Disorders of esophageal motility and sensation are relatively rare in the general population. Because their prevalence generally increases with age \[1,2\], more patients are expected to present with these disorders as the average age of the population increases. The rarity of these disorders, combined with the lack of specificity in their clinical presentation, makes early diagnosis a challenge. All of the currently available treatments are at best palliative, and their benefit may be offset by side effects and complications that require additional therapy. Despite treatment, progression of the underlying disorder occurs frequently, so that ongoing follow-up is necessary to manage symptom relapse and complications. Although rarely life-threatening, these disorders have substantial effects on the quality of life experienced by afflicted patients \[3,4\]. The magnitude of anxiety and suffering that these disorders engender is readily evident from Internet postings by members of disease-specific patient support groups. Quality care of these patients requires technical and cognitive mastery of the various diagnostic and treatment modalities, along with clinical acumen and compassion in helping patients cope with a chronic illness.

This article develops an algorithmic approach to the evaluation of idiopathic and secondary esophageal motor and sensory disorders, with the exception of those related to gastroesophageal reflux disease (GERD). Readers are strongly encouraged to review the article on GERD elsewhere in this issue. This article also does not cover sensory and motor disorders of the oropharynx.

Although the article title suggests that sensory and motor disorders are separate entities, a common clinical scenario is the conjoint manifestation of these problems in any single patient. Indeed, it is often hard to determine whether the sensory or the motor disturbance is the dominant agent for symptoms. A final introductory caveat is that although sensory and motor disorders comprise a wide range of conditions, their underlying mechanisms and many clinical effects share a common basis.
spectrum, the condition with the greatest body of information and consensus on clinical approach is esophageal achalasia. Evaluation and management of achalasia of necessity dominates the article, as does the use of achalasia to exemplify important concepts in the general approach to all such disorders.

**ARE SYMPTOMS PRESENT THAT SUGGEST AN ESOPHAGEAL MOTOR OR SENSORY DISORDER?**

The first step in diagnosing an esophageal sensorimotor disorder is to recognize that the patient's presentation is consistent with such a disorder (Fig. 1). The repertoire of presenting symptoms for esophageal sensorimotor disturbances is relatively limited. Symptomatic presentation of esophageal sensory and motor disorders is as follows:

- **Primary symptoms of disorder**
  - Dysphagia for solids and liquids
  - Chest pain or heartburn
  - Regurgitation or vomiting
  - Coughing or choking
  - Hiccups, eructation
  - Halitosis
  - Globus
  - Altered diet or eating behavior

- **Secondary symptoms from complications**
  - Weight loss
  - Fever
  - Respiratory symptoms
  - Hematemesis

Individual symptoms or constellations of symptoms are inconsistently present. For example, although the classic hallmark of motor disorders is dysphagia for both solids and liquids, dysphagia is an initial symptom in less than half of achalasia patients [5]. Certain features of the symptoms suggest the presence of a sensorimotor disorder. More difficulty is reported with cold or carbonated beverages, whereas warm drinks may improve symptoms. Patients may get up from the meal to walk around or arch their neck to move the swallowed material into the stomach [5]. Belching is not a spontaneous event that relieves a sense of gastric distention; instead, it is an event induced by air swallowing to try to remove air trapped in the top of the esophagus. Regurgitated food is not sour and has a taste similar to that when originally swallowed. Regurgitation of such food often occurs hours after it was consumed. Rather than food, the patient may bring up a bland foam-laden liquid, essentially the saliva that was swallowed throughout the day. Food particles are found on the bedclothes in the morning. Elicitation of these features often requires pointed questioning of the patient or family and at times direct observation of patient behavior during a challenge of eating and drinking.

The symptoms typically begin insidiously and progress gradually over the course of weeks-to-months. The course of symptom progression is not always
relentless. For milder disorders, symptoms may only appear intermittently (but, to the patient’s consternation, often not predictably). Patient modification of eating habits and diet can give a false semblance of remission or reversal of the disorder. The dominant symptom can also change as the disorder progresses. For example, a common history in achalasia is that the major symptom early in the course is chest discomfort, to be replaced by dysphagia and eventually regurgitation, as the esophagus progressively dilates. Rarely, the patient has no primary symptom. This is more likely to be the case in patients with cognitive disturbances or developmental disorders, as with achalasia in patients
with Down syndrome [6]. In such cases, presence of the disorder becomes recognized during the evaluation of a complication (eg, aspiration pneumonia), or by chance during evaluation of another condition (eg, dilated esophagus seen on a CT scan performed to rule out pulmonary embolism).

Symptoms in patients may reflect complications of the disease. Respiratory symptoms can result from aspiration pneumonia or a piece of regurgitated food lodged in a bronchus. Rarely, achalasia presents with life-threatening acute respiratory distress from occlusion of the airway by the distended esophagus [7]. Hematemesis may be from a Mallory-Weiss tear from retching or a bleeding esophageal cancer. Weight loss would seem to be an obvious symptom of a condition that makes eating a challenge. As the prevalence of obesity has increased in the United States population, however, more patients with achalasia have been encountered who continue to gain weight despite the disorder to the point of warranting bariatric surgery [8]. One should not conclude that the patient with weight gain cannot have a major esophageal sensorimotor disorder.

