Understanding and Managing the Patient with

Gastroesophageal Reflux Disease (GERD)

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Lesson description

Pharmacists are called upon by their patients to help them manage a variety of disorders, and one of the more common disorders is gastroesophageal reflux disease (GERD). GERD is present in a large proportion of the population with varying symptoms and can negatively affect the quality of life of these individuals. Pharmacists should be able to identify the symptoms and give patients direction to help them manage the disease. This lesson will review the epidemiology, pathophysiology, diagnosis, and symptoms of GERD. The treatment options, non-pharmacological and pharmacological including prescription and over-the-counter medications, will be discussed. In addition, a tool to help pharmacists evaluate the effectiveness of their treatments is included in this lesson.

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Learning objectives

Upon completion of this continuing education lesson, the reader will:

1. be able to provide a definition of gastroesophageal reflux disease
2. have a thorough understanding of the prevalence of GERD in the general population
3. have a comprehensive knowledge of normal gastroesophageal physiology
4. be able to list the physiological and anatomic factors that contribute to the development of GERD
5. be able to understand and list the complications of GERD
6. be able to recognize and list the typical, atypical, and complicated signs and symptoms of GERD
7. be able to identify the tools that can be used in the diagnosis of GERD
8. be able to identify which of the diagnostic tools is most appropriate, accurate, and/or practical in the diagnosis of GERD in a particular patient
9. be able to list the three treatment modalities for GERD
10. have an understanding of what lifestyle modifications patients can adopt in the treatment of GERD
11. have an understanding of pharmacological management of GERD and be able to
    a. list the classes of medications used in the treatment of GERD
    b. show a thorough knowledge of the mechanisms of action, side effects, dosing, and precautions associated with each medication or medication class
    c. define the role of each medication or medication class in the treatment of GERD based on current evidence
12. have a basic understanding of the principles of surgical management of GERD
13. be able to identify the patients in which surgical management of GERD is the most appropriate form of treatment
14. be able to apply the knowledge acquired in the lesson to choose the most appropriate medication(s) for the patient based on a thorough knowledge of GERD, patient specific factors, and current evidence
15. be able to apply the PASS Test to evaluate the effectiveness of maintenance treatment

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Topic Expertise: Marica Gaspic Piskovic attained her Bachelor of Science in Pharmacy from the University of Alberta in 1989. She completed a residency in hospital pharmacy at the McMaster University Medical Centre in 1990, where she did a rotation in gastroenterology. Marica spent a significant portion of her residency as a clinical pharmacist in geriatrics as well as chronic non-malignant pain at the Chedoke site, where she routinely managed patients with GERD. Ms. Gaspic Piskovic furthered her career in drug information at a multinational manufacturer and working as a consultant for a private payer. In addition, Ms. Gaspic Piskovic has worked in retail pharmacy, has taught pharmacy technicians pharmacology, and has consulted. Ms. Gaspic Piskovic also has a number of publications, one of which was a coauthored continuing education program on GERD. Currently Ms. Gaspic Piskovic works as a consultant and in community pharmacy.

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1. Introduction to GERD

1.1 Definition

Gastroesophageal reflux is the movement of gastric material in a retrograde direction into the esophagus. This occurs normally in most individuals and is characterized by episodes of asymptomatic and brief periods of reflux that does not result in injury to the esophagus. Gastroesophageal reflux disease is said to be present when the reflux of gastric material results in symptoms with or without the presence of injury to the esophagus. GERD can also be present when there are no symptoms but there is objective evidence of esophageal injury on endoscopic examination.[1] Patients can present with symptoms of GERD without evidence of esophageal injury on endoscopic examination.[1,2] This condition is referred to as endoscopic-negative reflux disease (ENRD).

The impact of GERD on the quality of life was added as another parameter to measure the severity of the disease by the Canadian Consensus Conference on the management of gastroesophageal reflux disease in adults.[1]

1.2 Epidemiology

GERD is most prevalent in Western countries and there appears to be no difference based on gender.[2] It should be noted that Barrett's esophagus, a complication of GERD, is more likely to occur in adult white males residing in Western countries. Esophagitis is also more likely to occur in white males.

Many patients do not seek medical attention for mild symptoms, preferring to self-medicate with over-the-counter antacids. In addition, there is no recognized gold standard for the diagnosis of GERD.[3]

Approximately 7–10% of people experience heartburn, a typical symptom of GERD, on a daily basis.[3,4] Of these people, 20–40% will suffer from abnormal levels of reflux, which commonly leads to symptoms and/or physical damage to the esophagus.[5]

The Canadian Adult Dyspepsia Empiric Treatment-Prompt Endoscopy (CADET PE) study investigated the prevalence of dyspepsia in adult patients who complained of symptoms with no prior endoscopy.[6] The purpose of this study was to better understand the prevalence in this group, and to determine the predictability of clinically significant upper gastrointestinal findings. A total 1040 patients representing 49 Canadian family practice sites were selected and underwent endoscopy within 10 days of referral. The patients were managed and followed by their respective physicians for a period of 6 months. Dyspepsia was subclassified into the following categories for which the patients were evaluated: ulcer-like dyspepsia, reflux-like dyspepsia, and dysmotility-like dyspepsia. The most common diagnosis in these patients was esophagitis (43%), and the subclassification of dyspepsia was deemed of limited value in predicting the presence of clinically significant upper gastrointestinal findings.

Esophagitis, one of complications of GERD, is said to occur in 50% of patients.[2] Barrett's esophagus, another complication of GERD, occurs in 8–15% of patients.[4]

1.3 Quality of life

A group of Canadian gastroenterologists came to a consensus that GERD is the most prevalent acid-related disease which can have a negative impact on the health-related quality of life (HRQL).[1] Although GERD has a low disease-related mortality, it can impair the quality of life to a degree that may surpasses the impact by other disease states (i.e., diabetes, heart failure).[1] This was substantiated by a survey of 102 GERD patients of which 41% reported a decrease in productivity and absenteeism.[7]

2. Pathophysiology of GERD

2.1 Normal gastroesophageal physiology

The esophagus moves from the thorax into the abdomen through the esophageal hiatus (an opening in the right crus of the diaphragm). The lower esophageal sphincter (LES) is a band of muscle at the most distal portion of the esophagus that lies just above the stomach and just below the diaphragm. This band of muscle cannot be distinguished from the esophageal body but is distinctly different from it. The LES is a 1–3.5 cm muscle band that maintains a resting pressure that is 10–45 mm Hg in excess of the pressure in the stomach (normal mean LES pressure is 13 mmHg). This creates a positive pressure gradient between the thorax and the abdominal cavity. The positive pressure gradient that is created prevents the reflux of gastric material into the esophagus. The crural diaphragm will contract during inspiration and pinch the distal portion of the esophagus, which also serves as a barrier to reflux of gastric material. This secondary mechanism will also serve as an adjunct to the actions of the LES in preventing reflux. The angle at which the esophagus meets the stomach is called *the angle of His*. This angle at the junction creates a one-way flap valve, which in turn prevents reflux. Finally, the most distal portion of the esophagus extends into the abdominal cavity,

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where increases in abdominal pressure pinch esophageal walls together and prevent reflux.

