Gastroenterology and Hepatology

Disorders of the Esophagus

Symptoms of Esophageal Disease

Dysphagia

Normal swallowing consists of three phases. The oral phase encompasses formation of a food bolus and transfer of the bolus to the back of the throat. The pharyngeal phase allows the bolus to be safely positioned in the upper throat; the soft palate elevates, the epiglottis protects the trachea, the tongue moves backward, and the pharyngeal wall moves forward. The esophageal phase starts with the bolus entering the esophagus with relaxation of the upper esophageal sphincter. Peristalsis (rhythmic contractions) propels the bolus down; primary peristalsis is initiated with the swallow, and secondary peristalsis is intended to clear residual bolus. This phase ends as the lower esophageal sphincter relaxes to allow the bolus to enter the stomach.

Dysphagia is a disruption in the swallowing mechanism, resulting in a bolus not passing from the mouth to the stomach. Determining whether the cause is oropharyngeal or esophageal is important in developing a differential diagnosis and management plan. **Table 1** highlights common causes of dysphagia.

Oropharyngeal Dysphagia

Oropharyngeal dysphagia, also called transfer dysphagia, occurs when the patient cannot transfer the food bolus from the mouth into the upper esophagus by swallowing. Common symptoms include choking, coughing, and nasal regurgitation of food and liquids. Patients are at risk for aspiration pneumonia. Stroke is a common cause, and an underlying neurologic disorder, such as Parkinson disease, may be suspected, particularly with concurrent neurologic findings. A pharyngoesophageal (Zenker) diverticulum should be considered when undigested food is brought up several hours after a meal or if a patient reports hearing a gurgling noise in the throat.

The initial study for suspected oropharyngeal dysphagia is a modified barium swallow and video fluoroscopy, with a range of liquid and solid consistencies. Routine upper gastrointestinal endoscopy and esophageal manometry have a limited role in the evaluation of oropharyngeal dysphagia. Management includes dietary changes and a swallowing exercise program implemented with a speech pathologist.

Esophageal Dysphagia

Patients with esophageal dysphagia can initiate the swallowing process but often feel chest discomfort. Patients also may not readily characterize dysphagia as difficulty swallowing. Common descriptions of the sensations of dysphagia include food "hanging up" or feeling lodged or stuck during a meal. Patients also may describe a bolus slow to go down or "sitting" in the chest. Occasionally they may present with vomiting of undigested food contents.

Esophageal dysphagia results from one of two causes: a mechanical obstruction or a motility disorder. Dysphagia with solids alone suggests a mechanical obstruction, whereas dysphagia with liquids alone or with liquids and solids favors a motility disorder. An urgent workup is indicated for complete obstruction, hematemesis, odynophagia, onset in an older patient, dysphagia associated with weight loss, or acute course. Food impaction may occur, wherein a food bolus lodges in the esophagus and obstructs the passage of additional food, fluid, or saliva. Food impaction is an indication for emergency endoscopy.

Mechanical esophageal obstruction may be benign or malignant and may be caused by masses, strictures, an esophageal ring (e.g., a Schatzki ring [**Figure 1**]), webs, or complex hiatal hernias. Strictures may be due to chronic reflux esophagitis (peptic strictures), eosinophilic esophagitis, radiation therapy, or caustic injury. Dysphagia that progresses from occurring only with solids to occurring with both solids and liquids is concerning because it may be indicative of malignancy or of benign strictures that have become high-grade obstructions. Achalasia often presents with dysphagia for both solids and liquids associated with nonacidic regurgitation of undigested food and fluid. Chest pain upon ingestion of very hot or very cold liquids may indicate esophageal spasm.

Upper endoscopy allows for diagnosis (biopsy and inspection) and therapeutic intervention (dilation) and is the usual initial test of choice. Barium esophagography may provide more information in specific situations, such as suspicion of motility disorders or proximal lesions (e.g., Zenker diverticulum). Clinical management is based on the underlying cause.

Odynophagia

Pain while swallowing defines odynophagia and suggests active mucosal inflammation and esophageal ulceration. Odynophagia is commonly associated with pill-induced damage, infection, or caustic ingestion and is less commonly caused by gastroesophageal reflux disease (GERD) or esophageal cancer. Upper endoscopy with biopsy is the most

