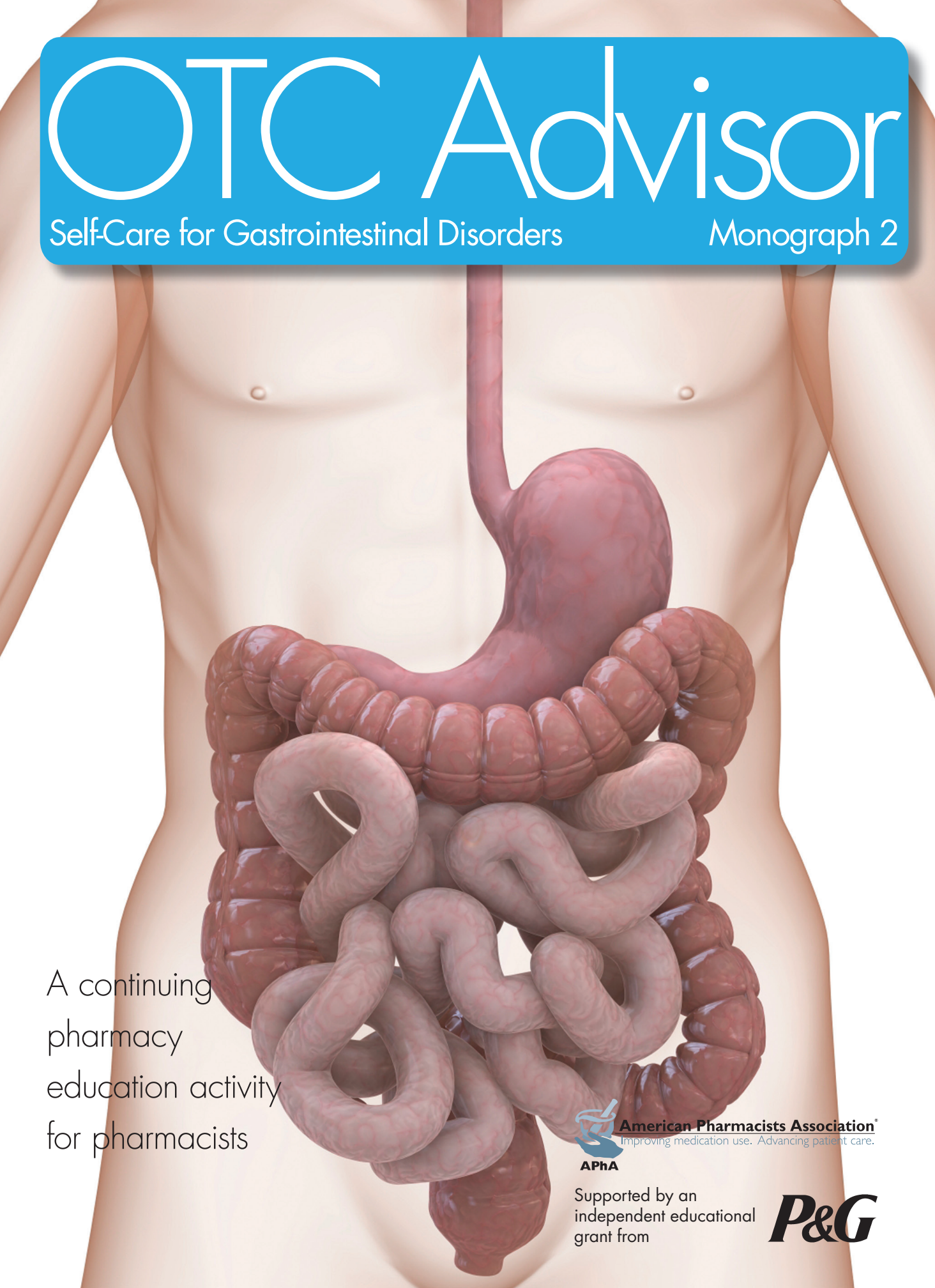
OTC Advisor

Self-Care for Gastrointestinal Disorders

Monograph 2



A continuing pharmacy education activity for pharmacists

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Supported by an independent educational grant from P&G

PROVIDER: American Pharmacists Association
TARGET AUDIENCE: Pharmacists
RELEASE DATE: January 15, 2010
EXPIRATION DATE: January 15, 2013

ACPE NUMBER: 202-000-10-103-H01-P
CPE CREDIT HOURS: 2.5 hours (0.25 CEU)
ACPE ACTIVITY TYPE: Knowledge-based
FEE: There is no fee associated with this activity.

ACTIVITY PREVIEW

Symptoms and complaints related to the gastrointestinal (GI) tract are some of the most common reasons why people take prescription or nonprescription medications or seek the advice of health care providers. Pharmacists are the logical health care professionals to assist patients with self-care decisions related to GI problems, because pharmacists are available at the point of purchase and are the only health care professionals who receive in-depth formal education and skill development in nonprescription pharmacotherapy.

This monograph addresses self-care for five common GI complaints: heartburn, dyspepsia, constipation, diarrhea, and anorectal disorders. Each condition is defined, and its pathophysiology is reviewed. Exclusions for self-treatment are presented and explained. Self-care options—nonprescription medications and nonpharmacologic interventions—are discussed in the context of a self-treatment algorithm. Each section of the monograph concludes with a list of POINTS TO REMEMBER that provides a quick summary of the major concepts and recommendations.

LEARNING OBJECTIVES

At the completion of this activity, the pharmacist will be able to:

1. Compare and contrast heartburn and dyspepsia in terms of usual causes and patient presentation.
2. Discuss the etiology and pathophysiology of constipation, diarrhea, and typical anorectal disorders.
3. Differentiate between patients with common GI disorders who are candidates for self-treatment and patients who should be seen by a primary care provider.
4. Describe nonpharmacologic interventions for heartburn, dyspepsia, constipation, diarrhea, and typical anorectal disorders.
5. Discuss the nonprescription medications used to manage heartburn, dyspepsia, constipation, diarrhea, and typical anorectal disorders, including product selection considerations, correct dosing and administration, contraindications, and adverse effects.

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This activity is supported by an independent educational grant from Procter & Gamble.

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DISCLOSURES

Rosemary R. Berardi, PharmD, FCCP, FAPhA, FASHP, has served as advisory board member for Procter & Gamble's National Heartburn Alliance.

Juliana Chan, PharmD, has served as an advisory board member for Novartis and Takeda Pharmaceuticals.

APhA's editorial staff declares no conflicts of interest or financial interests in any product or service mentioned in this activity, including grants, employment, gifts, stock holdings, and honoraria.

This publication was prepared by Cynthia Knapp Dlugosz, BPharm, of CKD Associates, LLC, on behalf of the American Pharmacists Association.

INTRODUCTION

According to the American Gastroenterological Association, symptoms and complaints related to the gastrointestinal (GI) tract are some of the most common reasons why people take prescription or nonprescription medications or seek the advice of health care providers. Widely quoted statistics indicate that 7% of American adults suffer from daily heartburn, 14% experience weekly heartburn, and 44% experience monthly heartburn. Dyspepsia—a heterogeneous group of upper abdominal symptoms that arise from disparate conditions—affects more than one fourth of the general population. More than 4 million Americans (particularly women and adults aged 65 years and older) have frequent constipation. The average adult has a bout of diarrhea about four times a year. About half of the U.S. population has hemorrhoids (a condition in which the veins around the anus or lower rectum are swollen and inflamed) by age 50 years.

This monograph discusses common nonpharmacologic measures and nonprescription medications used for the self-treatment of heartburn, dyspepsia, constipation, diarrhea, and anorectal disorders.

HEARTBURN AND DYSPEPSIA

Heartburn may best be described as a burning feeling rising from the stomach or lower chest up toward the neck or throat. It may be accompanied by acid regurgitation: the effortless return of acidic gastric contents to the pharynx, which causes a sour or bitter taste in the mouth. Heartburn frequently occurs within 1 to 2 hours after eating, especially after large or fatty meals. It may be aggravated by bending over or lying down.

Dyspepsia generally refers to consistent or recurrent discomfort centered in the upper abdomen (epigastrium). The discomfort may be characterized by or associated with bloating, belching, early satiety, postprandial fullness, nausea, or anorexia. However, the discomfort is not necessarily restricted to meal-related symptoms.

Patients who experience heartburn or dyspepsia may not distinguish between these symptoms. In fact, there is considerable overlap: many patients experience both heartburn and dyspepsia. Self-treatment of both heartburn and dyspepsia may involve similar lifestyle modifications or pharmacologic therapy with antacids, histamine H_2-receptor antagonists (H_2 antagonists), or proton pump inhibitors (PPIs).

Heartburn

Heartburn is most closely associated with gastroesophageal reflux: the retrograde movement of acidic gastric contents into the esophagus. Reflux usually is prevented by the lower esophageal sphincter (LES), an area of specialized smooth muscle located above the junction where the esophagus meets the stomach. The LES ordinarily is constricted; the resting tone of the LES normally is 10 to 30 mm Hg higher than intragastric pressure. When food is ingested, the LES relaxes briefly (5 to 10 seconds) during peristalsis to allow the swallowed bolus to enter the stomach.

Spontaneous, transient relaxations of the LES appear to be the most frequent mechanism for reflux in patients with normal LES pressure. Transient LES relaxations occur independently of swallowing or peristalsis and last substantially longer (up to 45 seconds) than do swallow-induced LES relaxations. They are most likely to occur when the proximal stomach is distended by either food or gas.

However, acid reflux alone is not necessarily sufficient to provoke heartburn. Everyone experiences some degree of reflux, especially after meals, but most reflux episodes go unperceived. The refluxed material (refluxate) usually is cleared rapidly from the esophagus by a combination of gravity (when a person is upright) and peristaltic contractions brought on by swallowing. Any residual acid remaining in the esophagus is neutralized by bicarbonate in swallowed saliva and in mucus secreted by glands in the esophageal mucosa and submucosa.

Additional research is needed to determine the exact mechanism or mechanisms that constitute the "missing link" between acid reflux and heartburn. Factors that currently are thought to influence the occurrence of heartburn include:

- *Prolonged esophageal acid clearance time.* Prolonged acid clearance results in prolonged exposure of the esophageal mucosa to the refluxate. Acid clearance time is prolonged when a person lies down (because gravity facilitates clearance) or sleeps (swallowing virtually ceases during sleep). Decreased salivation also contributes to prolonged acid clearance; the production of saliva decreases during sleep, with increasing age, and as a result of cigarette smoking.
- *Larger refluxate volumes.* Both overeating and delayed gastric emptying increase the amount of material available to be refluxed. Large volumes of refluxate increase the duration and "reach" (i.e., proximal extent) of reflux episodes.
- *Refluxate composition.* Although gastric acid alone may not cause much damage, acid in combination with even small amounts of the proteolytic enzyme pepsin is able to disrupt the esophageal mucosal barrier. The presence of duodenal contents (e.g., bile salts) in the refluxate also may be injurious to the esophageal mucosa.

Altered esophageal tissue resistance may prove to be the most important determinant of heartburn. If the normally tight intercellular junctions of the esophageal mucosa are damaged, hydrogen ions gain access to and acidify the intercellular space. Heartburn appears to be related to the stimulation of sensory neuron receptors within the intercellular space.

Heartburn vs Gastroesophageal Reflux Disease

For self-treatment purposes, heartburn is classified as episodic or frequent. Episodic heartburn typically is mild and sporadic. It often occurs predictably, after the ingestion of specific foods or beverages or after some types of exercise. Frequent heartburn is defined as heartburn that occurs 2 or more days per week.

It is important to keep in mind that heartburn is a symptom, not a

disease or diagnosis. Heartburn that is frequent and persistent (3 months or longer) is the most common symptom of gastroesophageal reflux disease (GERD). An international consensus panel recently defined GERD as a condition that develops when the reflux of stomach contents causes troublesome symptoms and/or complications. In clinical practice, the determination of whether or not heartburn is "troublesome" should be made by the patient.

When patients with GERD undergo endoscopy, about 20% to 30% are found to have evidence of esophageal damage (i.e., erosive esophagitis). Untreated erosive esophagitis can lead to potentially serious complications such as esophageal strictures (7% to 23% of patients) or hemorrhage (7% to 18% of patients). Another potential complication is Barrett esophagus—a condition in which the normal squamous epithelium of the distal esophagus is replaced by columnar epithelium. Barrett esophagus is believed to be an intermediate step in the development of esophageal adenocarcinoma.

Heartburn pain usually is substernal. However, GERD also can cause chest pain (often referred to as noncardiac chest pain) that is indistinguishable from ischemic cardiac pain. In addition, the refluxed acidic contents may damage the oropharynx, larynx, and respiratory system, resulting in extraesophageal manifestations of GERD. Examples of extraesophageal reflux syndromes include chronic laryngitis, sinusitis, chronic cough, asthma, and dental erosions.

Treatment Strategies

The treatment of heartburn (and GERD) most often involves dietary and lifestyle modifications in combination with drug therapy. Dietary and lifestyle modifications target various risk factors (TABLE 1) that may precipitate or aggravate heartburn through mechanisms such as decreasing LES pressure or irritating the esophageal mucosa. Although dietary and lifestyle modifications benefit many patients, there is little evidence of their effectiveness, and they are unlikely to control symptoms in the majority of patients in the absence of drug therapy.

Patients with episodic heartburn usually can manage their symptoms adequately with antacids, nonprescription H_2 antagonists, or combination therapy with both medications. Nonprescription PPIs are the only nonprescription medications indicated for the treatment of frequent heartburn.

Patients with GERD usually require long-term, possibly lifetime, maintenance therapy with prescription PPIs or H_2 antagonists. Antireflux surgery can be a maintenance option for selected patients with well-documented GERD.

Dyspepsia

The constellation of symptoms associated with dyspepsia may be caused by a number of foods, medications, GI tract diseases, and pathologic states in other organ systems (e.g., diabetes, thyroid disease, congestive heart failure). However, up to 60% of patients experience dyspepsia symptoms with no obvious biochemical or organic cause. These patients are labeled as having functional dyspepsia (also referred to as idiopathic dyspepsia or nonulcer dyspepsia). The pathophysiology of functional dyspepsia is not well understood. Both physiologic factors (e.g., delayed gastric emptying, impaired gastric accommodation, altered visceral sensation, *Helicobacter pylori* infection) and psychosocial factors, including increased life stress, may be involved.

Many patients report dyspepsia as a consequence of overeating or ingesting specific foods, especially fatty or spicy foods, coffee, or alcoholic beverages. Although meal-related symptoms are prevalent, there is little objective evidence to support a cause-and-effect relationship between dietary factors and symptoms. Lactose intolerance may coexist with dyspepsia, but it is not considered to be a common cause of dyspepsia.

