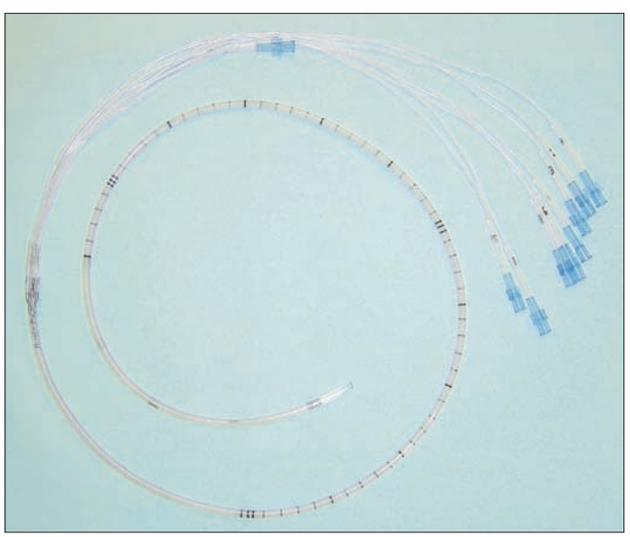
Manometry is performed after an overnight fast using a round 4 mm polyvinyl catheter continuously perfused with distilled water at a rate of 0.5 ml/min by a low compliance, pneumohydraulic capillary infusion system (**2.27**). The stationary pull-through technique is used to determine the location and length of the LES and UES.

Esophageal motility is then assessed by using 10 wet swallows (5 ml water each) with the distal recording site positioned 5 cm above the LES. *Tables 2.3* and *2.4* demonstrate normal and pathological values for manometry and figure **2.28** shows a typical esophageal manometric tracing.

Table 2.2 Indications for esophageal manometry

Indicated	*Possibly indicated*	*Not indicated*
Evaluation of dysphagia in patients without evidence of mechanical obstruction or if achalasia is suspected	Evaluation of dysphagia in patients treated for achalasia or undergone anti-reflux surgery	As the initial test for non-cardiac chest pain
Pre-op evaluation for anti-reflux surgery in patients suspected of having esophageal motility disorder, such as achalasia	Routine pre-op assessment of esophageal peristalsis prior to anti-reflux surgery	Diagnosis of GERD
Defining the location of LES for placement of intraluminal devices, such as pH probe, which requires positioning relative to LES		

GERD: gastroesophageal reflux disease; LES: lower esophageal sphincter

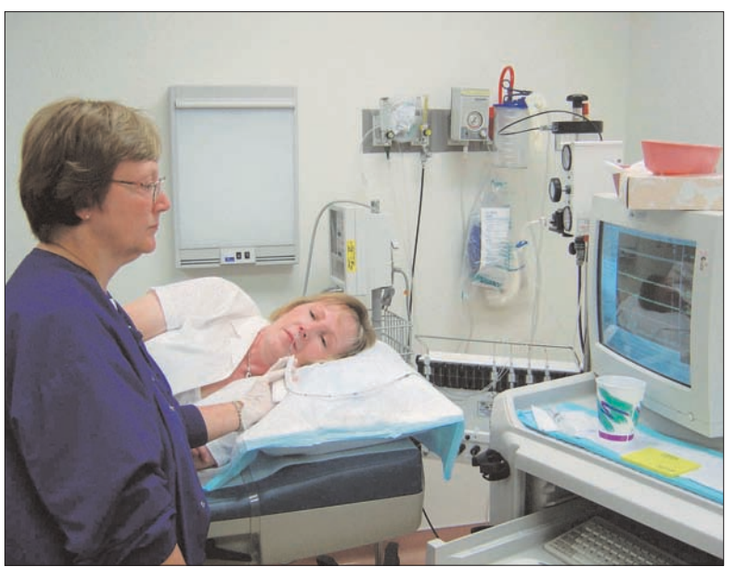


2.26 Esophageal manometry probe, consisting of a 4 mm polyvinyl catheter that contains several small caliber lumens that are perfused with water from a low compliance perfusion device. When a catheter port is occluded by an esophageal contraction, water pressure builds within the catheter exerting a force, which is conveyed to an external transducer. The electrical signals from the transducers are transmitted to a computer, which produces a graphic record.

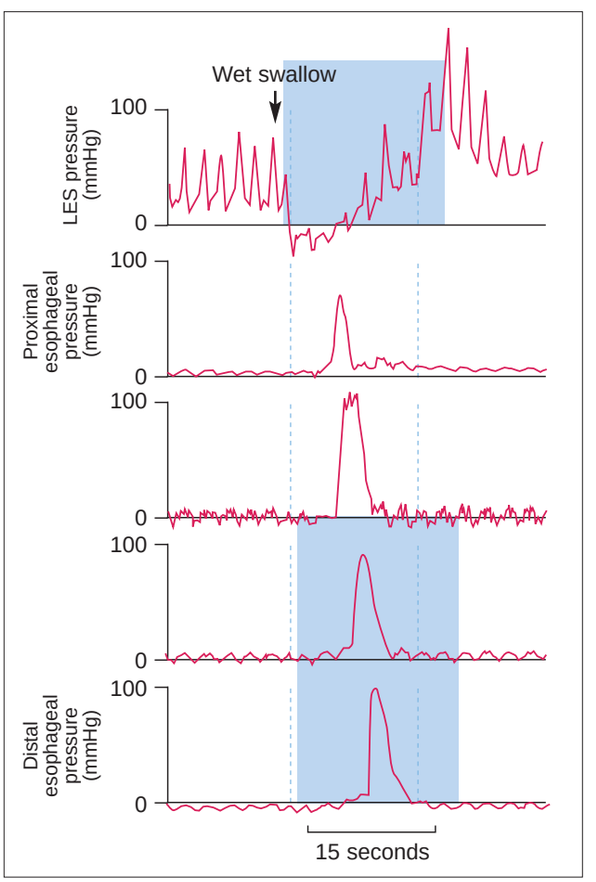
Table 2.3 Normal values for esophageal manometry

LESP	10.0–45.0 mmHg
Esophageal body amplitude	30.0–180.0 mmHg
Esophageal body contraction duration	1.0–6.0 seconds
Distal onset velocity	<8.0 seconds
UESP	30.0–118.0 mmHg

LESP: lower esophageal sphincter pressure
UESP: upper esophageal sphincter pressure



2.27 Esophageal manometry in a patient. The manometry probe is inserted into the esophagus via nares. The catheter is then advanced to approximately 60 cm, which is well within the stomach. At this point, the patient is placed supine on the left side and the catheter is calibrated. The stationary pull-through technique is then used. This involves slowly withdrawing the catheter through the LES, esophagus, and UES. Resting LES pressure and relaxation are thus evaluated by a series of wet swallows.



2.28 Normal manometric tracing. The wet swallow initiates a progressive peristaltic contraction in the body of the esophagus with wave amplitudes of 30–180 mmHg. The LES relaxes completely to gastric baseline at the end of peristalsis.

Table 2.4 Manometric criteria for esophageal motility disorders

Diagnosis	*Criteria*
Normal	≤20% ineffective; ≤10% simultaneous; average DEA <180 mmHg and >30 mmHg; normal LES resting pressure
Achalasia	Isobaric simultaneous contractions or aperistalsis; poorly relaxing LES
Scleroderma	Low amplitude or absent contraction in distal esophagus, with or without low LES pressure
DES	≥20% simultaneous normal amplitude esophageal contractions – intervening normal peristalsis
IEM	≥30% of swallows with amplitude <30 mmHg in either of the two distal sites at 5 and 10 cm above LES
Nutcracker esophagus	Normal peristalsis with DEA >180 mmHg
Poorly relaxing LES	Average LES residual pressure >8 mmHg
Hypertensive LES	LES resting pressure >45 mmHg
Hypotensive LES	LES resting pressure <10 mmHg

DEA: distal esophagueal amplitude; DES: diffuse esophageal spasm; IEM: ineffective esophageal motility; LES: lower esophageal sphincter

Ambulatory monitoring

24-hour pH

Introduction

This is an important tool in the diagnosis and management of GERD as it can detect and quantify gastroesophageal reflux and correlate symptoms temporally with reflux.

Indications

Indications for ambulatory pH monitoring are presented in *Table 2.5* and include:

- To document abnormal acid exposure in patients with suspected GERD but without endoscopic esophagitis.
- To evaluate the efficacy of medical or surgical therapies for GERD:
  - In patients with GERD who are refractory to proton-pump inhibitor (PPI) therapy.
  - In patients with anti-reflux surgery who have continued reflux symptoms.

Other possible indications include:

- Evaluation of non-cardiac chest pain.
- Evaluation of ear, nose and throat (ENT) manifestations associated with GERD that are refractory to aggressive PPI therapy.
- Evaluation of reflux-induced asthma in an adult patient with new-onset asthma. (A positive test does not prove causality.)

The test is *not* indicated to detect or confirm reflux esophagitis (reflux esophagitis is an endoscopic diagnosis), or for evaluation of non-acid reflux.

Table 2.5 Indications for pH monitoring

Indicated	*Possibly indicated*	*Not indicated*
Suspected GERD without endoscopic esophagitis	Non-cardiac chest pain	Detection of reflux esophagitis
Assessment of efficacy of medical or surgical therapies of GERD	ENT manifestation of GERD refractory to PPI therapy	Evaluation of non-acid reflux
	Reflux induced asthma	

ENT: ear, nose, and throat; GERD: gastroesophageal reflux disease; PPI: proton-pump inhibitor

Equipment

The pH probe consists of 2.1 mm monocrystal line catheters with antimony electrodes. There are three types of probe:

- Single: has one pH sensor at the catheter tip; it measures pH at the distal esophagus (5 cm above LES) (**2.29**).
- Double: has two pH sensors 15 cm apart to detect pH at the distal and proximal esophagus (**2.29**).
- Triple: composed of two catheters; one catheter has two pH sensors for hypopharyngeal and proximal esophageal pH monitoring and another catheter has one pH sensor for the distal esophagus (**2.30**).

Technique

The pH probe is inserted into the esophagus via the nares and a distal electrode is positioned 5 cm above the proximal border of the LES. LES location is usually determined prior to pH probe placement using esophageal manometry. The pH electrodes are connected to a portable digital data recorder (**2.31**) (Digitrapper Mark III Gold; Synectics Medical AB, Stockholm, Sweden) worn around the waist, which stores pH data samples every 4 seconds for up to 24 hours.

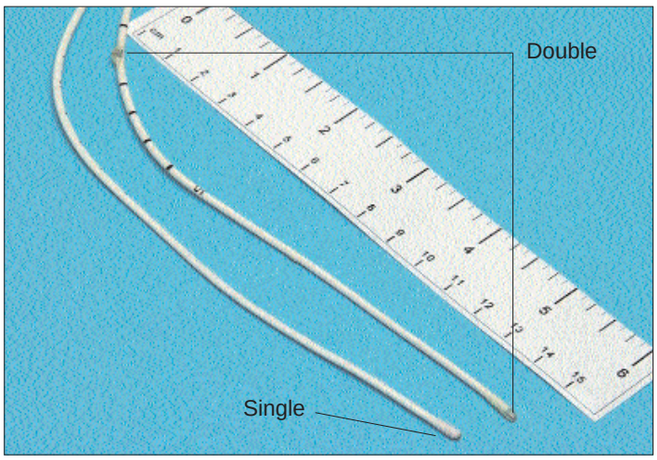
Patients are required to keep a diary of symptoms, meal times, time of lying down for sleep, and time of rising in the morning. They are instructed to perform normal daily activities, consume their usual diet without restrictions, and avoid taking naps during the daytime. Patients return on the following day after a minimum of 18 hours to have the probes removed and diaries reviewed. Data is analyzed using a dedicated computer program (Gastrosoft, Irving, TX, USA).

Normal values

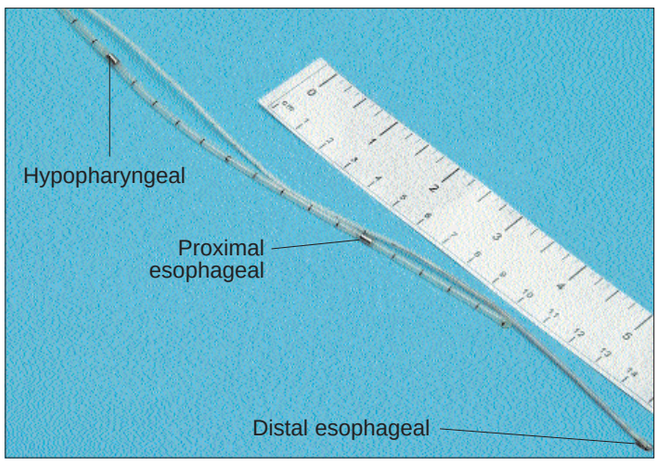
A pH <4 is used as a cutoff for acid reflux, as this is the level which is associated with the onset of heartburn (1) and has been shown to best discriminate between normal and GERD cases (2). It has been found that esophageal pH is normally <4.0 for a small percentage of the time (3) (*Table 2.6*, **2.32**–**2.35**).

Table 2.6 Normal values for pH monitoring

pH electrode	*Body position*	*% time pH <4.0*
Proximal	Total	>1.1
	Upright	>1.7
	Supine	>0.6
Distal	Total	>5.5
	Upright	>8.3
	Supine	>3.0

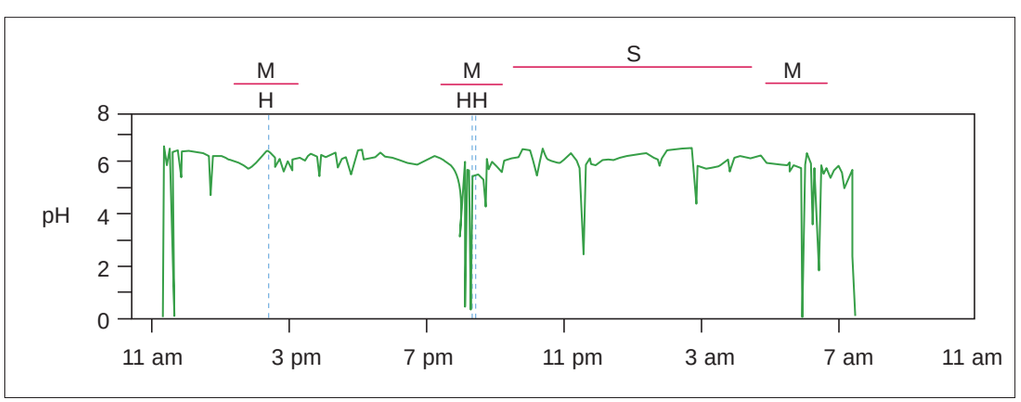


2.29 Single and double pH probes. A single pH probe contains one electrode which detects distal esophageal acid exposure at 5 cm above LES. The double pH probe has two electrodes 15 cm apart for acid exposure detection at both distal and proximal esophagus.

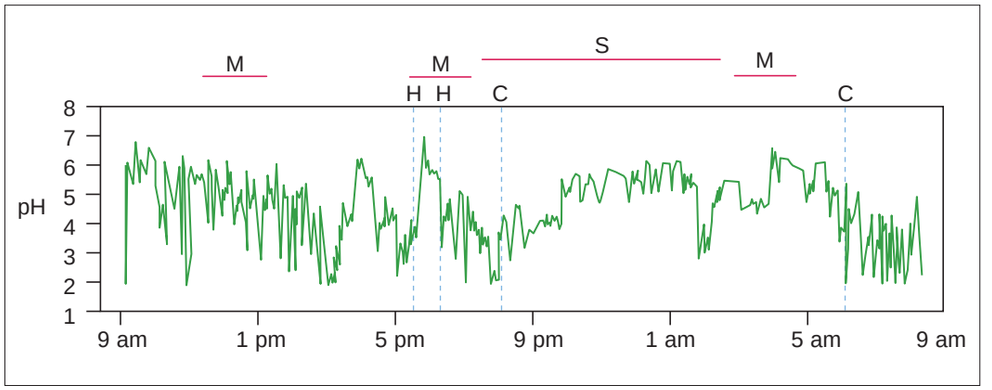


2.30 Triple pH probe. It consists of three electrodes which are used to detect acid exposure in the distal and proximal esophagus and in the hypopharynx.

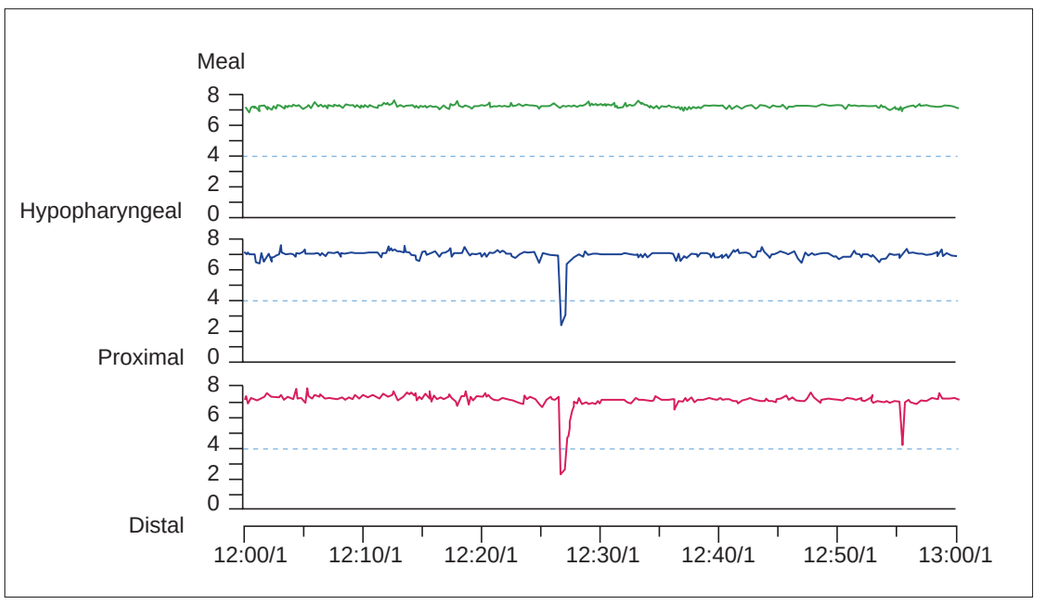
2.31 A triple pH probe with portable data logger. The data loggers use sampling rate of eight per minute with 0.1 pH unit resolution. There are input buttons on the data logger to indicate events such as heart burn, meal time, supine position, and so on.



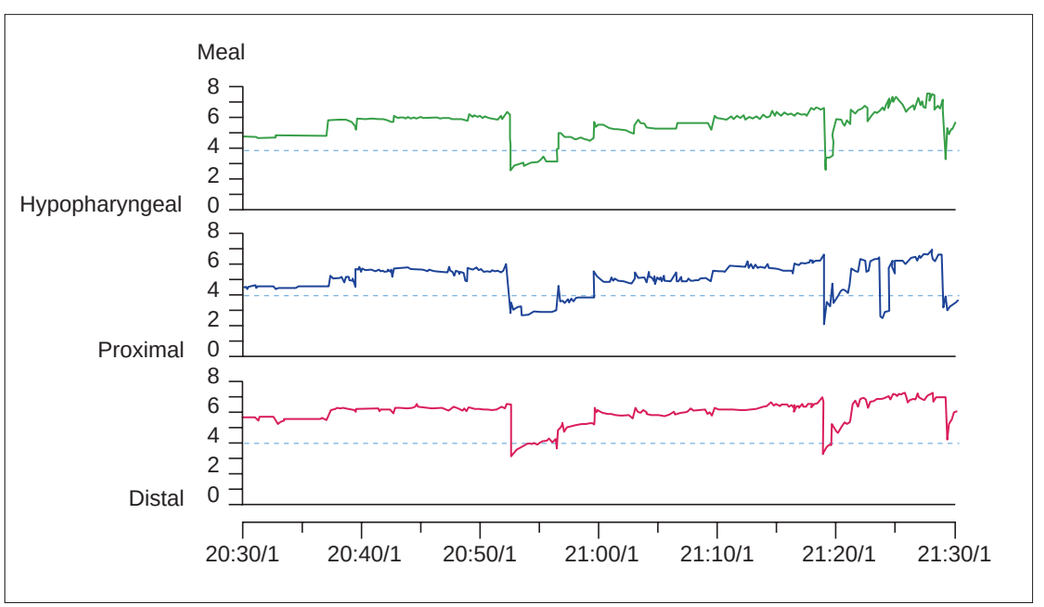
2.32 A 24-h ambulatory esophageal single probe pH tracing in a normal subject. Periods of meals and supine position are indicated by horizontal bars. For the majority of the time, the esophageal pH is >4.0. (H: heartburn; M: meal; S: supine.)



2.33 24-h ambulatory esophageal single probe pH tracing in a gastroesophageal reflux disease (GERD) subject. Esophageal pH tracing shows markedly increased prevalence of distal pH >4.0 (>5.5%) consistent with GERD. (C: chest pain; H: heartburn; M: meal; S: supine.)



2.34 pH tracing of proximal and distal acid exposure. This triple probe pH tracing shows a pH drop to <4.0 in both proximal and distal electrodes but not in the hypopharyngeal electrode. There is no hypopharyngeal acid exposure.



2.35 pH tracing of hypopharyngeal acid exposure, shown by a pH drop to <4.0 in all three electrodes. This is in contrast with figure **2.34** which does not show hypopharyngeal acid exposure.

Bravo wireless system

Introduction

Bravo pH (Medtronic, Shoreview, MN, USA) is a wireless ambulatory pH monitoring system approved by the FDA, which consists of two components, a small pH capsule (**2.36A**) and a pager-sized receiver (**2.36B**)(4).

Indications

The indications for Bravo pH monitoring are the same as for traditional 24-hour ambulatory esophageal pH monitoring.

Technique

The Bravo system comes in a pre-packaged assembly consisting of a pH capsule and a delivery system. Esophagogastroduodenoscopy (EGD) is performed prior to Bravo capsule deployment, to determine the GEJ. The pH capsule delivery system is then passed into the esophagus transorally or transnasally and positioned so that the pH capsule is 6 cm above the GEJ. After proper positioning, a vacuum is applied which fills the suction chamber of the pH capsule with the adjacent esophageal tissue. The safety pin is removed and the locking pin is advanced which securely attaches the Bravo capsule to the esophageal wall (**2.37**).

The capsule transmits pH data to the receiver via radio telemetry signals. The pH monitoring is performed over 24–48 hours and the patients are given the same instructions as for standard pH monitoring. After the testing period, the patient returns the receiver and the data is downloaded via an infrared link to the computer and analyzed using a dedicated software program.

The capsule is designed to slough off from the esophageal wall and pass through the GI tract.

Interpretation

The normal values are the same as traditional pH monitoring (**2.38**, **2.39**).

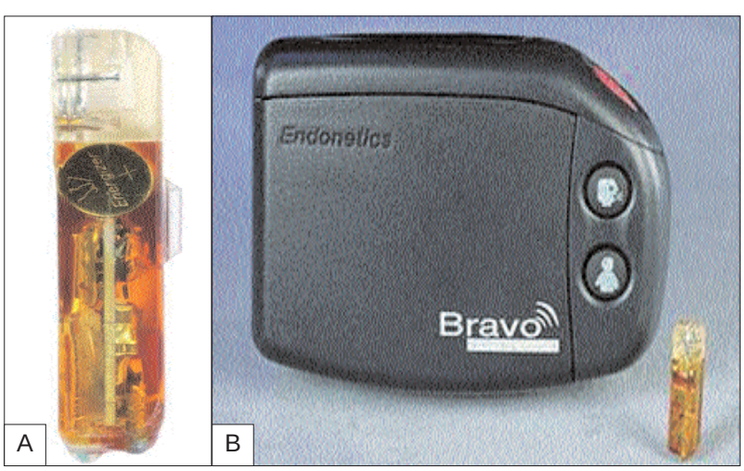
Bile reflux

Introduction

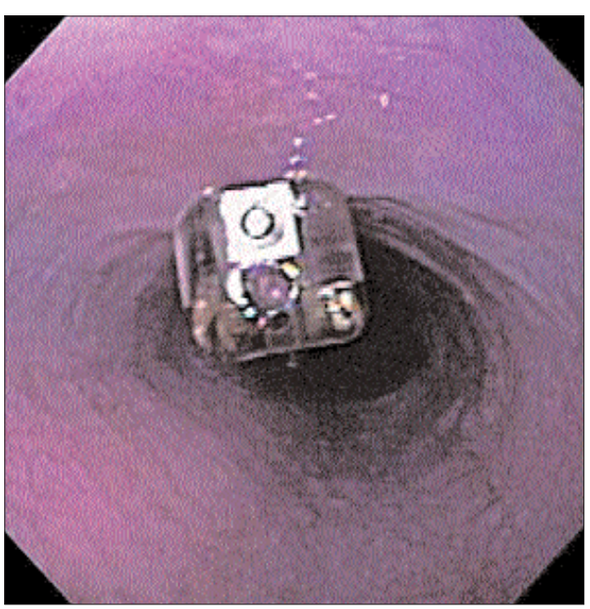
Bile reflux, or duodenogastroesophageal reflux (DGER), refers to regurgitation of duodenal contents through the pylorus into the stomach and subsequently into the esophagus. DGER may be important because factors other than acid, such as bile and pancreatic enzymes, may play a role in mucosal injury and symptoms in patients with GERD. Alkaline pH is a poor marker for DGER, which lead to the development of bilirubin monitoring.

Indications

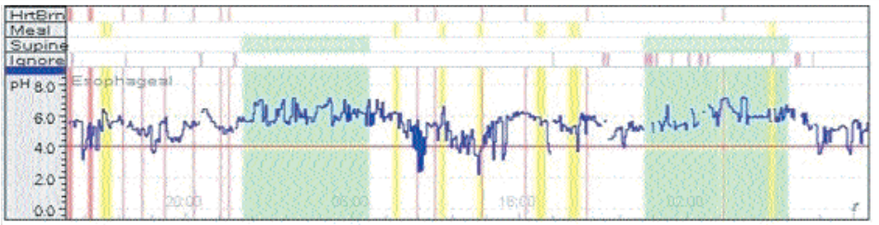
Indications for bile monitoring include detection of DGER. It has a limited clinical role as acid and bile reflux usually occur together.



2.36 A: Bravo pH capsule is 6 × 5.5 × 25 mm in size with antimony pH electrode and reference electrode located at the distal tip of the capsule. An internal battery and transmitter are also contained within the capsule. The pH capsule is placed 6 cm above the gastroesophagel junction determined by upper endoscopy. The pH capsule sends data using radio telemetry to the external receiver. **B**: Bravo external receiver and pH capsule.



2.37 Bravo capsule deployed on the esophageal lumen.



Reflux Table – Acid Reflux Analysis – Day 1

	Total	(Normal)	Upright	(Normal)	Supine	(Normal)
Fraction time pH <4 (%)	1.1	5.5	1.6	8.2	0.0	3.0

Reflux Table – Acid Reflux Analysis – Day 2

	Total	(Normal)	Upright	(Normal)	Supine	(Normal)
Fraction time pH <4 (%)	2.2	5.5	3.4	8.2	0.0	3.0

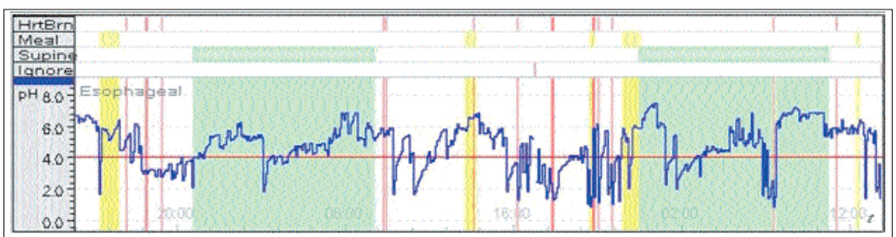
SI Table – Total

	Total
HrtBrn	5.6
ChestP	n/a
Regurg	n/a
Cough	n/a

SIP Table – Total

	Total
HrtBrn	64.3
ChestP	0.0
Regurg	0.0
Cough	0.0

2.38 Normal 48-hr Bravo pH monitoring. There is no increase in acid exposure in either day of monitoring.



Reflux Table – Acid Reflux Analysis – Day 1

	Total	(Normal)	Upright	(Normal)	Supine	(Normal)
Fraction time pH <4 (%)	17.6	5.5	27.1	8.2	5.9	3.0

Reflux Table – Acid Reflux Analysis – Day 2

	Total	(Normal)	Upright	(Normal)	Supine	(Normal)
Fraction time pH <4 (%)	21.9	5.5	26.5	8.2	16.6	3.0

SI Table – Total

	Total
HrtBrn	50.0
ChestP	n/a
Regurg	n/a
Cough	n/a

SIP Table – Total

	Total
HrtBrn	100.0
ChestP	0.0
Regurg	0.0
Cough	0.0

2.39 48-hr Bravo pH monitoring showing abnormal acid reflux. There is increased acid exposure in both days of monitoring. Additionally, the symptom index correlates in 50% of the episodes of heartburn reported.

Equipment

A fiberoptic spectrophotometer (**2.40**) (Bilitec 2000, Synectics, Stockholm, Sweden) uses the optical properties of bilirubin to detect DGER. Bilirubin has a characteristic spectrophotometric absorption band at 450 nm. Absorption near this wavelength implies the presence of bilirubin and, therefore, DGER.

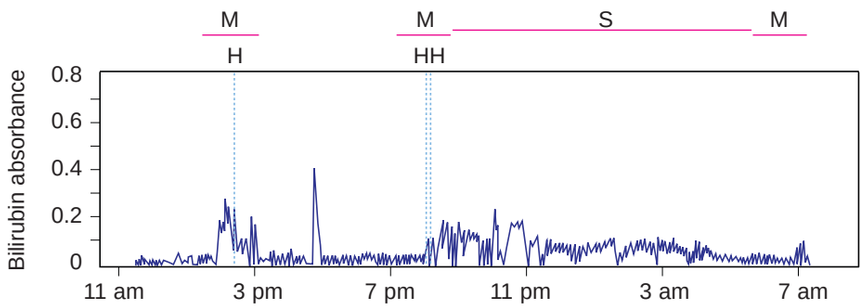
Technique

Ambulatory bilirubin monitoring can be employed, similar to pH monitoring. Data is recorded as percent time that bilirubin absorbance is >0.14, and can be analyzed for total, upright, and supine periods (**2.41**). Normal values for percent total, upright, and supine times bilirubin is >0.14 are 1.8%, 2.2%, and 1.6%, respectively.

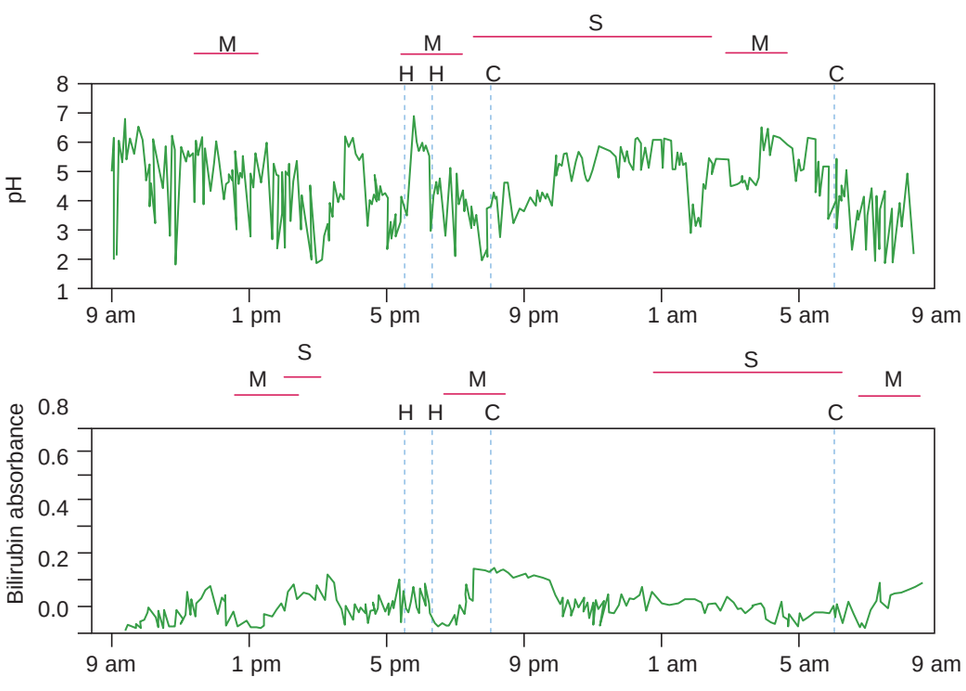
This instrument may underestimate bile reflux in an acidic medium, so must be accompanied by simultaneous pH monitoring (**2.42**). A modified diet is necessary to avoid interference and false readings, as the probe indiscriminately records any substance around 450 nm.

2.40 Bilitec 2000 monitor for duodenogastroesophageal reflux. The probe is a fiberoptic spectrophotometer designed for the detection of bilirubin in the distal esophagus.

High episode		*Total*	*Upright*	*Supine*	*Meal*	*Post P*	*Heart burn*
Duration	(HH:MM)	19:54	12:54	07:00	00:20	06:00	00:12
Number of episodes	(#)	30	28	2	0	21	1
Number of episodes longer than 30 minutes	(#)	0	0	0		0	0
Longest episode	(Min)	28	23	26	0	23	4
Total time absorbance above 0.14	(Min)	181	128	53	0	97	4
Fraction time absorbance above 0.14	(%)	15.2	16.2	12.7	0.0	26.8	33.3
Median absorbance value		–	–	–	–	–	–



2.41 Bilitec tracing of a patient with duodenogastroesophageal reflux. Reflux is defined as bilirubin absorbance >0.14. This patient has several postprandial episodes of reflux associated with heartburn (H). Also note the prolonged episode of duodenogastroesophageal reflux while supine (S). (M: meal.)



2.42 Simultaneous pH and bile monitoring. Note that the episodes of duodenogastroesophageal reflux correlating with meals (M) are associated with acid reflux as well. (C: chest pain; H: heartburn; S: supine.)

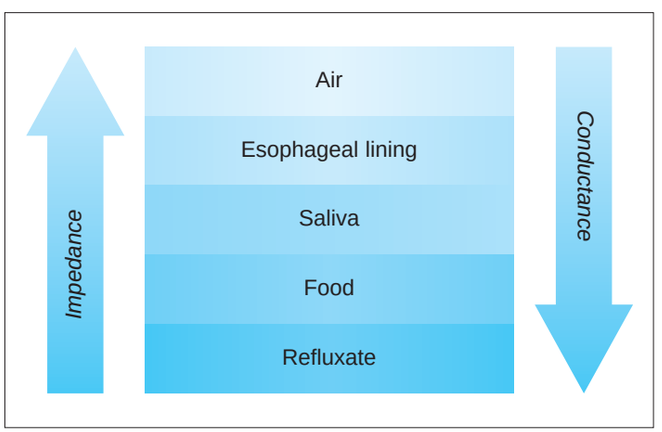
Intraluminal impedance

Introduction

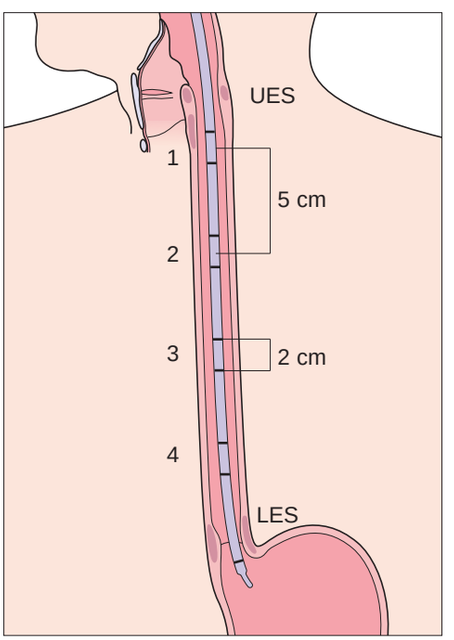
Multi-channel intraluminal impedance (MII) is an alternative technique available for the evaluation of GERD. Impedance is a measure of total resistance to the alternating current (AC) flow. Substances with high ionic concentration, such as liquids, have high conductance and low impedance. Conversely, substances with low ionic concentration, such as air, have low conductance and high impedance. A mixed (liquid and gas) bolus exhibits the characteristics of both (**2.43**)(5).

A typical MII catheter consists of multiple impedance measuring segments (i.e. multi-channel) mounted 5 cm apart on a 2.1 mm diameter polyvinyl catheter (Sandhill Scientific Inc., Denver, CO, USA) (**2.44**). Characteristic esophageal impedance tracing correlating with a liquid bolus movement across the impedance-measuring segment was validated with simultaneous video-fluoroscopy (**2.45**)(7). The direction of bolus movement is determined based on the time sequence of bolus entry and exit through different impedance measuring segments (**2.46**, **2.47**)(7).

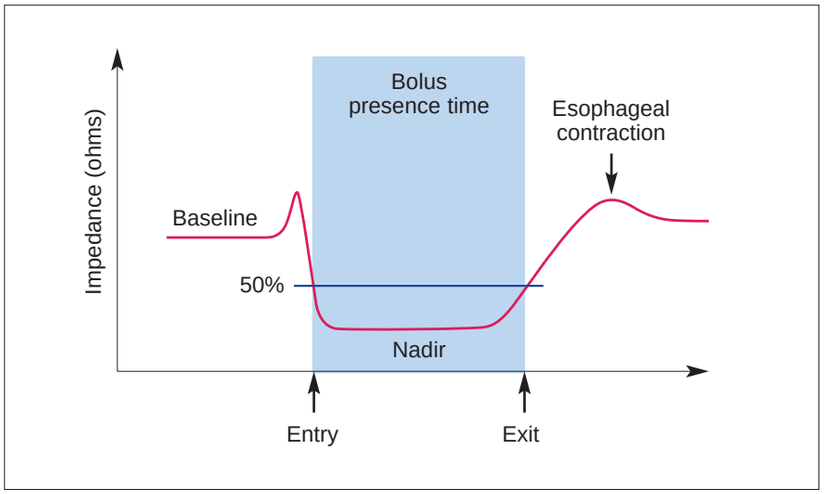
Two variations of MII have been introduced for clinical use: combined MII and pH monitoring (MII-pH) and combined MII and manometry (MII-EM). MII-pH permits differentiation of the refluxate as either acid or non-acid and is useful for evaluation of GERD. On the other hand, MII-EM allows concurrent measurement of the esophageal contraction and corresponding bolus movement and can be used for esophageal function testing.



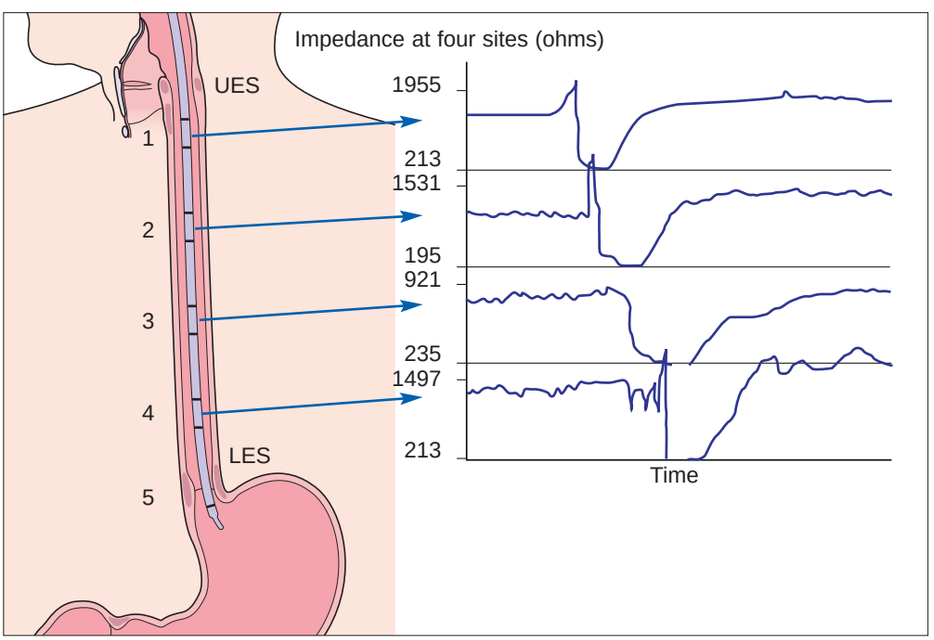
2.43 Relative impedance of various substances found in the esophageal lumen. Impedance is a total resistance of a substance to alternating current flow. Therefore, it is the opposite of conductance and is dependent on the ionic concentration. Substances with high ionic concentration have high conductance and low impedance (e.g. liquid). Conversely, substances with low ionic concentration have low conductance and high impedance (e.g. gas).



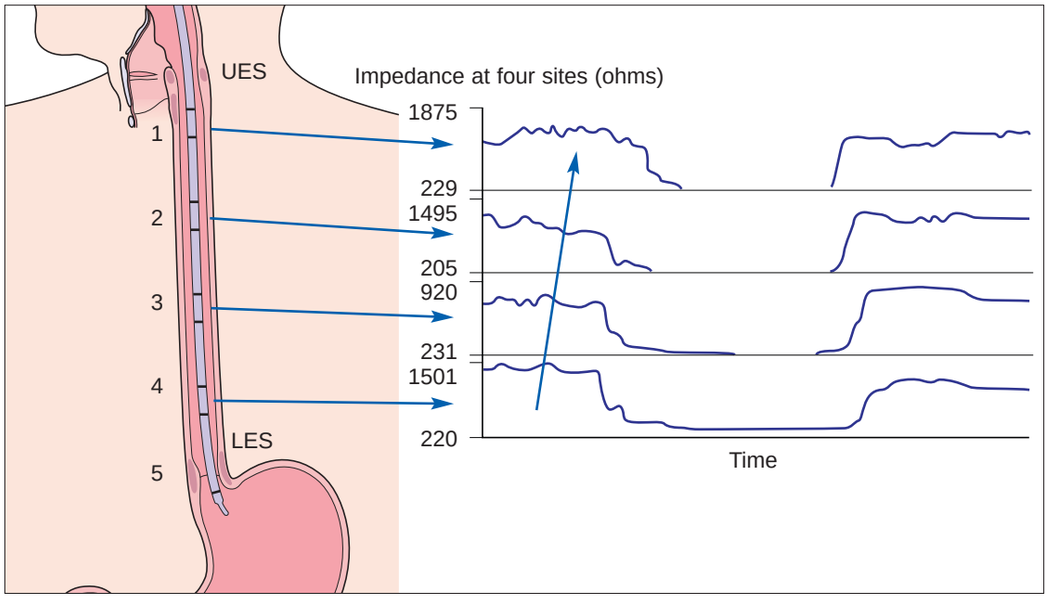
2.44 Multi-channel intraluminal impedance probe, consisting of four impedance-measuring segments spaced 5 cm apart. Each impedance-measuring segment consists of two electrodes 2 cm apart.



2.45 Characteristic impedance tracing of a liquid bolus. At baseline, the esophagus is a narrow, empty tube and the impedance is determined by the electrical properties of the esophageal mucosa. As the bolus reaches the impedance-measuring segment, the esophagus expands and the impedance rises sharply due to the air in front of the bolus head. This is followed by a rapid drop in impedance as the higher conductive liquid bolus passes the measuring segment. Bolus entry is considered to be at the 50% drop in impedance from baseline, and bolus exit at the 50% rise from the nadir. The impedance stays at nadir as long as the bolus is present on the impedance-measuring segment. Esophageal contraction causes lumen narrowing and passage of bolus, resulting in transient impedance elevation ('overshoot') above the baseline before returning to baseline.



2.46 Impedance tracing of antegrade bolus movement. Antegrade movement (or swallow) is shown by proximal to distal detection of bolus by the impedance-measuring segments.

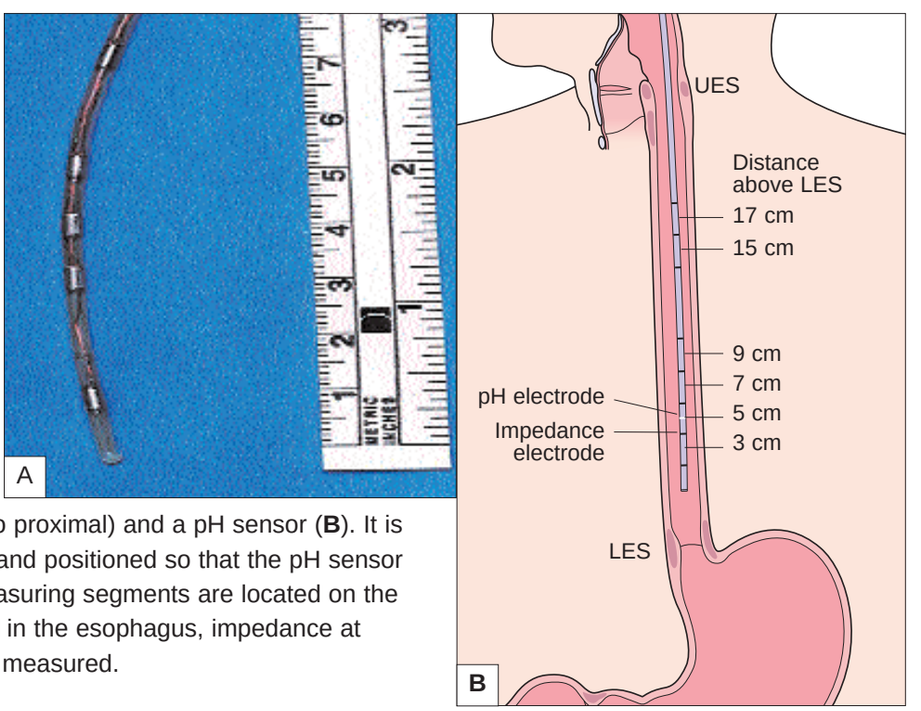


2.47 Impedance tracing of retrograde bolus movement. Retrograde movement (or reflux) is shown by distal to proximal detection of bolus by the impedance-measuring segments.