2.2 Physiological factors that contribute to GERD

2.2.1 Transient LES relaxation[8,9]

There are three main physiologic reasons why gastric material moves backward into the esophagus. First, and most common, is transient LES relaxation (TLESR). Normally, when food is swallowed, peristalsis will move it down the esophagus and the LES will relax (resting pressure decreases to zero) for a period of 3–10 seconds. This relaxation allows the food bolus to pass into the stomach. With GERD, LES relaxation can occur anytime and can last for periods up to 45 seconds. This prolonged drop in LES pressure does not allow the LES to serve as a barrier to reflux. TLESRs occur about 2 to 6 times per hour in normal individuals as part of the normal belching mechanism. In patients with GERD they can happen as many as 3 to 8 times per hour and more commonly will be associated acid reflux. The TLESR mechanism is an example of how a patient can have normal levels of acid production and still develop GERD.

2.2.2 Increased intra-abdominal pressure[8,9]

The second mechanism is due to increases in intra-abdominal pressure. Intra-abdominal pressure will transiently increase due to coughing, straining, bending over, or eating. This increase in pressure forces gastric material upward towards the gastroesophageal junction. If intra-abdominal pressure increases during a TLESR, the LES does not have sufficient pressure to prevent the movement of gastric material into the esophagus.

2.2.3 Atonic LES[8,9]

The third mechanism for GERD is due to an atonic LES. If the LES has no muscle tone it cannot maintain adequate resting pressure and will thus allow free reflux of gastric contents into the esophagus.

TLESRs will only usually occur in states of adequate resting LES pressure. Increases in intra-abdominal pressure and atonic LES occur only if the LES pressure is low. Common factors that can lower LES pressure are fatty foods and medications (see Table 2).

2.2.4 Abnormal esophageal clearance[8,9,10]

In a normal individual the clearance of acidic materials occurs quickly with the aid of four mechanisms: peristalsis, gravity, salivation (alkaline substance), and bicarbonate production. If this process works well, the acidic material does not remain in contact with the esophagus long enough to damage the tissue. There are conditions or situations that interfere with these mechanisms; for example:

- sleeping can remove the aid of gravity in clearing acidic material
- scleroderma can reduce peristalsis, allowing acidic material to remain in the esophagus for extended periods of time
- saliva production is minimal during sleep; therefore, acidic material cannot be neutralised

2.2.5 Esophageal epithelial resistance breakdown[8,9]

Normal esophageal epithelial lining consists of a mucous layer, a water layer, and a layer of bicarbonate ions. This lining is sufficient in normal individuals to protect the esophagus from degradation by acidic gastric material. In patients with GERD, this acidic gastric material is in contact with the esophagus for prolonged periods of time, causing the protective mechanisms of the lining to break down. Esophageal injury from this exposure ensues.

2.2.6 Composition of reflux material[8,9]

Gastric material can lead to esophageal injury if the pH is less than 4. The injury occurs as a result of direct denaturation of proteins. In addition, at a pH of less than 4, pepsinogen is converted to pepsin, which can begin to digest esophageal tissue.

The reflux of pancreatic juices and biliary juices is also possible. These alkaline solutions can increase the permeability of the esophageal lining to hydrogen ions. The alkaline solutions are also direct irritants to the esophageal lining. In general, a pH of less than 4 will contribute to the development of GERD.

2.2.7 Abnormal gastric emptying[8,9]

GERD can develop if there is a delay in the emptying time of gastric contents. In considering delayed gastric emptying it is important to understand the contribution of gastric volume. As gastric volume increases, so does the frequency of reflux episodes. In addition, the higher the gastric volume, the more gastric material there is to reflux. Smoking and fatty foods are known causes of delayed gastric emptying times, increased gastric volumes, and lowering of LES resting pressure.[10]

2.3 Anatomic factors that contribute to GERD[8,9]

Abnormalities in valves, external compression of the stomach, and location of the distal portions of the esophagus are potential anatomic factors related to the presence of GERD.

Sliding hiatus hernia refers to the protrusion of the gastroesophageal junction and of the distal portion of the esophagus through the crurae of the

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diaphragm and into the chest cavity. In this situation, the crurae can no longer serve as an adjunct to the LES to prevent reflux (even if the LES pressure is normal). In addition, if intra-abdominal pressure rises in this situation, the crurae will not pinch the distal esophagus to prevent reflux. Instead, the increase in intra-abdominal pressure will push a pocket of the stomach into the chest cavity, allowing the gastric contents of that pouch to easily flow into the esophagus.

It has been shown that the combination of low LES pressures and increased frequency and/or duration of TLESR promotes the development of GERD.[10,11]

2.4 Complications of GERD

2.4.1 Esophagitis

The direct irritation of the esophageal lining from exposure to gastric material can result in esophagitis. Esophagitis can be diagnosed by endoscopic examination; the findings are ulcerations and erosions of the squamous epithelium. Esophagitis can be present regardless of the presence of the typical symptoms of heartburn.

2.4.2 Esophageal strictures

The ulceration that takes place due to reflux can lead to a buildup of fibrous tissue typically in the distal esophagus. This fibrous tissue can cause a narrowing of the esophagus, which can lead to dysphagia of solid foods. These narrowings are known as *esophageal strictures*. The strictures are usually smooth, tapered narrowings with an average length of 1–2 cm. These can be seen on barium swallow, but a more sensitive test is endoscopy, as it can detect smaller narrowings that barium swallow may miss. In order to determine if these narrowings are malignant or benign, one must use endoscopy with biopsy and brush cytology.

There are several ways to deal with strictures. Aggressive acid suppression can reduce the need for dilation and reduce the incidence of dysphagia. Balloons or dilators can be used to treat strictures by passing these devices between the narrowing and then inflating the device. In rare cases of intractable strictures, surgical resection is required.

2.4.3 Barrett's esophagus

The damage that occurs from esophagitis or stricture formation triggers the body to try and repair the affected tissue. What results is the replacement of damaged tissue, namely squamous epithelium, with columnar epithelial cells. This is known as *Barrett's esophagus*. This condition is present in 8–15% of patients who have GERD;[2] most common in patients with chronic GERD and even more likely in those with severe GERD. Patients with Barrett's esophagus are asymptomatic despite the presence of tissue damage seen upon endoscopy. The condition is diagnosed at an average age of 55 years and is more common in men. Interestingly, once Barrett's esophagus is present, it does not appear to continue to progress and further affect the esophageal lining.