A number of medications are capable of causing dyspepsia through known mechanisms (e.g., direct mucosal irritation, alterations in

Table 1. Risk Factors That May Contribute to Heartburn

Dietary
- Alcohol (ethanol)
- Caffeinated beverages
- Carbonated beverages
- Chocolate
- Citrus fruit or juices
- Fatty foods
- Garlic or onions
- Mint (e.g., spearmint, peppermint)
- Salt and salt substitutes
- Spicy foods
- Tomatoes/tomato juice

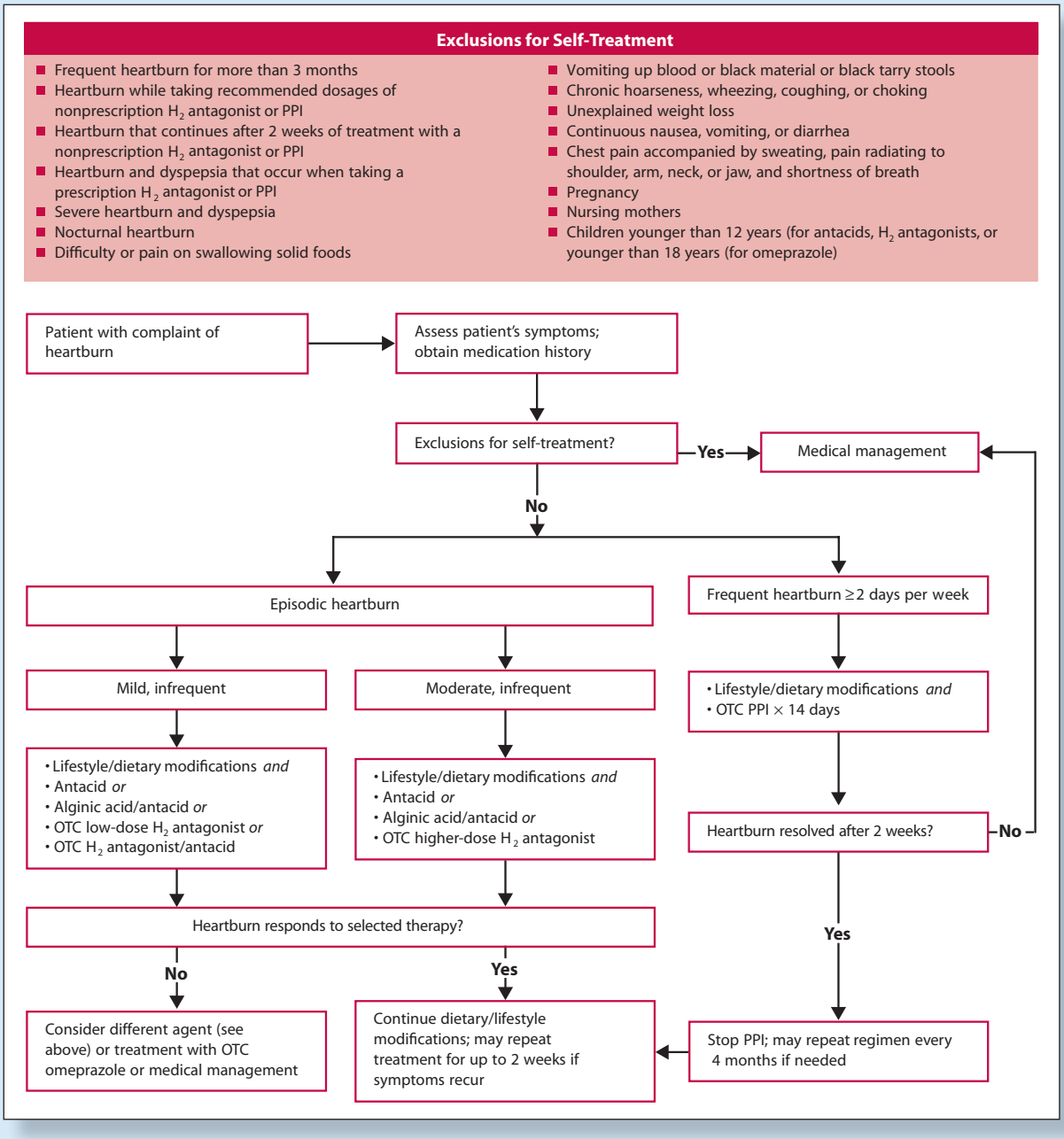
Diseases
- Motility disorders (e.g., gastroparesis)
- Peptic ulcer disease
- Scleroderma
- Zollinger-Ellison syndrome

Lifestyle
- Exercise
- Obesity
- Smoking (tobacco)
- Stress
- Supine body position
- Tight-fitting clothing

Medications
- α-Adrenergic antagonists
- Anticholinergic agents
- Aspirin and other nonsteroidal anti-inflammatory drugs
- β_2-Adrenergic agonists
- Barbiturates
- Benzodiazepines
- Bisphosphonates
- Calcium channel blockers
- Chemotherapy
- Dopamine
- Estrogen
- Iron
- Narcotic analgesics
- Nitrates
- Potassium
- Progesterone
- Prostaglandins
- Quinidine
- Tetracycline
- Theophylline
- Tricyclic antidepressants
- Zidovudine

Other
- Genetics
- Pregnancy

Figure 1. Algorithm for Self-Treatment of Heartburn



H_2 antagonist = histamine H_2-receptor antagonist; OTC = over-the-counter; PPI = proton pump inhibitor.

Source: Zweber A, Berardi RR. Heartburn and dyspepsia. In: Berardi RR, Ferreri SP, Hume AL, et al. *Handbook of Nonprescription Drugs: An Interactive Approach to Self-Care.* 16th ed. Washington, DC: American Pharmacists Association; 2009:235.

gastric motility) as well as unknown mechanisms. Medications commonly associated with dyspepsia are listed in TABLE 2. Notable among these are aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs), which provoke dyspepsia in as many as 20% to 25% of patients.

Common Organic Causes of Dyspepsia

The most common identifiable organic causes of dyspepsia are peptic ulcer disease, GERD, and gastric cancer.

Peptic Ulcer Disease. Peptic ulcer disease—ulcerations of the stomach, duodenum, or both resulting from acid-peptic injury—is the cause of dyspepsia in 5% to 15% of patients. The classic symptom of peptic ulcer disease is gnawing or burning epigastric pain. In patients with duodenal ulcers, the pain usually occurs 2 to 3 hours after meals and is relieved by eating or taking antacids. In patients with gastric ulcers, the pain occurs sooner after meals and is less reliably relieved by food or ant-

Table 2. Selected Medications That May Cause or Contribute to Dyspepsia

- Acarbose
- Antibiotics (especially macrolides, metronidazole, sulfonamides)
- Aspirin and other nonsteroidal anti-inflammatory drugs
- Bisphosphonates
- Colchicine
- Digitalis
- Estrogens
- Gemfibrozil
- Glucocorticoids
- Iron
- Levodopa
- Narcotics
- Niacin
- Oral contraceptives
- Orlistat
- Potassium supplements
- Quinidine
- Sildenafil
- Theophylline

acids; it also may awaken the patient from sleep.

As many as 90% of duodenal ulcers and 70% of gastric ulcers are caused by *H. pylori* infection. Therefore, current approaches to treating peptic ulcer disease seek to cure the condition by eradicating *H. pylori.* Use of aspirin (including low-dose aspirin) and NSAIDs accounts for the majority of gastric ulcers that are not caused by *H. pylori.*

Gastroesophageal Reflux Disease. As noted earlier, there is considerable overlap among the symptoms of dyspepsia and GERD. More than half of patients with proven GERD have dyspepsia in addition to heartburn; as many as 20% of patients experience dyspepsia only, without heartburn or regurgitation. Erosive esophagitis is found in 5% to 15% of patients with dyspepsia, regardless of whether they report experiencing heartburn.

Gastric Cancer. Gastric cancer is a rare (less than 2% of cases) but important cause of dyspepsia. The incidence of gastric cancer increases with age; in the United States, fewer than 10 out of 100,000 cases occur among persons younger than 55 years of age. The median age at diagnosis is 70 years in men and 74 years in women.

Treatment Strategies

Treatment strategies for dyspepsia are not as straightforward or well-defined as they are for heartburn. Whenever possible, treatment should be directed at the underlying cause of the symptoms (e.g., *H. pylori*–eradication therapy for patients with suspected peptic ulcer disease). Patients who experience dyspepsia in relation to specific foods or activities (e.g., overeating, smoking) should be encouraged to limit or avoid them; this often resolves a patient's symptoms, if only by means of a placebo effect. Drugs that are known to cause or contribute to dyspepsia should be discontinued or replaced with a more suitable agent whenever possible.

Antacids, nonprescription H_2 antagonists, and bismuth subsalicylate can be effective for the treatment of occasional episodes of acute dyspepsia. Symptoms in patients with chronic dyspepsia—including symptoms that persist after successful eradication of *H. pylori*—often respond to a single 4-week course of therapy with a prescription PPI. Nonprescription PPIs are not indicated for the treatment of dyspepsia.

Exclusions for Self-Treatment

Although occasional GI complaints usually are not harbingers of disease, both heartburn and dyspepsia can be symptoms of serious conditions that require medical attention.

Heartburn

Further diagnostic testing should be considered for patients with alarm symptoms suggesting complicated disease:

- Dysphagia (difficulty in swallowing).
- Odynophagia (painful swallowing).
- Upper GI bleeding.
- Unexplained iron-deficiency anemia.
- Unintended weight loss.

It may be necessary to ask specific, direct questions (e.g., "Do you feel pain when you swallow? When you eat, do you feel as though the food gets stuck or just doesn't go down right? Have you coughed up any blood or vomited black material that looks like coffee grounds?") to determine whether the patient has experienced any of these signs or symptoms.

Other exclusions for self-treatment of heartburn are listed in FIGURE 1.

Dyspepsia

Patients with dyspepsia who present with any of the following alarm symptoms need early investigation with endoscopy, primarily to rule out upper GI malignancy:

- Age older than 55 years with new-onset dyspepsia.
- Family history of upper GI cancer.
- Upper GI bleeding.
- Jaundice.
- Odynophagia.
- Palpable mass or lymphadenopathy.
- Persistent vomiting.
- Progressive dysphagia.
- Unexplained iron-deficiency anemia.
- Unintended weight loss.

Patients younger than 55 years of age with chronic or recurrent dyspepsia in the absence of obvious GERD or NSAID use should undergo testing for *H. pylori* infection. Patients who are *H. pylori*–positive should receive eradication therapy; patients who are *H. pylori*–negative should receive empiric treatment with a PPI for 4 to 8 weeks.

In addition, patients with dyspepsia who meet any of the exclusions for self-treatment listed in the algorithm in FIGURE 1 should be evaluated by a primary care provider.

Self-Treatment Strategies

Self-treatment usually is appropriate for all other patients who complain of heartburn or dyspepsia. In patients without alarm symptoms, the delay in diagnosis imposed by a relatively short course of self-treatment is unlikely to mask serious urgent problems or influence eventual treatment success.

Lifestyle Modifications

Patients who notice a temporal relationship between episodes of heartburn or dyspepsia and ingestion of specific foods or beverages should be advised to avoid the offend-

Table 3. Lifestyle Modifications That May Benefit Patients With Heartburn

- Avoid eating large meals
- Avoid foods, beverages, and activities that promote reflux
- If possible, avoid the use of medications that may aggravate heartburn
- If nocturnal symptoms are present:
  - Avoid lying down for at least 3 hours after eating
  - Elevate the head of the bed 6–10 inches using blocks, or use a foam wedge
- Lose weight if overweight
- Stop or reduce cigarette smoking[a]
- Wear loose-fitting clothing

[a]Nicotine may decrease lower esophageal sphincter pressure; the act of smoking decreases salivation.

ing items, or at least consume less of them. For some patients, these simple measures may be sufficient to eliminate symptoms completely.

If the offending agent is a medication, care should be taken to ensure that the patient is using the medication correctly. For example, bisphosphonates should be taken with a full glass of plain water, and patients should avoid lying down for at least 30 minutes after taking the medication. If an offending medication therapy cannot be discontinued, it ideally should be replaced with a therapeutic equivalent less likely to cause symptoms. If it cannot be replaced, consideration should be given to using the smallest possible effective dosage or using other strategies that might minimize symptoms. For example, if a patient must be treated with aspirin or an NSAID, a trial of cotherapy with an antacid, H_2 antagonist, or PPI may be considered (depending on the frequency and severity of dyspepsia).

Other lifestyle modifications that may be of benefit to patients with heartburn in particular are listed in Table 3.

Nonprescription Medications

Antacids. Antacids are basic compounds that contain inorganic salts, primarily sodium bicarbonate, calcium carbonate, aluminum salts (hydroxide, phosphate), and magnesium salts (hydroxide, carbonate, trisilicate). These compounds react with gastric acid to form a salt and water, resulting in a small but noticeable increase in intragastric pH. Increasing the intragastric pH above 5 inhibits the conversion of pepsinogen to pepsin, which is thought to contribute to the mechanism of action of antacids.

Antacids also may work by means of nonacid mechanisms. Aluminum hydroxide and calcium carbonate appear to adsorb pepsin, reducing its proteolytic activity more than would be predicted by pH changes alone. Both magnesium hydroxide and aluminum hydroxide bind bile acids, and they may have cytoprotective effects as well. Antacids also may increase LES pressure.

Most antacids are indicated for the relief of mild, infrequent heartburn; acid indigestion; and sour stomach in patients 12 years of age or older. (A product containing calcium carbonate is available as Children's Pepto and in generic versions; it is labeled for use in children as young as 2 years of age who weigh at least 24 lb.) Antacids cannot be used to prevent symptoms because they only neutralize existing gastric acid and have no effect on acid secretion. Antacids are sometimes used as adjunctive therapy, to relieve breakthrough symptoms of heartburn or dyspepsia, in patients who are being treated with prescription medications for GERD or peptic ulcer disease.

Available antacid dosage forms include liquid formulations (suspensions), chewable tablets, and effervescent powders and tablets that must be dissolved in water. New antacid products are introduced regularly, and existing products tend to be reformulated frequently, so it is important to check product labeling to confirm the current active and inactive ingredients.

The amount of acid buffered by a dose of antacid over a specified period is known as the acid-neutralizing capacity, expressed in terms of milliequivalents (mEq). Acid-neutralizing capacity is influenced by product formulation, ingredients, and concentration, so that equal volumes of liquid antacids or the same number of tablets are not equipotent. Despite these differences, currently marketed antacids are considered to be interchangeable when used at recommended dosages.

Antacids have the ability to begin neutralizing gastric acid immediately upon entering the stomach, although actual onset of action may be influenced by the active ingredients and product formulation. Tablet formulations must dissolve after they are swallowed; therefore, liquid formulations usually have a faster onset of action.

All antacids have a short duration of action, ranging from 20 minutes when taken on an empty stomach to 3 hours when taken postprandially. Additional doses may be taken every 1 to 2 hours, although patients should be cautioned not to exceed the product-specific maximum daily dosage. Patients who need to use antacids more than twice per week or regularly for more than 2 weeks may need to be switched to a different medication such as an H_2 antagonist, H_2 antagonist plus antacid, or PPI.

Some antacid products include alginic acid in the formulation (it is listed among the inactive ingredients on the Drug Facts label). Alginic acid reacts with sodium bicarbonate and saliva to form a highly viscous solution (sodium alginate) that floats on the surface of gastric contents. When reflux occurs, sodium alginate enters the esophagus first, acting as a mechanical barrier and theoretically minimizing the potential for irritation. There is some evidence that combined antacid/alginic acid therapy offers symptom control superior to that achievable with antacids alone, but these combination products also tend to be more expensive.

Adverse effects of antacid therapy usually are minimal in patients with normal renal function; all antacids

Table 4. Selected Medications That Should Not Be Administered Concurrently With Antacids

- Azithromycin
- Dasatinib
- Digoxin
- Fluoroquinolones
- Iron
- Isoniazid
- Itraconazole
- Ketoconazole
- Mycophenolic acid
- Tetracyclines
- Tipranavir

pose a risk of systemic adverse effects or electrolyte imbalances in patients with chronic renal failure. The risk of common adverse effects such as diarrhea (magnesium-containing products) and constipation (aluminum-containing and calcium-containing products) increases with higher dosages. The use of sodium bicarbonate is limited by associated risks of fluid overload (owing to sodium retention) and systemic alkalosis in susceptible patients (sodium bicarbonate can be absorbed into the systemic circulation and alter systemic pH). Hypercalcemia and the milk-alkali syndrome are becoming increasingly important concerns with the addition of calcium carbonate to many antacid products as well as current trends toward using calcium carbonate as a calcium supplement.

Antacids are capable of interacting with a wide variety of drugs through three primary mechanisms:

- Binding of another drug in the intestinal tract.
- Changes in GI pH.
- Changes in urinary pH.

To prevent the most common and potentially detrimental interactions, patients should not use antacids within 2 hours of enteric-coated products or any of the drugs listed in TABLE 4. Antacid-induced alkalinization of the urine may increase blood concentrations of amphetamines and quinidine and decrease concentrations of salicylates.