Combined MII-pH

MII-pH can characterize reflux events as liquid, gas, or mixed (liquid and gas) and acid, weak-acid, acid re-reflux, or non-acid (*Table 2.7*, **2.48**–**2.50**)(7).

The results are interpreted based on the normal values established by Shay *et al.* (*Table 2.8*)(8). MII-pH is useful for the evaluation of typical and atypical gastroesophageal reflux symptoms refractory to aggressive acid suppression therapy, and in elucidating the role of non-acid reflux in continued reflux symptoms.



2.48 Combined multi-channel intraluminal impedance and pH (MII-pH). Usually, impedance recording is performed in combination with pH monitoring. Combined they provide complementary information of the refluxate: the composition of the refluxate (liquid, gas, or mixed) and pH (acid vs. non-acid). Combined MII-pH catheter is a thin flexible 2.1 mm polyvinyl catheter (Sandhill Scientific Inc., Denver, CO, USA) similar to a standard pH catheter (**A**). On this catheter are six impedance-measuring segments (four distal and two proximal) and a pH sensor (**B**). It is placed into the esophagus transnasally and positioned so that the pH sensor is 5 cm above LES. The impedance-measuring segments are located on the catheter such that when properly placed in the esophagus, impedance at 3, 5, 7, 9, 15 and 17 cm above LES are measured.

2.49 A patient with MII-pH probe. The MII-pH test is performed similar to 24-hour ambulatory pH monitoring. Patients are instructed to fast 4–6 hours before the MII-pH probe is placed. During the monitoring period, the patients are instructed to perform normal daily activities, consume a usual diet, and keep a diary of symptoms, meal times, time of lying down for sleep, time of rising in the morning, and time of acid-suppression medication. The patients return the following day to have their probe removed and diaries reviewed. The MII-pH data are downloaded and analyzed using a dedicated computer program.

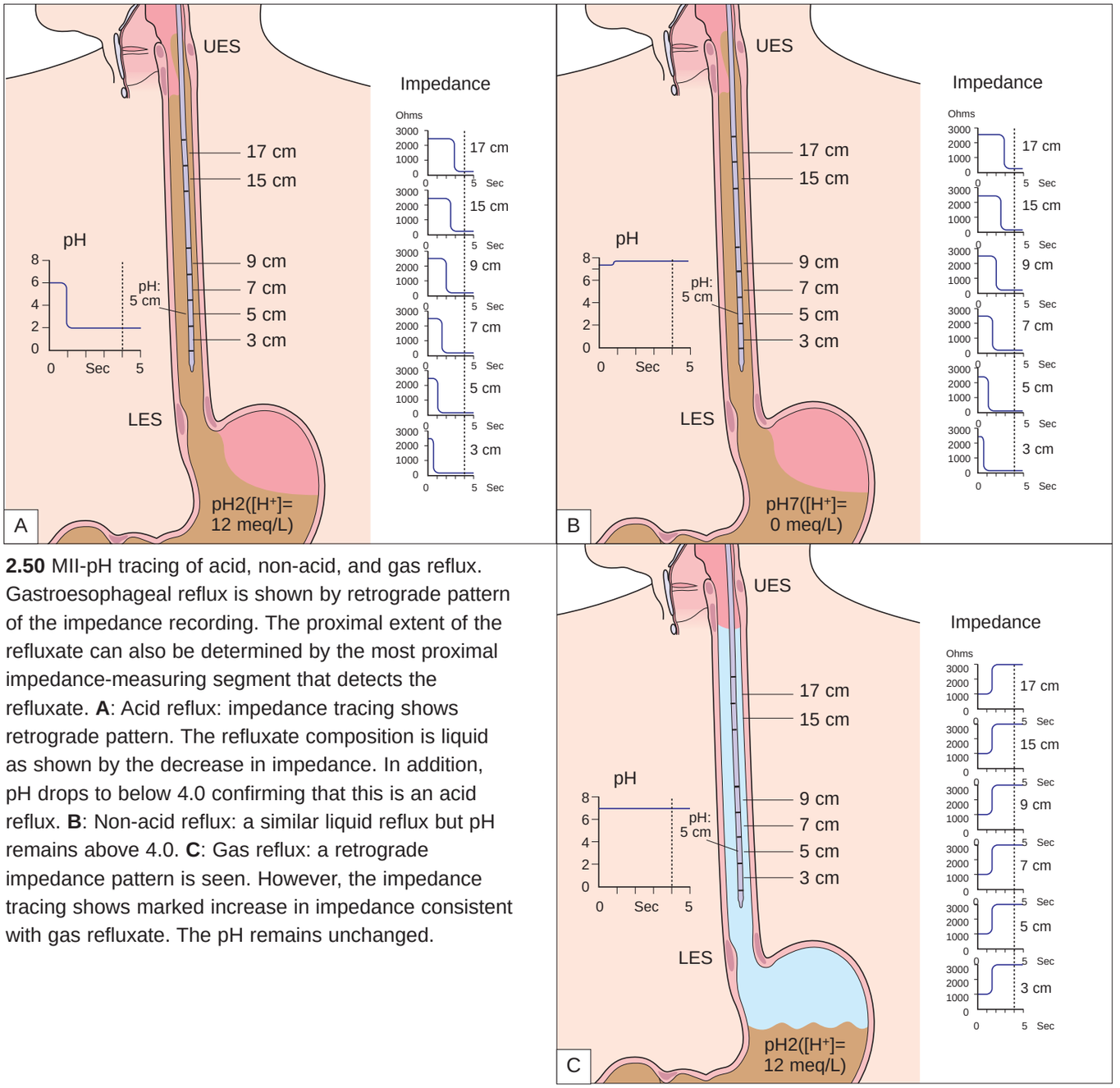
Table 2.7 Multi-channel intraluminal impedance-pH classifications of reflux (7)

Acid reflux	pH drop to <4.0 from baseline pH >4.0
Weak acid reflux	pH drop by >1 unit but pH remains >4.0
Acid re-reflux	Acid reflux when pH already <4.0
Non-acid reflux	pH remains >4.0 and does not drop by >1 unit

Table 2.8 Multi-channel intraluminal impedance-pH normal values (number of reflux events)

		Total	*Acid*	*Weak acid*	*Non-acid*	*Acid re-reflux*
Distal	Total	73	55	26	1	4
	Upright	67	52	24	1	4
	Recumbent	7	5	4	0	1
Proximal	Total	31	28	12	1	2
	Upright	29	25	11	1	2
	Recumbent	3	2	1	0	0

(Shay *et al*. (2000). *American Journal of Gastroenterology* **99**(6):1037–1043.)



2.50 MII-pH tracing of acid, non-acid, and gas reflux. Gastroesophageal reflux is shown by retrograde pattern of the impedance recording. The proximal extent of the refluxate can also be determined by the most proximal impedance-measuring segment that detects the refluxate. **A**: Acid reflux: impedance tracing shows retrograde pattern. The refluxate composition is liquid as shown by the decrease in impedance. In addition, pH drops to below 4.0 confirming that this is an acid reflux. **B**: Non-acid reflux: a similar liquid reflux but pH remains above 4.0. **C**: Gas reflux: a retrograde impedance pattern is seen. However, the impedance tracing shows marked increase in impedance consistent with gas refluxate. The pH remains unchanged.

Combined MII-EM

MII-EM is useful for esophageal function testing as it provides simultaneous assessment of esophageal motility and corresponding functional bolus transit (**2.51**, **2.52**). MII-EM classifications of swallows and normal values are shown in *Table 2.9* and *Table 2.10* respectively. The indications for MII-EM are similar to those for conventional esophageal manometry (dysphagia, non-cardiac chest pain, GERD, pre-operative evaluation for anti-reflux surgery).

2.51 Combined MII-EM. The MII-EM catheter is available as a 9 channel, 4.5 mm diameter flexible polyvinyl catheter with five pressure sensors (two circumferential and three unidirectional) and four impedance measuring segments (Sandhill Scientific Inc., Highlands Ranch, CO, USA). The two circumferential pressure sensors are located 5 and 10 cm from the catheter tip and three unidirectional pressure sensors at 15, 20, and 25 cm from the tip. The four impedance measuring segments, consisting of two ringed electrodes 2 cm apart each, are centered at 10, 15, 20, and 25 cm from the tip. The catheter is inserted transnasally and positioned in the esophageal lumen using stationary pull-through technique so that the most distal pressure sensor is placed at the high pressure zone of LES. Thus, the remainder of pressure sensors and impedance measuring segments are located 5, 10, 15, and 20 cm above LES.

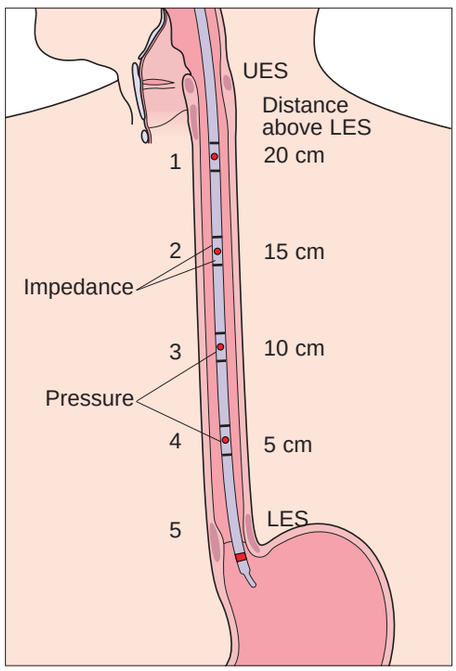
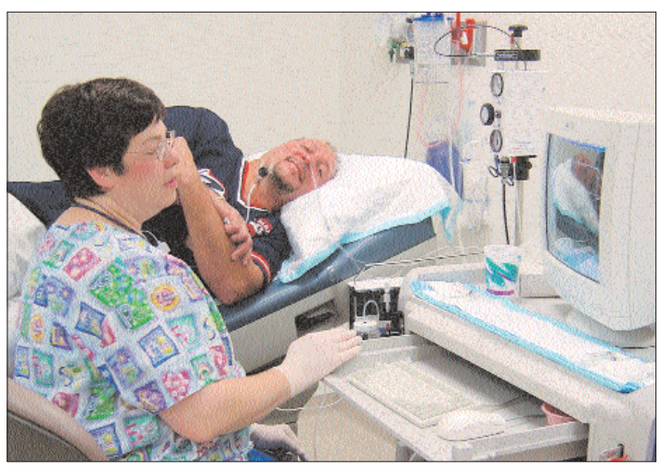


Table 2.9 Multi-channel intraluminal impedance-esophageal manometry classification of swallows (9)

Classification	Criteria
Manometry	
Normal	Amplitudes at 5 and 10 cm above LES ≥30 mmHg and distal onset velocity <8 cm/sec
Simultaneous	Amplitudes at 5 and 10 cm above LES ≥30 mmHg and distal onset velocity >8 cm/sec
Ineffective	Amplitudes at 5 or 10 cm above LES <30 mmHg
Impedance	
Complete bolus transit	Bolus entry detected at 20 cm shown to have bolus exit at all distal sites (15, 10, and 5 cm)
Incomplete bolus transit	Bolus entry detected at 20 cm which does not have bolus exit at any of the three distal sites

LES: lower esophageal sphincter



2.52 A patient undergoing MII-EM. MII-EM is performed in a similar fashion as standard esophageal manometry with few differences. Unlike manometry, 10 liquid swallows of normal saline, instead of water, are given since the former has standardized ionic concentration and known impedance characteristics. Additionally, 10 viscous swallows are performed with 'apple sauce' consistency material with known impedance. The data are recorded and analyzed using dedicated computer software (Insight Acquisition and Bio View Analysis, Sandhill Scientific Inc., Highlands Ranch, CO, USA).

Table 2.10 Multi-channel intraluminal impedance-esophageal manometry normal values (9)

N=43 (95th percentile)	*Liquid bolus*	*Viscous bolus*
Total bolus head advance time (entry @ 20 cm → entry @ 5 cm)	5.0 sec	7.5 sec
Total bolus transit time (entry @ 20 cm → exit @ 5 cm)	12.5 sec	12.5 sec
Smooth muscle segmental transit time (entry @ 10 cm → exit @ 5 cm)	10.5 sec	8.5 sec
% complete bolus transit	≥80	≥70

References

1 Johnson LF, Demeester TR (1974). Twenty-four-hour pH monitoring of the distal esophagus. A quantitative measure of gastroesophageal reflux. *Am J Gastroenterol* **62**:325–332.

2 Vitale GC, Cheadle WG, Sadek S, *et al.* (1984). Computerized 24-hour ambulatory esophageal pH monitoring and esophagogastroduodenoscopy in the reflux patient. A comparative study. *Ann Surg* **200**:724–728.

3 Richter JE, Bradley LA, DeMeester TR, Wu WC (1992). Normal 24-hr ambulatory esophageal pH values. Influence of study center, pH electrode, age, and gender. *Dig Dis Sci* **37**(6):849–856.

4 Pandolfino JE, Richter JE, Ours T *et al.* (2003). Ambulatory esophageal pH monitoring using a wireless system. *Am J Gastroenterol* **98**(4):740–749.

5 Sifrim D, Holloway R, Silny J, *et al.* (2001). Acid, nonacid, and gas reflux in patients with gastroesophageal reflux disease during ambulatory 24-hour pH-impedance recordings. *Gastroenterol* **120**(7):1588–1598.

6 Sifrim D, Silny J, Holloway RH, *et al.* (1999). Patterns of gas and liquid reflux during transient lower oesophageal sphincter relaxation: a study using intraluminal electrical impedance. *Gut* **44**(1):47–54.

7 Tutuian R, Vela MF, Shay SS, et al. (2003). Multichannel intraluminal impedance in esophageal function testing and gastroesophageal reflux monitoring. *J Clin Gastroenterol* **37**(3):206–215.

8 Shay S, Tutuian R, Sifrim D, *et al.* (2004). Twenty-four hour ambulatory simultaneous impedance and pH monitoring: a multicenter report of normal values from 60 healthy volunteers. *Am J Gastroenterol* **99**(6):1037–1043.

9 Tutuian R, Vela MF, Balaji NS, *et al.* (2003). Esophageal function testing with combined multichannel intraluminal impedance and manometry: multicenter study in healthy volunteers. *Clin Gastroenterol Hepatol* **1**(3):174–182.

Further reading

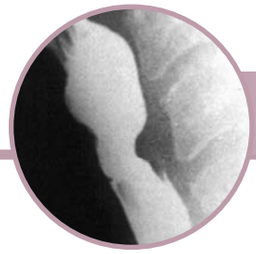
Pandolfino JE, Kahrilas PJ (2005). American Gastroenterological Association medical position statement: Clinical use of esophageal manometry. *Gastroenterol* **128**:207–208.

Pandolfino JE, Kahrilas PJ (2005). AGA Technical review on the clinical use of esophageal manometry. *Gastroenterol* **128**:209–224.

Park W, Vaezi MF (2005). Esophageal impedance recording: Clinical Utility and Limitations. *Curr Gastroenterol Rep* 7:182-189.

(1996). American Gastroenterological Association medical position statement: guidelines on the use of esophageal pH recording. *Gastroenterol* **110**:1981–1996.

Chapter 3



Esophageal symptom assessment

Typical symptoms

Heartburn (pyrosis) and acid regurgitation

Definition

Heartburn is a substernal burning sensation, usually occurring from 30 minutes to 2 hours post-prandial, that can radiate up to the neck and throat. Heartburn is usually worsened by lying down and bending over, and can awaken patients from sleep. Large meals before sleeping are associated with heartburn. Certain foods (alcohol, caffeine, coffee, chocolate, peppermint, tomatoes), as well as cigarettes and medications are also associated with an increased risk of heartburn. Symptoms are usually improved with antacids. Heartburn is extremely prevalent, and occurs in up to 33% of Americans on a monthly basis.

Acid regurgitation occurs when a small amount of acidic or bitter fluid that appears spontaneously and effortlessly in the back of the throat or mouth. It is most common after meals, but it can also awaken patients from sleep and can be associated with coughing or choking. It is separated from 'vomiting' by an absence of retching and associated nausea.

Diagnosis

These are the classic symptoms of GERD and, in the absence of warning signs (GI bleeding, weight loss, iron deficiency anemia, dysphagia), empiric therapy with acid-suppressive agents can be instituted. If symptoms do not improve after a sufficient trial (up to 12 weeks), or warning signs are present, further investigation is warranted. Upper endoscopy is often the first diagnostic test in the presence of warning signs, and pH monitoring is useful in associating symptoms with increased intraesophageal acid exposure.

Non-acid regurgitation

Definition

Non-acid regurgitation is described as food or fluid being present in the mouth without a recognized associated 'vomiting' episode. The food seems to effortlessly appear in the mouth.

Etiology

The contents that appear in the mouth can be undigested food, which is almost always associated with esophageal obstruction of some degree. This can be seen in association with strictures, rings, achalasia, or a pharyngeal pouch.

Water brash

Definition

Water brash is defined as a sudden filling of the mouth with a large amount of fluid, that is often clear and salty in taste.

Etiology

This is caused by a reflex secretion (cholinergic) from salivary glands in the mouth, in response to stimulation from distal esophageal acid irritation. Water brash is often associated with GERD, especially if acid regurgitation and heartburn are present.

Atypical symptoms

Globus

Definition

The globus sensation is defined as the feeling of fullness, or a lump in the throat. Patients may also describe a 'tickling' sensation in their throat. Globus is often a constant symptom, and may improve with swallowing.

Etiology

If pharyngeal, laryngeal, and neck physical and mechanical etiologies are excluded, globus can be associated with multiple esophageal etiologies. Possibilities include – hypertensive UES, altered visceral sensation, GERD, webs, diverticula, and dysmotility disorders (achalasia, ineffective esophageal motility).

Chest pain

Chest pain, often qualitatively similar to ischemic chest pain, can be secondary to an esophageal abnormality. This is due to a shared embryologic sensory innervation. As this symptom mimics the pain of myocardial ischemia, all evaluations must first definitively rule out a cardiac etiology. Like ischemic chest pain, it may be relieved by nitroglycerin. Esophageal chest pain is classically non-exertional, and can be spontaneous, post-prandial, or occur at night. Symptoms may last for minutes to hours. It is often associated with other esophageal symptoms, such as heartburn, regurgitation, and dysphagia. If thought to be non-cardiac, this chest pain is often secondary to an abnormal visceral nociception, an esophageal motor disorder, or GERD.

Respiratory

Multiple respiratory symptoms, such as asthma, bronchitis, and cough, have been associated with GERD. These symptoms may be due to GERD as well as oropharyngeal swallowing disorders. Continued acidic aspiration can lead to coughing, throat clearing, and hoarseness. Patients may also present with pneumonia from aspiration of gastric contents.

Hiccup

Definition

An acute, involuntary lowering of diaphragm with glottis closure – produces a characteristic sound.

Etiology

Uremia, reflux, obstruction (achalasia or stricture).

Odynophagia

Definition

The symptom of odynophagia is best defined as the sensation of pain with swallowing. This symptom is strongly associated with an esophageal or pharyngeal abnormality, and is produced from local inflammation or neoplasm in the mouth and pharynx. The symptom is described as burning or pain after swallowing, and can be associated with acidic, spicy, or hot or cold food.

Etiology

Odynophagia is most often associated with erosive esophagitis of any etiology – pill-induced, infectious (CMV, HSV, *Candida* sp.), acid related, radiation, or caustic injury, and is commonly seen in patients with AIDS and patients undergoing chemotherapy. When severe, cessation of swallowing may occur.

Dysphagia

Definition

The symptom of dysphagia, described by patients as a difficulty swallowing, is strongly associated with an esophageal abnormality. Patients describe the food 'sticking' or 'hanging up' during its passage down the esophagus, during a swallow. Although pain may coexist, dysphagia must be separated from odynophagia (pain with swallowing, see below). It is also important to differentiate oropharyngeal dysphagia from esophageal dysphagia.

Etiology

A detailed clinical history is often extremely helpful in finding an etiology. Dysphagia can be conceptualized as belonging to two main groups: obstructive and motility related (*Table 3.1*).

Diagnosis

Clues in the history that will aid in diagnosis include the following:

- If the dysphagia presents with liquids, solids, or both: a motility disorder may be indicated. Dysphagia to solids only is usually obstructive, and is usually progressive.
- If the dysphagia is progressive or intermittent: episodic dysphagia to liquids and solids can suggest a motor disorder, while intermittent dysphagia to solids suggests a fixed esophageal ring or web. Progressive dysphagia (solids to solids and liquids) suggests an obstructive etiology (stricture, neoplasm, or achalasia).
- If there associated heartburn: this may suggest a peptic stricture or scleroderma.

Other associated symptoms, such as pattern of onset, pain, weight loss, choking, and drugs, may narrow the differential diagnosis. If the progression of dysphagia is rapid, and is associated with weight loss, esophageal carcinoma must be suspected. The initial diagnostic modality for dysphagia depends on the diagnostic suspicion. In those whom a motility disorder is suspected, barium swallow should be the initial test. In those suspected of having structural (obstructive) causes of dysphagia, upper GI endoscopy may be the better initial diagnostic modality.

Table 3.1 Causes of dysphagia

Obstructive (mechanical)	*Motility (neuromuscular)*
Strictures	Achalaisa
Carcinoma	Ineffective esophageal motility
Rings	Diffuse esophageal spasm
Webs	Nutcracker esophagus
Diverticula	Scleroderma
Tumors – benign	Hypertensive LES
Pill-induced injury	Chagas' disease
Foreign body	
External compression – mediastinal, cervical osteoarthritis, vascular	

LES: lower esophageal sphincter

Oropharyngeal dysphagia

Epidemiology

Oropharyngeal dysplasia is an extremely common condition, and increases in prevalence with age. It occurs in one-third of all stroke patients and is common in patients with head injuries, Parkinson's, and Alzheimer's disease (20–40% prevalence). Up to 60% of nursing home occupants have feeding difficulties, with a substantial proportion having dysphagia. Consequences include malnutrition, aspiration, choking, pneumonia, and death. It therefore carries a high morbidity, mortality, and cost.

Etiology

Swallowing is a complex act, requiring interplay of multiple muscles and neurological pathways in order for the bolus to pass from the oral cavity into the esophagus. *Table 3.2* lists the common causes of oropharyngeal dysphagia. Common categories of underlying etiologies include central nervous system diseases, peripheral nervous system diseases, myogenic diseases (including drug-induced), metabolic abnormalities, infectious diseases, and structural disorders.

Clinical presentation

Oropharyngeal dysphagia can result from disturbance in any aspect of the swallow response, and can be seen as delayed swallow initiation, aspiration, nasopharyngeal regurgitation, and excessive post-swallow residue. The patient can often accurately localize the site of the dysfunction, as opposed to the case in distal esophageal obstruction. Patients have difficulty initiating a swallow, and have immediate coughing, choking, gagging, and nasal regurgitation.

Oral symptoms include drooling or spillage of food, sialorrhea, xerostomia, difficulty initiating swallowing, dysarthria, and piecemeal swallowing. Pharyngeal symptoms may include sensation of a bolus holding up in the neck, post-nasal regurgitation, repeated swallowing to clear food, coughing and choking, and dysphonia. Other symptoms include odynophagia and sore throat, dysphagia, and regurgitation of old food.

A neurological exam and evaluation of neurological symptoms is often helpful in discovering the cause of oropharyngeal dysphagia, as neurological or neuromuscular findings may assist in directing the physician to the underlying primary etiology of the dysfunction.

Table 3.2 Causes of oropharyngeal dysphagia

Neuromuscular

Cerebrovascular accident
Parkinson's disease
Brainstem tumors
Amyotrophic lateral sclerosis
Multiple sclerosis
Peripheral neuropathy (poliomyelitis)
Huntington's chorea
Tabes dorsalis
Spinocerebellar degeneration
Syringobulbia
Amyloidosis
Botulism
Wilson's disease
Progressive bulbar paralysis

Structural lesions

Zencker's diverticulum
Retropharyngeal abscess
Cricopharyngeal bar
Thyromegaly or thyroid tumor
Cervical osteophyte or spur
Oropharyngeal carcinoma
Esophageal carcinoma
Esophageal web
High esophageal stricture
Inflammatory disease – tonsilar abscess, pharyngitis
Foreign body
Post-surgical change
Vascular anomalies
Cervical lymphadenopathy
Plummer–Vinson syndrome

Skeletal muscle disorders

Myasthenia gravis
Metabolic myopathies
Polymyositis
Muscular dystrophies – myotonic and oculopharyngeal
Inflammatory myopathies
Dermatomyositis
Scleroderma
Mixed connective tissue disease
Inclusion body myositis
Myxedema
Sarcoidosis
Systemic lupus erythamatosis
Hyperthyroidism
Stiff-man syndrome

Cranial nerve diseases

Rabies
Lead poisoning
Diabetes mellitus
Recurrent laryngeal nerve palsy
Transection or injury
Diphtheria
Other neurotoxins

Miscellaneous

Cricopharyngeal dysfunction
Decreased saliva – radiation, Sjögren's syndrome, medications
Alzheimer's disease
Depression

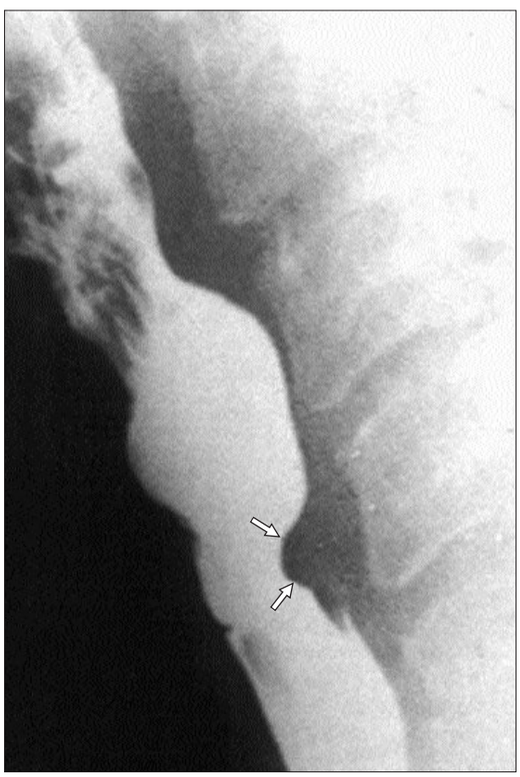
Diagnosis

Evaluation by a speech pathologist can assist with information about language, cognitive dysfunction, and the strength of the muscles involved in swallowing and speech.

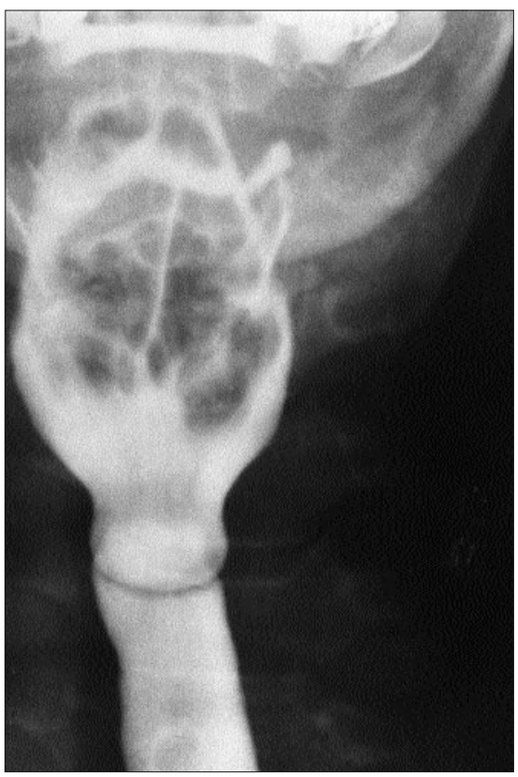
Barium swallow contrast radiography can detect structural causes of dysphagia, including cricopharyngeal bar diverticula, neoplasm, webs, and stenoses (**3.1–3.4**). However, these films cannot accurately assess the mechanics of swallowing. Videofluoroscopy is the best method of assessment, as it allows replay of the act of swallowing, which enables assessment of the mechanisms and the severity of dysfunction present to be established. Other important information from this examination includes the presence, timing, and severity of aspiration. Videofluoroscopy does not allow for quantification of contractile forces or intrabolus pressure, or detection of incomplete upper esophageal sphincter (UES) opening.

Nasoendoscopy is the gold standard for identifying and biopsying mucosal abnormalities. It is mandatory if malignancy is suspected in the differential diagnosis.

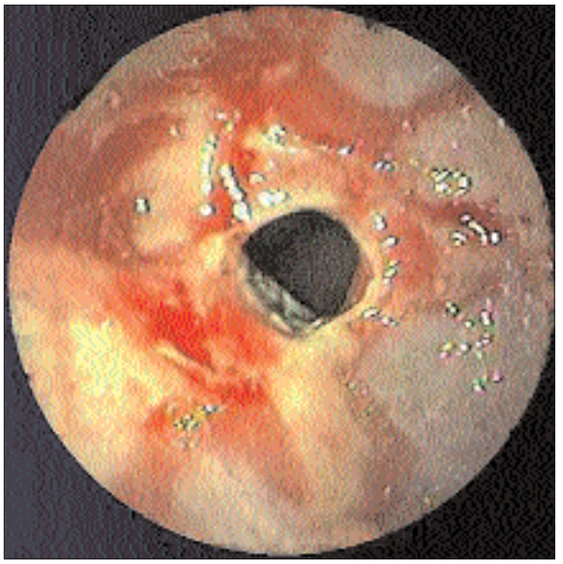
Manometry allows quantification of deglutitive forces, assesses UES relaxation, and assesses the coordination of pharyngeal contraction and UES relaxation. Manometry findings must be compared with appropriate age-specific standards.



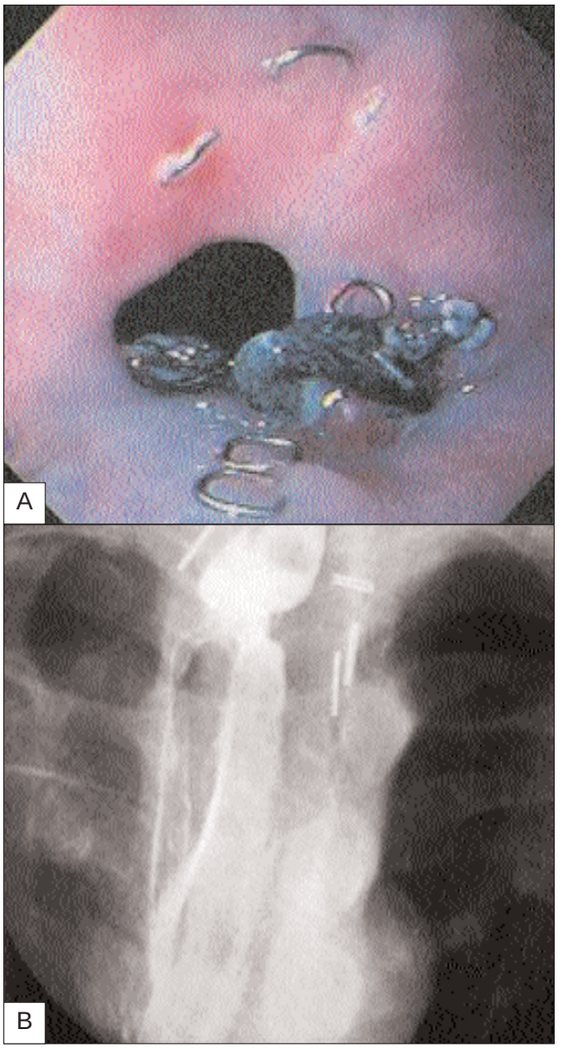
3.1 Barium study depicting a cricopharyngeal bar. Hypertrophy and fibrosis of the cricopharyngeus muscle, coupled with incomplete relaxation, causes this defect of the posterior cervical esophagus. This muscle comprises the UES, and progression of the bar can lead to oropharyngeal dysphagia. Surgical myotomy is sometimes used for symptomatic improvement in severe cases.



3.2 A patient with cervical dysphagia with esophageal web on barium swallow.



3.3 High degree of stenosis in a patient with cervical dsyphagia.



3.4 Endoscopic view (**A**) and barium x-ray (**B**) for a patient post-esophagectomy and cervical dysphagia.

Treatment

Response to treatment is variable and unpredictable, and depends on factors including the underlying cause, the severity and nature of mechanical dysfunction, the amount of cognitive dysfunction, and the prognosis of the underlying etiology. It therefore involves a multidisciplinary approach.

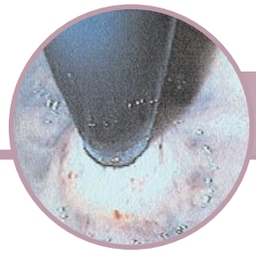
Aims of treatment include identifying and treating the underlying disease, along with attempting to circumvent or compensate for the specific mechanical disturbances. Structural problems may be amenable to surgery, dilation, or myotomy. Speech pathology should be involved in order to assess the risk for aspiration and to evaluate for possible institution of non-oral feeding options.

Botulinum toxin injection may be of benefit in oropharyngeal dysphagia secondary to failed muscle relaxation, but further studies are needed before this therapy can be strongly recommended. Swallow therapy maneuvers include dietary modification, changes in swallowing posture, and alterations in the techniques of swallowing. These changes aim to strengthen swallowing muscles and modify the mechanics of swallowing. Percutaneous gastrostomy (PEG) tubes may be necessary to reduce the risk of aspiration, although studies have not shown a decrease in the risk of aspiration pneumonia following initiation of PEG tube feeding.

Further reading

Cook IJ, Kahrilas PJ (1999). AGA technical review on the management of oropharyngeal dysphagia. *Gastroenterol* **116**:455–478.

Johnston BT, Castell DO (2004). Symptom overview and quality of life. In *The Esophagus*, DO Castell, JE Richter (eds). Lippincott Williams and Wilkins, New York, pp 37–46.



Chapter 4

Esophageal disease states

Achalasia

Definition

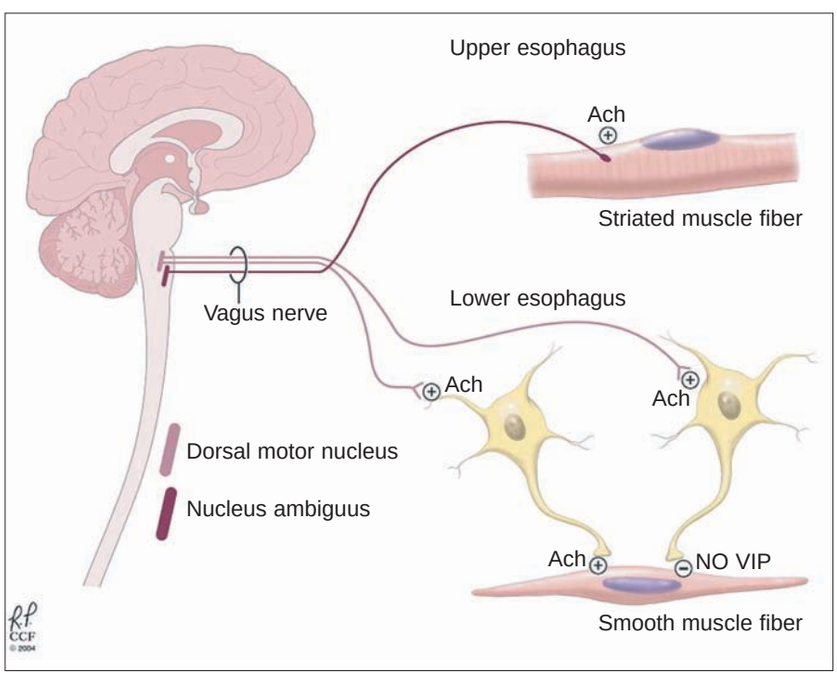
Achalasia is a primary esophageal motor disorder of unknown cause, which is characterized by insufficient lower esophageal sphincter (LES) relaxation and aperistalsis.

Etiology

The cause of achalasia remains unknown. Available data suggest degenerative, autoimmune, infectious and hereditary factors as possible causes (1).

Esophageal motor innervation and normal physiology

The proximal one-third of the esophagus (striated muscle) is innervated directly by the somatic efferent cholinergic fibers of the vagus nerve originating from the *nucleus ambiguus* (**4.1**). The distal two-thirds of the esophagus (smooth muscle) are controlled by the myenteric plexus, which is innervated by the pre-ganglionic cholinergic vagus nerve fibers from the *dorsal motor nucleus*. The myenteric



4.1 Esophageal motor innervation.The striated muscle of the proximal esophagus is innervated directly by the somatic efferent cholinergic fibers of the vagus nerve originating from the *nucleus ambiguus*. Smooth muscle of the distal esophagus is innervated by the pre-ganglionic vagus nerve fibers from the *dorsal motor nucleus*. The neurotransmitter released, acetylcholine, affects two types of post-ganglionic neurons in the myenteric plexus: excitatory cholinergic neurons and inhibitory nitrinergic neurons.

plexus has two types of post-ganglionic neurons: (i) excitatory cholinergic neurons; and (ii) inhibitory nitrinergic (nitric oxide, NO) neurons and vasoactive intestinal polypeptide- (VIP) containing neurons.

At baseline, the esophagus is in a contractile state mediated by excitatory cholinergic neurons. Deglutition induces inhibitory NO and VIP neuron excitation, resulting in esophageal and LES relaxation. Peristalsis results from coordinated relaxation and contraction mediated by the inhibitory and excitatory myenteric plexus neurons along the path of the esophagus.

Pathophysiology

The hallmark of achalasia is the loss of inhibitory NO and VIP neurons in esophageal myenteric plexus. In early achalasia, there is inflammation of the myenteric plexus (T-cell lymphocytic infiltration) without the loss of ganglion cells (**4.2**). In later stages, loss of myenteric ganglion cells and neural fibrosis ensues. In a selective manner, post-ganglionic inhibitory myenteric neurons containing NO and VIP are lost, whereas post-ganglionic excitatory cholinergic neurons are spared. The net result is unopposed cholinergic stimulation. This results in high basal LES pressure and failure of LES relaxation. In addition, loss of latency gradient along the esophageal body, which is mediated by nitric oxide, results in aperistalsis.

Epidemiology

The incidence is 1–2 per 200,000 (2). Both sexes are affected equally, with onset usually in the third to fifth decades, but can occur at any age.

Clinical presentation

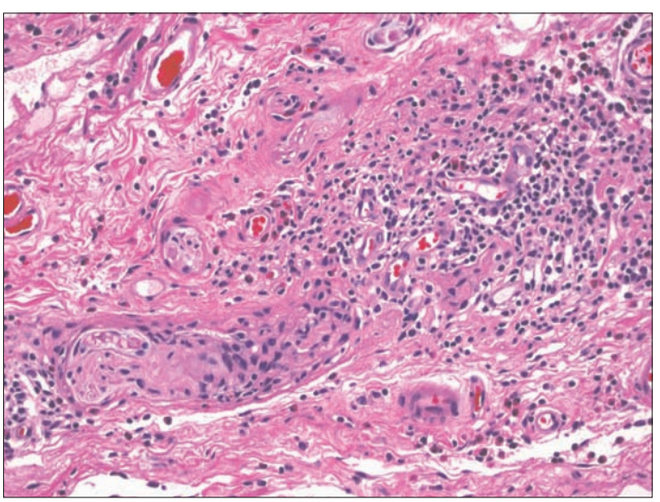
Dysphagia to solids is present in nearly all achalasia patients. Dysphagia to liquids present in two-thirds of achalasia patients. Regurgitation is found in 60–90% of achalasia patients. It usually occurs shortly after a meal, or while recumbent. Undigested food is regurgitated.

Chest pain is found in one-third of achalasia patients. It is located retrosternally and is typical of non-cardiac chest pain. Pain is precipitated by eating, which thus causes decreased intake and weight loss.

Other symptoms include weight loss (associated with advanced disease), pulmonary symptoms, and coughing spells secondary to aspiration.

Diagnosis

Diagnosis of achalasia requires radiographic, manometric, and endoscopic evaluation.



4.2 Histology of achalasia. There is inflammation of the myenteric plexus with T-cell lymphocytes.

Radiographic studies

Barium esophagram (**4.3, 4.4**)

This is the primary screening test for evaluation of achalasia, and has a 95% accuracy in diagnosing achalasia. Essential features are:

- 'Bird's beak' narrowing of the LES with incomplete opening.
- Loss of primary peristalsis.
- Delayed esophageal emptying.

Supportive features include a dilated or sigmoid-shaped esophagus, and epiphrenic diverticula.

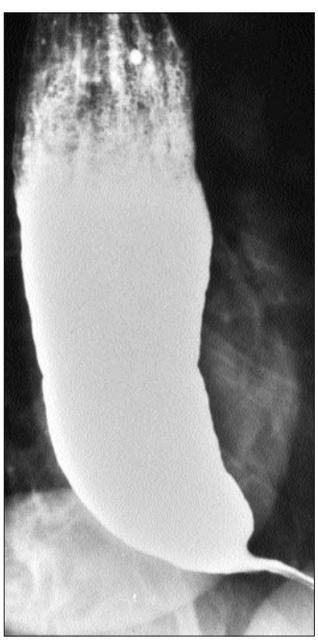
Timed barium swallow (**4.5**)

This provides objective evaluation of esophageal function. It is performed as a primary evaluation of achalasia or assessment of response to pneumatic dilation (3, 4).

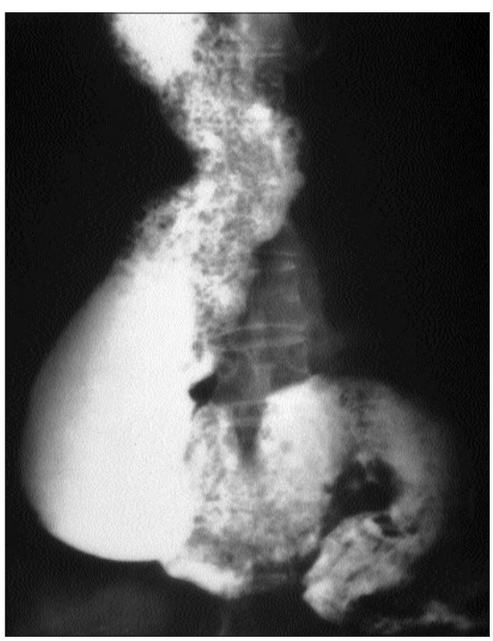
Three-on-one spot films are taken 1, 2, and 5 minutes after ingestion of 100–250 ml low-density barium. The volume ingested is based on patient tolerance. The degree of emptying is estimated qualitatively by comparing 1- and 5-minute films, or quantitatively estimated by measuring the height and width for both films. On subsequent follow-up studies, the same volume of barium is used for accurate serial assessment (3). In normal individuals, the esophagus is devoid of barium within 1 minute. The goal of therapy in achalasia is to normalize emptying by 5 minutes (3).