The standard physical examination is essentially unhelpful in determining the presence of a sensorimotor disorder per se. Physical findings may offer a clue to the presence of conditions causing secondary sensorimotor disturbances or the presence of complications from such disturbances.

**HAVE MORE COMMON CAUSES FOR THESE SYMPTOMS BEEN EXCLUDED?**

Two fundamental problems interact to impede attempts at making a presumptive diagnosis of an esophageal sensorimotor disorder based on symptoms. First, none of the individual symptoms are pathognomonic for a specific disorder or the general category of sensorimotor disorders. All of the primary and secondary symptoms listed previously have been reported in some fashion by patients with GERD. For example, in one series of patients studied manometrically for mixed solid-liquid dysphagia, GERD was over twice as prevalent as achalasia [9]. Second, sensorimotor disorders of the esophagus are extremely rare, especially when compared with the presence of GERD. As an example, the annual incidence of achalasia is about 1 per 200,000 population [10]. Given that about 1 out of 20 adults has daily symptoms caused by GERD, any given patient presenting with esophageal symptoms is about 10,000 times more likely to have GERD than achalasia. Even in a patient with multiple classic symptom features, the probability is still overwhelming that the patient has atypical GERD, not typical achalasia. More problematic still are the patients who initially have GERD and subsequently develop a separate disorder, such as achalasia [11,12].

The combination of rarity and symptom nonspecificity causes considerable delay between the onset of symptoms and the diagnosis of esophageal sensorimotor disorders. For achalasia, this diagnostic delay averages about 5 years [13,14]. Although it is frustrating for patients to be mistakenly diagnosed and treated initially as having GERD, most patients with similar symptoms are
going to have GERD and are likely to respond to treatment. Even patients who fail to respond to such treatment are more likely to be patients with GERD who need a different treatment regimen than patients with a separate sensorimotor disorder. For patients with alarm symptoms, such as progressive dysphagia, the standard diagnostic test (endoscopy) can be nondiagnostic for both conditions. Most patients undergo endoscopy and unsuccessful courses of treatment for GERD before the diagnosis of an esophageal sensorimotor disorder is considered.

GERD is the most common of a diverse range of other conditions that must be considered in the differential diagnosis of esophageal sensorimotor disorders, listed as follows:

<table>
<thead>
<tr>
<th>Structural esophageal disorders</th>
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<tbody>
<tr>
<td>Rings, webs, caustic and inflammatory strictures</td>
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<tr>
<td>Eosinophilic esophagitis</td>
</tr>
<tr>
<td>Intrinsic neoplasm</td>
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<tr>
<td>Extrinsic compression (neoplasm, vascular, inflammatory)</td>
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<tr>
<td>Congenital atresia or fistula</td>
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<td>Inflammatory esophageal disorders</td>
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<tr>
<td>Reflux esophagitis</td>
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<tr>
<td>Infection (fungal, viral)</td>
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<td>Radiation</td>
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<tr>
<td>Medication (pill injury)</td>
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<tr>
<td>Nonesophageal functional and motor disorders</td>
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<tr>
<td>Oropharyngeal motor disorders</td>
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<tr>
<td>Bulimia</td>
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<tr>
<td>Cyclic vomiting syndrome</td>
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<tr>
<td>Rumination</td>
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<tr>
<td>Gastroparesis</td>
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<tr>
<td>Hyperemesis gravidarum</td>
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<tr>
<td>Disorders of other organ systems</td>
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<tr>
<td>Cardiovascular disease</td>
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<tr>
<td>Pulmonary disease</td>
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<tr>
<td>Musculoskeletal disorders of the chest</td>
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<tr>
<td>Postherpetic and other sensory neuropathies</td>
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<td>Iatrogenic complications</td>
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<tr>
<td>Dysfunctional antireflux procedure</td>
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</tbody>
</table>

The presence of many of these as the cause for symptoms becomes readily apparent after a careful history, physical examination, and evaluation by standard tests, such as endoscopy, barium esophagrams, and CT imaging of the chest and abdomen. Among this broad list, several conditions warrant specific discussion. In the patient whose dominant symptoms are chest discomfort rather than altered bolus transit, great care should be taken to ensure that the symptoms are not a result of underlying cardiovascular disease. Although a delay in the accurate diagnosis of an esophageal sensorimotor disorder can affect quality of life, a delay in the diagnosis of coronary artery disease can be fatal. Eosinophilic esophagitis is being diagnosed with increasing frequency.
Although certain characteristic features have been identified, these are not universally present, nor are the endoscopic, radiographic, and pathologic features always recognized when they are present. To avoid missing this diagnosis, the endoscopist needs to obtain esophageal biopsies from multiple sites and the pathologist needs to quantify the number of eosinophils per high-powered field. Patients with a tight fundoplication wrap may have a normal endoscopic and radiographic evaluation. The standard esophagram misses oropharyngeal motor disorders; if these are in the differential diagnosis, a videotaped fluoroscopic swallow study with a speech pathologist should be performed.

