# Chapter 3
# Making an Accurate Diagnosis of GERD

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## Introduction

Gastroesophageal reflux disease (GERD) is a common problem, affecting 20% of the population in some manner on a monthly basis [1]. For most individuals with GERD, the gastric refluxate in the esophagus causes heartburn, the most common symptom associated with GERD. Most patients are both diagnosed and treated by a trial of acid antagonist, most commonly, proton pump inhibitors (PPIs). Although less common, a substantial number of patients experience symptoms outside the esophagus, usually in the throat or lungs. It is accepted that gastroduodenal contents refluxed into the esophagus and aspirated through the vocal cords may result in what is often referred to as extraesophageal or airway-type symptoms and pathology. These can range from cough and hoarseness to asthma and pulmonary fibrosis. It is important to realize that almost all of these presentations may have other etiologies and contributing factors. Therefore, although it is important to recognize the possible role that GERD may be playing, it is also imperative that GERD is worked up and diagnosed appropriately in order to select the proper patients to treat and to select the proper therapy.

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## Etiology of Reflux and Associated Symptoms

The primary anatomic cause for GERD is a dysfunction of the anti-reflux barrier complex located around the lower esophageal sphincter (LES). Within this complex are several components that all contribute to the prevention of reflux. The LES acts as a one-way valve that is designed to allow passage of food from the esophagus to the stomach while preventing the reflux of gastric contents into the esophagus. The LES maintains a resting pressure that is designed to relax during a swallow. A phenomenon of transient lower esophageal sphincter relaxation, in which the LES relaxes independent of swallow induction, has been associated with reflux events. When the pressure drops and is overcome by increased intra-abdominal pressure, the reflux episode is generated. In addition, there is a small group of patients who have a chronically hypotensive LES such that the resting pressure is insufficient, allowing free reflux to occur. Another component of the anti-reflux barrier complex is the angle of His, an angulation formed by the esophagus, hiatus of the diaphragm, and cardia of the stomach at the level of the gastroesophageal junction (GEJ). Most commonly, the angle of His is disrupted secondary to a hiatal hernia, a weakness of the diaphragmatic crura that results in a gap between the crus and the GEJ. The natural evolution of hiatal hernias is to gradually widen over time due to increased pressure and stress on the diaphragm. Common causes for this are chronic cough, obesity, pregnancy, and repetitive straining. The hernia defect allows the GEJ to slide in and out of the mediastinum. The loss of external compression in combination with the loss of the angle of His causes the anti-reflux complex and LES to become functionally incompetent allowing reflux to occur.

In addition to defects of the LES, reflux can be augmented by anatomic dysfunction proximal and distal to the LES. Dysmotility disorders of the esophagus can contribute to incomplete clearance of the esophagus. While this does not directly cause reflux, it can result in prolonged exposure of refluxate to the distal esophagus and regurgitation, thus accentuating reflux-related symptoms and manifestations. Similarly, delayed gastric emptying and gastric atony can cause pooling of material in the stomach, providing a larger pool of material that can be refluxed in a patient who already has LES dysfunction.

Understanding how dysfunction of the anti-reflux complex causes GERD helps explain why patients can develop a multitude of typical and atypical symptoms. Typical reflux symptoms are heartburn, regurgitation, acid/water brash, chest pain, and dysphagia. Heartburn and regurgitation have a high probability (and thus some diagnostic value) for being associated with GERD. As one proceeds further down the list of symptoms, there is a lower likelihood of association with GERD. Atypical symptoms of GERD include cough, hoarseness, aspiration, globus sensation, and nausea. These symptoms are called atypical because there are multiple disease processes other than reflux that can produce these symptoms. Patients with primary pulmonary disease can often present with atypical symptoms such as cough. Therefore, additional confirmatory testing is needed to help make an accurate diagnosis if GERD is suspected to play a role in a patient's symptoms or disease.

## Endoscopy

Flexible endoscopy of the esophagus and stomach can help identify anatomic etiologies for GERD and resultant pathologic changes. Examination of the esophageal mucosa allows for visual identification of erosions and changes in epithelium such as metaplasia that may be secondary to reflux and acid exposure. If any of these changes are visualized, biopsies should be taken to make a histologic diagnosis. Visualization of the esophagus at the level of the *Z*-line can also identify the presence of a hiatal hernia. Progressing further into the stomach, gastric dilation and retained food may suggest gastric dysmotility that could contribute to reflux. Visualization of bile may also suggest a component of bilio-duodenal reflux. Retroflexion of the endoscope in the stomach allows for visualization of the gastroesophageal junction and cardia of the stomach (Fig. 3.1). It is at this point that hiatal hernias can often be more clearly identified. With large hiatal hernias or paraesophageal hernias, patients can develop Cameron's ulcerations, which can contribute to the atypical presentation of anemia.