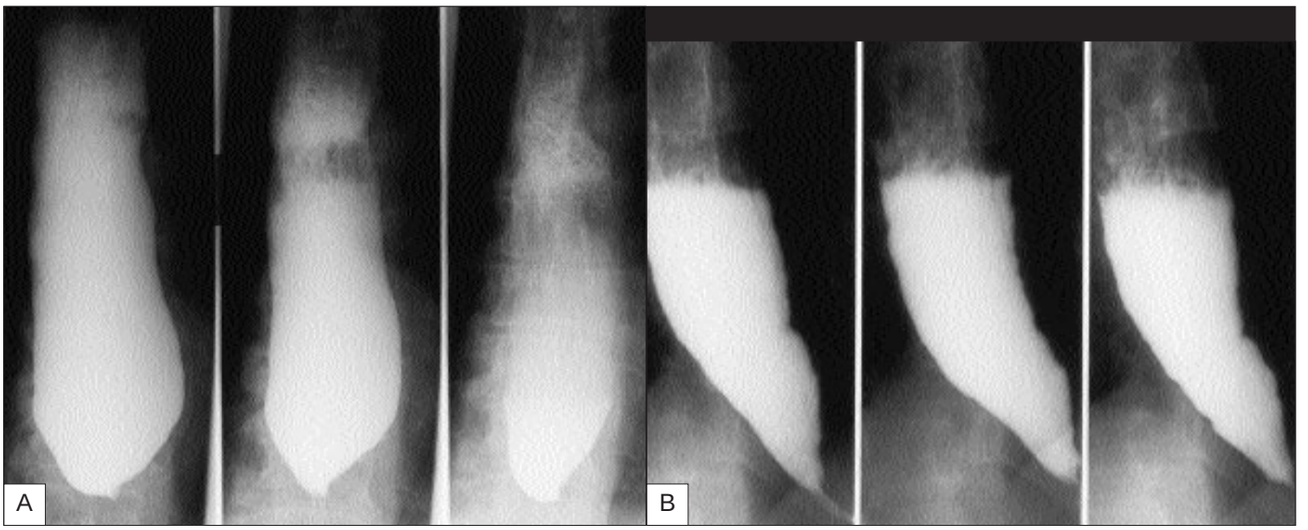
This technique has been shown to be a simple and reproducible method for objective assessment of esophageal function before and after treatment of achalasia (3). Additionally, it has been shown to be a reliable predictor of response to pneumatic dilation therapy and is an important tool in post-pneumatic dilation evaluation (4, 5).

4.3 Characteristic barium esophagram of achalasia. There is poor emptying of the barium from the esophagus which is dilated. There is a characteristic 'bird's beak' narrowing of the distal esophagus due to a non-relaxing LES.



4.4 End-stage achalasia (sigmoid esophagus). The esophagus is markedly dilated and tortuous, forming a sigmoid shape.





4.5 Timed barium swallow (TBS) in two patients (**A** and **B**) with significant delay in esophageal emptying. TBS provides objective evidence of esophageal function and is most useful in diagnosing achalasia and assessing the response to therapies such as pneumatic dilation, or surgical myotomy. It is performed with 250 ml of barium. After the barium is ingested, an X-ray is taken in upright position at time 1, 2, and 5 minutes. The barium height and width at 1, 2, and 5 minutes are measured. In normal population, the barium completely empties in 1 minute.

Esophageal manometry

This is needed to confirm or establish the diagnosis of achalasia, especially when an esophagram is inconclusive. Essential features are:

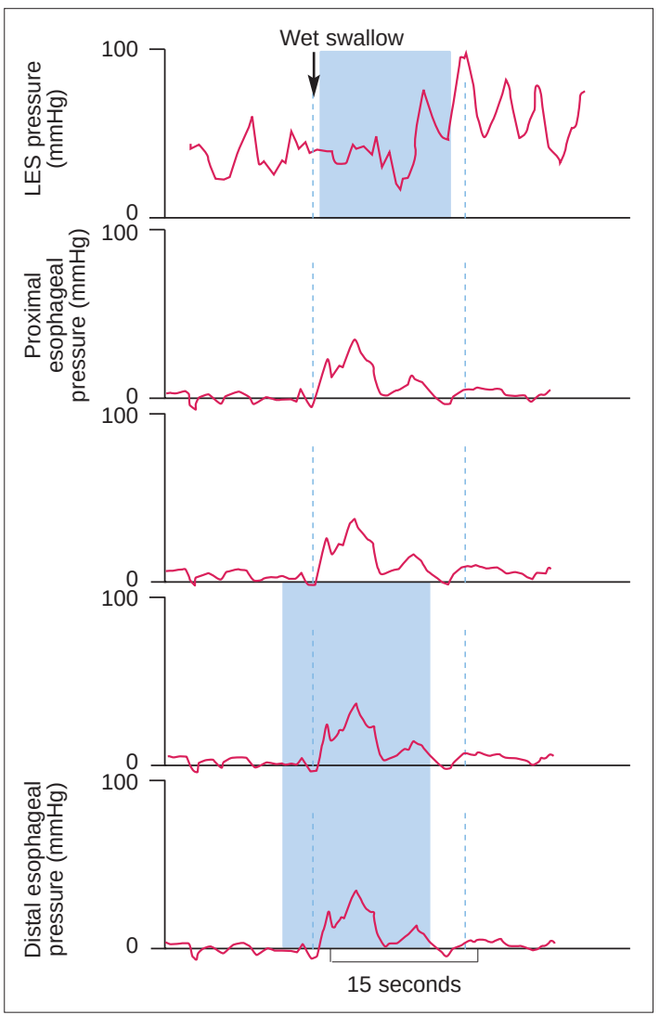
- Aperistalsis in the distal two-thirds of the esophagus (**4.6**).
- Simultaneous onset.
- Isobaric (identical pressure tracings in all leads).
- Abnormal LES relaxation with swallows.

Supportive features include hypertensive LES pressure (LES pressure >45 mmHg), and low amplitude esophageal contractions (contraction amplitude <30 mmHg).

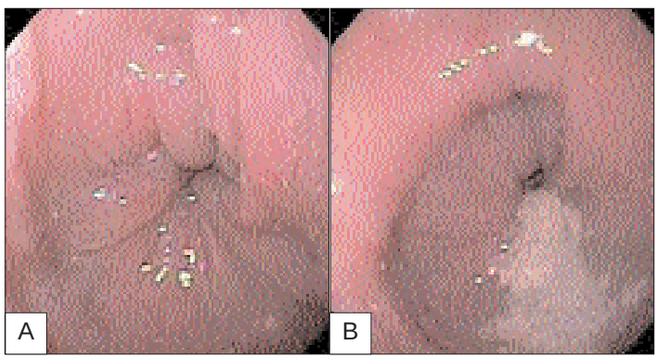
Endoscopy

Endoscopy is necessary to rule out pseudoachalasia secondary to malignancies at the esophagogastric junction.

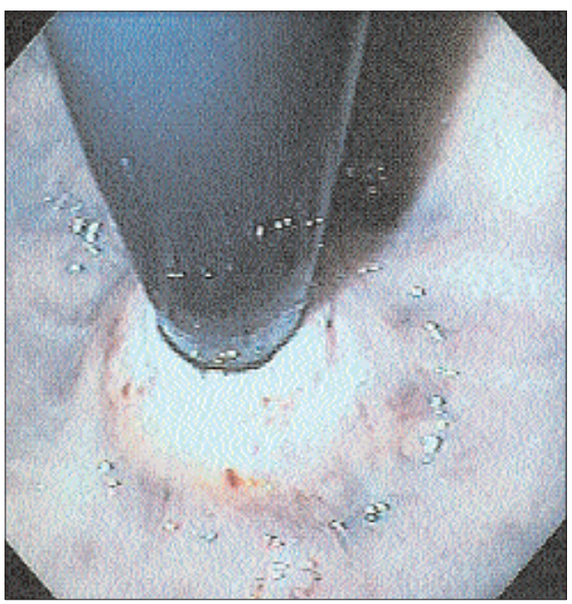
A typical esophagus on endoscopy in an achalasia patient is dilated and tortuous. It is not uncommon to find retained food debris and secretions in the esophagus. The LES remains closed with air insufflation and appears puckered (**4.7**). The gastroesophageal junction (GEJ) and gastric cardia (**4.8**) are carefully examined for evidence of tumors.



4.6 Manometric findings in achalasia. Achalasia is defined manometrically by aperistalsis and failure of LES relaxation. The pressure tracing shows low amplitude simultaneous contractions. Pressure tracings in all leads are identical or isobaric. Isobaric contractions are due to the esophagus being a closed chamber (dilated esophagus closed by sphincters on both ends), where pressure changes are detected by all manometric sites. In addition, LES does not relax with wet swallow.



4.7 Upper endoscopy of an achalasia patient reveals a characteristic puckered GEJ. Retained secretions and food in the esophagus are also frequently seen.



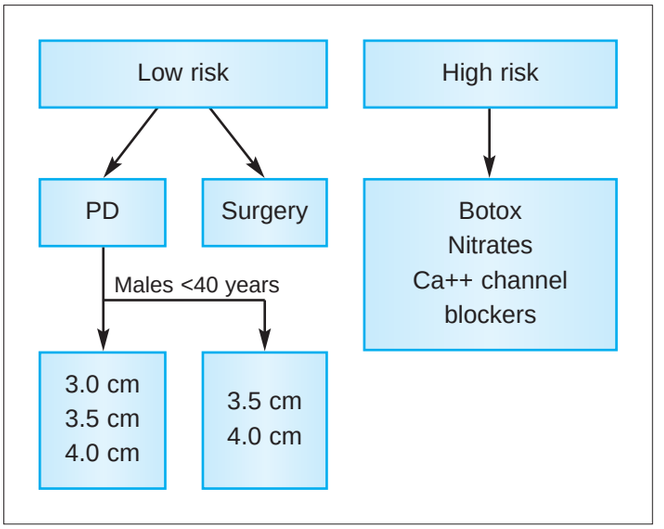
4.8 Retroflexed view of the gastric cardia shows very tight LES around the endoscope. There is no evidence of malignancy causing pseudoachalasia.

Differential diagnosis

Various disorders with similar manometric and radiologic features as achalasia (pseudoachalasia) should be considered in making a diagnosis of achalasia (*Table 4.1*).

The most important cause of pseudoachalasia is malignant neoplasm. Tumors cause pseudoachalasia by encircling or compressing the distal esophagus or infiltrating the esophageal myenteric plexus and impairing inhibitory LES innervation. Clinical features that suggest malignancy are:

- Duration of symptoms <6 months.
- Onset after age 60 years.
- Excessive weight loss.
- Difficulty with endoscope passage through GEJ during esophagogastroduodenoscopy (EGD).
- Computed tomography (CT) scan showing marked (>1 cm) and/or asymmetric esophageal wall thickening.



4.9 Achalasia treatment algorithm. (PD: pneumatic dilation.)

4.1 Disorders with manometric and radiologic features similar to achalasia

Malignancy
- Gastric adenocarcinoma
- Esophageal squamous cell carcinoma
- Lymphoma
- Lung carcinoma
- Pancreatic carcinoma
- Prostatic carcinoma
- Anaplastic carcinoma
- Colon carcinoma
- Esophageal lymphangioma
- Pleural mesothelioma

Chronic intestinal pseudo-obstruction
Amyloidosis
Sarcoidosis
Chagas' disease
Post-vagotomy
Pancreatic pseudocyst
Von Recklinghausen's neurofibromatosis
Anderson–Fabry's disease
Familial glucocorticoid deficiency syndrome
MEN type IIb

MEN: multiple endocrine neoplasia

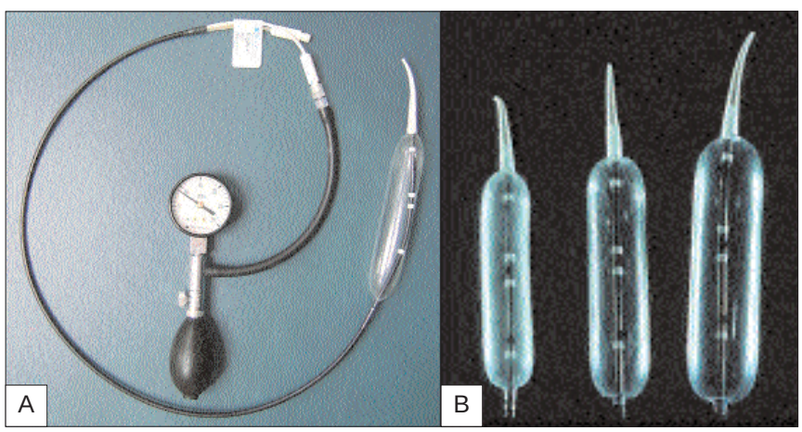
Treatment

There is no cure for achalasia. Treatment options include:

- Pneumatic dilation.
- Surgical myotomy (Heller).
- Botulinum toxin injection.
- Medical therapy (calcium channel blockers, nitrates) (see *Table 4.2*, **4.9**).

Pneumatic dilation

All patients considered for pneumatic dilation should be good surgical candidates because of the 2–5% risk of esophageal perforation. Pneumatic dilation uses air pressure to disrupt traumatically the circular muscle layer of the LES. Rigiflex balloon dilators are most commonly used and are available in three diameters (3.0, 3.5, and 4.0 cm) (**4.10**). A 3.0 cm balloon is usually used for initial dilation. With



4.10 A: Rigiflex pneumatic dilator. **B**: The dilator comes in three balloon sizes: 3.0, 3.5, and 4.0 cm. Pneumatic dilation uses air pressure to disrupt traumatically the circular muscle layer of the LES. A 3.0 cm balloon is usually used for initial dilation. With symptom recurrence, repeat dilations are performed in a stepwise graded fashion using larger sized balloons.

4.2 Comparison of treatments for idiopathic achalasia

	Pneumatic dilation	*Laparascopic myotomy*	*Botulinum toxin*	*Nifedipine/nitrates*
Response	60–90% at 1 year; 60% at 5 years	90% at 1 year; 85% at 5 years	90% at 1 month; 60% at 1 year	50–70% initially; <50% at 1 year
Complications	2–-5% perforation	10% symptomatic reflux	20% rash, transient chest pain	30% headache, hypotension
Advantages	Good response rates	Minimally invasive surgery	Low morbidity	Rapidly initiated
Disadvantages	Risk of perforation	Risks associated with general anesthesia; may need conversion to open procedure	Need frequent repeat injections within 1 year; causes fibroinflammatory reaction at LES	Poor effect on esophageal emptying; tachyphylaxis

LES: lower esophageal sphincter. (Adapted from Feldman M, Friedman LS, Sleisenger MH (2002). *Sleisenger & Fordtran's Gastrointestinal and Liver Disease*, 7th edn. Saunders, Philadelphia.)

symptom recurrence, repeat dilations are performed in a stepwise graded fashion using larger sized balloons. The balloon is positioned over a guidewire using either endoscopic or fluoroscopic control across the LES. The balloon is then inflated until the balloon waist (formed by the LES) is obliterated. The pressure applied is usually 10–14 psi (**4.11**, **4.12**). After dilation therapy, all patients undergo gastrografin esophagram followed by barium esophagram to rule out perforation (**4.13**).

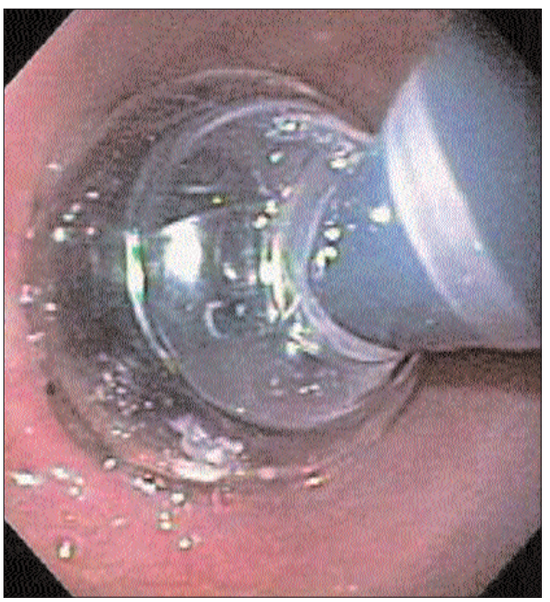
Studies have shown a 50–93% response rate with pneumatic dilation (6). A higher clinical response rate is seen with each successive dilation, with increasing balloon size. A recent evidence showed that males <40 years old will likely fail when a 3.0 cm balloon is used and that they may beneift from the use of a 3.5 cm balloon as initial therapy.

*Surgical therapy: Heller myotomy (**4.14**)*

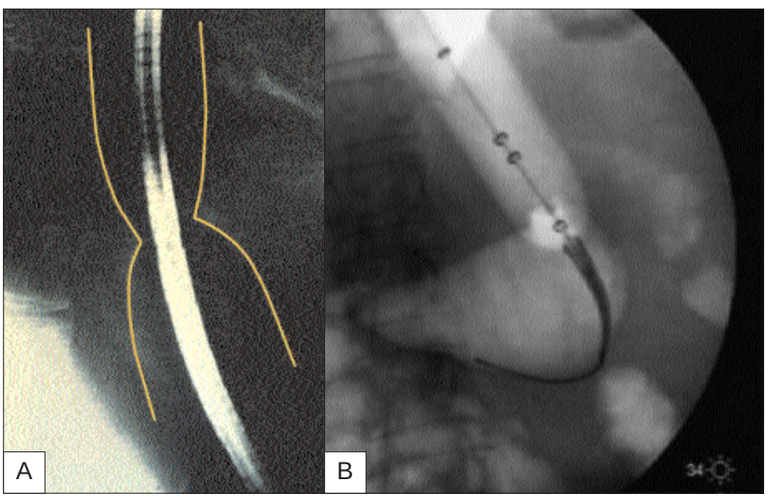
The goal of myotomy is to reduce LES resting pressure without causing gastroesophageal reflux. Heller myotomy consists of anterior myotomy across the LES, which is performed either laparoscopically (abdominal approach) or open (transthoracic approach). The circular muscle fibers are divided down to the level of the mucosa and the myotomy extends to several centimeters above the LES and <1 cm onto the stomach. Anti-reflux surgery (Dor fundoplication) is usually performed concomitantly. Good response rates are observed, from 80–90% (7).

*Botulinum toxin injection (**4.15**)*

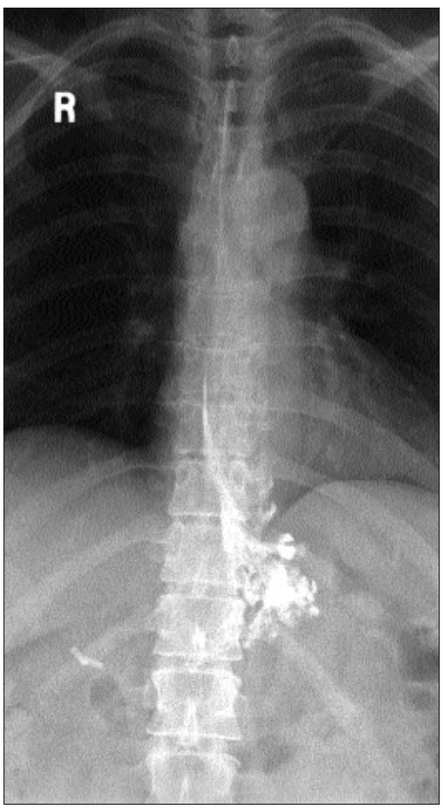
This can be performed on patients who are high risk for pneumatic dilation or surgical myotomy, such as the elderly or those with other co-morbidities. Botulinum toxin inhibits acetylcholine release from nerve terminals, thereby blocking excitatory effects of the cholinergic neurons. It is initially effective in about 85% of patients. However, the response only lasts about 6 months, with >50% symptom recurrence in 6 months.



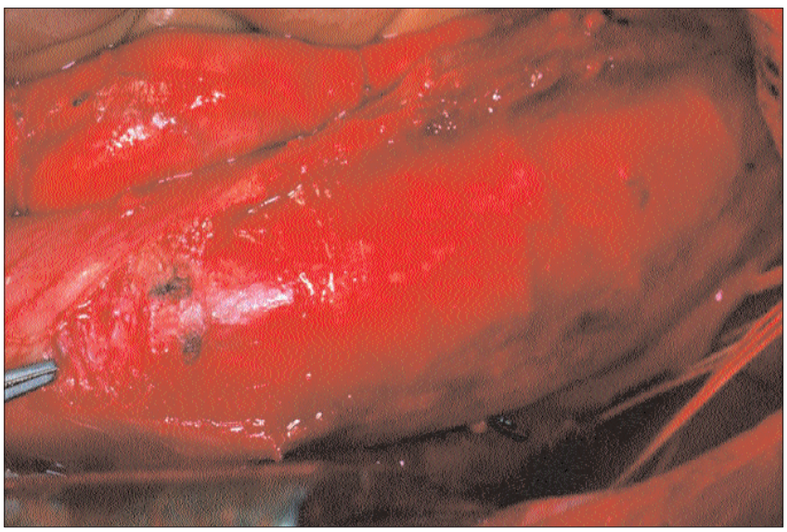
4.11 The balloon is positioned over a guidewire using either endoscopic or fluoroscopic control across the LES. Then, the balloon is inflated until the balloon waist detected on fluoroscopy (formed by the LES) is obliterated. The pressure applied is usually 10–14 psi.



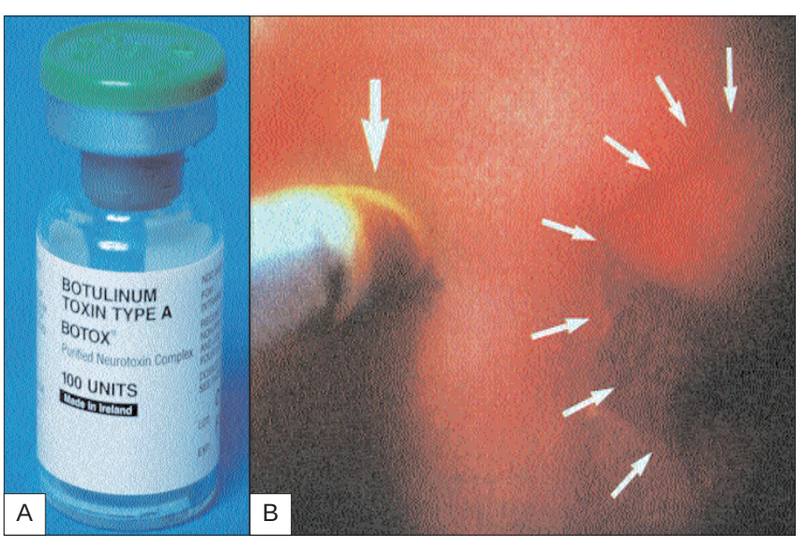
4.12 Pneumatic dilation is usually performed using fluoroscopic control. When the balloon is inflated, a waist is formed secondary to a poorly relaxing LES. The balloon is slowly inflated further until the waist is obliterated.



4.13 Esophageal perforation a patient with post-pneumatic dilation.



4.14 Open Heller myotomy. Heller myotomy consists of anterior myotomy across the LES. The circular muscle fibers are divided down to the level of mucosa. The myotomy extends to several centimeters above LES and <1 cm onto the stomach. Anti-reflux surgery (Dor fundoplication) is usually performed concomitantly.



4.15 A: Botulinum toxin injection is performed on patients who are high risk for pneumatic dilation or surgical myotomy, such as the elderly or those with other co-morbidities. Botulinum toxin inhibits acetylcholine release from nerve terminals, thereby blocking the excitatory effects of the cholinergic neurons. **B**: It is injected at about 1 cm above the gastroesophageal junction (large arrow). The LES is highlighted by the smaller arrows at the puckered GEJ. Botulinum toxin is initially effective in about 85% of patients. However, the response only lasts about 6 months with >50% symptom recurrence in 6 months.

Other pharmacologic options

Calcium-channel blockers and long-acting nitrates reduce LES pressure. The clinical response is not complete and is short lasting, with decreased efficacy over time. Therefore, medical therapy is recommended for those who are not candidates for pneumatic dilation or surgical myotomy and who fail to respond to botulinum toxin injection.

Complications

Complications are related to retention and stasis in the esophagus. They include esophagitis secondary to irritation of the mucosal lining, aspiration of esophageal contents (nocturnal coughing spells or aspiration pneumonia), and esophageal squamous cell carcinoma (SCC).

References

1 Park W, Vaezi MF (2005). Etiology and pathogenesis of achalasia: the current understanding. *Am J Gastroenterol* **100**(6):1404–1414.

2 Howard PJ, Maher L, Pryde A, *et al.* (1992). Five year prospective study of incidence , clinical features, and diagnosis of achalasia in Edinburgh. *Gut* **33**:1011.

3 de Oliveira JM, Birgisson S, Doinoff C *et al.* (1997). Timed barium swallow: a simple technique for evaluating esophageal emptying in patients with achalasia. *AJR* **169**:473–479.

4 Vaezi MF (2001). Quantitative methods to determine efficacy of treatment in achalasia. *Gastrointestinal Endoscopy Clinics of America* **11**(2):409–424.

5 Vaezi MF, Baker ME, Achkar E *et al.* (2002). Timed barium oesophagram: Better predictor of long term success after pneumatic dilation in achalasia than symptom assessment. *Gut* **40**:765–770.

6 Vaezi MF, Richter JE (1998). Current therapies for achalasia: comparison and efficacy. *J Clin Gastroenterol* **27**:21-35.

7 Vantrappen G, Hellemans J (1980). Treatment of achalasia and related motor disorders. *Gastroenterol* **79**:144.

Further reading

Vaezi MF, Richter JE (1999). Diagnosis and management of achalasia. *Am J Gastroenterol* **94**:3406–3412.

Summary

Definition: primary esophageal motor disorder.

Etiology: unknown.

Pathophysiology: loss of inhibitory neurons in myenteric plexus required for LES relaxation. Aperistalsis also occurs.

Symptoms: dysphagia, regurgitation, chest pain, weight loss, pulmonary symptoms and coughing.

Diagnosis: contrast radiography (barium esophagram), esophageal manometry and endoscopy.

DDx: pseudoachalasia due to neoplasia.

Treatment: pneumatic dilation, surgical myotomy, botulinum injection, medical therapy (calcium channel blockers, nitrates).

Complications: esophagitis, aspiration of esophageal contents, SCC.

Non-achalasia motility disorders

Introduction

Esophageal motility disorders are associated with abnormal manometric motility patterns primarily in patients with non-cardiac chest pain and non-obstructive dysphagia (*Table 4.3*). Their clinical significance is unclear (1), and they are associated with poor correlation between manometric findings and symptoms. In some cases, treatment may reduce symptoms but manometric findings are unchanged. In one study of 1,161 adult patients with chest pain or dysphagia, motility abnormality was found in 33% (2). Motility abnormality was more common in patients with symptoms of dysphagia than chest pain (53% and 28% respectively)(2).

Clinical presentation

Esophageal motility disorder should be considered in patients presenting with dysphagia, chest pain, or odynophagia. For symptoms of dysphagia, structural lesions must first be ruled out with barium esophagram or upper endoscopy. Cardiac chest pain cannot be distinguished from esophageal chest pain. Therefore, heart disease must be excluded before non-cardiac chest pain is entertained. Odynophagia is rare in primary esophageal motility disorder. It is usually due to infectious, pill-induced, or reflux esophagitis and work-up should be performed to rule out such causes.

Diagnosis

- Barium esophagram is sensitive and specific in detecting motility disorder when carefully performed with videofluoroscopy.
- EGD has little role in the evaluation of esophageal dysmotility. It is used in conjunction with barium studies to rule out structural lesions or esophagitis.
- Manometry is necessary in order to characterize and define esophageal motility disorder.

4.3 Manometric diagnosis of motility disorders

Functional defect	*Diagnosis*	*Manometric criteria*
Aperistalsis	Achalasia	Isobaric simultaneous contractions; poorly relaxing LES
	Scleroderma	Low amplitude or absent contraction in distal esophagus, with or without low LES pressure
Incoordinated motility	DES	≥20% simultaneous esophageal contractions
Hypercontractile	NE	Normal peristalsis with DEA >180 mmHg
	Hypertensive LES	LES resting pressure >45 mmHg
Hypocontractile	IEM	≥30% of swallows with amplitude <30 mmHg in either of the two distal sites at 5 and 10 cm above LES
	Hypotensive LES	LES resting pressure <10 mmHg

DEA: distal esophageal amplitude: DES: diffuse esophageal spasm; IEMD: ineffective esophageal motility; LES: lower esophageal sphincter; NE: nutcracker esophagus

Diffuse esophageal spasm (DES)

Etiology and pathophysiology

The etiology of DES is unknown. Suggested mechanisms of disease include a hypersensitivity response to cholinergic and hormonal stimulation, mediated by defects in neural inhibition.

Clinical presentation

Recurrent chest pain is indistinguishable from cardiac chest pain and is relieved with nitroglycerin. It is associated with meals but rarely exertionally induced. Dysphagia is intermittent and non-progressive.

Diagnosis

Manometry is the only way to diagnose DES accurately. The diagnostic criteria are the presence of normal peristalsis intermixed with simultaneous contractions in ≥20% of wet swallows (**4.16**)(3).

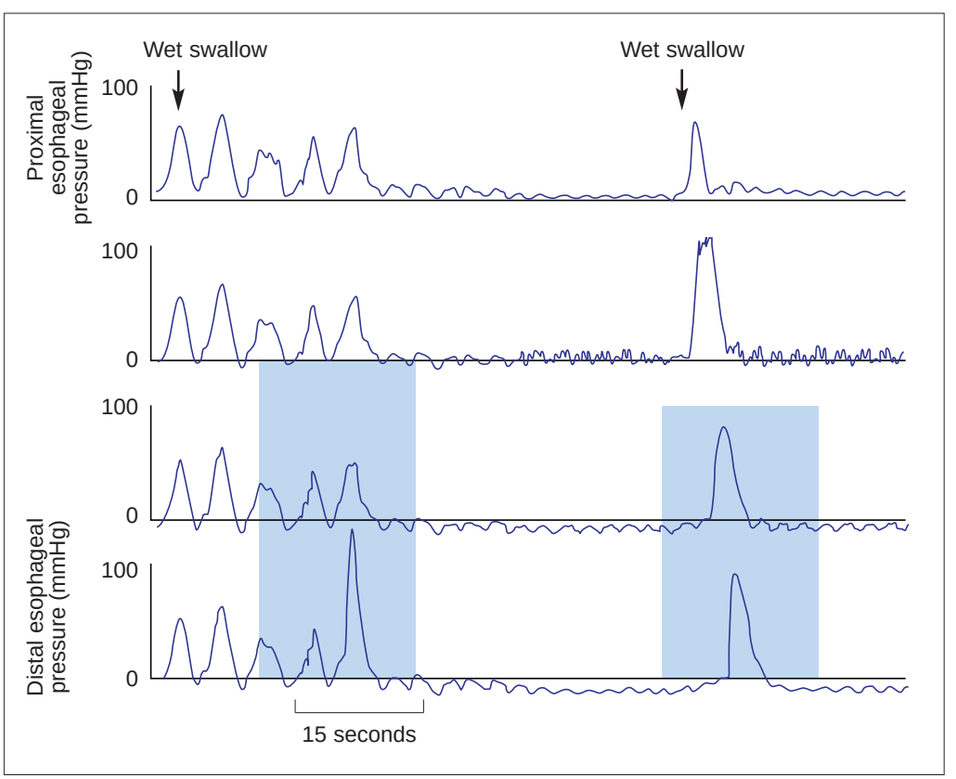
Finding from barium swallows are variable and are usually normal. Therefore, normal radiographic study does not rule out the diagnoses. Tertiary activity produces esophageal coiling appearance ('corkscrew') (**4.17**). The LES region is usually normal.

Natural history

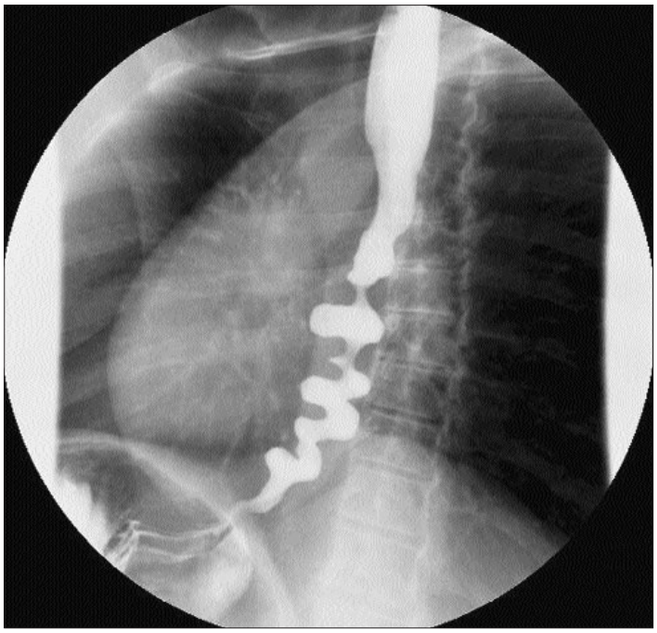
Patients with DES have an excellent prognosis in general. Transition to achalasia occurs in approximately 3–5% (4).

Treatment

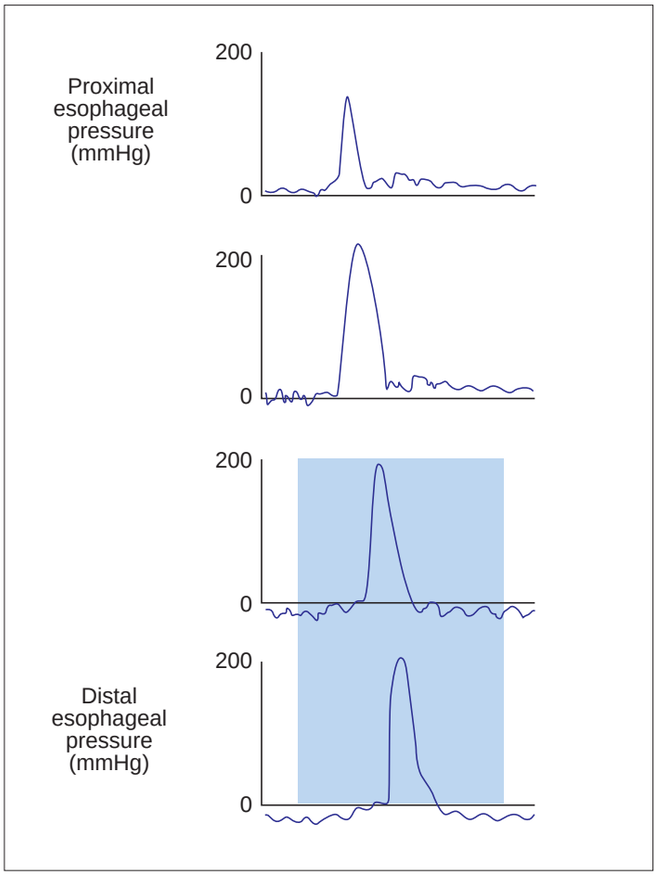
Treatment consists of medications that relax the esophagus, including nitrates and calcium channel blockers. They are usually not effective.



4.16 Manometric finding in DES. There are repetitive simultaneous contractions in the esophageal body, but some normal peristalsis is maintained. LES relaxation is normal and complete.



4.17 Barium esophagram in DES. The barium swallow study shows characteristic 'corkscrew' appearance.



4.18 Manometric finding in NE. NE is diagnosed manometrically as high amplitude (≥180 mmHg) peristaltic contractions with wet swallows.

Nutcracker esophagus

Etiology

The cause of nutcracker esophagus (NE) is unknown. However, findings of infrequent transition to achalasia suggests it may be an early part of a spectrum of disease that results in achalasia (5). Some believe it may be a functional disorder similar to irritable bowel syndrome and associated with increased visceral pain perception (6).

Clinical presentation

Chest pain is the most common (90%) symptom. Dysphagia is less frequent. These patients usually present to gastroenterologists after cardiac chest pain is ruled out by their internist and cardiologist.

Diagnosis

Manometry is required to diagnose NE. Diagnostic criteria require that all contractions are peristaltic and that the contraction amplitude is ≥180 mmHg (**4.18**). Patients with NE may present later as normal or with different manometric tracing, such as DES (7).

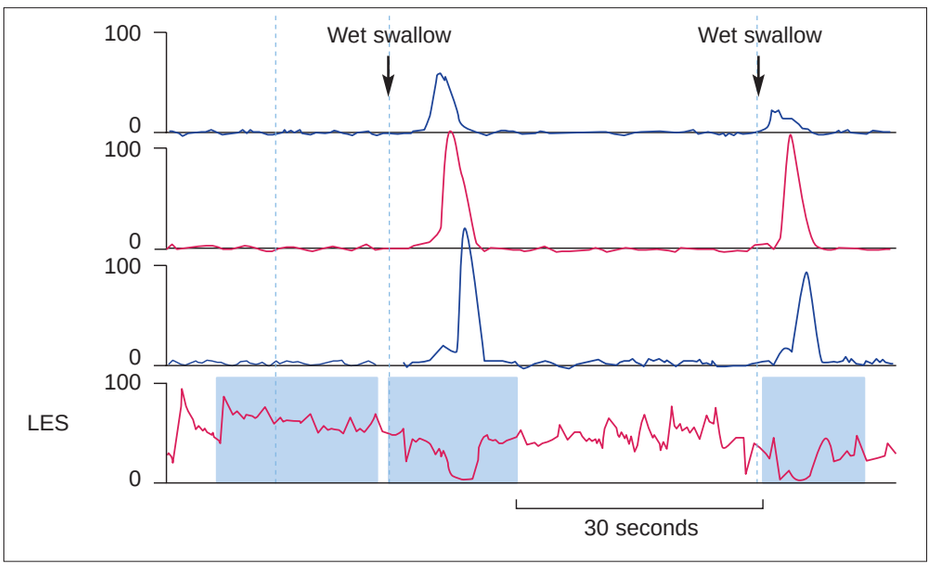
Radiographic findings are usually normal, since all patients have normal peristalsis by definition.

Hypertensive lower esophageal sphincter

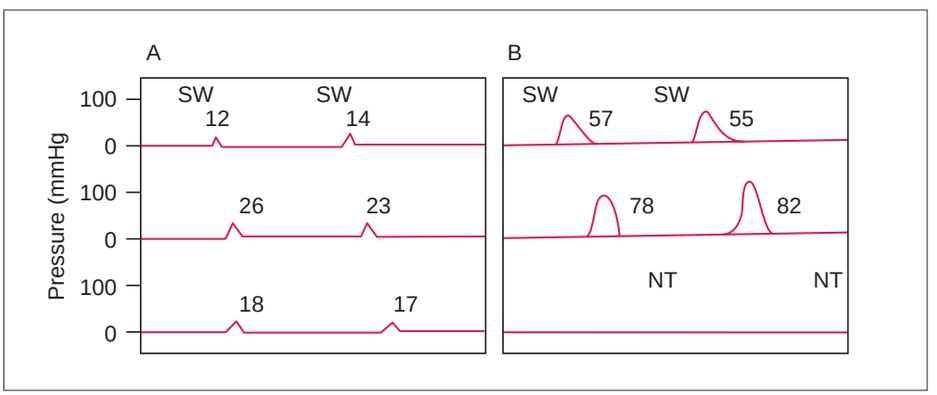
Hypertensive LES is defined by a resting LES pressure >45 mmHg. As part of a peristaltic sequence, LES relaxation occurs with normal residual pressure (**4.19**). Of unknown etiology, it is typically seen in patients with symptoms of chest pain. Dysphagia can also be seen. Barium swallow is usually normal with normal esophageal function.

Ineffective esophageal motility (4.20)

The manometric abnormality is characterized by a hypocontractile esophagus, which is defined as distal esophageal contraction amplitude <30 mmHg in ≥30% of wet swallows. It is commonly associated with gastro-esophageal reflux disease (GERD).



4.19 Manometric finding in hypertensive LES. The resting pressure of the LES is >45 mmHg. As part of the peristaltic sequence, LES relaxation occurs with normal residual pressure.



4.20 Manometry tracing of a patient with ineffective esophageal motility showing normal weak amplitude peristaltic contractions (A) and non-transmitted (NT) esophageal contraction in distal esophagus (B). (Adapted from *Dig Dis Sci* [1997] **42**: 9.)

Treatment (Table 4.4)

GERD should be treated if present. Sublingual nitrates are given as needed if symptoms are mild and intermittent. For unexplained chest pain in patients with depressive or anxiety component, trazodone 50–100 mg three times daily or imipramine 50 mg at bed time is recommended. Calcium-channel blockers are prescribed in those who are refractory to the above treatment: diltiazem 60–90 mg three times daily, or nifedipine 10– 20 mg three times daily. For severely refractory patients with LES dysfunction, botulinum toxin, pneumatic dilation, or myotomy should be considered.

References

1 Richter JE (2001). Oesophageal motility disorders. *Lancet* **358**:823–828.

2 Katz PO, Dalton CB, Richter JE, *et al.* (1987). Esophageal testing of patients with noncardiac chest pain and/or dysphagia. Results of a three year experience with 1161 patients. *Ann Intern Med* **106**:593.

3 Richter JE, Castell DO (1984). Diffuse esophageal spasm: Reappraisal. *Ann Intern Med* **100**:242.

4 Rhoton AJ, *et al.* (1992). The natural history of diffuse esophageal spasm (DES): a long term follow-up study. *Am J Gastroenterol* **87**:A1256.

5 Anggiansah A, Bright NF, McCullagh M, *et al.* (1990). Transition from nutcracker esophagus to achalasia. *Dig Dis Sci* **35**:1162.

6 Richter JE, Obrecht WF, Bradley LA, *et al.* (1986). Psychological comparison of patients with nutcracker esophagus and irritable bowel syndrome. *Dig Dis Sci* **31**:131.

7 Narducci F, *et al.* (1985). Transition from nutcracker esophagus to diffuse esophageal spasm. *Am J Gastroenterol* **80**:242.

Table 4.4 Therapeutic options for esophageal motility disorders

Nitrates	Nitroglycerin 0.4 mg sublingually before meals or as needed Isosorbide 10–30 mg orally 30 minutes before meals
Viceral analgesic	Imipramine 50 mg orally at bedtime
Sedatives/antidepressants	Alprazolam 2–5 mg orally four times daily Trazadone 50 mg orally three or four times daily
Calcium-channel blockers	Nifedipine 10–30 mg orally four times daily Diltiazem 60–90 mg orally four times daily
Smooth muscle relaxant	Hydralazine 25–50 mg orally three times daily Botulinum toxin 80 U (injected into LES using endoscopy)
Dilation	50–60 French bougie Pneumatic dilation

LES: lower esophageal sphincter

Webs and rings

Table 4.5 shows the similarities and differences between esophageal webs and the two types of esophageal rings (A and B). Although the terms 'web' and 'ring' are often used interchangeably, there do exist several important differences, and an accurate distinction should be made in describing these lesions.

Proximal web

Definition

A proximal web is a thin, transverse membrane of squamous mucosal epithelium occurring anywhere in the esophagus, though most often in the proximal esophagus.

Epidemiology

The prevalence of webs is not well described, although an estimate is 1–8% of the population. Webs have been found in 5–15% of patients with benign causes of dysphagia who undergo endoscopic evaluation. They can be located anywhere in the esophagus, but typically occur in the post-cricoid area of the upper esophagus, located on the anterior cervical wall. The prevalence of webs increases with age, and symptomatic rings are more common in women.

Pathophysiology

The cause of webs is unclear, and most are classified as being idiopathic. GERD has been suggested as a possible cause. Several other conditions have been associated with webs, but the cause and effect relationship is uncertain. These conditions include thyroid disease, duplication cyst, Zenker's diverticula, chronic graft-versus-host disease (GVHD), blistering skin diseases (pemphigoid and epidermolysis bullosa), psoriasis, Stevens–Johnson syndrome, and laryngeal carcinoma.

Table 4.5 Webs and rings

Characteristic	*Esophageal web*	*Mucosal (B ring)*	*Muscular (A ring)*
Location	Posterior cricoid region along anterior wall	Schatzki's ring, squamocolumnar junction – associated with hiatal hernia	1.5 cm proximal to squamocolumnar junction – at upper LES
Histology	Mucosa and submucosa covered by epithelium	Mucosa and submucosa covered by squamous and columnar epithelium	Hypertrophied muscle covered by squamous epithelium
Symptoms	Intermittent solid food dysphagia	Intermittent solid food dysphagia – size dependent	Usually asymptomatic – solid food dysphagia if symptomatic
Imaging	Thin projection off anterior surface of post-cricoid esophagus	Thin, transverse, circumferential ridge	Smooth, symmetrical narrowing
Treatment	Bougie or balloon dilation	Maloney dilation – 50–60 French	Maloney dilation – 50–60 French

LES: lower esophageal sphincter

Clinical presentation

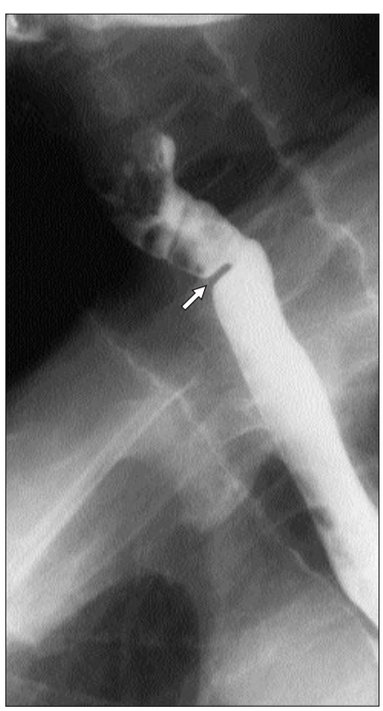
The majority of all rings and webs are asymptomatic. The most common complaints of patients with esophageal webs who do experience symptoms are solid food or pill-induced dysphagia. The proximal location of the web leads to a sensation of choking while eating.