DO TEST FINDINGS SUPPORT THE DIAGNOSIS OF AN ESOPHAGEAL SENSORIMOTOR DISORDER?

Because the symptoms of esophageal sensorimotor disorders are nonspecific, once likely alternative causes for the symptoms are excluded, additional testing is required to support the clinical hypothesis that such a disorder is present. Testing for these disorders is imperfect and should serve as adjuncts to, not substitutes for, diagnostic reasoning.

Testing for Esophageal Motor Disorders

Testing for esophageal motor disorders is fraught with several conceptual and methodologic difficulties. First, the tests currently clinically available only provide information on the phenotype of the disorder. That is, they delineate alterations in esophageal morphology, muscle activity, and bolus transit without elucidating the underlying pathophysiologic disturbances contributing to the phenotype. Different disease processes may manifest an indistinguishable phenotype on a given test, the classic example being the similar manometric findings of idiopathic achalasia and pseudoachalasia from adenocarcinoma of the cardia [16].

Second, because the underlying pathophysiology is unknown, constellations of findings on the diagnostic test have been used as the gold standard for deciding that the disorder is present. Such gold standards have commonly been determined by expert consensus or statistical parameters (ie, a value on a given measurement that is outside the 95% confidence interval of a control group). In many cases, these gold standards lack rigorous evidence for validity (in terms of predicting natural disease course or response to therapy) or reproducibility. Diagnoses based on a finding being outside the normal range are particularly problematic because, by definition, 5% of normal subjects have this finding, and these normal “outliers” may be over 100 times more prevalent in the population than patients with true motor disorders who have similar outlying values. Because there can be considerable random variation in a parameter over time, a group of patients who are categorized as abnormal based on an outlier value on a single test have some members of that group revert to a normal value on repeat testing (regression to the mean), as has been demonstrated with hypertensive peristalsis [17].

Third, considerable functional variability can exist within a diagnosis. For example, by definition, diffuse esophageal spasm can range from a patient
with infrequent (20%) normal amplitude simultaneous contractions but otherwise normal motility to a patient in whom nearly every swallow results in high-amplitude, long-duration simultaneous contractions. Even in such a disorder as esophageal achalasia, which has considerable expert consensus about the diagnostic criteria, variant forms have been recognized [18]. Fourth, published diagnostic criteria for different disorders are inconsistently applied to manometric findings by different clinicians [19].

Fifth, there is little consensus for the testing apparatus used or the testing protocol followed among different motility centers. Normal values may vary greatly among manometry laboratories if they use different catheters and score pressure phenomena differently. Lack of uniformity in formatting of manometry data across different systems can make it nearly impossible for a person in one laboratory to interpret the raw data from a manometric study performed in another laboratory. Finally, one needs to distinguish between testing to document the presence of an esophageal sensorimotor disorder and testing to determine if the disorder is the cause of a particular symptom. This is especially true when motor disorders are identified, but the symptoms are more related to pain than abnormal bolus transport.

Several tests are available to help establish the diagnosis of an esophageal motor disorder.

**Tests for motor dysfunction**
- Endoscopy
- Barium radiography
- Esophageal scintigraphy
- Manometry
- Impedance testing
- Endosonography

Endoscopy is used more to exclude other causes for the symptoms than to diagnose a sensorimotor disorder. Certain findings on endoscopy can suggest the presence of some disorders. An obviously dilated esophageal lumen with substantial fluid retention and no obstructing structural lesion is highly suggestive of achalasia. Failure to observe peristaltic contractions with swallows on endoscopy, and abnormal opening patterns of the gastroesophageal junction with swallows, have been reported to be accurate in distinguishing the extreme motor disorders of achalasia and scleroderma esophagus from normal motility [20]. The use of endoscopy to detect more subtle motor disturbances remains untested.

Both fluoroscopy and scintigraphy have been used in the evaluation of esophageal motor disorders. Both are excellent at detecting the gross disturbances in bolus transit through the esophagus that can be a consequence of some motor disorders. Abnormal temporal patterns of bolus deformation on radiology can suggest the presence of failed or weak contractions; simultaneous (spastic) contractions; or retrograde contractions. Neither modality can identify a contraction abnormality in a region of esophagus that has been cleared of bolus material, so that patients with hypertensive peristalsis are usually not detected by these.
techniques [21,22]. These tests are operator-dependent, and some radiologists fail to appreciate the characteristic features of even a standard motor disorder, such as achalasia [23]. Variant and early forms of achalasia are even less well recognized, so that the sensitivity for radiology and scintigraphy in the detection of achalasia is suboptimal [24]. This is becoming more of a problem as radiologists in training in the United States devote less time and enthusiasm to mastery of these techniques. This author’s clinical perception is that unseasoned radiologists are often overcalling motor disturbances, because of a failure to appreciate the effects of normal physiologic processes on bolus transport, such as deglutitive inhibition and refractory periods with closely spaced swallows, the normal degree of retrograde bolus escape seen in the transition zone region between the striated and smooth muscle in the proximal esophagus, and the normal inefficient clearance of solid boluses with single swallows [25,26]. The risks of radiation exposure limit the duration of these studies.