Upon endoscopic retroflexion, the flap valve of the GE junction can be graded, based on the Hill classification to assess the competency of the valve. The Hill classification grades the gastroesophageal valve from I to IV. The grading system is as follows: Grade I—prominent fold of tissue close to the endoscope extending 3–4 cm along the lesser curve, Grade II—less prominent fold with occasional opening and closing of the valve around the endoscope during respiration, Grade III—no prominent fold and loose gripping of the endoscope by the tissue, and Grade IV—hiatal hernia with no fold or gripping of the endoscope by the tissue resulting in visible esophageal squamous epithelium. The altered geometry of the gastroesophageal flap valve is associated with deterioration of LES pressure and a mechanically compromised sphincter. Grade I valves are seldom associated with reflux, while Grade IV valves have a high

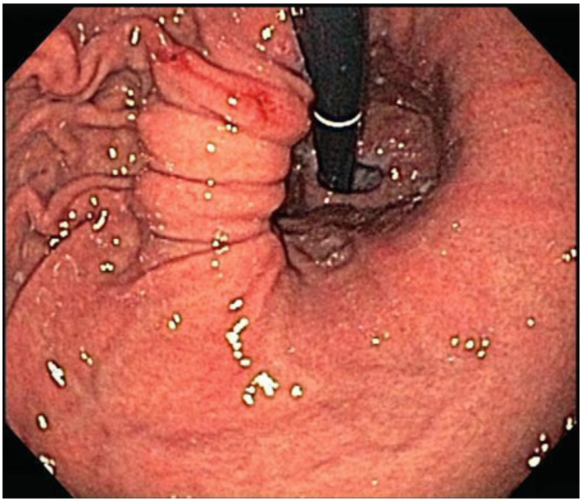

**Fig. 3.1** Endoscopic gastroduodenoscopy (EGD) showing a hiatal hernia

association with reflux. There is more of a gray area with Grade II and Grade III valves, and prediction of GERD strictly based on these endoscopic findings is not strong. Therefore, additional testing should be performed to confirm GERD [2].

## Upper Gastrointestinal Esophagram

A real-time esophagram performed under fluoroscopy can help identify anatomic abnormalities that can cause GERD. For example, being able to identify the location of the GEJ relative to the diaphragm can determine the presence of a sliding hiatal hernia. Stomach that is visualized above the diaphragm can help with the diagnosis of a more severe hiatal hernia or a paraesophageal hernia. As discussed earlier, these changes in the LES and angle of His are major contributors to the development of reflux. Watching a contrast bolus being swallowed can provide the unique view of active reflux of contrast material from the stomach into the esophagus. An esophagram can also identify other etiologies for reflux-like symptoms that are due to other disorders. For example, patients with dysphagia could have esophageal dysmotility disorders such as achalasia or esophageal spasm as opposed to a reflux etiology such as a peptic stricture. The esophagram for these motility disorders shows characteristic findings of a dilated esophagus with bird's beak tapering or a corkscrew esophagus that are pathognomonic for nonreflux etiologies of dysphagia. Esophageal neoplasms and diverticula can also cause dysphagia, yet can be visualized as specific anatomic entities on an upper gastrointestinal (UGI) series in which reflux is not related to the abnormality. While these are just some of the findings that can be seen on esophagram, these examples emphasize the importance of differentiating anatomic etiologies for reflux from other anatomic pathologies that share overlapping symptomatic presentations, since the treatment plans for each disease process is very different. Because obtaining an UGI esophagram is a relatively noninvasive way to characterize the anatomy of the esophagus, GEJ, and stomach, it should be considered when evaluating a patient for reflux. Given its particular benefit of displaying the relational anatomy of the esophagus and stomach, it is particularly useful to surgeons involved in the evaluation of GERD (Fig. 3.2).

## Manometry

Just as characterizing the anatomy of the GEJ and LES is important for understanding reflux, characterizing the physiology of the LES also contributes to making the diagnosis of GERD and helping to develop a treatment plan. Esophageal manometry is a diagnostic tool that characterizes esophageal pressure, propulsion, and coordination. This procedure involves insertion of a multichannel catheter transnasally, across the esophagus, and beyond the LES into the stomach. Typically, ten liquid swallows are performed. With each swallow, the catheter's transducers capture the pressure generated by the segments of the esophagus in a temporal fashion.