Diagnosis

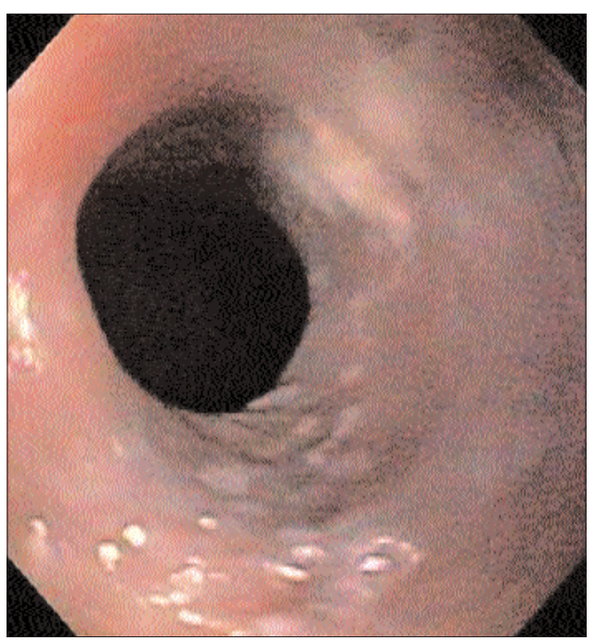
The diagnosis of webs is difficult, and they are often missed during endoscopic evaluation as well as on radiographic examination. The most sensitive test for diagnosis is a barium esophagram, and the radiologist must focus on the proximal esophagus to detect the webs (**4.21**). Webs will appear as a thin membranous filling defect just below the upper esophageal sphincter (UES), and they are best visualized on lateral images. Webs are 2–3 mm thick, and lie at the lower border of the cricoid cartilage. They may be unilateral or circumferential. Endoscopy is less reliable, but webs may be seen as a thin, eccentric lesion with normal appearing mucosa (**4.22**) compromising the esophageal lumen. The webs may impinge on the passage of the scope depending on their size. The passage of the scope may also disrupt the webs without the endoscopist being aware.

Treatment

The most common treatment is Savary dilation over a guidewire, with most physicians using dilators 15 mm or greater in diameter. Webs may persist even following symptom relieving therapy. Other methods of treatment include endoscopic biopsy, balloon dilation, laser ablation, and surgery.



4.21 Barium esophagram showing a proximal esophageal web (arrow). This is the most sensitive test to detect this lesion. The most common location for this lesion is the posterior cricoid area of the upper esophagus.



4.22 Endoscopic appearance of a proximal esophageal web. The web appears to be a thin, eccentric lesion. The mucosa is normal in appearance. If located proximally, it is possible to fracture the web during passage through the UES without being aware of its presence.

Plummer–Vinson or Patterson-Kelly syndrome

This syndrome is a triad of esophageal web, iron-deficiency anemia, and dysphagia.

The webs are typically hypopharyngeal or in the upper esophagus, may be single or multiple, and may be associated with stricture formation. It is more common in the middle-aged, and in white women.

Ringed esophagus

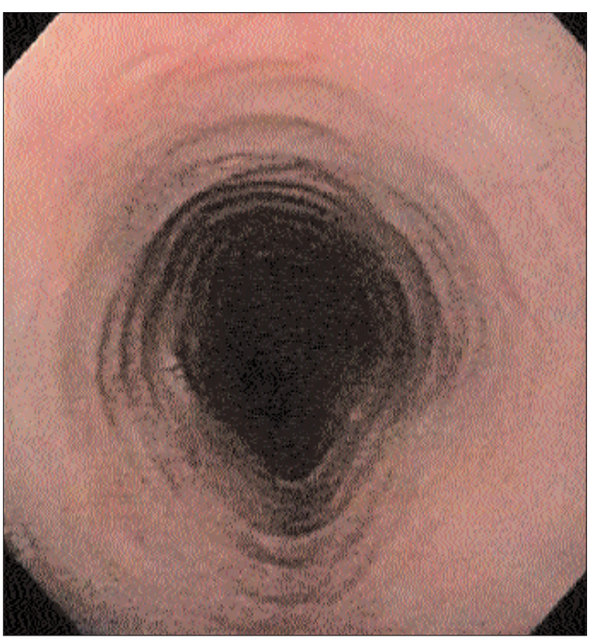
This is a rare condition that most often occurs in young males, with most patients being younger than 30 years. Clinical presentation is often a complaint of long-standing solid food dysphagia, usually going back to early childhood. Patients may present with an acute food impaction, after spending years accommodating their chronic dysphagia.

Proposed etiologies include GERD, congenital abnormalities, and possible allergic conditions (eosinophilic esophagitis) (**4.23, 4.24**). Endoscopy shows multiple esophageal rings, often associated with an area of esophageal narrowing. The esophageal mucosa appears normal throughout.

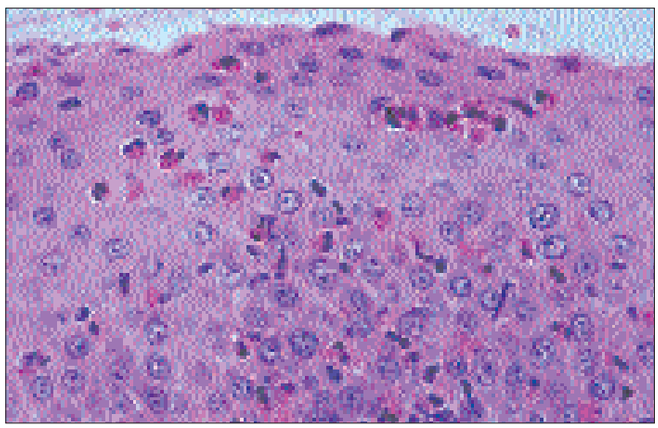
Treatment is with mechanical bougienage and a consideration of acid suppressive therapy. It is not uncommon to require multiple dilations, and these patients are at increased risk of painful, deep mucosal tears.

Schatzki's rings

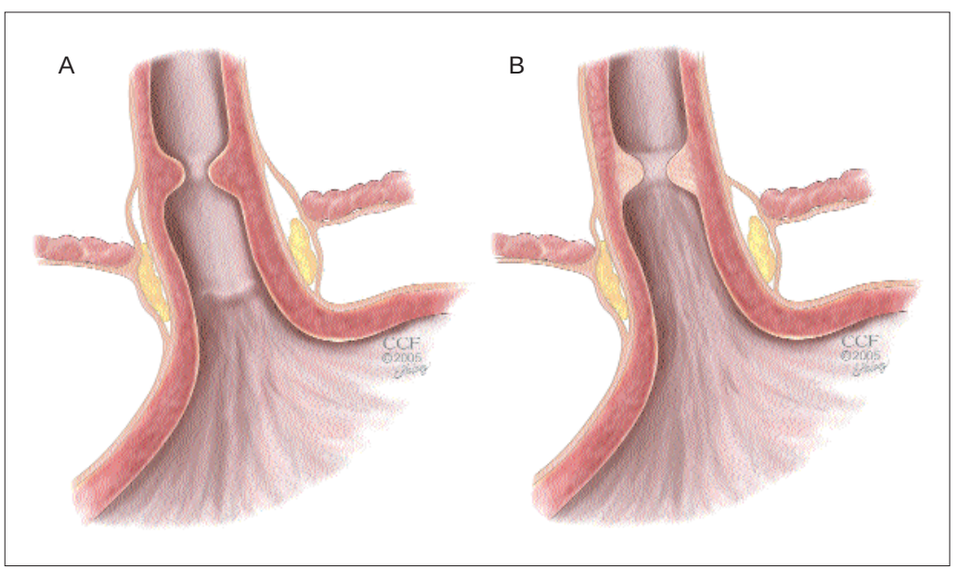
A prevalence of 0.2–14% in the general population has been reported, with an increase in incidence with increasing age (most occur after the age of 40 years). The rings are located at the GEJ, at the distal margin of the LES, and are composed of annular membranes of mucosa and submucosa. Due to their location, the proximal aspect is usually squamous mucosa, with gastric columnar mucosa distally (**4.25**). By definition, there is a hiatal hernia present with all Schatzki's rings. Schatzki's rings are the most



4.23 Endoscopy depicting a ringed esophagus. This rare condition is most prevalent in young men, and presents with dysphagia. There are multiple esophageal rings seen on endoscopy, and treatment includes dilation and possible addition of an acid suppressive agent. Complications, such as deep mucosal tears, are more common with treatment of this condition.



4.24 Histology from an esophageal biopsy in a patient with eosinophilic esophagitis. This condition is most common in young males, and patients present with chronic solid food dysphagia. Associated conditions are often present, and include allergies, asthma, and atopy. Endoscopy will show multiple mucosal rings, and a narrow, slender esophagus. The demonstration of eosinophils on biopsy is necessary in order to make the diagnosis.



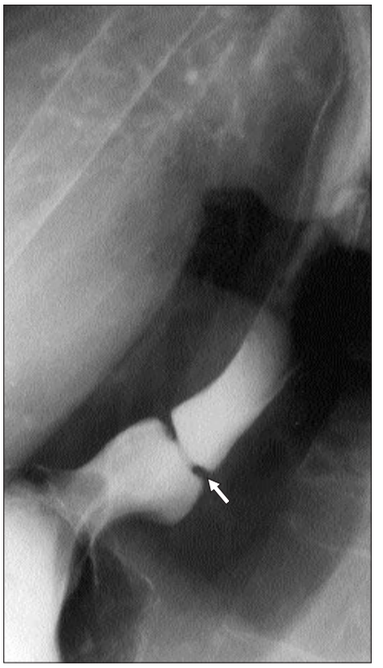
4.25 Schematic figure to show the difference in appearance of esophageal 'A' rings (**A**) and 'B' rings (Schatzki's ring) (**B**). The 'A' ring is located proximal to the SCJ, and is an annular ring composed of hypertrophied muscle. The 'B' ring, or Schatzki ring, is located at the SCJ, and is always located in association with a hiatal hernia. This ring is composed of normal esophageal epithelium, but may have a columnar mucosa on the gastric side.

common cause of intermittent solid food dysphagia, which may be slowly progressive over years. Other clinical presentations include food impaction and, rarely, perforation.

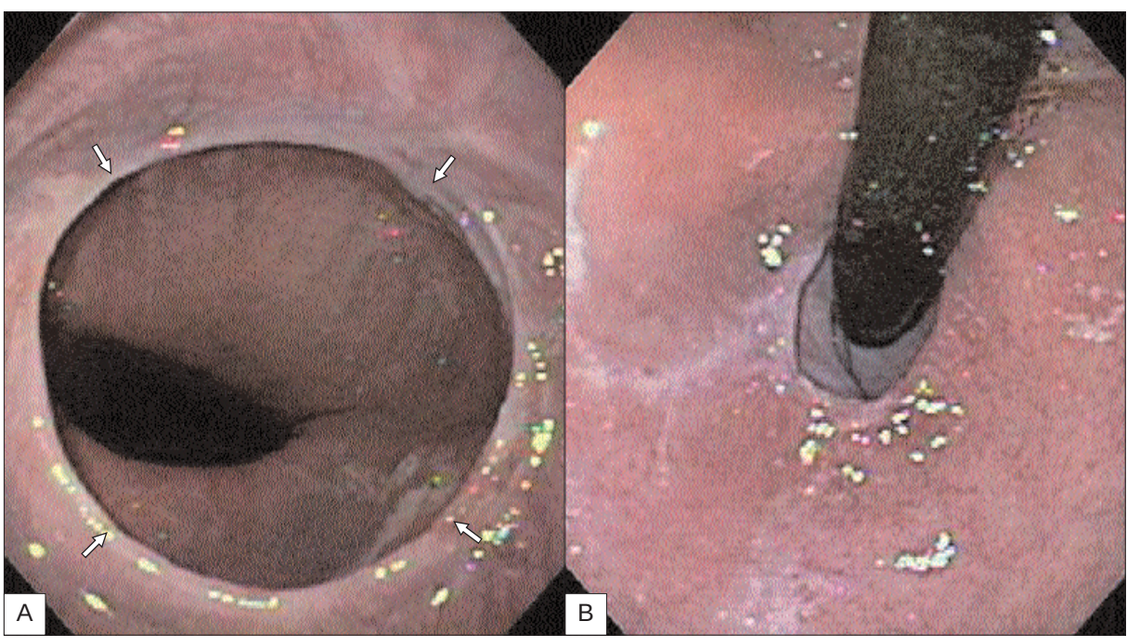
The presence of symptoms depend on luminal diameter: if <13 mm the patient will have symptoms; if >20 mm the patient will almost never have symptoms. Symptoms are variable at diameters between 13 and 20 mm. Pathogenesis is controversial, and proposed etiologies include congenital abnormalities and GERD.

For diagnosis the most sensitive test is the barium esophagram (**4.26**), and yield may be enhanced by using a barium bolus (tablet, marsh mallow). Most rings can also be seen on endoscopy (**4.27**) using patience, air insufflation, or the Valsalva maneuver.

Treatment is only necessary if the patient is symptomatic. In these cases, mechanical bougienage is the treatment of choice, usually using a single pass with a large bore (48 F) dilator. It is not uncommon to have recurrent symptoms requiring repeat dilation. Acid suppressive therapy may be used considering the possible association with GERD.



4.26 Esophagram showing a Schatzki's ring after barium swallow (arrow). Notice the presence of the hiatal hernia. Presence of dysphagia is dependent on the diameter of the ring, with nearly all patients having symptoms if <13 mm.



4.27 An endoscopic view of a Schatzki's ring, depicting a significant narrowing of the esophageal lumen (**A**: esophageal view (arrows); **B**: retroflex gastric view). Endoscopists may use air insufflation to identify these rings better during the examination.

'A' ring

An 'A' ring is a muscular ring located in the lower esophagus at the proximal margin of the LES, approximately 2 cm proximal to the squamocolumnar margin (SCM) (**4.25**). This ring is composed of hypertrophic bands of circular muscle, covered with normal squamous epithelium. The incidence increases with age, with most symptomatic patients being older than 40 years of age. These rings are rarely symptomatic, but can lead to intermittent solid food dysphagia.

Diagnosis is made by barium swallow, which shows a smooth, symmetrical narrowing of the distal esophagus (**4.28**). This may also be seen on endoscopy. As with other rings, treatment is with large-bore dilation (>50 F), and should only be considered if the patient is symptomatic.

Summary

Definition: a transverse membrane of squamous mucosal epithelium anywhere in the esophagus, usually proximally.

Etiology: unknown, possible association with GERD.

Pathophysiology: partially occlude lumen.

Symptoms: dysphagia (solid food or pill-induced), majority are asympomatic.

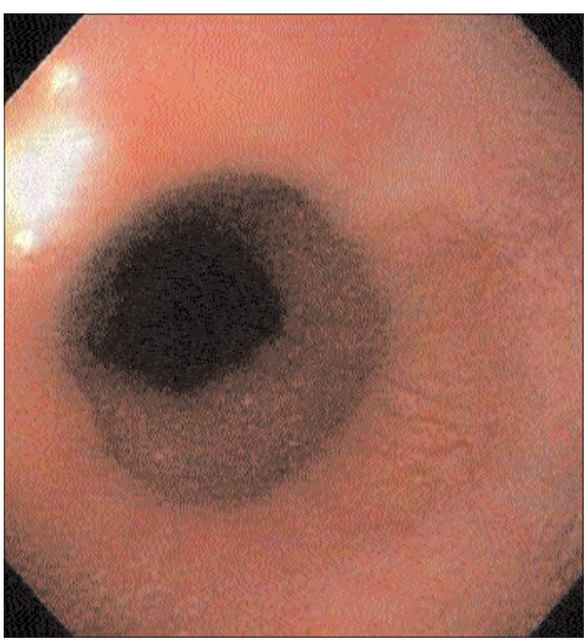
Diagnosis: contrast radiography (barium esophagram). Endoscopy is less reliable.

Treatment: dilation (Savary), endoscopic biopsy, laser.

Further reading

Castell DO, Richter JE (eds) (2003). *The Esophagus*, 4th edn. Lippincott, Williams, and Wilkins, Philadelphia.

Tobin RW (1998). Esophageal rings, webs, and diverticula. *J Clin Gastroenterol* **27**(4):285–295.



4.28 The 'A' ring is most often detected on barium swallow, and is rarely symptomatic. The location is approximately 2 cm proximal to the SCJ.

Strictures

Definition

An esophageal stricture is any loss of lumen area within the esophagus.

Clinical presentation

The predominant clinical symptom is dysphagia which usually is most prevalent when the luminal diameter is <15 mm (normal is 20 mm). Less severe strictures can cause intermittent dysphagia to large food pieces, such as meat and bread.

Causes

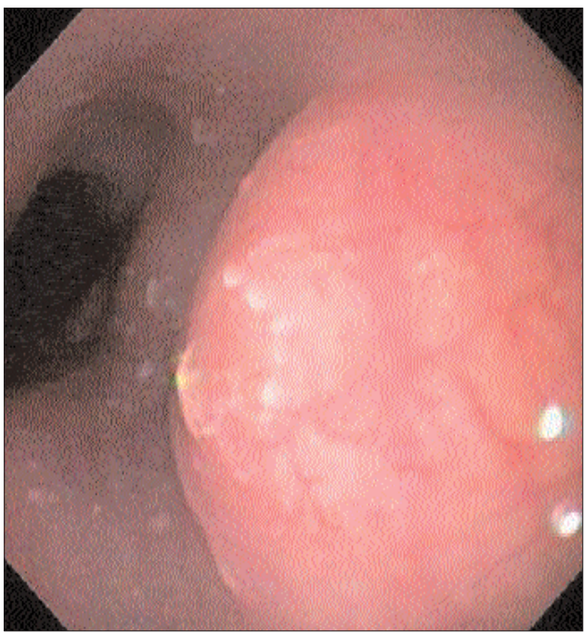
There are multiple intrinsic and extrinsic causes for esophageal strictures (*Table 4.6*). Intrinsic strictures are most common, with acid/peptic disease accounting for a majority of the cases. (Rings/webs and neoplasms are discussed in separate sections.)

Diagnosis

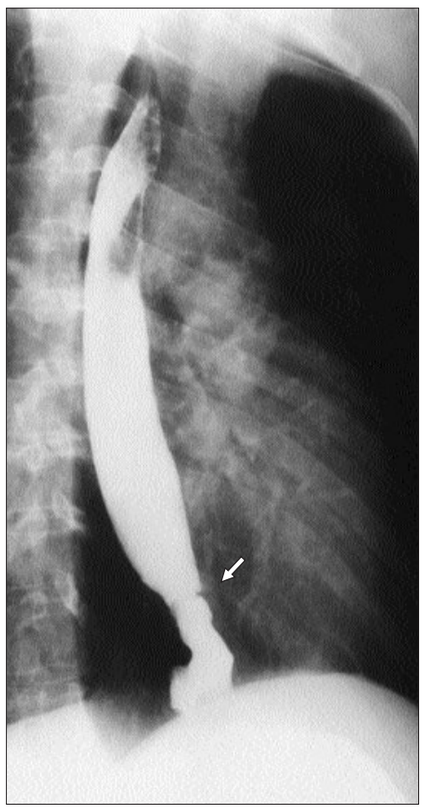
Strictures may be diagnosed by barium swallow or endoscopy (**4.29–4.32**). Barium swallow is particularly useful to assess for the presence of subtle strictures or rings. Endoscopy is usually necessary to allow biopsy for diagnosis and for treatment.

Table 4.6 Etiology of esophageal strictures

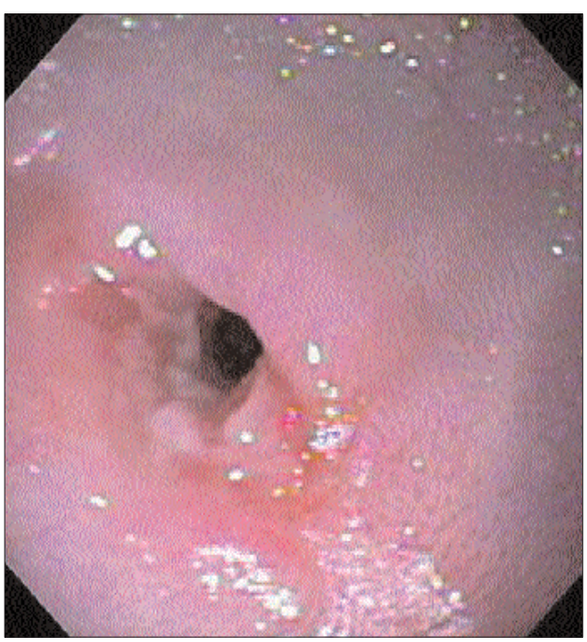
Intrinsic	*Extrinsic*
Acid peptic	Pulmonary/mediastinal malignancies
Pill-induced	Anomalous vessels and aneurysms
Chemical/lye	Metastatic submucosal infiltration (breast cancer, mesothelioma, adenocarcinoma of gastric cardia)
Post-nasogastric tube	
Infectious esophagitis	
Sclerotherapy	
Radiation-induced	
Esophageal/gastric malignancies	
Surgical anastomotic	
Congenital	
Systemic inflammatory disease	
Epidermolysis bullosa	



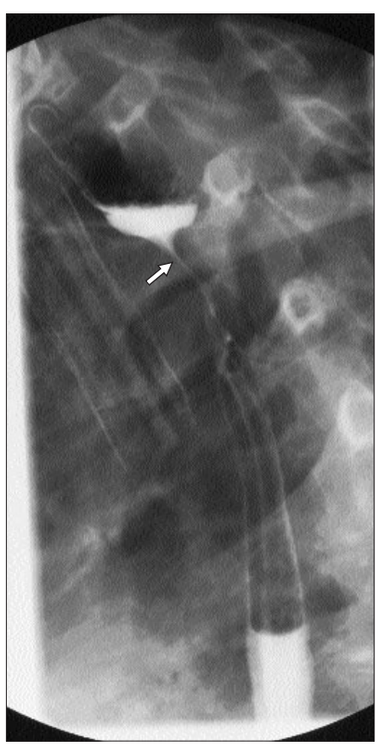
4.29 Aortic arch causing external compression of the proximal esophagus. The aortic arch normally causes minor narrowing in the proximal esophagus. Occasionally, this can results in symptoms and is known as ‘dysphagia lusoria’.



4.30 Barium esophagram of a peptic stricture (arrow). Peptic strictures usually occur in the distal esophagus and are associated with intermittent or progressive dysphagia. Strictures are treated with gentle dilation and PPI therapy. PPIs are superior to H2 blockers in preventing the recurrence of acid-related strictures.



4.31 Endoscopic photograph of a tight radiation-induced stricture. Initially the standard upper GI endoscope was unable to pass through the narrow lumen.



4.32 Barium esophagram of the stricture in **4.31** (arrow). Note the residual lumen is only several millimeters in width. Stricture length can also be determined easily based on this barium study.

Treatment

The hallmark for treating benign stricture disease is esophageal dilation (**4.33–4.35**), and there are several different types of dilators (**4.36**, **4.37**). To minimize the risk of perforation, the 'rule of threes' applies: no more than three sequential dilators should be passed per session. The goal is to obtain an objective diameter of >15 mm.

Complications from stricture dilation are uncommon: perforation (0.5%), bleeding (0.3%), and bacteremia (20–50%).

Refractory strictures

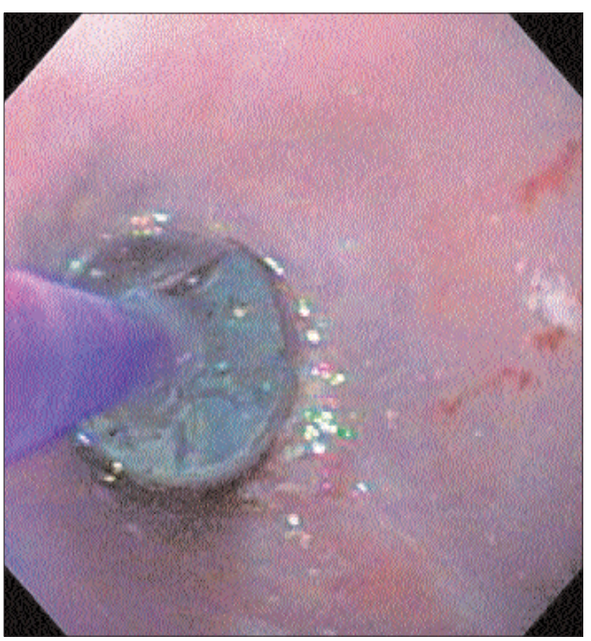
Refractory strictures are defined by lack of response to two or more dilations. Causes include ongoing insults from pills or non-steroidal anti-inflammatory drugs (NSAIDs) (see Pill-induced injury. below), uncontrolled acid reflux, and inadequate lumen diameter with dilations.

Treatment is by elimination of offending agents (pills) and acid suppression with proton-pump inhibitors (PPIs). Gentle dilation to 15 mm is used. Intralesion steroids injected before dilation are safe and probably effective. Removable plastic stents are a recent advance (**4.38**). Surgery is extremely rare for benign disease.

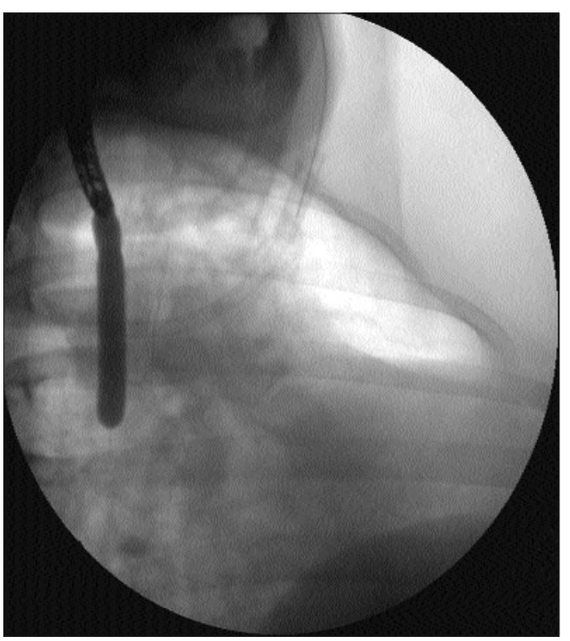
Further reading

Ferguson DD (2005). Evaluation and management of benign esophageal strictures. *Dis Esophagus* **18**(6):359-64.

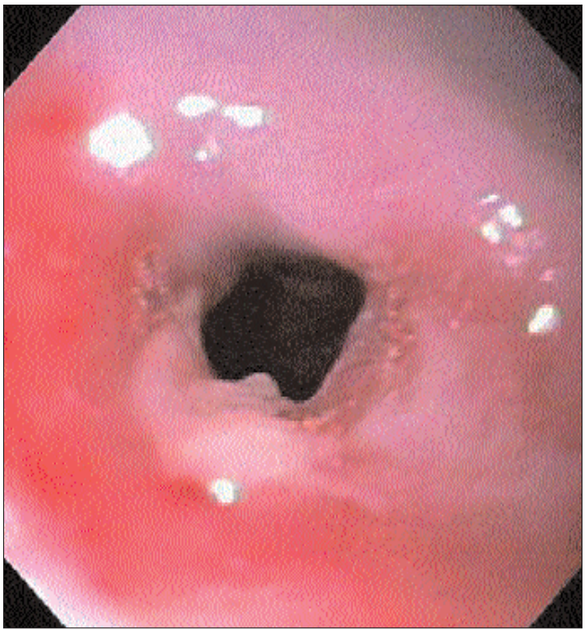
Richter JE (1999). Peptic strictures of the esophagus. *Gastroenterol Clin North Am* **28**(4):875–891.



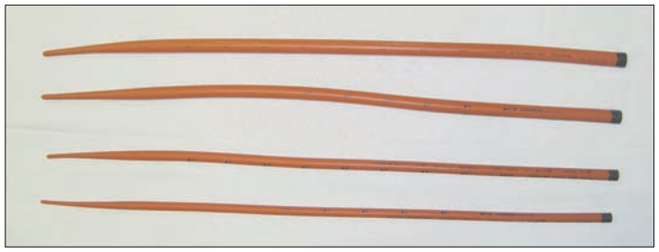
4.33 Endoscopic photo of balloon dilation. A 'through-the-scope' balloon has been passed under fluoroscopic guidance through the stricture. Balloon insufflation creates radial force to dilate the stricture.

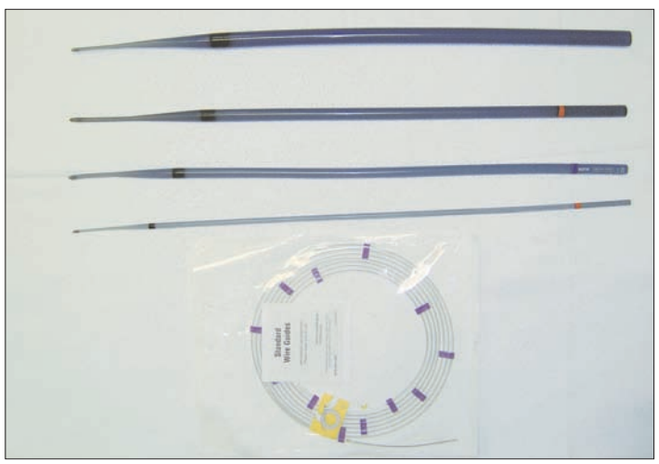


4.34 Fluoroscopic image of the dilation in **4.33**. The balloon expands fully and there is no residual 'waist'.

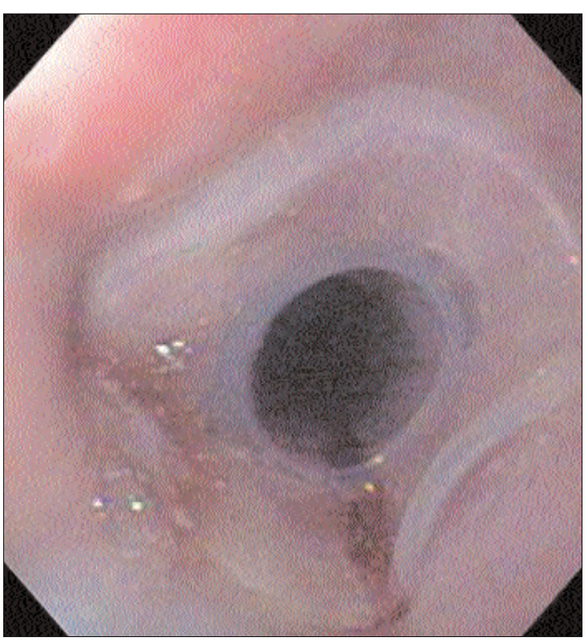


4.35 Endoscopic image post-dilation. The lumen is now larger, allowing for passage of the upper endoscope.





4.36, **4.37** There are several different types of dilators available (in addition to the 'through-the-scope' balloons as in **4.33**). **4.36** Mercury-filled Maloney dilators (top). **4.37** Wire-guided rigid Savary–Gilliard dilators. Choice of dilator often depends on the anatomy of the stricture and operator expertise. In general, Maloney bougies are used in uncomplicated, short, straight strictures. The wire-guided Savary–Gilliard and TTS balloons are best suited for long, tight, or tortuous strictures.



4.38 Plastic stent in an esophageal stricture. Removable plastic stents are now available for use in refractory benign strictures.

Neoplasms

Epidemiology

Approximately 12,000 cases of esophageal carcinoma occur each year in the US.

Two main culprits are adenocarcinoma and SCC, with over 50% of cases being adenocarcinoma. The diseases share similar presentations but their epidemiology is quite different (*Table 4.7*).

Clinical presentation

Patients typically present with rapidly progressing solid food dysphagia caused by mechanical obstruction. Up to 75% of patients experience weight loss. Other symptoms include odynophagia, iron deficiency, or hoarseness from recurrent laryngeal nerve injury.

SCC is locally aggressive and complications related to local invasion are common and include tracheoesophageal fistulas and recurrent laryngeal nerve injury with vocal cord paralysis. Distant metastases occur in the lung, liver, bone, and brain. Adenocarcinoma, while not as locally invasive, will often have lymphatic and liver metastases secondary to the rich lymphatic supply in the lamina propria.

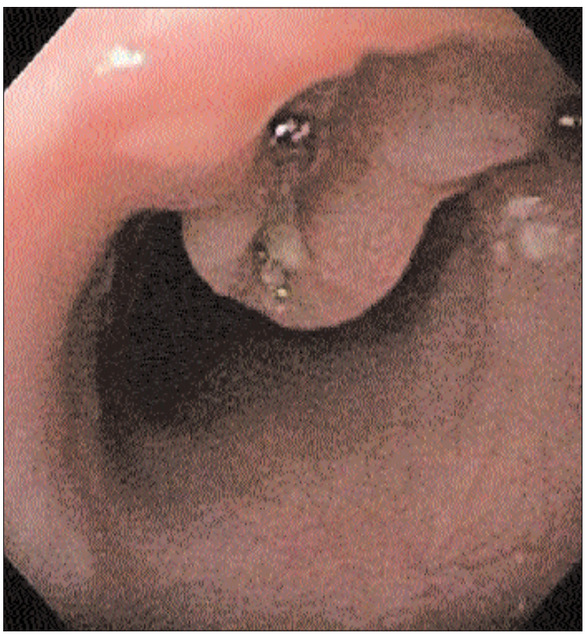
Diagnosis

Endoscopy with biopsy is usually diagnostic (**4.39–4.42**).

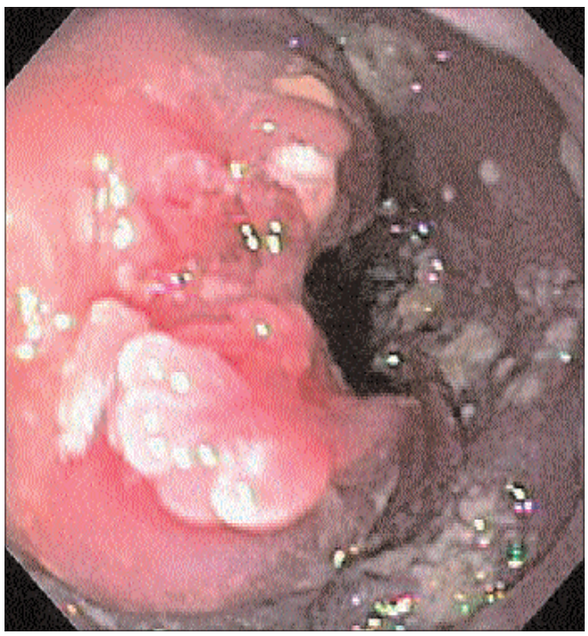
Table 4.7 Epidemiology of esophageal cancer

	Squamous cell carcinoma	*Adenocarcinoma*
Gender	Males	Males
Ethnicity	African Americans	Caucasians
Risk factors	Tobacco/alcohol, achalasia, caustic injury HPV	GERD; Barrett's
Site	Mid-esophagus	Distal esophagus

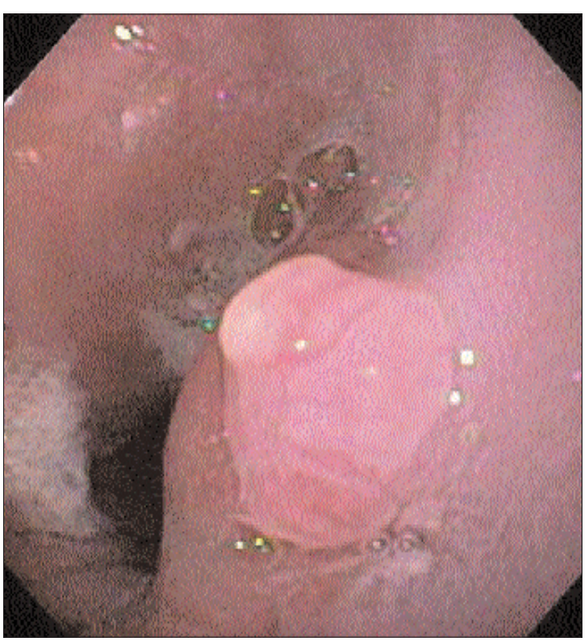
GERD: gastroesophageal reflux disease; HPV: human papilloma virus



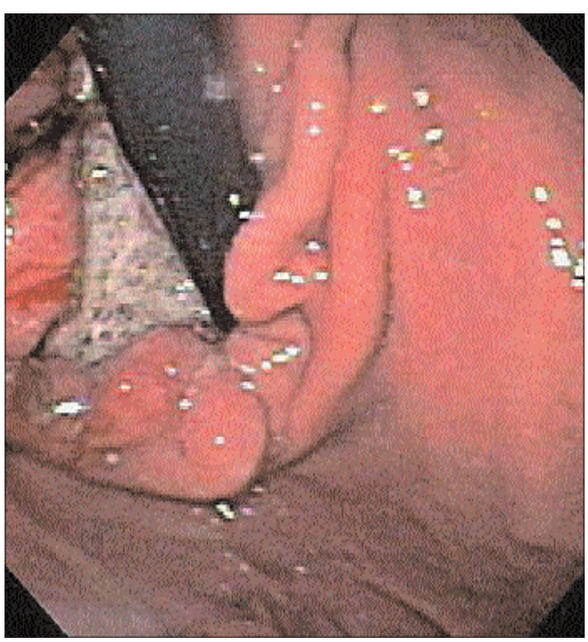
4.39 Endosocopic photo of an ulcerated mid-esophageal mass. Biopsy confirmed the presence of esophageal SCC.



4.40 Endoscopic photo of a large mass present at the GEJ. Biopsy confirmed adenocarcinoma.



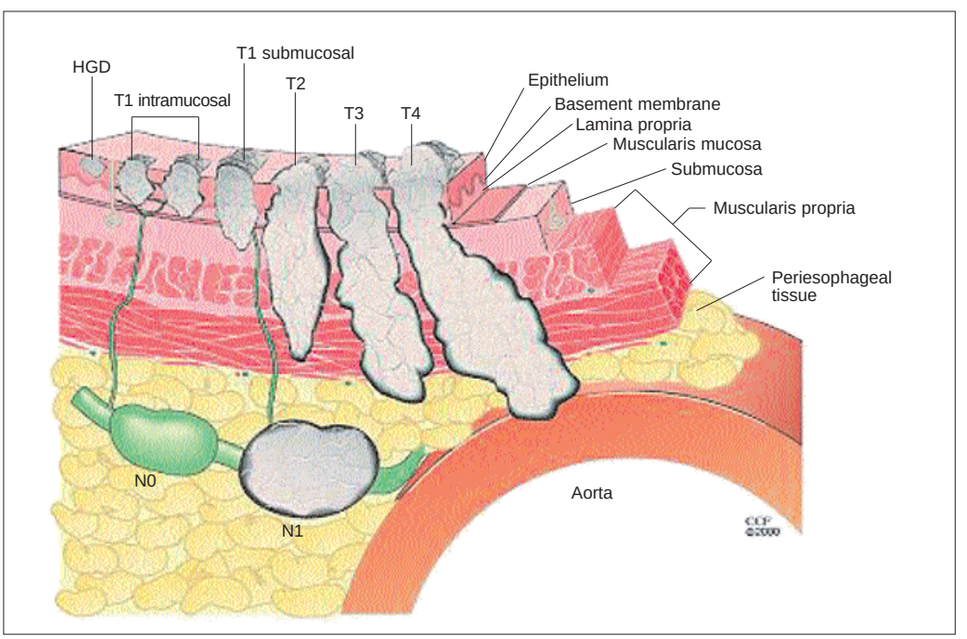
4.41 Endoscopic photo of a nodule arising at the proximal end of Barrett's esophagus. Biopsy documented adenocarcinoma within the nodule.



4.42 Retroflexed view of the GEJ. An ulcerated adenocarcinoma is seen. Tumors located at the GEJ can mimic the signs and symptoms of achalasia and is known as 'pseudoachalasia'.

Treatment

Outcome and treatment will depend upon the stage of the malignancy, so rigorous staging is used (*Table 4.8*, **4.43**). Staging usually includes CT scan, endoscopic ultrasound (EUS), and positron emission tomography (PET) scan. EUS is the most accurate technique for identifying the depth of tumor invasion (**4.44–4.48**) and lymph node metastases. EUS has the added advantage of allowing fine-needle aspiration (FNA) of suspicious lymph nodes (**4.49, 4.50**). CT scan and PET scans are important for identifying distant metastases.



4.43 Tumor, nodes, and metastasis (TNM) classification of esophageal cancer. T class is based on the depth of tumor invasion. T1 tumors are limited to the submucosa, T2 tumors extend to the muscularis propria, T3 tumors extend through the muscularis propria into the adventitia, and T4 tumors invade adjacent structures (i.e. aorta). N class is based on the present or absence of involved lymph nodes. Early lymph node metastases are common secondary to the rich lymphatic supply of the esophageal wall.

Table 4.8 TNM staging classification of esophageal cancer

Primary tumor (T)

TX: Primary tumor cannot be assessed

T0: No evidence of primary tumor

Tis: Carcinoma *in situ*

T1a Tumor invades lamina propria

T1b: Tumor invades submucosa

T2: Tumor invades muscularis mucosa

T3: Tumor invades adventitia

T4: Tumor invades adjacent structures

Regional lymph nodes (N)

NX: Lymph nodes cannot be assessed

N0: No lymph node metastasis

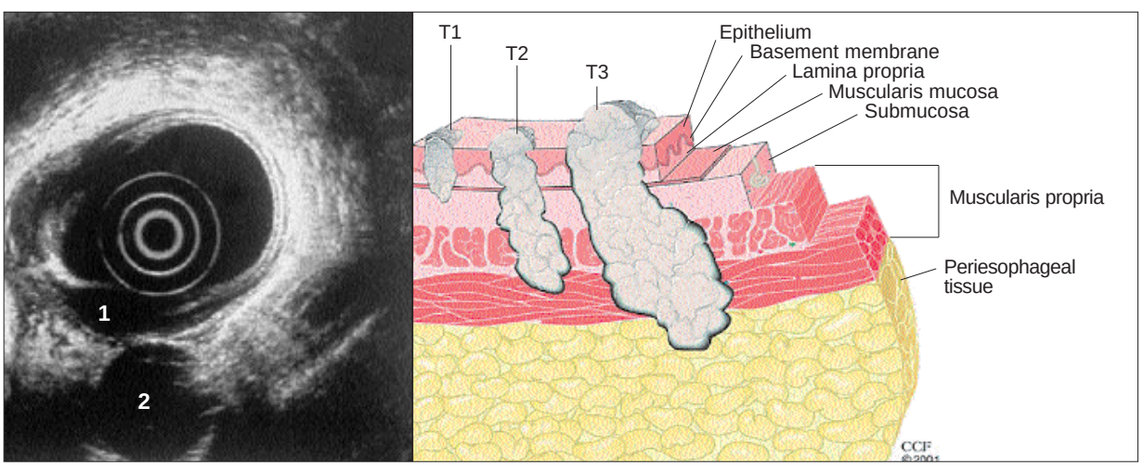
N1: Lymph node metastasis

Distant metastasis (M)

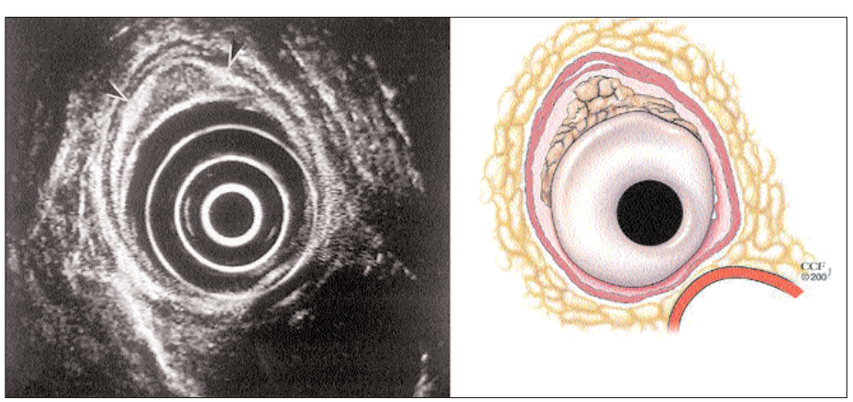
MX: Distant metastasis cannot be assessed

M0: No distant metastasis

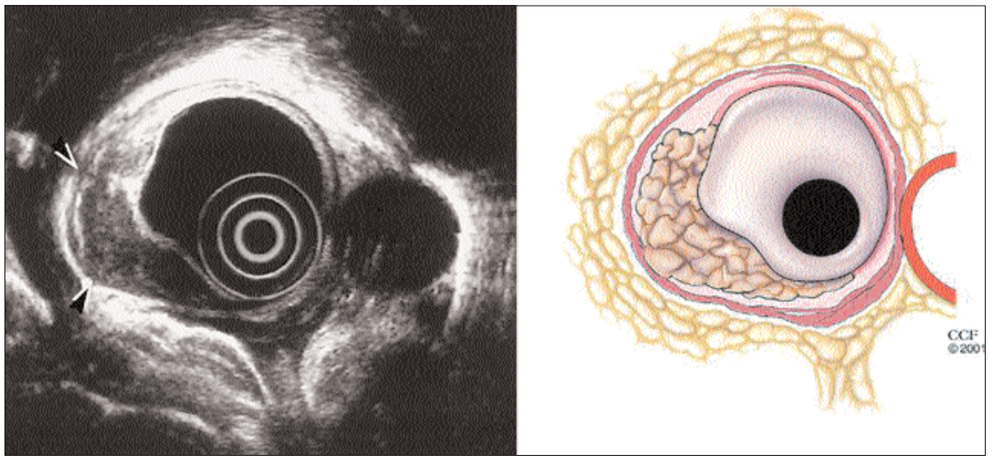
M1: Distant metastasis



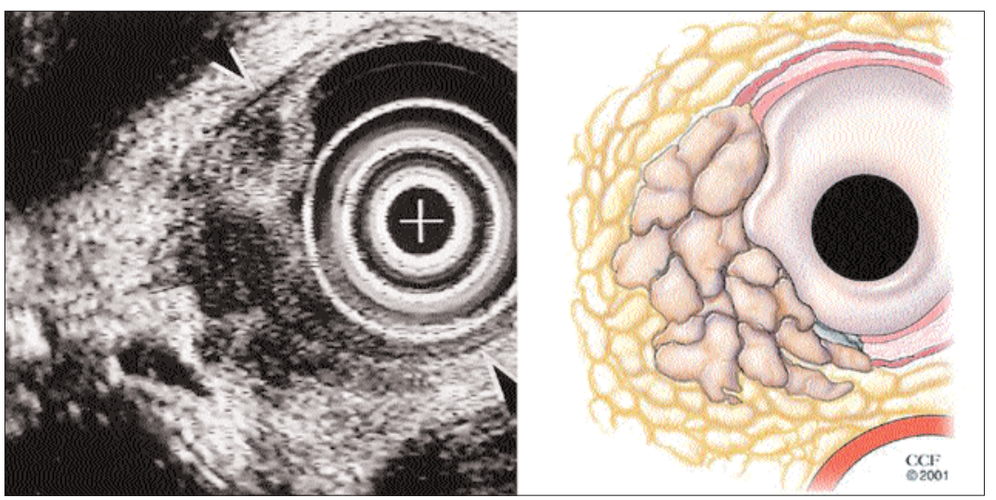
4.44 EUS correlates to the layers of the esophageal wall. (1: submucosa; 2: aorta.)



