1. What is the most difficult substance to swallow?
Water. Swallowing involves several phases. First, a preparatory phase involves chewing, sizing, shaping, and positioning of the bolus on the tongue. Then, during an oral phase, the bolus is propelled from the oral cavity into the pharynx while the airway is protected. Finally, the bolus is transported into the esophagus. Water is the most difficult substance to size, shape, and contain in the oral cavity. This makes it the hardest to control as it is passed from the oral cavity into the pharynx. Thus, viscous foods are used to feed patients with oropharyngeal dysphagia.

2. What sensory cues elicit swallowing?
The sensory cues are not entirely known, but entry of food or fluid into the hypopharynx, specifically the sensory receptive field of the superior laryngeal nerve, is paramount. Swallowing may also be initiated by volitional effort if food is present in the oral cavity. The required signal for initiation of the swallow response is a mixture of both peripheral sensory input from oropharyngeal afferents and superimposed control from higher nervous system centers. Neither is capable of initiating swallowing independent of the other. Thus, swallowing cannot be initiated during sleep when higher centers are turned off or with deep anesthesia to the oral cavity when peripheral afferents are disconnected.

3. What is the difference between globus sensation (globus hystericus) and dysphagia?
Globus sensation is the feeling of a lump in the throat. It is present continually and is not related to swallowing. It may even be temporarily alleviated during a swallow. Dysphagia is difficulty in swallowing and is noted by the patient only during swallowing.

4. What are common etiologies of globus sensation?
- Gastroesophageal reflux disease
- Anxiety disorder (must exclude organic disease)
- Early hypopharyngeal cancer
- Goiter

5. Do patients accurately localize the site of dysphagia?
Patients with oropharyngeal dysphagia usually recognize that the swallow dysfunction is in the oropharynx. They may perceive food accumulating in the mouth or an inability to initiate a pharyngeal swallow. They can generally recognize aspiration before, during, or after a swallow. Patients with esophageal dysphagia correctly localize the abnormal site only 60% to 70% of time. They report it proximal to the actual site in the remainder. Differentiating between proximal and distal lesions may be difficult based on only the patient’s perception. Associated symptoms, such as difficulty with chewing, drooling, coughing, or choking after a swallow, are more suggestive of oropharyngeal than of esophageal dysphagia.

6. What are the differences between esophageal and oropharyngeal dysphagia?
See Table 1-1.

7. What symptoms can be seen in oropharyngeal dysphagia?
- Inability to initiate a swallow
- Sensation of food getting stuck in the throat
- Coughing or choking (aspiration) during swallowing
- Nasopharyngeal regurgitation
- Changes in speech or voice (nasality)
- Ptosis
- Photophobia or visual changes
- Weakness, especially progressive toward the end of the day
8. What are the causes of oropharyngeal dysphagia?
Oropharyngeal dysphagia can be viewed as resulting from propulsive failure or structural abnormalities of either the oropharynx or esophagus. Propulsive abnormalities can result from dysfunction of the central nervous system control mechanisms, intrinsic musculature, or peripheral nerves. Structural abnormalities may result from neoplasm, surgery, trauma, caustic injury, or congenital anomalies. If dysphagia occurs in the absence of radiographic findings, motor abnormalities may be demonstrable by more sensitive methods such as electromyography or nerve stimulation studies. If all studies are normal, impaired swallowing sensation may be the primary abnormality. (See Table 1-2.)

9. What causes oropharyngeal dysphagia in the elderly?
Eighty percent of cases of oropharyngeal dysphagia in elderly patients are attributable to neuromuscular disorders. Of these, cerebrovascular accidents account for the vast majority. Parkinson disease, motor neuron disorders, and skeletal muscle disorders are also well known etiologies. Structural disorders are seen in less than 20% of elderly patients with dysphagia.

10. Why is a brainstem stroke more likely to cause severe oropharyngeal dysphagia than a hemispheric stroke?
The swallowing center is situated bilaterally, in the reticular substance below the nucleus of the solitary tract, in the brainstem. Efferent fibers from the swallow centers travel to the motor neurons controlling the swallow musculature located in the nucleus ambiguous. Therefore, brainstem strokes are more likely to cause the most severe impairment of swallowing with difficulty in initiating a swallow or absence of the swallow response.

11. When is it appropriate to evaluate stroke-related dysphagia?
About 25% to 50% of strokes will result in oropharyngeal dysphagia. Most stroke-related swallowing dysfunction improves spontaneously within the first 2 weeks. Unnecessary diagnostic or therapeutic procedures, such as percutaneous gastrostomy, should be avoided immediately after a cerebrovascular accident. If symptoms persist beyond the 2-week period, swallowing function should be evaluated.

12. Is a barium swallow examination adequate to evaluate oropharyngeal dysphagia?
A barium swallow focuses on the esophagus, is done in a supine position, and takes only a few still images as the barium passes through the oropharynx. Therefore, aspiration may be missed if a conventional barium swallow is ordered. Oropharyngeal dysphagia is best evaluated with a cineradiographic or videofluoroscopic swallowing study, commonly called the modified barium swallow. Because the oropharyngeal swallow is rapid and transpires in less than 1 second, images must be obtained and recorded at a rate of 15 to 30/sec to adequately capture the motor events. The recorded study can be played back in slow motion for careful evaluation. This study is done with the patient in the upright position and resembles the normal eating position more than does the conventional barium swallow.