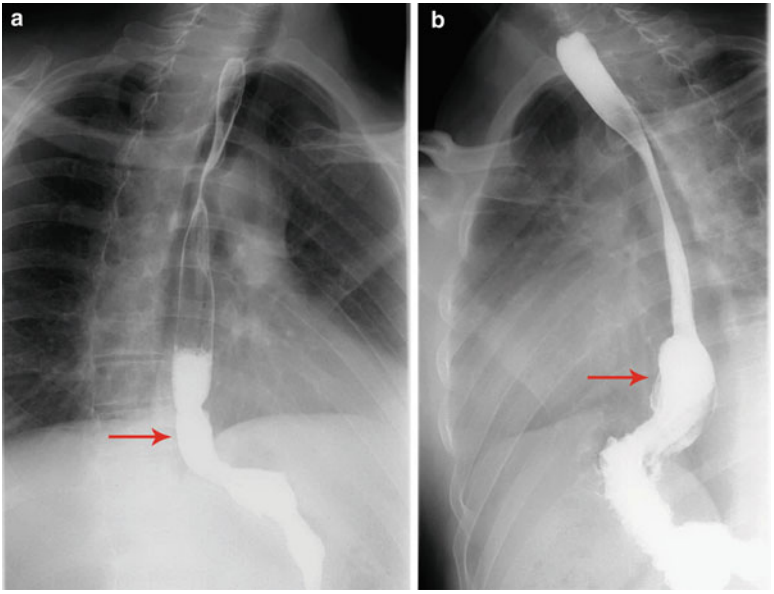


**Fig. 3.2** (**a**, **b**) UGI esophagram demonstrating a hiatal hernia

In doing so, the upper esophageal sphincter, esophageal body, and lower esophageal sphincter are evaluated. The exact location of the lower esophageal sphincter can be identified, which is important for accurate placement of a pH probe. pH monitoring, discussed later in this chapter, is the gold standard for the detection of reflux and requires exact placement of the distal probe 5 cm above the LES in order to provide accurate measurements.

A temporal view of the peristaltic waveform helps to characterize the coordination of the esophageal contraction and give insight into the efficiency of propulsion. Weakness of the lower esophageal sphincter (defined by low resting pressure) in the absence of motility disorders can help identify an anatomic cause of reflux [3]. The length of the LES can also be measured with manometry. Short LES length has been shown to be associated with reflux. In addition, a dual high-pressure zone on esophageal manometry testing can help identify the presence of a hiatal hernia that can also result in reflux (Fig. 3.3).

As discussed earlier, abnormalities with esophageal motility and LES function can result in pathologies that are not related to reflux, but have reflux-like symptoms. Esophageal dysmotility can result in uncoordinated propulsion of food into the stomach. Coupled with an incompetent LES this can result in stasis of gastric contents in the esophagus and regurgitation, particularly in the supine position. While a patient may be regurgitating and having dysphagia symptoms, treatment for dysmotility is very different from treatment for reflux, and in the case of surgical treatment, the operations are completely different. Because of the ability of manometry to differentiate between primary esophageal motility disorders from reflux, it is an