Histamine H_2-Receptor Antagonists. H_2 antagonists competitively inhibit the action of histamine on the H_2 receptor of gastric parietal cells, causing a dose-dependent inhibition of both basal and meal-stimulated gastric acid secretion. All four H_2 antagonists (cimetidine, famotidine, nizatidine, and ranitidine) are available on a nonprescription basis (TABLE 5) at one half the usual prescription dose; famotidine and ranitidine also are available on a nonprescription basis at the usual prescription dosages (famotidine 20 mg and ranitidine 150 mg). Although there are modest differences among the nonprescription H_2 antagonists in terms of potency, duration, onset of action, and potential for drug interactions, they generally can be used interchangeably. (Cimetidine has the shortest duration of action and the greatest potential for serious hepatic cytochrome P450 [CYP] drug interactions, and is associated with impotence in men.)

Compared with antacids, the nonprescription H_2 antagonists have a slightly slower onset of action (30 to 45 minutes) but a longer duration of action (as long as 6 to 10 hours). The slower onset makes the nonprescription H_2 antagonists particularly useful for preventing heartburn symptoms in patients who can predict when they will suffer from episodes of reflux (e.g., after a heavy meal, during exercise).

Nonprescription H_2 antagonists are indicated for use in patients 12 years of age and older for the treatment of mild to moderate, infrequent, episodic heartburn, as well as for the prevention of heartburn associated with acid indigestion and sour stomach. They may be used at the onset of symptoms or up to 60 minutes before a meal or exercise that may provoke heartburn. The H_2 antagonists also provide moderate improvement in patients with mild dyspeptic symptoms.

Patients should not take more than two doses of a nonprescription H_2 antagonist in 24 hours. Tolerance to the gastric antisecretory effect may develop when H_2 antagonists are taken daily (versus as needed) and may be responsible for diminished effect;

Table 5. Nonprescription Acid Suppressants

Drug and Strength	Brand Name(s)
Histamine H_2-Receptor Antagonists	
Cimetidine 200 mg	Tagamet HB
Famotidine 10 mg	Pepcid AC
Famotidine 20 mg	Pepcid AC Maximum Strength
Nizatidine 75 mg	Axid AR
Ranitidine 75 mg	Zantac 75
Ranitidine 150 mg	Zantac 150
Histamine H_2-Receptor Antagonist Plus Antacid	
Famotidine 10 mg/calcium carbonate 800 mg/magnesium hydroxide 165 mg	Pepcid Complete
	Tums Dual Action
Proton Pump Inhibitors	
Lansoprazole 15 mg	Prevacid 24HR
Omeprazole 20 mg	Prilosec OTC[a]
Omeprazole 20 mg/sodium bicarbonate 1,100 mg	Zegerid OTC

[a] Each tablet contains omeprazole magnesium 20.6 mg, equivalent to omeprazole 20 mg.

therefore, it is preferable for these agents to be used on an as-needed basis only.

The nonprescription H_2 antagonists are generally well tolerated, with a low incidence of adverse effects. The adverse effects reported most frequently by patients using the nonprescription products are headache, diarrhea, constipation, dizziness, and drowsiness. All four H_2 antagonists are eliminated by a combination of renal and hepatic metabolism, with renal elimination being most important. Consideration should be given to reducing the dose in patients with renal failure and patients of advanced age.

Proton Pump Inhibitors. PPIs bind irreversibly to hydrogen/potassium adenosine triphosphatase (the "proton pump") in gastric parietal cells, thereby blocking the final step in gastric acid secretion. The resulting inhibition of gastric acid secretion is potent and long-lasting, permitting once-daily dosing.

Omeprazole was the first PPI available on a nonprescription basis, as Prilosec OTC. Lansoprazole recently became available for nonprescription use as Prevacid 24HR. Other PPIs are under consideration for a switch from prescription to nonprescription (Rx-to-OTC) status.

Nonprescription PPIs are indicated for the treatment of frequent heartburn (i.e., heartburn that occurs 2 or more days per week) in patients 18 years of age and older. They are *not* intended for the immediate relief of heartburn or occasional, as-needed use. Although onset of symptom relief can occur within 2 to 3 hours, complete relief may take 1 to 4 days. Product labeling instructs patients to swallow (not chew or crush) one tablet or capsule daily for 14 consecutive days. The 14-day course of therapy may be repeated once every 4 months.

PPIs are acid-labile compounds that must be protected from degradation by gastric acid during oral administration. Most PPIs (including nonprescription omeprazole and lansoprazole) are formulated as delayed-release, enteric-coated tablets or capsules. The dual-ingredient product Zegerid—which recently was approved for an Rx-to-OTC switch as Zegerid OTC—is an immediate-release capsule formulation containing omeprazole 20 mg and sodium bicarbonate 1,100 mg. The sodium bicarbonate serves to raise the gastric pH, thereby protecting omeprazole from acid degradation.

After PPIs are absorbed, they accumulate in the parietal cells and bind only to proton pumps that are actively secreting acid. To ensure that the maximal number of pumps are activated when serum drug levels are highest, the daily dose of a PPI should be taken up to 30 minutes before breakfast (or the first substantial meal of the day).

PPIs generally are well tolerated, with a low incidence of adverse effects. The most commonly reported adverse effects are headache, diarrhea, and constipation. Omeprazole may interact with other medications that depend on hepatic CYP 2C19 for metabolism; in particular, it can delay the clearance of diazepam, phenytoin, and warfarin. (See Acid Reducers and Clopidogrel for information about concomitant use of those agents.) Because PPIs cause such a profound inhibition of gastric acid secretion, they may interfere with the absorption of drugs for which gastric pH is an important determinant of bioavailability (e.g., ketoconazole, digoxin).

Bismuth Subsalicylate. Bismuth subsalicylate is another nonprescription option for patients seeking relief from heartburn, indigestion, or upset stomach. It is the active ingredient in a growing number of products—especially reformulated products. The mechanism of action in upset stomach may involve a topical effect on the gastric mucosa; the mechanism of action in heartburn is not known. The usual adult dosage is 262 to 500 mg every 30 to 60 minutes as needed, with a maximum of eight doses in 24 hours and a maximum length of therapy of 2 days. Patients should be warned that a temporary, harmless darkening of the stool, tongue, or both may occur. Mild tinnitus is a dose-related adverse effect. (See the Diarrhea section for additional information.)

Acid Reducers and Clopidogrel

In November 2009, the U.S. Food and Drug Administration (FDA) issued a public health advisory concerning an interaction between the platelet aggregation inhibitor clopidogrel and omeprazole. Clopidogrel is converted into its active form by hepatic CYP 2C19, which is inhibited by omeprazole. According to the advisory, new data had revealed a reduction in active metabolite levels of about 45% in patients who received both clopidogrel and omeprazole, compared with those taking clopidogrel alone. The effect of clopidogrel on platelets was reduced by as much as 47% in patients receiving clopidogrel and omeprazole together; these reductions were seen regardless of whether the drugs were given at the same time or 12 hours apart.

The advisory recommended avoiding concomitant use of clopidogrel and omeprazole. Because cimetidine and esomeprazole (Nexium), which also inhibit CYP 2C19, were expected to have similar interactions with clopidogrel, the advisory also recommended against those combinations. No recommendations were made about drug interactions between clopidogrel and other H_2 antagonists or PPIs because of insufficient information.

Product Selection and Use Considerations

As depicted in Figure 1, the decision about which medication to recommend to a specific patient will be based on the timing and frequency of the patient's symptoms as well as patient preferences and cost. Because antacids offer rapid but short-lived symptomatic relief, they are most appropriate for patients who experience mild, infrequent symptoms. Tablet formulations are more portable than liquids, so many patients find it most convenient to use tablets during the day and liquids at night. The palatability of antacid preparations varies widely and is a matter of individual preference for most patients; patients may need to take a trial-and-error approach to finding the most accept-

CASE 1. HEARTBURN

A 44-year-old woman has experienced sporadic heartburn symptoms in the past, which she had been able to manage adequately with a nonprescription H_2 antagonist. But her symptoms have increased substantially during the last 2 months, to the point where she currently experiences heartburn about 3 days per week. She attributes this increase to a recent promotion at work that has necessitated more frequent travel, poor eating habits, and a lot of stress. The patient asks whether she can keep treating the symptoms herself or needs something "stronger." A medication history reveals the following:

- Flonase (fluticasone propionate) 50 µg, one spray in each nostril every day for allergic rhinitis.
- Claritin (loratadine) 10 mg daily.
- Multivitamin daily.

What advice would you offer this patient?

a. Tell the patient that she should undergo a diagnostic work-up and most likely needs to be treated with a prescription medication.
b. Recommend that she try a 14-day course of therapy with a nonprescription PPI.
c. Encourage her to try taking antacids instead of the nonprescription H_2 antagonist.
d. Recommend that she take double the recommended dose of the nonprescription H_2 antagonist, twice daily, for a 2-week period.

Case study responses appear on page 26.

able product.

H_2 antagonists are a better choice for patients with mild to moderate symptoms who require more prolonged relief. The higher-dose products should be reserved for patients with moderate symptoms. H_2 antagonists are the only current option for patients with episodic heartburn who are able to predict when they are going to suffer from symptoms and therefore able to premedicate.

Concurrent use of antacids and H_2 antagonists has been shown to provide an incremental improvement in efficacy compared with the individual agents. This approach offers patients the benefits of rapid neutralizing effect and long duration of action. Famotidine, calcium carbonate, and magnesium hydroxide are available in combination products (TABLE 5); single agents also may be administered consecutively (i.e., an antacid followed by an H_2 antagonist).

Product labeling for antacids and nonprescription H_2 antagonists recommends a maximum length of therapy of 14 days. A stepwise approach may be tried, beginning with antacids and progressing to H_2 antagonists (or antacids plus an H_2 antagonist) if antacids fail to control symptoms adequately. Continuous therapy with either type of agent should not exceed 2 weeks (or a total of 4 weeks if a drug from each class is tried).

Patients who experience heartburn symptoms 2 or more days per week or have symptoms that do not respond to nonprescription H_2 antagonists are candidates for treatment with a nonprescription PPI. Patients should not use PPIs for more than 14 days, or repeat the course of therapy more frequently than every 4 months, unless they are directed to do so by their primary care provider.

As many as 30% to 80% of pregnant women experience heartburn, usually during the third trimester. Dietary and lifestyle modifications should be tried before drug therapy is considered. Antacids containing calcium or magnesium generally are considered to be safe for use during pregnancy, as long as the recommended daily dosages are not exceeded. However, care should be taken to avoid excessive ingestion of calcium (more than 2,500 mg per day) from antacids, prenatal vitamins, and other possible sources. Because data about the safety of H_2 antagonists and PPIs are limited, pregnant women should be directed to use antacids unless instructed otherwise by a health care provider.

Follow-Up

Patients whose symptoms persist or worsen after an appropriate trial of self-treatment (no longer than 14 days), as well as patients who need to use doses of nonprescription medications that are larger or more

Points to Remember

- Heartburn and dyspepsia are common GI symptoms. Many patients experience both. When heartburn (with or without acid regurgitation) is the dominant symptom, it usually is associated with gastroesophageal reflux.
- Patients with heartburn or dyspepsia who report alarm symptoms, initially or during self-treatment, should undergo a diagnostic work-up. All patients 55 years of age or older with new-onset dyspepsia should undergo diagnostic testing to rule out the presence of gastric cancer.
- All patients—especially those with heartburn—may benefit from adopting lifestyle modifications, although objective evidence of the effectiveness of these measures is lacking.
- Antacids and nonprescription H_2 antagonists are the mainstays of treatment for the relief or prevention (H_2 antagonists only) of episodic heartburn symptoms and dyspepsia. In general, antacids provide faster relief; H_2 antagonists take slightly longer to work but provide a longer duration of action. Patients who can anticipate meal-induced heartburn or dyspepsia may be able to prevent their symptoms by taking an H_2 antagonist up to 1 hour before eating. Concurrent use of antacids and H_2 antagonists provides immediate relief of heartburn and a longer duration of action.
- Nonprescription PPIs offer a self-treatment option for patients with frequent heartburn symptoms (2 or more days per week). Patients take one dose (tablet or capsule) per day for 14 days and may repeat this 14-day course of therapy every 4 months.

Table 6. Selected Medications That Can Cause Constipation

- Analgesics (including nonsteroidal anti-inflammatory drugs)
- Antacids containing aluminum or calcium
- Anticholinergic agents (e.g., benztropine)
- Anticonvulsants (e.g., carbamazepine)
- Antihistamines (e.g., diphenhydramine)
- Antihypertensive agents (e.g., angiotensin-converting enzyme inhibitors, β-adrenergic blocking agents)
- Antimotility agents (e.g., diphenoxylate, loperamide)
- Barium sulfate
- Benzodiazepines (especially alprazolam and estazolam)
- Bismuth
- Calcium channel blockers (e.g., verapamil)
- Calcium supplements
- Diuretics (e.g., thiazides)
- Iron supplements
- Lipid-lowering agents (e.g., cholestyramine, pravastatin, simvastatin)
- Memantine
- Monoamine oxidase inhibitors (e.g., phenelzine)
- Opiates (e.g., codeine, morphine)
- Parasympatholytics (e.g., atropine)
- Parkinsonism agents (e.g., bromocriptine)
- Polystyrene sodium sulfate
- Psychotherapeutic drugs (e.g., phenothiazines, butyrophenones)
- Sucralfate
- Tricyclic antidepressants
- Vinca alkaloids (e.g., vincristine)

frequent than recommended, should be directed to consult their primary care provider. All patients who develop any of the alarm symptoms described earlier (see the EXCLUSIONS FOR SELF-TREATMENT section) while taking nonprescription medications for heartburn or dyspepsia should undergo further medical evaluation.

CONSTIPATION

Constipation is a symptom-based disorder characterized by infrequent stools, difficult passage of stool, or both. For patients, constipation represents a subjective interpretation of a real or imagined disturbance of bowel function. A person who says "I am constipated" may be referring to any of a broad set of complaints, including:

- Straining to pass stools.
- Passing excessively hard or small stools.
- Unproductive urges.
- Passing stools less frequently than the person thinks he or she should.
- A sensation of incomplete bowel evacuation.
- Lower abdominal bloating or discomfort.
- Inability to defecate at will.

In the United States, constipation is reported more frequently by women than men and by nonwhites than whites. Constipation is common during pregnancy, particularly during the first and third trimesters. The prevalence of constipation rises with increasing age, although there does not appear to be an age-related decrease in the frequency of bowel movements. Some studies have found correlations between constipation and both low socioeconomic status and fewer years of education.

Many people are unaware that the normal frequency of bowel movements in humans ranges from about three times per day to three times per week in adults. Bowel movement patterns vary more widely in children. Some people believe that daily bowel movements are required for health and well-being, or fear that toxic substances will accumulate in the colon if they (or their children) fail to have a daily bowel movement. For these people, the only intervention needed may be reassurance that irregular bowel habits are common in the healthy general population and that their symptoms are not harmful.

Causes of Constipation

Constipation may be classified as primary or secondary. Secondary causes of constipation include mechanical small and large bowel obstruction as well as a wide variety of disorders of the GI tract (e.g., irritable bowel syndrome, diverticulitis), metabolic disorders (e.g., diabetes), endocrine disorders (e.g., hypothyroidism), neurologic disorders (e.g., Parkinson disease, multiple sclerosis), and psychogenic factors (e.g., depression, eating disorders). Primary constipation most often is associated with disordered function of the colon or rectum (known as functional constipation). Slow-transit constipation is characterized by slower than normal movement of fecal contents. Defecatory disorders, which include pelvic floor dysfunction, anismus, and rectal prolapse, are characterized by failure to empty the rectum effectively because of an inability to coordinate the abdominal, rectoanal, and pelvic floor muscles.

A number of medications can cause constipation (TABLE 6). Most of these medications inhibit the neurologic or muscular function of the GI tract (particularly the colon), and the inhibitory effects usually are dose-dependent. Opiates, anticholinergic agents, and antacids containing aluminum or calcium are the most frequent causes of drug-induced constipation. Although excessive use or abuse of stimulant laxatives had been thought to lead to a paradoxical worsening of constipation, there is no evidence to support this common belief.