13. What is the characteristic feature of dysphagia in myasthenia gravis?
Myasthenia gravis is an autoimmune disorder characterized by progressive destruction of acetylcholine receptors at the neuromuscular junction. It affects the striated portion of the esophageal musculature. A distinct feature is increasing muscle weakness with repetitive muscle contraction such that dysphagia worsens with repeated swallows or as the meal progresses. Resting to allow reaccumulation of acetylcholine in nerve endings improves pharyngoesophageal functions and symptoms simultaneously. Muscles of facial expression, mastication, and swallowing are frequently involved and dysphagia is a prominent symptom in more than one third of cases. An anticholinesterase antibody test is about 90% sensitive in diagnosing myasthenia gravis. If clinical suspicion is strong, a therapeutic trial with an acetylcholinesterase inhibitor, such as Tensilon, or a cholinomimetic, such as Mestinon, should be considered even in the absence of the anticholinesterase antibody.

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### Table 1-1. Esophageal Versus Oropharyngeal Dysphagia

<table>
<thead>
<tr>
<th>ESOPHAGEAL DYSPHAGIA</th>
<th>OROPHARYNGEAL DYSPHAGIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Associated symptoms: chest pain, water brash, regurgitation</td>
<td>Associated symptoms: weakness, ptosis, nasal voice, pneumonia, cough</td>
</tr>
<tr>
<td>Organ-specific diseases (e.g., esophageal cancer, esophageal motor disorder)</td>
<td>Systemic diseases (e.g., myasthenia gravis, Parkinson disease)</td>
</tr>
<tr>
<td>Treatable (e.g., dilation)</td>
<td>Rarely treatable</td>
</tr>
<tr>
<td>Expendable organ (only one function)</td>
<td>Nonexpendable organ (functions include speech, respiration, and swallowing)</td>
</tr>
</tbody>
</table>
14. Why is simultaneous involvement of the oropharynx and esophagus extremely unusual for any disease process other than infection?
The oropharynx and the esophagus are fundamentally different in respect to musculature, innervation, and neural regulation (Table 1-3). Because most disease processes are specific for a particular type of muscle or nervous system element, it is unlikely that they would involve such diverse systems.

15. What is Zenker diverticulum?
Zenker diverticulum is a diverticulum of the hypopharynx. It is located posteriorly in an area of potential weakness at the intersection of the transverse fibers of the cricopharyngeus and the obliquely oriented fibers of the inferior pharyngeal constrictors also called the Killian dehiscence (Fig. 1-1).

16. Are Zenker diverticula the result of an obstructive or a propulsive defect?
It was previously believed that the pathogenesis of the diverticulum was due to abnormally high hypopharyngeal pressures caused by defective coordination of upper esophageal sphincter (UES) relaxation during pharyngeal...
bolus propulsion. It is now known that Zenker diverticulum is caused by a constrictive myopathy of the cricopharyngeus (poor sphincter compliance). Increased resistance at the cricopharyngeus and increased intrabolus pressures above this relative obstruction cause muscular stress in the hypopharynx with herniation and diverticulum formation. Thus, Zenker diverticulum is an obstructive rather than a propulsive disease.

17. What are the treatment options for Zenker diverticula?
The most common treatments are open surgical diverticulectomy with or without myotomy, rigid endoscopic myotomy, and, recently, cricopharyngeal myotomy using flexible endoscopes. Beware of comorbid conditions causing poor pharyngeal contraction, such as Parkinson disease, because these patients may have poor pharyngeal contraction and may not improve clinically after myotomy.

18. How does flexible endoscopic therapy differ from standard surgical therapies?
Surgical therapy usually involves rigid endoscopic therapy in the operating under general anesthesia and requires hyperextension of the neck. The myotomy is done using stapling devices, although laser division has been done.

Endoscopic therapy is usually performed in the endoscopy suite usually with moderate sedation or monitored anesthesia care. During endoscopic therapy, the septum between the diverticulum and esophagus that contains the cricopharyngeus is divided. The septum is reduced to less than 1 cm. Electrocautery is used to divide the muscle, and the usual cutting methods have included needle knife and argon plasma coagulation (APC), although forceps coagulation has been described.

19. What are the early complications following endoscopy therapy for Zenker diverticulum?
Complications are those related to aspiration, sedation, perforation, and bleeding. Perforation occurs in up to 23% of patients and usually represents microperforation. Most endoscopists routinely obtain chest radiographs or water-soluble contrast esophagograms after the procedure to look for the presence of mediastinal air or leak from perforation. Bleeding after myotomy occurs in 0% to 10% of patients.

20. What are the indications and late risks of a cricopharyngeal myotomy?
See Table 1-4.

21. When should you consider performing flexible endoscopic therapy for Zenker diverticula?
Flexible endoscopic treatment may be a better choice for elderly patients who are at high risk for surgery and who may benefit from avoiding general anesthesia and hyperextension of the neck.