TABLE 1. Causes of Dysphagia

Condition	Diagnostic Clues
Oropharyngeal Dysphagia	
Structural disorders	
Cervical osteophytes	High dysphagia, degenerative joint disease
Cricoid webs	High dysphagia, iron deficiency
Pharyngoesophageal (Zenker) diverticulum	Aspiration, neck mass, and regurgitation of foul-smelling food
Goiter	Neck mass
Neurologic/myogenic disorders	
Amyotrophic lateral sclerosis	Upper and lower motoneuron signs, fasciculations
Central nervous system tumor	Headache, vision changes, nausea, seizures, balance problem
Stroke	Focal neurologic deficits
Muscular dystrophy	Slow progression of muscular weakness over years
Myasthenia gravis	Weakness with repetitive activity
Multiple sclerosis	Episodes of neurologic dysfunction with variable degrees of recovery
Parkinson disease	Bradykinesia, rigidity, tremor
Dementia	Altered cognition
Sjögren syndrome	Dry mouth, dry eyes
Esophageal Dysphagia	
Structural disorders	
Dysphagia lusoria (vascular dysphagia)	Vascular extrinsic compression of the esophagus on imaging
Epiphrenic/traction diverticulum	Outpouching of the esophagus at any level on imaging
Esophageal strictures	Progressive dysphagia, especially for solid food; history of reflux
Eosinophilic esophagitis	Food impactions, atopic history, rings or strictures on endoscopy
Esophageal webs or rings	Intermittent dysphagia; upper esophageal webs may be associated with iron deficiency anemia
Neoplasms	Rapidly progressive dysphagia for solids, then liquids; anorexia; weight loss
Motility disorders	
Achalasia	Concomitant liquid and solid dysphagia
Diffuse esophageal spasm	Chest pain
Systemic sclerosis	Skin hardening, telangiectasias, sclerodactyly, gastroesophageal reflux disease, Raynaud phenomenon

appropriate diagnostic test to determine the degree of inflammation and underlying cause.

Globus Sensation

Patients commonly report globus sensation as a lump in the throat or throat tightness, usually not linked to meals. Causes of globus include GERD (with or without heartburn), motility disorders, stress, and psychiatric conditions (e.g., anxiety disorder, panic disorder, and somatic symptom disorder). Globus should not be diagnosed if the patient reports other esophageal symptoms, such as dysphagia or odynophagia. Assessment for the cause should include evaluation for thyroid goiter and an underlying pharyngeal lesion, which can be diagnosed by transnasal endoscopy or barium swallow.

Treatment with acid suppression or cognitive behavioral therapy may be initiated once a structural cause has been ruled out.

Reflux and Chest Pain

The development of chest pain from an esophageal cause can mimic chest pain from cardiac disease. A cardiac cause must be ruled out first. The most common cause of noncardiac chest pain is GERD. Another possible cause is an esophageal motility disorder, particularly hypercontractile motility disorders. Reports of heartburn with a history of Raynaud phenomenon could signify a systemic condition, such as systemic sclerosis. Starting a course of an acid-reducing agent can be both diagnostic and therapeutic. Patients whose symptoms do not respond require further evaluation, including upper

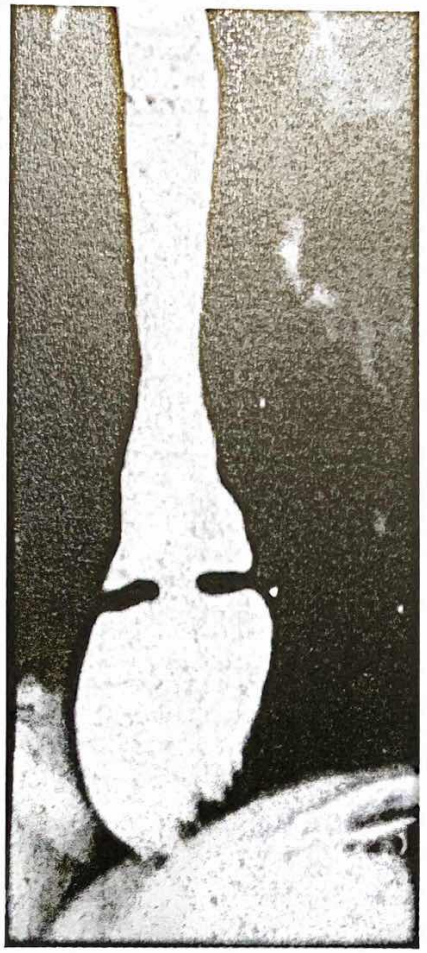

FIGURE 1. Barium esophagram showing a Schatzki ring, a subtype of esophageal ring located at the squamocolumnar junction and a common cause of dysphagia.

endoscopy, and possibly ambulatory pH testing with or without esophageal manometry.

See Gastroesophageal Reflux Disease for information about diagnosis and management.

