Dysphagia is the perception that there is an impediment to the normal passage of swallowed material. Odynophagia is the sensation of pain on swallowing. Dysphagia can be caused by a number of disorders, benign and malignant, that involve either the oropharynx or the esophagus. The purpose of this report is to develop a rational approach to the treatment of adult patients who have dysphagia caused by benign disorders of the distal esophagus. The report provides a critical review of pertinent literature on which to base this approach. Patient care strategies that emerge from the review are summarized in the accompanying American Gastroenterological Association (AGA) Medical Position Statement. For this report, the distal esophagus is defined, somewhat arbitrarily, as the segment of esophagus that extends from the level of the aortic arch to the gastric cardia. The muscularis propria in this esophageal segment is composed predominantly of smooth muscle. Thus the distal esophagus is susceptible to three general categories of disease processes that can cause dysphagia (Table 1): (1) mucosal (intrinsic) diseases that narrow the lumen of the esophagus through inflammation, fibrosis, or neoplasia; (2) mediastinal (extrinsic) diseases that encase and obstruct the esophagus by direct invasion or through lymph node enlargement; and (3) diseases affecting the esophageal smooth muscle and its innervation that disrupt peristalsis, interfere with lower esophageal sphincter relaxation, or both. This review considers clinical reports on these disorders that have been published in peer-reviewed journals since 1966. The reports were identified primarily by a MEDLINE search using the following MeSH terms: deglutition disorders, esophageal dysphagia, esophageal stenosis, esophageal motility disorders, and esophageal achalasia. Clinical studies published only in abstract form are not included. However, even the peer-reviewed literature on the treatment of patients with dysphagia due to benign esophageal disorders consists predominantly of retrospective, uncontrolled studies of small, heterogeneous patient populations who were followed up only briefly. The conclusions that can be drawn from these reports often are limited, and the serious deficiencies in study design and execution often preclude meaningful meta-analyses. This report highlights the strengths and weaknesses of the most relevant studies.

Diagnosis

History

It has been estimated that the cause of dysphagia can be determined with an accuracy of approximately 80% on the basis of a careful history alone. Some key elements of the history for patients with dysphagia are highlighted below.

Is the dysphagia for solid foods, liquids, or both? Mucosal and mediastinal diseases that involve the distal esophagus cause dysphagia by narrowing the esophageal lumen. Such narrowings usually pose little barrier to the passage of liquids, and consequently these diseases characteristically cause dysphagia only for solid foods. In contrast, diseases that disrupt peristalsis by affecting the smooth muscle and its innervation may cause dysphagia for both solids and liquids. In achalasia, persistent contraction of the lower esophageal sphincter (LES) causes complete mechanical obstruction of the esophagus that persists until either the sphincter relaxes or the hydrostatic pressure of the retained material exceeds the pressure generated by the sphincter muscle. Even in the absence of peristalsis, gravity often can empty the esophagus of liquid material effectively if the LES is relaxed. Therefore, patients who have disordered peristalsis and profoundly hypotensive LESs often experience no dysphagia or dysphagia only for solid foods.

Where does the patient perceive that ingested material sticks? Patients with esophageal obstruction often perceive that swallowed material sticks at a point that is either above or at the level of the lesion causing the obstruction. In a recent radiographic study of 12 patients with lower esophageal mucosal rings that impeded the passage of a marshmallow bolus, the perceived level of the obstruction was localized to the neck in 7, to the sternal angle in 2, to the midsternum in 2, and to the lower chest in 1. It is uncommon for patients to perceive
that swallowed material sticks at a level substantially below that of the obstructing lesion. In a recent endoscopic study of 139 patients with dysphagia caused by esophageal strictures, the patients' perception of the level of obstruction agreed with the endoscopists' localization of the stricture with an accuracy of ±4 cm in 74% of cases. Eighteen percent of patients with strictures of the distal esophagus localized obstruction to the proximal esophagus, whereas only 5% of patients with proximal esophageal strictures perceived obstruction in the distal esophagus. Thus, the perception that a swallowed bolus sticks above the suprasternal notch is of little value for localization of the obstruction because this sensation could be caused by a lesion located anywhere from the pharynx to the most distal esophagus. However, if the patient localizes the obstruction to a point below the suprasternal notch, the chances are excellent that the dysphagia is caused by a disorder that involves the distal esophagus.

Are there symptoms of oropharyngeal dysfunction? Dysphagia caused by oropharyngeal dysfunction is the subject of another AGA Technical Review and is not discussed in detail in this report. Oropharyngeal dysphagia often results from diseases that affect the striated muscles of the oropharynx or their innervation (e.g., muscular dystrophies, cerebrovascular accidents). Patients with these neuromuscular diseases may experience difficulty in initiating swallowing, and swallowing may be accompanied by nasopharyngeal regurgitation, pulmonary aspiration, and a sensation that residual material remains in the pharynx. If any of these symptoms are prominent, evaluation for oropharyngeal dysfunction may precede tests for esophageal disorders.

Is the dysphagia intermittent or progressive? Patients who have lower esophageal mucosal (Schatzki) rings typically complain of dysphagia that is intermittent and nonprogressive. These patients characteristically experience discrete, short-lived episodes of dysphagia for solid foods, often during a meal in a restaurant (hence the term “steak-house syndrome”) or at a social function. Episodes may be separated by weeks, months, or years, and the patient typically experiences no swallowing difficulty between discrete episodes. In contrast, esophageal strictures usually cause dysphagia that is progressive in frequency and severity. With benign strictures, the progression is typically slow and insidious (over a period of months to years), and weight loss is minimal. Malignant esophageal strictures usually cause dysphagia that progresses rapidly (over a period of weeks to months), and weight loss may be profound.

Is there a history of chronic heartburn? Heartburn is the cardinal symptom of gastroesophageal reflux disease (GERD), and a history of chronic heartburn supports the possibility that dysphagia may be caused by a peptic esophageal stricture. However, the history of pyrosis should be interpreted with caution because the sensation of burning, substernal chest discomfort is not specific for GERD. For example, patients with achalasia frequently complain of a heartburn sensation that may be caused by abnormal motor activity as well as by esophageal acid exposure. Conversely, many patients who develop peptic strictures as a result of GERD have no antecedent history of heartburn. In one study of 154 patients with benign (mostly peptic) esophageal strictures, for example, only 75% of the patients related a history of chronic heartburn. Finally, approximately two thirds of patients with dysphagia caused by adenocarcinoma in Barrett’s esophagus have a history of longstanding heartburn. Although the history of heartburn provides useful clinical information, conclusions regarding the etiology of dysphagia in an individual patient should not be based primarily on the presence or absence of heartburn.

Is the patient taking medications likely to cause pill esophagitis? A number of medications taken in pill form are potentially caustic to the esophagus and can cause deep ulceration with stricture formation if they have prolonged contact with the esophageal mucosa. Although the list of medications that can cause pill esophagitis is long, most cases reported in the United States have been caused by antibiotics (e.g., doxycycline), potassium chloride preparations, nonsteroidal anti-inflammatory drugs (NSAIDs), or quinidine. Recently, a number of cases of pill esophagitis have been attributed to alendronate sodium, an agent used in the treatment of osteoporosis in postmenopausal women.

Is there a history of collagen-vascular disease? Collagen-vascular diseases such as scleroderma, rheuma-
toid arthritis, and systemic lupus erythematosus can affect the distal esophagus and cause disordered motility. Esophageal dysmotility in these disorders is often, but not invariably, associated with Raynaud's phenomenon. In scleroderma and related collagen-vascular disorders, fibrosis and vascular obliteration in gut smooth muscle cause poor esophageal contractility and weakness of the LES that predisposes to severe GERD. In addition, patients with collagen-vascular disease are often treated with medications such as NSAIDs that can cause pill esophagitis. Consequently, dysphagia associated with collagen-vascular disease may be the result of disordered esophageal motility, severe GERD, pill esophagitis, or some combination of these abnormalities. Although it seems logical to assume that pill esophagitis should occur more frequently in patients with esophageal motor disorders, there are few published data to support this notion.

Is the patient immunosuppressed? Infectious esophagitis occurs frequently in patients whose immune system has been compromised severely by infection with the human immunodeficiency virus, by advanced malignancy, or by organ transplantation with the administration of potent immunosuppressive drugs. It has been estimated that 30%–40% of patients who have the acquired immunodefiency syndrome develop symptoms of esophageal disease. Most esophageal infections are caused by one or a combination of only three organisms: candida, cytomegalovirus, and herpes simplex virus. Odynophagia is usually the predominant symptom for patients with infectious esophagitis, but most patients experience dysphagia as well. Esophageal stricturing is an uncommon late complication of infectious esophagitis.

Physical Examination

Physical examination is important for assessment of the patient's nutritional status and ability to tolerate the invasive procedures that may be necessary to manage the esophageal disorder. However, the physical examination infrequently provides specific clues to the cause of dysphagia. For patients with dysphagia caused by collagen-vascular diseases, physical examination may show characteristic features such as joint abnormalities, calcinosis, telangiectasias, sclerodactyly, and rashes. A palpable left supraclavicular (Virchow's) lymph node suggests dysphagia caused by a malignancy within the abdomen (e.g., adenocarcinoma of the esophagogastric junction). Diffuse dental erosions may be a sign of GERD. Finally, the physical examination may show evidence of neuromuscular disorders that can interfere with swallowing such as Parkinson's disease, although most neuromuscular diseases that cause dysphagia do so by involving the striated muscle of the oropharynx and proximal esophagus (not the smooth muscle of the distal esophagus).