### Table 1-3. Comparison of the Oropharynx and the Esophagus

<table>
<thead>
<tr>
<th>OROPHARYNX</th>
<th>ESOPHAGUS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Striated muscle</td>
<td>Striated muscle (proximal), smooth muscle (middle and distal)</td>
</tr>
<tr>
<td>Direct nicotinic innervation</td>
<td>Myenteric plexus within longitudinal and circular smooth muscles</td>
</tr>
<tr>
<td>Cholinergic</td>
<td>Cholinergic, nitric oxide, vasoactive intestinal peptide</td>
</tr>
</tbody>
</table>

### Table 1-4. Indications and Late Risks of a Cricopharyngeal Myotomy

<table>
<thead>
<tr>
<th>INDICATIONS</th>
<th>LATE RISKS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zenker diverticulum</td>
<td>Aspiration in patients with gastroesophageal reflux</td>
</tr>
<tr>
<td>Cricopharyngeal bar with symptoms</td>
<td>Worsening of swallow function</td>
</tr>
<tr>
<td>Parkinson’s disease with impaired upper esophageal sphincter relaxation</td>
<td></td>
</tr>
</tbody>
</table>
22. What is the differential diagnosis of dysphagia in a patient who has had surgery, radiation, and chemotherapy for head and neck cancer?
- Radiation myositis and/or fibrosis
- Xerostomia (hyposalivation)
- Anatomic defects due to surgery
- Recurrence of malignancy

23. Are swallowing disorders related to an increased morbidity and mortality?
Yes. Patients with dysphagia have an increased risk of aspiration pneumonia. Relative risk for aspiration is highest in patients with dementia followed by those who are institutionalized. Liquid aspiration is the most common type of aspiration in elderly patients.

24. What therapies can be used to improve swallowing?
The goals of swallow therapy are to help minimize the risk of aspiration and to optimize oral delivery of nutrition.
- Direct swallow therapies attempt to improve the swallow physiology. Examples include treatment of the primary disease, oral and maxillofacial prosthetics, cricopharyngeal myotomy, and swallow maneuvers such as the supraglottic swallow.
- Compensatory techniques help eliminate symptoms but do not change the swallowing dysfunction. These techniques include adjustment of the patient’s head and neck, changing food viscosity, and optimizing the volume and rate of food delivery.
- Indirect swallow therapies address the neuromuscular coordination needed for swallowing. Examples include exercise regimens for tongue coordination and chewing.

25. Which patients are ideal candidates for swallow therapy?
Patients who are mentally competent and motivated have the best results with swallow therapy. Therapy is most effective for aspiration (during and after swallow) and unilateral pharyngeal paresis.

26. What are the etiologies of dysphagia in gastroesophageal reflux disease?
- Inflammation: 30% of patients with esophagitis experience dysphagia.
- Stricture: Dysphagia occurs when the lumen diameter is less than 11 to 13 mm.
- Peristaltic dysfunction: This is seen with advanced disease.
- Hiatus hernia: Up to 30% of patients with a hiatus hernia may have dysphagia.
- Coexisting eosinophilic esophagitis

27. What are the common symptoms and causes of xerostomia?

<table>
<thead>
<tr>
<th>SYMPTOM</th>
<th>CAUSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dysphagia</td>
<td>Sjögren syndrome</td>
</tr>
<tr>
<td>Dry mouth with viscous salvia</td>
<td>Rheumatoid arthritis</td>
</tr>
<tr>
<td>Bad taste in mouth</td>
<td>Drugs (e.g., anticholinergics, antidepressants)</td>
</tr>
<tr>
<td>Oral burning</td>
<td>Radiation therapy</td>
</tr>
<tr>
<td>Dental decay</td>
<td>Poor oral hygiene, other</td>
</tr>
<tr>
<td>Bad breath</td>
<td>Multiple</td>
</tr>
</tbody>
</table>

28. Why is cricopharyngeal achalasia a misnomer? How does it differ from classic achalasia?
The UES is a striated muscle that is dependent on tonic excitation to maintain contractility. If innervation to the cricopharyngeus is lost, the UES relaxes and becomes flaccid. This is in contrast to the lower esophageal sphincter (LES). The LES a 3- to 4-cm-long segment of tonically contracted smooth muscle located at the distal end of the esophagus. LES tonic contraction is a property of both the muscle itself and of its extrinsic innervation. Normal resting tone of the LES varies from 10 to 30 mm Hg, being least in the postcibal period and greatest at night. Classic achalasia is caused by loss of the inhibitory myenteric plexus neurons in the distal esophagus, thereby leaving no mechanism to inhibit myogenic contraction (Table 1-5).

29. When is botulinum toxin (BTx) used for dysphagia?
BTx has been best studied in dysphagia caused by achalasia. Achalasia is the result of selective loss of inhibitory neurons at the LES, resulting in unopposed (tonic) excitation of the LES. BTx injection into the distal esophagus can reduce LES pressure by blocking acetylcholine release from the presynaptic cholinergic nerve terminals in the myenteric plexus. Surgical myotomy is the definitive treatment for achalasia, as repeated BTx therapy is required to maintain efficacy. Ideal candidates for BTx are the elderly and those at high operative risk.
Endoscopic injection of BTx into the diverticular spur, as an alternative to surgical cricopharyngeal myotomy, has been successful in case reports. The use of BTx in Parkinson disease with dysphagia due to impaired relaxation of the UES has also shown improvement by videofluoroscopic and electromyographic studies. Potential side effects include persistent stenosis and the risk of local BTx diffusion into the larynx or hypopharynx.