KEY POINTS

- Oropharyngeal dysphagia occurs when the patient cannot transfer the food bolus from the mouth into the upper esophagus by swallowing and should be evaluated with a modified barium swallow with video fluoroscopy.
- Esophageal dysphagia with solids alone suggests a mechanical obstruction, whereas dysphagia with liquids alone or with liquids and solids favors a motility disorder.
- Upper endoscopy is diagnostic and may be therapeutic for esophageal dysphagia.
- Chest pain is common in patients with gastroesophageal reflux disease, but a cardiac cause of chest pain must be ruled out first.

TABLE 2. Factors Associated With Reflux

Category	Factor
Lifestyle	Cigarette smoking
Eating habits	Eating large meals
	Eating late at night
	Lying supine shortly after eating
Foods and beverages	Alcohol
	Chocolate
	Citrus fruits and juices
	Coffee
	Fatty and fried foods
	Onions
	Peppermint
Medications	Anticholinergic agents
	Aspirin and NSAIDs
	Calcium channel blockers
	Nitrates
	Progesterone
	Opioids (due to delayed gastric emptying)
Body position	Bending over, exercising (both result in increased intra-abdominal pressure)
Other	Obesity
	Pregnancy
	Tight-fitting clothing
	Hiatal hernia

Nonmalignant Disorders of the Esophagus

Gastroesophageal Reflux Disease

GERD is characterized by contents refluxing from the stomach into the esophagus. It has a prevalence of 10% to 20% in the Western world. There is a strong relationship between GERD and obesity. The most common symptoms reported are heartburn, regurgitation, and chest pain, for which a cardiac cause must be excluded. Many factors can trigger reflux (**Table 2**). Protective mechanisms to minimize esophageal exposure to acid and its effects include swallowed salivary bicarbonate, peristalsis, a competent lower esophageal sphincter (LES), and gastric emptying; reflux occurs when these physiologic protectors become ineffective. Uncontrolled GERD can negatively affect quality of life because of poor sleep, low productivity, and work absences. Long-standing GERD can lead to complications, including reflux esophagitis, stricture, Barrett esophagus, and esophageal adenocarcinoma. Commonly attributed extraesophageal conditions include chronic cough, hoarseness (laryngitis), wheezing (asthma), and dental erosions. Pregnant women may experience GERD during any trimester of pregnancy, symptoms may worsen as the pregnancy progresses, and symptoms typically resolve after delivery.

Diagnosis

Strategies for diagnosing GERD include consideration of clinical history and response to medical therapy; testing, such as endoscopy and ambulatory pH monitoring; and exclusion of a motility disorder by manometry. There is no single gold-standard diagnostic test. Clinical symptoms of heartburn and regurgitation strongly suggest GERD. Alarm features include dysphagia, weight loss, hematemesis, or melena. Patients with GERD symptoms but without alarm features may undergo an empiric trial of a proton pump inhibitor (PPI). In patients with alarm features or failure to respond to treatment, upper endoscopy is warranted to rule out an underlying ring, web, malignancy, eosinophilic esophagitis, erosive esophagitis, stricture, or Barrett esophagus. Most patients with GERD have normal findings on upper endoscopy.

Ambulatory pH monitoring can quantify acid exposure in the esophagus. Impedance-pH testing can help differentiate between acid and nonacid reflux. Testing to detect active acid reflux can be done with a 24-hour transnasal catheter or 48-hour or 96-hour wireless capsule endoscopy. pH monitoring may be performed while the patient is not receiving acid-suppressive therapy to confirm acid exposure and support a diagnosis of GERD. Esophageal manometry should be considered as part of the evaluation for patients with dysphagia or atypical reflux symptoms and before antireflux surgery to rule out motility disorders.

Treatment

An algorithm outlining evaluation of GERD is presented in **Figure 2**.

Lifestyle Changes

Patients with recent weight gain or who are overweight should have a weight-loss plan. Patients with nocturnal GERD should not eat within at least 3 hours before going to sleep and should consider raising the head of the bed. Avoiding large meals and rich or fatty foods that stay in the stomach for longer periods is helpful.

Additional dietary modification should focus on eliminating specific foods that trigger an individual patient's GERD symptoms rather than globally eliminating all common trigger foods (caffeine; chocolate; spicy foods; acidic foods, such as citrus fruits; and fatty foods). Cessation of alcohol and tobacco use is recommended.

Medical Therapy

Pharmacologic therapy includes antacids, H_2 blockers, and PPIs. A PPI once daily for 8 weeks is the therapy of choice for symptom relief and for treatment of erosive esophagitis. Most PPIs should be taken once daily, 30 to 60 minutes before the first meal of the day. Patients with partial response to PPI therapy should increase the dosage to twice daily. Given the risks and potential adverse effects of PPI therapy (**Table 3**), the goal should be to use the lowest dose required to control symptoms and to discontinue if there is not an appropriate indication. Similarly, patients requiring long-term maintenance therapy should be prescribed the lowest effective PPI dose, including on-demand or intermittent use. For patients with uncomplicated GERD, stopping or reducing long-term PPI therapy should be attempted once a year.