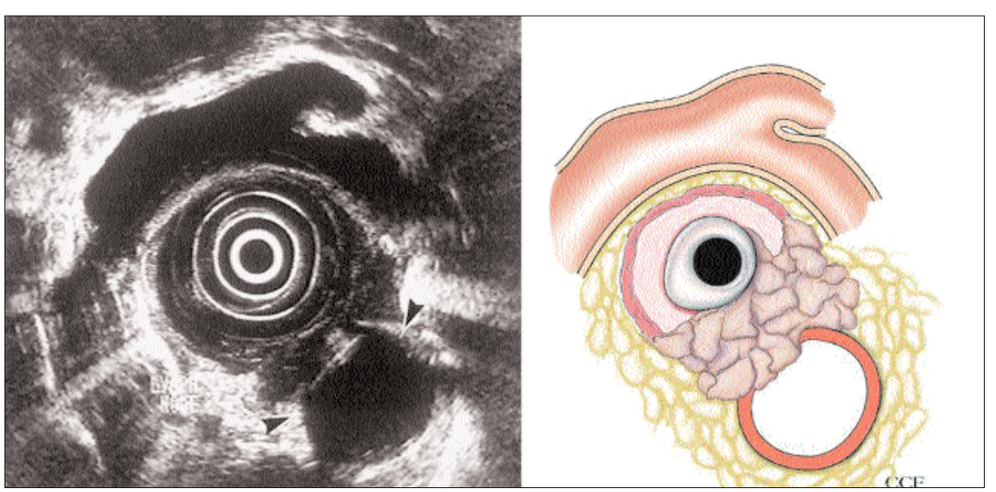
4.45 EUS of T1 tumor. The tumor extends into the third hyperechoic layer (submucosa but not beyond).



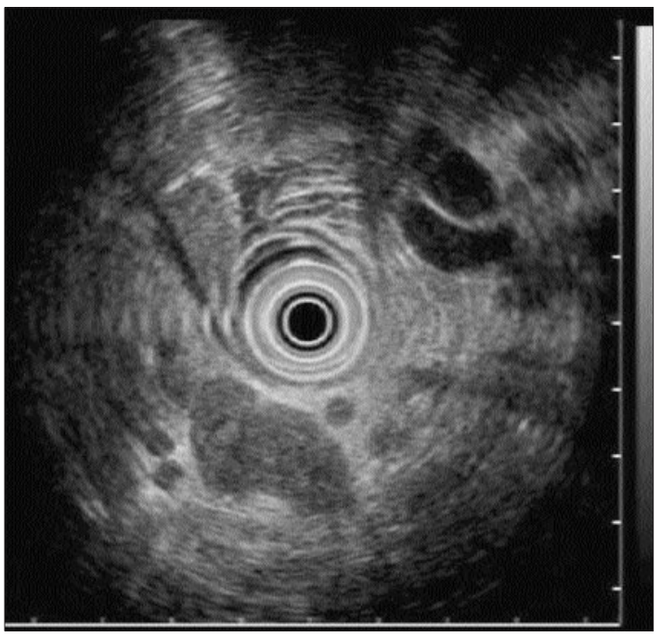
4.46 EUS of T2 tumor. The tumor extends to the fourth hypoechoic layer, the muscularis propria.



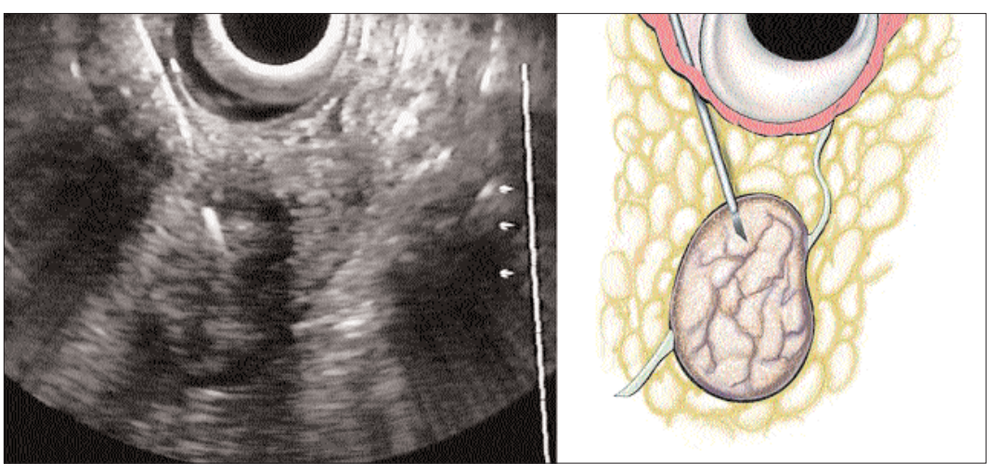
4.47 EUS of T3 tumor. The tumor now invades through the fourth hypoechoic layer and into the fifth hyperechoic layer, adventitia.



4.48 EUS of T4 tumor. The tumor now invades the aorta.



4.49 EUS of multiple enlarged abdominal lymph nodes. EUS is the most accurate technique for determining lymph node involvement.



4.50 FNA of an enlarged lymph node. EUS with FNA allows sampling of suspicious nodes which increases the accuracy of staging.

Staging is based on the TNM classification (*Table 4.8*, **4.43**). Patients with early stage disease, namely T1 or T2, without nodal or metastatic disease can be treated with surgery alone. Patients with more advanced disease, T3 or N1, may benefit from neoadjuvant chemotherapy/radiation before surgical resection. Those with late stage disease receive palliative treatment. Palliative endoscopic measures include repeated dilation, laser/photodynamic ablation, esophageal stent placement (**4.51**, **4.52**), and percutaneous gastrostomy (PEG) tube placement.

Prognosis

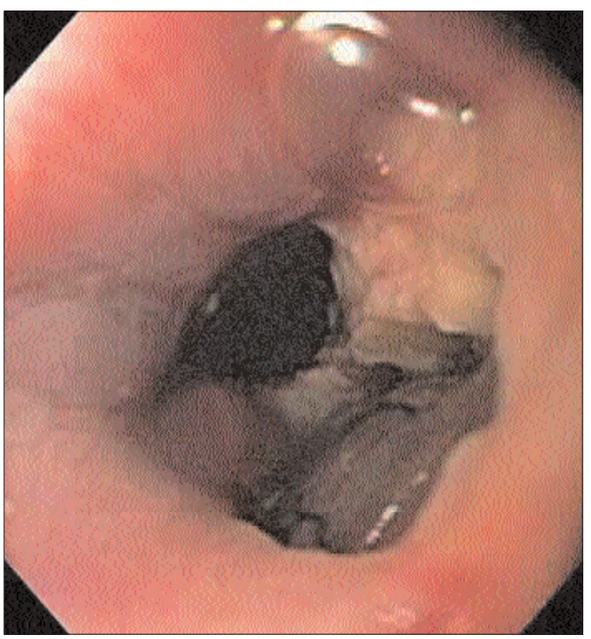
Esophageal cancer is usually identified at a late, incurable stage. Five-year survival rates for SCC are <10% and are <15% for adenocarcinoma. Survival is stage-dependent with 5-year survival rates for T1 lesions and T4 lesions of 46% and 7% respectively.

Benign neoplasms

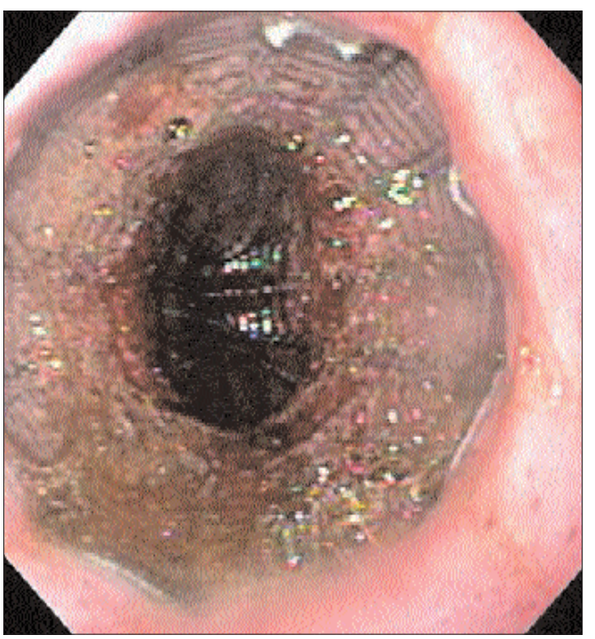
Benign neoplasms of the esophagus are rare and include leiomyoma (**4.53**), granular cell tumors, and papillomas. Many of these lesions present as submucosal masses.

Further reading

Wang KK, Wongkeesong M, Buttar NS (2005). American Gastroenterological Association technical review on the role of the gastroenterologist in the management of esophageal carcinoma. *Gastroenterol* **128**(5):1471–1505.



4.51 Tracheoesophageal fistula. This patient had a proximal SCC and symptoms suggestive of aspiration. Endoscopy diagnosed the T-E fistula (smaller 'lumen' to the upper left). T-E fistula is a common complication of SCC. This patient was managed with an endoscopically placed metal stent.



4.52 Endoscopic view after metal stent deployment.

Summary

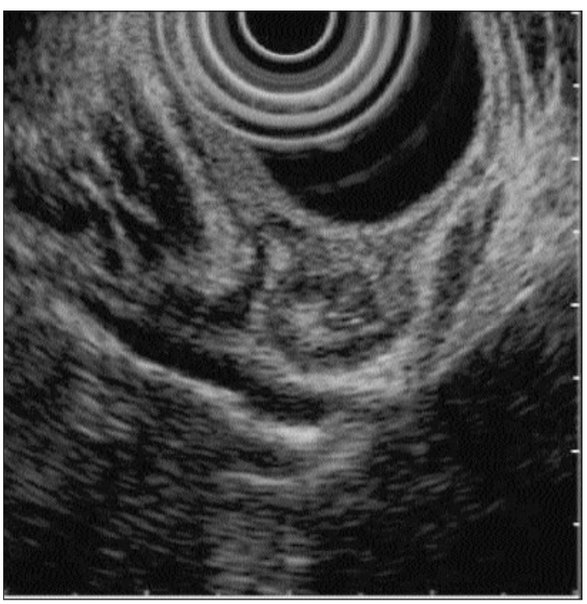
Squamous cell carcinoma (SCC) and adenocarcinoma.

Symptoms: rapidly progressing solid food dysphagia, weight loss, odynophagia, iron deficiency, hoarseness.

Diagnosis: endoscopy with biopsy.

Treatment: depends on tumor stage; surgery alone for early disease (T1 and T2), combined with chemo/radiotherapy for T3 or N1. Late stage disease – palliative treatment.

Prognosis: fairly poor as identified late. 5-year survival: SCC < 10%, adenocarcinoma <15%.



4.53 Endoscopic ultrasound of a leiomyoma. Note the mass arises from the second hypoechoic layer (muscularis mucosa) which is highly suggestive of leiomyoma. FNA can be performed for diagnostic purposes.

Gastroesophageal reflux disease (GERD)

Introduction

GERD is defined as chronic symptoms or mucosal damage caused by the abnormal reflux of gastric contents into the esophagus (1). Reflux esophagitis refers to a subset of GERD that has endoscopic or histopathologic characteristic changes in the esophageal mucosa.

Non-erosive reflux disease (NERD) refers to patient with typical GERD symptoms who have normal upper endoscopy. Barrett's esophagus is a complication of chronic GERD and is defined as intestinal columnar metaplasia characterized by mucin-containing goblet cells. GERD patients can be subdivided as follows (**4.54**)(2):

- NERD: 50%.
- Reflux esophagitis: 30–40%.
- Barrett's esophagus: 10–20%.

Epidemiology

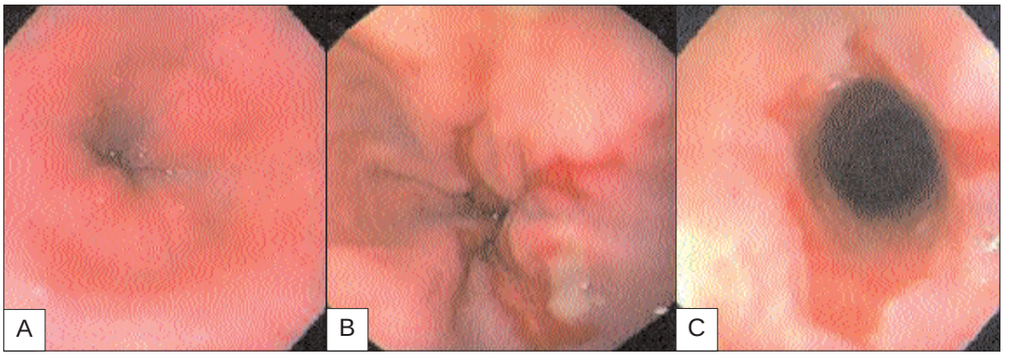
There is a 58.7% prevalence of symptoms of heartburn or acid regurgitation, based on a population-based study of Olmsted County, Minnesota (3). GERD is equally prevalent in men and women; however, there is male predominance for esophagitis (2–3:1) and Barrett's metaplasia (10:1)(4). Pregnancy is associated with the highest incidence of GERD, with 48–79% of pregnant woman complaining of heartburn (5). White races are more frequently affected than other races, with a low prevalence in Africa and Asia and high rates in North America and Europe (6).

Clinical presentation

Esophageal and extra-esophageal symptoms of GERD are presented in *Table 4.9*. Typical symptoms include heartburn or pyrosis, acid regurgitation, and dysphagia or odynophagia. Heartburn presents as an intermittent, restrosternal burning discomfort that may radiate towards the neck. Aggravating factors include meals (usually within 60 minutes of eating), exercise, and lying down. Heartburn is typically relieved with antacids or by drinking water.

Acid regurgitation presents with the sensation of sour or burning fluid in the mouth or throat. It is due to effortless return of esophageal or gastric contents into the pharynx.

Dysphagia or odynophagia usually presents in the setting of chronic heartburn due to impaired peristalsis, peptic strictures, and/or erosive esophagitis.



4.54 Patients with GERD symptoms may have endoscopically normal (NERD [A]) or abnormal (GERD [B], Barrett's [C]) findings.

Table 4.9 Symptoms of gastroesophageal reflux disease

Esophageal	*Extra-esophageal*
Heartburn	Cough
Acid regurgitation	Wheezing
Odynophagia	Hoarseness
Dysphagia	Throat clearing
Non-cardiac chest pain	Globus
Water brash	Tracheal stenosis
	Aspiration pneumonia
	Pulmonary fibrosis
	Apnea (infants)

Atypical symptoms include:

- Posterior laryngitis.
- Asthma.
- Cough.
- Chest pain.
- Dental erosions.

Etiology and pathophysiology

Table 4.10 lists the common causes of GERD. GERD can occur when there is transient or permanent impairment of the antireflux barrier between the stomach and the esophagus (7). This can be caused by LES incompetence (hypotensive LES) (*Table 4.11*), transient LES relaxation (TSLER)(8), hiatal hernia, and scleroderma.

TSLER is a primary mechanism for gastroesophageal reflux in healthy persons and in those with mild GERD, and occurs as short periods of relaxation of the LES that is not associated with swallowing. Those with severe GERD and related complications usually have more permanent structural defects, such as hiatal hernia. An increased gastroesophageal pressure gradient, due to delayed gastric emptying (diabetic gastroparesis, intestinal pseudo-obstruction, collagen vascular disease), pregnancy, and obesity can result in GERD.

Another cause is prolonged esophageal acid clearance,

Table 4.10 Causes of gastroesophageal reflux

Barrier defect	*Poor esophageal clearance*
TLESR	Ineffective esophageal motility
Hiatal hernia	Re-reflux due to hiatal hernia
Hypotensive LES	Impaired salivary function
Scleroderma	Cigarette smoking
LES disruption (status post myotomy, balloon dilatation)	Sjögren's syndrome
Increased gastroesophageal pressure gradient	*Increased gastric acid production*
Delayed gastric emptying (diabetic gastroparesis, intestinal pseudo-obstruction)	Zollinger–Ellison syndrome
Pregnancy	
Obesity	
Tight fitting clothes	

LES: lower esophageal sphincter; TLESR: transient lower esophageal sphincter relaxation

Table 4.11 Substances that affect lower esophageal sphincter pressure

	Increases resting LESP	*Decreases resting LESP*
Food	Protein	Fat, chocolate, ethanol, peppermint
Medications	Metoclopramide, domperidone, cisapride	Nitrates, calcium channel blockers, morphine, meperidine, barbiturates, diazepam
Neural agents	α-adrenergic agonists, β-adrenergic agonists, cholinergic agonists	α-adrenergic antagonists, β-adrenergic antagonists, cholinergic antagonists, serotonin
Hormones	Gastrin, motilin, substance P	Secretin, cholecystokinin, glucagon, gastric inhibitory polypeptide, progesterone

LESP: lower esophageal sphincter pressure

which can be due to impaired esophageal emptying in the case of abnormal peristalsis (ineffective esophageal motility), re-reflux of acid due to hiatal hernia or impaired salivary function. This results in reduced neutralization of acid by salivary bicarbonate and is observed in smokers (9) and Sjögren's syndrome.

Breakdown of esophageal tissue resistance may be involved in the etiology of GERD. This occurs when gastroduodenal contents, such as acid, pepsin, and bile, damage the intercellular junction of the esophageal epithelium. As a result, there is increased permeability allowing hydrogen ion penetration. Consequent acidification of the cytosol leads to cell edema and death. Acid hypersecretion, such as that in Zollinger–Ellison syndrome, is also a causal factor of GERD.

Histopathology

The normal esophagus is lined with non-cornified stratified squamous epithelium. At the squamocolumnar junction, the squamous epithelium is in continuity with the columnar cells of the stomach. Reactive epithelial cell changes are seen in GERD even though upper endoscopy may be normal. These include hyperplasia of the basal zone and elongation of the papillae, as well as increased mitotic figures and increased vascularization of the epithelium. When there is endoscopic evidence of esophagitis, epithelial cell injury is evident and there is inflammatory cell infiltrate (neutrophilic or eosinophilic) (**4.55**).

Differential diagnosis

Table 4.12 presents the differential diagnosis for GERD.

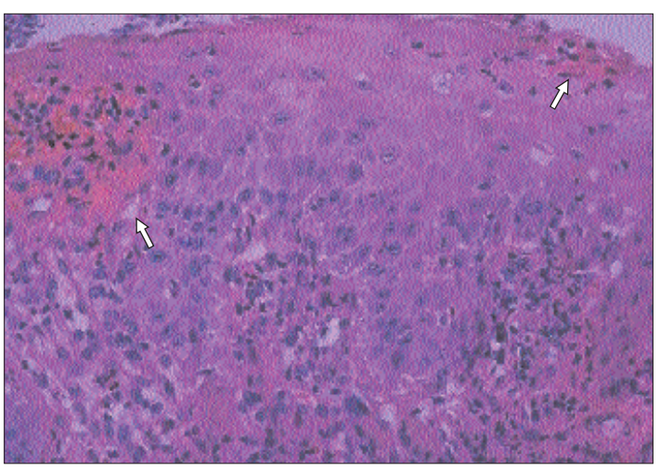
Diagnosis

There is no diagnostic gold standard for detecting GERD. Classic symptoms of acid regurgitation and heartburn are specific but not sensitive for the diagnosis of GERD, as determined by abnormal 24-hour pH monitoring. Therefore, if only heartburn and/or acid regurgitation is present, empiric antisecretory therapy (PPI) can be started. The diagnosis of GERD is confirmed by the resolution of symptoms with antisecretory therapy. Further diagnostic testing (such as upper endoscopy) should be performed in cases of therapy failure, extremely chronic GERD (to rule out Barrett's) or if certain 'alarm signs' are present, such as dysphagia, odynophagia, weight loss, or GI bleeding.

If chest pain is present, coronary artery disease should be ruled out with appropriate tests.

Table 4.13 lists the tests used in the diagnosis of GERD, and their advantages and disadvantages. Upper endoscopy is the technique of choice to evaluate esophageal mucosa in suspected GERD. It allows detection and management of complications of GERD and also exclusion of other diseases. Endoscopy is diagnostic for GERD if reflux esophagitis or Barrett's esophagus is present. The severity of reflux esophagitis is characterized by grading systems:

- Los Angeles classification (*Table 4.14*, **4.56**, **4.57**).
- Savary–Miller classification (*Table 4.15*).



4.55 Histopathology of GERD. The esophageal biopsy of GERD shows squamous cell hyperplasia and numerous inflammatory cells (predominantly eosinophils) (arrows). (Courtesy of Mary Bronner M.D., Department of Anatomic Pathology, Cleveland Clinic, Ohio.)

Table 4.12 Differential diagnosis of gastroesophageal reflux disease

Infectious esophagitis	Peptic ulcer disease
Pill-induced esophagitis	Non-ulcer dyspepsia
Esophageal motor disorders	Biliary colic
Gastritis	Coronary artery disease

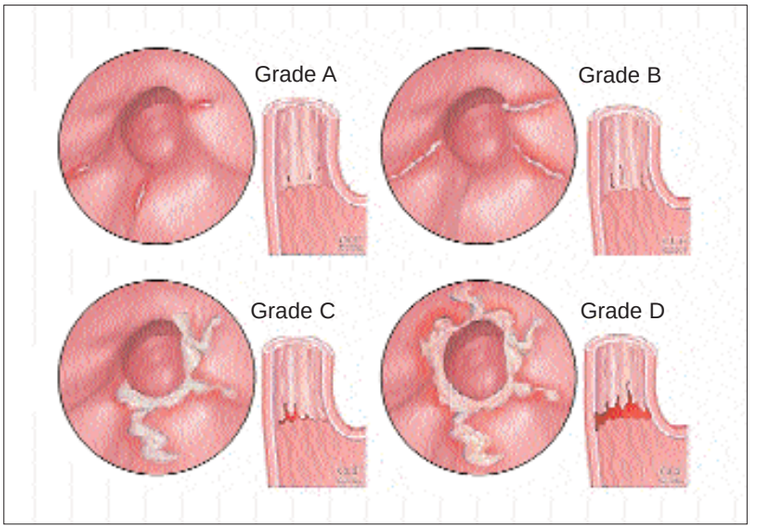
Table 4.13 Diagnostic tests for gastroesophageal reflux disease

Test	*Advantages*	*Disadvantages*
Empiric PPI therapy	Diagnostic and therapeutic; low cost; no referral needed to the specialist	May mask underlying disease; disease severity unknown; poor diagnostic accuracy with atypical reflux symptoms
Endoscopy	Visual establishment of severity of esophagitis; screening for Barrett's	Often normal; costly
Ambulatory 24/48-hour esophageal pH monitoring	Diagnosis of 'acid' reflux; quantifies acid reflux events and allows symptom correlation; when used on-therapy, monitors therapy efficacy	Low sensitivity with catheter-based system; improved sensitivity with the wireless 48-hour device; costly
Barium esophagram	Good test for defining anatomy	Often normal; non-specific
Esophageal manometry	Measures LESP; pre-op evaluation for anti-reflux surgery	Limited use in GERD management
Esophageal impedance	Identifies non-acid reflux events; useful in evaluating for non-acid reflux in patients who are refractory to high dose PPI therapy	Role of non-acid reflux in GERD is not defined

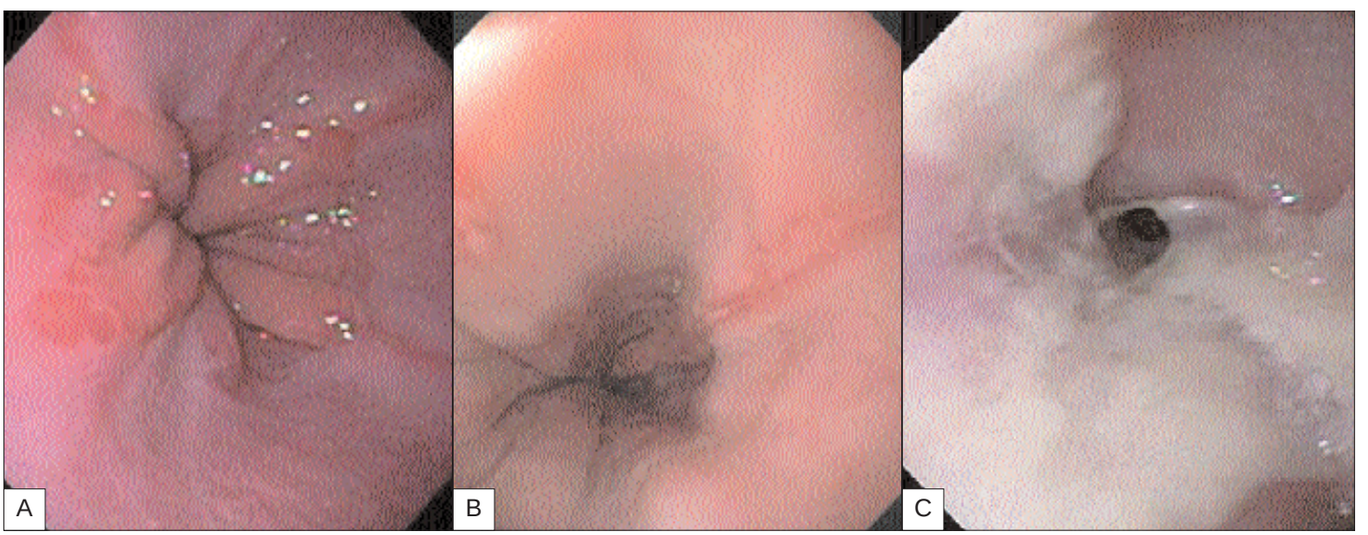
GERD: gastroesophageal reflux disease; LESP: lower esophageal sphincter pressure; PPI: proton-pump inhibitor

Table 4.14 Los Angeles classification of esophagitis

Grade	*Pathology*
A	One or more mucosal breaks <5 mm and not contiguous with adjacent mucosal fold tops
B	One or more mucosal breaks >5 mm and not contiguous with adjacent mucosal fold tops
C	Mucosal breaks contiguous between tops of two or more folds but involving <75% of esophageal circumference
D	Mucosal breaks contiguous between tops of two or more folds and involving ≥75% of esophageal circumference



4.56 Los Angeles classification of esophagitis.



4.57 Endoscopic view of esophagitis. **A**: Los Angeles grade A; **B**: Los Angeles grade B; **C**: Los Angeles grade D.

Table 4.15 Savary–Miller classification of esophagitis

Grade	*Pathology*
I	One of more non-confluent lesions with erythema or reddish spots
II	Confluent but not circumferential erosive and edematous lesions in the distal esophagus
III	Circumferential erosions in the distal esophagus
IV	Chronic complications, such as ulcers, strictures, or Barrett's metaplasia

Ambulatory 24-hour pH monitoring has limited use in the diagnosis of GERD as results are normal in 25% of erosive esophagitis and 33% of NERD (10). However, it is a useful test to quantitate esophageal acid exposure and correlate symptoms to reflux events. A barium esophagram is useful in identifying strictures and esophageal ulcers but it is not a good test for detecting esophagitis or Barrett's metaplasia.

Treatment

The goals of therapy in GERD should be to relieve symptoms, heal esophagitis, prevent recurrence of symptoms, and prevent complications. Therapies are presented in *Table 4.16*. Modifying the patient's lifestyle may be of benefit, especially for mild GERD. They should be advised to avoid fatty foods, alcohol, caffeine, etc, avoid recumbency for 3 hours after meals, elevate their bed, stop

Table 4.16 Treatment for gastroesophageal reflux disease

Treatment	*Method*	*Comments*
Lifestyle modifications	Diet: avoid large meals, high fat diets, avoid meals at bedtime. Avoid caffeine, alcohol, smoking, mints, chocolate; weight loss; elevate head of bed 6 inches; sleep on left side rather than right; avoid tight fitting clothes; smoking cessation	All patients with GERD should be advised. There is minimal data to support efficacy of lifestyle modification. It is likely to be suitable only for mild GERD
H2RAs	Cimetidine 400 mg po qac, qhs Ranitidine 150 mg po bid Famotidine 20–40 mg po bid Nizatidine 150 mg po bid	Most effective acid suppressive occurs during fasting and during sleep. Efficacy is limited by tachyphylaxis and inadequate suppression of acid related to meals
PPI	Omeprazole 20–40 mg po, qd-bid Lansoprazole 15–30 mg po qd-bid Rabeprazole 20 mg po qd-bid Pantoprazole 40 mg po qd-bid Esomeprazole 20–40 mg po qd-bid	Better acid suppression than H2RAs. Should be administered 30 minutes before meals for optimal acid suppression. Rebound hypersecretion occurs with discontinuation due to secondary hypergatrinemia
Promotility agents	Metoclopramide 5–15 mg qac, qhs (Cisapride)	Metoclopramide side-effects: tremor, parkinsonism, depression, tardive diskinesia; cisapride is not available due to cardiotoxic effects (prolonged QT)
Endoscopic	Radiofrequency ablation (Stretta); endoscopic suturing (Bard EndoCinch); endoscopic injection; gatekeeper reflux repair system	Currently, only Stretta is FDA approved for endoscopic therapy of GERD
Surgical	Fundoplication: Nissen, Toupet, Dor	

bid: twice daily; GERD: gastroesophageal reflux disease; po: by mouth, qac: before meals; qd: once daily; qhs: before sleep

smoking, wear loose fitting clothes, and lose weight. Acid suppressive therapy can be used to provide symptomatic relief and heal esophagitis. Histamine receptor antagonists (H2RAs) in standard divided doses have been shown to achieve complete symptom relief in approximately 60% of patients and to heal esophagitis in about 50%. PPIs are superior to H2RAs in both symptom relief and healing esophagitis, with a success rate of up to 90% (11).

Because GERD is a chronic relapsing disease for most patients, with almost universal recurrence, maintenance therapy may be required in many patients. Long-term use of PPIs is superior to H2RAs, with remission maintained at 80% and 50% respectively (12). 'Step down' therapy is recommended in clinical practice. Patients are initially treated with PPIs; when clinical response is achieved, H2RAs and PPIs are used as needed.

Prokinetic drugs, such as metoclopramide and cisapride, have been used with minimal effect, and their use is also limited by significant side-effects.

Anti-reflux surgery may be required. Basic methods of fundoplication (**4.58**, **4.59**) involve pulling down the GEJ into the abdominal cavity and the fundus of the stomach is wrapped around the distal esophagus. The net result is the creation of an artificial valve and prevention of the LES sliding back into the thorax. The procedure can be performed either with open or laparoscopic laparotomy. There are multiple variations to this procedure:

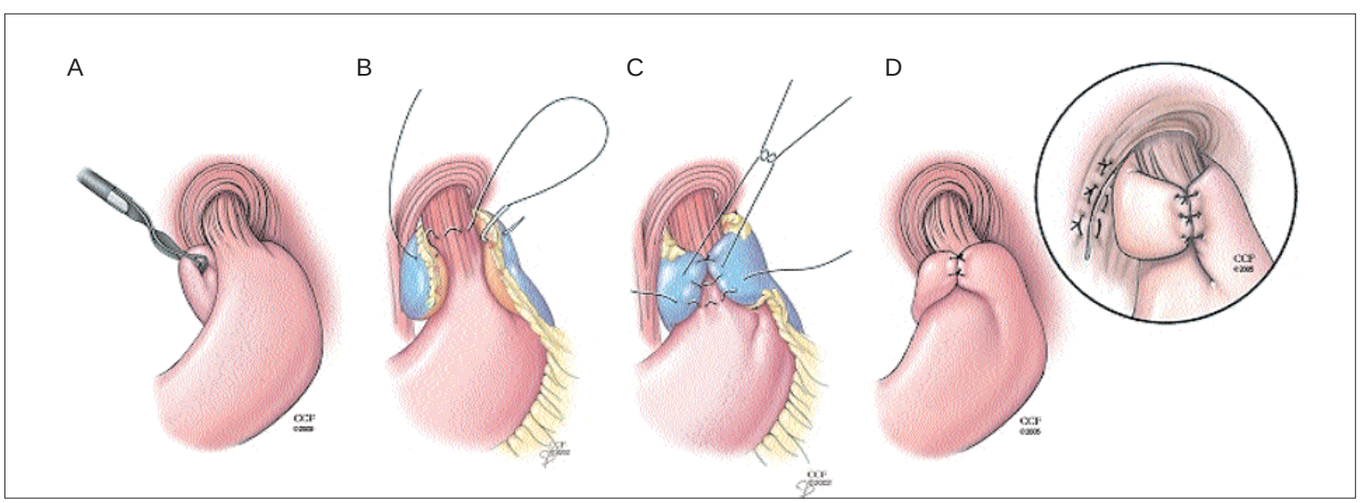
- Nissen: complete fundoplication; the wrap encircles the entire (360°) esophagus (**4.58**, **4.59**).
- Toupet: posterior partial fundoplication; the wrap encircles two-thirds (270°) of the esophagus posteriorly.
- Dor: anterior partial fundoplication; the wrap encircles one-third (120°) of the esophagus anteriorly; usually performed with Heller myotomy in achalasia.

Complete fundoplication provides better acid reflux control than partial (13).

Indications include persistent symptoms refractory to medical therapy, severe esophagitis by endoscopy, benign stricture, Barrett's esophagus (without dysplasia or carcinoma), and recurrent pulmonary symptoms associated with GERD. Patients with large hiatal hernia with predominant regurgitation symptoms should also be considered for surgery.

The ideal candidate is the patient with typical symptoms that respond completely to antisecretory therapy.

Patients who are refractory to acid suppression therapy on high dose PPIs are poor candidates and surgery should be considered with caution. In this setting, ongoing

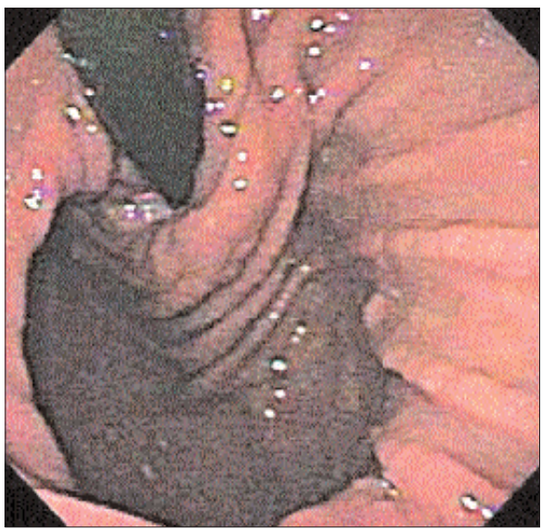


4.58 Nissen fundoplication. **A**: The mobilized fundus is brought behind the esophagus. Tightness of the wrap is usually controlled by passing a 56F to 60F bougie into the esophageal lumen (not shown). **B**–**D**: Left and right fundal wrap is approximated and sutured. The esophageal muscle wall is also sutured to hold the wrap in place (circle). Before the wrap is sutured, the crura is approximated behind the esophagus.

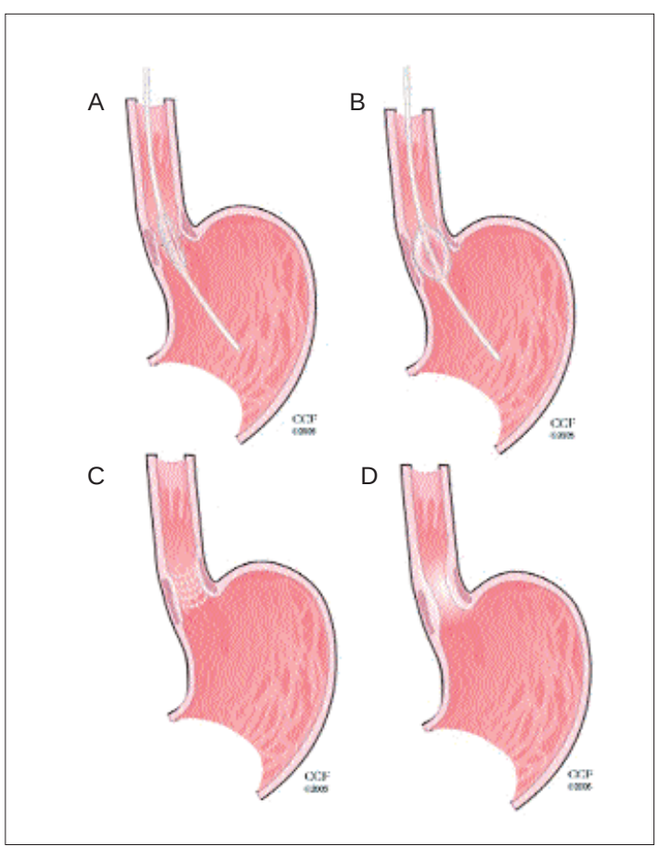
esophageal acid exposure while on medication should be documented. If acid is well controlled on therapy, non-acid reflux may cause symptoms and this should be investigated by impedance monitoring. Otherwise, surgery is not recommended in those who are unresponsive to high dose PPIs and who have no evidence of esophageal acid exposure while on therapy.

Complications of fundoplication include acute perioperative complications, such as pneumonia, sepsis, wound infection, pulmonary embolism, pneumothorax, esophageal or gastric perforation, spleen damage, and death. Technical failures can occur, such as transdiaphragmatic herniation, fundoplication disruption, slipped or misplaced fundoplication, too tight or loose wrap, or twisted fundoplication. Symptomatic failures are those patients with persistent or recurrent heartburn, dysphagia, chest pain, nausea, gas-bloat syndrome, and inability to belch or vomit.

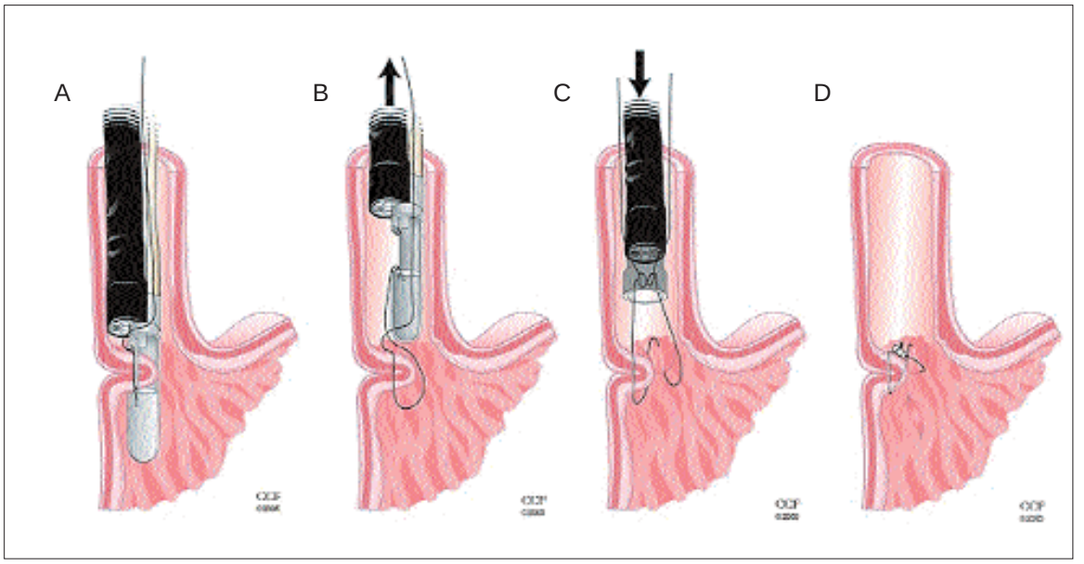
Endoluminal therapies include radiofrequency (RF) ablation of the GEJ (Stretta) (**4.60**), in which radiofrequency energy delivers heat to the GEJ which causes nerve tissue to ablate and scar tissue form. It results in reduction of transient LES relaxation. Scarring at the GEJ functions as an additional barrier to reflux. Other endoluminal therapies include endoscopic suturing of the GEJ (Bard EndoCinch) (**4.61**), endoscopic injection of the GEJ (**4.62**), and gatekeeper reflux repair system (**4.63**).



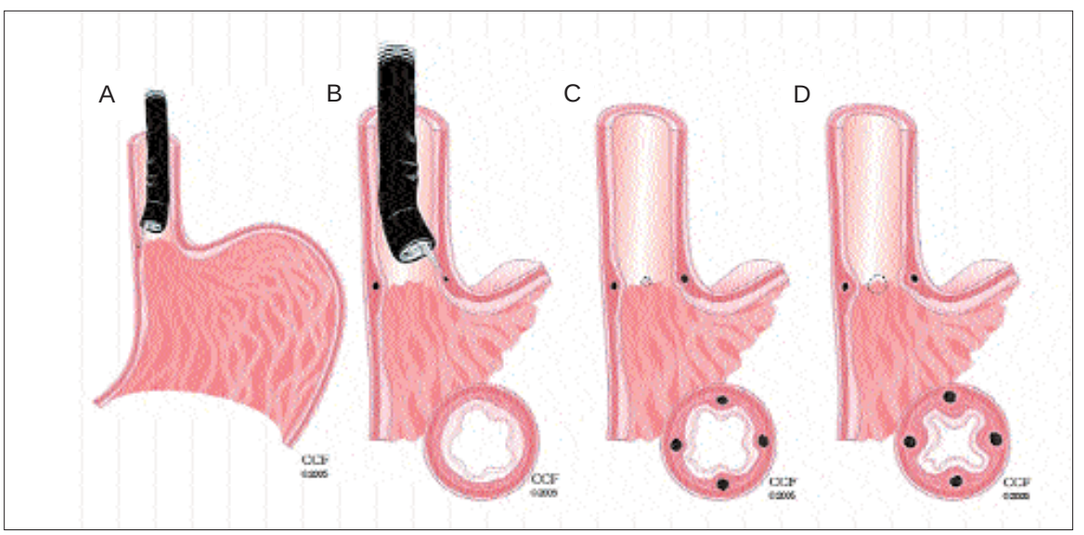
4.59 Endoscopic view of the Nissen fundoplication. The retroflexed view of the gastric cardia shows fundus wrapped around the esophagus.