### Table 1-5. Comparison of the Lower and Upper Esophageal Sphincters

<table>
<thead>
<tr>
<th></th>
<th>LOWER ESOPHAGEAL SPHINCTER</th>
<th>UPPER ESOPHAGEAL SPHINCTER</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resting tone</td>
<td>Myogenic</td>
<td>None</td>
</tr>
<tr>
<td>Result of denervation</td>
<td>Contraction</td>
<td>Relaxation</td>
</tr>
<tr>
<td>Cause of impaired opening</td>
<td>Failure of relaxation</td>
<td>Failure of traction (pulling open)</td>
</tr>
<tr>
<td>Source of opening force</td>
<td>Bolus</td>
<td>Suprahyoid and infrahyoid musculature</td>
</tr>
</tbody>
</table>

Endoscopic injection of BTx into the diverticular spur, as an alternative to surgical cricopharyngeal myotomy, has been successful in case reports. The use of BTx in Parkinson disease with dysphagia due to impaired relaxation of the UES has also shown improvement by videofluoroscopic and electromyographic studies. Potential side effects include persistent stenosis and the risk of local BTx diffusion into the larynx or hypopharynx.

### WEBSITES

1. [http://www.radiologyassistant.nl/en/440bca82f1b77](http://www.radiologyassistant.nl/en/440bca82f1b77)

### Bibliography

1. **What is gastroesophageal reflux disease (GERD)? How common is it?**

GERD is a pathologic condition of symptoms and injury to the esophagus caused by percolation of gastric or gastroduodenal contents into the esophagus. GERD is extremely common. One survey of hospital employees showed that 7% experienced heartburn daily, 14% experienced symptoms weekly, and 15% experienced symptoms monthly. Other studies have suggested a 3% to 4% prevalence of GERD among the general population, with a prevalence increase to approximately 5% in people older than 55 years. Pregnant women have the highest incidence of daily heartburn at 48% to 79%. The distribution of GERD between the sexes is equal, but men are more likely to have complications of GERD—esophagitis (2–3:1) and Barrett’s esophagus (10:1).

2. **What are the typical symptoms of GERD?**

Heartburn is usually characterized as a midline retrosternal burning sensation that radiates to the throat and occasionally to the intrascapular region. Patients often place the open hand over the sternal area and flip the wrist in an up-and-down motion to simulate the nature and location of the heartburn symptoms. Mild symptoms of heartburn are often relieved within 3 to 5 minutes of ingesting milk or antacids. Other symptoms of GERD include the following:

- **Regurgitation** consists of eructation of gastric juice or stomach contents into the pharynx and often is accompanied by a noxious bitter taste. Regurgitation is most common after a large meal and usually occurs with stooping or assuming a recumbent posture.
- **Dysphagia** (difficulty in swallowing) usually is caused by a benign stricture of the esophagus in patients with longstanding GERD. Solid foods, such as meat and bread, are often precipitants of dysphagia. Dysphagia implies significant narrowing of the esophageal lumen, usually to a luminal diameter of less than 13 mm. Prolonged dysphagia, associated with inability to swallow saliva, requires prompt evaluation and often endoscopic removal (see Chapter 61, Fig. 61-1).
- **Water brash** is an uncommon symptom but highly suggestive of GERD. Patients literally foam at the mouth as the salivary glands produce up to 10 mL of saliva per minute as an esophagosalivary reflex response to acid reflux.

3. **Is gastrointestinal (GI) hemorrhage a common symptom of GERD?**

No. Endoscopic evaluation of patients with upper GI hemorrhage has identified erosive GERD as the cause in only 2% to 6% of cases.

4. **What is odynophagia? Is it a common symptom of GERD?**

Odynophagia is a painful substernal sensation associated with swallowing that should not be confused with dysphagia. Odynophagia rarely results from GERD. Instead, odynophagia is caused by infections (monilia, herpes simplex virus, and cytomegalovirus), ingestion of corrosive agents or pills (tetracycline, vitamin C, iron, quinidine, estrogen, aspirin, alendronate [Fosamax], or nonsteroidal anti-inflammatory drugs), or cancer.

5. **What clues about GERD can be gleaned from the physical exam?**

- Severe kyphosis often is associated with hiatal hernia and GERD, especially when a body brace is necessary.
- Tight-fitting corsets or clothing (in men or women) can increase intra-abdominal pressure and may cause stress reflux.
- Abnormal phonation may suggest high GERD and vocal cord injury. When hoarseness is due to high GERD, the voice is often coarse or gravelly and may be worse in the morning, whereas in other causes of hoarseness, excessive voice use or abuse leads to worsening later in the day.
- Wheezing or asthma and pulmonary fibrosis have been associated with GERD. Patients often give a history of postprandial or nocturnal regurgitation with episodes of coughing or choking caused by near or partial aspiration.
- Loss of enamel on the lingual surface of the teeth may be seen in severe GERD, although it is more common in patients with ruminating syndrome or bulimia (Fig. 2-1).
- Esophageal dysfunction may be the predominant component of scleroderma or mixed connective tissue disease. Inquiry about symptoms of Raynaud syndrome and examination for sclerodactyly, taut skin, and calcinosis are important.
- Cerebral palsy, Down syndrome, and mental retardation are commonly associated with GERD.
- Children with peculiar head movements during swallowing may have Sandifer syndrome.
- Some patients unknowingly swallow air (aerophagia) that triggers a burp, belch, and heartburn cycle. The observant clinician may detect this behavior during the interview and physical exam.
6. Do healthy persons have GERD?
Yes. Healthy persons may regurgitate acid or food contents into the esophagus, especially after a large meal late at night. In normal persons, the natural defense mechanisms of the lower esophageal sphincter (LES) barrier and esophageal clearance are not overwhelmed, and symptoms and injury do not occur. Ambulatory esophageal pH studies have shown that healthy persons have acid reflux into the esophagus during less than 2% of the daytime (upright position) and less than 0.3% of the nighttime (supine position).