Barium Swallow

For decades, physicians have debated whether barium swallows should be performed early in the evaluation of esophageal dysphagia, or whether it is more cost-effective to bypass the radiographic examination entirely and proceed directly to endoscopic evaluation. Proponents of the latter approach argue that endoscopy is almost always required in the evaluation of esophageal dysphagia for both diagnostic and therapeutic purposes and that barium swallows usually do not provide enough additional information to justify the expense, inconvenience, and potential risk from radiation exposure. Those who advocate the former approach contend that a well done barium swallow provides valuable anatomic information about the esophagus that may help to direct therapy and prevent procedural complications. In the absence of studies validating the cost-efficacy of either approach, this debate will continue.

Despite the lack of data on cost-efficacy, a number of observations suggest that the practice of early radiographic evaluation for patients with esophageal dysphagia is useful. Barium contrast examination appears to be more sensitive than endoscopy for the detection of subtle narrowings of the esophagus such as those caused by rings and by peptic strictures that are >10 mm in diameter. In one study of 60 patients with lower esophageal rings, for example, barium swallows showed the rings in 95% of cases, whereas rings were demonstrated by endoscopic examination in only 58% of the patients. However, this study is more than 12 years old, and few data have been published that confirm these observations. Having the patient perform a Valsalva maneuver or swallow a solid bolus such as a marshmallow may increase the sensitivity of the radiographic evaluation for detection of structural and functional lesions of the esophagus. Furthermore, fluoroscopic examination can identify abnormalities in esophageal motility. When the patient swallows barium while in the supine or right oblique position, the fluoroscopist can assess the efficacy of esophageal peristalsis. Barium swallow may be especially helpful in suggesting the diagnoses of achalasia and diffuse esophageal spasm, conditions that may be difficult to identify endoscopically in early cases. In one study that assessed the accuracy of esophageal radiography in patients with manometrically verified esophageal motility disorders, for example, barium swallows identified achalasia in 18 of 19 cases (95%) and diffuse esophageal spasm...
in 5 of 7 cases (71%). Early radiographic demonstration of achalasia may prevent the situation in which endoscopic examination is performed initially for diagnostic purposes and then repeated later for therapy because the endoscopist either did not recognize the disorder or was not prepared to perform a pneumatic dilation or botulinum toxin injection on the initial evaluation. Barium swallow can identify lesions that may pose potential hazards or create confusion for the endoscopist such as large Zenker's or epiphrenic diverticula or large paraesophageal hernias. For patients with esophageal strictures, barium esophagram can provide information on the length and tightness of the lesion that may be helpful in choosing the type of dilator to be used for treatment and in deciding whether dilation should be done with fluoroscopic guidance (see below). Finally, initial barium swallow provides an objective baseline record of the esophagus that can be useful in assessing the response to therapy or progression of disease. Despite all these proposed advantages of early radiographic evaluation, however, no study yet has verified the contention that barium swallow performed before endoscopy decreases complications or improves outcome.

Endoscopy

Unless contraindicated by serious comorbidity, endoscopic evaluation is recommended for most patients with dysphagia of esophageal origin to establish or confirm a diagnosis, to seek evidence of esophagitis, to exclude malignancy, and when appropriate to implement therapy. Unlike the radiologist, the endoscopist can obtain biopsy and brush cytology specimens of esophageal lesions that may establish a diagnosis of neoplasms or specific infections. Endoscopy is more sensitive than radiology for identification of subtle mucosal lesions of the esophagus (e.g., mild esophagitis caused by gastroesophageal reflux or infection). The precise sensitivity of endoscopy for identification of mucosal lesions is not entirely clear, however, because endoscopy often has been used as the gold standard for establishment of the presence of mucosal disease. Therefore, if a subtle mucosal lesion is missed by endoscopic examination, it would probably be missed or dismissed as a spurious finding on an alternative diagnostic study such as barium swallow. The acceptance of endoscopy as a gold standard test for mucosal disease also results in bias in evaluation of the sensitivity of other diagnostic modalities. For example, reported estimates on the sensitivity of barium swallow for identification of moderate esophagitis range between 79% and 93%. Because endoscopy was used as the gold standard for mucosal disease in these studies, the sensitivity of radiology could not possibly exceed that of endoscopy.

Esophageal Manometry

The clinical use of esophageal manometry is the subject of a recent AGA technical review, and the reader is referred to that report for details about the procedure. Esophageal manometry is the gold standard test for esophageal motility disorders. Esophageal manometry has been shown to be especially useful for establishment of diagnoses of achalasia and diffuse esophageal spasm and for detection of esophageal motor abnormalities associated with collagen-vascular diseases.

For patients with dysphagia of esophageal origin, history and results of barium swallow or endoscopy can be used to decide whether esophageal manometry is necessary. Esophageal motility study usually is not needed at all for patients with mechanical causes of dysphagia such as strictures or rings. These patients can be treated with esophageal dilation and antireflux therapy if necessary, and manometry can be considered for those whose dysphagia persists despite adequate treatment of the mechanical and inflammatory lesions. For patients thought to have dysphagia caused by motility disorders other than achalasia, it usually is not critical that manometry precede endoscopy because there are no specific endoscopic therapies for these disorders. Therefore, these patients generally will not require second endoscopy solely for therapeutic purposes, as might occur if the diagnosis of achalasia were not established before the endoscopic evaluation. Endoscopy is performed in patients with motility disorders to assess the degree of esophagitis and to seek mechanical lesions (e.g., esophageal rings) that might be contributing to the dysphagia. Any mechanical lesions noted at endoscopy can be treated during or immediately after the procedure, irrespective of the precise nature of the underlying motility problem.

For patients thought to have dysphagia as a result of motility abnormalities associated with collagen-vascular diseases, manometry need not be performed routinely if dysphagia disappears with treatment of any associated reflux esophagitis and esophageal stenoses. For patients whose dysphagia persists despite such treatment, manometry can establish the nature of the motility problem. However, it is not clear that the information provided by esophageal manometry justifies the expense and inconvenience of the procedure, even in this setting. There are no specific treatments for motility disorders other than achalasia and its variants, so esophageal manometry often does not alter patient treatment. One might argue that the results of the motility study can be used to direct therapy with prokinetic agents. According to this argu-
ment, prokinetic agents that augment smooth muscle contraction would be used only for patients with disorders characterized by weak esophageal motility such as scleroderma and would be avoided for patients with spastic motility disorders such as diffuse esophageal spasm. However, the esophageal effects of the few available prokinetic agents often are only marginal for patients with weak esophageal motility, and the effects are not specific for any individual disorder. Although it seems logical to assume that prokinetic agents would have detrimental effects for patients with spastic motility disorders, few published data support this notion. Many patients with dysphagia caused by esophageal motility disorders are treated empirically with prokinetic agents without the benefit of a motility study, and it is not clear that documentation of the disorder by manometric examination has a substantial influence on patient management or outcome. One older study of 363 patients referred for esophageal manometry concluded that the procedure changed the course of treatment in only 4% of cases. One recent report provides a more optimistic assessment of the procedure, reporting that esophageal manometric examination resulted in a change in patient treatment in 49% of 268 patients referred to a motility laboratory. However, this report provides no details on precisely how the results of manometry changed treatment. Furthermore, the investigators considered manometric confirmation of certain clinical diagnoses to be a change in treatment. Thus it is not clear that early esophageal manometry for patients with conditions other than achalasia is preferable to a course of empiric therapy with prokinetic agents.

As discussed above, an esophageal motility study ideally should precede endoscopy for patients thought to have achalasia. Ordinarily, the motility catheter is passed blindly through the nose or mouth into the stomach. In patients with achalasia whose esophagus is dilated and tortuous, however, it may not be possible to advance the motility catheter blindly into the stomach because the flexible catheter curls in the capacious esophagus rather than passing through the hypertensive sphincter. In this situation, the information on LES function necessary to establish a manometric diagnosis of achalasia is not available. Few published data guide clinicians on how to deal with this problem. The options are (1) to pass the motility catheter using fluoroscopic guidance; (2) to pass the motility catheter over a guidewire placed endoscopically in the stomach; (3) to drag the motility catheter into the stomach using endoscopic techniques; and (4) to dispense with the motility study altogether. The first three options for catheter passage can be cumbersome and uncomfortable, and the success rate is not well documented. Furthermore, endoscopic methods for catheter placement often require the administration of sedatives that can influence esophageal motility. When the clinician is unable to position the motility catheter successfully in a patient with suspected achalasia, it seems reasonable to review the case critically before using invasive techniques for catheter passage. If the diagnosis of achalasia appears clear-cut based on typical clinical and radiographic features, the motility study usually can be deferred and endoscopy can be performed for diagnostic and therapeutic purposes. For such patients, the diagnostic problem usually involves distinction among primary (idiopathic) achalasia, secondary achalasia (e.g., caused by malignancy), and hypotonic contraction disorders (e.g., scleroderma) with peptic stricture formation. Manometry cannot reliably distinguish primary and secondary achalasia, and endoscopy usually can differentiate between achalasia (in which the esophageal narrowing caused by the sphincter muscle can be traversed easily with gentle pressure on the endoscope) and peptic stricture (in which the fibrotic, and typically inflamed, stricture poses substantial resistance to passage of the endoscope). Invasive techniques for positioning of the manometry catheter can be considered for patients who have clinical or radiographic features that are suggestive but not entirely typical of achalasia.