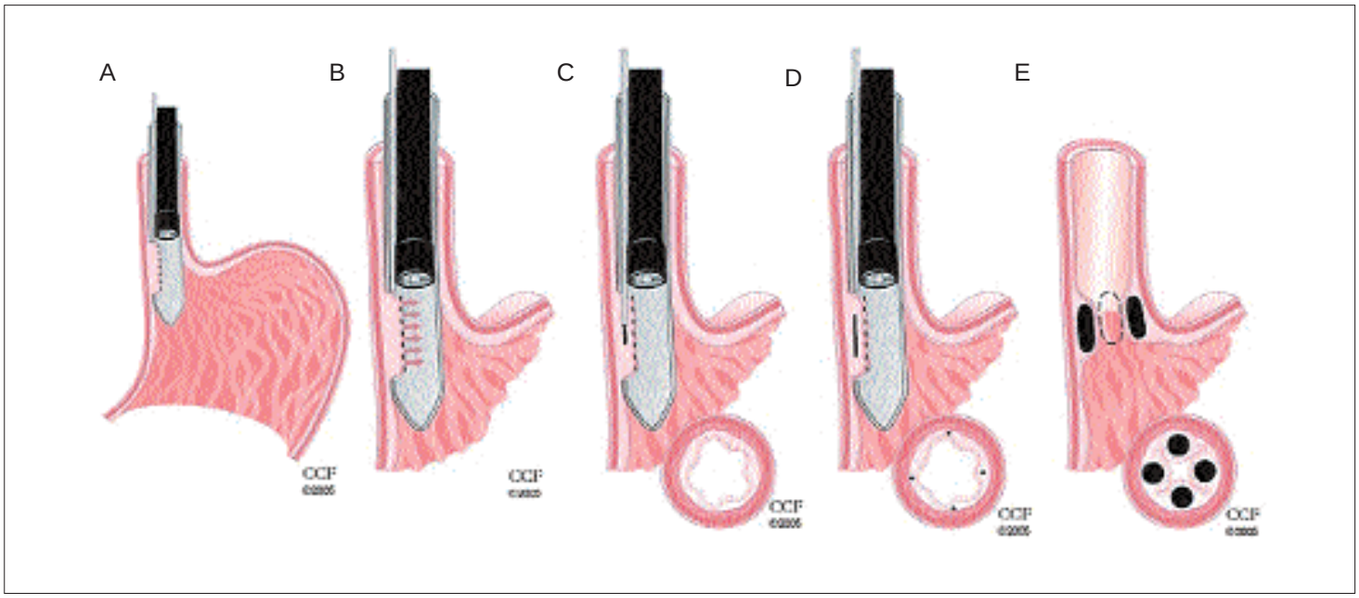
4.60 Endoscopic radiofrequency (RF) ablation therapy (Stretta). The instrument consists of a balloon surrounded by four curved metal needle electrodes. **A**: After the GEJ is measured using the standard EGD, the Stretta catheter is inserted into the esophagus and positioned at the GEJ. **B**: The balloon is inflated deploying the four needle electrodes. Each electrode delivers RF energy to achieve target temperature of 85°C for 90 seconds, resulting in a ring of lesions. **C**: The catheter is rotated and repositioned linearly to create several rings of lesions 2 cm above and below gastric cardia. **D**: The net result is nerve ablation and scarring at the GEJ which acts as a reflux barrier.



4.61 Endoscopic suturing of the GEJ (Bard EndoCinch). The Bard EndoCinch sewing capsule is attached to the standard EGD scope and inserted into the esophagus via an overtube to the GEJ. **A**, **B**: Suction is applied to the capsule drawing the adjacent tissue into the capsule. The needle with pre-loaded suture is then advanced and the endoscope is removed. **C**, **D**: In the original technique, half-stitches were hand-tied and pushed with knot-pusher and the suture cut using a separate guillotine catheter. Further refinements have been made and the new cinch/cutting catheter (not shown) is used to place a cinch tag and cut the suture in one step.



4.62 Endoscopic injection of the GEJ. **A**, **B**: Using a standard endoscope and injection catheter under fluoroscopic guidance, a liquid polymer dissolved in solvent is injected into the LES in four quandrants. **C**, **D**: The solvent separates away and the polymer solidifies into a spongy material, enhancing the LES barrier against reflux.



4.63 Gatekeeper reflux repair system. **A**, **B**: A gatekeeper overtube is positioned over the LES and suction is applied, drawing adjacent tissue into the overtube. **C**, **D**: A radiopaque removable hydrogel (Polyacrylonitril) is injected into the submucosa via the delivery sheath. **E**: Submucosal placement of the gatekeeper narrows the esophageal lumen, enhancing the barrier effect of the LES.

References

1 Devault KR, Castell DO (1999). Updated guideline for the diagnosis and treatment of gastroesophageal reflux disease. *Am J Gastroenterol* **94**:1434–1442.

2 Achem SR (1999). Endoscopy-negative gastroesophageal reflux disease: the hypersensitive esophagus. *Gastroenterol Clin North Am* **28**:893–904.

3 Locke GR III, Talley NJ, Fett SL, *et al.* (1997). Prevalence and clinical spectrum of gastroesophageal refulx: A population-based study in Olmsted County, Minnesota. *Gastroenterol 112*:1448–1456.

4 Wienbeck M, Barnert J (1989). Epidemiology of reflux disease and reflux esophagitis. *Scand J Gastroenetrol* **Suppl 156**:7–13.

5 Bainbridge ET, Temple JG, Nicholas SP, *et al.* (1983). Symptomatic gastroesophageal reflux in pregnancy: A comparative study of white Europeans and Asians in Birmingham. *Br J Clin Pract* **37**:53–57.

6 Sonnenberg A, El-Serag HB (1999). Clinical epidemiology and natural history of gastroesophageal reflux disease. *Yale J Biol Med* **72**:81–92.

7 Orlando RC (2002). Pathogenesis of gastroesophageal disease. *Gastroenterol Clin North Am* **31**:S35–S44.

8 Mittal RK, Holloway RH, Penagini R, *et al.* (1995). Transient lower esophageal sphincter relaxation. *Gastroenterol* **109**:601–610.

9 Kahrilas PJ, Gupta RR (1989). The effect of cigarette smoking on salivation and esophageal acid clearance. *J Lab Clin Med* **114**:431–438.

10 Fass R, Fennerty MB, Vakil N (2001). Nonerosive reflux disease – current concepts and dilemmas. *Am J Gastroenterol* **96**:303–314.

11 Chiba N, De Gara CJ, Wilkinson JM, *et al.* (1997). Speed of healing and symptom relief in grade II to IV gastroesophageal reflux disease: a metaanalysis. *Gastroenterol* **112**:1798–1810.

12 Vigneri S, Termini R, Leandro G, *et al.* (1995). A comparison of five maintenance therapies for reflux esophagitis. *N Engl J Med* **333**:1106–1110.

13 Sonnenberg A (2004). Review article: anti-reflux surgery and endoluminal therapies. *Alimentary Pharmacolology & Therapeutics* **20**(Suppl 5):81–88.

Further reading

DeVault KR, Castell DO (2005). Updated guidelines for the diagnosis and treatment of gastroesophageal reflux disease. *Am J Gastroenterol* **100**(1):190–200.

Extra-esophageal GERD

Introduction

Patients with GERD may present with symptoms other than heartburn and regurgitation.

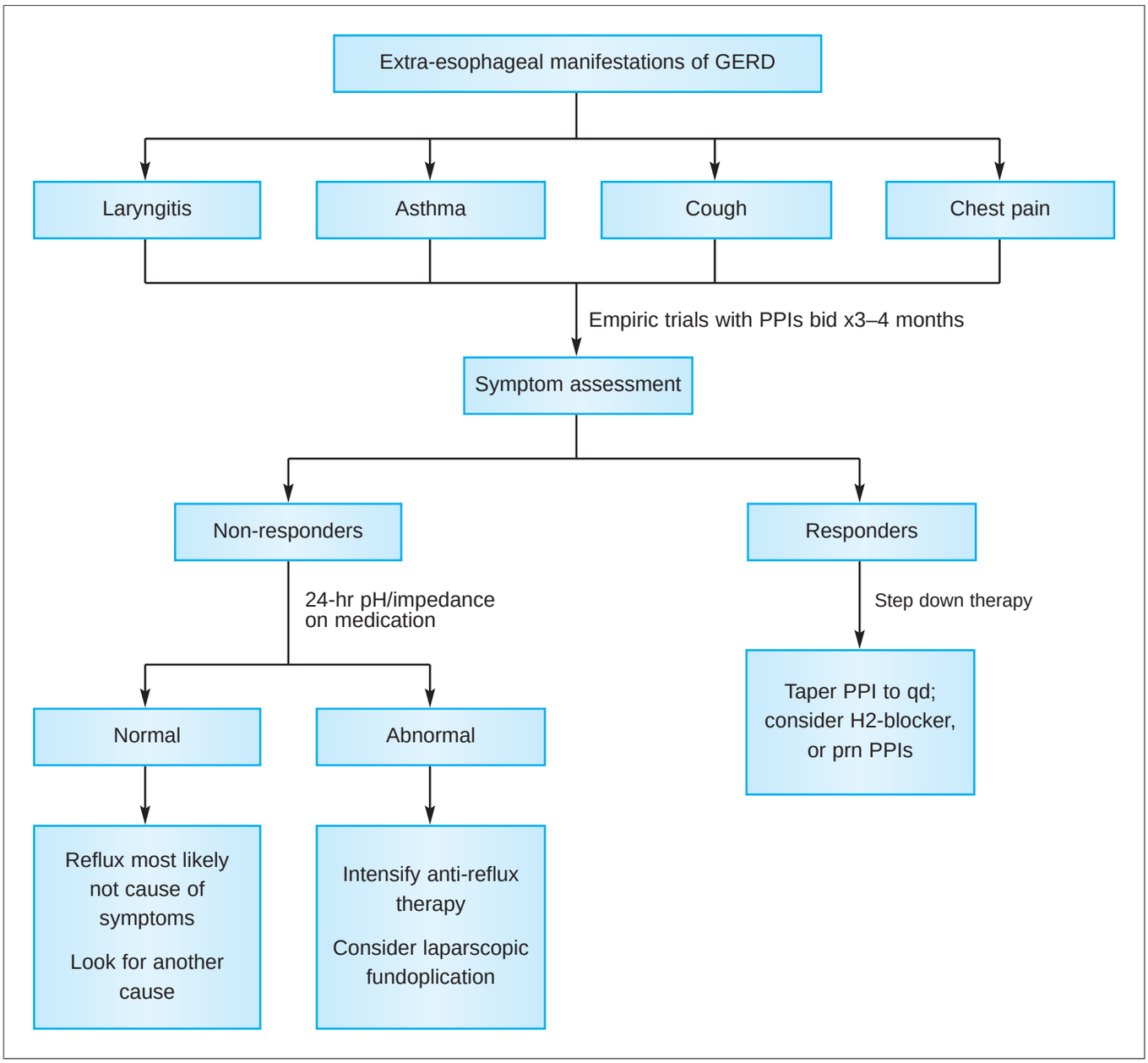
Extra-esophageal symptoms include asthma, chest pain, chronic cough, laryngitis, and dental erosions. In most patients, esophagitis or Barrett's esophagus is not present. Response to anti-reflux surgery and acid suppression is less predictable. An empiric trial of PPIs bid is indicated as the initial treatment as there is no definitive diagnostic gold standard for GERD (**4.64**). If treatment fails, a full evaluation with ambulatory pH monitoring is recommended.

Laryngitis

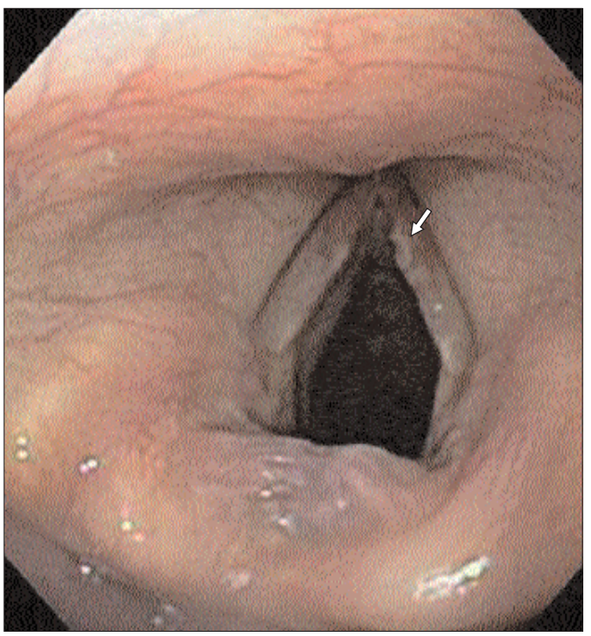
There is increasing evidence that GERD causes laryngeal signs and symptoms, so called reflux laryngitis (LR) or laryngopharyngeal reflux (LPR). GERD may cause significant laryngeal changes including erythema, edema, pharyngeal ulcerations, vocal cord nodules and polyps, granulomas, or even leukoplakia and cancer, but these findings are not specific for GERD (*Table 4.17*, **4.65–4.69**). The most specific laryngeal lesions for GERD-induced injury are vocal cord lesions and arytenoid medial wall erythema and edema. Overall, only 50% of patients with laryngoscopic signs of GERD have abnormal esophageal acid exposure on pH monitoring (**4.70**). PPIs should be first line of therapy, initially twice daily and then tapering to once daily in responders.

Table 4.17 Potential laryngopharyngeal signs associated with gastroesophageal reflux disease

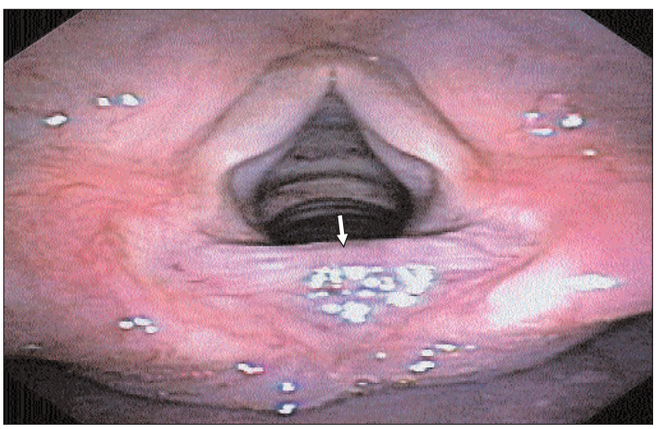
Edema and hyperemia of larynx
Hyperemia and lymphoid hyperplasia of posterior larynx (cobblestoning)
Interarytenoid changes
Granuloma
Contact ulcers
Laryngeal polyps
Reinke's edema
Tumors
Subglottic stenosis
Posterior glottic stenosis
Strictures
Apnea
Sudden infant death syndrome (SIDS)



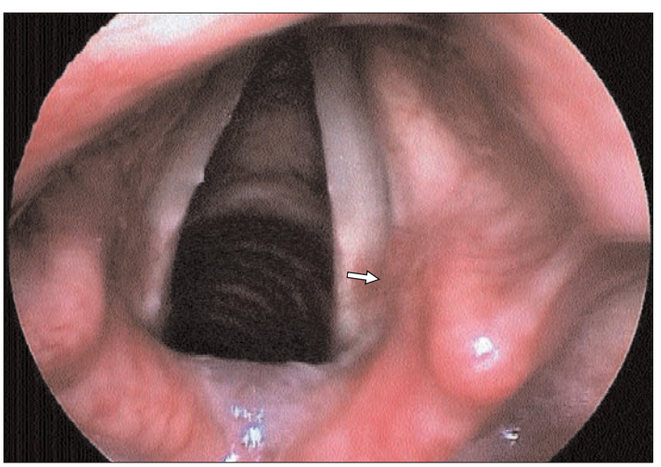
4.64 Treatment algorithm for extra-esophageal manifestations of GERD. (bid: twice daily; prn: as needed; qd: once daily.)



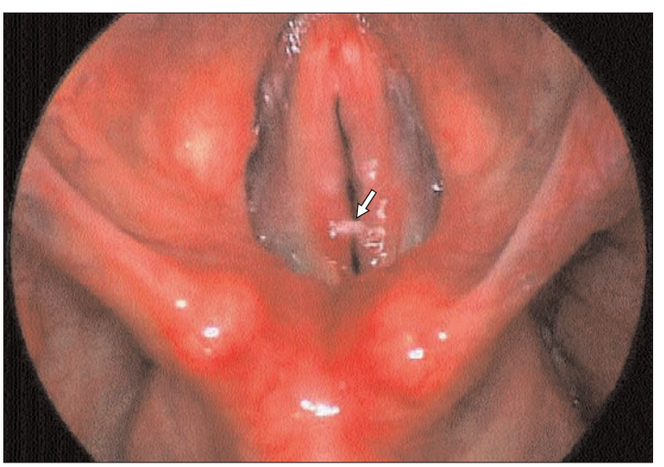
4.65 Laryngeal signs of GERD: vocal cord nodule (arrow).



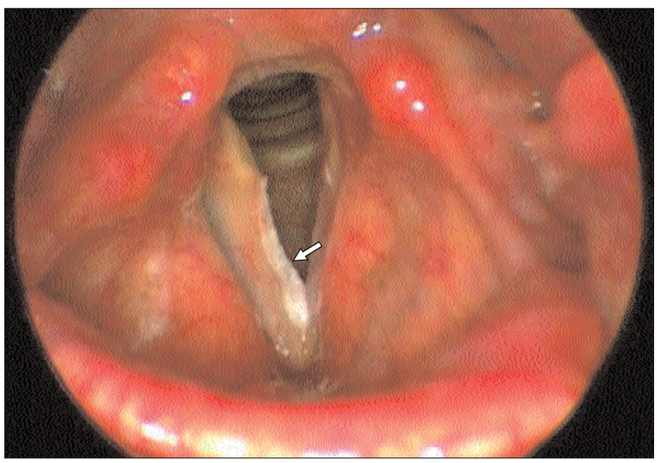
4.66 Interarytenoid bar (arrow).



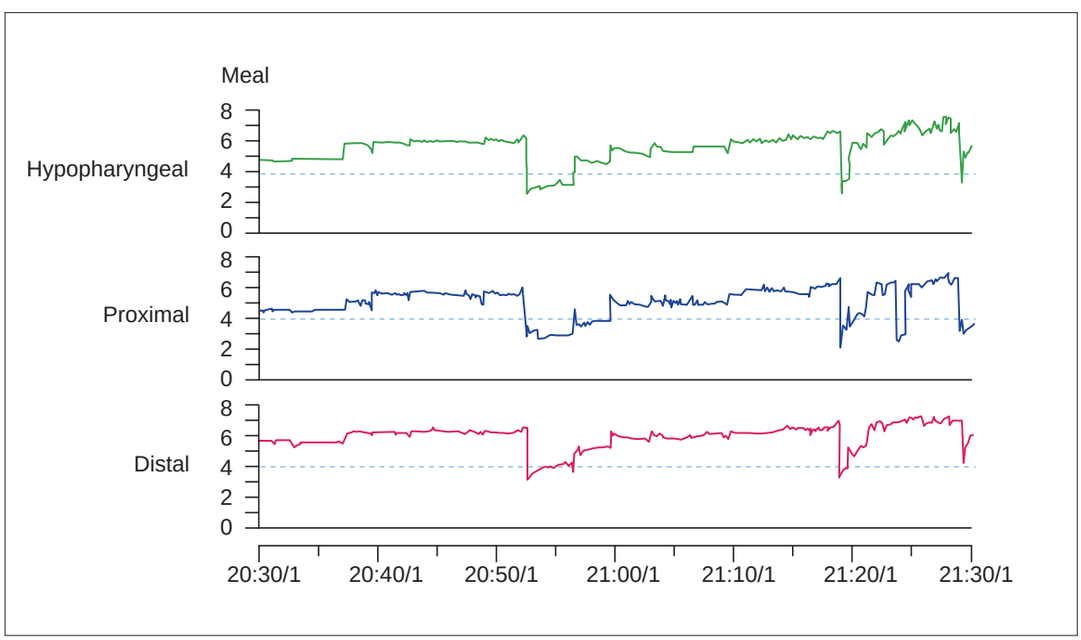
4.67 Laryngeal signs of GERD: artynoid medial wall erythema (arrow).



4.68 Laryngeal signs of GERD: vocal cord erythema (arrow).



4.69 Vocal cord leukoplakia (arrow).



4.70 Hypopharyngeal acid exposure is shown by a pH drop to <4.0 in all three electrodes. Only 50% of patients with laryngoscopic signs of GERD have abnormal acid exposure on pH monitoring.

Asthma

Approximately 70–80% of asthma patients have GERD. There are two pathophysiological mechanisms: proximal esophageal reflux leading to microaspiration/bronchospasm, and vagally-mediated esophageal–bronchial reflex, resulting in bronchospasm. Treatment of GERD improves respiratory symptoms in 69% and reduces asthma medication use by 62%.

Chest pain

Non-cardiac chest pain may be due to pulmonary, muscoskeletal, or esophageal etiologies. The most common esophageal cause is GERD, accounting for 40–60% of patients. The most cost effective initial option is a trial of PPIs for 3 months.

Chronic cough

GERD is the third most common cause of chronic cough after post-nasal drip and asthma (**4.71**). Patients with chronic cough from GERD have normal chest radiographs, are non-smokers, are not taking medications (such as angiotensin-converting enzyme [ACE] inhibitors) known to cause cough, and have had no response to treatment for asthma and post-nasal drip. PPIs twice daily are the best initial management, and a GERD-related cough can take 3 months to resolve. A pH study can be helpful as it allows temporal correlation between reflux events and cough. If cough precedes the pH drop, this suggests secondary reflux.

Dental erosions

Dental erosion is a loss of tooth structure resulting from a chemical rather than bacterial cause (**4.72**). Chronic exposure to acid can lead to a loss of enamel and tooth substance. Reported prevalence of dental erosions in patients with GERD is 17–68%.

Further reading

Vaezi MF, Hicks DM, Abelson TI, Richter JE (2003). Laryngeal signs and symptoms and gastroesophageal reflux disease: a critical assessment of cause and effect association. *Clin Gastroenterol Hepatol* **1**:333–44.

Summary

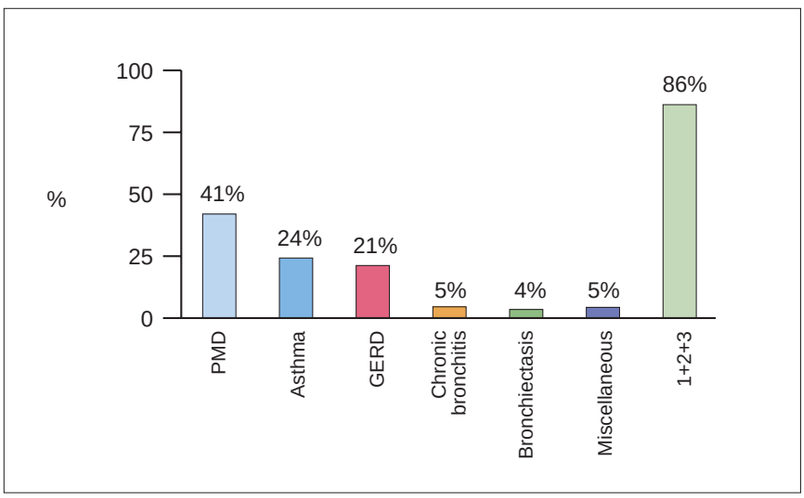
Definition: chronic symptoms or mucosal damage caused by reflux of gastric contents into the esophagus.

Pathophysiology: impaired anti-reflux barrier at LES, increased gastroesophageal pressure gradient, prolonged acid clearance, reduced esophageal tissue resistance, acid hypersecretion.

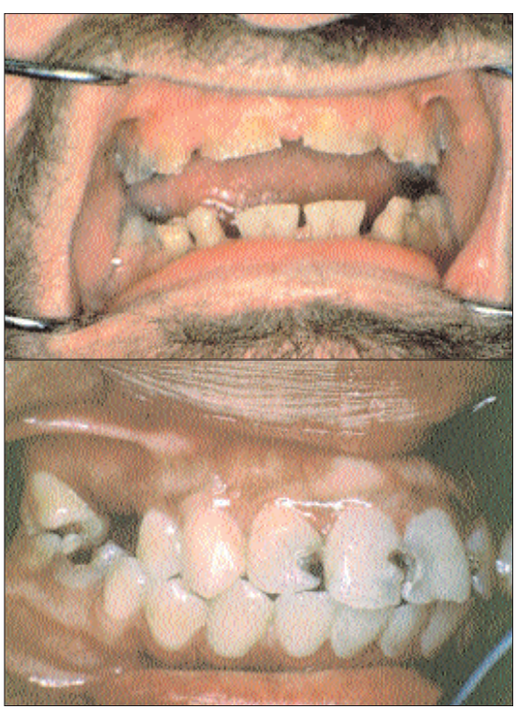
Symptoms: heartburn (pyrosis), acid regurgitation, dysphagia or odynophagia, atypical symptoms (asthma, cough, chest pain, dental erosions).

Diagnosis: no gold standard. pH monitoring or empirical PPI therapy. Endoscopy to examine mucosa.

Treatment: lifestyle modification, acid suppressive therapy (PPIs, H2RAs), anti-reflux surgery (fundoplication).



4.71 Causes of chronic cough. GERD is the third most common cause after post-nasal drip and asthma. (Data derived from Irwin RS, Curley FJ, French CL *et al*. (1990) Chronic cough. The spectrum and frequency of causes, key components of the diagnostic evaluation, and outcome of specific therapy. *Am Rev Respir Dis*, **141**:640–647.)



4.72 Dental erosions secondary to GERD.

Barrett's esophagus

Definition

Normal stratified squamous epithelium of the distal esophagus is replaced with intestinal columnar metaplasia (**4.73**). Barrett's metaplasia can be divided into short-segment and long-segment, based on the length of Barrett's metaplasia of greater or less than 3 cm (**4.74**, **4.75**).

Epidemiology

It is estimated that 6–12% of patients with GERD will have Barrett's esophagus, with the highest risk in older Caucasian males. It is a significant outcome of chronic GERD and predisposes to the development of esophageal adenocarcinoma. There are no specific symptoms related to Barrett's esophagus, but it is associated with more severe GERD. However, secondary to impaired acid sensitivity, some patients are no worse than uncomplicated GERD, so it is recommended that patients with prolonged GERD symptoms undergo endoscopic screening.

Diagnosis

Barrett's esophagus is suspected endoscopically when the pale pink-appearing squamous mucosa of the distal esophagus is replaced to various lengths with salmon pink columnar mucosa. Thus the SCJ is displaced proximal to the GEJ. It is confirmed when intestinal metaplasia is noted on biopsy (**4.76**).

Treatment

The risk of adenocarcinoma increases by approximately 0.5% per year, thus it is recommended that patients undergo continued endoscopic surveillance to detect the development of dysplasia and adenocarcinoma (*Table 4.18*). Current endoscopic surveillance guidelines suggest four-quadrant biopsies at 2 cm intervals along the entire length of Barrett's every 3 years. Surveillance biopsies are examined for the presence of dysplasia. Surveillance intervals are based on the presence and degree of dysplasia as outlined in the updated guidelines of the American College of Gastroenterology (ACG) (*Table 4.18*). Several endoscopic methods can be used as alternatives to surgery for high grade dysplasia or intramucosal cancer. These include argon plasma coagulation (**4.77**), photodynamic therapy, cryoablation, and endoscopic mucosal resection (**4.78**).

Further reading

Falk GW (2002). Barrett's esophagus. *Gastroenterol* **122**(6):1569–1591.

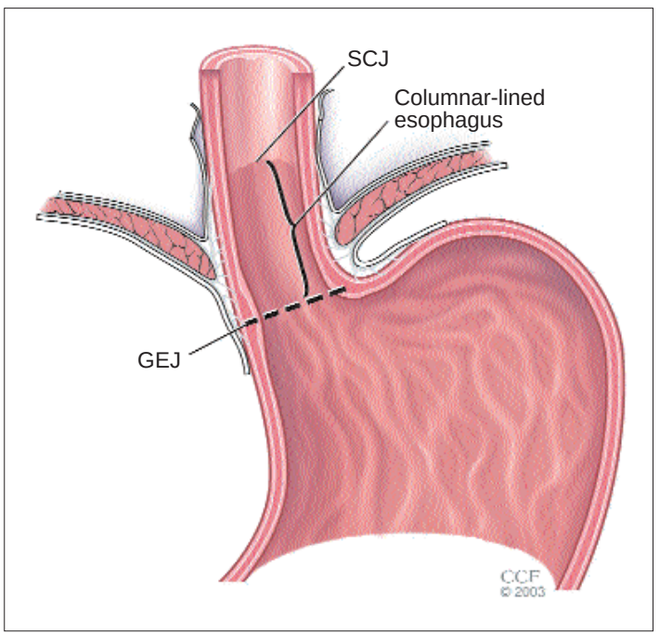
Sampliner RE (2002). Updated guidelines for the diagnosis, surveillance, and therapy of Barrett's esophagus. *Am J Gastroenterol* **97**:1888–1895.

Sharma P, McQuaid K, Dent J, *et al.* (2004). A critical review of the diagnosis and management of Barrett's esophagus: the AGA Chicago Workshop. *Gastroenterol* **127**(1):310–330.

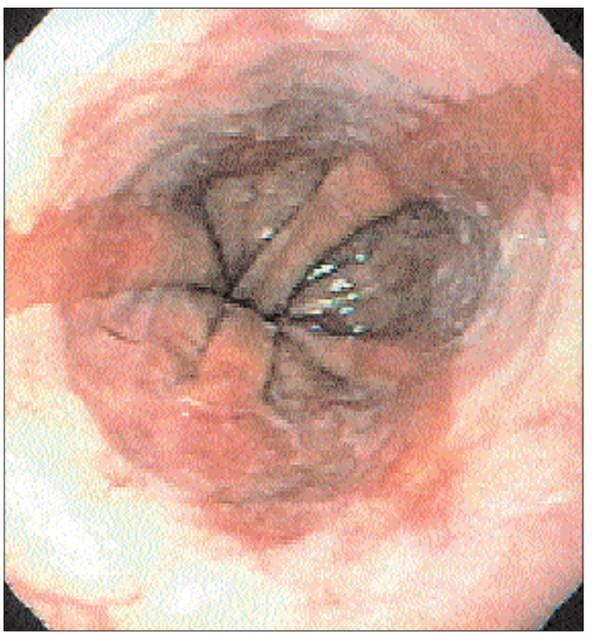
Table 4.18 Management of Barrett's metaplasia

Dysplasia	*Confirmation*	*Intervention*
None	2 EGDs with 4-quadrant biopsies every 2 cm	Surveillance endoscopy every 2–3 years
Low grade	Highest grade on repeat EGD with biopsy remains low grade	Surveillance endoscopy every year until no dysplasia
High grade	Repeat EGD with 4-quadrant biopsies every 1 cm Expert pathologist confirmation	Focal HGD surveillance-endoscopy every 3 months Multifocal HGD-esophagectomy, ablation therapy, or esophageal mucosal resection

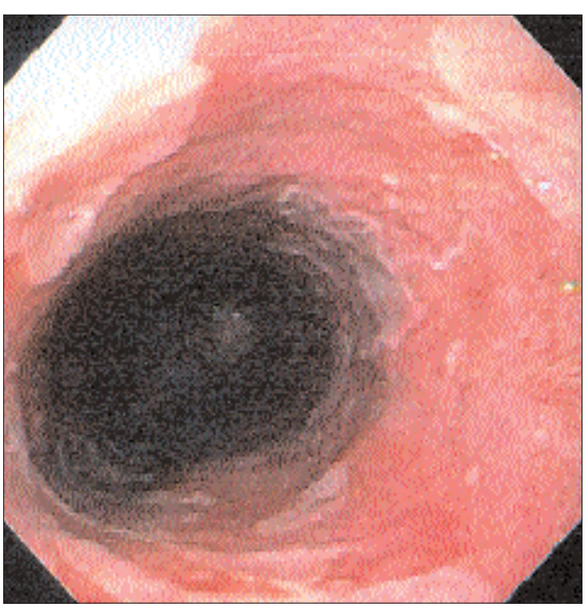
EGD: esophagogastroduodenoscopy; HGD: high grade dysplasia



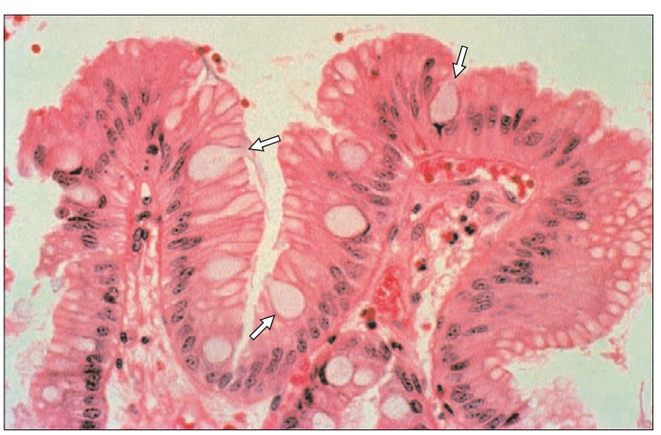
4.73 Schematic diagram of Barrett's esophagus. The SCJ is proximal to the GEJ.



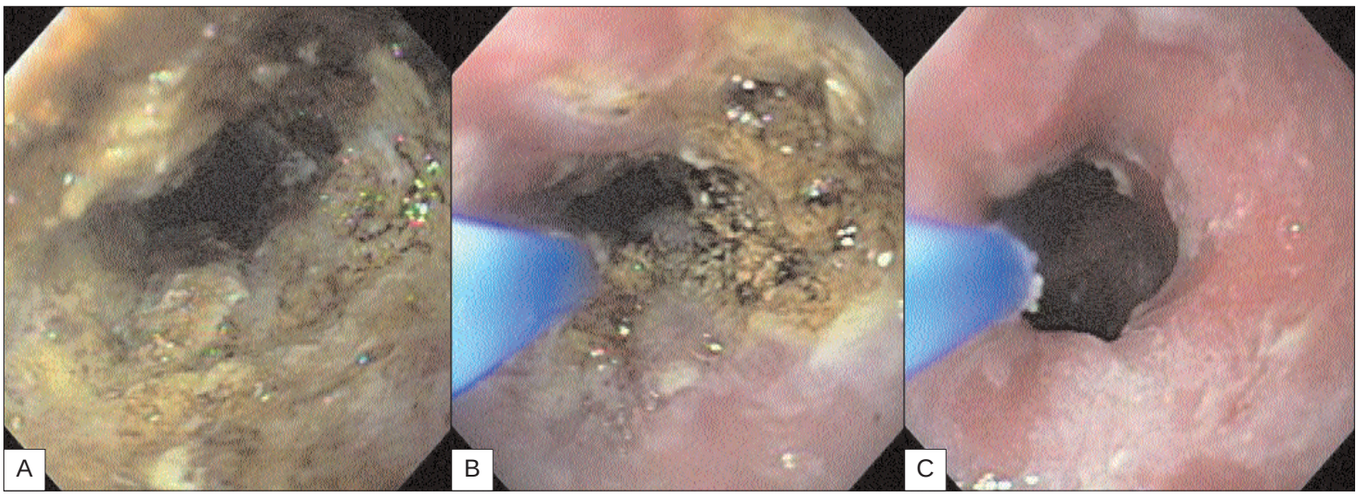
4.74 Short-segment Barrett's esophagus. 'Tongues' of red columnar mucosa extending <3 cm above the GEJ. Dysplasia and cancer are more common in patients with long-segment Barrett's esophagus, but patients with short-segment Barrett's are also at increased risk.



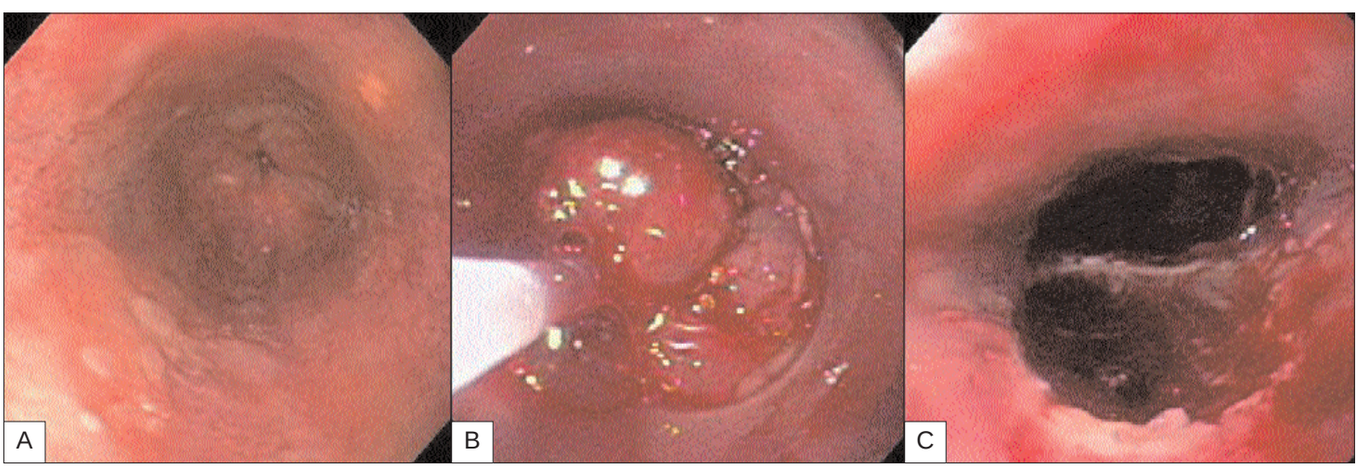
4.75 Long-segment Barrett's esophagus. The columnar mucosa extends >3 cm above the GEJ. Islands of normal squamous mucosa are present within the Barrett's metaplasia.



4.76 Histology of a distal esophageal biopsy, demonstrating goblet cells (arrows) diagnostic of Barrett's metaplasia. Alcian blue stain could be used if there is difficulty identifying goblet cells by routine H&E stain.



4.77 A–C: Argon plasma coagulator (APC) ablation of Barrett's esophagus. The patient was a non-surgical candidate with high grade dysplasia. APC is used to ablate the mucosa and the patient is followed with close surveillance.



4.78 A–C: Nodule arising in Barrett's esophagus. Biopsies show high grade dysplasia at the nodule only. The nodule is then resected with a cap-assisted endoscopic mucosal resection (EMR) technique. A large amount of tissue can be removed with EMR.

Hiatal hernia

Introduction

Hiatal hernia is a prolapse of stomach or other abdominal contents through the diaphragmatic esophageal hiatus into the thorax. Hiatal hernia is usually asymptomatic, but can potentially result in life-threatening conditions. Prevalence is estimated from 0.8–2.9% of all patients undergoing upper endoscopy (1). There are four types of hiatal hernia, which can be grouped as esophageal or paraesophageal (*Table 4.19*).

Etiology

It is thought to be an acquired condition due to multiple factors compromising the integrity of the hiatus. Some of these factors may include:

- Age-related degeneration.
- Repeated mechanical stresses of inspiration, vomiting, postural change, swallowing, heavy lifting.
- Increased abdominal pressure due to obesity or pregnancy.

Other possible causes are trauma, congenital malformations, or iatrogenic.

Table 4.19 Types of hernia

Sliding	
Type I	Herniation of gastric cardia into the posterior mediastinum; most common type (95%); usually asymptomatic but can cause symptomatic GERD; usually an acquired condition
Paraesophageal	
Type II	Herniation of gastric fundus; due to localized defect of phrenoesophageal membrane and laxity of gastrosplenic and gastrocolic ligaments; stomach is fixed at GEJ; stomach may rotate around its longitudinal axis resulting in organoaxial volvulus, or infrequently rotate around its transverse axis resulting in mesenteroaxial volvulus
Type III	Combination of types I and II hernias; due to progressive enlargement of type II
Type IV	Herniation of other intra-abdominal organs, such as colon, spleen, pancreas, and small intestine; due to a large defect in the phrenoesophageal membrane

GEJ: gastroesophageal junction; GERD: gastroesophageal reflux disease

Type I or sliding hiatal hernia

Type I hernia involves an upward herniation of the gastric cardia through the esophageal hiatus into the posterior mediastinum (**4.79–4.81**). This is the most common type of hiatal hernia (95% of all hiatal hernias). It is usually asymptomatic but there is increased likelihood of gastro-esophageal reflux and patients often present with GERD symptoms.

It is caused by widening of the muscular hiatus and laxity of phrenoesophageal membrane.

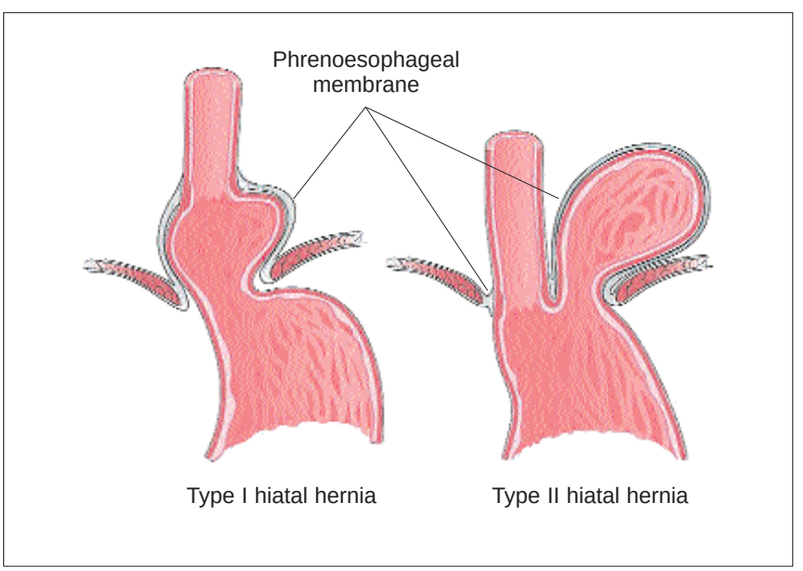
Type II hernia

This is caused by a localized defect in the phrenoesophageal membrane. The gastric fundus is herniated while the GEJ remains fixed. The hernia gets progressively worse over time, so that the entire stomach may eventually herniate. Rotation of the herniated stomach around its longitudinal axis (organoaxial volvulus) may occur as a result of stomach being fixed at the GEJ. The stomach may also infrequently rotate around its transverse axis, resulting in mesenteroaxial volvulus.

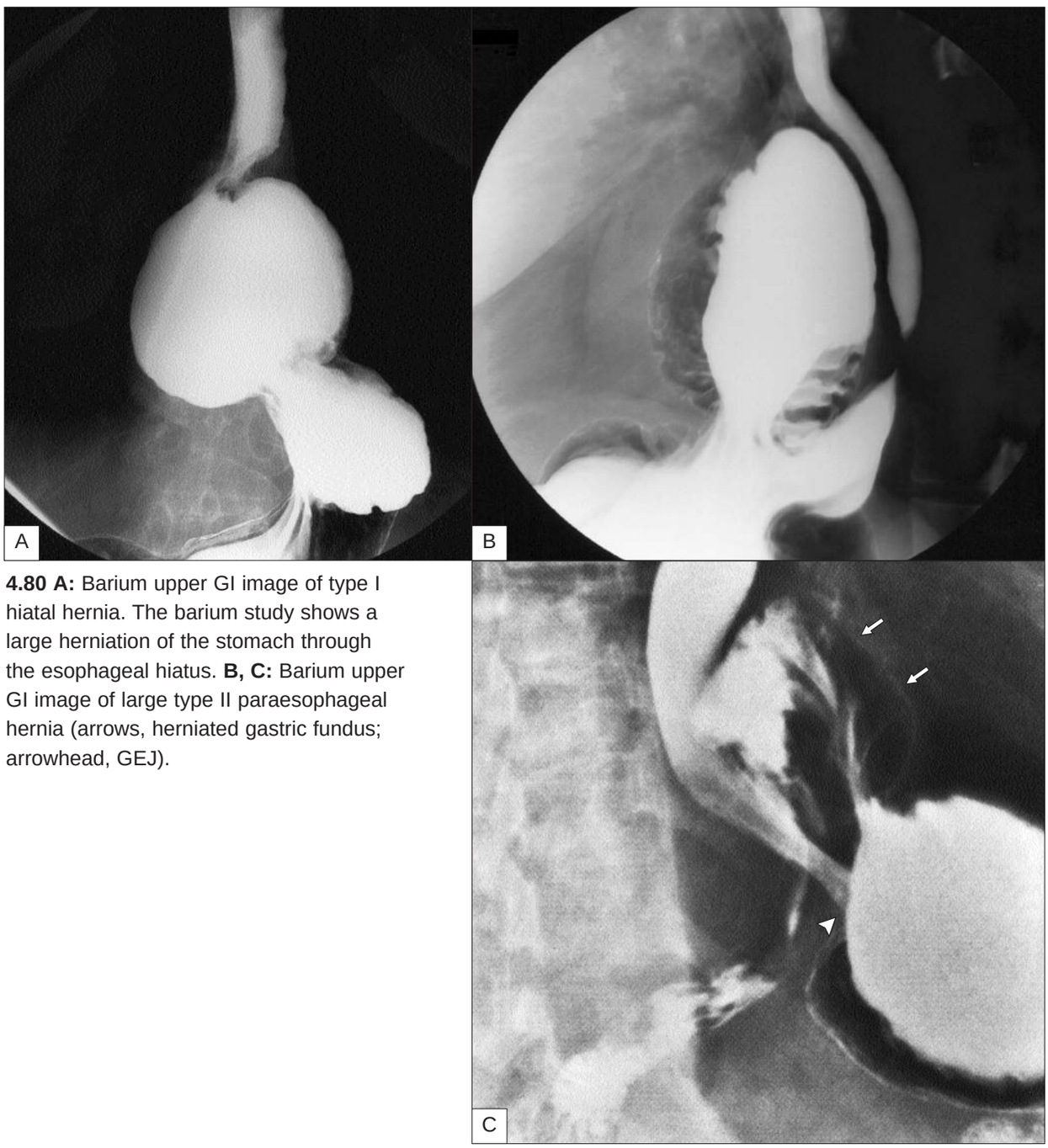
Types III and IV hiatal hernias

These are variations of type II hernia. Type III hiatal hernia is a combination of both types I and II hernias and occurs due to progressive enlargement of the type II hernia.