7. How can swallowing and salivary production be associated with GERD?
Reflux of gastric contents into the esophagus often stimulates salivary production and increased swallowing. Saliva has a neutral pH, which helps to neutralize the gastric refluxate. Furthermore, the swallowed saliva initiates a peristaltic wave that strips the esophagus of refluxed material (clearance). During the awake upright period, persons swallow 70 times an hour; this rate increases to 200 times an hour during meals. Swallowing is least common during sleep (less than 10 times per hour), and arousal from sleep to swallow during GERD may be reduced by sedatives or alcohol ingestion. Patients with Sjögren syndrome and smokers have reduced salivary production and prolonged esophageal acid clearance times.

8. What are the two defective anatomic mechanisms in patients with GERD?
Ineffective clearance and defective GE barrier.

9. What clearance defects are associated with GERD?
- Esophageal. Normally, reflux of gastric contents into the esophagus stimulates a secondary peristaltic or clearance wave to remove the injurious refluxate from the esophagus. The worst case of ineffective esophageal clearance is seen in patients with scleroderma. The LES barrier is nonexistent, and there is no primary or secondary peristalsis of the esophagus (hence, no clearance).
- Gastric. Gastroparesis may lead to excessive quantities of retained gastroduodenal and food contents. Larger volumes of stagnant gastric contents predispose to esophageal reflux.

10. How may the GE barrier be compromised?
The normal LES is 3 to 4 cm long and maintains a resting tone of 10 to 30 mm Hg pressure. The LES acts as a barrier against GERD. When the LES pressure is less than 6 mm Hg, GERD is common; however, the presence of normal LES pressure does not predict the absence of GERD. In fact, LES pressure of less than 10 mm Hg is found in a minority of people with GERD. Recent studies have shown that transient LES relaxations are important in the pathogenesis of GERD. During transient LES relaxations, the sphincter inappropriately relaxes and free gastric reflux occurs.

11. What foods and medications influence resting LES pressure?
See Table 2-1.

---

Table 2-1. Increased Versus Decreased Lower Esophageal Sphincter (LES) Pressure

<table>
<thead>
<tr>
<th>Food</th>
<th>INCREASED LES PRESSURE</th>
<th>DECREASED LES PRESSURE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Food</td>
<td>Protein</td>
<td></td>
</tr>
<tr>
<td>Medication</td>
<td>Antacids</td>
<td>Calcium channel</td>
</tr>
<tr>
<td>Metoclopramide</td>
<td></td>
<td>antagonists</td>
</tr>
<tr>
<td>Cisapride</td>
<td></td>
<td>Theophylline</td>
</tr>
<tr>
<td>Domperidone</td>
<td></td>
<td>Diazepam</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Meperidine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Morphine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dopamine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Diazepam</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Barbiturates</td>
</tr>
</tbody>
</table>
12. What other medical conditions may mimic symptoms of GERD?
The differential diagnosis of GERD includes coronary artery disease, gastritis, gastroparesis, infectious and pill-induced esophagitis, peptic ulcer disease, biliary tract disease, and esophageal motor disorders.

13. What medical condition clinically presents with dysphagia and is often mistaken for GERD?
Eosinophilic esophagitis. The condition is usually accompanied by atopy, allergies, or asthma. Symptoms of heartburn are usually mild or nonexistent. Endoscopic findings include coiled rings, vertical linear lines, and a narrowed esophageal lumen (Chapter 44, Fig. 44-4). Esophageal biopsy showing greater than 25 eosinophils per high-power field is diagnostic.

14. How can GERD be distinguished from coronary artery disease?
In the evaluation of patients with retrosternal chest pain, the clinician must always be mindful that patients with GERD do not die but patients with new-onset angina or an acute myocardial infarction with symptoms mimicking GERD can. Clues that a patient’s chest pain is cardiac in origin include radiation of the pain to the neck, jaw, or left shoulder/upper extremity; associated shortness of breath and/or diaphoresis; precipitation of pain by exertion; and relief of pain with sublingual nitroglycerin. Physical findings of new murmurs or gallops or abnormal rhythms are also suggestive of a cardiac origin. Although positive findings on an electrocardiogram (ECG) are helpful in the evaluation of patients with chest pain, the absence of ischemic ECG changes should not discourage the clinician from excluding a cardiac etiology for the patient’s symptoms.