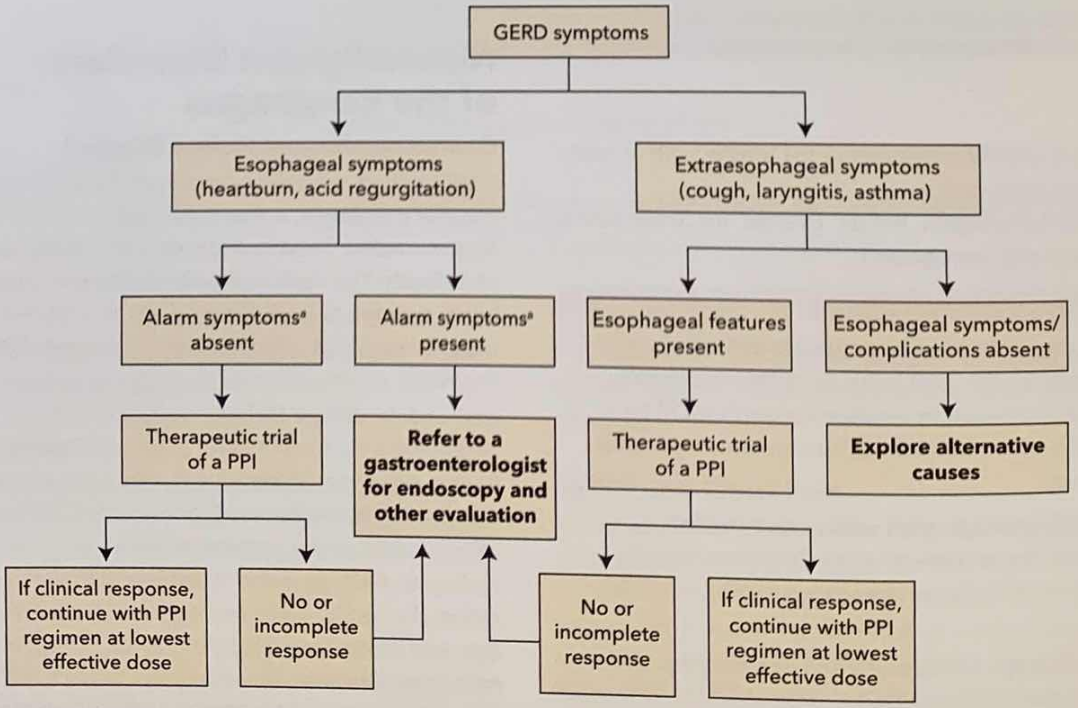

FIGURE 2. Management of gastroesophageal reflux disease.

GERD = gastroesophageal reflux disease; PPI = proton pump inhibitor.

[a]Alarm symptoms include dysphagia, unintentional weight loss, hematemesis, and melena.

TABLE 3. Adverse Effects of Proton Pump Inhibitors

Common	Unusual	Proposed Associations
Headache	Vitamin B_{12} deficiency	Kidney injury[a]
Diarrhea	Hypomagnesemia	Dementia[a]
Dyspepsia	Community-acquired pneumonia[a]	
	Clostridioides difficile infection[a]	
	Hip fracture	

[a]A large randomized controlled trial published in 2019 failed to demonstrate increased risk for these outcomes over 3 years (Moayyedi P, Eikelboom JW, Bosch J, et al; COMPASS Investigators. Safety of proton pump inhibitors based on a large, multi-year, randomized trial of patients receiving rivaroxaban or aspirin. Gastroenterology. 2019;157:682-691.e2. [PMID: 31152740] doi:10.1053/j.gastro.2019.05.056).

Switching to a different PPI may be warranted for adverse reactions or unresponsive symptoms. PPIs are safe in pregnant patients.

Prokinetic agents, such as metoclopramide, should not be used to treat GERD unless gastroparesis is present.

Antireflux Surgery

Surgery is infrequently required; indications include failure of optimal PPI therapy, a desire to stop the medication, and intolerable medication side effects. Patients should undergo objective testing, such as pH monitoring and manometry, before surgery. Surgical treatments for GERD are laparoscopic fundoplication or bariatric surgery for obesity as well as magnetic sphincter augmentation (a magnetic ring is placed around the LES without surgical alteration of the stomach). Surgery is most effective in patients with typical symptoms of heartburn and regurgitation that respond to PPI therapy. However, about one third of patients require resumption of a PPI 5 to 10 years after surgery. Postoperative complications include dysphagia, diarrhea, and inability to belch because of a tight fundoplication.