Manometric studies of esophageal motor function have traditionally been used as the gold standard for determining the presence and classification of an esophageal motor disorder. Clear advantages for manometry over radiology and scintigraphy are the ability to perform prolonged studies and detect motor abnormalities in regions of the esophagus not occupied by a bolus at the time of observation. Methodologic limitations for manometry until recently have been a lack of adequate spatial resolution for most systems. This can result in two problems. One is the likelihood of missing focal abnormalities (uncoordinated or weak contractions) that occur between two widely spaced sensors. The other is the axial dislocation of a high-pressure zone off of a point sensor, resulting in the spurious finding of relaxation. The manometric sleeve device was developed to allow continuous recording of high-pressure zones, such as the lower esophageal sphincter (LES), during axial movement [27], identifying the failed relaxation of the LES with deglutition in achalasia. Accurate interpretation of sleeve findings requires careful positioning of the sleeve relative to the sphincter. If the sphincter is located too close to the proximal end of the sleeve, the sphincter moves off of the sleeve with deglutition, imparting a false sense of relaxation. Although the customary position of the top of the sleeve is 2 cm above the top of the sphincter high-pressure zone, it is clear that in some circumstances more vigorous axial displacement is possible [28]. Such displacement may well account for the unexpectedly frequent occurrence of LES relaxations in conjunction with vigorous esophageal body contractions during ambulatory sleeve recordings in achalasia patients [29]. As a practical rule, if the sleeve seems to record LES relaxations that are simultaneous with vigorous proximal esophageal body contractions, recordings should be repeated with the sleeve repositioned at least 2 cm more proximally.

Like radiographic methods, esophageal manometry is exceedingly dependent on the expertise of the operator. Few trainees in gastroenterology devote sufficient time and concentration in the technique. Failure to appreciate the limitations of the manometric recording apparatus, and a lack of knowledge about esophageal anatomy and physiology, are the major reasons for the need to
repeat studies performed elsewhere. In this author’s experience, the most common errors are a failure to identify incomplete LES relaxations because of use of a single point sensor, misdiagnosis of ineffective motility by recording from a hiatal hernia instead of the distal esophagus, misinterpretation of intrabolus pressures as esophageal contractions, and failure to appreciate the effect of dry swallows and upright body position on peristaltic amplitude and velocity [30–32]. Because atypical features are inconsistently interpreted and consensus criteria for diagnosis are not uniformly applied, diagnostic agreement on study interpretation, even at expert centers, can be poor for certain disorders [19]. Given these difficulties in assigning diagnostic labels to manometric findings, a reasonable approach may be instead to report the component abnormalities in sphincter and esophageal body motor function [33,34].

Newer techniques of high-resolution solid-state manometry, esophageal impedance, and endosonography may revolutionize the assessment of these patients in the future. The performance characteristics of these tests are covered in more detail elsewhere in this issue.

Testing for Esophageal Sensory Disorders
Positive diagnosis of esophageal sensory disorders remains problematic. Sensory disorders tend to be considered only after nonesophageal disorders (eg, cardiac disease), GERD, and esophageal motor disorders have been ruled-out by testing. Evidence against this approach comes from studies indicating that these different disorders may occur together in groups of patients with chest pain [35–37]. Ideally, a diagnostic test for esophageal sensory disturbances has reproducibility and clinical validity even when other disorders are present. Diagnostic tests for esophageal sensory and motor disorders include the following:

- Tests for sensory dysfunction
- Esophageal distension
- Esophageal electrical stimulation
- Pharmacologic provocation
- Esophageal acid perfusion

A variety of stimuli have been applied to the esophagus to demonstrate that selected groups of patients with chest symptoms have reduced thresholds for discomfort or higher perceptions of pain, when compared with normal subjects. Some of these stimuli could potentially cause symptomatic motor responses; however, response to noxious stimuli after blockade of motor responses supports the presence of visceral hypersensitivity [38].

Several factors have limited the clinical use of provocative sensory testing for diagnosing esophageal sensory disorders. First, the techniques for stimulus production vary considerably among laboratories, with accompanying variation in normal values. The manner in which the stimulus is applied can significantly affect the threshold for symptom induction [39]. Second, there is a high risk of response bias, requiring blinding of the test administrator and the patient to the stimulus [40]. Third, studies have shown significant age and gender differences in sensory thresholds [41,42].
Fourth, although studies have shown significant differences between patients with chest symptoms and asymptomatic controls, the range of responses between the two groups often overlaps. Some otherwise normal subjects have been identified as having esophageal hypersensitivity, based on their outlier responses to testing [43]. For most tests, data on sensitivity and specificity are either not available or inadequate because of a lack of sufficient sample size or performance of a receiver operating characteristic curve analysis to determine the optimal test threshold for diagnosis. Fifth, patients may have a positive response to one stimulus but not another. Use of multiple stimuli is likely to improve sensitivity at the expense of specificity. Use of multiple sequential stimuli at the same test setting also runs the risk of inducing altered responses because of central sensitization [44].