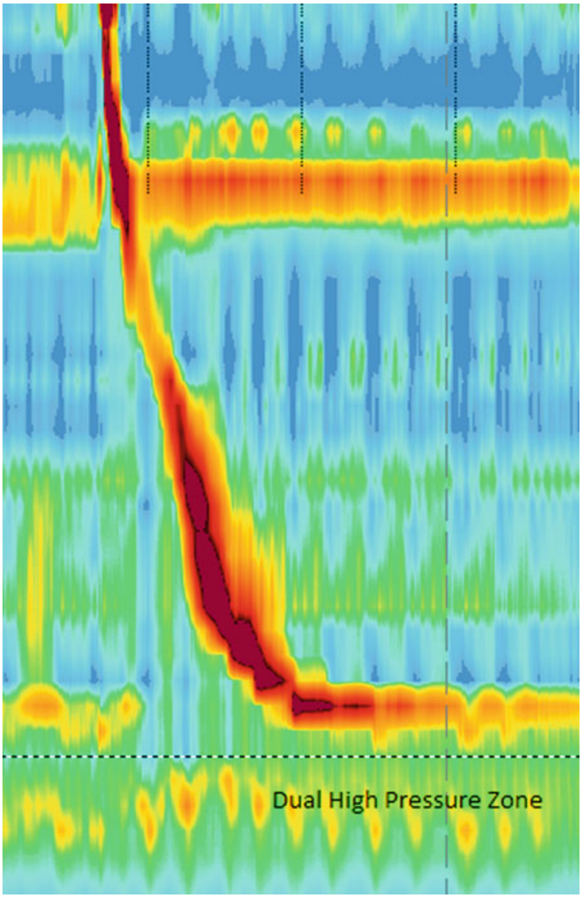


**Fig. 3.3** High-resolution manometry tracing showing decreased LES pressure and a hiatal hernia

important and necessary preoperative test to help operative decision-making should an anti-reflux operation be indicated. Specifically, for a patient who has been identified to have reflux and is a candidate for a surgical anti-reflux operation, if the patient is also shown to have severe esophageal dysmotility, a complete fundoplication may cause a functional esophageal obstruction, resulting in worsening symptoms and inappropriate treatment of disease.

## Ambulatory pH Monitoring

Ambulatory pH monitoring has long been established as the gold standard for measuring GERD [4–6]. pH monitoring is performed most commonly with a transnasally placed catheter that has a pH electrode at the distal tip (Fig. 3.4). The electrode

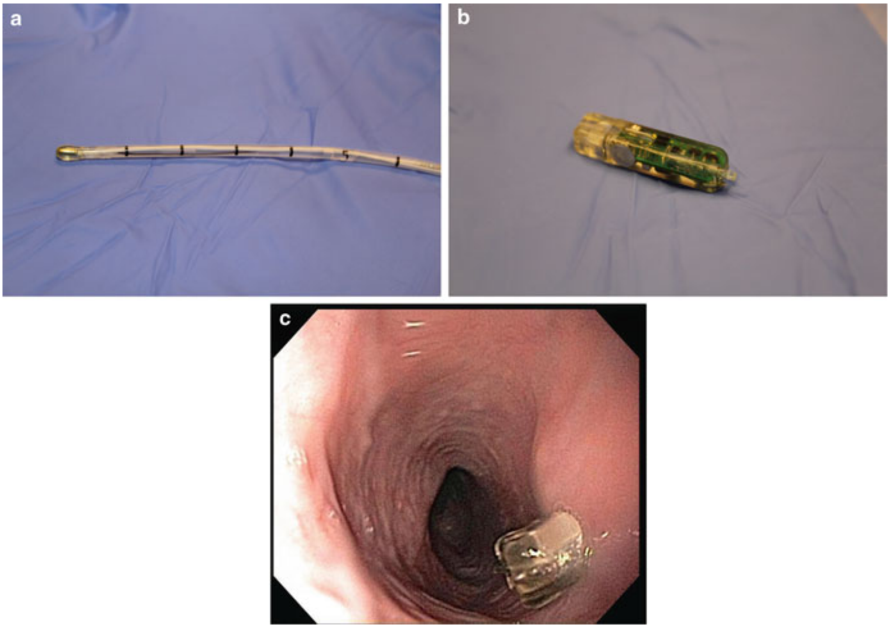

**Fig. 3.4** (**a**) pH catheter. (**b**, **c**) A Bravo probe

is positioned 5 cm above the GEJ as determined by an in-line pressure transducer and pull-through technique, esophageal manometry, or upper endoscopy (though by far the most accurate method is manometry). The electrode is connected to a portable recording device that streams continuous pH readings from the electrode. The recorder also allows the patient to simultaneously mark when symptoms are present to allow for symptomatic correlation analysis. Alternatively, a wireless capsule with a pH electrode can be placed in a similar fashion to record continuous distal esophageal pH (Bravo system, Medtronic, Minneapolis, MN). The probe communicates to a portable recording device via a radio signal and is often tolerated better by patients because of the lack of transnasal catheter (Fig. 3.4).

All acid-suppression and promotility medications are stopped prior to testing. Proton pump inhibitors are withheld for 7 days, and H2 blockers are withheld for 48 h prior to the testing to determine maximum esophageal acid exposure. The probe is worn for a 24-h period during which the patient is instructed not to alter their daily routine or diet in order to most accurately represent a typical day. After the 24-h period is complete, the pH catheter is removed, and the data are downloaded and analyzed. Alternatively, the wireless capsule pH probe disengages over time and is expelled from the body.