Videofluoroscopy

Videofluoroscopy, in which a motion recording is made of swallows involving barium suspensions and barium-coated materials, is an excellent technique for assessment of oropharyngeal function. However, this technique is of little value for evaluation of esophageal disorders.

Esophageal Transit Scintigraphy

In esophageal transit scintigraphy, patients swallow a radiolabeled liquid (e.g., water mixed with technetium-99m sulfur colloid), and radioactivity within the esophagus is measured over time using a gamma camera. Patients with esophageal motility disorders typically have delayed disappearance of the radiolabel from the esophagus. The test provides a quantitative estimate on the efficacy of emptying in different regions of the esophagus and is well tolerated by patients because it requires no intubation. Radionuclide transit studies are less sensitive and specific than manometry for establishment of the diagnosis of specific esophageal motility disorders, but scintigraphy provides information on bolus transit through the esophagus that can complement manometric data. Esophageal transit scintigraphy presently is used primarily for research, and routine
attention from gastroenterologists. Recent studies of stricture dilation, this report received relatively little patients treated with antireflux surgery alone (without blockers but no reduction in the need for stricture dilation. Although a small surgical series published in 1975 had shown a significant improvement in dysphagia and a substantial increase in stricture diameter for patients treated with antireflux surgery alone (without stricture dilation), this report received relatively little attention from gastroenterologists. Recent studies of patients with peptic strictures have shown that chronic, aggressive acid suppression therapy with proton pump inhibitors both improves dysphagia and decreases the need for subsequent esophageal dilations. For example, in one study of 366 patients with peptic esophageal strictures who were randomly assigned to receive medical therapy with either omeprazole (20 mg daily) or ranitidine (150 mg twice daily) for 1 year after baseline stricture dilation, repeat dilation was required in only 30% of patients in the omeprazole group compared with 46% in the ranitidine group (P < 0.01). In a study correlating esophageal stricture diameter (measured radiographically), grade of esophagitis (determined endoscopically), and severity of dysphagia (estimated using a numerical scoring system), Dakkak et al. found that stricture diameter alone could explain only 30% of the variation in dysphagia score, whereas the combination of stricture diameter and severity of esophagitis could account for 66% of that variation. The authors concluded that the degree of esophagitis is as important as stricture diameter in causing dysphagia. In summary, these studies show a reversible component of reflux esophagitis that contributes to dysphagia in some patients with peptic esophageal strictures. This esophagitis can be controlled with either proton pump inhibitors or antireflux surgery. For patients who remain symptomatic despite treatment with proton pump inhibitors or fundoplication, 24-hour esophageal pH monitoring can be used to document the adequacy of therapy in controlling acid reflux.

In addition to aggressive antireflux therapy, patients with benign esophageal strictures usually are treated (at least initially) with dilation. Esophageal dilation has been practiced since the 16th century, when physicians used tapered wax wands to dislodge material stuck in the esophagus. The name bougie is derived from Boujiyah, the name of an Algerian city that was the center of the medieval wax candle trade. Today, three major types of esophageal dilating devices are used commonly: (1) mercury-filled bougies that are passed blindly through the mouth (e.g., tapered-tipped Maloney dilators, blunt-tipped Hurst dilators); (2) polyvinyl bougies that can be passed over a fine guidewire that is positioned within the stenosis using either fluoroscopic or endoscopic guidance (e.g., Savary dilators); and (3) balloon dilators that are passed over a guidewire or through the endoscope (so called “through-the-scope,” or TTS, balloons). The first two types of dilators are pushed through the stenotic segment and thus deliver axially directed shearing forces as well as radially directed dilating forces to the stricture. In contrast, balloon dilators deliver only radially directed dilating forces. In theory, therefore, balloon dilators should stretch the stricture uniformly while eliminating complications associated with the application of shearing stresses.
these proposed advantages for balloon dilators over bougies, no study yet published has demonstrated convincingly that any commonly used dilator is superior to another in efficacy or safety. Indeed, historical data suggest that mercury-filled rubber bougies may have the best safety record for any of the dilator types, although no meaningful comparative study has been conducted to prove this contention.⁵² There are relatively few published reports of studies directly comparing the different dilator types for patients with esophageal strictures.⁵³–⁵⁸ Among five randomized trials that compared balloon dilation to push dilation (Table 2), three found a modest advantage for push dilation, one found no difference between the two, and one described a modest advantage for balloon dilation. None of these studies has established the superiority of one dilator type over another. In considering the cost of dilation therapy, however, the fragility of the TTS balloons is a disadvantage because unlike bougies, the balloons break easily with repeated usage.

Although many physicians have abandoned mercury-filled bougies in favor of the newer balloon dilators and guided polyvinyl bougies, a strong case can be made for mercury-filled bougies as the dilators of choice for esophageal strictures with diameters larger than 10–12 mm.⁵²,⁵⁹,⁶⁰ First, these bougies have a record of excellent efficacy and safety that has been established over a period of more than 80 years. Next, mercury dilators are passed without a guidewire, and fluoroscopic guidance usually is not necessary for dilation of simple strictures. Thus the added time, inconvenience, expense, and risk associated with guidewire passage and fluoroscopy are obviated. Finally, mercury-filled bougies often can be passed with minimal or no sedation, a major advantage for patients who require frequent bougienage. The flexibility of the mercury dilators that undoubtedly contributes to their safety becomes a disadvantage in dilation of strictures complicated by tightness, length, and tortuosity. Mercury dilators with diameters of less than 10 mm (30F) are so floppy that they tend to curl in the esophagus rather than to traverse such complicated strictures. Therefore, guided dilation using polyvinyl bougies or balloons may be necessary for stenoses that are exceptionally tight, long, or tortuous. Also, guided dilation should be considered for patients in whom strictures are associated with esophageal diverticula (either true or pseudodiverticula) whose thin walls might be perforated by the tip of a blindly passed dilator. The choice between balloons and polyvinyl bougies for patients with complicated strictures should be based on the availability of the dilators in a given institution and on the operator’s experience and comfort in using them because published experience has not convincingly established the superiority of one dilator type over another. Once an adequate esophageal luminal diameter has been achieved using a guided dilation technique, it may be possible to perform subsequent dilations using mercury-filled bougies.

Fluoroscopic guidance has been proposed as a means of enhancing the safety of esophageal dilation, but the published data to support this proposal are few and unconvincing.⁵² Fluoroscopic guidance usually is not necessary in dilation of esophageal strictures with mercury-filled rubber bougies, but fluoroscopy can be helpful in selected cases to ensure that the dilator has traversed the stricture. In a study of 145 patients with peptic esophageal strictures or Schatzki’s rings treated with Maloney dilators, fluoroscopy was found to alter the dilation technique in 24%.⁶¹ Fluoroscopy was especially useful for ensuring proper dilator passage in patients who had large hiatal hernias. Fluoroscopic guidance is used commonly for passing of bougies over a guidewire, but recent retrospective studies have challenged the need for fluoroscopy even in this setting.⁶²–⁶⁴ Kadakia et al.⁶² used endoscopy alone (without fluoroscopy) to pass a marked

Table 2. Results of Randomized Trials Comparing Balloon and Push Dilators

<table>
<thead>
<tr>
<th>Study (yr)</th>
<th>No. of patients</th>
<th>Dilators compared</th>
<th>Perforations</th>
<th>Significant differences</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kelly⁴⁹ (1988)</td>
<td>71</td>
<td>Balloon vs. Celestin and Eder-Puestow</td>
<td>0</td>
<td>Bougie modestly better than balloon for reduction of dysphagia and maintenance of stricture patency</td>
</tr>
<tr>
<td>Tytgat⁵⁰ (1990)</td>
<td>60</td>
<td>Balloon vs. Savary-Gilliard</td>
<td>0</td>
<td>Bougie modestly better than balloon for reduction of dysphagia</td>
</tr>
<tr>
<td>McBride and Ergun⁵¹ (1992)</td>
<td>71</td>
<td>Balloon vs. Eder-Puestow</td>
<td>1 Bougie, 1 balloon</td>
<td>None</td>
</tr>
<tr>
<td>Tulman and Boyce⁵² (1994)</td>
<td>93</td>
<td>Balloon vs. Celestin and Eder-Puestow</td>
<td></td>
<td>Bougie modestly better than balloon for reduction of dysphagia and maintenance of stricture patency</td>
</tr>
<tr>
<td>Cox et al.⁵³ (1995)</td>
<td>34</td>
<td>Balloon vs. Savary</td>
<td>0</td>
<td>Balloon modestly better than bougie for prevention of stricture recurrence; required fewer treatment sessions, produced less procedural discomfort</td>
</tr>
</tbody>
</table>

*This series includes the patients described in the study by Kelly.⁴⁹*
guidewire through esophageal strictures in 138 patients and successfully performed bougienage over the guidewire without fluoroscopic guidance and without complications in all of these cases. However, it is not clear whether the relatively simple strictures in these patients could have been dilated successfully even with no guidewire using only mercury-filled rubber bougies. Kozarek et al. found that fluoroscopic guidance was necessary in only 8% of more than 300 patients who had esophageal strictures dilated successfully with polyvinyl bougies. Thus it appears that fluoroscopically guided dilation should be necessary only in the minority of patients who have complicated esophageal strictures or large hiatal hernias.