Specific lifestyle factors are associated with constipation. Individuals who are inactive or immobile (e.g., because of an injury or degenerative joint disease) often complain of constipation. Inadequate intake of fluids, calories (i.e., ingestion of small amounts of food), or carbohydrates specifically (e.g., Atkins diet) can lead to diet-related constipation. Somewhat surprisingly, no study has

Table 7. Types of Fiber Supplements

Type of Fiber	Examples of Common Brands
Products Classified as Bulk-Forming Laxatives	
Malt soup extract	Maltsupex
Methylcellulose	Citrucel
Polycarbophil	FiberCon
Psyllium	Metamucil
Products Classified as Dietary Supplements	
Inulin	FiberChoice, Metamucil Clear & Natural
Partially hydrolyzed guar gum	Sunfiber
Powdered cellulose	UniFiber
Wheat dextrin	Benefiber

demonstrated a link between low dietary fiber intake and constipation. In young children, constipation may be associated with the transition from breast milk to cow's milk or formula. People of all ages may become constipated when their normal diet and daily routines are disrupted (e.g., when traveling).

Adults and children can develop constipation if they suppress or ignore the urge to empty the bowel, because the rectal muscles eventually lose tonicity and the nerve pathways may degenerate. Patients with painful lesions of the anal canal (e.g., ulcers, fissures, thrombosed hemorrhoidal veins) may suppress defecation to avoid pain. Some adults may suppress the urge to have a bowel movement because they believe they are too busy or do not want to use toilets outside the home; children may ignore the urge as a result of stressful toilet training or because they do not want to take a break from play.

Exclusions for Self-Treatment

The majority of patients who complain of constipation have no structural, biochemical, or physiologic abnormalities. Nevertheless, the underlying cause of constipation should be determined and treated whenever possible. The exclusions for self-treatment listed in FIGURE 2 help to identify patients with secondary constipation as well as patients with signs and symptoms of potentially serious GI problems.

A detailed medication history can reveal possible drug-induced constipation. Additional questions should be directed at lifestyle factors (including diet, fluid intake, and physical activity) as well as previous laxative use.

Self-Treatment Strategies

The primary goals of treatment are to:

- Relieve constipation and reestablish normal bowel function.
- Establish dietary and exercise habits consistent with preventing recurrences.
- Promote the safe, effective, and rational use of laxatives.

As shown in FIGURE 2, initial treatment is based on nonpharmacologic interventions, including a gradual increase in fiber intake (through dietary fiber, fiber supplements, or a combination of both) and increased fluid intake. Nonprescription laxatives can be used as an adjunct to lifestyle modifications if more immediate relief is needed or desired. In general, a bulk-forming agent should be tried first, if it is not being used already for fiber supplementation. If the bulk-forming agent is ineffective or more rapid laxation is needed, the hyperosmotic agent polyethylene glycol 3350 (PEG 3350) should be considered.

Lifestyle Changes and Fiber Supplements/Bulk-Forming Agents

Fiber adds bulk to stools, improves retention of stool water, and increases the rate of stool transit through the intestine. Patients should be encouraged to increase dietary fiber to the level recommended in the current *Dietary Guidelines for Americans:* 14 g per 1,000 calories consumed. For most adults, this translates to about 20 to 35 g per day, compared with an average daily intake in the United States of 14 g per day for women and 19 g per day for men. Patients should be advised simultaneously to limit their intake of foods that have little or no fiber, such as ice cream, cheese, meat, and processed foods.

Fiber typically is divided into two

CASE 2. CONSTIPATION

A 72-year-old woman shows you an empty box of Dulcolax (bisacodyl 5 mg) tablets and asks, "Do you have this? It has always worked well for me. I'm having some problems again now and I used up this box. But there seem to be a lot more products named Dulcolax now. "Upon questioning, the woman explains that she has been using Dulcolax daily for the last 3 weeks. The product worked well to relieve her constipation during the first 2 weeks, but then seemed markedly less effective during the past week.

What information should you communicate to this patient?

a. The patient should discontinue use of this product and focus on adding more fiber to her diet.
b. She most likely has developed tolerance to the effect of the stimulant laxative in this product. She should stop using the product for 1 week, and then start taking it again.
c. Because of the duration of this patient's constipation and her recent daily use of laxatives (exceeding 1 week), she should undergo a diagnostic work-up.

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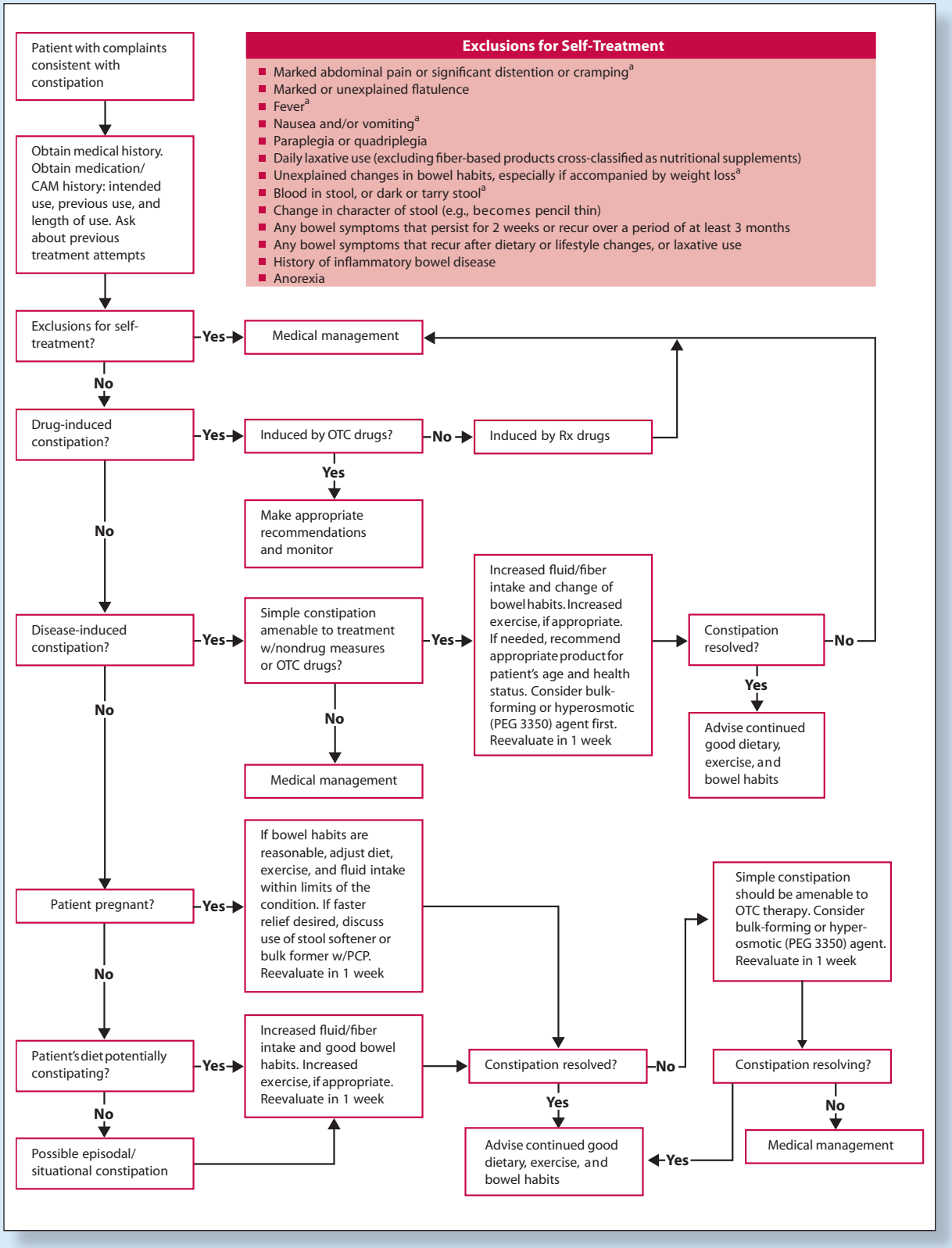
Figure 2. Algorithm for Self-Treatment of Constipation



[a]Denotes "alarm" or red flag symptoms.

CAM = complementary and alternative medicine; OTC = over-the-counter; PCP = primary care provider; PEG = polyethylene glycol; Rx = prescription.

Source: Curry CE Jr., Butler DM. Constipation. In: Berardi RR, Ferreri SP, Hume AL, et al. *Handbook of Nonprescription Drugs: An Interactive Approach to Self-Care.* 16th ed. Washington, DC: American Pharmacists Association; 2009:266–7.

categories: soluble and insoluble. Insoluble fiber, which is found in foods such as whole grains, wheat bran, and many vegetables, passes through the intestines essentially unchanged. It is considered to be most effective for the treatment of constipation. Soluble fiber, which is found in foods such as oat bran, beans, barley, peas, carrots, citrus fruits, and apples, dissolves easily in water and assumes a soft, gel-like texture in the intestines. Soluble fiber is associated with improved glycemic control, lowered serum cholesterol, and enhanced fluid and electrolyte absorption.

Patients who cannot achieve their daily fiber goal through diet alone may benefit from the use of commercial fiber supplements. Fiber supplements are available in a number of dosage forms, including powders, caplets, wafers, and chews. They offer the benefits of convenience as well as a uniform amount of fiber per dose. Some fiber supplements are classified as bulk-forming laxatives (Table 7) and carry a Drug Facts label. Many newer fiber supplements—for example, products containing inulin or powdered cellulose—are classified as dietary supplements (Table 7). A number of these newer products are formulated as flavor-free, texture-free powders that can be mixed into hot or cold foods or beverages or added as an ingredient to cooked foods and baked goods.

Patients should be cautioned to increase their intake of fiber gradually and slowly. Flatulence, abdominal distention, and bloating are common adverse effects of increased fiber intake, although these effects tend to resolve with continued use. Patients also should be advised to drink adequate amounts of fluid, preferably water. This is especially important for patients who use products containing psyllium; obstruction of the esophagus, stomach, small intestine, and colon has been reported when psyllium was consumed without fluid or with insufficient fluid. Recommendations for adequate fluid intake vary considerably, from 1 L (approximately 32 oz) to 4 L (approximately 128 oz) per day. In general, 2 L of fluid per day (approximately 64 oz) is recommended.

Patients should be aware that the effects of increased fiber consumption are unlikely to be apparent immediately. The effects of a high-fiber diet may not be noticed for 3 to 5 days; package labeling for fiber supplements classified as bulk-forming laxatives states an onset of effect within 12 to 72 hours. Some patients require a considerably longer time to realize the benefits of increased fiber intake, and some patients (especially those who complain initially of passing small stools) may not realize any significant benefit.

A high fiber intake may reduce the bioavailability of oral medications because of binding to the fiber or other mechanisms. Whenever possible, medications should not be taken within 1 to 2 hours of ingesting fiber supplements.

Pharmacologic Agents

Occasional short-term use of nonprescription laxative medications generally is acceptable in patients with simple or acute constipation (Figure 2). The pharmacologic agents described in this section should be used as infrequently as possible, at the lowest effective dosage, and usually for periods not exceeding 1 week. Patients who feel a need to continue the use of laxative medications beyond 1 week should be evaluated for the presence of chronic constipation.

Laxatives traditionally have been classified according to their mechanism of action (Table 8) despite the fact that the mechanism of many products is not understood clearly. In general, laxatives work by reversing the normal physiology of the intestine, turning it from an organ that primarily absorbs water and electrolytes to an organ that primarily secretes them.

In recent years, a number of active ingredients in nonprescription laxative products (especially stimulant laxatives) have been reviewed and in some cases reclassified by the FDA as category II (not generally recognized as safe and effective). Because of these decisions, many laxative products that contained those ingredients have been reformulated recently or may be reformulated

Table 8. Major Classes of Laxatives and Representative Products

Classification	Agent (Example of Brand)	Onset of Action (hr)	Possible Adverse Effects
Hyperosmotic	Polyethylene glycol 3350 (MiraLAX)	24–72	Bloating, abdominal discomfort, cramping, flatulence
	Glycerin (Fleet Suppositories)	0.25–1	Rectal irritation
Emollient	Docusate sodium (Colace)	12–72	Diarrhea, mild abdominal cramping
Lubricant	Mineral oil	6–8	Anal irritation and pruritus, malabsorption of fat-soluble vitamins
Saline	Milk of magnesia (Phillips)	0.5–3	Abdominal cramping, fluid or electrolyte imbalances
Anthraquinone stimulant	Senna (Ex-Lax)	6–10	Severe abdominal cramping, fluid and electrolyte deficiencies
Diphenylmethane stimulant	Bisacodyl (Correctol)	6–10	Severe abdominal cramping, fluid and electrolyte deficiencies

subsequent to pending FDA actions. All health care professionals should take special care to check product labeling to confirm the current composition.

Hyperosmotic Agents. The hyperosmotic agents PEG 3350 and glycerin contain poorly absorbed ions or molecules that draw water into the intestinal lumen. The resultant increased intraluminal pressure exerts a mechanical stimulus that increases intestinal motility.

PEG 3350 was switched from prescription to nonprescription status in 2006. It is available as a powder for oral administration; the powder must be mixed with 4 to 8 oz of water or another beverage (hot, cold, or room temperature). The onset of action usually occurs within 24 to 72 hours.

PEG 3350 is considered to be very safe for short-term treatment of constipation. Most of an oral dose remains within the GI tract; the very small amount (0.2%) that is absorbed systemically is excreted rapidly in the urine. Possible adverse effects with recommended doses include bloating, abdominal discomfort, cramping, and flatulence. No clinically important drug-drug interactions have been reported. Patients with renal disease should consult with their primary care provider before using PEG 3350.

Glycerin usually is administered in suppository form. The onset of action generally occurs within 30 minutes. Glycerin is considered to be a very safe laxative for intermittent use in all age groups. Adverse effects from glycerin suppositories are minimal; some rectal irritation may occur. No clinically important drug-drug interactions have been reported. Use may be inappropriate in patients with a previous condition involving rectal irritation. Chronic use or overuse may lead to reduced serum potassium concentrations.

Emollient Agents. Emollient laxatives—also known as "stool softeners"—contain docusate calcium or docusate sodium. Emollients are anionic surfactants that function as detergents: when administered orally, emollients facilitate the mixing of aqueous and fatty substances within the intestinal tract, which softens the fecal mass. Although they are classified as laxatives, emollients are used mainly to prevent constipation. The onset of effect usually occurs in 1 to 2 days but may take as long as 3 to 5 days in some patients.

Emollient laxatives are most useful for patients who suffer from anorectal disorders or who should avoid straining at stool, including:

- Patients with severe hypertension or cardiovascular disease.
- Patients who recently had a myocardial infarction.
- Patients who recently underwent rectal or abdominal surgery.
- Women who recently gave birth.

Emollient laxatives potentially can cause mild abdominal cramping and diarrhea. They may enhance the intestinal absorption of agents administered concurrently and alter their toxic potential.

Lubricant Agents. Liquid petrolatum (mineral oil) is the only nonprescription lubricant laxative. When administered orally in a dose of 15 to 45 mL, mineral oil coats the stool and prevents colonic absorption of fecal water. The onset of action occurs within 6 to 8 hours. Emulsified mineral oil preparations are more palatable than plain mineral oil, and they penetrate and soften fecal matter more effectively.

The indications for use of mineral oil are similar to those for emollient laxatives. However, the emollients generally are considered to be the safer and more effective choice. Mineral oil should not be administered to children younger than 6 years of age or to pregnant women. It should be used with care, if at all, by older adults.

Most adverse effects of mineral oil are associated with repeated and prolonged use. Especially at higher doses, mineral oil may seep from the rectum, causing anal irritation and pruritus as well as soiling of skin and clothing. Aspiration of mineral oil can cause lipid pneumonia. Aspiration is a particular concern in young children, older patients, and debilitated patients who must remain recumbent; mineral oil should not be administered to these patients or to any patient before lying down. Mineral oil may impair the absorption of fat-soluble vitamins (vitamins A, D, E, and K) and many orally administered drugs, including oral anticoagulants, oral contraceptives, and digoxin.