Barrett's esophagus increases the risk of developing esophageal adenocarcinoma by 30 to 60 times.[2,12] The precursor to this invasive malignancy is a condition known as dysplasia. There is no definite treatment of Barrett's esophagus other than the aggressive treatment of GERD. Early surgical intervention may be warranted in the management of Barrett's esophagus to prevent further pathophysiologic changes or damage.[2] Endoscopic surveillance is recommended in patients with chronic or severe, complicated GERD.

3. Signs and symptoms of GERD

3.1 Typical symptoms

The most common symptom of GERD is heartburn. Heartburn can be described as a warm or burning feeling that is present at the sternal level and may move up into the neck. Patients commonly describe this feeling by waving their hand vertically along the sternal area (cardiac pain is often described by waving the hand horizontally across the chest). Heartburn usually occurs when gastric pH falls below 4. Heartburn comes and goes but is most likely to occur with eating high-fat foods, lying down, and bending over, all of which aggravate reflux of gastric material. It is important to note that the diagnosis of GERD based on typical symptoms alone is only correct in 70% of patients.[4]

Heartburn can be aggravated by certain foods that are known to lower LES pressure (see Table 2). The passive movement of liquid or food from the esophagus into the mouth is known as *regurgitation*. Regurgitation is the second most common symptom of GERD in adults and is very common in infants that suffer from GERD.

Acidic and spicy foods do not lower LES pressure; rather, they directly irritate esophageal tissue, thereby mimicking heartburn. In addition, heartburn can be caused by bending over, straining to defecate, or lifting heavy objects. This type of heartburn is obviously not GERD-related.

Water brash is also common in GERD. This symptom is described by hypersalivation, regurgitation, and belching. Eating large fatty meals and lying down or bending over soon after eating triggers water brash.

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3.2 Atypical symptoms

Chest pain occurs often in patients with GERD. It is sometimes mistaken for cardiac chest pain. 50% of patients with normal ECG and chest pain have GERD as the source of the pain. Non-allergic asthma is often a complaint, and gastric acid reflux directly irritates the vagus nerve, causing bronchospasm or cough. It has also been shown in one study that approximately 50% of asthmatic patients have GERD.[9] Gastric reflux material can also be aspirated and produce a chemical pneumonia or pulmonary fibrosis.

Dental erosions can also be common in GERD. This occurs due to the regurgitation of gastric material into the oral cavity.

3.3 Severity assessment

Assessment of the severity of GERD should include the frequency, intensity, and duration of the symptoms in relation to the extent that they have an impact on a patient's daily activities and HRQL.[1] In mild GERD, symptoms are infrequent (less than 3 times/week) and of low intensity and short duration with minimal to no effect on daily activities. Patients classified with moderate or severe disease would have a higher frequency (greater than 3/week) of symptoms that would be considered as intense or prolonged in duration. Generally, patients with moderate or severe disease would complain of an impact on activities of daily living and loss of productivity.

3.4 "Alarm" symptoms

Complicated symptoms are usually the result of chronic GERD. Patients with chronic untreated GERD can complain of the following symptoms:

- bleeding
- choking
- dysphagia
- weight loss
- continuous pain
- persistent vomiting
- emesis
- melena
- anemia

In patients with alarm symptoms, alternate diagnoses (e.g., PUD or gastric ulcers) should be ruled out.

4. Diagnosis of GERD

4.1 Signs and symptoms

Signs and symptoms are the most useful way to diagnose GERD. The presence of heartburn and regurgitation would lead us to believe a patient may have GERD. A study of primary care in 3 European countries demonstrated that primary care physicians were able to accurately diagnose GERD based on these 2 common symptoms.[36] At this point it is reasonable to prescribe acid suppression therapy along with counselling on appropriate lifestyle modifications. If patients respond, a diagnosis can be made. Further testing may be warranted for patients who have complicated symptoms, patients at risk of Barrett's esophagus due to chronic symptoms, and those who need continuous treatment to relieve their symptoms of GERD.

If atypical symptoms are present, the most important first step is to rule out a cardiac and/or respiratory pathology. Upon ruling out other causes of the symptoms, a proton pump inhibitor (PPI) can be prescribed for its management. The trial of a PPI could be initiated for a period of 2 to 4 weeks and the patient evaluated for effectiveness in reducing symptoms. If there is no response then the PPI should be discontinued. If a reduction in symptoms is noted, then GERD can be suspected with an option to increase the dosing of the PPI. Progress of GERD management should be evaluated at a later date.

4.2 Esophageal manometry

With esophageal manometry, a multi-lumen tube is placed down the esophagus into the stomach. The tube is then drawn up, measuring pressures across the LES, esophagus, and oral pharynx. The main purpose of this diagnostic test is to assess peristaltic function and LES function. Esophageal manometry is only useful for patients who are candidates for esophageal surgery.

4.3 Ambulatory 24-hour pH monitoring

With this type of testing, a small tube is placed intra-nasally to a point about 5 cm below the LES. Patients are then asked to keep a diary of when they have symptoms and the circumstances at the time of these symptoms. This is done to determine if the pH is actually lower than normal during symptoms.

This form of testing has a specific purpose. It is used for patients who have symptoms despite the lack of evidence of physical damage, patients who do not respond to treatment, and patients who have atypical symptoms after cardiac or respiratory pathology has been ruled out.

4.4 Endoscopy

Endoscopy is performed by placing a tube with a fibre-optic camera on the end into the mouth and down the esophagus, past the LES, and into the

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Table 1. The Modified Los Angeles Classification of GERD Description

A	One (or more) mucosal break no longer than 5 mm that does not extend between the tops of 2 mucosal folds
B	One (or more) mucosal break more than 5 mm that does not extend between the tops of 2 mucosal folds
C	One (or more) mucosal break that is continuous between the tops of 2 or more mucosal folds but that involves less than 75% of the circumference
D	One (or more) mucosal break that involves at least 75% of the esophageal circumference

American Society for Gastrointestinal Endoscopy. Role of Endoscopy in the Management of GERD. Gastrointestinal Endoscopy:219–224: 66;2:2007. Accessed at www.giejournal.org 05/01/09

stomach. One purpose of endoscopy is to objectively identify if a patient has GERD. Keep in mind, however, that only 30–50% of patients with severe heartburn have any noticeable endoscopic findings suggestive of esophagitis.[8]

Endoscopy can also be used to determine if a patient with GERD has physical changes suggestive of Barrett's esophagus. There are also some conditions that have symptoms that mimic GERD, such as peptic ulcer disease, and endoscopy can be used to rule out these other diseases.