Esophageal dilators are sized using the French gauge system in which the dilator's diameter can be estimated using the following formula: Dilator Diameter (in mm) = French Gauge Size ÷ 3. For example, a 30F dilator has a diameter of 10 mm. There is no clear consensus on the optimal size to which a peptic stricture should be dilated. For patients with Schatzki rings, dysphagia is the rule when the ring diameter is less than 13 mm (39F) and uncommon when the ring diameter exceeds 20 mm (60F). In a number of published series of patients with predominantly peptic esophageal strictures, progressive dilation to a gauge size between 40 and 60F resulted in good relief of dysphagia in approximately 85% of cases with a very low rate of complications. In theory, successful dilation might decrease the mechanical barrier to gastroesophageal reflux imposed by the stricture and thereby result in an increase in heartburn and regurgitation. One investigation on this issue did not find a significant overall postdilatation increase in acid reflux by protracted esophageal pH monitoring in a group of 10 patients with peptic strictures, although certain individuals in that group experienced a marked exacerbation of acid reflux after the dilating procedure. With the availability of highly effective antisecretory medications such as proton pump inhibitors, concerns about exacerbation of reflux disease should not be a major factor in limiting the extent of esophageal dilation. Nevertheless, it seems preferable to individualize dilation therapy rather than to aim for the same arbitrary dilator size for all patients. Although no study on benign strictures has documented clearly that the risk of esophageal perforation increases with dilator sizes up to 60F, it seems logical to assume that fibrotic strictures have a critical size beyond which they cannot stretch without rupturing. Furthermore, the extent of initial stricture dilation does not seem to influence either stricture recurrence or the requirement for subsequent dilation; therefore, there is little support for the concept that strictures should be dilated aggressively to prevent recurrence. For a patient who has experienced complete relief of dysphagia with dilation to 48F, there is little to be gained by dilation to larger diameters. Most patients experience good relief of dysphagia when dilated to a bougie size between 40 and 54F. The extent of dilation in an individual patient should be based on the symptomatic response to therapy and on difficulties encountered during the dilation procedure.

When dilating a stricture with bougies, the initial choice of dilator size is based on an estimate of stricture diameter provided by a barium swallow or endoscopic examination. A more physiological approach to estimation of stricture diameter involves having the patient swallow barium spheres of known diameter, but this technique is seldom used in clinical practice and has not been shown to improve the results of dilation. It is generally recommended that the first bougie passed have a diameter approximately equal to that estimated for the stricture. The “rule of threes” is a clinical maxim that holds that no more than three bougies of progressively increasing size should be passed at any one dilation session to minimize the risks of esophageal perforation and hemorrhage. Mercury-filled rubber bougies (for which the rule of threes originally was formulated) increase in size by 2F units, so the diameter of the third bougie is only 1.3 mm larger than the first (e.g., dilation of a stricture using 36, 38, and 40F bougies increases the stricture diameter 12-13.3 mm). Although the rule of threes seems reasonable as a clinical guideline, no studies verify that adherence to the rule improves dilation efficacy or safety. Furthermore, with balloon dilation, strictures are routinely dilated in one session to a diameter far greater than that which could be achieved with the passage of three bougies. Balloons are designed to burst if a certain pressure is exceeded during dilation, but it is not clear that the burst pressure is less than that required to rupture the diseased esophagus. One report described no perforations among 35 patients with a mean stricture diameter of 7.6 mm who underwent dilation in a median of 13 sessions using a 60F balloon. This represents a mean increase in stricture diameter of 11.4 mm. To achieve this degree of dilation, the balloon dilators are progressively increasing diameter would require the passage of at least 20 bougies. No study has systematically evaluated the safety of passing so many bougies in one sitting. If one elects to dilate a stricture with mercury-filled bougies rather than balloons, it seems a reasonable concession to the unvalidated rule of threes to pass bougies of progressively increasing diameter until resistance is first encountered, and to pass no more than two bougies after that in the same session. This may not be a reasonable approach
when using polyvinyl dilators passed over a guidewire, because these dilators may not provide the operator with a meaningful tactile impression of stricture resistance.\textsuperscript{50} With polyvinyl dilators, the resistance to passage perceived by the operator may be more a function of friction produced by the guidewire than of resistance provided by the esophageal stenosis. Nevertheless, esophageal dilation using polyvinyl dilators has an excellent safety record, and it is not clear that adherence to the rule of threes enhances safety. In one recent study, benign esophageal strictures in more than 400 patients were dilated using either a single, large polyvinyl dilator (\(\geq 45\)F) or multiple polyvinyl dilators so that the stricture diameter increased by \(>2\) mm in one session.\textsuperscript{64} Despite this flagrant violation of the rule of threes, only one perforation was observed in 662 dilation sessions. If one elects to dilate a stricture using balloon dilators, it seems prudent to limit the initial dilation to no more than 45F. Although a previously mentioned report found no complications in a small series of patients dilated initially with 60F balloons,\textsuperscript{51} it seems preferable to be more conservative until results of future studies on the safety and efficacy of balloon dilation are available.

The major complications of esophageal dilation are perforation and bleeding. These two complications appear to occur with approximately equal frequency, although there is substantial variation among the reported series. For example, the 1974 American Society for Gastrointestinal Endoscopy survey found rates of perforation and bleeding of 0.1% and 0.3%, respectively, among 13,139 esophageal dilations performed with mercury-filled rubber bougies.\textsuperscript{72} In contrast, Patterson et al.\textsuperscript{11} observed 5 perforations and only 1 hemorrhage during esophageal dilation in 154 patients, most of whom had multiple sessions of bougienage performed over a period of up to 87 months. In another American Society for Gastrointestinal Endoscopy survey conducted in 1984, 10 hemorrhages and 2 perforations were reported among 456 patients treated with balloon dilation of esophageal strictures for an overall complication rate of 2.5%.\textsuperscript{73} It is difficult to provide precise estimates on the rate of complications for esophageal dilation because of inconsistencies in the available studies. The patient populations in most reported series were heterogeneous, composed of patients with strictures of varying complexity caused by a number of different disease processes. It is likely that the complication rate is highest for dilations performed for strictures that are exceptionally tight, long, or tortuous, but most reports do not supply specific information regarding these stricture variables. If guided dilation techniques are used preferentially for patients with complex strictures (those most likely to be associated with procedural complications), then guided dilation may spuriously appear to be more dangerous than blind bougienage. Many reports do not specify precisely the criteria used for the choice of dilation technique, few studies are randomized, and it is difficult to perform a blinded trial of dilation therapy. With one or more of these deficiencies present in virtually every reported study on esophageal dilation, it is difficult to perform a meaningful meta-analysis. Based on a review of the flawed studies available, it appears that serious complications can be expected in approximately 0.5% of all dilation procedures. With such a low rate of complications, a meaningful comparative study seeking to demonstrate a significant safety benefit of one procedure over another will require large numbers of patients, numbers far greater than those included in any comparative study reported to date (Table 2).

Bacteremia complicates esophageal dilation more often than any other procedure performed by gastroenterologists.\textsuperscript{53} A number of reports suggest that bacteremia accompanies esophageal dilation in 20%–45% of cases.\textsuperscript{74–76} Despite the high frequency of bacteremia, clinically recognizable infectious complications of esophageal dilation such as endocarditis and brain abscesses have rarely been reported.\textsuperscript{77–80,82} Although antibiotic prophylaxis for esophageal dilation generally is recommended routinely only for patients at high risk for endocarditis according to the American Heart Association’s guidelines,\textsuperscript{82,83} some authorities recently have suggested that such prophylaxis should be given routinely even to patients with “intermediate risk” lesions such as mitral valve prolapse with insufficiency.\textsuperscript{75}

After initial dilation, stricture recurrence is a frequent phenomenon. Before proton pump inhibitors became available, a number of investigations suggested that only approximately 40% of patients would experience protracted relief of dysphagia after a single dilation session, and approximately 60% would require multiple dilations.\textsuperscript{11,69,84,85} With proton pump inhibitor therapy, as few as 30% of patients may require repeat dilations within 1 year.\textsuperscript{47} For patients with peptic strictures, factors associated with the need for multiple dilations include a history of weight loss and absence of heartburn at the time of initial dilation.\textsuperscript{86} Neither the severity of the initial stenosis nor the type and size of dilator used appears to have a major influence on the likelihood of stricture recurrence.\textsuperscript{11,69,86} Therefore, for individual patients there is no reliable method to predict the need for repeated dilation. Patients require close follow-up after initial dilation, and the procedure should be repeated if dysphagia returns.