Saline Agents. Saline laxatives contain relatively nonabsorbable cations and anions: magnesium citrate, magnesium hydroxide, magnesium sulfate, monobasic or dibasic sodium phosphate, or sodium biphosphate. The mechanism of action is believed to be mainly osmotic.

Milk of magnesia (an 8% suspension of magnesium hydroxide) is considered to be safe for occasional (every few weeks) use in otherwise healthy patients with mild constipation. A standard dose typically produces a bowel movement within 6 hours. Other saline laxatives are used primarily as cathartics for acute evacuation of the bowel (e.g., when preparing for endoscopic examination or after poisoning). The onset of action (i.e., producing a watery evacuation) occurs within 30 minutes to 3 hours for oral doses and 2 to 5 minutes for rectal doses.

All saline laxatives are capable of causing serious, potentially life-threatening electrolyte imbalances with long-term use or overdosage. Up to 20% of magnesium ions may be absorbed from magnesium-containing products; excessive doses of magnesium salts can cause hypermagnesemia. These products should be used with caution in patients with renal impairment, in children, and in older patients. Products containing sodium phosphates can cause hypocalcemia, hyperphosphatemia, and hypernatremia and thus should be used with caution in patients with renal impairment or cardiac disease (their use is contraindicated in patients with congestive heart failure) and in patients being treated with drugs that may affect serum electrolyte concentrations (e.g., diuretics).

Some deaths among patients who ingested more than 45 mL of sodium phosphate oral solution (including patients without medical contraindications) prompted the FDA to limit package sizes to 90 mL in 1998. These products since have been voluntarily

Points to Remember

- The term *constipation* may encompass any of a number of complaints related to bowel movements, including reduced frequency, increased straining, problems with the consistency or size of stools (e.g., hard stools, small stools), unproductive urges, a sense of incomplete bowel evacuation, or lower abdominal bloating or discomfort.
- Education may be needed to dispel patient misconceptions, including the belief that daily bowel movements are required for health and well-being and the fear that toxic substances will accumulate in the colon if bowel movements do not occur daily.
- Many patients who complain of constipation benefit from increased fluid intake, increased exercise, and increased intake of fiber, either through dietary changes or use of commercial fiber supplements.
- Occasional use of laxative medications is acceptable in most patients with acute constipation. These medications should be used as infrequently as possible, at the lowest effective dosage, and usually for periods not exceeding 1 week. In general, bulk-forming agents should be tried first; the hyperosmotic agent PEG 3350 should be considered if bulk-forming agents prove ineffective or if more rapid laxation is needed.

withdrawn from the nonprescription market.

Stimulant Agents. Stimulant laxatives are divided into two main groups on the basis of chemical structure: anthraquinone derivatives and diphenylmethane derivatives. Both groups are thought to increase intestinal propulsive peristaltic activity through local mucosal irritation or by means of interaction with the intramural nerve plexus of intestinal smooth muscle. Subsequent to the ongoing FDA review of nonprescription drug products, senna is the only currently marketed anthraquinone derivative, and bisacodyl is the only marketed diphenylmethane derivative.

Although senna and bisacodyl are considered to be appropriate for patients with simple constipation, they are considered to be second-line agents (after bulk-forming laxatives or PEG 3350). Both senna and bisacodyl are finding wide use in the treatment of chronic constipation caused by opiate analgesics. Doses of senna are expressed in terms of sennosides or standardized senna concentrate and vary considerably among products. Bisacodyl is available as 5-mg tablets; the usual daily dosage range for adults is 10 to 30 mg. The onset of laxative action (i.e., producing either a soft or semifluid stool) occurs within 6 to 10 hours for oral formulations of senna or bisacodyl. Bisacodyl also is available as a suppository; the onset of effect occurs within 15 to 60 minutes.

The action of stimulants is the least physiologic of all laxative classes. Possible adverse effects include severe cramping, electrolyte and fluid deficiencies, enteric loss of protein, malabsorption resulting from excessive hypermotility and catharsis, and hypokalemia. Prolonged use of anthraquinone derivatives has been associated with a reversible accumulation of dark pigment in the colon (melanosis coli), although this condition appears to be harmless. Patients who use senna should be alerted to the possibility of discolored urine (pinkish red, reddish violet, or reddish brown).

Bisacodyl has been associated with gastric irritation and is formulated as enteric-coated tablets. The tablets should not be chewed or crushed before administration. The tablets also should not be taken within 1 hour of milk, antacids, H_2 antagonists, or PPIs, because rapid erosion of the enteric coating may occur.

Stimulant laxatives have been considered to be especially prone to overuse and dependence. However, recent data show tolerance to be uncommon in all but the relatively few patients with severe slow transit constipation. There are no data to support the development of "rebound" constipation (i.e., constipation that worsens after laxative use), and there is no potential for addiction to laxatives. A proportion of patients with chronic constipation may become dependent on laxatives to achieve bowel movements without complaints such as severe straining, but this usually is not the result of prior laxative intake.

Castor Oil. Castor oil usually is considered to be a stimulant laxative, but it is sometimes classified as an anionic surfactant (emollient) laxative. Castor oil provides a strong purgative action at therapeutic doses, and its use generally is discouraged. The irritant effects of castor oil can induce premature labor in pregnant women.

Combination Products. A wide variety of combination laxative products are available. These products generally seek to take advantage of multiple mechanisms of action (e.g., an emollient laxative combined with a stimulant laxative). Few clinical comparisons have been conducted, and data supporting the use of combinations are very limited. In general, use of single-agent products is preferred.

Enemas. Laxative enemas are used to prepare patients for surgery or diagnostic procedures and to treat certain cases of constipation. Prepackaged enema units containing mineral oil, bisacodyl, glycerin, or sodium phosphate are available. Tapwater enemas also are used in the treatment of simple constipation.

To administer a laxative enema, the patient should lie (1) on the left side with knees bent or (2) in a knee-to-chest position facing toward the floor. The lubricated enema nozzle should be inserted gently 2 to 3 inches into the rectum. The solution should be allowed to flow into the rectum slowly (a dose usually is 500 mL or less). The enema solution should be retained until definite lower abdominal cramping is felt. The entire procedure may take as long as 1 hour.

Enemas have the potential to produce significant morbidity if instructions for administration are disregarded. The rectal mucosa is vulnerable to trauma from misdirected or inadequately lubricated nozzles. Dangerous water intoxication can occur if large volumes are used for

tap-water enemas. Phosphate enemas can lead to dangerous electrolyte disturbances (i.e., hyperphosphatemia and hypocalcemia) if they are retained too long. Patients should be cautioned to follow all directions for enema products carefully.

Follow-Up

The effectiveness of treatment for constipation is determined by how rapidly constipation is relieved and to what degree normal bowel habits have been restored. If an adequate response is not achieved after an appropriate trial—several days to several weeks for bulk-forming agents, 1 week for other types of laxatives—the patient should be referred to a primary care provider for further evaluation. Patients should be cautioned that overuse or extended use of some laxatives can alter the normal physiologic functioning of the gut.

DIARRHEA

Diarrhea is an abnormal increase in stool frequency, liquidity, or weight compared with a person's normal bowel pattern. Diarrhea is classified as acute, persistent, or chronic. Episodes of acute diarrhea usually have a sudden onset, are self-limiting, and resolve within 3 to 7 days, although diarrhea is considered to be acute if it lasts less than 14 days. Persistent diarrhea lasts from 14 days to 4 weeks; chronic diarrhea lasts more than 4 weeks.

Self-treatment options are appropriate only for patients with acute diarrhea. Persistent or chronic diarrhea may indicate the presence of any number of GI and systemic conditions (e.g., inflammatory bowel disease, irritable bowel syndrome, malabsorption syndromes, diabetic neuropathy) that should be evaluated and managed by a primary care provider.

Causes of Acute Diarrhea

Most cases of acute diarrhea are caused by infectious agents: viruses, bacteria, or protozoa. Noroviruses account for up to 75% of viral gastroenteritis; rotaviruses account for about 12% of all acute gastroenteritis and up to 50% of infantile gastroenteritis. The bacterial pathogens most commonly responsible for acute gastroenteritis in the United States are *Campylobacter* sp., *Salmonella* sp., *Shigella* sp., diarrheagenic strains of *Escherichia coli, Staphylococcus* sp., *Clostridium* sp., *Yersinia enterocolitica*, and *Bacillus cereus*. Acute infectious diarrhea may be accompanied by symptoms including nausea, vomiting, abdominal pain, and fever.

Foodborne transmission of pathogens accounts for more than one third of cases of acute gastroenteritis in the United States. Most foodborne infection is caused by viruses, *Salmonella* sp., or *Campylobacter* sp. Outbreaks may be linked to poor sanitary conditions in meat-processing plants, grocery stores, or restaurants as well as to specific foods (e.g., milk, raw eggs, chicken, melons, hummus, raspberries). *E. coli* strains have contaminated undercooked hamburger, unpasteurized apple cider, spinach, lettuce, and raw milk.

Traveler's diarrhea is the most predictable travel-related illness. It affects 30% to 70% of travelers each year, especially those who travel to high-risk destinations such as most of Africa, Asia, Central and South America, Mexico, and the Middle East. The most common presentation of traveler's diarrhea is a sudden onset of frequent (three to eight or more per day), loose or watery bowel movements, often accompanied by abdominal cramps and pain. Symptoms usually appear within the first week of travel but may occur at any time, even after the traveler returns home. Contrary to popular belief, the causative organisms (primarily bacteria, notably enterotoxigenic *E. coli*) are found more often on foods (e.g., fruits, vegetables, raw meat, seafood, hot sauces) than in the local water supply.

The ingestion of poorly absorbable sugars or sugar alcohols (e.g., mannitol, sorbitol) or poorly absorbed cations or anions (e.g., magnesium, sulfate, phosphate) can cause an osmotic diarrhea. Patients with lactase deficiency, which accounts for lactose intolerance, experience diarrhea because they are unable to hydrolyze the disaccharide lactose to absorbable monosaccharides. Some people develop diarrhea after eating fatty or spicy foods, or foods that contain large amounts of fiber or seeds. Diarrhea also may occur secondary to a food allergy (e.g., to dietary proteins).

Examples of medications that can cause diarrhea are shown in Table 9. Temporal correlation between the initiation of drug therapy and onset of diarrhea occurrence may be difficult to recognize; a careful and detailed medication history is extremely important in identifying drug-induced diarrhea. Diarrhea also may be a sign of laxative abuse. Patients with suspected medication-related diarrhea should be evaluated by a primary care provider.

Prevention of Diarrhea

Acute infectious diarrheal illness, especially viral gastroenteritis, usually is spread by person-to-person

Table 9. Selected Medications That Can Cause Diarrhea

- Acid-reducing agents (e.g., histamine H_2-receptor antagonists, proton pump inhibitors)
- Antacids containing magnesium
- Antiarrhythmic agents (e.g., digoxin, quinidine)
- Antibiotics
- Antihypertensive agents (e.g., angiotensin-converting enzyme inhibitors)
- Antineoplastic agents
- Antiretroviral agents
- Auranofin (gold salt)
- Cholinergic agents (e.g., bethanechol)
- Colchicine
- Misoprostol
- Nonsteroidal anti-inflammatory drugs
- Vitamin and mineral supplements

contact. Anyone who must come into contact with infected individuals should heighten hygiene measures by washing hands more frequently. Workers in day care centers and long-term care facilities should follow basic preventive measures, including isolating the individual with diarrhea and using sterile techniques.

The growing problem of food-borne illness prompted the U.S. Department of Agriculture to add the following consumer food safety recommendations to its update of the *Dietary Guidelines for Americans*:

- Wash hands, food contact surfaces (e.g., countertops, cutting boards), and fruits and vegetables.
- Keep raw foods separate from cooked or ready-to-eat foods while shopping, preparing, and storing foods.
- Cook foods to a safe temperature.
- Refrigerate perishable foods promptly and defrost foods properly.
- Avoid raw (unpasteurized) milk or any products made from unpasteurized milk, raw or partially cooked eggs or foods containing raw eggs, raw or undercooked meat and poultry, unpasteurized juices, and raw sprouts.
- "If in doubt, throw it out."

Travelers who will be going to high-risk areas may take a number of precautions to help minimize the risk of diarrhea. They should be encouraged to eat foods that are freshly cooked and served steaming hot (>138°F [59°C]). Travelers should avoid drinking tap water or beverages diluted with water (e.g., reconstituted fruit juices); beverages containing ice made from local water also should be avoided. (Carbonated beverages and beverages that are bottled and sealed are considered to be safe.) Foods that should be avoided include:

- Foods washed in water, such as salads.
- Fruits and vegetables with intact skins.
- Meat or seafood that is raw, undercooked, or served at room temperature.
- Hot sauces on tabletops.
- Food and beverages sold by street vendors.

However, travelers should be aware that people who follow these rules still become ill; poor hygiene practices in local restaurants may be the largest contributor to the risk for traveler's diarrhea.

Bismuth subsalicylate (e.g., Pepto-Bismol) has been shown to reduce the incidence of traveler's diarrhea from 40% to 14% when used prophylactically at a dosage of two chewable tablets or 2 fl oz (60 mL) four times daily (with meals and at bedtime) for up to 3 weeks. Prophylactic antimicrobial therapy is not recommended for most travelers, but it may be considered for short-term travelers who are high-risk hosts (e.g., immunocompromised patients) or are undertaking critical trips during which even a short bout of diarrhea could impact the purpose of the trip.

Exclusions for Self-Treatment

Because diarrheal illness may cause serious fluid and electrolyte imbalances, assessment of the patient's risk for dehydration and degree of dehydration is critical to determining the appropriateness of self-treatment for acute diarrhea. Specific signs and symptoms of dehydration (Table 10) are associated with the severity of diarrhea and related to the etiology and degree of fluid and electrolyte losses. Children younger than 5 years of age and adults 65 years of age and older are at particular risk for dehydration from diarrhea, especially severe, life-threatening dehydration. The following types of patients also are at increased risk:

- Patients with diabetes.
- Patients with severe cardiovascular or renal diseases.
- Patients with multiple chronic medical conditions.
- Immunocompromised patients (e.g., patients with acquired immunodeficiency syndrome, patients receiving cancer treatment, organ transplant recipients).

Patients with severe diarrhea and dehydration (more than 9% loss of body weight) may need to be hospitalized and managed with intravenous fluid therapy.

Other exclusions for self-treatment are listed in Figures 3A and 3B. Many of these exclusions help to identify patients with signs and symptoms of potentially serious GI problems.

Self-Treatment Strategies

Most cases of acute diarrhea are self-limited and generally improve clinically within 24 to 48 hours. The main goals of self-treatment are to (1) prevent or correct fluid and electrolyte loss and acid-base disturbance and (2) relieve symptoms. The treatment of acute diarrhea in children 6 months to 5 years of age and in patients older than 5 years is outlined in Figures 3A and 3B.

Fluid Therapy and Dietary Considerations

The most important treatment of diarrhea is to ensure that fluid and electrolyte deficits are replenished. Otherwise healthy adults who do not show signs of dehydration can accomplish this by increasing their intake of sports drinks (e.g., Gatorade), diluted juices, salty crackers, soups, and broths until the diarrhea resolves. Commercially available oral rehydration solutions, which are specially formulated to increase fluid and electrolyte absorption, are the preferred treatment for fluid therapy in all other patients.

Fluid therapy is carried out in two phases: rehydration therapy and maintenance therapy. Rehydration over 3 to 4 hours quickly replaces water and electrolyte deficits to restore normal body composition. In the maintenance phase, electrolyte solutions are given to maintain normal body composition.

Oral rehydration solutions are available primarily as premixed solutions. Although some dry powders requiring reconstitution are available, premixed products are preferred for use in children because they eliminate the possibility of improper reconstitution, which can lead to patient complications and injury. Both dextrose-based and rice-based preparations are available; there is no evidence that one product is clinically superior to another in effecting rehydration.