One of the major advantages of endoscopy is that it enables a biopsy to be taken in order to accurately determine the presence of Barrett's esophagus or histologic changes suggestive of esophageal adenocarcinoma.

There are a group of patients who have GERD based on symptoms, but will not have any signs of the disease on endoscopy. These patients are classified as having endoscopy-negative reflux disease.

Endoscopy also allows a grading of the stage or severity of esophagitis if this is present (see Table 1 classification).

4.5 Radionuclide imaging of gastric emptying

Barium esophagogram, or barium swallow, is very useful in those patients who complain of dysphagia. Patients are asked to drink a barium-containing liquid and then radiography is performed to follow the path of the barium. This test will help identify the location and presence of any strictures that may impair normal swallowing. The test can also be used to help quantify the size of a hiatal hernia and help identify its shape.

Barium swallow is also useful to identify if there are other signs of GERD such as esophageal fold thickening, ulcerations, or erosions.

4.6 "PPI test"[9]

A trial of any PPI in a standard dose or double dose for a period of time has been used to diagnose GERD. If a patient responds to the regimen, the diagnosis of GERD can be made. This test may be as useful as ambulatory pH monitoring and is cheaper and more readily available.

The test seems to be very useful in patients with persistent symptoms in which other diseases (peptic ulcers, esophageal erosions, carcinoma) have been ruled out by endoscopy. The major problem with this diagnostic method is the lack of a standard dose and duration of therapy.

Some examples of dosing regimens for this method are omeprazole 60 mg daily for seven days, omeprazole 20 mg twice daily for seven days, and omeprazole 40 mg in the morning and 20 mg in the evening for seven days.[9]

4.7 The PASS Test[13]

PASS Test

Are you taking a prescription medication for any of the following stomach problems/symptoms?

- ☐ Stomach pain or discomfort
- ☐ Heartburn
- ☐ Sour taste in your mouth/acid regurgitation
- ☐ Excessive burping/belching
- ☐ Increased abdominal bloating
- ☐ Nausea
- ☐ Early satiety

If "yes," then ask patient the following questions:

1. Are you still experiencing stomach symptoms?
   ☐ Yes ☐ No

2. In addition to your main medications, are you taking any of the following medications to control your symptoms: antacids (e.g. Tums®, Rolaids®, Maalox®), acid-lowering medications like Zantac®, ranitidine, Pepcid AC®, Losec®, Pantoloc®, Prevacid®, Nexium®, Pariet®, motility medications like Motilium®, or others like Gaviscon®, Pepto-Bismol®, or herbal supplements?
   ☐ Yes ☐ No

3. Is your sleep affected by your stomach symptoms?
   ☐ Yes ☐ No

4. Are your eating and drinking habits affected by your stomach symptoms?
   ☐ Yes ☐ No

5. At any time do your stomach symptoms interfere with your daily activities?
   ☐ Yes ☐ No

Adapted from Armstong D, et al: Can J Gastroenterol 2005;19:350–8

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GERD is a chronic condition with up to 90% of patients experiencing recurrent symptoms upon discontinuation of treatment. Persistent symptoms are seen in patients who continue treatment. Physicians may not have a good grasp as to the extent that their patients continue to experience symptoms despite treatment. Armstrong et al. created a questionnaire called the PPI Acid Suppression Symptom Test (PASS Test), which can be administered to patients on continuous acid suppression therapy to identify these patients. The questionnaire above was developed in both English and French and validated.

Although this questionnaire was designed for physicians to give to their patients, it can be easily applied by pharmacists when counselling their patients. The second question includes a number of different drug treatments, prescription as well as non-prescription, and it should be used as a guide by a pharmacist depending on their familiarity with a particular patient. If, upon completing the questionnaire, the patient is continuing with GERD symptoms, it is an opportunity for the pharmacist to intervene and contact the prescribing physician to share the results.

5. Treatment modalities

5.1 Lifestyle modifications

It is important to understand that lifestyle modifications do not usually eliminate the symptoms of GERD on their own. Despite strict modification of lifestyle, only 20% of patients will see a resolution of their symptoms of GERD.[14] Most patients require a combination of pharmacological therapy and lifestyle changes in order to limit the amount of reflux and the time duration that reflux material is in contact with esophageal tissue. It is also recommended that lifestyle modification continue at all times, even in combination with pharmacologic therapy or surgical intervention, despite the lack of evidence supporting its efficacy.

The recommended lifestyle modifications are listed in Table 2. Weight loss has not been shown to reduce GERD symptoms, but obese patients are twice as likely to develop GERD.[15] It is therefore necessary to counsel obese patients on the potential benefits of weight loss. Similar to this, smoking cessation has never been shown to improve the symptoms of GERD, but it is known that smoking can increase regurgitation and belching.[16] For this reason, patients should be encouraged to quit smoking. There are certain medications that exacerbate the symptoms of GERD. It is important in this case for the patient and health care provider to weigh the benefits of the drug against the risk of worsening GERD. Medications known to exacerbate GERD are listed in Table 3. Keep in mind that certain medications cannot be avoided. In such cases, a therapy aimed at symptom relief may be an option.

There are a number of foods that can also exacerbate GERD symptoms; these foods should be avoided if at all possible. Patients are also counselled to elevate the head of the bed with a below-the-mattress foam wedge to reduce the amount of time reflux material is in contact with esophageal tissue.[17]

Table 2. Lifestyle modifications for the management of GERD

Elevate head of bed 15–20 cm with a foam wedge under mattress
Quit smoking to reduce LES spontaneous relaxation
Change diet: • avoid chocolate, alcohol, peppermint, spearmint, high-fat foods (they reduce LES pressure) • avoid spicy foods, acidic foods, caffeine products (they are direct irritants to the esophagus)
Avoid bedtime snacks
Lose weight
Avoid tight-fitting clothes

Table 3. Medications that can aggravate GERD[18]

Drugs that promote reflux (decrease LES pressure):	Drugs that are direct irritants to the esophagus:
• beta-adrenergic blockers • calcium channel blockers • nitrates • theophylline • alpha blockers • anticholinergic drugs • barbiturates • benzodiazepines • estrogen • glucagon • opiates • progesterone • prostaglandins • sildenafil • tricyclic antidepressants	• NSAIDS • ASA • iron salts • quinidine • antibiotics • potassium chloride • bisphosphonates • glyburide • phenytoin

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5.2 Pharmacotherapy

The goals of pharmacotherapy are to relieve symptoms, prevent complications, reduce the number of reflux episodes, and promote healing of lesions secondary to esophagitis. Various drug classes have been shown to achieve these goals in the short term. It is also known that most patients with esophagitis will relapse within one year if their medication is stopped, regardless of which medication they use. For this reason it is common for patients to require long-term maintenance therapy with standard doses of acid-suppressing agents (especially those with more severe GERD). In patients with more severe GERD, maintenance therapy is used to limit symptoms and to prevent complications such as Barrett's esophagus.