The role of surgical treatment for benign esophageal
strictures remains disputed. There are two major approaches to the surgical treatment of esophageal strictures: (1) antireflux surgery with intraoperative stricture dilation for patients with peptic strictures caused by GERD (for patients whose peptic strictures are associated with substantial esophageal shortening, a lengthening procedure such as a Collis gastroplasty may be necessary for successful fundoplication), and (2) esophageal reconstruction for patients with strictures of any etiology that are not responsive to dilation. Esophageal reconstruction may rarely involve a procedure that widens the stricture without a resection (e.g., Thal fundic patch) or, more commonly, the stenotic esophagus may be resected and reconstructed either by use of a gastric pull-up procedure or by interposition of a loop of bowel (colon or jejunum) between the remaining esophagus and the stomach. For patients with peptic strictures treated by antireflux surgery and intraoperative dilation, the success rate for relief of dysphagia is similar to that reported for nonsurgical dilation therapy.87–92 The major advantage of this approach is that successful antireflux surgery obviates lifelong medical therapy with its attendant expense and inconvenience. However, there is no clear benefit for surgical treatment of esophageal strictures over medical therapy for relieving dysphagia per se, and there is a small operative mortality rate (usually <1%) associated with fundoplication. The requirement for repeated dilation after antireflux surgery for strictures ranges between 1% and 31% and appears to be somewhat smaller than that described for medical treatment of esophageal stenoses.87–92 One might argue that the small risk of operative mortality might be offset by the reduced need for repeated esophageal dilation with its attendant mortality rate. However, there has been no meaningful comparative study of medical and surgical treatments for peptic esophageal strictures, so it is not clear that surgery is truly superior to medical therapy in prevention of stricture recurrence. Physicians should be especially cautious in recommending antireflux surgery for patients with peptic esophageal strictures caused by esophageal motility disorders such as scleroderma. The combination of abnormal esophageal motor function and mechanical obstruction imposed by fundoplication can result in severe postoperative dysphagia. However, scleroderma is not an absolute contraindication to antireflux surgery, and some reports have described excellent outcomes for fundoplication in small series of selected patients with peptic esophagitis and strictures caused by scleroderma.93 Finally, in rare cases, intractable esophageal strictures will require surgical resection and reconstruction. Operative morbidity and mortality are substantially higher for esophageal resection and reconstruction procedures than for antireflux surgery.

There are several reports on the use of endoscopic steroid injection for the treatment of patients with refractory esophageal strictures.94–96 All of these studies involve small numbers of patients with benign strictures of diverse etiology that had not responded to at least one attempt at esophageal dilation. Some patients appeared to respond dramatically to steroid injection by exhibiting substantial improvement in dysphagia and decreases in their requirement for repeated dilations. These small studies were not randomized or controlled, and the conclusions that can be drawn regarding the efficacy of steroid injection are very limited. Also, the mechanisms by which steroid injection might improve esophageal stenoses are not clear. Nevertheless, steroid injection appears to be a relatively safe procedure, and a trial of this unproved therapy seems reasonable for those rare patients with benign esophageal strictures who derive no or short-lived relief of dysphagia despite repeated attempts at stricture dilation and aggressive control of reflux esophagitis. Finally, the technique of self-bougienage can be taught to patients who require very frequent esophageal dilation despite intensive medical therapy and steroid injection and for whom surgery is either contraindicated or unacceptable. The very limited published data available on self-bougienage suggest that the technique can be both safe and effective.97

Lower Esophageal (Schatzki) Rings

In 1953, two independent groups of investigators published descriptions of patients who had dysphagia associated with ringlike constrictions of the distal esophagus.98,99 The investigators had differing opinions about the nature of these lower esophageal rings. Ingelfinger and Kramer98 proposed that the ringlike narrowings were caused by contraction of an overactive band of esophageal muscle, whereas Schatzki and Gary99 believed that esophageal rings were fixed structures that were not contractile. Although it is now clear that lower esophageal rings are quite common, controversy persists regarding the precise nature and pathogenesis of these structures.100 Based on an extensive review of the literature and on an autopsy study of the distal esophagus, Goyal et al.101,102 concluded that some of the controversy had arisen because several different disorders had been included under the rubric “lower esophageal ring” (e.g., muscular rings, mucosal rings, and ringlike peptic strictures). Muscular rings (also called A rings) are caused by a thickened band of esophageal muscle fibers. The location of these rings corresponds with an annular thickening in the muscularis propria of the distal esophagus that anatomists have
called the inferior esophageal sphincter (a structure that should not be confused with the LES described functionally by physiologists). Muscular rings are located approximately 2 cm above the esophagogastric junction and rarely cause dysphagia. Most of the discussion that follows pertains to lower esophageal mucosal rings (also called Schatzki rings or B rings), which are by far the most common type of lower esophageal ring found in patients with dysphagia.

The lower esophageal mucosal ring is a thin, diaphragm-like, circumferential fold of mucosa that protrudes into the lumen of the distal esophagus, thereby posing a physical barrier to the passage of solid material. Mucosal rings usually are located at the squamocolumnar junction with squamous epithelium lining the upper surface and columnar epithelium lining the lower aspect of the ring. Fibrous tissue often can be found in the lamina propria. Some authorities have challenged the contention that mucosal rings occur primarily at the squamocolumnar junction, but the contrary evidence presented is unconvincing. Schatzki rings are best appreciated on barium swallow, where they are usually, if not invariably, associated with hiatal hernias. With careful radiological techniques aimed at distending the distal esophagus, a lower esophageal ring can be found in approximately 15% of all patients who have barium swallows. However, few of these rings cause dysphagia.

The pathogenesis of the lower esophageal mucosal ring is not clear, but a number of hypotheses have been proposed. One hypothesis holds that the ring is merely a pleat of redundant mucosa that forms when the esophagus shortens either transiently (during contraction of the longitudinal muscle) or permanently (from unknown cause). Another hypothesis suggests that rings are congenital in origin. Few data either strongly support or clearly refute these two hypotheses. A third hypothesis suggests that lower esophageal mucosal rings are thin peptic strictures that develop as a consequence of GERD. If this hypothesis is correct, treatment of patients with rings might be directed at controlling reflux esophagitis. However, data on the association of GERD and Schatzki rings are inconclusive and contradictory. Goyal et al. found no evidence of reflux esophagitis associated with any of 9 esophageal mucosal rings identified at postmortem examination. Jamieson et al. found that GERD symptoms and abnormal acid reflux (identified by esophageal pH monitoring) were less frequent among 32 patients with Schatzki rings than among 32 control patients who had hiatal hernias without rings. In contrast, Marshall et al. found evidence of GERD (abnormal acid reflux by 24-hour pH monitoring or endoscopic signs of reflux esophagitis) in 13 of 20 patients with symptomatic Schatzki rings. Also supporting a potential role for GERD in the pathogenesis of lower esophageal mucosal rings are the observations that demonstrable rings are virtually always associated with hiatal hernias and that serial radiographic examinations in some patients with rings have shown progression in the esophageal stenoses over time to the point that they resembled peptic strictures more than rings. Finally, a role for pill esophagitis has been suggested in the pathogenesis of Schatzki rings. In one study, 62% of patients with rings who had no signs or symptoms of GERD had a history of ingestion of medications known to cause pill esophagitis.

The hypotheses on the pathogenesis of lower esophageal mucosal rings need not be mutually exclusive. For example, a congenital ring might be narrowed further by scarring from reflux or pill esophagitis. It is also conceivable that subtle rings do not cause symptoms unless there is a supervening disorder that further interferes with esophageal clearance such as esophagitis or dysmotility. This could explain an apparent association between rings and GERD, even if GERD plays no role in the pathogenesis of the rings per se.

Treatment of patients with dysphagia caused by lower esophageal mucosal rings begins with reassurance that the condition is benign and with advice that food be chewed slowly and carefully. However, there are no data to show that this advice is beneficial, and dilation therapy is recommended for most patients. Traditionally, initial dilation therapy for Schatzki rings involves the passage of a single large bougie or balloon (45–60F) aimed at fracturing (rather than merely stretching) the mucosal fold. This approach differs from that discussed above for peptic strictures, which are treated by gradual stretching for fear of rupturing the fibrotic esophagus with a single, abrupt dilation. The safety of abrupt dilation for esophageal rings has been well established, and most reported series limited to patients with Schatzki rings describe no complications of the procedure. However, the contention that abrupt dilation is more effective than gradual dilation for relief of dysphagia has not been verified. Furthermore, the notion that ring fracture by abrupt dilation should result in a low rate of recurrent dysphagia has not been substantiated by published experience. Indeed, a number of reports suggest that recurrence is the rule rather than the exception after dilation of symptomatic Schatzki rings. For example, one recent report describes 33 patients with symptomatic Schatzki rings who were treated by abrupt dilation with the passage of a single, large bougie (46–58F) and were followed up for a mean duration of 2 years. Initial results were excellent, with all patients...
reporting complete relief of dysphagia at a 4-week follow-up examination. However, actuarial life-table analysis showed that only 68% would remain free of dysphagia after 1 year, whereas only 11% of patients were estimated to be symptom-free by year 5. In another study of 61 patients with symptomatic Schatzki rings who were followed up for a mean duration of 75 months, 63% developed recurrent dysphagia after initially successful dilation.\(^{110}\)

No clinical features have been identified that are consistently useful for predicting which patients will need repeated dilations for Schatzki rings. The initial diameter of the ring has not been found to correlate significantly with recurrence.\(^{109,110}\) Some investigators have suggested that recurrence is more likely in patients who have GERD associated with their Schatzki rings,\(^{105}\) whereas others have found no correlation between the presence of GERD and the need for repeated ring dilations.\(^{109}\) For patients who have both Schatzki rings and GERD, antireflux therapy aimed at eliminating the signs and symptoms of reflux esophagitis clearly is appropriate despite the lack of proof that such treatment reduces the frequency of recurrent dysphagia. All patients with rings who are treated with dilation should be advised that recurrence is likely and that dilation may need to be repeated if dysphagia returns.