Endoscopic Therapy

Transoral incisionless fundoplication (an endoscopic fundoplication created with full-thickness suture) has had initial success; long-term data are limited. Additional endoscopic therapies for GERD are based on thermal radiofrequency energy, silicone injection, suturing, and endoscopic resection, but long-term benefits are unproven.

Extraesophageal Manifestations

Asthma, chronic cough, and laryngitis are linked to GERD (see Figure 2). When these symptoms are present, other non-GERD causes should be eliminated. Laryngoscopy should not be used to diagnose GERD-related laryngitis, and edema and erythema as potential signs of reflux-induced laryngitis are nonspecific. A PPI trial is recommended in patients who have concomitant typical GERD symptoms. For patients with atypical symptoms only, ambulatory esophageal pH monitoring should be considered before a PPI trial. Surgery is less effective in this group and should be considered only in patients whose symptoms respond to PPI therapy.

Refractory GERD

The first step in addressing refractory GERD is to optimize PPI therapy by emphasizing the importance of taking medication 30 to 60 minutes before eating, increasing the dosage to twice daily, or switching to another PPI. If symptoms are still unresponsive, alternative causes must be considered. For typical symptoms, endoscopy is used to rule out eosinophilic esophagitis or erosive esophagitis. Adequacy of acid suppression therapy may be confirmed by esophageal impedance-pH testing while the patient is receiving optimized PPI therapy. For atypical symptoms, other causes should be evaluated, and referral to otorhinolaryngology, pulmonary, or allergy specialists to identify and treat the cause should be considered. In these patients, impedance-pH testing conducted off acid-suppression therapy may help confirm the diagnosis of acid reflux. If results of impedance-pH and pH testing are normal but symptoms persist, therapy for functional heartburn may be attempted with selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, or tricyclic antidepressants.

Eosinophilic Esophagitis

Eosinophilic esophagitis (EoE) is commonly associated with dysphagia and food bolus obstruction, which may be recurrent. Most patients are diagnosed between the second and fifth decades of life, and EoE is more common in men. Patients often have other atopic conditions, such as asthma, rhinitis, dermatitis, and seasonal or food allergies. The reported U.S. prevalence is 40 to 90 per 100,000. The diagnostic criteria for EoE are esophageal symptoms (dysphagia), esophageal biopsy specimens showing persistent eosinophil counts of 15/hpf or greater, and exclusion of other causes of eosinophilia. Other causes include GERD, hypereosinophilic syndrome, infections (fungal, viral), autoimmune and connective tissue disorders, Crohn disease with esophageal involvement, and drug hypersensitivity reactions. EoE is diagnosed in the absence of eosinophilia elsewhere.

Endoscopic findings include rings, longitudinal furrows, luminal narrowing, and sometimes strictures (**Figure 3**). If assessment identifies no other causes of eosinophilia, EoE can be diagnosed and appropriate therapy initiated with a PPI and/or swallowed topical glucocorticoids (fluticasone or budesonide). Limited evidence suggests that diet modification may be effective in the prevention of EoE. An empiric elimination diet–removing the foods most commonly associated with food allergies, such as egg, soy, wheat, peanuts, cow's milk, and fish/shellfish–has been used. Endoscopic dilation should be considered in patients with continued dysphagia caused by esophageal stricture not responding to medical therapy.

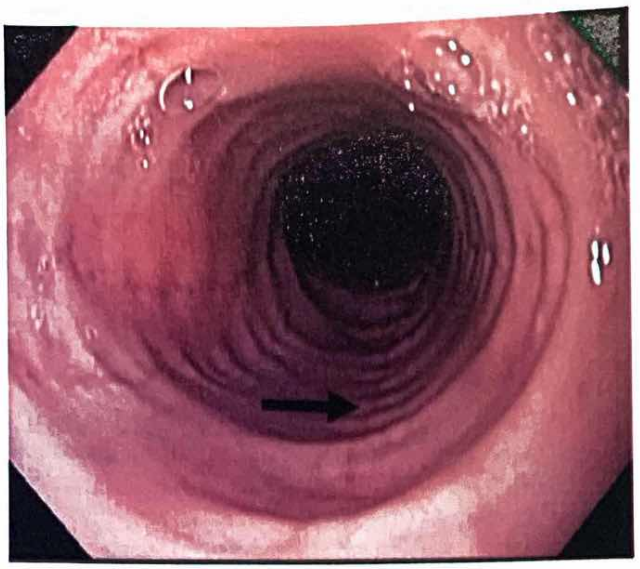

FIGURE 3. The characteristic findings of eosinophilic esophagitis on endoscopy include rings and longitudinal furrows; strictures may also be seen.