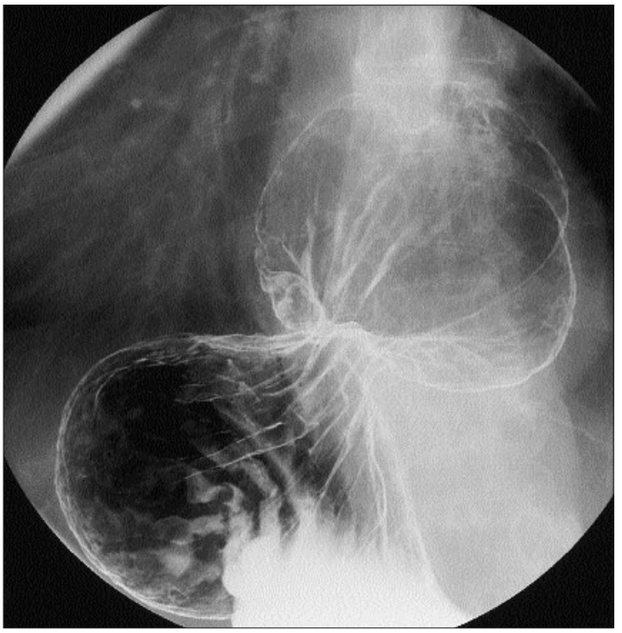
Type IV hiatal hernia is due to a large defect in the phrenoesophageal membrane. As a result, other intra-abdominal organs, such as colon, spleen, pancreas, and small bowel, may enter the hernia sac.



4.79 Type I and type II hiatal hernia. In type I (or sliding) hernia, the gastric cardia is upwardly herniated through the esophageal hiatus into the posterior mediastinum. It is secondary to widening of the muscular hiatus and laxity of phrenoesophageal membrane. Type II hiatal hernia is caused by a localized defect in the phrenoesophageal membrane. The gastric fundus is herniated while the GEJ is fixed.



4.80 A: Barium upper GI image of type I hiatal hernia. The barium study shows a large herniation of the stomach through the esophageal hiatus. **B, C:** Barium upper GI image of large type II paraesophageal hernia (arrows, herniated gastric fundus; arrowhead, GEJ).



4.81 Barium upper GI image of a large hiatal hernia with mesenteroaxial volvulus.

Associated conditions

GERD

There is a 50–94% prevalence of hiatal hernia in patients with GERD (2). The LES becomes incompetent in the setting of hiatal hernia due to the loss of diaphragmatic contribution. Additionally, hiatal hernia impairs esophageal emptying.

Bleeding

Bleeding is usually subtle and may be asymptomatic; massive bleeding is rare (2). Bleeding sites include the esophagus, esophogastric junction, or hiatal hernia sac. Risk factors for bleeding include NSAID use. Hiatal hernia increases the risk of developing a Mallory–Weiss tear. Cameron lesions can occur, which are linear gastric erosive changes in the hernia sac. They are usually found at or near the diaphragm, and may cause obscure bleeding evidenced by iron deficiency anemia. They are not associated with *Helicobacter pylori*.

Incarceration and volvulus

Two types of gastric volvulus can occur (**4.82**): organoaxial (rotation of stomach on its longitudinal axis) and mesenteroaxial (rotation of stomach on its transverse axis). Volvulus may result in obstruction, necrosis, and perforation which can be catastrophic.

Table 4.20 Treatment of hiatal hernia

Sliding	
Type I	Observation if aymptomatic; if GERD symptoms start PPI therapy; consider surgery if PPI therapy fails
Paraesophageal	
Types II, III, IV	Surgery is indicated due to increased risk of catastrophic complications

GERD: gastroesophageal reflux disease; PPI: proton-pump inhibitor

Schatzki's ring

Hiatal hernia can be associated with a mucosal lower esophageal ring (B ring), located within 3 mm proximal to the SCJ.

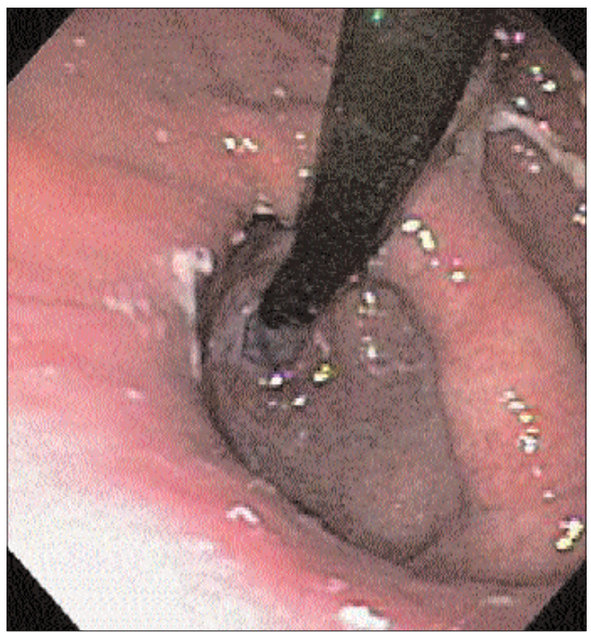
Treatment

Treatment of hiatal hernia is described in *Table 4.20*. Type I hiatal hernia can be managed by observation, if asymptomatic. If there are GERD symptoms, medical treatment should be initiated first with PPIs. Surgical treatment may be needed if medical therapy fails (see GERD section for more detail).

Enlarging type II, III, and IV hiatal hernias have a high risk of serious complications of incarceration, necrosis, and perforation. Therefore, they should be treated surgically even if asymptomatic.

References

1 Pridie RB (1966). Incidence and colincidence of hiatus hernia. *Gut* **7**:188–189.
2 Johnson DA, Ruffin WK (1996). Hiatal hernia. *Gastrointest Endosc Clin N Am* **6**(3):641–66.



4.82 Endoscopic retroflexed view of hiatal hernia. The diaphragmatic hiatus is easily visualized in the retroflexed view allowing easier visualization of the hernia.

Summary

Definition: a prolapse of stomach or other abdominal contents through the diaphragmatic esophageal hiatus into the thorax.
Etiology: acquired condition due to multiple factors, such as age, mechanical stresses, increased intra-abdominal pressure.
Type I: most common, usually asymptomatic or GERD symptoms.
Type II: due to localized defect in phrenoesophageal membrane.
Types III and IV are variations of type II.
Symptoms and sequelae: GERD, bleeding, incarceration and volvulus (especially types II-IV), Schatzki's ring.
Treatment: Type I – as for GERD, PPIs +/- surgery; type II–IV – surgical treatment even if asymptomatic.

Diverticula

Definition

An esophageal diverticulum is a sac that protrudes from the esophageal wall. A true diverticulum contains all layers of the wall of the esophagus, while a false diverticulum only consists of mucosa and submucosa that have herniated through a weak area of the esophageal wall (**4.83**).

Zenker's diverticulum

A Zenker's diverticulum is located proximal to the esophagus above the UES, and is, in reality, a hypopharyngeal diverticulum. These protrusions occur in an area called Killian's triangle, an area of relative weakness, which is located between the cricopharyngeal sphincter and the inferior pharyngeal constrictor muscle (**4.84**). The formation of this diverticulum is related to incomplete relaxation of the UES, increased UES resting pressure, or incoordination between the UES and the hypopharynx. GERD has also been implicated as a possible cause of Zenker's diverticula. Zenker's are false diverticula, involving only the mucosa and submucosa.

The incidence of Zenker's increases with age, possibly secondary to an increase in tissue elasticity. The prevalence reaches 50% in the seventh and eighth decades of life, and is higher in women. Many of these diverticula are asymptomatic, and are incidentally discovered during a radiologic study. Symptoms typical of a Zenker's include oropharyngeal dysphagia, regurgitation of undigested food, intermittent solid food dysphagia, halitosis, excessive salivation, cough, and aspiration pneumonia.

The best diagnostic test for this diverticulum is a barium swallow, with special attention to the oropharyngeal phase of swallowing. The diverticulum protrudes posteriorly, and may best be seen on lateral and oblique views. Endoscopy does not add to the diagnosis, and may lead to perforation of the diverticulum.

Treatment should only be offered to patients who are symptomatic secondary to large diverticula; small asymptomatic diverticula may be followed with serial barium studies.

Treatment includes open surgical resection of the diverticulum, with division of the cricopharyngeus muscles. Another treatment option is a diverticulopexy, which involves suspension of the diverticulum in a cranial direction. Endoscopic therapeutic maneuvers are beginning to emerge, including the use of lasers and stapling devices.

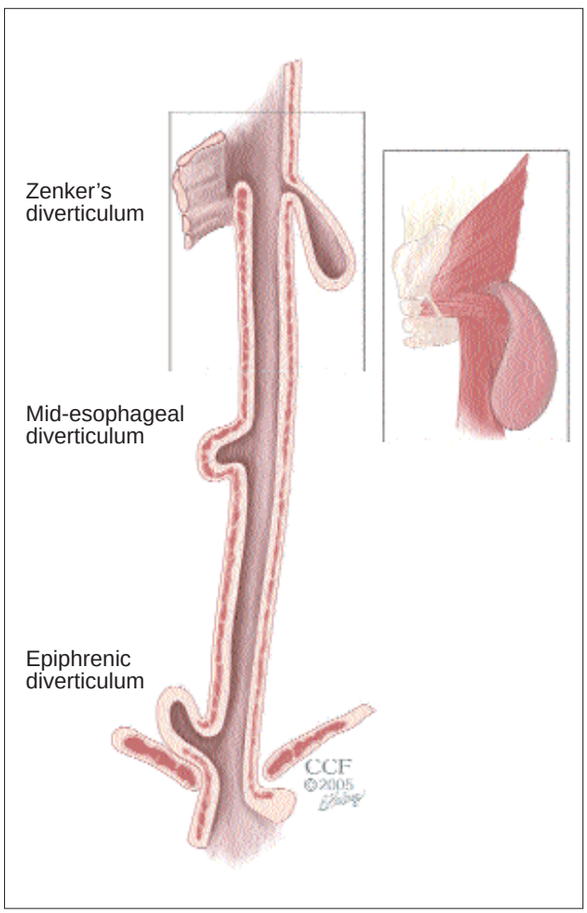
Mid-esophageal diverticula

These diverticula, also known as traction diverticula, and are formed secondary to external pulling of the esophageal wall by adjacent inflammatory or fiberoptic tissue (as can be seen in tuberculosis mediastinitis). These formations are located in the middle third of the esophagus, and are the only true diverticula seen in the esophagus. A pulsion type diverticulum also occurs in the mid-esophagus, which is a false diverticulum formed due to abnormal forces applied to the esophageal wall resulting in an outpouching.

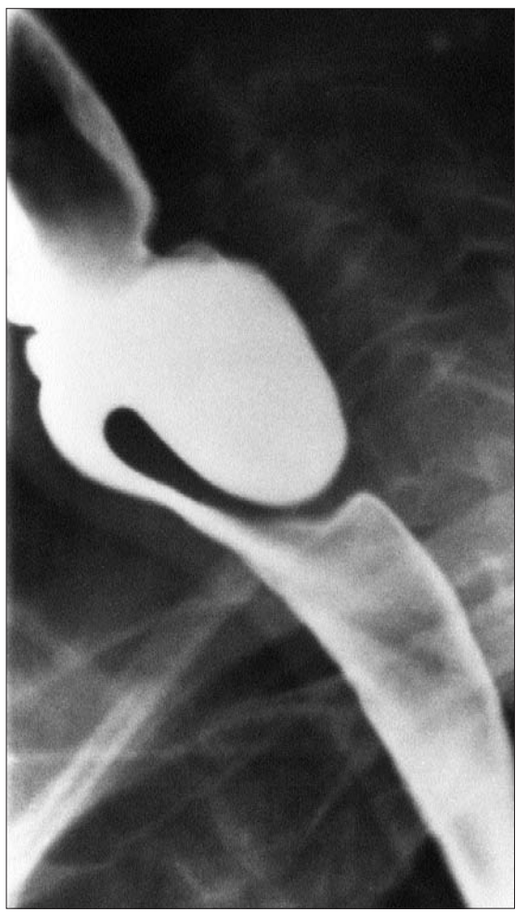
Most traction diverticula are asymptomatic, and tend to be small. Patients may present with chest pain and dysphagia, but this usually occurs in subjects with a motility disorder.

Complications are rare, and include rupture, aspiration, exsanguinations, fistula formation, and carcinoma. Diagnosis is often made incidentally during a barium study carried out for other reasons. As with Zenker's diverticula, endoscopy does not add to the diagnosis.

Treatment is not required for most mid-esophageal diverticula, as they are asymptomatic and uncomplicated. If necessary, the standard treatment is diverticulectomy with or without myotomy, but the presence of a motility disorder must be ruled out prior to surgery.



4.83 Schematic diagram showing the three major types of diverticula. A false diverticula is secondary to the herniation of mucosa and submucosa through the muscular wall. True diverticula contain all the layers of the esophageal wall. The most proximal diverticulum, a Zencker's diverticulum, forms in an area of weakness known as Killian's triangle. Mid-esophageal diverticulum is the only true diverticulum in the esophagus, and is a traction diverticulum formed as a result of pulling of the esophageal wall by inflammatory or fibrotic tissue. The epiphrenic diverticulum, located near the diaphragm, is often secondary to achalasia or another motility disorder.



4.84 A barium swallow esophagram showing a Zencker's diverticulum. These occur between the cricopharyngeal sphincter and the inferior pharyngeal constrictor muscle. Treatment, which consists of surgical resection, is only offered to patients with large, symptomatic diverticula.

Epiphrenic diverticula

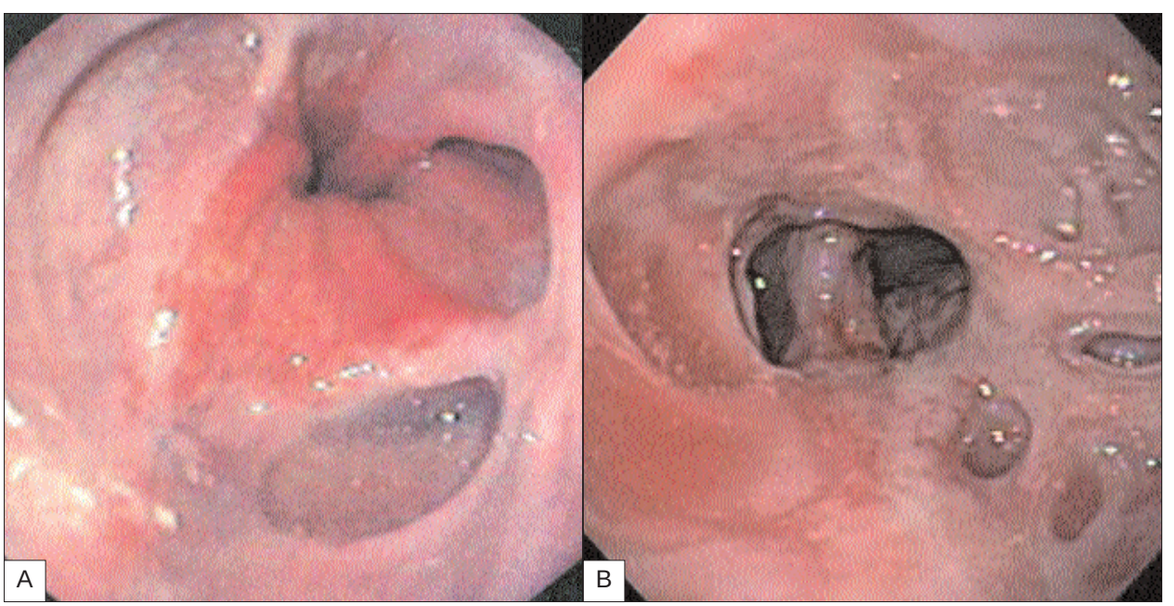
These outpouchings are located in the distal esophagus, near the LES and the diaphragmatic hiatus (**4.85**). This term is usually use for diverticula in the distal 3–4 cm of the esophagus. Epiphrenic diverticula are almost always the result of a motility disorder, such as achalasia or diffuse esophageal spasm, or incoordination between the distal esophagus and the LES. Epiphrenic diverticula can occur in all age groups, with a range in a large case series of 18–88 years. The incidence of epiphrenic diverticula is low, with a frequency estimated to be only 20% that of Zenker's diverticula.

The majority of epiphrenic diverticula are asymptomatic, but symptoms, when present, may include chest pain or regurgitation. Symptoms also depend on the associated motor abnormality. Diagnosis of these diverticula includes manometric testing to rule out an associated motility disorder. As with other diverticula, diagnosis is made by barium esophagram, and multiple views aid in defining the size of the pouch and the location of the mouth. A modified barium swallow is useful in identifying an associated motor abnormality.

One aspect of treatment of epiphrenic diverticula includes management of the underlying motility disorder. This will aim to avoid further enlargement of the diverticulum. Surgical treatment of an epiphrenic diverticulum is diverticulotomy, with or without myotomy, if the diverticulum is symptomatic.

Intraluminal pseudodiverticula

Esophageal intramural pseudodiverticula are most often seen as multiple small outpouchings on barium esophagram or upper endoscopy (**4.86**, **4.87**). These are not actual diverticula, rather they are composed of dilated submucosal glands. The etiology of these diverticula is unclear, although it has been postulated that they are due to extensive chronic inflammation leading to dilated ducts, which then develop small cysts. Other associations, with GERD, esophageal strictures, candidiasis, motility disorders, and esophageal carcinoma, have also been described.



4.85 A, B: Endoscopic views of an epiphrenic diverticulum. These are seen in close proximity to the LES, and these diverticula are often asymptomatic.

The prevalence is unknown, but it is thought to be a rare condition. On radiological evaluations for all causes, two series have found prevalences of 0.09% and 0.15%. Most cases occur in the sixth and seventh decades of life, and occur in both males and females.

Patients present with dysphagia, mostly to solid foods, and which may be acute in onset. These diverticula are associated with strictures, and usually occur proximal to the narrowing.

Diagnosis is made on barium esophagram, and they are best seen with a double air contrast technique. They may also be noted as pinpoint openings in the esophageal wall on endoscopy. Treatment is with esophageal dilation, often achieving symptomatic relief for several years. Serial dilations may be required in some patients.

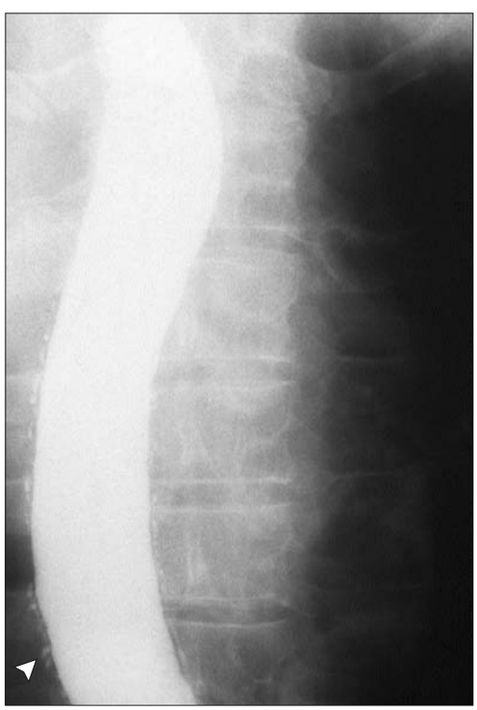
Summary

Definition: a sac that protrudes from the esophageal wall, and contains all the layers of the wall.
Zenker's: false diverticula above UES, involving mucosa and submucosa only.
Mid-esophageal: secondary to adjacent inflammatory or fiberoptic tissue.
Epiphrenic: distal, near LES.
Intraluminal pseudodiverticula: not true diverticula, but dilated submucosal glands.
Symptoms: often asymptomatic, dysphagia, regurgitation, and chest pain.
Diagnosis: barium esophagram.
Treatment: surgical resection if symptomatic.

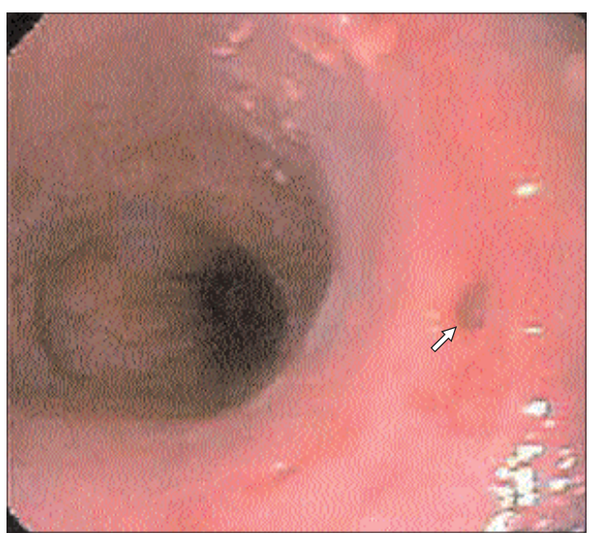
Further reading

Cassivi SD, Deschamps C, Nichols FC, *et al.* (2005). Diverticula of the esophagus. *Surg Clin North Am* **85**(3):495–503.

Castell DO, Richter JE (eds) (2003). *The Esophagus*, 4th edn. Lippincott, Williams, and Wilkins, Philadelphia.



4.86 Esophageal pseudodiverticula (arrowhead) are seen on barium esophagram as multiple small out-pouchings in the wall of the esophagus. These are not diverticula, but are rather dilated submucosal glands.



4.87 Pseudodiverticula (arrow) seen at endoscopy. Although the cause of these lesions is not clear, they are associated with strictures, acid reflux, and esophageal cancer. The number of pseudodiverticula in a single patient can number from a few to dozens.

Foreign body

Epidemiology

The annual incidence of food impaction has been estimated to be 13/100,000. Foreign bodies cause significant morbidity and mortality, with 1,500 deaths per year attributed to foreign bodies. Children tend to ingest objects such as coins, toys, safety pins, button batteries, marbles, screws, and pen caps. Adults tend to have problems with impaction of meat and bones. Special populations at risk of foreign body ingestion include psychiatric patients and prisoners. Food impaction in adults tends to increase with advancing age, secondary to the use of dentures. Men tend to have problems more than women, and impaction tends to be more common in overweight individuals.

Pathophysiology

Most foreign bodies are lodged at levels of natural narrowing – cricopharyngeus, thoracic inlet, aortic arch, tracheal bifurcation, and LES. Studies have shown that 88–97% of adults with meat impaction had distal esophageal disease (stricture, esophagitis, or hiatal hernia). In adults, 63–75% of foreign bodies are impacted at the LES, 8–10% at the aortic arch, and 35–40% at the UES.

Clinical presentation

Common symptoms following ingestion of a foreign body include dysphagia, odynophagia, foreign body sensation, and excessive salivation. In children, respiratory symptoms may be more common than GI symptoms. Other symptoms that should raise concern include stridor, persistent cough, drooling, and refusal to take feedings.

In adults, a life-threatening situation can occur when food becomes lodged at the level of the UES, which may cause acute airway obstruction and death from asphyxiation. This responds to the Heimlich maneuver. Physical findings are usually rare, and may include pharyngeal erythema or oral abrasions. Subcutaneous emphysema may indicate perforation. The presence of a penetrating foreign body may present with hematemesis and shock, secondary to an aortoesophageal fistula.

Diagnosis

A thorough history may assist in discovering the type of object, the size, the timing of the event, and any prior esophageal pathology. The most important step in management is determining the exact location of the foreign body. Plain radiographs can localize objects as well as give insight into size and shape (**4.88**). They can also give information about complications, such as perforation, aspiration, or pleural effusion. CT scans are of particular value in evaluating foreign bodies present in the cervical esophagus, even after plain films and endoscopy have been negative. CT scans can also show pseudoaneurysms, abscesses, or inflammatory changes in adjacent structures. Endoscopy plays an essential role in diagnosis, as it can help to show location, type of object, configuration, and can also provide a means of therapy (**4.89**). It may also identify other mucosal changes not seen on radiography. Diagnostic and therapeutic endoscopy should be performed as early as possible in situations of foreign body ingestion. There is no role for barium studies, unless being used to confirm disimpaction.

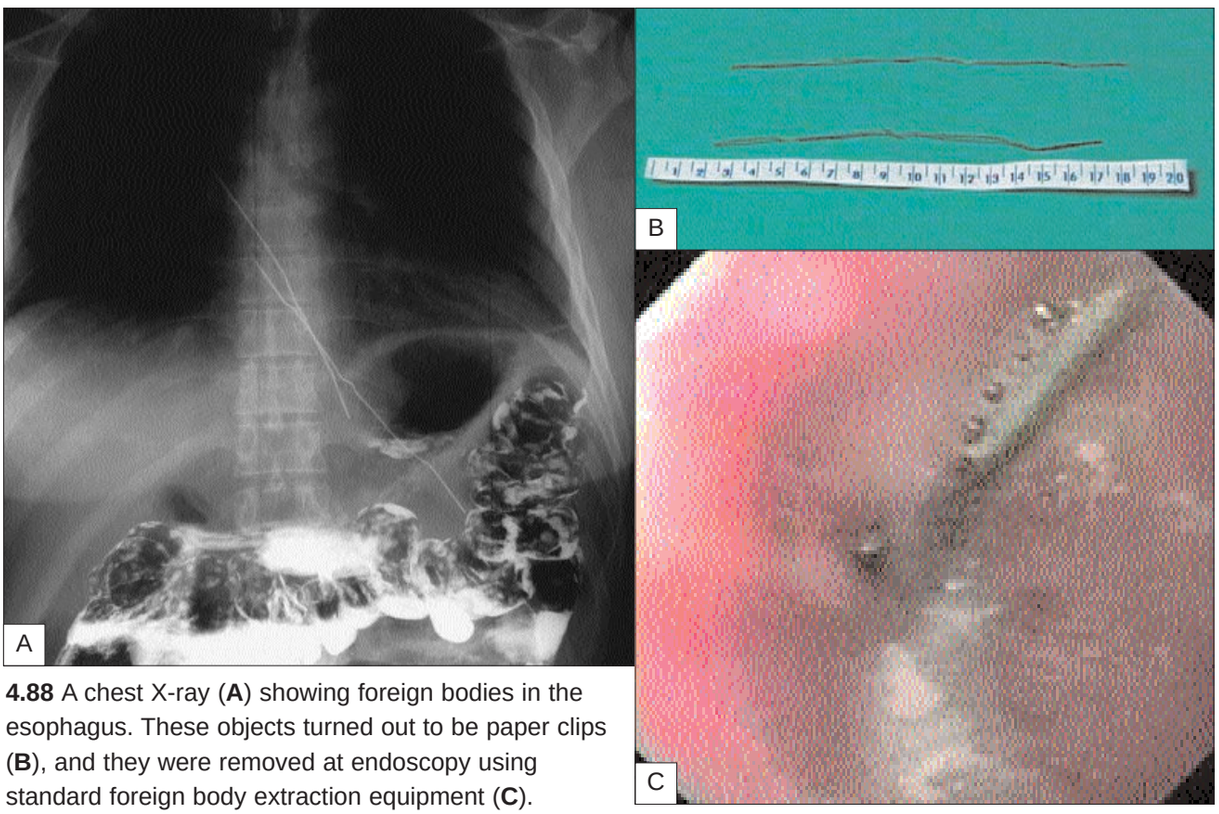
Treatment

Important information for the physician to consider in the management of foreign bodies includes location, type and nature of object, size of object, timing of ingestion, associated symptoms, number of objects, stability of object, radiologic evaluation, previous esophageal pathology, and safety of retrieving the object.

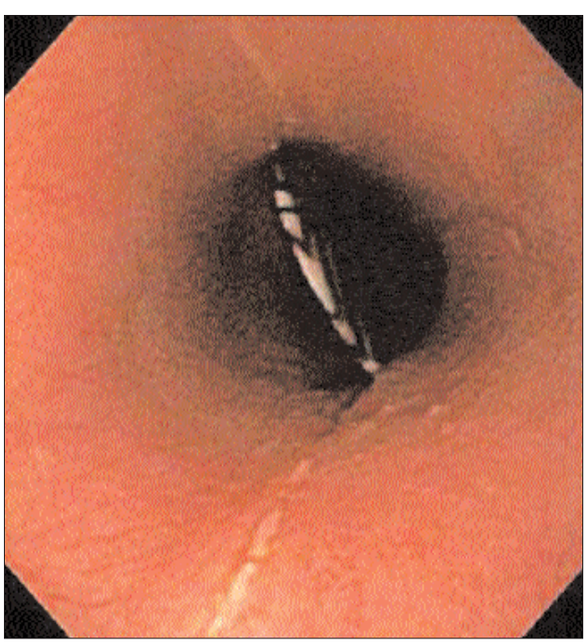
Endoscopic removal is the only safe way to remove bodies that are sharp; it should be remembered that the leading edge of the object has the potential for perforation.

Button batteries should be removed urgently to avoid the possibility of full thickness mucosal injury. Illicit drugs in balloons or condoms should not be removed endoscopically, as rupture can lead to sudden death.

There are non-endoscopic techniques for the treatment of food impaction; however, they are rarely used today. Glucagon has been used to relax the musculature of the LES. Other agents that relax the LES include calcium channel blockers, nitrates, benzodiazepines, and anti-cholinergics. Meat tenderizer, or papain, has been used, although severe complications preclude its usage. Gas-forming agents have also been shown to have complications that outweigh the benefits of their usage.



4.88 A chest X-ray (**A**) showing foreign bodies in the esophagus. These objects turned out to be paper clips (**B**), and they were removed at endoscopy using standard foreign body extraction equipment (**C**).



4.89 An endoscopic view of a guitar pick stuck in the esophagus of a young patient.

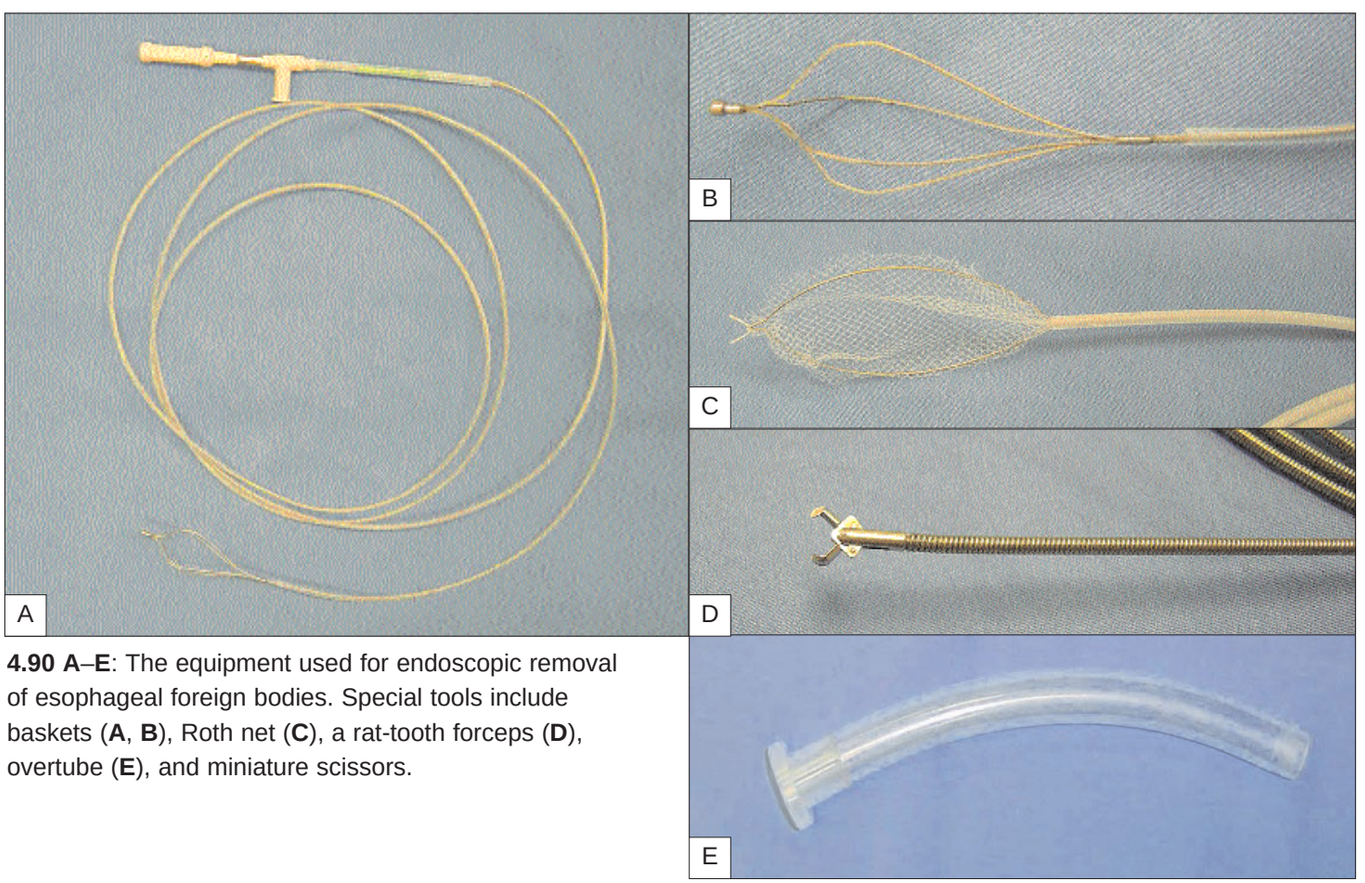
Endoscopic removal has been found to have high rates of success for treating food impaction. Surgical backup must be available, and intervention should not be delayed longer than 24 hours, as complication rates will increase. Some impactions may be pushed through to the stomach by the endoscope, which may be attempted if luminal patency distal to the object can be confirmed. A number of snares, forceps, baskets, and nets are passed through the biopsy channel of the endoscope, and the food is removed whole or in pieces (**4.90**). Following disimpaction, the esophagus should be assessed for underlying pathology, which is present in 90% of cases.

Complications

Complications are estimated to occur in <5% of cases. The most common complications are associated with esophageal mucosal changes, and include tears, ulcers, bleeding, perforation, edema, and luminal obstruction. Respiratory complications can also be seen, including aspiration and airway obstruction. Complications in the thorax can occur secondary to migration of the body from the esophagus, and include arterioesophageal fistulae, aortoesophageal fistulae, mediastinitis, pericarditis, and pericardial effusions.

Further reading

American Society of Gastrointestinal Endoscopy (ASGE) Guidelines (2002). Guideline for the management of ingested foreign bodies. *Gastrointestinal Endoscopy* **55**:802–806.



4.90 A–E: The equipment used for endoscopic removal of esophageal foreign bodies. Special tools include baskets (**A**, **B**), Roth net (**C**), a rat-tooth forceps (**D**), overtube (**E**), and miniature scissors.

Pill-induced injury

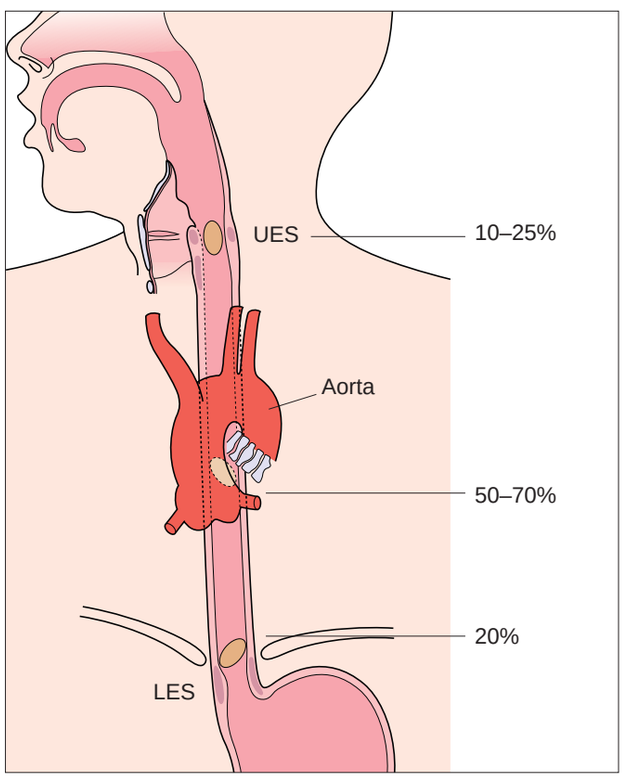
Epidemiology

Since first being described in 1970, approximately 1,100 cases of pill-induced injury have been reported, although this is likely to be a gross under-representation of actual incidence. A study in Sweden in the 1970s reported an incidence of 4/100,000 per year, although this figure is probably higher today. Pill-induced esophageal injury affects patient of all age groups, with reports in patients from 3–98 years old.

In reported cases, women have been injured 71% of the time, with more women being injured by antibiotics, NSAIDs, and alendronate. Other risk factors for pill-induced injury are advanced age, decreased peristalsis, and extrinsic compression of the esophagus.

Pathophysiology

Patients who experience pill-induced injury usually have normal esophageal function and structure. Even in normal subjects, there are three natural areas of esophageal narrowing which provide a potential site for pills to become lodged: the cricopharyngeus muscle, the aortic arch, and the cardia. An enlarged left atrium provides another area of narrowing that a pill may lodge in (**4.91**).



4.91 Schenatic figure showing the most prevalent sites of pill-induced injury to the esophagus. Injury occurs at areas of esophageal narrowing, where the transit of the pill can be arrested. The most common site is in the mid-esophagus, where a narrowing exists at the level of the right atrium. The distal esophagus, at the level of the lower esophageal sphincter, is the site of 20% of injuries. The most proximal site of pill-induced injury is at the level of the UES.

As can be seen in *Table 4.21*, a wide variety of medications can cause injury, including NSAIDs, antibiotics, anti-hypertensives, minerals, and steroids. Injury occurs due to the direct irritant effects of the medications on the esophageal mucosa. Medication factors that predispose to sticking include gelatin capsules, sustained release medications, and larger pill size. When a pill becomes lodged, it will dissolve and release the contents directly onto the esophageal mucosa. These contents can be caustic, which will cause mucosal injury. In other cases, such as ferrous sulfate and tetracycline, the contents may lead to an acid burn. Other mechanisms of injury may include stimulation of gastroesophageal reflux, production of hyperosmolarity, and intracellular poisoning.

Clinical presentation

The most common presentation of pill-induced injury is the abrupt onset of odynophagia in a patient taking a potentially injurious medication. There is usually sudden onset and progression of retrosternal pain over a period of 1–4 days, and the pain is often worsened with swallowing. Patients may report that they had the sensation of the pill sticking in their throat prior to the onset of the symptoms. The pain may remain mild, or may progress to the point that the patient is unable to swallow adequately enough to maintain their nutrition and hydration. Symptoms typically last for days to a few weeks.

Differential diagnosis

The main differential diagnosis for pill-induced esophageal injury is infectious esophagitis. If the pain is more burning in nature, GERD may be suspected as a possible diagnosis. If the retrosternal pain becomes constant, myocardial infarction may be considered. If the dysphagia is more slowly progressive, esophageal cancer may be a consideration.

Diagnosis

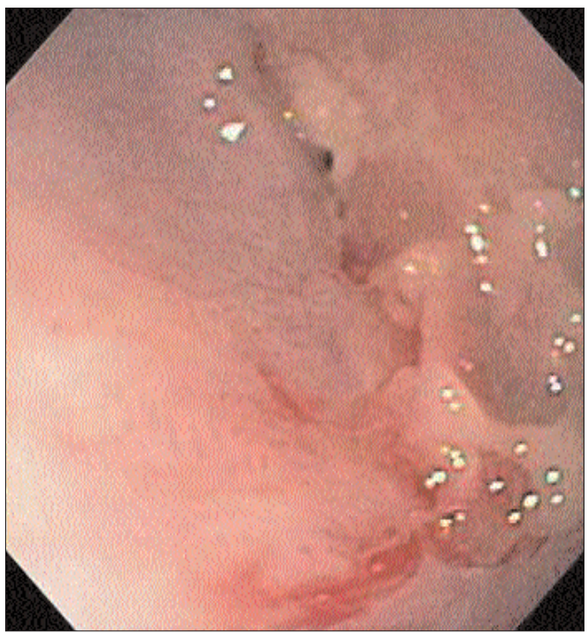
If history reveals pill-induced injury as an obvious etiology, diagnosis is aimed at assessing predisposing factors or complications, and finding alternative therapy. When symptoms are gradual, atypical, or persistent, or when the relation to use of a suspect pill is unclear, endoscopy is indicated. Endoscopy is also indicated in this setting for immunocompromised patients, or for those with hemorrhage. Barium esophagrams are lower in cost, and may show extrinsic compression, but initial endoscopy is superior for its ability to biopsy and provide an alternative diagnosis. On endoscopy (**4.92**), the physician will see discrete ulcers with normal surrounding mucosa. Biopsies will show acute inflammation.

Treatment

The initial treatment of pill-induced injury is to discontinue the offending agent.

Table 4.21 Medications causing esophageal mucosal injury

Non-steroidal anti-inflammatory drugs	Alendronate	Mexiletine
Aspirin	Tetracycline	Pancreatic enzyme capsules
Ferrous sulfate (especially sustained release form)	Doxycycline	Penicillamine
	Clindamycin	Percogesic
Potassium chloride	Ciprofloxacin	Phenobarbitone
Quinidine	Cloxacillin/dicloxacillin	Retinoic acid
Verapamil	Alprenolol	Theophylline (sustained release)
Captopril	Cellulose/fiber tablets	Zidovudine (AZT)
Glucocorticoids	Chloroquine	Lincomycin
Oral contraceptives	Cromolyn	Minocycline
Ascorbic acid (vitamin C)	Clozapine	Spiramycin
Phenytoin	Foscarnet	Emepronium bromide



4.92 An endoscopic view of pill-induced esophagitis. Injury is most often seen as a superficial ulcer, but can evolve to a deep ulcer with perforation. There can also be formation of a stricture. Patients should be counselled to remain upright after taking their medications, and to take all medications with copious amounts of fluids.

Anti-reflux therapy may be initiated to prevent an exacerbation of the injury by gastric refluxate. Severe pain may be symptomatically relieved by use of a topical anesthetic.

On rare occasions, for severe injury, patients may require intravenous hydration or nutrition while the injury is healing. Patients who develop strictures may require repeat dilations.

Patients with complications of pill-induced injury, such as esophageal perforation, mediastinitis, hemorrhage, and fiber-optic stricture, require further treatment of their specific condition.

Prevention

Patients should drink 4 oz of fluid with all medications, and should drink more if they are taking pills that commonly cause injury. Patients should remain upright for 10 minutes after taking medications, and up to 30 minutes after particularly injurious medications. Those who are bedridden, or have structural esophageal problems should avoid pills that are likely to cause esophageal injury.

Further reading

Kikendall JW (1991). Pill-induced esophageal injury. *Gastroenterol Clin North Am* **20**(4):835–846.

Infectious esophagitis

Introduction

Infectious esophagitis is a common condition, especially in certain high-risk groups. Commonly affected individuals include immunocompromised patients, such as transplant patients, chemotherapy patients, and patients infected with the human immunodeficiency virus (HIV).

Clinical presentation

The most common symptom of infectious esophagitis due to any of the possible organisms is odynophagia. In immunocompromised patients, other symptoms may present including heartburn, nausea, fever, and GI bleeding.

Etiology

The three most common causes of infectious esophagitis are cytomegalovirus (CMV), herpes simplex virus (HSV), and *Candida albicans*. In addition to the above common causes, other infections may be implicated, including varicella-zoster virus, Epstein-Barr virus, human papilloma virus, diptheria, various bacterial causes, syphilis, and the human immunodeficiency virus (HIV).

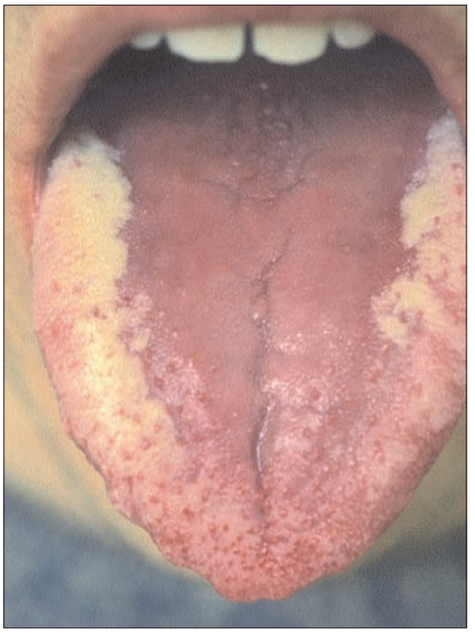
Candida albicans

This yeast is a normal component of oral flora, and is the most common cause of clinically relevant infectious esophagitis. In addition to the high risk groups listed above, other groups at increased risk of candida esophagitis include those with diabetes mellitus, alcoholics, those on glucocorticoid therapy, those on antibiotics, the elderly, patients with motility disorders, malnutrition, radiation therapy, and hypochlorhydrics.