A number of different treatments have been used for patients with “defiant” rings that do not respond to abrupt dilation using standard balloons and bougies, or that recur quickly after initial relief of dysphagia. There are anecdotal reports on the successful use of pneumatic dilation with large balloon dilators such as those usually reserved for the treatment of achalasia.\(^{111}\) Some investigators have performed endoscopic electrosurgical incision of the rings with good results.\(^{112,113}\) Others have used surgery either to rupture or excise the rings, and to repair the associated hiatal hernias.\(^{114,115}\) However, one report of such surgical therapy describes the recurrence of symptoms in 14 of 36 patients (39%).\(^{114}\) A concomitant motility disorder could explain the frequent recurrence of symptoms in some patients with defiant Schatzki rings, but few studies have systematically searched for esophageal dysmotility in these patients. The possibility of a motility disorder should be explored with a manometric examination before one of the potentially hazardous therapies mentioned above is used for patients with defiant lower esophageal mucosal rings.

Physicians occasionally encounter patients who have intermittent dysphagia for solid foods suggestive of a Schatzki ring but have no demonstrable abnormality on barium swallow or endoscopic examination of the esophagus. Few reports have addressed the treatment of such patients. One study explored the role of empiric esophageal dilation in patients who had “esophageal dysphagia” and a normal esophagoscopy, barium swallow, or both.\(^{116}\) Among 20 such patients who had dysphagia for solid foods only, empiric bougienage to 54F resulted in immediate and complete resolution of dysphagia in 19 cases (95%). During a median follow-up period of 20 months, furthermore, 13 of those 19 patients experienced no recurrence of dysphagia. In contrast, complete resolution of dysphagia was seen after empiric dilation in only 2 of 17 patients (12%) who had dysphagia for both solids and liquids. It seems likely that empiric dilation was effective in the former patients because they had subtle rings, webs, or strictures that were missed by the diagnostic studies, whereas the latter patients probably had motility disorders. Although the design of this study was far from ideal, the report suggests that a trial of empiric bougienage is reasonable for patients who complain of dysphagia for solid food and who have normal findings on endoscopic examinations.

Achalasia

Primary achalasia is an esophageal disease of unknown cause in which there is degeneration of neurons in the wall of the esophagus.\(^{117,118}\) This degenerative process preferentially involves the nitric oxide–producing inhibitory neurons that effect the relaxation of esophageal smooth muscle.\(^{119,120}\) In some patients, degenerative changes are found in brainstem ganglion cells in the dorsal motor nucleus of the vagus, and Wallerian degeneration has been observed in vagal fibers that supply the esophagus.\(^{121}\) However, the disordered motility that characterizes achalasia appears to result primarily from the degeneration of inhibitory neurons within the esophagus itself. The smooth muscle of the LES is tonically contracted at rest and relaxes when intramural neurons release their inhibitory neurotransmitters. Loss of inhibitory innervation in the LES causes basal sphincter pressures to increase and renders the sphincter muscle incapable of normal relaxation. Unlike the LES, the smooth muscle of the esophageal body does not exhibit resting tone; therefore, the loss of inhibitory neurons has little effect on resting pressure in the body of the esophagus. However, inhibitory influences are necessary for normal peristalsis, and the loss of inhibitory neurons results in aperistalsis.

Although the etiology of primary achalasia is not known, certain recognized diseases can cause esophageal motor abnormalities similar or identical to those of primary achalasia. This condition is called secondary achalasia or pseudoachalasia. In Chagas’ disease, seen in Central and South America, for example, esophageal
infection with the protozoan parasite Trypanosoma cruzi can result in a loss of intramural ganglion cells that causes aperistalsis and incomplete LES relaxation.\textsuperscript{122} Malignancies rarely can cause pseudoachalasia either through direct invasion of esophageal neural plexuses (e.g., adenocarcinoma of the esophagogastric junction) or through release of uncharacterized humoral factors that disrupt esophageal function as part of a paraneoplastic syndrome.\textsuperscript{123} It is important to exclude the diagnosis of pseudoachalasia caused by malignancy before invasive therapies such as pneumatic dilation or surgical myotomy (see below) are implemented. It seems likely that these procedures would be especially hazardous for patients with infiltrating neoplasms of the distal esophagus, although few published data are available to support this contention. In most cases, a careful history and endoscopic examination are sufficient to exclude the diagnosis of pseudoachalasia. However, if the clinical history is strongly suggestive of achalasia caused by malignancy (e.g., onset in old age, rapid progression of symptoms, profound weight loss), additional tests such as computed tomography or endosonography might be necessary to exclude an infiltrating neoplasm.

Presently, no therapy can reverse or even halt the degeneration of enteric neurons that occurs in primary achalasia. Therefore, the treatment of this disorder is functional, aimed at decreasing resting pressure in the LES (by pharmacological or mechanical means) to the point that the sphincter no longer poses a substantial barrier to the passage of ingested material. This therapeutic attack on the LES does not reliably restore function in the body of the esophagus, although the return of peristaltic activity has been observed in some patients after the administration of various therapies designed solely to decrease LES pressure.\textsuperscript{124–126} Nitrates and calcium channel blockers have been shown to relax the smooth muscle of the LES both in normal individuals and in patients with achalasia, and these agents have been used to treat the disorder with variable success.\textsuperscript{127–135} Sublingual isosorbide dinitrate causes a substantial decrease in LES pressure within minutes, and the effect often lasts for more than 1 hour. Limited studies suggest that more than 75% of patients with achalasia experience substantial improvement in dysphagia when they take isosorbide in a dose of 5–10 mg sublingually 10 minutes before meals.\textsuperscript{127,128} One comparative trial in 15 patients with achalasia found that nitrates were superior to nifedipine both for decreasing LES pressure (64% decrease from baseline for nitrates vs. 47% decrease for nifedipine) and for relieving dysphagia (swallowing improved in 87% of patients on nitrates vs. 53% of patients on nifedipine).\textsuperscript{128} However, nitrate therapy often must be discontinued because many patients experience intolerable side effects (predominantly headache) and because some patients become refractory to the nitrates after an initial good response.\textsuperscript{127,128} Like nitrates, calcium channel blockers administered sublingually also result in substantial decreases in LES pressure for more than 1 hour.\textsuperscript{135} However, the results of studies on the effects of calcium channel blockers on the symptoms of achalasia are contradictory; some investigators report good,\textsuperscript{133,135} marginal,\textsuperscript{130} and no\textsuperscript{134} relief of dysphagia in small groups of patients treated with these agents. Although verapamil and diltiazem have been used, most published experience has involved nifedipine given in a dose of 10–20 mg sublingually 30 minutes before meals. Adequate plasma levels have been observed when calcium channel blockers are administered orally (rather than sublingually) to patients with achalasia,\textsuperscript{134} but the absorption of orally administered drugs may be erratic for patients with advanced disease in whom the pills can linger for hours in the flaccid esophagus. In summary, pharmacotherapy for achalasia is inconvenient, often ineffective, and frequently associated with side effects and tachyphylaxis. It appears that pharmacotherapy is best reserved for patients who are unwilling or unable to tolerate the more effective invasive forms of therapy discussed below.

At one time, authorities recommended esophageal dilation using large, mercury-filled rubber bougies (50–60F) as the initial therapy for achalasia.\textsuperscript{136} As techniques for forceful dilation of the LES in achalasia became popular, bougienage was dismissed as a procedure that, at best, provided only transient and incomplete relief of dysphagia.\textsuperscript{137} In 1982, Mandelstam et al.\textsuperscript{136} reported that bougienage to 58F resulted in relief of dysphagia for months to years in 4 of their 5 patients with achalasia and called for a reappraisal of the role of bougienage in the treatment of this disorder. More recently, McJunkin et al.\textsuperscript{138} reviewed their experience with achalasia and reported that bougienage was successful when used as initial therapy in 10 of 20 patients. Despite these reports, most modern authors continue to dismiss bougienage as a procedure that provides only temporary and incomplete relief for patients with achalasia. Consequently, few modern gastroenterologists have any experience with bougienage in the treatment of achalasia. In the absence of well-designed, prospective studies, it is difficult to draw firm conclusions regarding the efficacy of bougienage for achalasia. Presently, it appears that bougienage, like pharmacotherapy, is best reserved as an alternative treatment for patients who are unwilling or unable to tolerate the more invasive forms of therapy discussed below.