5.2.1 Antacids

Antacids neutralize acid that is produced by the parietal cells of the gastric mucosa. There are many different types of antacids. Some are either single- or multiple-ingredient preparations that consist of one or more of the following: aluminum salts, magnesium salts, calcium salts, alginic acid.

Antacids have been a mainstay for the management of mild GERD and are commonly used in combination with more potent acid-suppressing agents for more severe GERD. They are found to be useful for reducing the symptoms of GERD. Despite their perceived effectiveness, there are no clinical trials that show that these agents are any more efficacious than placebo.[17,19]

Pepsinogen gets converted to pepsin at a pH of less than 4. Antacids neutralise gastric material so less pepsin is produced, reducing the irritation of the esophagus. In addition, at a pH above 4, gastric reflux material will not reduce LES pressure.

Antacids that contain alginic acid are particularly useful, as the alginic acid forms a viscous layer that floats on top of gastric material. This barrier that is formed reduces the number of reflux episodes and thereby reduces symptoms of GERD. At this time there is no clinical evidence to suggest antacids with alginic acid aid in healing.[14,20,21]

Antacids have a short duration of action (usually about an hour). Dosing therefore needs to be frequent and is usually a half an hour prior to meals and at bedtime. The duration of action can be extended to 3 hours by giving the antacid after meals. Dosing can also be as frequent as every hour to as little as an as-needed basis.

Antacids have many drug interactions and adverse effects. Aluminum-containing antacids can cause constipation, while magnesium-containing antacids may cause diarrhea. Phosphate in the gut can be bound by aluminum in antacids and can cause demineralization of bones.

Drug interactions caused by antacids occur by several different mechanisms. Antacids can bind medications to prevent absorption; can increase gastric pH, reducing absorption; can increase urinary pH, delaying drug clearance; and can form insoluble drug complexes, reducing drug absorption.

5.2.2 Histamine-2 receptor antagonists (H2A)

H2As reduce the production of stomach acid by inhibiting the secretion of acid from gastric parietal cells and histamine from enterochromaffin-like (ECL) cells. They bind reversibly and competitively to the histamine-2 receptors on the parietal cells in order to exert their action. ECL cells store histamine, which when released stimulates parietal cells to release acid.[22] These agents have no anticholinergic effect and they do not bind to histamine-1 receptors.

The use of H2As in GERD is very common in patients with disease of mild severity and infrequent symptoms. Effectiveness is limited in patients who have more severe GERD, including erosive esophagitis.[1] The consensus from the literature is that these agents produce endoscopic healing in approximately 50% of patients.[23] In addition, H2A therapy produces improvement of symptoms in 60% of patients.[16] The literature has not shown a difference between agents with respect to efficacy. There are, however, differences between agents with respect to cost, side effects, and drug interactions.

Dosing of these agents is dependent on severity and duration of GERD. Intermittent heartburn or meal-provoked heartburn can be effectively treated with as-needed over-the-counter doses of H2As.[24] The higher the dose of an H2A, the greater the acid suppression and the higher the rate of endoscopic healing.[25,26] In addition, acid secretion occurs throughout the day and night. Therefore, the more frequent the dosing schedule (e.g., qid vs. bid), the more successful the H2A will be at maintaining the gastric pH above 4. It is important, however, to commence therapy at usual doses and to reserve high-frequency dosing regimens for patients who do not respond.

For mild GERD, H2As at over-the-counter as-needed doses can be useful. For patients with mild to moderate non-erosive GERD, standard twice-daily dosing is more efficacious. For patients who do not respond and/or have erosive disease (e.g., patients with acid hypersecretion), higher doses are often needed. For patients requiring higher doses of H2A, it may be better to switch them to a proton pump inhibitor, as they have been shown to be superior to H2As in most patients.[9] There is no data to support the combination of a PPI and

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Table 4. Histamine-2 receptor antagonists[24]

Drug	Dose	Recommended duration for GERD
cimetidine	800 mg bid or 400 mg qid	12 weeks
famotidine	20 mg bid for symptoms only	6 weeks
	40 mg bid for esophagitis	12 weeks
nizatidine	150 mg bid	12 weeks
ranitidine	150 mg bid for symptoms	No limit specified
	150 mg qid for esophagitis	

an H2A at this time. The safety of high-dose H2A regimens is not well documented.

Side effects of the H2As are usually uncommon and involve diarrhea, constipation, headache, dizziness, somnolence, and fatigue. Drug interactions are only commonly seen with cimetidine. Cimetidine will reduce the metabolism of drugs that use the cytochrome P450 enzyme system for their metabolism. Examples of drugs that may accumulate with cimetidine therapy are warfarin, theophylline, and phenytoin.

5.2.3 Proton pump inhibitors (PPI)

PPIs inhibit the action of the H^+/K^+/ATP-ase pumps that are present on parietal cells in the gastric mucosa. Once these pumps are inhibited, gastric acid secretion is reduced by approximately 90% with standard PPI doses. This produces a condition in which gastric pH remains above 4 for the majority of the time, even in the presence of gastric acid surges.

The PPIs are used in patients with mild to moderate non-erosive GERD, severe erosive esophagitis, endoscopy-negative disease, or Barrett's esophagus and strictures. In patients with severe esophagitis, standard PPI doses can produce healing rates of 80–100%.[8] In patients with grade 4 esophagitis, healing rates decrease to 60%.[8] For these types of patients, an increase in the dose of PPI can improve healing rates.[9] Symptomatic relief is also exceptional, with an average success rate of approximately 80% in most patients.[9]

When comparing PPIs to H2As, it is clear that PPIs are superior to H2As (for endoscopic-positive esophagitis patients) for a number of reasons.[27] PPIs keep gastric pH above 4 for a greater period of time. For this reason, PPIs produce more extensive and faster healing of lesions compared to H2As.[27] PPIs also relieve symptoms at a faster rate than H2As. In addition, they have demonstrated superior efficacy for long-term maintenance of GERD. The superior efficacy of PPIs in improving symptoms of erosive esophagitis has been shown to be more cost-effective than H2As.[1,28] Currently the majority of the PPIs are available from different generic manufacturers at a significantly reduced price, making them more favourable from a cost perspective.