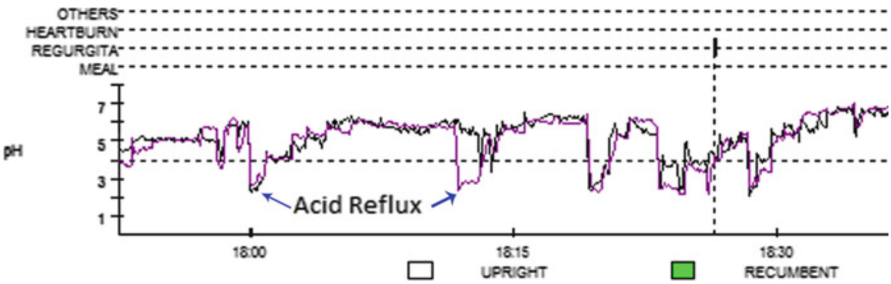


**Fig. 3.5** 24-h Ambulatory pH tracing

Several parameters are measured to analyze for GERD: (1) Percentage of time pH < 4.0, (2) number of reflux episodes, (3) number of reflux episodes >5 min, (4) mean duration of reflux episodes, and (5) longest reflux episode. These are analyzed for both upright and supine periods and for the total duration of the test (Fig. 3.5). A calculation is performed based on these parameters, and a score is generated based on the work by Johnson and DeMeester [7]. The DeMeester score is positive for acid reflux when the value is greater than 14.72. The score has been shown to have good correlation with a diagnosis of acid reflux. When a score is borderline, correlation of a patient's symptoms with quantitative measurements of pH can be further examined to assist in making a diagnosis of GERD.

Despite the excellent predictive value of pH testing for diagnosing GERD, the sensitivity for detecting reflux that travels more proximally and is at risk for aspiration is not ideal. Therefore, discerning the role of GERD in patients with respiratory symptoms with traditional pH monitoring is less clear. Studies have been performed to measure pharyngeal pH as a surrogate for pharyngeal reflux by positioning the probes relative to the upper esophageal sphincter as opposed to the LES [3, 8]. The value of doing so is that there can be objective measurement of pharyngeal acid exposure. Studies have shown good correlation between positive pharyngeal pH testing with response to medical and surgical therapies for reflux, thus adding value to pharyngeal pH monitoring [9, 10]. Interestingly, however, based on the current data, the correlation between positive pharyngeal pH and esophageal pH is not strong, which emphasizes that patients can still have reflux and associated respiratory symptoms or microaspiration without a quantitatively positive study [3]. Ultimately, the current opinion is that in a patient who has a positive esophageal pH test with related respiratory symptoms without other identifiable causes for those respiratory symptoms, there is a reasonable probability that reflux is the etiology. Similarly, in a patient with a positive pharyngeal pH test, there is a strong correlation with microaspiration and respiratory symptoms. Nonetheless, the pH monitoring still should be evaluated in the context of the patient's symptoms, anatomy, and other functional information obtained from studies described above.

## pH Impedance Testing

A limitation of pH testing is the inability to determine reflux while patients are on acid-suppression medication. In addition, pH testing also does not detect the presence of nonacidic gastroduodenal reflux. Impedance testing has been used in combination with pH monitoring to attempt to evaluate these patients [11, 12]. Impedance probes have multiple sensors placed in a circumferential orientation along the length of the catheter (Fig. 3.6). As refluxate progresses proximally up the esophagus, the resistance measured by the electrode decreases (liquid conducts electrical current more easily than air). As the refluxate continues to move proximally, the resistance measurements decrease in sequence along the more proximal electrodes. The progressive decrease in resistance results in a characteristic tracing. The accuracy of impedance testing is controversial, though some studies have suggested that the combination of traditional pH testing with impedance monitoring provides a more sensitive test for acid and nonacid reflux. However, there are still few definitive studies available showing the ability of impedance monitoring to predict the response to medical or surgical GERD therapies.