From these considerations, it is evident that any laboratory proposing to perform a diagnostic test battery for abnormal esophageal sensitivity cannot assume that its protocol precisely matches those from published studies. This means that each laboratory needs to develop its own set of normal data for its specific protocol. Such a data set needs to include subjects rigorously tested for the presence of other symptomatic disorders and report normal value ranges adjusted for age and gender.

Although the usual clinical emphasis is on hypersensitive disorders, some patients may have reduced esophageal sensitivity. Reduced sensitivity has been demonstrated in patients with achalasia [45] and Chagas’ disease [46]. Abnormal sensory pathways may result in a failure to elicit normal clearing peristaltic contractions in response to a retained esophageal bolus [47]. Despite its potential importance, testing for esophageal hyposensitivity is almost never performed clinically.

IS THE SENSORIMOTOR DISORDER IDIOPATHIC, OR DOES IT RESULT FROM ANOTHER CONDITION?
When esophageal sensorimotor abnormalities have been identified, the clinician needs to determine whether they are primary (idiopathic) or are a secondary manifestation of another disorder. Secondary etiologies for esophageal sensory and motor disorders include the following:

- Neoplastic
  - Adenocarcinoma of the cardia
  - Small cell carcinoma (anti-Hu)
  - Amyloidosis
- Neurologic disorders
  - Parkinson’s disease
  - Multiple sclerosis
  - Autonomic or sensory neuropathies
- Inflammatory or autoimmune disorders
  - Chagas’ disease
  - Connective tissue disorders
  - Eosinophilic esophagitis
For some conditions, the medical history, examination findings, and other laboratory tests may have already confirmed the presence of the underlying disorder, and the role of esophageal function testing is to confirm that this organ is also affected and causing symptoms. The esophageal manifestations, however, can sometimes be the presenting feature of the disease. An important example of this is the development of an achalasia phenotype as a paraneoplastic response months before the underlying small cell carcinoma can be detected [48]. In patients with Allgrove’s syndrome, the esophageal motor disturbance can develop before the life-threatening adrenal insufficiency [49]. The entity of pseudoachalasia arising from adenocarcinoma of the gastric cardia requires specific mention, because this condition can on manometry be indistinguishable from idiopathic achalasia. Although frequently identified at endoscopy, at times CT scanning or endosonography is required to identify the lesion. Pseudoachalasia should be suspected in patients presenting at an older age, with a rapid symptom course and substantial weight loss [50]. Rare cases of eosinophilic esophagitis presenting as secondary motor rather than mucosal disorders can be extremely difficult to diagnose [51].

**ARE THERE ADDITIONAL DISORDERS PRESENT TO CAUSE OR MODULATE SYMPTOMS?**

At times, one is fortunate to identify an esophageal sensorimotor disorder relatively early in the presentation and diagnostic work-up. In such cases, one has to be cognizant of the potential for a more common disorder to be present also and contributing to the clinical picture. The 65-year-old hyperlipidemic smoker with dysphagia and chest pain may have both achalasia and unstable angina. Abnormal esophageal acid exposure is a common finding in hypertensive peristalsis. Symptoms may result from a complication of the disorder, rather than the inherent pathophysiology of the disorder. An example is odynophagia from an ulcer caused by a retained caustic medication. For secondary
disorders, symptoms may be another manifestation of the underlying disorder, such as chest pain resulting from diabetic sensory neuropathy.

Since the classic studies of Wolf and Almy [52], it has been known that psychologic stressors can modulate esophageal sensorimotor disorders. Psychiatric disorders are common among patients with esophageal motor disorders referred for diagnostic testing [53], although patients with similar symptoms and no motor disorders are also found to have evidence for depression, anxiety, and somatization [54]. In such patient groups, psychiatric disturbance is more closely associated with symptoms of chest pain than dysphagia [54]. Acute stress can modify esophageal contractions [55] and perception thresholds for heartburn [56]. Often unappreciated is the effect of stress on diaphragmatic crural function [57], contraction of which can impair esophageal emptying [58]. One has to be wary of this phenomenon in anxious patients, to avoid misdiagnosis of a disorder of smooth muscle LES relaxation.