It is common for patients to require long-term maintenance, as demonstrated by relapse when medications are stopped. Long-term healing at 4 and 8 weeks is greater with PPIs regardless of high or low doses being used. In general, for most conditions, PPIs (when compared to H2As) have a number needed to treat of 3. In other words, you would need to treat 3 GERD patients with PPIs in order to heal one more lesion that would not have been healed with an H2A.[29]

There are several PPIs on the market at this time. These agents and their usual doses are listed in Table 5. In most comparisons, 4- and 8-week healing rates are similar between agents when comparable doses are used.[27] Two recently published systematic reviews that include all currently relevant clinical trials provide some insight into which PPI to choose in the treatment of patients with GERD. The Oregon Health Resources Commission conducted an in-depth review of PPIs in the management of GERD.[28] They conclude that there is insufficient evidence at this time to demonstrate a difference between PPIs with respect to esophagitis healing, relief of symptoms, or prevention of relapse in adult patients with GERD. This systematic review takes into account the results of three recent clinical trials that demonstrated a significant advantage with esomeprazole compared to omeprazole 20 mg daily and lansoprazole 30 mg daily. The authors suggest that trials comparing omeprazole 40 mg daily to esomeprazole 40 mg or 20 mg daily would need to be done if a true difference between these agents is to be proven. This review was funded by non-profit government organisations in Oregon, USA.

In contrast, the other systematic review[29] on PPIs in patients with GERD (and peptic ulcer disease) concluded that esomeprazole has been shown to be superior with respect to esophagitis healing in head-to-head comparisons. For GERD symptom relief, they suggest all PPIs are equivalent after 1 to 2 weeks of treatment, but lansoprazole and esomeprazole may provide a quicker onset of symptom relief. The authors conclude at the end of the review that there is currently no agent or dose that has been shown to be superior for all PPI

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indications at this time. This review also takes into account the same three clinical trials that demonstrated superiority of esomeprazole 40 mg daily versus omeprazole 20 mg daily or lansoprazole 30 mg daily. This review was funded by the manufacturers of esomeprazole.

PPIs are also the agents of choice in most patients who require maintenance therapy for GERD. For patients without endoscopic evidence of esophagitis (ENRD), all evidence at this time suggests that PPIs and H2RAs are equivalent in symptomatic relief.[28]

The side effect profile of PPIs is similar to that of H2As. They are usually well tolerated; however, patients infrequently complain of somnolence, headache, dizziness, diarrhea, constipation, and nausea. The literature does cite possible bone fractures, *Clostridium difficile*-associated diarrhea, and community-acquired pneumonia with prolonged use of PPIs.[29] Due to the increased nasogastric pH, there exists the potential to alter the normal oropharyngeal and gastrointestinal flora, predisposing individuals to infection. The increase in pH can decrease the absorption of pH-dependent medications (such as calcium) and cause bone fracture.

The development of *C. difficile* diarrhea is believed to be caused by the vegetative form of the bacteria, which is activated when exposed to a high pH. Although studies identify patients on long-term PPI therapy with *C. difficile*-associated diarrhea, the evidence is not conclusive as to the PPI being the cause, even though antibiotics were ruled out as the potential cause in one study. More rigid studies need to be designed to fully establish the risk of *C. difficile*-associated diarrhea in patients on continuous PPI therapy.[29]

Community-acquired pneumonia (CAP) is believed to result from two mechanisms, the increase in nasogastric pH and a change in neutrophil function.[29] The association between PPI treatment and CAP was noted, as there appeared to be a large proportion of patients who developed the infection while on GERD treatment. Confounding factors were that the pneumonia was not diagnosed conclusively, and there was no comparison with non-PPI-treated patients.

The increase in bone fractures, also noted as being of a higher proportion in patients who were also taking PPIs, is not conclusive.[29] Although studies did see increase in hip fractures, other sites were not tracked and potential confounding factors were not noted.

Although the above side effects are being noted and cited in the literature, strong causality has not been substantiated. However, for pharmacists interacting with patients taking PPIs, it may be beneficial to be vigilant and monitor for any effects that might be suggestive of these side effects.

Of concern in the past was the risk of gastric carcinoma with long-term use (>1 year) of PPIs. To date, there has been no link established between gastric carcinoma and the use of omeprazole.

Drug interactions with PPIs will depend on which PPI is being used. All the PPIs use the cytochrome P450 system for metabolism to some extent, specifically CYP3A4 and CYP2C19. Pantoprazole has an alternate metabolic pathway and therefore appears to have the fewest drug interactions. Omeprazole may inhibit the metabolism of warfarin, diazepam, and phenytoin. Patients with a polymorphic gene variation that classifies them as "slow metabolizers" are more susceptible to the drug interactions that may occur with omeprazole. Rabeprazole can also increase digoxin concentrations by about 20%. The general approach to patients on PPIs with other potentially interacting drugs is to monitor them closely.

Juurlink et. al. published a population-based study in the January 2009 issue of CMAJ discussing an interaction between clopidogrel and PPIs.[50] The group reviewed a total of 13,635 patients who were prescribed clopidogrel following acute myocardial infarction. It was noted that 734 patients were readmitted to the hospital with myocardial infarction. Upon in-depth analysis by the study authors, it was noted that the individuals who had a second episode were also prescribed PPIs. Clopidogrel, a prodrug, is converted in the liver to an active metabolite by the CYP450 isoenzyme 2C19. All the PPIs (omeprazole, lansoprazole, rabeprazole and esomeprazole), except pantoprazole, act as inhibitors of CYP450 2C19, thus reducing the anti-platelet

Table 5. Proton pump inhibitors[1]

Drug	Dose	Duration†
esomeprazole	20–40 mg qd	4–8 weeks symptom relief 8–16 weeks lesion healing
lansoprazole	15–30 mg qd or bid	same as above
omeprazole	20 mg qd or bid	same as above
pantoprazole (oral formulation only)*	40 mg qd or bid	same as above
rabeprazole	20 mg qd or bid	same as above

*Pantoprazole IV is available but is not indicated for the treatment of GERD.
†Duration refers to the approved duration of treatment by the manufacturer based on indication listed.

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effects of the following PPIs: omeprazole, lansoprazole, rabeprazole, and esomeprazole.

When counselling patients on time of day when to take their PPI, a pharmacist should determine the period when a patient is most affected by their GERD symptoms. If symptoms are present during the waking hours, then counsel patients to take the medication approximately 30 minutes before the morning meal. This ensures maximum efficacy, as these agents only inhibit the action of actively working proton pumps. If symptoms are present during the night, then bedtime dosing is most appropriate, about an hour before retiring for the night. Lansoprazole also requires special counselling, as it is the only agent that may have reduced absorption when given directly with food.

5.2.4 Prokinetic agents

There are three prokinetic agents that have been studied in the management of GERD. They are metoclopramide, bethanechol, and cisapride.