15. How should patients with symptoms of GERD be evaluated?
Evaluation of patients with GERD may be guided by the severity of symptoms. Patients without symptoms of high GERD (aspiration or hoarseness) or dysphagia may be given careful instruction about lifestyle modification and a diagnostic trial of H₂ blocker therapy and followed clinically. Diagnostic evaluation is warranted when symptoms of GERD are chronic or incompletely responsive to medical therapy. Esophagogastroduodenoscopy (EGD) is the best test for evaluation of GERD. Up to 50% of patients with GERD do not have macroscopic evidence of esophagitis at the time of endoscopy. In this group, more sensitive GERD testing may be necessary or alternative diagnoses considered.

16. Describe a commonly used endoscopic grading system for GERD.
Grade 0  Macrocopically normal esophagus; only histologic evidence of GERD
Grade 1  One or more nonconfluent lesions with erythema or exudate above the GE junction
Grade 2  Confluent, noncircumferential, erosive, and exudative lesions
Grade 3  Circumferential erosive and exudative lesions
Grade 4  Chronic mucosal lesions (ulceration, stricture, or Barrett’s esophagus)

17. What are the more sophisticated esophageal function tests? How can they be used appropriately in the evaluation of patients with GERD?
Clinical tests of GERD may be divided into three categories:
• Acid sensitivity
  ○ Acid perfusion (Bernstein) test
  ○ 24- to 48-hour ambulatory esophageal pH monitoring
• Esophageal barrier and motility
  ○ Esophageal manometry
  ○ GE scintiscanning
  ○ Standard acid reflux (modified Tuttle) test
  ○ 24- to 48-hour ambulatory esophageal pH monitoring
• Esophageal acid clearance time
  ○ Standard acid reflux (clearance) test (SART)
  ○ 24- to 48-hour ambulatory esophageal pH monitoring

18. Do all patients with GERD need esophageal function testing?
No. Testing should be reserved for patients who fail medical therapy or in whom the correlation of reflux symptoms is in doubt.

19. What is the use of multichannel intraluminal impedance and pH (MII-pH) technology in the evaluation of GERD?
The normal pH of the esophagus ranges between 5.0 and 6.8, making it difficult for conventional intraesophageal pH measurements to detect non–acid reflux events. The MII-pH (impedance) technology is a major advance in esophageal testing that can aid in the detection of both acid and non–acid reflux events.
20. When is ambulatory esophageal pH monitoring helpful?
Ambulatory esophageal pH monitoring is helpful in evaluating patients refractory to standard medical therapy. Acid hypersecretion is often seen in patients with GERD, and esophageal pH monitoring may be helpful in titrating the dose of H₂ blocker or proton pump inhibitor (PPI). Persistence of acid reflux on adequate doses of a PPI should raise the possibility of patient noncompliance or Zollinger-Ellison syndrome.

The Bravo capsule (Medtronic, Inc.) is a new wireless technology that permits more physiologic intraesophageal monitoring for acid reflux. The Bravo capsule is the size of a gel cap and is placed with or without endoscopic assistance 6 cm above the squamocolumnar junction. The capsule is stapled to the esophageal mucosa, permitting more physiologic and prolonged intraesophageal monitoring. Some investigators have begun to staple the capsule in the proximal esophagus to evaluate patients with atypical reflux symptoms, such as hoarseness, throat tightness, asthma, and interstitial lung disease.

21. When are esophageal manometry and scintiscanning helpful?
Esophageal manometry is helpful in evaluating the competency of the LES barrier and the body of the esophagus for motor dysfunction. Severe esophagitis may be the sole manifestation of early scleroderma. When ambulatory pH testing is not available, scintiscanning has been shown to be helpful.

22. Define the various types of medical therapy for GERD and give a logical approach to prescription therapy for patients with longstanding GERD.
For patients with mild, uncomplicated symptoms of heartburn, empiric H₂ blocker therapy without costly and sophisticated diagnostic testing is reasonable. For patients recalcitrant to conventional therapy or with complications of high GERD (aspiration, asthma, hoarseness), Barrett's esophagus, or stricture, diagnostic and management decisions become more complicated. Medical or surgical therapy depends on patient preference, health care cost, risk of medical or surgical complications, and other related factors (Table 2-2).