**WHAT THERAPIES SHOULD BE USED IN PATIENTS WITH SENSORIMOTOR ESOPHAGEAL DISORDERS?**

When devising a treatment plan for esophageal sensorimotor disorders, several issues must be considered. The first issue is whether the severity of the disturbance and its effect on the patient’s overall health and quality of life are severe enough to warrant treatment. A patient with isolated episodes of brief chest discomfort or bolus hesitancy every few days or weeks from a focal and intermittent discoordination of contractions in the esophageal body may require no treatment other than an explanation and reassurance. Studies have suggested that following confirmation of an esophageal disorder by testing, patients have less hospital use and fewer absences from work and social functions [59]. Many patients who are found to have less severe motor disorders exhibit improvement in symptoms over time [60]. At the other extreme, the patient with substantial weight loss and dehydration from near daily regurgitation and vomiting or with recurrent aspiration pneumonia is going to require more definitive therapy.

The second issue when considering treatment is that none of the therapies available at present correct the underlying disorder. These treatments are at best palliative for the dominant symptoms of the patient. All available treatments have the potential for side effects and complications, which need to be considered carefully in the context of the patient’s overall health, comorbid illnesses, and life expectancy. Treatments often lack a durable response or lose their benefit as the underlying disease progresses. The evidence for many treatments is anecdotal at best, with few controlled clinical trials to support efficacy. When competing treatments are available for a disorder, few have undergone comparisons in appropriately designed clinical trials of adequate length.

If symptoms are severe enough to warrant active treatment, one then has to decide which pathophysiologic processes are responsible for the symptoms. Although the dichotomy is not perfect, motor disturbances are more likely to
have symptoms of bolus transport (eg, dysphagia, regurgitation), whereas hyper-sensitivity is more likely to result in symptoms of pain.

**Treatment of Motor Disorders**

Motor disorders from a functional standpoint can be divided into two broad categories: disorders of outflow obstruction from an inadequately relaxing LES and disorders of peristaltic bolus transport in the esophageal body. Esophageal body disorders can be divided into disorders of inadequate peristaltic propulsive strength and disorders of abnormal contraction sequencing (spasm). Interactions between LES and esophageal body dysfunction determine the pattern of abnormal bolus transport and the therapeutic approach (Fig. 2). Findings on manometric and radiographic studies can help identify the disturbances of bolus transport.

![Selection of Therapeutic Options for Motor Disorders Based on Pattern of Motor Disturbances](image)

**Fig. 2.** Algorithm for selecting therapies for esophageal motor disorders. LES, lower esophageal sphincter.
Isolated disorders of inadequate propulsive strength leave bolus residue in the esophageal body. In the upright position the combined effects of gravity and the feeble propulsive force are usually sufficient to overcome resistance at the gastroesophageal junction and intragastric pressure, so that liquid boluses are almost completely cleared into the stomach. Nondeforming boluses that adhere to the esophageal wall may not clear at all until dissolved. The goal of therapy is to improve the strength of contractions, when possible.

Isolated disorders of contraction sequencing are commonly accompanied by a failure of descending inhibition [61,62]. Contractions distal to the bolus impair its entry into the stomach and can move the bolus retrograde. In the absence of outflow obstruction and with the benefit of gravity, however, there is no progressive retention of bolus with repeated swallows. The goal of currently available therapy is to diminish or abolish these abnormal contractions.

When outflow obstruction is present from abnormal LES relaxation, this needs to be reduced or eliminated to facilitate esophageal emptying. If peristaltic or spastic contractions can raise the pressure in the bolus sufficiently to propel it into the stomach, then significant esophageal retention is usually not observed.Symptoms may result from activation of pain receptors in regions where higher intrabolus pressures result in increased intramural tension. In this situation, reduction of both LES tone and esophageal body contractions may be beneficial.

When esophageal body contractions are insufficiently vigorous to generate an adequate pressure gradient to force the bolus through the LES, however, then esophageal retention occurs and esophageal contractions cannot occlude the lumen (Fig. 3). On manometry isobaric pressure waves are observed [63]. In this situation, pharmacologic agents that relax all smooth muscle are not helpful, because the reduction in LES pressure is offset by the reduction in esophageal body contractility that serves to move the bolus into the stomach. In this situation, targeted reduction of the outflow resistance is required.

Modifications of diet and lifestyle are the first line of treatment for motor disorders. Patients should eat and drink in an upright position and remain that way postprandially, so that gravity can facilitate esophageal clearance. Swallowing hot (60°C) water with meals may aid in bolus passage [64]. Peppermint may decrease spastic contractions [65]. Foods the patient identifies as provoking spasm should be avoided [66]. Patients with poor esophageal propulsive ability need to wash down food with liberal use of liquids. Carbonated beverages can also be helpful if significant outflow obstruction is absent.

A limited number of pharmacologic agents are available to alter tonic and phasic contractions of the LES and esophageal body. For increasing contractions, the only pathway available at present is through agents that mimic acetylcholine or enhance the availability of acetylcholine. Bethanechol has been shown acutely to increase esophageal contractions and improve bolus clearance in patients with GERD and severe ineffective motility [67,68]. This has not been evaluated in chronic studies in patients with disorders of ineffective motility.