Historically, patients with diarrhea have been advised to refrain from

Table 10. Assessment of Dehydration and Severity of Acute Diarrhea

	Minimal or No Dehydration (Self-Treatable)	Mild to Moderate Dehydration/Diarrhea (Self-Treatable)	Severe Dehydration/Diarrhea (Not Self-Treatable)
Degree of dehydration (loss of body weight)	<3%	3%–9%	>9%
Signs of dehydration[a]			
Mental status	Well; alert	Normal; fatigued or restless; irritable	Apathetic; lethargic; unconscious
Thirst	Drinks normally; might refuse liquids	Thirsty; eager to drink	Drinks poorly; unable to drink
Heart rate	Normal	Normal to increased	Tachycardia; bradycardia in most severe cases
Quality of pulses	Normal	Normal to decreased	Weak; thready; impalpable
Breathing	Normal	Normal; fast	Deep
Eyes	Normal	Slight sunken[b]	Deeply sunken[b]
Tears	Present	Decreased[b]	Absent
Mouth and tongue	Moist	Dry	Parched
Skin fold	Instant recoil	Recoil in <2 seconds	Recoil in >2 seconds
Capillary refill	Normal	Prolonged	Prolonged; minimal
Extremities	Warm	Cool	Cold; mottled; cyanotic
Urine output	Normal to decreased	Decreased[b]	Minimal[b]
Number of unformed stools per day	<3	≤5	6–9
Other signs/symptoms of diarrhea	Afebrile; normal blood pressure; no orthostatic changes in blood pressure/pulse	May be afebrile or may develop fever >102.2°F (39°C); normal blood pressure; mild orthostatic blood pressure/pulse changes with or without mild orthostatic-related symptoms may be present; sunken fontanelle[c]	Fever >102.2°F (39°C); low blood pressure; dizziness; severe abdominal pain

[a] If signs of dehydration are absent, rehydration therapy is not required. Maintenance therapy and replacement of stool losses should be undertaken.
[b] Signs and symptoms experienced especially by young children.
[c] Of particular concern for young infants.

eating, then to resume eating slowly over a period of several days. However, most forms of acute diarrhea are not improved by fasting, and fasting may increase patient morbidity. A normal, age-appropriate diet should be reintroduced once the patient has been rehydrated. Although the BRAT (bananas, rice, applesauce, and toast) diet is prescribed frequently, it provides insufficient calories, protein, and fat and is not recommended. To avoid aggravating their condition, patients should be advised to avoid fatty or spicy foods, foods high in simple sugars, and caffeine-containing beverages.

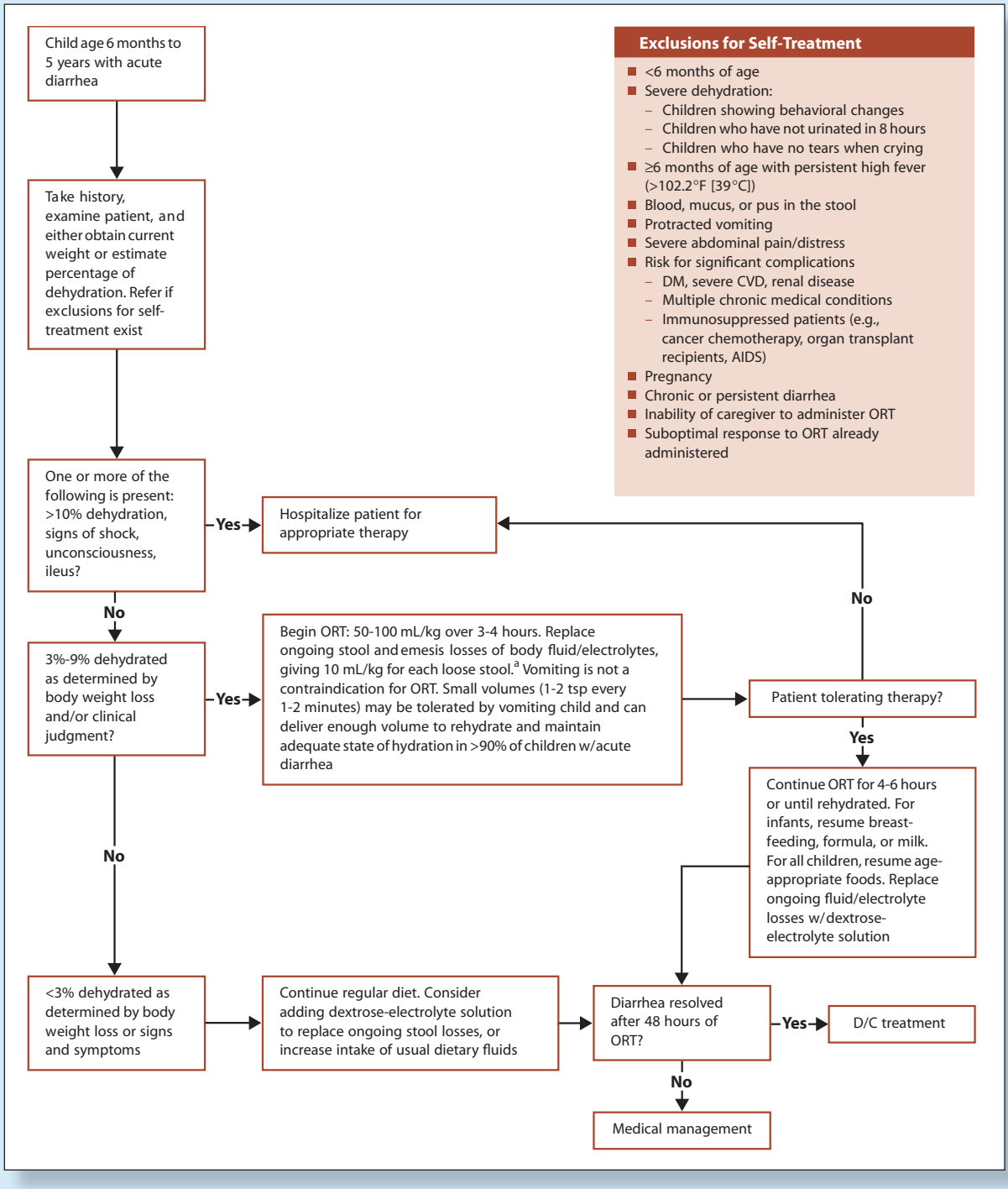
Pharmacologic Therapy

Although episodes of acute diarrhea usually are self-limiting and resolve within several days, patients still may seek relief from symptoms. Nonprescription antidiarrheal agents may provide relief and usually will do no harm when used according to label instructions.

A change in stool consistency toward more formed stools does not necessarily indicate that antidiarrheal therapy has treated the underlying problem successfully. Formed stools can have a high water content, and substantial water losses may continue despite the change in consistency. Moreover, reliance on pharmacologic agents shifts the focus away from fluid and electrolyte management.

Loperamide. Loperamide is considered to be a safe and effective choice for the treatment of acute diarrhea in patients as young as 6 years of age. It is a synthetic opioid agonist that stimulates μ-opioid receptors on intestinal circular muscles and reduces intestinal motility, which slows the intraluminal flow of liquid and facilitates intestinal absorption. Use of loperamide is not recommended in children younger than 6 years of age because it produces only modest, clinically insignificant effects on stool

Figure 3A. Algorithm for Self-Treatment of Diarrhea in Children 6 Months to 5 Years of Age

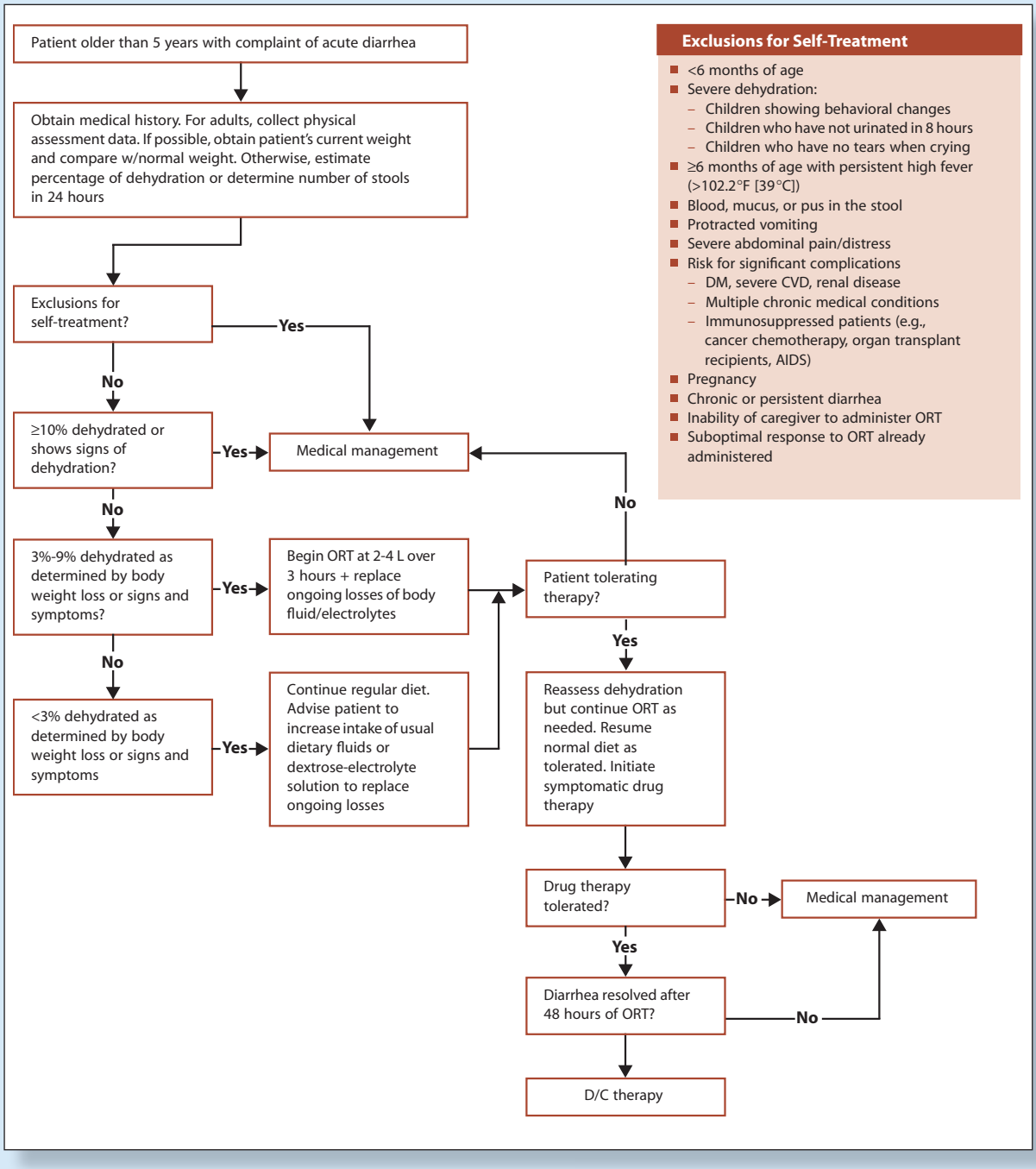


[a]Alternatively: <10 kg BW, give 60-120 mL ORT for each diarrheal stool or vomiting episode; ≥ 10 kg BW, give 120-240 mL ORT.

AIDS = acquired immunodeficiency syndrome; BW = body weight; CVD = cardiovascular disease; D/C = discontinue; DM = diabetes mellitus; ORT = oral rehydration therapy.

Source: Walker PC. Diarrhea. In: Berardi RR, Ferreri SP, Hume AL, et al. *Handbook of Nonprescription Drugs: An Interactive Approach to Self-Care*. 16th ed. Washington, DC: American Pharmacists Association; 2009:296.

Figure 3B. Algorithm for Self-Treatment of Diarrhea in Patients Older Than 5 Years of Age



AIDS = acquired immunodeficiency syndrome; CVD = cardiovascular disease; D/C = discontinue; DM = diabetes mellitus; ORT = oral rehydration therapy.

Source: Walker PC. Diarrhea. In: Berardi RR, Ferreri SP, Hume AL, et al. *Handbook of Nonprescription Drugs: An Interactive Approach to Self-Care.* 16th ed. Washington, DC: American Pharmacists Association; 2009:297.

Table 11. Nonhemorrhoidal Anorectal Disorders

Disorder	Etiology/Pathophysiology	Common Signs and Symptoms	Comments
Anal abscess	Obstruction of anal glands, resulting in painful swelling in perianal or anal canal; usually leads to bacterial infection	Fever, local swelling, redness, tenderness, and a continuously painful bulge in the rectal or gluteal regions	Usually identified on history and physical examination; possible life-threatening sepsis if not identified and treated promptly
Anal fistula (or groove)	Unhealed or incomplete drainage of anorectal abscess located between internal and external opening of fistula tract, and manifested as hollow fibrous area lined with granulation tissue	Chronic, persistent drainage; pain; possible bleeding on defecation	Surgical repair required
Anal fissure	Slit-like ulcer in anal canal within or around anal verge	Pain during and after defecation, lasting several minutes to several hours; if bleeding is present, blood is usually seen on toilet tissue	Underlying disorders: inflammatory bowel disease, tuberculosis, sexually transmitted infections, neoplasm, or human immunodeficiency virus/acquired immunodeficiency syndrome
Anal neoplasms	Any of a variety of histologic types classified as epidermoid carcinomas	Bleeding; changes in bowel habits, constipation, diarrhea, anal discharge, an internal or external mass, pain, pruritus, or rash; asymptomatic in about 25% of patients	Relatively uncommon, accounting for 1%–2% of all gastrointestinal malignancies; most are curable, but poor prognosis with anorectal melanomas (approx. 20% 5-year survival rate)
Polyps	Pedunculated growth that arises from gastrointestinal mucosa and extends into lumen of body cavity; usually found in colon but may also be present in anal canal	Bleeding	May be benign or malignant
Pruritus ani	Usually associated with primary underlying condition (e.g., anorectal or dermatologic disorder); other causes: diet (e.g., caffeinated or dairy products), lifestyle preferences (e.g., dyed or scented toilet paper or soaps, tight clothing), or medications (e.g., mineral oil, antibiotics)	Persistent itching in perianal region; more bothersome at bedtime or when patient is not preoccupied	Affects men more often than women

volume and duration of illness, but an unacceptably high risk of adverse effects including life-threatening ileus and toxic megacolon.

Loperamide is available in caplet, chewable tablet, and liquid formulations. The usual dosage for patients 12 years of age and older is 4 mg after the first loose bowel movement followed by 2 mg after each subsequent loose movement, to a maximum of 8 mg per day. The usual dosage for children 6 to 11 years of age is 2 mg after the first loose bowel movement followed by 1 mg after each subsequent loose movement, to a maximum of 6 mg per day in children who weigh 60 to 95 lb and 4 mg per day in children who weigh 48 to 59 lb. Duration of use should not exceed 48 hours.