Infectious Esophagitis

Infectious esophagitis can be caused by fungal, viral, bacterial (uncommon), or parasitic pathogens. It most commonly occurs in immunocompromised patients. Patients most often present with odynophagia or dysphagia. *Candida* esophagitis frequently causes dysphagia with or without odynophagia, whereas viral esophagitis produces odynophagia. Other organisms associated with esophagitis include *Lactobacillus*, β-hemolytic streptococci, *Cryptosporidium* species, *Pneumocystis jirovecii*, *Mycobacterium avium* complex, and *Mycobacterium tuberculosis*.

Candida infection can occur in immunocompetent or immunocompromised hosts. Diagnosis is usually made clinically on the basis of compatible symptoms and oral candidiasis, although not all patients have oral involvement. Endoscopy and biopsy can be considered for patients who do not respond to empiric therapy or who have atypical symptoms. Endoscopy shows small, white, raised plaques, and esophageal brushings confirm the diagnosis (**Figure 4**). The most common species is *Candida albicans*, which is treated with oral fluconazole.

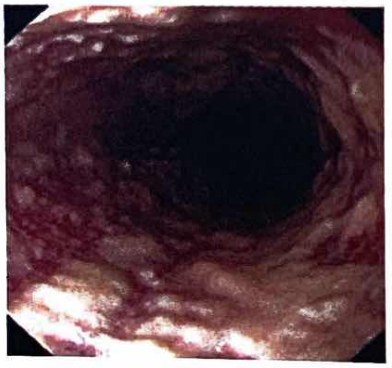

FIGURE 4. White adherent plaques suggesting *Candida* esophagitis, as seen on upper endoscopy.

Herpes simplex virus and cytomegalovirus are seen in immunodeficient or immunosuppressed individuals but rarely occur in immunocompetent patients. Endoscopy with biopsy is needed to confirm the diagnosis. Herpes simplex virus infection is treated with acyclovir, and cytomegalovirus infection is treated with ganciclovir; oral valganciclovir is also an option.

Pill-Induced Esophagitis

Medications can cause esophageal injury that results in esophagitis. Risk factors for pill-induced esophagitis include decreased salivary output, esophageal dysmotility, large pills, medications that increase the LES tone (opioids), and ingestion of medications in the supine position. Patients commonly report chest pain, dysphagia, and odynophagia several hours to days after taking the medication. Pill-induced esophagitis has occurred with alendronate, quinidine, tetracycline, doxycycline, potassium chloride, ferrous sulfate, and mexiletine. Medications associated with stricture formation include alendronate, ferrous sulfate, NSAIDs, and potassium chloride. Pill-induced esophagitis can be diagnosed by history alone, but upper endoscopy should be performed for severe symptoms, persistent symptoms, or atypical symptoms (such as hematemesis or abdominal pain). Preventive strategies include drinking sufficient water with medications and remaining upright for 30 minutes after pill ingestion.

Esophageal Motility Disorders

The esophagus is a muscular tube that passes a food bolus from the hypopharynx to the stomach through peristalsis. The upper third of the esophagus is composed of skeletal muscle innervated by axons of lower motor neurons. The lower two thirds is smooth muscle innervated by the vagus nerve. High-resolution esophageal manometry is used to evaluate suspected esophageal motility disorders.

Hypertonic Motility Disorders

Hypertonic motility disorders are characterized by dysphagia with both liquids and solids. Other symptoms can include regurgitation of undigested food, particularly when the patient is in a recumbent position.

Achalasia and Pseudoachalasia

Achalasia is defined by inadequate relaxation of the LES and aperistalsis. Achalasia can be idiopathic or associated with viral, autoimmune, and neurodegenerative disorders and infection (Chagas disease). Damage to the ganglion cells and myenteric plexus in the esophageal body and LES leads to uncontested cholinergic nerve activation, which prevents LES relaxation. Achalasia affects men and women equally, with an annual incidence of 1 in 100,000 individuals. It commonly occurs between 30 and 60 years of age. Patients have dysphagia with both solids and liquids along with nonacidic regurgitation of undigested food. Additional symptoms include heartburn, weight loss, and chest pain unresponsive to acid-reducing

FIGURE 5. Barium esophagram showing the typical appearance of a dilated esophagus and "bird's beak" narrowing at the gastroesophageal junction in a patient with achalasia.

agents. Extrinsic compression from surgical procedures, such as fundoplication or bariatric surgery (gastric band), can also cause secondary achalasia.

There is a spectrum of achalasia-type disorders. Classic achalasia is characterized by a hypertonic LES and aperistalsis. Another subtype may include hypertonic LES, aperistalsis, and panesophageal pressurization (increased pressure of the entire esophageal body between the lower and upper esophageal sphincters).