Bethanechol's use is limited, as it has been shown to be less effective than H2A therapy. Metoclopramide increases LES pressure and speeds gastric emptying. Despite this, metoclopramide, like bethanechol, has not been shown to be as effective as H2A therapy. There is no evidence to suggest these agents have any effect on endoscopic healing. In addition, the extensive side effect profile of metoclopramide (extrapyramidal side effects, sedation, increased prolactin secretion) has limited its use. The use of these two agents cannot be recommended at this time due to lack of clinical evidence.[30]

Cisapride, on the other hand, has efficacy comparable to that of H2As, as it increases esophageal clearance. It has been demonstrated that cisapride is equivalent to H2As in resolution of symptoms, healing rates, and symptom relief in endoscopy-negative reflux patients.[30–36] Cisapride, when added to either an H2RA or a PPI, has not been shown to provide any additional symptom improvement.[44] Cisapride is no longer used routinely due to withdrawal from the market. However, it can be obtained from Health Canada through the Drug Special Access program for refractory upper gastrointestinal motility disorders, e.g., diabetic gastroparesis.

Domperidone, a motility agent that can help with the nausea and epigastric distress, is a safer alternative to cisapride and metocloperamide.[45]

Prokinetic agents do have a place in therapy when combined with H2As. This combination can be useful in patients with a documented motility disorder.

Table 6. Prokinetic agents[32–38]

Drug	Dose	Duration
bethanechol	10–15 mg bid-qid	12 weeks
cisapride (no longer available)	10–20 mg qid	no limit specified
domperidone	10 mg tid-qid	no limit specified
metoclopramide	10–15 mg qid	12 weeks

5.2.5 Sucralfate

Sucralfate is used in the management of symptoms of patients with mild GERD. It has comparable efficacy to H2As in this type of patient.[38–42] In more severe GERD it is less effective than H2As. The role of sucralfate in the management of GERD is therefore limited at this time.

5.2.6 Approach to drug therapy

The historical approach to managing patients with GERD depended on the severity and duration of their symptoms. A step-wise approach to care seemed to be the most appropriate guide to therapy for GERD patients, but this is now an issue of debate. Studies in primary-care GERD patients have demonstrated that symptoms are similar in endoscopy-positive versus endoscopy-negative GERD patients.[43] This seems to imply that duration and severity of symptoms does not help predict a response to therapy.[45] This being known, currently available evidence suggests that in patients with ENRD, PPIs and H2RAs are equally effective in symptom resolution.[27]

The Canadian Dyspepsia working group (CanDys) has reviewed GERD and all available clinical evidence pertaining to treatment.[44] In the absence of evidence they have also provided some recommendations based on consensus opinion. CanDys recommends PPIs as the drug class of choice based on the large body of clinical evidence indicating their superiority (better symptom relief, faster healing, higher healing rates).[44]

The CanDys working group makes the following treatment recommendations:[44]

1. Patients with mild symptoms may try lifestyle modifications and antacids. There is no documented efficacy of this therapy (consensus).
2. Patients with heartburn and/or regurgitation should be prescribed (in the following order):
   a. PPI monotherapy*
   b. H2A monotherapy*
   c. prokinetic (cisapride) – not available

**Adding a H2RA to a PPI or vice versa has not been shown to add any benefit.*

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The CanDys group reviewed all pertinent clinical trial data comparing PPIs with each other and H2As with each other and found a limited number of comparison trials. Their recommendation is to consider all agents within each class equally effective.[44] It is also important to consider the findings of two more recent systematic reviews, as mentioned earlier, when deciding on which PPI to choose.[31,32]

It is the recommendation of the CanDys working group that patients be reassessed after 4 weeks of therapy. This is based on the fact that most patients will see symptom resolution with PPIs in 4 weeks if they are going to respond.[32,46] In addition, patients will either respond to H2A or prokinetic therapy in 4 weeks or not respond at all. At this point, continuing therapy with these agents is unlikely to produce a response.

In the 2004 Update of the Canadian Consensus conference on the management of GERD in adults, the working group added two new treatment options, "intermittent" and "on-demand."[1] "Intermittent" therapy is a medical maintenance therapy that has a defined daily intake of medication for a predetermined, finite period that results in resolution of reflux symptoms or healing of erosions after a relapse. "On-demand" was defined as the daily intake of a medication, PPI or H2RA, for a period long enough to attain resolution of reflux symptoms.[1] Medication would be stopped until the symptoms reappear, and the same form of treatment restarted.

These new treatment approaches can help guide pharmacists to better inform patients regarding GERD management.

The CanDys working group did not mention the use of over-the-counter as-needed doses of H2As. There is evidence to suggest that this may be a therapeutic option for patients with mild, intermittent symptoms of GERD or in patients with meal-provoked GERD.[24] In addition, antacids may also be a reasonable initial therapeutic choice along with lifestyle modifications in patients with mild, intermittent symptoms.

The choice of drug therapy for the maintenance of GERD would be the same as for short-term management. PPIs have demonstrated superiority over H2As with respect to relapse rates.[46] It is recommended that patients with chronic symptoms use standard doses of PPIs for maintenance therapy, as lower doses have not been effective. In some patients, a higher-dose PPI is needed for long-term maintenance.[8]

5.3. Surgical treatment

Surgical intervention is considered in patients who:

- do not respond to conventional drug therapy
- respond to therapy but do not like the inconvenience of taking medications
- have Barrett's esophagus, strictures, or grade 4 esophagitis (see Table 1 for classification system)
- have reflux documented on 24-hour ambulatory pH monitoring
- have atypical symptoms (cough, wheezing, aspiration, ear/nose/throat involvement, dental erosions)

The goal of surgical intervention is to restore a reflux barrier, repair any hiatal defect, and position the LES in a situation of positive pressure. The mortality rate for laparoscopic surgical intervention is reported as 0.2–0.4%.[8] It has been reported that approximately 85% of surgical patients will have resolution of the signs and symptoms of GERD after the procedure.[8]

Laparoscopic fundoplication is the most common type of surgical intervention. There are many types, but they all have certain things in common. The procedures all involve wrapping a portion of the gastric fundus around the distal esophagus, repairing hiatal hernias, and creating an intra-abdominal segment of the esophagus. This all serves to produce a barrier to gastroesophageal reflux. It should be noted that patients who have had surgical intervention might need to use acid suppression therapy and that there is still a risk for developing Barrett's esophagus or esophageal adenocarcinoma.[8]

There are two endoscopic procedures that are approved by the FDA in the United States. One involves suturing the gastroesophageal junction (Bard procedure) and the other involves using microwave energy to create thermal lesions in the muscle of the LES (Stretta system).[8] The efficacy and safety of these procedures have not been adequately studied in clinical trials and therefore their role in the management of patients with GERD is unclear.