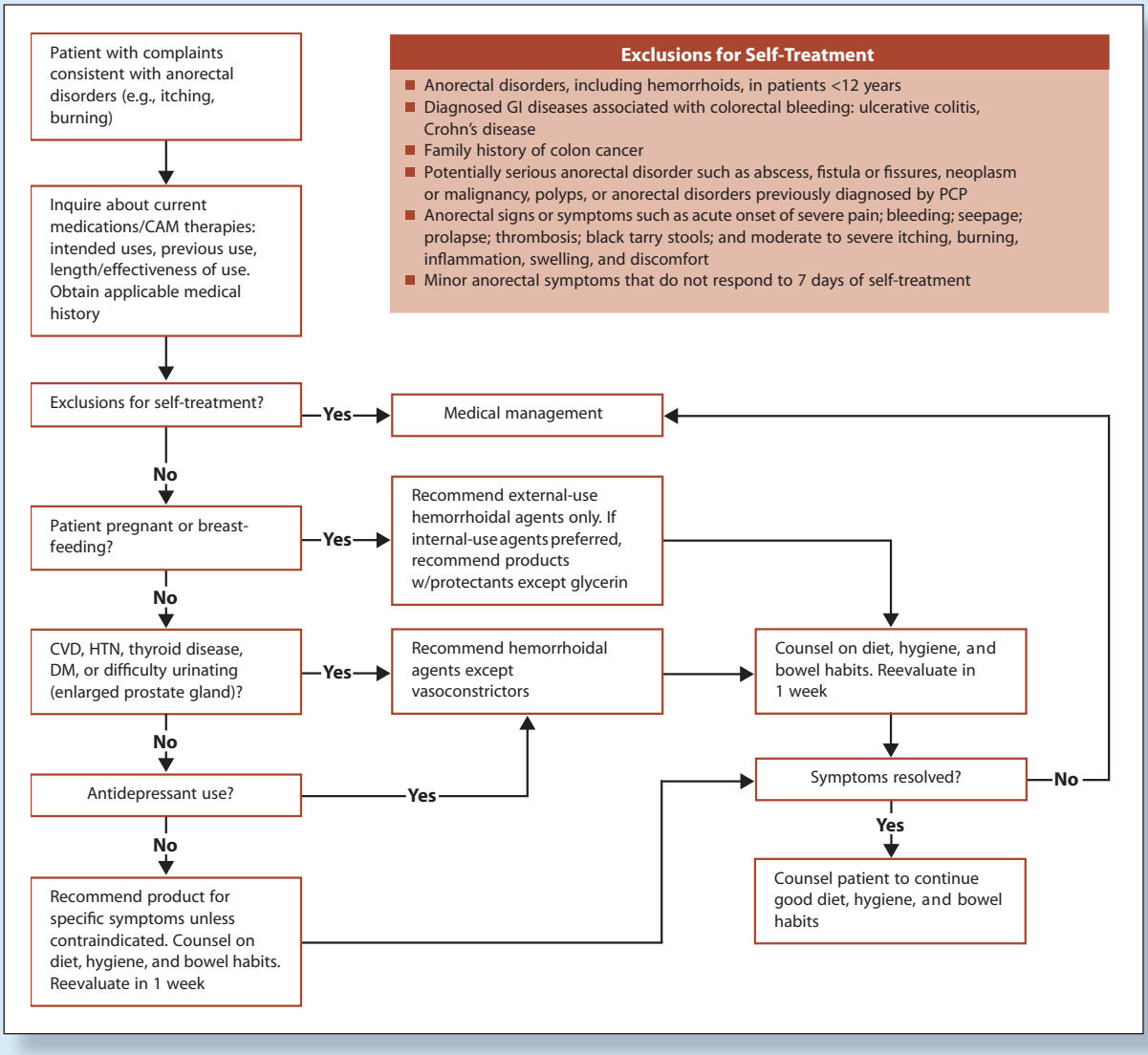
When used as directed, loperamide has few adverse effects other than occasional dizziness and constipation. Loperamide should not be used in patients with fecal leukocytes, high fever, or blood or mucus in the stool (dysentery). These signs suggest infection with invasive organisms or antibiotic-associated diarrhea.

Bismuth Subsalicylate. Bismuth subsalicylate reacts with hydrochloric acid in the stomach to form bismuth oxychloride and salicylic acid. Both moieties are pharmacologically active; each contributes to reducing the frequency of unformed stools, increasing stool consistency, and relieving symptoms of abdominal cramping.

Bismuth subsalicylate is approved for use in adults and children 12 years of age or older. Although products containing bismuth subsalicylate previously were labeled for use in children as young as 3 years of age, they are not recommended for use in young children, and the Drug Facts label no longer provides dosing information for children younger than 12 years of age.

Bismuth subsalicylate is available as tablets, chewable tablets, caplets, and liquid. The usual dosage is 524 mg taken every 30 to 60 minutes, to a maximum of eight doses per 24 hours. Duration of use for acute diar-

Figure 4. Algorithm for Self-Care of Hemorrhoids



CAM = complementary and alternative medicine; CVD = cardiovascular disease; DM = diabetes mellitus; GI = gastrointestinal; HTN = hypertension; PCP = primary care provider.
Source: Chan J, Berardi RR. Anorectal disorders. In: Berardi RR, Ferreri SP, Hume AL, et al. *Handbook of Nonprescription Drugs: An Interactive Approach to Self-Care.* 16th ed. Washington, DC: American Pharmacists Association; 2009:313.

rhea should not exceed 48 hours.

Bismuth salts react with hydrogen sulfide produced by bacteria in the mouth and colon; the resulting compound, bismuth sulfide, has a black color. Consequently, use of bismuth subsalicylate can cause a temporary and harmless darkening of the tongue or stool, which can be alarming to patients who are not advised of this effect beforehand.

Bismuth products contain various amounts of salicylate. If a patient takes aspirin or other salicylates simultaneously, toxic salicylate levels could be reached even if the patient follows all dosing directions closely. Mild tinnitus is a dose-related adverse effect that could be a sign of moderate to severe salicylate toxicity. As with all salicylates, bismuth subsalicylate should not be administered to children or adolescents who have or are recovering from chickenpox or flu because of the risk of Reye syndrome. Overdosage of bismuth products has caused neurotoxicity.

Bismuth subsalicylate may interact adversely with a number of other drugs, including:

- Warfarin and valproic acid—increased toxicity because of decreased plasma protein binding.
- Methotrexate—increased toxicity because of decreased plasma protein binding and decreased renal clearance.
- Probenecid—decreased uricosuric effect.
- Tetracycline and quinolone antibiotics—decreased absorption because of complex formation.

Patients who are using bismuth subsalicylate to treat traveler's diarrhea

Points to Remember

- Most cases of acute diarrhea are caused by infectious agents, especially viruses. Acute diarrhea usually resolves within a few days but may persist for up to 14 days. Only patients with mild to moderate acute diarrhea are appropriate candidates for self-treatment. All patients with persistent or chronic diarrhea should be referred to a primary care provider.
- The major complications of diarrheal illness are dehydration, and fluid and electrolyte imbalances. Otherwise healthy patients who do not show signs of dehydration should maintain normal hydration and replace fluids and electrolytes lost through stool. Patients who show signs of mild to moderate dehydration or who are at increased risk of dehydration (e.g., children, older patients, immunocompromised patients) should receive rapid rehydration therapy with oral rehydration solutions, followed by replacement of ongoing losses.
- Most forms of acute diarrhea are not helped by fasting; conversely, fasting may increase patient morbidity. No special diet is recommended, although patients should refrain from ingesting fatty or spicy foods, foods high in simple sugars, and caffeine-containing beverages.
- Nonprescription antidiarrheal agents can reduce stool frequency and stool weight as well as reduce coexisting symptoms such as abdominal cramps. Concerns about slowing the clearance of pathogens from the intestine are largely unsubstantiated. Loperamide is considered to be a safe and effective choice for the symptomatic relief of acute diarrhea in patients as young as 6 years of age. Bismuth subsalicylate is an alternative for adults and children 12 years of age or older.
- Patients should be educated about measures for preventing diarrhea, including thorough hand washing; proper handling, preparation, and storage of food; and precautions to take when traveling to high-risk areas.

should discontinue use if therapy with ciprofloxacin is initiated.

Follow-Up

Pharmacists should plan to follow up with patients after 48 hours of self-treatment. If a patient's diarrhea continues beyond 48 hours—or if the patient develops a high fever, bloody or mucoid stools, signs of worsening dehydration, or any other signs of worsening illness—the patient should be referred to a primary care provider for further evaluation.

ANORECTAL DISORDERS

Anorectal disorders involve the perianal area, the anal canal, and the lower portion of the rectum. Symptoms consistent with minor anorectal disorders include:

- Burning
- Discomfort
- Inflammation
- Irritation
- Itching
- Swelling

Many of these signs and symptoms are caused by hemorrhoids, and most can be self-treated successfully. Pain, bleeding, seepage, change in bowel patterns, prolapse, and thrombosis may signal the presence of more serious conditions that require medical management.

Hemorrhoids

Hemorrhoids are abnormally large, bulging, symptomatic conglomerates of hemorrhoidal vessels, supporting tissues, and overlying mucous membranes or skin in the anorectal region. Many factors have been implicated in the etiology of hemorrhoids. The most widely accepted pathophysiologic theory is that vascular cushions are part of the normal anatomy and are located around the circumference of the anal canal, above the dentate line. (The dentate line marks the transition from the top of the anal canal, which is lined with columnar epithelium like the rectum, to the lower portion of the anal canal, which is lined with squamous epithelium that is structurally similar to the skin covering other parts of the body.) The vascular cushions contain blood vessels, smooth muscle, and supportive connective tissue; they are subjected to downward pressure during defecation. The muscle fibers supporting the vascular cushions become weakened with increasing age, and the vascular cushions slide, become congested, bleed, and eventually protrude into the lower anal canal.

Internal hemorrhoids are graded using a degree system:

- First-degree hemorrhoids are enlarged but do not prolapse into the anal canal.
- Second-degree hemorrhoids protrude into the anal canal during defecation but return spontaneously to their normal position.
- Third-degree hemorrhoids protrude into the anal canal during defecation but can be returned manually into the anus.
- Fourth-degree hemorrhoids are prolapsed permanently.

External hemorrhoids develop below the dentate line. They are covered with squamous epithelium and have sensory fibers. External hemorrhoids are frequently visible as bluish lumps at the external or distal boundary of the anal canal. The blue color may be caused by thrombosed blood vessels in the complex. Symptoms of thrombosed external hemorrhoids range from minimal discomfort to severe pain.

Exclusions for Self-Care

Although hemorrhoids are the most common anorectal problem, a number of other serious disorders may present with similar symptoms. These disorders, which are described in Table 11, are not amenable to self-treatment.

Other exclusions to the self-treatment of anorectal symptoms are listed in Figure 4.

Self-Treatment Strategies

The goals of treatment for patients with minor anorectal symptoms such as burning, itching, irritation, discomfort, and swelling are to (1) alleviate and maintain remission of anorectal symptoms and (2) prevent complications that lead to adverse consequences. The appropriate self-care of hemorrhoidal complaints is depicted in Figure 4.

Nonpharmacologic Measures

Patients should be advised to maintain a well-balanced diet—preferably high in fiber and bulk—and good perianal hygiene. Fiber softens the stool and may prevent further irritation or formation of small symptomatic hemorrhoids. (See the section on CONSTIPATION for more information about fiber supplementation.)

Proper bowel habits should be encouraged. Patients should avoid sitting on the toilet longer than 10 minutes to reduce straining and decrease pressure on hemorrhoidal vessels. Avoiding the urge to defecate may lead to constipation and the formation of hemorrhoids.

Good perianal hygiene may help to relieve symptoms and prevent the recurrence of itching. Patients should clean the anorectal area regularly and after each bowel movement with a mild, unscented soap and water or, more practically, by using commercially available hygienic and lubricated wipes or pads. Avoiding excessive scrubbing of the anorectal area may minimize aggravation to this sensitive region.

A sitz bath (also called a hip bath) is a type of bath in which only the hips and buttocks are soaked in water or saline solution. Sitz baths promote good hygiene and often relieve hemorrhoidal symptoms, especially after bowel movements. When possible, the patient should sit in warm water (110°F to 115°F [43.3°C to 46.1°C]) two to three times a day for about 15 minutes. Plastic sitz tubs that fit over the toilet rim are convenient, easily cleaned, and readily available at pharmacies and medical supply vendors.

In addition, patients diagnosed with or suspected of having hemorrhoids should be advised to avoid lifting heavy objects and minimize the consumption of foods and beverages (e.g., caffeinated beverages) that may irritate or aggravate symptoms. NSAIDs or aspirin may promote bleeding and should be avoided to the extent possible.

Pharmacologic Therapy

The nonprescription pharmacologic agents used to relieve anorectal symptoms include local anesthetics, vasoconstrictors, protectants, astringents, keratolytics, analgesics/anesthetics/antipruritics, and corticosteroids. Only certain astringents, protectants, and vasoconstrictors may be used for internal hemorrhoids.

Table 12. Patient Instructions for Applying Anorectal Products

- Cleanse the affected area after bowel movement with a mild, nonmedicated, unscented soap and warm water; rinse thoroughly.
- If applying products that contain aluminum hydroxide gel or kaolin, clean the anorectal area prior to application, taking care to remove any previously used petrolatum-containing or greasy ointment.
- Gently dry the area by patting or blotting with unscented, uncolored toilet tissue or a soft cloth prior to product application.
- When using an anorectal product externally, apply the ointment as a thin covering to the perianal area and the anal canal.
- When inserting an anorectal product intrarectally, insert the ointment using an intrarectal applicator or a finger.
  - Intrarectal applicators are preferred to digital application because using the applicator enables the drug product to be applied to the rectal mucosa, which cannot be reached by using a finger.
  - Intrarectal applicators should have lateral openings, as well as a hole in the tip, to facilitate application and coverage of the rectal mucosa.
  - Intrarectal applicators should be lubricated before insertion by spreading ointment around the applicator tip.
- Do not use a product with an applicator if the introduction of the applicator into the rectum causes additional pain.
- Do not exceed the recommended daily dosage unless directed to do so by a primary care provider.

General instructions for applying these products are summarized in TABLE 12. The frequency of application varies by product; thus, patients should be encouraged to read the Drug Facts label carefully and not to exceed the recommended maximum frequency. Patients who fail to obtain the desired relief after 7 days of self-treatment should consult a primary care provider.

Local Anesthetics. Local anesthetics temporarily relieve itching, irritation, burning, discomfort, and pain by reversibly blocking the transmission of nerve impulses. Agents approved for use in anorectal preparations are benzocaine, benzyl alcohol, dibucaine, dyclonine, lidocaine, pramoxine, and tetracaine. Local anesthetics should be used with caution because they have the potential to mask the pain associated with a more severe anorectal disorder and delay appropriate intervention. Use of these products should be limited to the perianal region or the lower anal canal because the rectum is not innervated with sensory nerve fibers. Local anesthetics also can produce allergic reactions.

Vasoconstrictors. Vasoconstrictors stimulate α-adrenergic receptors in vascular beds, an action that promotes constriction of arterioles and produces a modest, transient reduction in swelling. These agents relieve itching, discomfort, and irritation when used topically in the anal region—effects attributable at least partially to a slight anesthetic effect of undetermined mechanism. Vasoconstrictors should not be used to control anorectal bleeding.

Ephedrine sulfate, epinephrine hydrochloride, epinephrine base, and phenylephrine hydrochloride are approved for external use. Ephedrine sulfate and phenylephrine hydrochloride also may be used for internal hemorrhoids.

Vasocontrictors may cause contact dermatitis. They are absorbed readily from mucous membranes and may produce nervousness, tremor, sleeplessness, nausea, and loss of appetite. Prolonged use may lead to rebound vasodilation, anxiety, and (rarely) paranoia. Serious adverse ef-

Table 13. Protectants for Anorectal Use

- Aluminum hydroxide gel
- Calamine
- Cocoa butter
- Cod liver oil
- Glycerin
- Hard fat
- Kaolin
- Lanolin
- Mineral oil
- Petrolatum and white petrolatum
- Shark liver oil
- Topical starch
- Zinc oxide

fects such as elevation of blood pressure, aggravation of hyperthyroidism, cardiac arrhythmias, and irregular heart rate are less likely.

Rectally administered vasoconstrictors may attenuate the effects of antihypertensive agents and increase blood pressure. Alternatively, the hypertensive effects of vasoconstrictors may be potentiated by monoamine oxidase inhibitors and tricyclic antidepressants. Concomitant use may lead to serious and even lethal outcomes including cerebral hemorrhage or stroke. Patients with diabetes, thyroid disease, hypertension, angina pectoris, or an enlarged prostate and those taking antidepressants, antihypertensive agents, or cardiac medications should not use hemorrhoidal agents with vasoconstrictors without first consulting their primary care provider.

Protectants. The protectant drug class includes absorbents, adsorbents, demulcents, and emollients (Table 13). These agents form a physical barrier on the skin that prevents irritation of the anorectal area. They also decrease water loss from the stratum corneum, which helps to soften the dry anal area. Protectants are approved for the temporary relief of discomfort, itching, irritation, and burning associated with internal and external hemorrhoids (glycerin is approved for external use only). Products that contain aluminum hydroxide or kaolin also are approved for the temporary relief of anorectal itching.