More agents are available to inhibit contractions and tone. The major classes are nitrates, calcium channel blockers, anticholinergics, and phosphodiesterase
Fig. 3. Progression from nonisobaric to isobaric waves in an achalasia patient. Manometric tracing shows a sequence of one dry swallow followed by five wet (5 mL water) swallows. The top seven channels show pressure data from recording sites in the esophageal body (E1–6) placed 3 cm apart and from the LES (recorded with a sleeve device). Channel E1-LES is the difference between these two channels, with a positive value being favorable for bolus passage from the esophagus through the LES. Pressure scales are 0 to 100 mm Hg, except for the bottom channel (−50–+50 mm Hg.) Note that the periods of favorable pressure differential for esophageal emptying are of short duration and low magnitude, insufficient to allow complete esophageal emptying. The first few swallows show pressure waveforms that are different throughout the esophagus (nonisobaric). As the esophagus fills with retained fluid, however, the basal pressure rises, and the contractions are no longer able to occlude the esophageal lumen. The pressure they generate is transmitted uniformly throughout the retained fluid, resulting in the same pressure waveform being recorded on all of the sensors in the esophageal body (isobaric waves) by the third wet swallow. DS, dry swallow; LES, lower esophageal sphincter; WS, wet swallow.
inhibitors. Essentially, they serve to inhibit muscle tone directly or block the excitatory actions of acetylcholine. None work specifically on the LES or esophageal body. This may explain why nifedipine is reported to be beneficial in early achalasia [69], but does not improve esophageal emptying in most patients with established achalasia [70]. Symptomatic improvement in patients with spastic esophageal disorders has also been reported in patients with nitrates [71], and injection of botulinum toxin into the esophageal body [72,73]. With sildenafil, changes in motility were not accompanied by consistent improvement in symptoms [74]. All of these studies are unblinded and lack appropriate controls.

Selective reduction in LES pressure can be achieved currently by injection of botulinum toxin into the LES, pneumatic dilation of the LES, or myotomy of the LES. The published trials of these therapies are largely confined to patients with the diagnosis of achalasia. Of the three, botulinum toxin has the least risk for complications. The treatments must be repeated, however, and some patients develop resistance, likely from the development of antibodies to the toxin. Comparative trials of botulinum toxin to pneumatic dilation have shown similar initial results but more durable results long term with pneumatic dilation [75]. Botulinum toxin should be reserved for patients who are too frail to undergo pneumatic dilation or myotomy, have a life expectancy of less than 6 months, or require a short-term intervention until more definitive therapy can be arranged.

Pneumatic dilation is usually performed as an outpatient endoscopic procedure, with the patient able to return to usual activities the following day. The major immediate risk of the procedure is esophageal perforation, which occurs in about 2% and may require surgical repair. The risk for perforation increases with use of balloon pressures above 10 psi [76]. Patients often require one or two additional dilations to achieve a satisfactory clinical response in 80% to 90% of patients [77,78]. Younger patients, especially young men, are less likely to have a successful response [78,79].

Surgical myotomy has evolved to a laparoscopic abdominal procedure for most patients. The success with a single operation is in the range of 90% [78]. Although the need to add an antireflux to the myotomy is controversial [80], a recent randomized trial showed a benefit of a Dor antireflux procedure on esophageal acid exposure in the early postoperative period [81]. In patients with dysphagic symptoms from spastic esophageal contractions, extension of the myotomy up through the smooth muscle portion of the esophageal body can be considered, but the outcomes are not as uniformly beneficial as those for achalasia [82,83]. Rarely, patients with a dilated, completely dysfunctional esophagus require esophagectomy. Patients too frail to undergo esophagectomy may require feeding by placement of a percutaneous endoscopic gastrostomy.

**Treatment of Sensory Disorders**

Diet and lifestyle modifications for patients with a hypersensitive esophagus are mostly a matter of avoiding foods and drinks that reproducibly cause
symptoms. Patients with a hyposensitive esophagus require counseling to avoid scalding liquids and pills that could injure the esophagus if their failed passage was not recognized. Such patients are also at risk for damage from unperceived acid reflux. Medical treatment for the hypersensitive esophagus has largely been with the use of low-doses of tricyclic antidepressants and trazodone [84,85]. Acute or short-term studies of the antidepressant citalopram [43], the 5-hydroxytryptamine4 receptor agonist tegaserod [86], and the phosphodiester-ase inhibitor theophylline [87] have shown reduction in symptoms or elevation of experimental pain thresholds. Their potential for long-term benefit is unclear. Patients with an acid-sensitive esophagus may benefit from acid-suppression therapy. Anticonvulsive agents are being used for other pain disorders, but there are no reported trials of their use in patients with esophageal sensory disorders to date.

Because patients can have both motor and sensory disorders of the esophagus, concurrent treatment for both may be indicated. The usual clinical practice is first to identify and treat motor disorders, with treatment for sensory disorders initiated on an empiric basis when symptoms persist and studies indicate that the motor disturbance has been reasonably palliated. Care must be taken, however, to avoid overly aggressive treatment of a motor disturbance when the symptoms are likely sensory in origin. For example, chest pain in patients with nutcracker esophagus responds poorly to myotomy [82].