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Questions

Questions 1–3 deal with the following scenario:
JK *comes to the counter of the local pharmacy in need of help. He is a 54-year-old male who currently works in a diner by a very busy industrial complex. He has been working long hours lately and finds he does not have time to prepare a lunch for himself to take to work. What he ends up doing is fixing a burger and fries at the diner for his dinner. He eats his dinner out in the back of the diner and then reads the paper while having a cigarette. Due to his change in eating habits he has put on 10 pounds, and he is already overweight. He has been complaining of heartburn lately on a regular basis and is wondering what over-the-counter medication will work for him.*

1. Which of the following is **not** a risk factor for JK to develop GERD?
   a. smoking
   b. fatty foods
   c. stress
   d. obesity

2. Over-the-counter H2As would be the first thing you would recommend for JK at this time.
   a. true
   b. false

3. Lifestyle modifications are likely to be helpful in relieving symptoms of GERD in
   a. 10% of patients
   b. 20% of patients
   c. 60% of patients
   d. 94% of patients

Questions 4–7 deal with the following scenario:
LM *is an 82-year-old female who lives alone in an apartment building with many other senior citizens. She has suffered from GERD for a number of years and has always used cimetidine 400 mg tid to relieve her symptoms. She recently went to a new family doctor, as her previous doctor retired. She mentioned to this doctor that she still feels as though she has heartburn that interfered with her sleep at least three times a week and caused significant chest pain at least once a week. Her new doctor prescribes esomeprazole 40 mg daily for her in hopes she will have better control of the heartburn. Her neighbour uses esomeprazole with great success and LM thinks this may be better for her as well.*

4. Which of the following statements is correct?
   a. LM would be better off trying a bigger dose of cimetidine.
   b. Esomeprazole is unlikely to be better than cimetidine.
   c. PPIs are generally as effective than H2As and LM will not notice an improvement in her condition.
   d. A combination of lifestyle modification, as-needed antacids, and esomeprazole would likely improve LM's condition.

5. LM will need esomeprazole for 4–8 weeks and then she can use on-demand therapy to control her GERD.
   a. true
   b. false

6. Which of the following statements does not describe the PPI class?
   a. All PPIs are not equally efficacious when comparable doses are used.
   b. Lansoprazole is the PPI that has shown superiority for fast symptom relief and esophagitis healing.
   c. Response to a particular PPI may differ from patient to patient.
   d. The choice of PPI may be based on the severity classification of the GERD.

7. LM should be counselled with regards to which potential side effect with her new PPI prescription?
   a. LM unlikely to experience any side effects
   b. abnormal heart rhythm
   c. agitation
   d. drowsiness

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8. Which of the following statements best defines GERD?
   a. GERD involves reflux symptoms **and** evidence of esophageal injury.
   b. GERD involves reflux symptoms **and/or** evidence of esophageal injury.
   c. GERD involves reflux of acidic fluid from the small intestine into the stomach.
   d. GERD involves the anterograde movement of reflux material from the esophagus into the stomach.

9. Reflux of gastric material occurs on a daily basis only in people with GERD.
   a. true
   b. false

10. What percentage of patients who experience heartburn will have GERD?
   a. 5%
   b. 10–20%
   c. 20–40%
   d. 60%

11. Lower esophageal sphincter pressure is ideally
   a. 10 mm Hg
   b. 13 mm Hg
   c. 30 mm Hg
   d. 35 mm Hg

12. A pH of less than 4
   a. is the aim of antacid therapy
   b. converts pepsinogen to pepsin
   c. is always associated with grade 4 esophagitis
   d. is a reason for delaying treatment until pH is less than 2

13. Physiological factors that contribute to GERD are
   a. TLESR, increased intra-abdominal pressure
   b. TLESR, hiatus hernia
   c. hiatus hernia, spicy foods
   d. hiatus hernia, atonic LES

14. Complications of GERD include everything except
   a. esophagitis
   b. adenocarcinoma
   c. stomach muscle atrophy
   d. Barrett's esophagus

15. An atypical symptom of GERD is coughing.
   a. true
   b. false

16. An atypical symptom of GERD is dysphagia.
   a. true
   b. false

17. The recognized gold standard for diagnosing GERD is
   a. the "PPI test"
   b. ambulatory pH monitoring
   c. manometry
   d. endoscopy
   e. there is no recognized gold standard

18. The treatment modalities of GERD include everything except
   a. acid suppression medications
   b. lifestyle modifications
   c. surgical intervention
   d. radiotherapy

19. Lifestyle modifications should not be recommended, as they are relatively ineffective.
   a. true
   b. false

20. Antacids with alginic acid
   a. have the benefit of two acid-neutralizing substances
   b. create a physical barrier in the esophagus to help raise LES pressure
   c. create a barrier on gastric fluid in the stomach in order to reduce the amount of reflux
   d. are useless, as the alginic acid decreases gastric pH even further

21. H2As inhibit acid secretion by blocking
   a. the action of H^+/K^+/ATP-ase pumps on the mast cells in the gastric mucosa
   b. the activity of parietal cells in the esophageal lining
   c. the activity of parietal cells of the gastric mucosa by binding to histamine-1 and histamine-2 receptors
   d. histamine release from ECL cells in generation of gastrin

22. PPIs have demonstrated superior healing compared to H2As except in patients with mild GERD.
   a. true
   b. false

23. Metoclopramide can be combined with H2As in patients with resistant GERD symptoms with or without evidence of a motility disorder.
   a. true
   b. false

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24. The surgical management of GERD is accomplished by using laparoscopic fundoplication techniques that aim to reduce the amount of strictures present in the esophagus.
   a. true
   b. false

25. The CanDys working group has put together GERD management recommendations based on
   a. expert consensus
   b. best available clinical evidence
   c. expert consensus and best available clinical evidence
   d. case reports and anecdotal evidence

26. Based on the recommendations of the CanDys working group,
   a. the drug of choice for most GERD patients is an antacid
   b. there is some evidence to suggest that antacids work as well as H2A
   c. PPIs and antacids are better than PPIs alone
   d. the drug of choice for most patients with GERD is a PPI

27. Patients should be followed after how many weeks of initiating a drug for GERD?
   a. 2–4 weeks
   b. 8 weeks
   c. weekly
   d. 4 weeks

28. PASS Test stands for:
   a. Pantoprazole Acid Suppression Symptom Test
   b. Particular Acid Suppression Symptom Test
   c. PPI Acid Suppression Symptom Test
   d. Prognosis Aid Supreme Symptom Test

29. The PASS Test is used to diagnose new patients with GERD.
   a. true
   b. false

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