The initial diagnostic test is barium esophagography, which shows dilation of the esophagus with narrowing at the gastroesophageal junction, known as a "bird's beak" (**Figure 5**). Upper endoscopy reveals retained food and saliva, no signs of mechanical obstruction or mass, and "tightness" at the gastroesophageal junction while the scope is advanced into the stomach. In classic achalasia, esophageal manometry shows incomplete LES relaxation and aperistalsis and confirms the diagnosis. Manometry may also detect evolving achalasia variants or spastic achalasia variants.

Pseudoachalasia results from malignant tumor infiltration or other secondary causes leading to myenteric plexus damage and can present similarly to achalasia. Unlike achalasia, pseudoachalasia has been associated with sudden weight loss later in life. Three clinical features suggest cancer as a cause of pseudoachalasia: short duration of dysphagia (<1 year), weight loss (>6.8 kg), and age older than 55 years. Suspected pseudoachalasia should be evaluated with CT, endoscopy, or endoscopic ultrasonography.

Treatment of achalasia includes endoscopic or surgical intervention with the goal of lowering LES pressure, which relieves symptoms. Medical therapy is uncommonly used.

Endoscopy with botulinum toxin injection into the LES inhibits acetylcholine release, relaxing the LES. However, after 1 year, only 40% of patients have continued symptom relief. Botulinum toxin injection can be repeated, but successive treatments are often less effective for symptom management. Pneumatic dilation is an effective nonsurgical therapy. Dilators ranging from 30 mm to 40 mm are used to disrupt the circular muscle. Clinical symptom relief ranges from 50% to 90%, and the most common complication is perforation.

Surgical treatment consists of laparoscopic myotomy of the circular muscle fibers. A partial fundoplication may also be done laparoscopically to prevent reflux symptoms after myotomy. Advantages of laparoscopic myotomy include the ability to address any hiatal hernia, if present, and perform a concurrent antireflux procedure. Peroral endoscopic myotomy (POEM) is a newer procedure that entails creation of an esophageal submucosal tunnel extending to the LES and then a myotomy. Advantages of POEM include the lack of skin incisions and ability to perform a longer myotomy, which may be beneficial in spastic achalasia. Disadvantages include risk for reflux. Choice of therapy depends on patient factors, type of disease, and available local expertise.

Medical therapy is reserved for poor candidates for endoscopic or surgical therapy. LES pressure can be reduced with medical therapy, including calcium channel blockers (nifedipine) or long-acting nitrates.

Patients with achalasia for more than 10 years have increased risk for squamous cell carcinoma and may benefit from surveillance endoscopy, but there are no established guidelines for frequency of surveillance.

Diffuse Esophageal Spasm and Jackhammer Esophagus

Spastic disorders of the esophagus may present with chest pain or dysphagia. Diffuse esophageal spasms are characterized by premature contractions, and the esophagus has a "corkscrew" (**Figure 6**) or "rosary bead" appearance on esophagography. Jackhammer esophagus occurs in patients with high-vigor peristaltic contractions.

Symptoms often respond to nitroglycerin, suggesting a flaw in esophageal nitric oxide production. Any GERD symptoms should be treated with a PPI. In patients without GERD symptoms, medical therapy with antidepressants (trazadone, imipramine) or a phosphodiesterase inhibitor (sildenafil) can relieve chest pain. Dysphagia may respond to calcium channel blockers. Botulinum toxin injection has alleviated dysphagia symptoms.

Hypotonic Motility Disorders

Hypotonic disorders of the esophagus are marked by lack of contractility and incomplete peristalsis. Patients may report GERD symptoms, which result from decreased LES pressure or dysphagia from incomplete peristalsis. In most cases, the cause of hypotonic esophageal disease is unknown. However, secondary causes include smooth-muscle relaxants, anticholinergic agents, estrogen, progesterone, connective