For decades, pneumatic dilation of the LES using large
balloons has been a popular form of treatment for achalasia.\textsuperscript{139–155} This therapy was designed to weaken the LES by tearing its muscle fibers, although experimental evidence that the procedure indeed works by inducing muscular tears is scant.\textsuperscript{148} Many different balloon dilators have been used over the years for treatment of achalasia (e.g., Mosher bag, Sippy dilators, Brown–Mchardy dilator, Rider–Möller dilator), but most are no longer being manufactured. Presently, the two most popular pneumatic dilators in the United States are the Rigiflex dilator (similar in design to the Gruntzig angioplasty catheter), which is passed over a guidewire and positioned fluoroscopically,\textsuperscript{150} and the Witzel dilator, which is mounted on an endoscope and inflated under direct vision.\textsuperscript{144}

There is no clear consensus on the optimal method for performing pneumatic dilation, and reported protocols have varied widely with regard to the types of medications used for sedation (which theoretically could affect the outcome if the sedatives cause LES relaxation, and which have ranged from no sedatives whatsoever to general anesthesia), the types of dilators used (e.g., Mosher, Sippy, Brown–Mchardy, Rider–Möller, Rigiflex, Witzel), the maximum diameter of the balloon (reported range, 2.4–5.0 cm), the pressure to which the balloon is inflated (reported range 105 to >1000 mm Hg), the rate of balloon inflation (rapid vs. gradual), the duration of balloon inflation (reported range, several seconds to more than 5 minutes), and the number of balloon inflations per dilating session (reported range, 1–5).\textsuperscript{155} Most investigators have used a single pneumatic dilator at each treatment session, with the need for subsequent dilations determined empirically by the symptomatic response to the initial dilation.\textsuperscript{154} Others have used the method of progressive pneumatic dilation advocated by Vantrappen and Janssens\textsuperscript{148} in which a series of balloons of progressively increasing diameter are inflated until there is manometric and radiographic evidence of adequate LES disruption. With so many possible permutations and combinations of the various components of pneumatic dilation, and with so few reports of prospective studies, it is difficult to perform a meaningful meta-analysis on the outcome of the procedure.

Despite the many variations in technique described above, most studies (primarily retrospective reviews of an institution’s experience) describe good to excellent short-term results in 60%–85% of patients with achalasia treated with a single session of pneumatic dilation. The duration of follow-up in most of these retrospective reports is relatively brief; consequently, few data are available on the long-term outcome of pneumatic dilation. One large retrospective study found that only 65% of 313 patients with achalasia treated with one or more pneumatic dilations still reported good to excellent results after a median follow-up of 11 years.\textsuperscript{140} In one of very few prospective studies on patients with achalasia treated initially with pneumatic dilation, 28 of 54 subjects (52%) were found to require repeat dilations during a median follow-up of 4.1 years.\textsuperscript{156} The estimated probability of remaining in remission after a single dilation was 59% at 1 year and 26% at 5 years. In a retrospective investigation of 123 patients treated initially with pneumatic dilation, Parkman et al.\textsuperscript{157} found that 42% required further treatment during a mean follow-up of 4.7 years. These investigators also noted that repeat pneumatic dilations became progressively less effective than the initial procedure. For example, 58% of patients who had a second pneumatic dilation required further treatment, whereas 73% required additional therapy after a third dilation. In a recent, more optimistic report of a retrospective study, Katz et al.\textsuperscript{158} found that pneumatic dilation was successful in relieving the symptoms of achalasia in 85% of 72 patients who were followed up for a mean of 6.5 years, and only 4 patients required more than one dilation procedure. Overall, these studies suggest that approximately 50% of patients with achalasia treated initially with a single pneumatic dilation will require further therapy within 5 years and that subsequent pneumatic dilations are progressively less likely to result in a sustained remission. Some authors have recommended that other forms of therapy be considered after two or three unsuccessful pneumatic dilations.\textsuperscript{117}

A number of studies have sought to identify clinical and technical factors that might help clinicians predict responses to pneumatic dilation.\textsuperscript{156–161} Young age consistently has been shown to be associated with a poor response.\textsuperscript{156–159} In one prospective study, for example, the 2-year sustained remission rate for patients under age 40 was only 29%, compared with 67% for those age 40 years and older.\textsuperscript{156} Perhaps young muscle is less susceptible to damage by forceful dilation than old muscle. Among the technical factors, LES pressure after dilation appears to be the best predictor of outcome. In the aforementioned prospective study, the 2-year remission rate was 100% for patients whose postdilation LES pressure was <10 mm Hg, 71% for those whose postdilation LES pressure was 10–20 mm Hg, and 23% for those with postdilation LES pressures of ≥20 mm Hg.\textsuperscript{156} The size of the dilating balloon also appears to influence the outcome (i.e., the long-term remission rate may be higher when larger diameter balloons are used), although few studies have specifically explored this issue.\textsuperscript{151,154,156} Factors that do not appear to have a substantial influence on the response
to pneumatic dilation include gender, duration of esophageal symptoms before treatment, diameter of the esophagus, pretreatment LES pressure, duration of balloon inflation, number of balloon inflations per dilating session, maximum inflation pressure, and chest pain present during the procedure. Finally, although many clinicians have been taught to look for blood on the dilating balloon as proof that the procedure has been consummated, this finding has not been found to be a useful predictor of outcome.

Despite the wide variations in equipment and techniques used for pneumatic dilation, reported complication rates are remarkably similar. Esophageal perforation is the most common serious complication of the procedure, and most large series describe rates of perforation in the range of 2%–6%. Mortality from pneumatic dilation is rare and has been estimated at approximately 0.2%. The new Rigiflex dilators do not appear to have any safety advantage over the older balloons, and some investigators even suggest that perforation rates are higher with the newer instruments. There are very few reports of studies that have prospectively compared the different dilator types for safety and efficacy, and those that have been published are primarily of historical interest because some of the dilators compared are no longer available. Achalasia is an uncommon disease, and the perforation rate for pneumatic dilation is relatively low. Consequently, it is difficult to conduct a meaningful study on factors that might predispose to esophageal perforation. A number of potential predisposing factors have been suggested, including malnutrition, weight loss, low LES pressure, high-amplitude contractions in the distal esophagus, previous pneumatic dilations, administration of anesthesia, large balloon size, and high inflation pressures. However, none of these factors has been shown consistently to influence the safety of pneumatic dilation. In addition, the presence of a large epiphrenic diverticulum has been regarded as a contraindication to pneumatic dilation because of anecdotal reports of perforations in this setting. However, the risk of perforation imposed by these diverticula has not been well established. Although it once was standard clinical practice to hospitalize patients for pneumatic dilation, it appears that performing the procedure in an outpatient setting for otherwise healthy individuals does not substantially increase the risk of complications.

A number of authorities recommend that esophagography be performed shortly after pneumatic dilation (usually as soon as the sedation has worn off) to seek evidence of perforation. Although water-soluble contrast (e.g., Gastrografin) is commonly recommended for this study, such hypertonic agents can cause a chemical pneumonitis if they are aspirated into the lungs. Consequently, these agents should not be used in sedated patients or in neurologically impaired individuals who are at risk for aspiration. Indeed, it may be preferable to use dilute barium rather than water-soluble contrast agents routinely for these postdilation esophagrams, but this contention has not been validated by formal investigation. Finally, it has been estimated that approximately 2% of patients treated with pneumatic dilation will develop reflux esophagitis because of the resulting LES hypotension. Indeed, aggressive pneumatic dilation essentially changes the manometric features of achalasia to those of scleroderma, a disorder often associated with severe GERD. One recent study describes abnormal acid reflux by 24-hour esophageal pH monitoring in 6 of 17 patients who had pneumatic dilation. With the availability of highly effective antireflux therapies such as proton pump inhibitors, concerns about the induction of GERD by pneumatic dilation need not be overriding.

Surgical myotomy, in which the surgeon weakens the LES by cutting its muscle fibers, traditionally has been viewed as the primary alternative to pneumatic dilation for achalasia. Cardiomyotomy was first performed in 1913 by Ernst Heller, and modern surgeons now use modifications of Heller’s original procedure. The standard “open” myotomy can be performed using either an abdominal or, more commonly, a thoracic approach. Recently, a number of centers have reported their preliminary results with minimally invasive surgery for achalasia in which laparoscopic or thoracoscopic techniques are used to perform the myotomy. Other important differences in technique among centers include variations in the length and depth of the myotomy incision and whether or not the myotomy is combined with an antireflux procedure. Surgical myotomy results in good to excellent relief of symptoms in 70%–90% of patients, with few serious complications and a mortality rate similar to that reported for pneumatic dilation (approximately 0.3%). Reflux esophagitis (which may be complicated by esophageal ulceration, stricture, and Barrett’s esophagus) has been found to develop in approximately 11% of patients treated by surgical myotomy, and surgeons continue to debate the need for the addition of an antireflux procedure. The addition of a fundoplication appears to reduce the rate of symptomatic, postmyotomy GERD to approximately 4% but may increase the frequency of postoperative dysphagia by imposing a valve between the aperistaltic esophagus and the stomach. In the absence of well-designed prospective studies, the debate over the need for fundoplication in this setting remains unresolved. However, the recent availability of highly effective medical antireflux therapies such as...
proton pump inhibitors should simplify the management of postoperative GERD considerably and perhaps obviate routine fundoplication.