Table 2-2. Medical Therapy for Gastroesophageal Reflux Disease

<table>
<thead>
<tr>
<th>MEDICATION</th>
<th>DOSAGE</th>
<th>SIDE EFFECTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Topicals</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antacids</td>
<td>1–2 tablets after meals and at bedtime, as needed</td>
<td>Diarrhea (magnesium containing) and constipation (aluminum and calcium containing)</td>
</tr>
<tr>
<td>Sucralfate</td>
<td>1 g 4 times/day</td>
<td>Incomplete passage of pill, especially in patients with esophageal strictures; constipation; dysgeusia</td>
</tr>
<tr>
<td>H₂ Blockers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cimetidine</td>
<td>400–800 mg 2–4 times/day</td>
<td>Gynecomastia, impotence, psychosis, hepatitis, drug interactions with warfarin, theophylline</td>
</tr>
<tr>
<td>Ranitidine</td>
<td>150–300 mg 2–4 times/day</td>
<td>Same, less common</td>
</tr>
<tr>
<td>Famotidine</td>
<td>20–40 mg 1–2 times/day</td>
<td>Same, less common</td>
</tr>
<tr>
<td>PPIs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Omeprazole</td>
<td>20–60 mg/day</td>
<td>Drug interaction due to cytochrome (CYP) P-450 (CYP2C19: warfarin, phenytoin, diazepam, clopedogrel)</td>
</tr>
<tr>
<td>Lansoprazole</td>
<td>30 mg/day</td>
<td>CYP-1A2 inducer; decreases theophylline levels</td>
</tr>
<tr>
<td>Dexlansoprazole</td>
<td>30–60 mg/day</td>
<td>CYP2C19 inhibition and drug interaction</td>
</tr>
<tr>
<td>Rabeprazole</td>
<td>20 mg/day</td>
<td>Probably none</td>
</tr>
<tr>
<td>Pantoprazole</td>
<td>40 mg/day</td>
<td>Probably none</td>
</tr>
<tr>
<td>Esomeprazole</td>
<td>20–40 mg/day</td>
<td>Probably none</td>
</tr>
<tr>
<td>Prokinetic Agents</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bethanechol</td>
<td>10–25 mg 4 times/day or at bedtime</td>
<td>Urinary retention in patients with detrusor-external sphincter dysynergia or prostatic hypertrophy, worsening asthma</td>
</tr>
<tr>
<td>Metoclopramide</td>
<td>10 mg 3 times/day or at bedtime</td>
<td>Extrapyramidal dysfunction, Parkinsonian-like reaction; cases of irreversible tardive dyskinesia have been reported</td>
</tr>
<tr>
<td>Cisapride</td>
<td>10–20 mg 3 times/day</td>
<td>FDA recall, because of potential fatal arrhythmia</td>
</tr>
</tbody>
</table>

FDA, U.S. Food and Drug Administration; PPI, proton pump inhibitor.
23. Describe the commonly recommended approach to graded treatment of GERD.
Stage I—Lifestyle modifications
   Antacids, prokinetics, over-the-counter H₂ blockers, or sucralfate
Stage II—H₂ blocker therapy
   Reinforce need for lifestyle modifications
Stage III—I—PPIs
   Reinforce need for lifestyle modifications
Stage IV—I—Surgical or endoscopic antireflux procedure
   The authors favor initiation of aggressive lifestyle modification (especially weight reduction and dietary changes) and pharmacologic therapy to achieve endoscopic healing of esophagitis (usually a PPI). When esophagitis is healed, the dose of the PPI should be lowered or an effective dose of an intermediate-potency H₂ blocker is substituted for the PPI. Then the patient is counseled about the risks, benefits, and alternatives to long-term medical therapy. Surgery is encouraged for the fit patient who requires chronic high doses of pharmacologic therapy to control GERD or dislikes taking medicine. Endoscopic treatments for GERD are very promising, but controlled long-term comparative trials with PPIs and/or surgery are lacking.

24. Do patients scheduled for surgical antireflux procedures need to undergo sophisticated esophageal function testing before surgery?
   There is no absolute correct answer. However, it is prudent to conduct esophageal motility studies to ensure that esophageal motor disease is not present. Patients with scleroderma may have a paucity of systemic complaints, and the diagnosis may go undetected without esophageal manometry. Generally, surgical antireflux procedures are avoided or modified in such patients. In addition, esophageal motility studies and ambulatory 24-hour pH monitoring may confirm or refute that the patient’s symptoms are attributable to GERD before the performance of a surgical procedure.

25. What are some of the new endoscopic treatments for GERD?
   • Endoluminal gastroplication (ELGP)—Endocinch by CR Bard, Inc., or Endoscopic Suturing Device (ESD), Wilson Cook Inc.
   • Single full-thickness plication—NDO Endoplication System by NDO Surgical, Inc.
   • Coagulation injury—Stretta by Curon Medical, Inc.
   • Polymer injection—Enteryx by Boston Scientific Corp. (recalled from U.S. market, 2005).

26. How should esophageal strictures be managed?
   • Prevention of peptic stricture with early institution of effective medical or surgical therapy appears to be particularly important for patients with scleroderma.
   • For patients with symptoms of dysphagia due to peptic stricture, esophageal dilation is effective. Dilation can be accomplished using mercury-filled polyvinyl Maloney bougies, wire-guided hollow Savary-Guilliard or American dilators, or through-the-scope (TTS) pneumatic balloons. Usually, the esophagus is dilated to a diameter of 14 mm or 42 to 44 French. After successful dilation of a peptic stricture, the patient should be placed on chronic PPI therapy to avoid recurrent stricture formation.
   • Surgery is an effective method of managing esophageal strictures. Usually, preoperative and intraoperative dilation is combined with a definitive antireflux procedure.

27. What is Barrett’s esophagus? How is it managed?
   Barrett’s esophagus is a metaplastic degeneration of the normal esophageal lining, which is replaced with a premalignant, specialized columnar epithelium. It is seen in roughly 5% to 7% of patients with uncomplicated reflux but in up to 30% to 40% of patients with scleroderma or dysphagia. Currently, there is no proven method to eliminate Barrett’s esophagus. Preliminary studies of laser or BiCAP ablation of the metaplastic segment followed by alkalization of the GE refluxate are encouraging. The need for cancer surveillance is discussed elsewhere in this book.

28. List some of the atypical symptoms and signs of GERD.
   Asthma, lingual dental erosions, chest pain, recurrent otitis in children, cough, throat-clearing, hiccups, throat tightness, hoarseness.