Systemic absorption of protectants is minimal; therefore, adverse reactions to these agents as a class are uncommon. Preparations containing aluminum hydroxide gel and kaolin are required to contain a warning stating that petrolatum or greasy ointments should be removed before applying these agents. This warning appears because greasy substances interfere with the ability of aluminum hydroxide gel and kaolin to adhere properly to the skin.

Astringents. Calamine, witch hazel, and zinc oxide are used as astringents in anorectal preparations. They are approved for the temporary relief of itching, irritation, and burning symptoms associated with anorectal disorders. Astringents act by coagulating the protein in skin cells, thereby protecting the underlying tissue while decreasing cell volume. They also cause contracting, wrinkling, and blanching of the affected area and decrease secretions, which makes the region drier.

Calamine and zinc oxide are approved for both internal and external use. Witch hazel is approved for external use only.

Adverse effects are uncommon with the topical use of calamine, zinc oxide, or witch hazel. Witch hazel may cause a slight stinging sensation when applied because of the alcohol used to prepare the compound; volatile oil in witch hazel can cause contact dermatitis. Systemic zinc toxicity (e.g., nausea, vomiting, lethargy, severe pain) may develop if calamine or zinc oxide is used for a prolonged period of time, especially for internal anorectal disorders.

Keratolytics. The keratolytic agents alcloxa and resorcinol are somewhat useful in reducing external anorectal itching and discomfort, although the exact mechanism of action is unknown. They are known to cause desquamation and debridement, or sloughing, of epidermal surface cells. Because mucous membranes do not contain a keratin layer, intrarectal use of keratolytics is not justified and may be harmful.

If resorcinol is absorbed, possible adverse effects range from ringing in the ears, increased pulse rate, sweating, and shortness of breath to potentially serious problems such as methemoglobinemia, circulatory collapse, unconsciousness, and convulsions. Products containing resorcinol carry a warning against use on open wounds near the anus, to minimize resorcinol absorption through abraded mucosal lining and decrease the potential for systemic toxicity.

Local Analgesics/Anesthetics/Antipruritics. The local analgesics/anesthetics/antipruritics previously were classified as counterirritants. The agents in this class suitable for anorectal use—camphor, juniper tar, and menthol—produce a local cooling sensation that distracts from complaints of pain, itching, burning, or discomfort. They should not be used internally because the rectum has no identifiable nerve fibers.

Points to Remember

- Anorectal itching, discomfort, irritation, burning, inflammation, and swelling generally are considered to indicate minor disorders amenable to self-treatment. The treatment of patients with pain, bleeding, seepage, recent change in bowel patterns, prolapse, or thrombosis should be managed by a primary care provider.
- Mild anorectal symptoms, usually associated with hemorrhoids, can be managed with nonpharmacologic measures, pharmacologic therapy, or a combination of these approaches. Nonpharmacologic measures include a high-fiber diet, good toileting practices and anal hygiene, and occasional use of sitz baths.
- Pharmacologic therapy encompasses local anesthetics, vasoconstrictors, protectants, astringents, keratolytics, analgesics/anesthetics/antipruritics, and corticosteroids. Products containing approved ingredients in appropriate dosages appear to be therapeutically similar when used to treat indicated anorectal signs and symptoms. Patients who need to use these products for more than 7 days should be evaluated by a primary care provider.

CASE 3. HEMORRHOIDS

A 44-year-old man describes a recent history of painful bowel movements accompanied by small amounts of blood on the toilet tissue. Upon further questioning, he expresses concern because his father had colon cancer. "It's hemorrhoids, right?" he asks. "I mean, I would know if it were a serious problem, wouldn't I?"

Which of the following responses is most appropriate?

a. Reassure the patient that his symptoms most likely are related to hemorrhoids and recommend a topical product.
b. Without alarming the patient unduly, convince him of the need for a diagnostic work-up.

Case study responses appear on page 26.

Extensive application of menthol to the torso has caused laryngospasm, dyspnea, and cyanosis. Thus, it is important to use anorectal preparations with this ingredient sparingly.

Corticosteroids. Topical hydrocortisone—the only topical corticosteroid contained in nonprescription anorectal products (at a maximum concentration of 1%)—acts as a vasoconstrictor and antipruritic. It has a relatively slow onset of action (up to 12 hours) but a longer duration of action than most other agents.

Hydrocortisone may mask the symptoms of bacterial and fungal infections.

Combination Products. Many nonprescription anorectal products contain various combinations of the pharmacologic agents discussed in this section. Although combination products are a reasonable option for treating anorectal disorders, there is no evidence that they are more effective than preparations containing a therapeutic amount of a single ingredient.

Product Selection Considerations

Product selection for anorectal disorders is based largely on the suitability of the active ingredient or ingredients for the patient's symptoms as well as patient preference for a specific dosage form. It may be necessary for patients to use more than one product (or a combination product) if they have multiple symptoms that cannot be treated adequately with a single product.

Products for external use are available as creams, ointments, gels, pastes, liquids, and foams. These dosage forms do not appear to have important clinical differences. Foam products theoretically should provide more rapid release of active ingredients than ointments, but they usually are more expensive. In addition, the foam may not remain in the affected area, and variations in the size of the foam bubbles may result in different concentrations of the active ingredient.

Suppositories for internal use provide a lubricating effect, which may ease straining at defecation, thereby easing or alleviating hemorrhoidal symptoms. However, suppositories should not be recommended as an initial dosage form when treating anorectal disorders, because they may leave the affected anal region and ascend into the rectum and lower colon when the patient is in a prone position (lying with the face downward). If the patient remains prone after inserting a suppository or an ointment, the active ingredients may not distribute evenly over the anal mucosa. Also, suppositories are relatively slow acting because they must melt to release the active ingredients.

Follow-Up

Pharmacists should plan to follow up with patients who are self-treating anorectal disorders after 7 days. If the patient's symptoms resolve, the patient should be encouraged to maintain a well-balanced diet, good personal hygiene, and good bowel habits. If symptoms persist beyond 7 days—or if alarm signs or symptoms such as blood in the stool or severe anal pain develop—the patient should be counseled to seek immediate medical attention.

CASE STUDY RESPONSES

Case 1. Heartburn

a. Tell the patient that she should undergo a diagnostic work-up and most likely needs to be treated with a prescription medication.
Incorrect. This patient is an appropriate candidate for self-treatment because her symptoms are consistent with frequent heartburn (2 or more days per week), and she does not exhibit any contraindications to self-treatment.

b. Recommend that she try a 14-day course of therapy with a nonprescription PPI.
Correct. This patient's symptoms are consistent with frequent heartburn (2 or more days per week), and she does not exhibit any contraindications to self-treatment.

c. Encourage her to try taking antacids instead of the nonprescription H_2 antagonist.
Incorrect. This patient's symptoms are consistent with frequent heartburn, so antacids are not the best or most convenient treatment option.

d. Recommend that she take double the recommended dose of the nonprescription H_2 antagonist, twice daily, for a 2-week period.
Incorrect. Although this may be a viable strategy, this patient is most likely to obtain symptomatic relief from a PPI. It also is possible that she developed tolerance to the H_2 antagonist if she had been taking it frequently.

Case 2. Constipation

a. The patient should discontinue use of this product and focus on adding more fiber to her diet.
Incorrect. Although she probably should discontinue use of this product and might need to add more fiber to her diet, this patient should be referred to her primary care provider.

b. She most likely has developed tolerance to the effect of the stimulant laxative in this product. She should stop using the product for 1 week, and then start taking it again.
Incorrect. This patient should discontinue use of the product and consult her primary care provider.

c. Because of the duration of this patient's constipation and her recent daily use of laxatives (exceeding 1 week), she should undergo a diagnostic work-up.
Correct. This patient should be referred to a primary care provider.

Case 3. Hemorrhoids

a. Reassure the patient that his symptoms most likely are related to hemorrhoids and recommend a topical product.
Incorrect. Although there is a strong possibility that this patient's symptoms are caused by hemorrhoids, the presence of blood and a family history of colorectal cancer point to the need for a diagnostic work-up.

b. Without alarming the patient unduly, convince him of the need for a diagnostic work-up.
Correct. The presence of blood and a family history of colorectal cancer point to the need for referral to a primary care provider to rule out more serious conditions.

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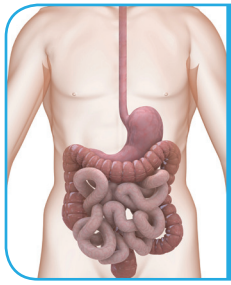

CPE EXAM

Instructions: The assessment questions printed below allow you to preview the online CPE exam. Please review all of your answers to be sure you have marked the proper letter on the online CPE exam. There is only one correct answer to each question.

1. A 72-year-old man complains of a 2-month history of heartburn. He experiences these symptoms once or twice a week, usually when he lies down after lunch to take his afternoon nap. He has tried using antacids to relieve his symptoms, but he finds that the symptoms return relatively quickly. He wants to obtain more long-lasting relief and asks for your recommendations. What advice would be appropriate for this patient?
   a. Advise him to refrain from lying down for at least 3 hours after eating.
   b. Encourage him to avoid or limit consumption of foods that might be contributing to his symptoms.
   c. Recommend that he try using a nonprescription H_2 antagonist, either before lunch (if the symptoms are predictable) or after lunch (perhaps in combination with an antacid).
   d. Any of the recommendations listed above would be appropriate.

2. For self-treatment purposes, frequent heartburn is defined as heartburn that:
   a. Occurs predictably, after eating certain foods or engaging in exercise.
   b. Occurs 2 or more days per week.
   c. Persists for 3 months or longer.
   d. All of these responses are characteristics of frequent heartburn.

3. The medications that provoke dyspepsia in as many as 20% to 25% of patients are:
   a. Antibiotics.
   b. Aspirin and other NSAIDs.
   c. Narcotics.
   d. Potassium supplements.

4. Which of the following lifestyle modifications might be helpful in a patient who complains of heartburn?
   a. Drinking carbonated beverages.
   b. Eating larger meals.
   c. Wearing loose-fitting clothing.
   d. None of the above.

5. Product labeling for antacids and nonprescription H_2 antagonists recommends a maximum length of therapy of:
   a. 1 week.
   b. 2 weeks.
   c. 3 weeks.
   d. 4 weeks.

6. An advantage of antacids compared with H_2 antagonists is:
   a. Rapid onset of action.
   b. Long duration of action.
   c. Once-daily dosing.
   d. All of the above.

7. An advantage of H_2 antagonists compared with antacids is:
   a. Rapid onset of action.
   b. Long duration of action.
   c. Once-daily dosing.
   d. All of the above.

8. Which of the following statements about PPIs is true?
   a. PPIs offer the convenience of once-daily administration.
   b. PPIs are the only nonprescription option for the treatment of frequent heartburn.
   c. PPIs are not intended to be used for the immediate relief of heartburn symptoms.
   d. All of these statements are true.

9. The proper dosage regimen for nonprescription PPIs is:
   a. One tablet as needed to relieve heartburn symptoms, not to exceed 14 continuous days of use.
   b. One tablet daily at bedtime for 7 days, not to exceed eight courses of therapy per year.
   c. One tablet daily with dinner for 14 days, not to exceed one course of therapy per year.
   d. One tablet daily before breakfast for 14 days, not to exceed four courses of therapy per year.

10. The normal frequency of bowel movements in adults ranges from:
    a. Once per day to three times per day.
    b. Once per day to once per week.
    c. Three times per day to three times per week.
    d. Only daily bowel movements are considered to be normal.

11. Which of the following categories of medications is identified in this monograph as a possible cause of constipation?
    a. Antacids containing magnesium.
    b. Antihistamines.
    c. Antimicrobial agents.
    d. Antineoplastic agents.

12. Adult patients with constipation should be encouraged to increase their daily intake of fiber to:
    a. 10–15 g per day.
    b. 15–25 g per day.
    c. 20–35 g per day.
    d. >35 g per day.

13. Examples of newer fiber supplements (classified as dietary supplements, not bulk-forming laxatives) include all of the following *except:*
    a. Inulin.
    b. Polycarbophil.
    c. Powdered cellulose.
    d. Wheat dextrin.

14. When patients use a nonprescription laxative medication to treat constipation, the total length of treatment should not exceed:
    a. 1 week.
    b. 2 weeks.
    c. 3 weeks.
    d. 4 weeks.

15. Which of the following saline laxatives is considered to be safe for occasional use in otherwise healthy patients with mild constipation?
    a. Magnesium citrate oral solution.
    b. Milk of magnesia.
    c. Sodium phosphate oral solution.
    d. All of the above.

16. According to the self-treatment algorithm depicted in Figure 2, which of the nonprescription laxatives listed below should be considered first for the treatment of simple or acute constipation?
    a. Bisacodyl.
    b. Milk of magnesia.
    c. PEG 3350.
    d. Senna.

17. Which type of laxatives exhibit the *least* physiologic mechanism of action?
    a. Emollient laxatives.
    b. Hyperosmotic laxatives.
    c. Saline laxatives.
    d. Stimulant laxatives.

18. Most cases of acute diarrhea in the United States are caused by:
    a. Antimicrobial therapy.
    b. Food intolerances.
    c. Infectious agents.
    d. Irritable bowel syndrome.

19. An adult patient with diarrhea should *not* attempt self-treatment if he or she exhibits which of the following symptoms?
    a. Fever of 99°F (37.2°C).
    b. Increased thirst.
    c. Severe abdominal pain.
    d. Three or more unformed stools per day.

20. When patients use a nonprescription antidiarrheal medication to treat acute diarrhea, the total length of treatment should not exceed:
    a. 24 hours.
    b. 48 hours.
    c. 1 week.
    d. 2 weeks.

21. Which of the following products can be used to prevent traveler's diarrhea?
    a. Loperamide.
    b. Bismuth subsalicylate.
    c. Kaolin.
    d. Lactobacillus.

Questions 22 and 23 pertain to the following case:

A 58-year-old woman presents to the pharmacy with a chief complaint of diarrhea of 1 day's duration (three to four loose stools). She says that she feels "a little weak" but reports no fever or other symptoms. The patient's medical history includes hypertension, which is well controlled with medication, and osteoarthritis. Her current medications include:

- Lisinopril 20 mg daily.
- Hydrochlorothiazide 25 mg daily.
- Etodolac 400 mg twice daily

She also notes occasional use of diphenhydramine as a sleep aid and Correctol tablets (bisacodyl 5 mg) for constipation. She denies overuse of the latter and suspects that her diarrhea "may have been picked up at church yesterday." She attended a picnic luncheon after the late service, and several other women who ate the meal also developed diarrhea.

22. Which of the following actions is most appropriate in this case?
    a. No action should be taken. The patient most likely is suffering from food poisoning, and any attempts to stop the diarrhea could prolong the course of illness.
    b. Recommend treatment with an oral rehydration solution and loperamide for up to 48 hours.
    c. Tell the patient to stop taking the etodolac and contact the prescriber to discuss a suitable alternative.
    d. Inform the patient of the need to undergo a diagnostic work-up.

23. If the woman had complained of diarrhea of 3 days' duration, accompanied by fever and severe abdominal pain, which of the following actions would be most appropriate?
    a. No action should be taken. The patient most likely is suffering from food poisoning, and any attempts to stop the diarrhea could prolong the course of illness.
    b. Recommend treatment with an oral rehydration solution and loperamide for up to 48 hours.
    c. Tell the patient to stop taking the etodolac and contact the prescriber to discuss a suitable alternative.
    d. Inform the patient of the need to undergo a diagnostic work-up.

24. Which of the following types of pharmacologic agents may be used for internal hemorrhoids?
    a. Analgesics.
    b. Keratolytics.
    c. Local anesthetics.
    d. Protectants.

25. When patients use a nonprescription product to treat an anorectal disorder, the total length of treatment should not exceed:
    a. 1 week.
    b. 2 weeks.
    c. 3 weeks.
    d. 4 weeks.

CPE INSTRUCTIONS

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