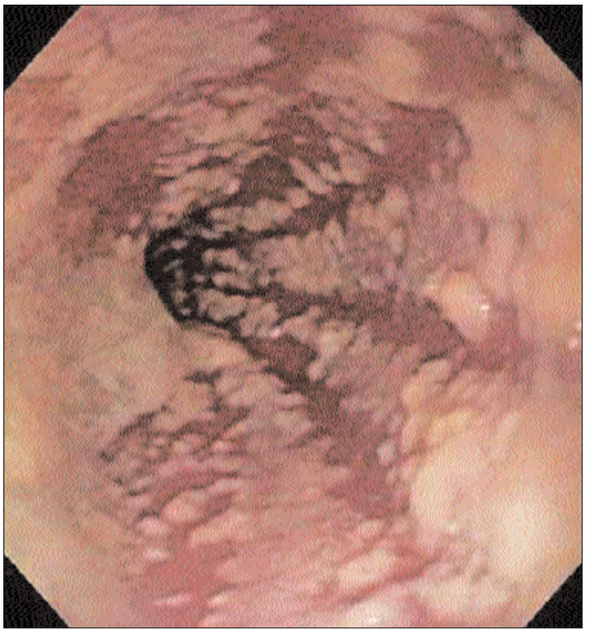
If oral thrush is seen on exam it assists in the diagnosis of candida esophagitis, as 75% of those with thrush and esophageal symptoms will have esophagitis (**4.93**).

Although empiric therapy is often instituted, diagnosis is made by endoscopy with biopsy and brushings (**4.94**). Microscopic examination of the brushings will reveal budding yeast and hyphae. There is a distinctive endoscopic appearance of candida esophagitis, with the esophageal mucosa being covered by adherent white-pale yellow plaques. The most common radiographic appearance of candida esophagitis is diffuse plaque-like lesions in a linear configuration. The plaques may become confluent with progression of disease, and resemble ulcers (**4.95**).

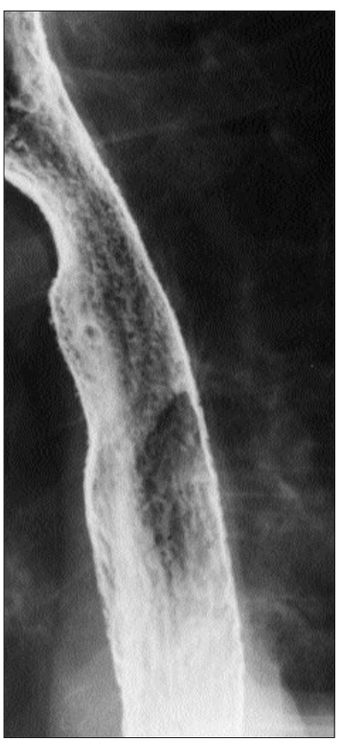
Treatment of candida esophagitis is with antifungal



4.93 A patient with oral thrush secondary to infection with *Candida albicans*. (Photo courtesy of the Department of Dermatology, Cleveland Clinic Foundation.)



4.94 Endoscopic view of esophagitis caused by *Candida albicans*. This is the most common form of infectious esophagitis in immunocompromised patients. Endoscopy classically shows white-pale yellow plaques that are adherent to the esophageal epithelium. Brushings will show hyphae along with budding yeast.



4.95 Esophagram of a patient with candida esophagitis. The diffuse, adherent plaques give the appearance of multiple long, linear ulcers in this study.

agents, usually fluconazole for 10–14 days (*Table 4.22*). If only mild immunocompromise is present, topical agents may be a reasonable alternative. Treatment in patients who are granulocytopenic requires amphotericin B to prevent progression to systemic fungal infection.

Cytomegalovirus (CMV)

CMV is the most common cause of esophageal ulcer in patients with acquired immunodeficiency syndrome (AIDS), and causes >50% of ulcers in this group. In CMV esophagitis, the virus infects the submucosal fibroblasts and endothelial cells, as opposed to the squamous epithelium. Due to a greater tendency for systemic infection with CMV, patients may present with more widespread GI symptoms, such as abdominal pain, nausea, and vomiting, in addition to odynophagia.

Endoscopy is necessary in order to confirm a tissue diagnosis, and biopsy specimens should be taken from the base of the CMV ulcers due to the subepithelial nature of the infection. The endoscopic appearance of CMV shows serpiginous erosions and ulcers, which often coalesce to form larger, deep ulcers (**4.96**). A barium study in CMV esophagitis will show well circumscribed ulcers, that can be vertical, linear, and deep, and are often serpiginous (**4.97**).

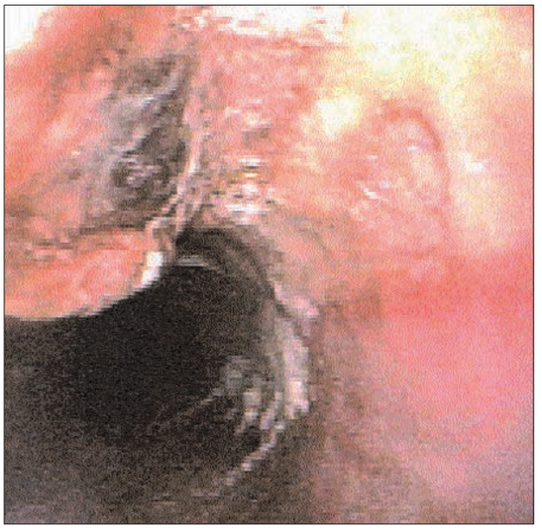
When examined under the microscope, biopsy specimens of CMV infected cells will show intranuclear and cytoplasmic inclusions, and a halo surrounding the nucleus (**4.98**). In addition to histologic examination, biopsy specimens should be sent for viral culture, which is more sensitive for the diagnosis.

Treatment options include both foscarnet and ganciclovir, and patients with CMV esophagitis often

Table 4.22 Treatment of infectious esophagitis

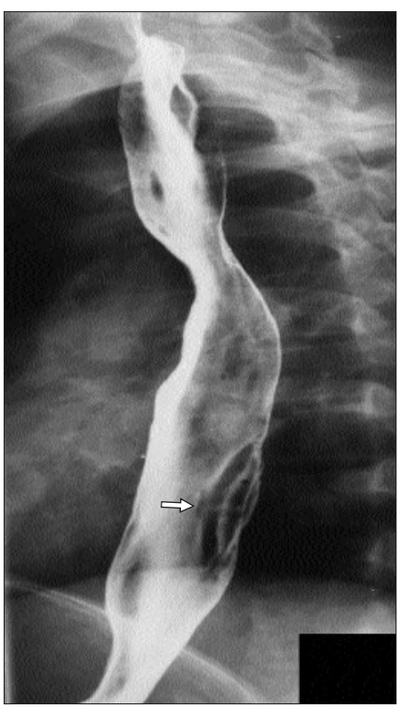
Organism	*Patient immune status*	*Treatment*
Cytomegalovirus		Ganciclovir 5 mg/kg iv q12h for 14–21 days. Follow with maintenance therapy 90–120 mg/kg/day *Or* foscarnet 90 mg/kg iv q12h for 12–21 days. Follow with maintenance therapy 90–120 mg/kg/day
Herpes simplex virus		Acyclovir 250 mg/m^2 iv q8h for 7–10 days *Or* foscarnet 90 mg/kg iv q12h for 14–21 days *Or* famciclovir 500 mg po bid for 14 days
Varicella-zoster virus		Acyclovir 250 mg/m^2 iv q8h for 7–10 days *Or* foscarnet 90 mg/kg iv q12h for 14–21 days *Or* famciclovir 500 mg po bid for 14 days
Candida albicans	Immunocompetent	Nystatin suspension 1–3 x 10^6 units po qid for 7 days *Or* clotrimazole troche 10 mg dissolved in mouth 5 times daily for 7 days
	Immunosuppressed	Fluconazole 100 mg po qd for 14 days *Or* ketoconazole 200 mg po qd for 14 days *Or* clotrimazole troche 100 mg dissolved in mouth tid for 14 days *Or* fluconazole 100–200 mg iv qd
	Immunosuppressed and granulocytopenic	Amphotericin B 0.5 mg/kg/day iv to a cumulative dose of 1.5–2.0g over 6–12 weeks

bid: twice daily; iv: intravenous; po: by mouth; qd: once daily; qid: three times daily

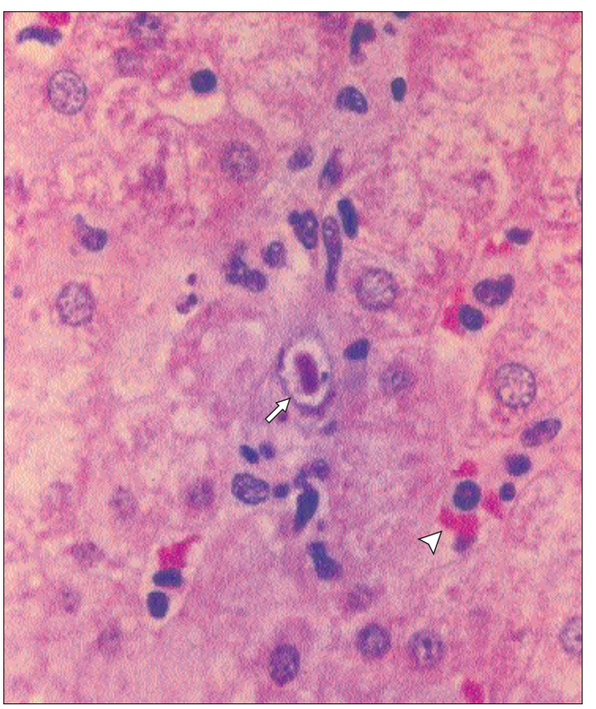


require a maintenance dose after an initial period of therapy of 2–3 weeks. Most patients who are immunocompromised will require a period of maintenance therapy after the initial 2-week treatment course (*Table 4.22*). In patients with AIDS, an ophthalmic exam should be pursued in patients with CMV esophagitis to rule out a concomitant CMV retinitis.

4.96 Endoscopic view of CMV esophagitis. Patients present with odynophagia, but may also complain of more systemic GI symptoms. Findings include erosions and ulcers that are classically serpiginous in nature. These ulcers can coalesce, forming larger, deep ulcers.



4.97 CMV esophagitis on a barium swallow esophagram can be differentiated from other infectious etiologies by the presence of large, deep, serpiginous ulcers (arrow).



4.98 Histology from an esophageal biopsy in a patient with CMV esophagitis. Diagnosis is made by demonstration of cytoplasmic and intranuclear inclusions (arrowhead), as well as the nucleus of CMV infected cells being surrounded by a halo (arrow).

Herpes simplex virus (HSV)

HSV is the most common viral cause of esophagitis. HSV esophagitis most often occurs secondary to reactivation of a latent infection, and it can occur in both immunocompromised and competent hosts. As with other causes of infectious esophagitis, diagnosis is made by endoscopy. Endoscopic findings will show characteristic esophageal vesicles, which eventually rupture to form ulcers with raised edges. Barium esophagram findings include focal small ulcerations with a normal mucosa.

HSV infects the epithelial cells, therefore biopsy specimens must be taken from the margins of the ulcers, where there is squamous epithelium present (**4.99**). Histologic examination of biopsy specimens shows multinucleated giant cells, ground glass nuclei, and Cowdry's type A intranuclear inclusion bodies. As with CMV, viral culture is more sensitive and should also be performed (**4.100**).

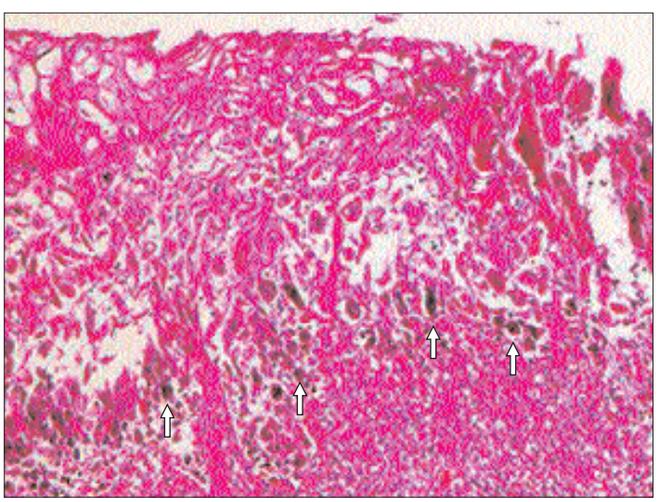
Treatment of HSV esophagitis is with intravenous acyclovir until the patient can tolerate oral therapy (*Table 4.22*). The total duration of therapy is 7–10 days. Immunocompetent patients will experience spontaneous resolution of the esophagitis in 2 weeks without any therapy.

Summary

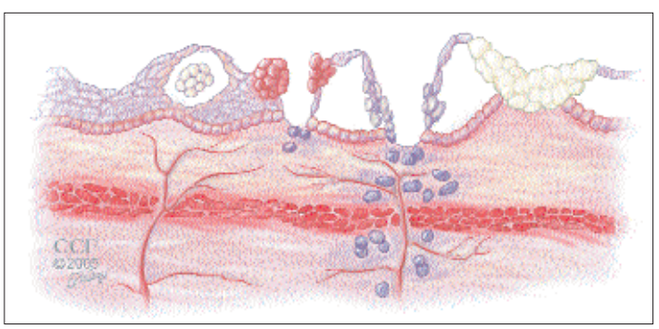
Symptoms: odynophagia +/- heartburn, nausea, fever, GI bleeding (especially in immunocompromised patients).
Etiology: CMV is most common cause of ulcers.
HSV: reactivation of latent infection can occur.
Candida albicans: yeast, often with oral infection.
Diagnosis: endoscopy and histology of biopsy specimens.
Treatment: CMV – foscarnet and ganciclovir.
HSV – acyclovir.
C. albicans – fluconazole.

Further reading

Baehr PH, McDonald GB (1994). Esophageal infections: risk factors, presentation, diagnosis, and treatment. *Gastroenterol* **106**(2):509–532.
Castell DO, Richter JE (eds) (2003) *The Esophagus*, 4th edn. Lippincott, Williams, and Wilkins, Philadelphia.
Sutton FM, Graham DY, Goodgame RW (1994). Infectious esophagitis. *Gastrointest Endosc Clin N Am* **4**(4):713–729.



4.99 Histology in HSV esophagitis. Typical findings are multinucleated giant cells (arrows), along with ground glass intranuclear inclusion bodies. Viral culture can also be obtained in order to increase the sensitivity of the diagnosis.



4.100 Schematic diagram to show biopsy sites. Different organisms that cause infectious esophagitis infect different regions of the esophageal wall. For this reason, biopsy specimens must be taken from different areas of the lesions in order to increase the likelihood of isolating the organism. *Candida albicans* can be recovered from the surface of ulcers and plaques, and either brushings or biopsies may be used. CMV infection is subepithelial, and the ulcer base should be sampled. HSV is an infection of epithelial cells, and biopsy of the ulcer margins will yield optimal results.

Caustic injury

Epidemiology

Most caustic ingestion injuries occur in children younger than 3 years of age, and there have even been reports of caustic injuries to neonates. In the US, there are approximately 5,000 accidental caustic injuries each year, with an increasing trend. Data from Denmark have found an incidence of pediatric ingestion of 34/100,000, with esophageal burns in 16/100,000. The most common offending agents are lye and drain cleaners, dishwasher detergent, denture cleanser, and batteries. In adults, most injuries are associated with suicide attempts. In adults in Denmark, an incidence of ingestion of 1/100,000 was reported, with 61% being suicide attempts.

Pathophysiology

Alkali injury (or lye injury) follows a specific sequence of injury. There is initial submucosal edema and congestion, followed by inflammation with vessel thrombosis. The superficial layers then slough, followed by necrosis of the muscularis, and organizing and fibrosis of the deep layers, with delayed re-epithelialization. Superficial burns often heal normally, burns involving the muscularis show delayed healing with fibrosis, and circumferential burns may lead to strictures. Stricture formation may take up to 4 weeks following the initial insult. If there is transmural liquefactive necrosis, esophageal perforation may occur.

Injury is worse with a more alkaline solution, with the most severe injury being cause by substances with pH of 14. Acid-induced injuries are less common than alkaline, and the mechanism involves coagulation necrosis, and the formation of a protective eschar.

Clinical presentation

Injuries can result in a range of findings, from mild oral burns or sore throat, to rapidly progressive life-threatening complications. Establishing the timing and nature of ingestion is an important part of the history, and it is often necessary to obtain history from surrogates. There is a poor correlation between the severity of symptoms and the extent of the esophageal injury. Oropharyngeal symptoms include pain, odynophagia, ulceration, drooling, and tongue edema. Stridor, aphonia, and hoarseness may be signs of laryngeal injury. Esophageal insult leads to dysphagia, odynophagia, chest pain, and back pain. Physicians must be alert for signs of serious injury (airway obstruction, aspiration, and perforation), including agitation, cyanosis, hypoxia, fever, leukocytosis, tachycardia, and shock. Following initial stabilization, injuries may continue to progress to esophageal stricture.

Table 4.23 Classification of caustic injury

Grade	*Endoscopic findings*
0	Normal
1	Edema and erythema of esophageal mucosa
2A	Superficial ulcers, exudates, and bleeding
2B	Deep focal or circumferential ulcers
3A	Focal necrosis; deep ulcers with gray, black, or brown discoloration
3B	Extensive necrosis
4	Perforation

Diagnosis

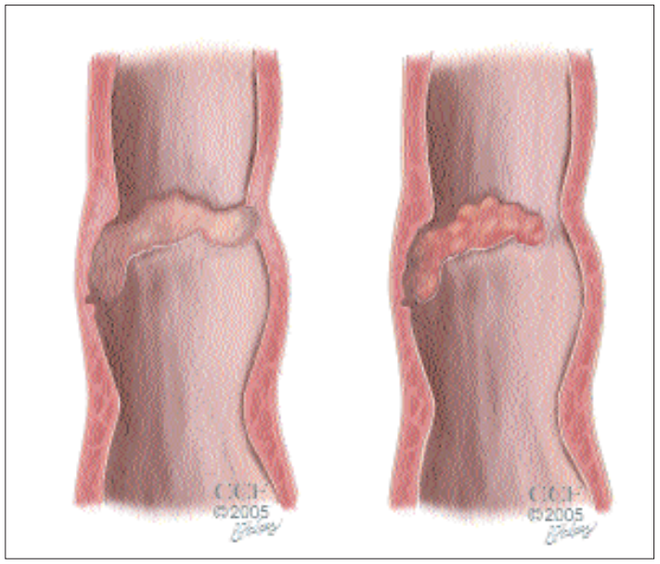
Fiberoptic laryngoscopy is an easy and safe way to examine the larynx and pharynx in most settings. Endoscopy is the most valuable tool in evaluating caustic injury, but the physician must be careful to avoid perforation (*Table 4.23*, **4.101**). In this setting, endoscopy should be used only for diagnostic purposes, and it should be stopped before passing the scope through any area of severe or circumferential burn. The endoscopy should be performed within 48 hours of the ingestion, while the wall retains its strength.

A chest radiograph is the most important radiological study, as it can reveal pulmonary infiltrates and signs of perforation, such as subcutaneous emphysema, pneumothorax, and pneumomediastinum. Contrast swallowing studies can be used to rule out perforation, but are more important in planning future evaluation and treatment after the initial insult has resolved (approximately 3 weeks after the injury).

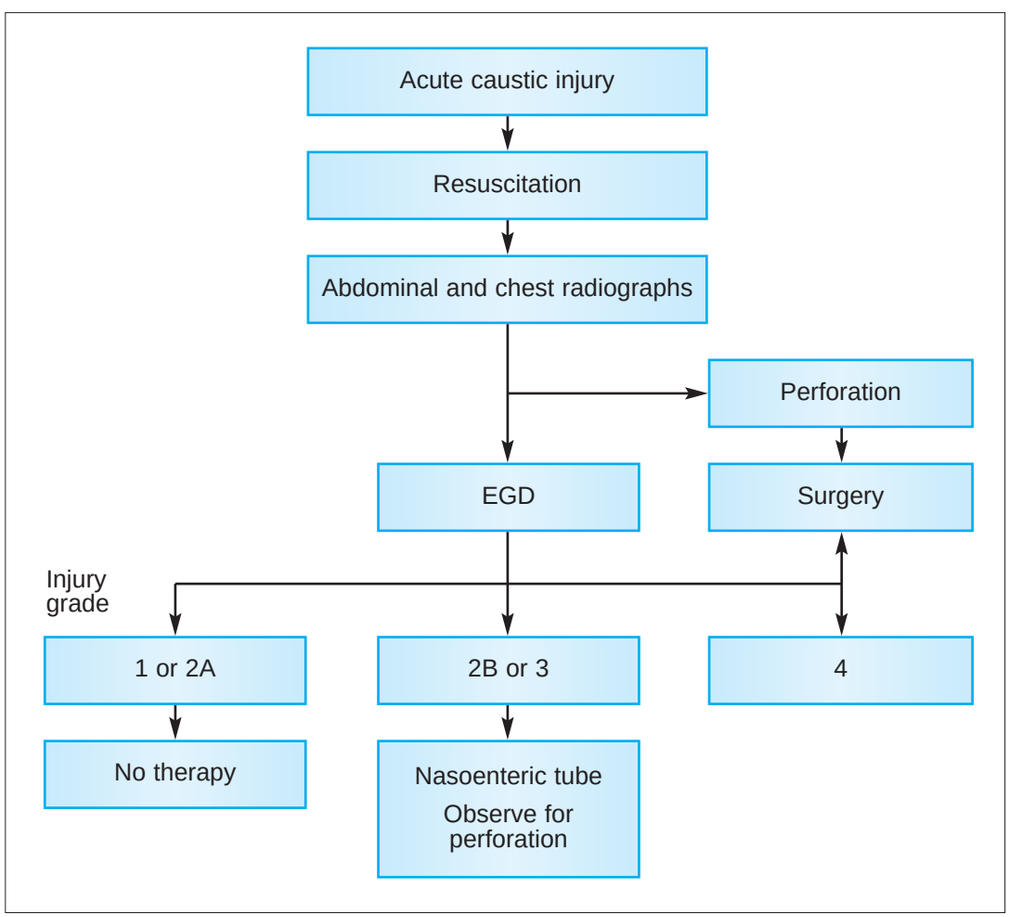
Treatment

Figure **4.102** presents treatment algorithm for caustic injury. Initial treatment of caustic injury involves basic resuscitation with intravenous fluids, obtaining intravenous access, giving prophylactic antibiotics, and providing airway support as warranted. Endoscopy should take place within 24–48 hours after the patient is stabilized. Patients who can swallow can start a liquid diet 48 hours after being stabilized, but those who cannot swallow may require total parenteral nutrition (TPN) or nasogastric tube feeding (with endoscopic guidance).

Steroids have been studied to prevent the development of esophageal stricture, especially in second and third degree burns. If used, steroids should always be given with antibiotics, and they should be given early and in high doses (2 mg/kg/day). Stenting may also be used in order to avoid stricture formation. Dilation is currently used for the treatment of secondary esophageal strictures (**4.103**), using the technique of antegrade dilation. If there are multiple or extensive segments, retrograde dilation may be considered.



4.101 Schematic diagram showing the findings that can be expected with the different grades of caustic esophageal injury (grade 2A left, grade 2B right).



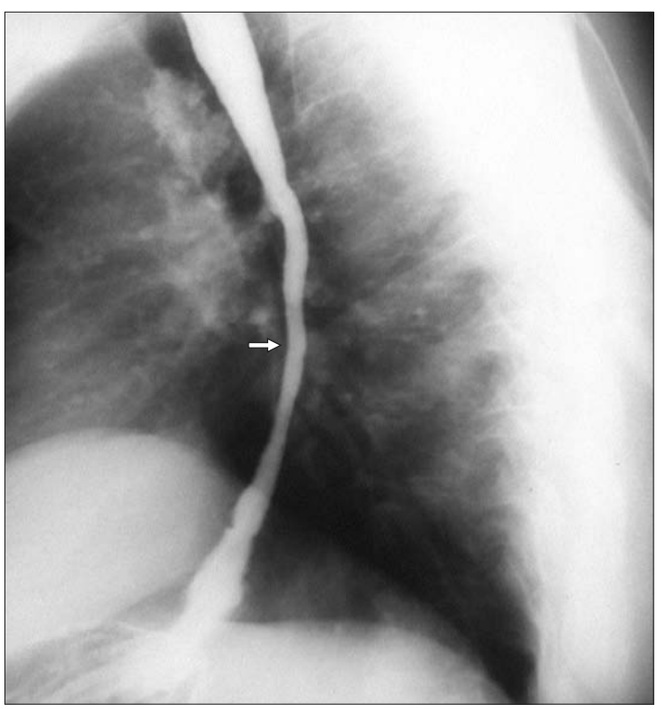
4.102 Treatment algorithm for caustic injury. Due to the possibility of airway compromise and esophageal perforation, caustic injuries must be aggressively treated. Initial treatment includes resuscitation, including intravenous fluids and intubation if there is airway involvement. Endoscopy should be done in the first 24–48 hours, to help establish prognosis and guide therapy. Those with grade 1 or 2A usually do well, but strictures develop in 70–100% of those with 2B or 3A injuries. Patients with grade 3B have a 65% early mortality rate, and often require esophageal resection. (EGD: esophagogastro-duodenoscopy.)

Perforation is a concern with dilation, and treatments should be gentle with an aim of slow improvement.

Surgery is indicated for the emergency treatment of esophageal necrosis and perforation. This type of injury is life-threatening, as it leads to mediastinitis, sepsis, and shock. Surgery may also be used for delayed reconstruction, following an emergency resection or following failed conservative therapy.

Prognosis

Patients with grade 1 and 2A injury have an excellent prognosis, without acute morbidity or chronic stricture formation. Grade 2B/3A injuries develop strictures in 70–100% of cases. Grade 3B is associated with an early mortality rate of 65%, and a high rate of esophageal resection. There is an association with the development of SCC of the esophagus following caustic injury, with a reported 1,000-fold increase in risk.

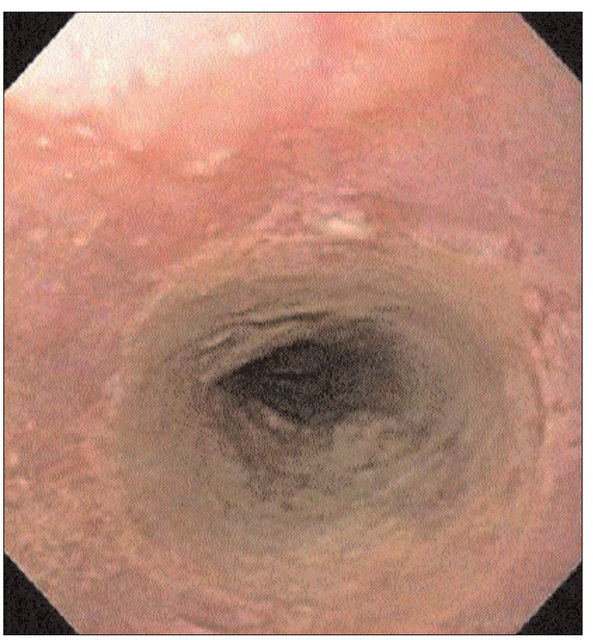


4.103 Esophagram showing a stricture formed after ingestion of a caustic substance. Caustic strictures usually require esophageal dilation, and are often longer and narrower than benign strictures. There is a high rate of complications associated with dilation of esophageal strictures, and up to 50% may require surgery.

Upper gastrointestinal bleeding

Epidemiology

Upper GI bleeding is a common indication for endoscopic examination, and this is often performed on an emergency basis. Upper GI bleeding may be secondary to pathology in any area of the GI tract from the mouth to the ligament of Treitz, and there are several conditions involving the esophagus and proximal stomach which are important causes. The common esophageal causes of bleeding are esophageal varices, reflux esophagitis (**4.104**), and ulcers (NSAID-induced or infectious), with less common causes being Mallory–Weiss tear, Cameron's ulcer (**4.105**), Dieulafoy's lesion, vascular malformations, aortoenteric fistulae, and neoplasms. Patients with upper GI bleeding are at risk of cardiac, pulmonary, renal, and neurological complications.



4.104 Esophagitis and esophageal ulceration are part of the spectrum of disease most often located near the SCJ, and most commonly secondary to acid reflux injury of the esophageal mucosa. Other causes of esophagitis include infection, medications, and radiation. Classification systems, such as the LA Classification, help to assess prognosis and guide therapy, as esophagitis and ulceration can be a cause of upper GI bleeding if severe.

Clinical presentation

Patients may present with signs of hemodynamic instability, such as fatigue, palpitations, chest pain, syncope, and dyspnea. Other presenting symptoms may include nausea, pallor, and diaphoresis. Orthostatic hypotension occurs after approximately 20% blood loss, with pronounced tachycardia and hypotension presenting after 25–40% loss of blood volume. Patients with upper GI bleeding usually present with signs of hemorrhage, including melena and hematemesis, and may present with hematochezia if the rate of blood loss is brisk.

Diagnosis

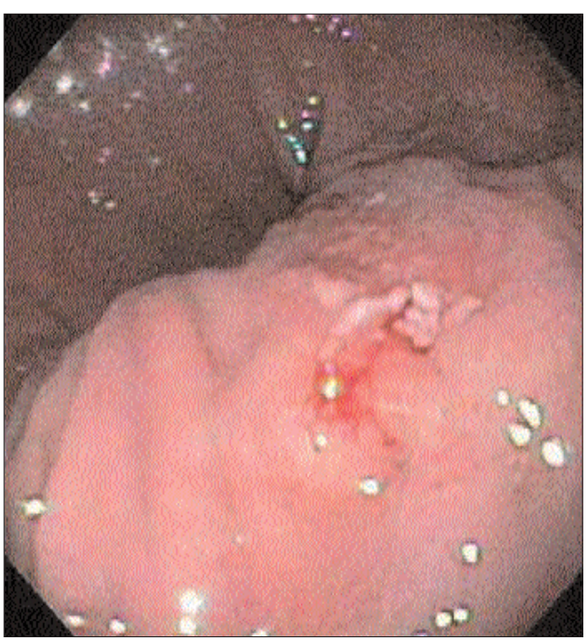
Nasogastric aspiration should be performed, and may show 'coffee ground' material if the bleeding is from an upper source, or frank blood if the bleeding is continual. A saline lavage should be started if frank blood or coffee ground material is found. Endoscopy is the diagnostic gold standard, and offers therapeutic options as well. If nasogastric aspiration is clear, endoscopy can be performed on an elective basis, but the presence of frank blood or coffee ground material requires emergency endoscopic evaluation.

Treatment

The goals of treating GI bleeding are hemodynamic support, minimization of complications, and providing effective therapy to control the bleeding. Initial resuscitation should be with intravenous fluids and blood products, and airway protection is essential. After hemodynamic stability is achieved, the patient with signs of continued bleeding should undergo upper endoscopy to localize the site of bleeding, and to identify possible therapeutic options (sclerotherapy, epinepherine injection, or electrocautery).

Further reading

Huang CS, Lichtenstein DR (2003). Nonvariceal upper gastrointestinal bleeding. *Gastroenterol Clin North Am* **32**(4):1053–1078.



4.105 The endoscopic appearance of a Cameron's lesion. This ulcer appears as a linear gastric erosion in a hiatal hernia. This is a diagnosis to be considered in the evaluation of occult GI blood loss.

Varices

Epidemiology

Esophageal varices (**4.106, 4.107**) are enlarged portal-systemic collateral veins that form as a consequence of increased portal pressure secondary to portal hypertension.

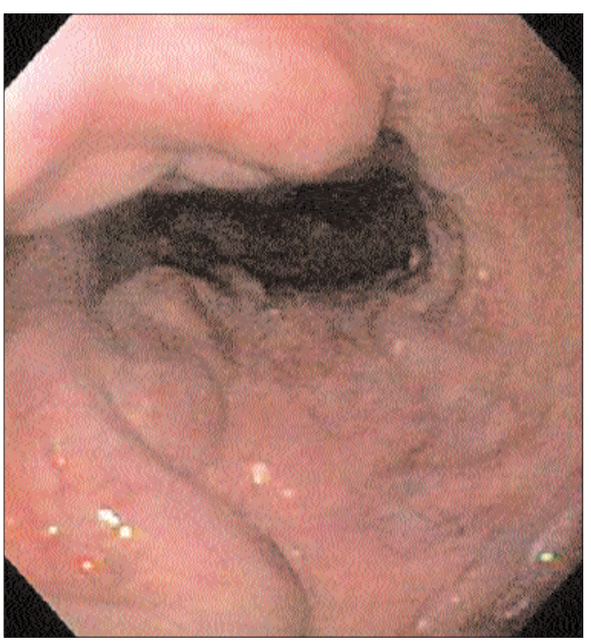
While varices develop in most patients with portal hypertension, bleeding occurs in only one-third of patients with varices. An episode of variceal hemorrhage carries a 30–50% risk of death. This is the most common cause of bleeding in patients with cirrhosis or portal hypertension. *Table 4.24* shows the grading system used to classify esophageal varices, based on the endoscopic appearance of the veins. This classification is important as it gives information on prognosis and likelihood of imminent variceal bleed. Classification also helps to guide therapy and helps the physician decide when banding is appropriate.

Clinical presentation

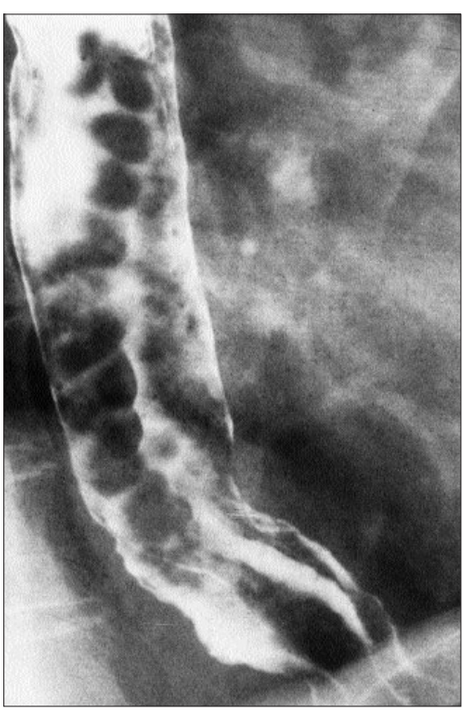
Patients may present with other stigmata of chronic liver disease, such as spider angiomata, gynecomastia, testicular atrophy, palmar erythema, jaundice, ascites, or hepatosplenomegaly which may assist the physician in the

Table 4.24 Classification of esophageal varices

Grade	*Endoscopic appearance*
I	Dilated veins (<5 mm) still at the level of the surrounding tissue
II	Dilated veins (>5 mm), straight, protruding into the esophageal lumen without obstruction
III	Large, winding, and tense veins with considerable obstruction of the esophageal lumen
IV	Obstruction of the esophageal lumen nearly complete, with signs of danger of impending hemorrhage (cherry red spots)



4.106 Endoscopy showing esophageal varices of moderate size.



4.107 Barium esophagram showing esophageal varices.

diagnosis. Variceal bleeding is usually painless and massive, and is associated with other signs of GI bleeding, such as tachycardia and shock. Risk factors for bleeding in individuals with varices include the degree of portal hypertension and the size of the varices. Varices are extremely unlikely to bleed if portal pressure is <12 mmHg.

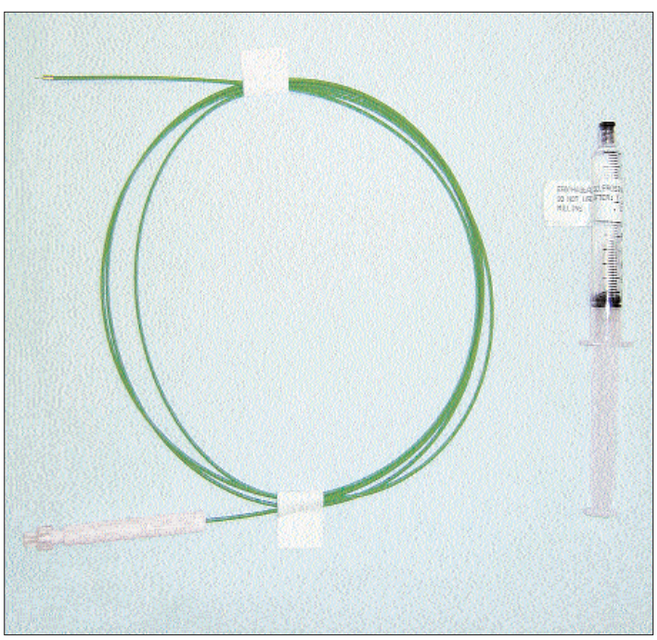
Diagnosis

On upper endoscopy, varices may be oozing blood, or may show a 'red wale' sign or a cherry red spot, signifying a recent bleed.

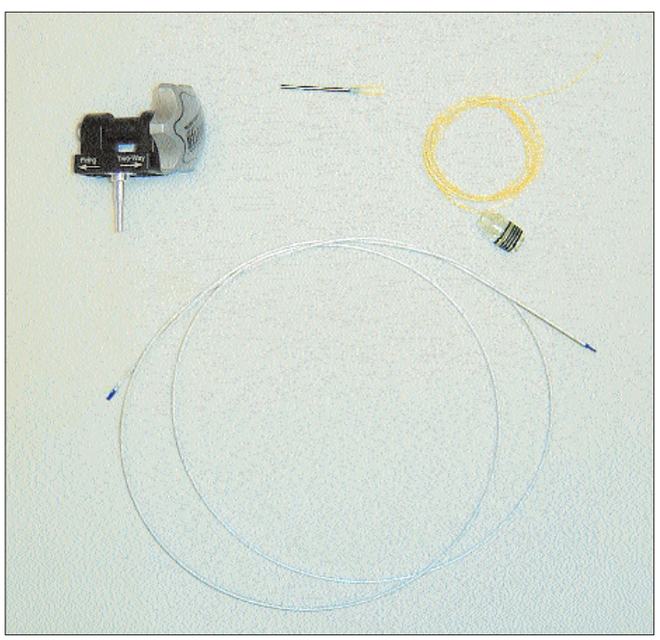
Treatment

An acute variceal bleed resolves spontaneously in 50% of patients. Patients with variceal bleeding often have concomitant coagulopathies, and clotting factors should be replaced at the initial resuscitation. Variceal bleeding often requires endoscopic intervention to control, although bleeding may also respond to intravenous octreotide or vasopressin as an initial adjunctive therapy.

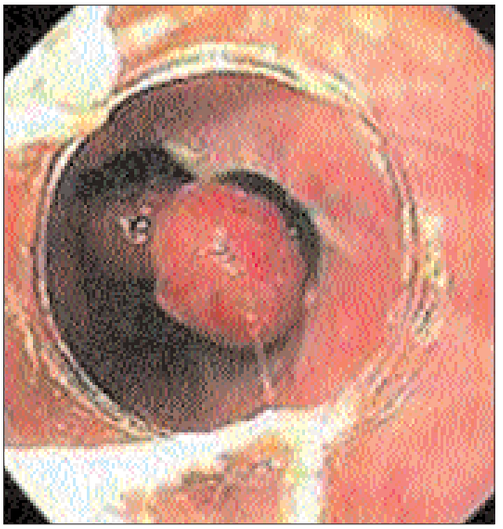
Sclerotherapy (**4.108**) is effective for variceal bleeding, and is currently the first line treatment. Banding (**4.109**, **4.110**) is also now being used to control bleeding, and this



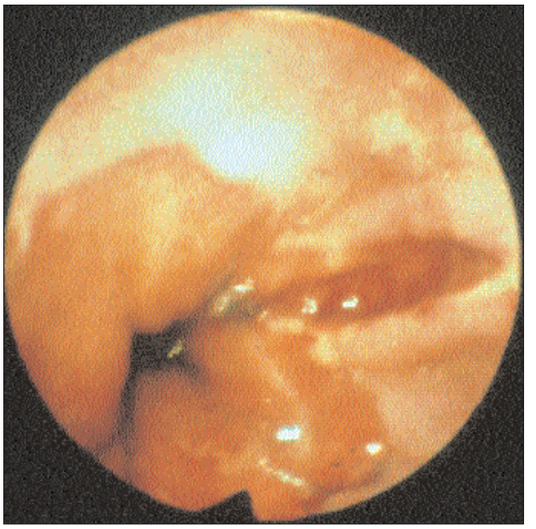
4.108 Tools used for endoscopic sclerotherapy. This treatment is used to achieve hemostasis in the setting of bleeding esophageal varices. The long, flexible sclerotherapy needle is passed through one of the ports of the endoscope. The needle is unsheathed, advanced, and the sclerosing solution is injected into the vein and/or the surrounding area. Sclerosants that are commonly used to control hemorrhage include sodium tetradecyl sulfate and ethanolamine.



4.109 Equipment used for band ligation. The barrel is placed at the end of the endoscope, and the scope is inserted. The varix is identified, and the barrel is positioned with the varix entering the barrel. The rubber band is then released, and the scope is withdrawn. Current kits allow the deployment of multiple bands without changing equipment.



4.110 Endoscopic view of esophageal varices after being banded using the band ligator instrument. The barrel can be seen at the end of the endoscope, and a varix, with a blue rubber band around it, is seen through the barrel. After banding, the varices typically slough off in 2–3 days following treatment.



4.111 A Mallory-Weiss lesion is a tear in the mucous membrane that occurs at the junction of the esophagus and the stomach. It is caused by prolonged vomiting or coughing, and can lead to massive hematemesis and hematochezia. A minor tear can heal on its own, but a more severe tear may require endoscopic intervention and blood transfusions.

method carries a lower risk of stricture formation and systemic toxicity. If local therapy does not control the bleeding, balloon tamponade with a Blakemore tube may be used. This tube provides temporary relief by direct compression of the bleeding vessel, but definitive therapy must still be performed. Other considerations include avoidance of subsequent bleeding, which may be addressed with beta-blocker therapy or with placement of a transhepatic intrajugular portosystemic shunt (TIPS).

Complications and further management

Following an acute bleed, patients are at risk of re-bleeding for up to 6 weeks, with the greatest risk being during the first 48 hours after their initial bleed. The risk of re-bleeding at 1 year is approximately 70%, and prevention of subsequent hemorrhage is essential. Screening endoscopy should be routinely performed, with a frequency determined by bleeding history and number and size of varices. Prophylactic banding is often done on a scheduled basis. Early re-bleeding is more common in patients with renal failure, over 60 years old, and those with a severe hemorrhage. Late re-bleeding is common in patients with renal failure, large varices, severe liver disease, alcohol abuse, and hepatocellular carcinoma.

Mallory–Weiss tear

A Mallory–Weiss tear is an esophagogastric mucosal tear, which occurs in the region of the GEJ, with an incidence of 4/100,000 (**4.111**). Patients often report a history of retching, or non-bloody vomiting, which was followed by hematemesis, although this history is not necessary. Prolonged coughing may also lead to this type of tear. They usually stop bleeding spontaneously and recurrences are uncommon.

Gastroenterology Society Guidelines

Achalasia

ACG Guidelines: Vaezi MF, Richter JE (1999). Diagnosis and management of achalasia. *American Journal of Gastroenterology* **94**:3406–3412.

Ambulatory 24-Hour esophageal pH monitoring

AGA (1996) American Gastroenterological Association medical position statement: guidelines on the use of esophageal pH recording. *Gastroenterology* **110**:1981–1996.

Barrett's esophagus

ACG Guidelines: Sampliner RE (2002). Updated guidelines for the diagnosis, surveillance, and therapy of Barrett's esophagus. *American Journal of Gastroenterology* **97**:1888–1895.

Esophageal manometry

Pandolfino JE, Kahrilas PJ (2005). American Gastroenterological Association medical position statement: Clinical use of esophageal manometry. *Gastroenterology* **128**: 207–208.

Pandolfino JE, Kahrilas PJ (2005). AGA Technical Review on the Clinical Use of Esophageal Manometry, *Gastroenterology* **128**:209–224.

Foreign body

ASGE Guidelines: (2002). Guideline for the management of ingested foreign bodies. *Gastrointestinal Endoscopy* **55**:802–806.

Gastroesophageal reflux disease

ACG Guidelines: DeVault KR, Castell DO (2005). Updated guidelines for the diagnosis and treatment of gastroesophageal reflux disease. *American Journal of Gastroenterology* **100**(1):190–200.

Oropharyngeal dysphagia

AGE (1999) AGA Technical Review on the Management of Oropharyngeal Dysphagia. *Gastroenterology* **116**:455–478.

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Note: Page numbers in **bold** refer to major references to the topics; those in *italic* refer to tables or boxed material