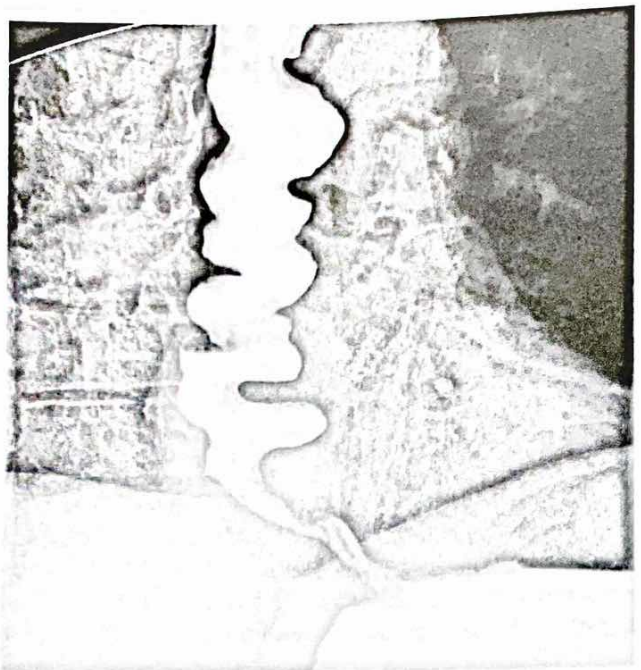

FIGURE 6. Findings of a "corkscrew" esophagus (caused by multiple simultaneous contractions) on esophagography are typical of diffuse esophageal spasm.

tissue disorders (e.g., systemic sclerosis), and pregnancy. Esophageal manometry shows weak nonperistaltic contractions in the distal esophagus. Findings can mimic those of achalasia.

Treatment includes lifestyle changes, such as eating upright and consuming liquid or semisolid rather than solid food. Medical therapy includes acid-reducing agents for GERD and low-dose antidepressants to reduce chest discomfort. Prokinetic agents (e.g., metoclopramide) are not recommended.

KEY POINTS

HVC
- In patients with symptoms of gastroesophageal reflux disease but without alarm features, an empiric trial of a proton pump inhibitor is the initial management.
- The diagnostic criteria for eosinophilic esophagitis are esophageal symptoms (most commonly dysphagia), esophageal biopsy specimens showing persistent eosinophil counts of 15/hpf or greater, and exclusion of other causes of eosinophilia.

HVC
- *Candida* esophagitis can be diagnosed clinically on the basis of compatible symptoms, such as dysphagia and oral candidiasis.
- Herpes simplex virus and cytomegalovirus esophagitis are seen in immunodeficient or immunosuppressed individuals; endoscopy with biopsy is needed to confirm the diagnosis.
- Treatments for achalasia include botulinum toxin injection, pneumatic dilation, and surgical myotomy; botulinum toxin injection is associated with high relapse rates.

Metaplastic and Neoplastic Disorders of the Esophagus

Barrett Esophagus

Epidemiology and Screening

Barrett esophagus is the replacement of the squamous epithelium with metaplastic columnar epithelium in the esophagus. It is a consequence of GERD, even in patients without clinical symptoms, and is a precursor lesion for esophageal cancer. Risk factors associated with Barrett esophagus include chronic GERD (for >5 years), age older than 50 years, male sex, white race, tobacco use, and obesity. Drinking alcohol is not associated with increased risk for Barrett esophagus, and wine consumption might be protective.

The annual cancer risks are 0.2% to 0.5% per year for Barrett esophagus without dysplasia, 0.7% per year for Barrett esophagus with low-grade dysplasia, and 7% per year for Barrett esophagus with high-grade dysplasia.

About 10% of patients with GERD are found to have Barrett esophagus on endoscopy. Evidence does not support routine screening for Barrett esophagus based on GERD symptoms for the general population. Studies suggest that individuals with multiple risk factors for esophageal carcinoma and chronic GERD might benefit from screening. Men older than 50 years with GERD symptoms for more than 5 years and additional risk factors (nocturnal reflux symptoms, hiatal hernia, elevated BMI, intra-abdominal distribution of body fat, tobacco use) may benefit from screening endoscopy. Women generally do not require routine endoscopic screening for Barrett esophagus and should be selected for screening on a case-by-case basis.

Diagnosis and Management

Barrett esophagus is diagnosed by endoscopic findings (**Figure 7**) with biopsy, which are then confirmed by pathology showing specialized intestinal metaplasia with acid-mucin–containing goblet cells. Barrett esophagus is categorized by endoscopy measurements as short-segment (≤3 cm) or long-segment (>3 cm). Long segments are at a higher risk for cancer progression than are short segments.

Barrett esophagus progresses along a continuum: intestinal metaplasia, indefinite for dysplasia, low-grade dysplasia, high-grade dysplasia, intramucosal carcinoma, and, finally, invasive adenocarcinoma. The stage informs surveillance and treatment recommendations (**Table 4**).

In patients with Barrett esophagus, medical therapy should be used to treat reflux symptoms and to heal reflux esophagitis. No strong evidence suggests that antireflux surgery can prevent progression of Barrett esophagus to adenocarcinoma when compared with medical therapy with PPIs.

Endoscopy-based therapies for patients with confirmed dysplasia include endoscopic mucosal resection for all visible lesions and radiofrequency ablation; experience with other ablative methods, such as cryotherapy, is growing.