Late recurrence of dysphagia after surgical myotomy or pneumatic dilation may be caused by a return of tone in the damaged LES muscle, by GERD with peptic stricture formation, or very rarely by squamous cell carcinoma of the esophagus that develops with increased frequency in patients with achalasia.\(^\text{192}\) Endoscopic examination should readily differentiate these disorders. Late recurrence of dysphagia appears to be less common after surgical myotomy than after pneumatic dilation, but postoperative recurrence of dysphagia is not unusual after surgical treatment. For example, Jara et al.\(^\text{176}\) describe a sustained remission rate of 81% after 10 years for patients treated with esophagomyotomy. Ellis et al. performed a Kaplan-Meier analysis on the results of esophagomyotomy in 81 patients and estimated sustained remission rates of 86% at 15 years and 67% at 20 years.\(^\text{193}\) Malthaner et al.\(^\text{194}\) also found a deterioration of surgical results over time with good to excellent results reported by 21 of 22 patients (95%) at 1 year, 17 of 22 (77%) at 5 years, 15 of 22 (68%) at 10 years, 11 of 16 (69%) at 15 years, and 6 of 9 (67%) at 20 years or more.

Relatively few studies have directly compared the results of myotomy and pneumatic dilation. In one retrospective study, Okike et al.\(^\text{177}\) reported good to excellent relief of dysphagia in 85% of 468 patients treated with myotomy compared with only 65% of 431 patients who underwent pneumatic dilation for achalasia. In another retrospective review, Anselmino et al.\(^\text{195}\) concluded that surgery was safer and more effective than pneumatic dilation, although the outcome of pneumatic dilation in this study was far worse than that reported by most investigators (i.e., 15% rate of esophageal rupture, 39% rate of dysphagia relief after a mean follow-up of 55 months). In contrast, Abid et al.\(^\text{196}\) reviewed their experience with pneumatic dilation (36 patients) and surgical myotomy (9 patients) in patients followed up for a mean interval of approximately 2 years and concluded that the procedures are equally effective (success rate for both procedures, approximately 90%) if both are performed by skilled operators. In one of the two prospective, randomized trials of myotomy and pneumatic dilation reported to date, Csendes et al.\(^\text{197}\) describe excellent results after a median follow-up of approximately 5 years in 40 of 42 (95%) patients in the surgical group, compared with 24 of 37 (65%) patients who underwent pneumatic dilation. This study has been criticized for using a pneumatic dilation protocol that may have been suboptimal (i.e., use of atropine as premedication, low balloon inflation pressures, short duration of inflation),\(^\text{198}\) but as noted above, these technical factors have not been shown to affect the outcome of pneumatic dilation. A recent, smaller randomized trial of balloon dilation and myotomy found the two procedures equally effective in relieving dysphagia for up to 3 years.\(^\text{199}\) Despite the limitations of the available studies, it appears that surgery generally is superior to pneumatic dilation for both short-term and long-term relief of dysphagia. Furthermore, the rate of serious complications such as esophageal perforation appears to be less for surgically treated patients, and the mortality rates for the two procedures are approximately equal. The major disadvantages for surgery are the high initial cost, protracted recovery period, and frequent development of GERD postoperatively. A recent cost analysis comparing open surgery and pneumatic dilation concluded that initial pneumatic dilation (with surgery reserved for dilation failures) was the most cost-effective approach.\(^\text{157}\) However, this analysis did not consider myotomy performed by minimally invasive techniques. The short-term relief of dysphagia by minimally invasive surgery appears to be at least as good as that described for the open procedure, but long-term results are not yet available because the procedures are so new. Prospective, comparative studies are sorely needed in this area. If laparoscopic or thoracoscopic techniques enable surgeons to perform myotomy at reduced cost and with shorter recovery periods, if the operation is shown to be durable, and if the incidence of severe GERD is acceptably low, then myotomy by minimally invasive techniques may well be more cost-effective than pneumatic dilation. Pending the results of long-term studies on minimally invasive surgery, however, the decision between pneumatic dilation and myotomy as initial therapy for achalasia should be based on a consideration of the patient's preferences and on the availability of personnel experienced in the two techniques.

Recently, an interesting new approach to the treatment of achalasia has been introduced by Pasricha et al.\(^\text{200–203}\) These investigators noted that botulinum toxin, a potent inhibitor of the release of acetylcholine from nerve endings, has been used successfully for decades to treat certain spastic disorders of skeletal muscle such as blepharospasm. They hypothesized that the local, perendoscopic injection of botulinum toxin into the LES of patients with achalasia would poison the excitatory (acetylcholine-releasing) neurons that contribute to LES smooth muscle tone, thereby effecting a therapeutic decrease in LES pressure. The investigators tested their hypothesis in an animal model and verified that local botulinum toxin injection caused a significant decrease in LES pressure in piglets.\(^\text{200}\) Later, a pilot study in 10
patients with achalasia suggested a beneficial therapeutic effect for botulinum toxin injection of the LES, an effect that was confirmed in a double-blind, placebo-controlled trial in 21 patients. Most recently, this group has described the results of botulinum toxin injection in 31 patients with achalasia. Twenty-eight of the 31 patients (90%) showed immediate symptomatic improvement, but this effect was short-lived in many cases. Despite repeated injections of the toxin when symptoms returned, only 20 of the 31 patients (65%) remained in remission 6 months after the initial treatment. In these 20 responders, botulinum toxin injection caused resting LES pressure to decrease by 45% compared with baseline values. During a median follow-up of 2.4 years, however, 19 of the 20 responders experienced a relapse of symptoms that required further therapy. Among 15 of these patients who were treated with another botulinum toxin injection, only 9 had sustained remission. Kaplan–Meier analysis suggested that only 68% of patients in remission at 6 months would remain in remission at the end of 1 year. The median duration of remission after initial treatment was 16 months, and the longest remission observed was 28 months. Other groups have confirmed the short-term efficacy of botulinum toxin injection. Pasricha et al. note that like pneumatic dilation, botulinum toxin injection was more effective in older patients (82% response rate for patients age ≥50 years vs. 43% in younger patients). They also note that the toxin was 100% effective for patients with vigorous achalasia (defined by the presence of pressure waves in the esophageal body with amplitudes >40 mm Hg), whereas only 52% of patients with classic achalasia showed a clinical response at 6 months. However, another group of investigators did not find a difference in response to botulinum toxin injection between patients with vigorous and classic achalasia. Botulinum toxin injection appears to be remarkably safe. Approximately 25% of patients experience transient, mild chest pain immediately after the procedure, and fewer than 5% of patients develop symptomatic GERD. The most serious complication reported to date is a case report of a patient who developed severe, ulcerative esophagitis (probably caused by acid reflux) after toxin injection. This patient also was found to have adhesions and peri-esophageal inflammation when he subsequently underwent surgical treatment for achalasia. These studies suggest that botulinum toxin injection of the LES is a remarkably safe procedure that can induce a clinical remission for at least 6 months in approximately two thirds of patients with achalasia. However, most patients need repeated injections to maintain the remission, and only approximately two thirds of those patients in remission at 6 months will remain in remission at 1 year despite repeated injections. Vaedi et al. recently reported the results of a prospective study in which 42 patients with achalasia were randomly assigned to receive either botulinum toxin injection or pneumatic dilation. At 12 months, only 32% of patients treated with botulinum injection were in symptomatic remission, compared with 70% of patients in the pneumatic dilation group.

Castell and Katzka point out that botulinum toxin therapy is expensive (approximately $300 just for the botulinum toxin used at each treatment session), the failure rate is substantial, patients frequently need repeated injections, and the long-term efficacy of the procedure is unknown. These concerns, combined with the very poor response rate found in patients under the age of 50, suggest that botulinum toxin injection may not be the ideal choice of therapy for young patients with achalasia. Further studies are needed before the procedure can be recommended for clinical application outside of research protocols. Presently, botulinum toxin injection can be considered for the treatment of patients who have serious comorbidities and for whom pneumatic dilation or surgical myotomy poses inordinate risks.

Other experimental therapies have been proposed for the treatment of achalasia, including endoscopic myotomy of the LES using a needle-knife and perendoscopic injection of ethanamine into the LES. Although preliminary reports are interesting, far more investigation is needed before these potentially hazardous treatments can be recommended for clinical use. In very rare patients in whom all reasonable therapies have failed, esophageal resection and reconstruction may be considered as a last resort. Finally, a feeding gastrostomy can be considered for patients in whom all reasonable primary therapies for achalasia have failed or for very elderly and infirm patients for whom other therapies may be hazardous. Few published data are available on the use of gastrostomy for patients with achalasia, but many neurologically intact patients undoubtedly will find this therapy unacceptable.

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