**Fig. 3.6** (**a**) Impedance catheter. (**b**) Tracing showing reflux

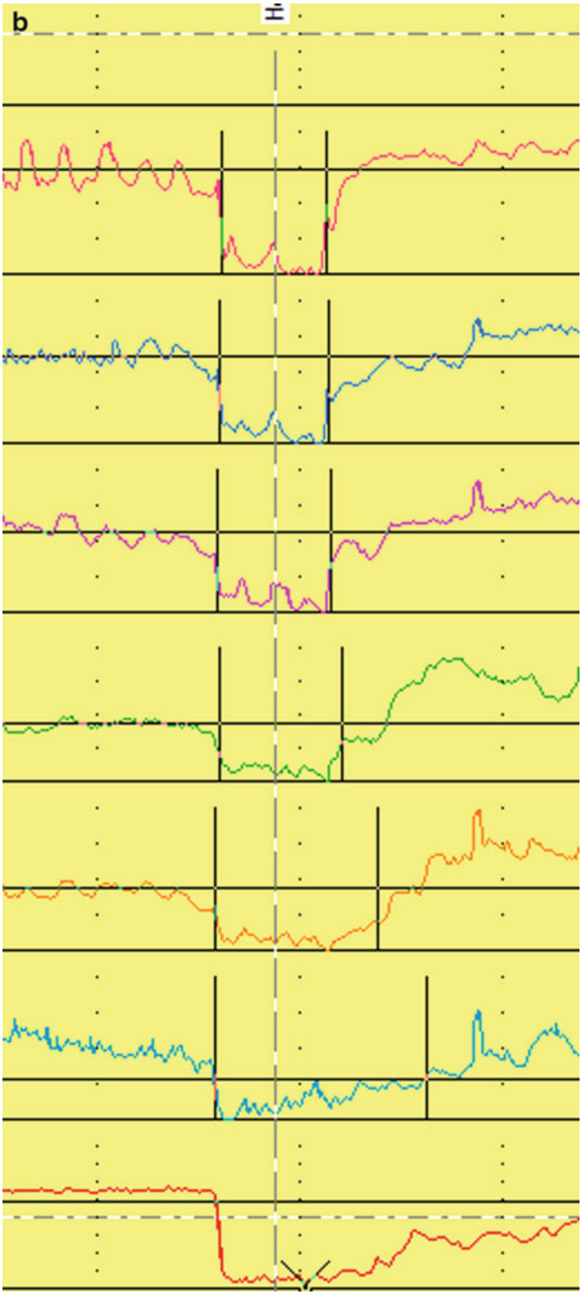


**Fig.3.6** (continued)

## Alternative Testing Modalities for Reflux

Several other tests are being investigated that may help with the diagnosis of reflux. These tests are based on the reflux and subsequent microaspiration of unique gastric markers. In addition to being more specific for microaspiration, they may also be less invasive tests compared to traditional 24-h pH monitoring and BRAVO probe placement. Sputum pepsin analysis is one such test. Pepsin is made only in the stomach and when refluxed out of the esophagus is phagocytosed by laryngeal epithelium. Therefore, induced sputum can be analyzed with immunoassay testing to identify the presence and quantify the density of pepsin protein [13, 14]. This test appears to have a high specificity for reflux based on initial studies. A similar test involves analyzing macrophages of induced sputum specimens for the presence of lipid [15, 16]. The lipid-laden macrophage index (LLMI) is a calculation of intracellular lipid that comes from food particles that are refluxed and aspirated. Alveolar macrophages are isolated and stained. The amount of lipid is then graded by a pathologist or, more recently, with high-resolution automated 3-D imaging. The LLMI is then calculated, and if it exceeds a defined threshold, suggests a diagnosis of reflux. While these are both new methods that still require more validation, they may offer less invasive alternatives to assist in the diagnosis of reflux.

## Conclusion

Gastroesophageal reflux disease is a common problem that affects the general population. GERD can manifest itself in multiple ways and can present with atypical respiratory symptoms. Because multiple disease processes can share these same symptoms, accurate diagnosis of GERD is critical in order to select the correct patients for treatment. Understanding the gastroesophageal anti-reflux complex and how changes in gastroesophageal and hiatal anatomy contribute to reflux will allow the practitioner to understand and interpret the tests that are available in order to differentiate GERD from other diagnoses. Each diagnostic test and a further understanding of the unique information each provides adds components for making an accurate diagnosis of GERD. pH testing is the gold standard test for diagnosing reflux. Endoscopy and upper gastrointestinal esophagram can help characterize the esophageal, LES, and gastric anatomy. Esophageal manometry contributes valuable information about the physiology of the esophagus and LES, findings of which may contribute to augmentation of reflux symptoms. By synthesizing all of the data, the practitioner can then differentiate GERD from other disease processes that have similar symptoms and select the appropriate patients for treatment.

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