29. Is there an association between obstructive sleep apnea (OSA) and GERD?
   Yes. Nocturnal acid reflux is seen in 54% to 72% of persons with OSA. Administration of nighttime continuous positive airway pressure (CPAP) and/or PPI therapy has been shown to decrease apnea events and acid reflux events.

30. Does the presence of heartburn symptoms predict a GERD-related cough etiology?
   No. There is poor correlation between symptoms of heartburn and cough. Between 43% and 75% of patients with GERD-related cough do not have heartburn symptoms. Both medical treatment with PPIs and surgical antireflux procedures have been reported to be effective for GERD-related cough. Caveats include the following:
35% response rate to omeprazole 40 mg twice a day after 2 weeks

Results of surgical antireflux procedures are best when preoperative esophageal manometry is normal and response to PPI is positive.

31. **What is the best method to evaluate for possible GERD-related cough?**

The first step is to exclude non–GERD-related etiologies: angiotensin-converting inhibitors, environmental irritants, smoking, parenchymal lung disease, allergic rhinitis and pneumonia, asthma and sinusitis, which are often silent. Symptom relief after a 2-week trial of high-dose PPI (40 mg twice a day) is a cost-effective approach. Patients who do not respond should be considered for further evaluation, including esophageal manometry/pH testing and/or EGD.

32. **What laryngeal conditions are associated with GERD?**

The most common laryngeal manifestation of high reflux or esophagopharyngeal reflux (EPR) is hoarseness. Other laryngeal conditions associated with EPR are listed:

- Arytenoid fixation
- Carcinoma of the larynx
- Contact ulcers and granuloma
- Globus pharyngeus
- Hoarseness
- Laryngomalacia
- Pachydermia laryngitis
- Paroxysmal laryngospasm
- Recurrent leukoplaikia
- Vocal cord nodules

33. **How often do people with EPR and hoarseness relate symptoms of heartburn?**

The prevalence of GERD symptoms among patients with reflux laryngitis is low (6%–43%).

34. **What is the most efficient, cost-effective method to evaluate hoarse patients for EPR?**

The first step in the evaluation of hoarseness should be exclusion of structural ear, nose, and throat (ENT) disorders, including neoplasm. The next step is an empiric trial of double-dose PPI for 2 to 3 months. Most EPR-related hoarseness improves with acid suppression (60%–96%). Patients responding to PPIs may stop the medication and be monitored for recurrence of symptoms. Hoarse patients with a negative ENT evaluation who fail PPI therapy should undergo formal esophageal pH analysis.

35. **Can GE reflux worsen asthma?**

Yes. Numerous studies have shown that reflux symptoms are common among asthmatics (65%–72%) and that medical and surgical antireflux treatment may improve pulmonary function.

36. **How does GE reflux worsen asthma?**

Several mechanisms are theorized to explain GERD-induced bronchospasm:

- Asthmatic patients with GERD have been shown to have autonomic dysregulation with heightened vagal response, which is presumed to be responsible for the decrease in LES pressure and more frequent transient relaxations of the LES, which promote reflux.
- Esophageal reflux may incite a vagal-mediated esophagobronchial reflex of airway hyperreactivity.
- Microaspiration of gastric juice has been shown to activate a local axonal reflex involving release of substance P, which leads to airway edema. The finding of lipid-laden alveolar macrophages among asthmatic patients demonstrates aspiration of gastric material into the pulmonary tree.

37. **What cytochrome P-450 (CYP-450) systems are involved in the metabolism of PPIs?**

All of the PPIs undergo some hepatic metabolism through the CYP-450 system. The CYP-2C19 and CYP-3A4 microsomal enzymes are responsible for the majority of PPI hepatic metabolism. Genetic polymorphism with CYP-2C19 is common; about 5% of Americans and 20% of Asians are deficient in this enzyme. Omeprazole decreases the metabolism of phenytoin and warfarin R-isomer (CYP-2C9), diazepam (CYP-2C19), and cyclosporine (CYP-3A4).

38. **How do esomeprazole (Nexium) and omeprazole (Prilosec) differ?**

Omeprazole is a racemic mixture of both the S- and R-isomers, whereas esomeprazole is a pure form of the S-isomer. Less esomeprazole (S-isomer) is metabolized by the CYP-2C19 pathway, leading to greater area under the curve and better intragastric acid suppression for 24 hours. Esomeprazole is the only PPI shown to be statistically superior to omeprazole in healing erosive esophagitis at 8 weeks (90%–94% efficacy rate).
39. Which patients with GERD should be considered for a surgical antireflux procedure?

Any young, healthy patient with chronic GERD requiring lifelong PPI medical therapy may be considered for an antireflux procedure. Other indications include failed medical therapy, complicated GERD (e.g., bleeding, recurrent strictures), medical success at excessive cost in young, otherwise healthy patients, and problematic symptoms due to regurgitation (asthma, hoarseness, cough).

40. Which patients are poor candidates for a surgical antireflux procedure?

- Elderly patients with substantial comorbid disease
- Patients with poor or absent esophageal peristalsis
- Patients with highly functional symptoms

Lack of available surgical expertise is also a contraindication for antireflux procedures.

WEBSITES


Bibliography