**WHAT ARE THE CAUSES OF PERSISTENT OR RECURRENT SYMPTOMS AFTER TREATMENT?**

A fairly long list of conditions needs to be considered when the patient has symptoms after treatment (Table 1). When symptoms persist early after

<table>
<thead>
<tr>
<th>Category</th>
<th>Specific Causes</th>
<th>Timeframe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary treatment failure</td>
<td>Incomplete myotomy</td>
<td>Early</td>
</tr>
<tr>
<td>Complication of treatment</td>
<td>GERD, peptic ulcer, stricture</td>
<td>Early–late</td>
</tr>
<tr>
<td></td>
<td>Myotomy site scarring</td>
<td>Early–late</td>
</tr>
<tr>
<td></td>
<td>Postoperative hematoma</td>
<td>Early</td>
</tr>
<tr>
<td></td>
<td>Paraesophageal herniation</td>
<td>Early–late</td>
</tr>
<tr>
<td></td>
<td>Neuroma in operative field</td>
<td>Early–late</td>
</tr>
<tr>
<td></td>
<td>Refeeding edema</td>
<td>Early</td>
</tr>
<tr>
<td>iatrogenic injury</td>
<td>Obesity</td>
<td>Late</td>
</tr>
<tr>
<td>Comorbid condition</td>
<td>Pill injury</td>
<td>Early–late</td>
</tr>
<tr>
<td></td>
<td>Cardiovascular disease</td>
<td>Early–late</td>
</tr>
<tr>
<td></td>
<td>Psychiatric disorder or stress</td>
<td>Early–late</td>
</tr>
<tr>
<td></td>
<td>Second sensory or motor disorder</td>
<td>Early–late</td>
</tr>
<tr>
<td>Progression of disease</td>
<td>Dilated, sigmoid esophagus</td>
<td>Late</td>
</tr>
<tr>
<td>Complication of disease</td>
<td>Aspiration pneumonia</td>
<td>Early–late</td>
</tr>
<tr>
<td></td>
<td>Esophageal cancer</td>
<td>Late</td>
</tr>
</tbody>
</table>

Table 1: Etiologies for symptoms after treatment of esophageal sensory and motor disorders
treatment, the most likely problem is that the treatment simply failed to work. The reason for failure is often not evident, and the patient may need to be tried on a different therapy. A specific identifiable and remediable cause for treatment failure in achalasia is an incomplete myotomy, which could be treated with surgical completion of the myotomy or pneumatic dilation.

The two most common reasons for patients with achalasia to develop symptoms after an initially successful course of therapy are the development of GERD and progression of the underlying disease. Although GERD can develop following pneumatic dilation, it is much more common after a myotomy and becomes more prevalent with time even when an antireflux procedure has been performed. Disease progression can result from redevelopment of esophageal outflow obstruction, further deterioration in the contractile ability of the esophageal body, or a combination of the two. With sufficient follow-up, nearly half of achalasia patients treated by pneumatic dilation or surgery develop recurrent or new symptoms that require additional treatment. For this reason, patients with achalasia should remain in on-going follow-up after therapy to monitor for symptoms of disease progression or complications.

Diagnostic testing of persistent or recurring symptoms usually starts with endoscopy to look for the presence of esophagitis, stricture, neoplasm, and disrupted antireflux procedures. A timed barium esophagram can assess the functional impairment in esophageal emptying, and a solid bolus challenge may help detect a subtle stenosis. Manometry may be necessary to identify an incomplete myotomy, tight antireflux wrap, or inadequate reduction in LES pressure after pneumatic dilation. Esophageal pH-impedance monitoring can document symptomatic reflux. Rarely, CT scans of the chest are needed to identify seromas or hematomas that are causing outflow obstruction.

There are two additional points worth making for motor disorders when the posttreatment symptom is primarily pain, rather than dysphagia or regurgitation. First, another disorder may be present: the patient who develops new chest pain years after stable symptom remission may have angina. Second, the patient may have visceral hypersensitivity compounded by the coexistence of a psychiatric disorder or psychosocial stressors. This constellation of problems is unlikely to be solved by ever more aggressive attempts at improving motor function. The depressed achalasia patient, whose dominant problem of chest pain persists after an esophagectomy for same, is the epitome an unacceptable clinical outcome.

**SUMMARY**

Despite advances in pharmacologic, endoscopic, and surgical treatment, esophageal motor and sensory disorders remain a challenging problem for management, especially when complicated by the additional problems of psychiatric disease and psychosocial stressors. Although symptoms from minor disorders may respond to reassurance, patients with more significant disorders require a lifetime of follow-up. Patients require counseling about the nature and prognosis of their disease and instruction on dietary and lifestyle modifications.
Careful clinical reassessment is necessary when new symptoms emerge or old ones recur, because their cause and treatment may be different from those present at the outset of the disorder.

References


[90] Lopushinsky SR, Urbach DR. Pneumatic dilatation and surgical myotomy for achalasia. JAMA 2006;296(18):2227–33.
