(NSAIDs) develop ulcers. As with idiopathic gastroparesis, some cases of functional dyspepsia result from prior infection.

Ulcer Disease In most GERD patients, there is no destruction of the esophagus. However, 5% develop esophageal ulcers, and some form strictures. Symptoms cannot distinguish nonerosive from erosive or ulcerative esophagitis. A minority of cases of dyspepsia stem from gastric or duodenal ulcers. The most common causes of ulcer disease are *H. pylori* infection and use of NSAIDs. Other rare causes of gastroduodenal ulcers include Crohn's disease (Chap. 351) and Zollinger-Ellison syndrome (Chap. 348), resulting from gastrin overproduction by an endocrine tumor.

Malignancy Dyspeptic patients often seek care because of fear of cancer, but few cases result from malignancy. Esophageal squamous cell carcinoma occurs most often with long-standing tobacco or ethanol intake. Other risks include prior caustic ingestion, achalasia, and the hereditary disorder tylosis. Esophageal adenocarcinoma usually complicates prolonged acid reflux. Eight to 20% of GERD patients exhibit esophageal intestinal metaplasia, termed *Barrett's metaplasia,* a condition that predisposes to esophageal adenocarcinoma (Chap. 109). Gastric malignancies include adenocarcinoma, which is prevalent in certain Asian societies, and lymphoma.

Other Causes Opportunistic fungal or viral esophageal infections may produce heartburn but more often cause odynophagia. Other causes of esophageal inflammation include eosinophilic esophagitis and pill esophagitis. Biliary colic is in the differential diagnosis of unexplained upper abdominal pain, but most patients with biliary colic report discrete acute episodes of right upper quadrant or epigastric pain rather than the chronic burning, discomfort, and fullness of dyspepsia. Twenty percent of patients with gastroparesis report a predominance of pain or discomfort rather than nausea and vomiting. Intestinal lactase deficiency as a cause of gas, bloating, and discomfort occurs in 15–25% of whites of northern European descent but is more common in blacks and Asians. Intolerance of other carbohydrates (e.g., fructose, sorbitol) produces similar symptoms. Small-intestinal bacterial overgrowth may cause dyspepsia, often associated with bowel dysfunction, distention, and malabsorption. Eosinophilic infiltration of the duodenal mucosa is described in some dyspeptics, particularly with postprandial distress syndrome. Celiac disease, pancreatic disease (chronic pancreatitis, malignancy), hepatocellular carcinoma, Ménétrier's disease, infiltrative diseases (sarcoidosis, eosinophilic gastroenteritis), mesenteric ischemia, thyroid and parathyroid disease, and abdominal wall strain cause dyspepsia. Gluten sensitivity in the absence of celiac disease is reported to evoke unexplained upper abdominal symptoms. Extraperitoneal etiologies of indigestion include congestive heart failure and tuberculosis.

APPROACH TO THE PATIENT: **Indigestion**

HISTORY AND PHYSICAL EXAMINATION

Care of the indigestion patient requires a thorough interview. GERD classically produces heartburn, a substernal warmth that moves toward the neck. Heartburn often is exacerbated by meals and may awaken the patient. Associated symptoms include regurgitation of acid or nonacidic fluid and water brash, the reflex release of salty salivary secretions into the mouth. Atypical symptoms include pharyngitis, asthma, cough, bronchitis, hoarseness, and chest pain that mimics angina. Some patients with acid reflux on esophageal pH testing do not report heartburn, but note abdominal pain or other symptoms.

Dyspeptic patients typically report symptoms referable to the upper abdomen that may be meal-related, as with postprandial distress syndrome, or independent of food ingestion, as in epigastric pain syndrome. Functional dyspepsia overlaps with other disorders including GERD, IBS, and idiopathic gastroparesis.

TABLE 54-3 ALARM SYMPTOMS IN GASTROESOPHAGEAL REFLUX DISEASE

Odynophagia
Unexplained weight loss
Recurrent vomiting
Occult or gross gastrointestinal bleeding
Jaundice
Palpable mass or adenopathy
Family history of gastrointestinal malignancy

The physical exam with GERD and functional dyspepsia usually is normal. In atypical GERD, pharyngeal erythema and wheezing may be noted. Recurrent acid regurgitation may cause poor dentition. Dyspeptics may exhibit epigastric tenderness or distention.

Discriminating functional and organic causes of indigestion mandates excluding certain historic and exam features. Odynophagia suggests esophageal infection. Dysphagia is concerning for a benign or malignant esophageal blockage. Other alarm features include unexplained weight loss, recurrent vomiting, occult or gross bleeding, jaundice, palpable mass or adenopathy, and a family history of gastrointestinal neoplasm.

DIAGNOSTIC TESTING

Because indigestion is prevalent and most cases result from GERD or functional dyspepsia, a general principle is to perform only limited and directed diagnostic testing of selected individuals.

Once alarm factors are excluded (Table 54-3), patients with typical GERD do not need further evaluation and are treated empirically. Upper endoscopy is indicated to exclude mucosal injury in cases with atypical symptoms, symptoms unresponsive to acid suppression, or alarm factors. For heartburn >5 years in duration, especially in patients >50 years old, endoscopy is advocated to screen for Barrett's metaplasia. The benefits and cost-effectiveness of this approach have not been validated in controlled studies. Ambulatory esophageal pH testing using a catheter method or a wireless capsule endoscopically attached to the esophageal wall is considered for drug-refractory symptoms and atypical symptoms like unexplained chest pain. High-resolution esophageal manometry is ordered when surgical treatment of GERD is considered. A low LES pressure predicts failure of drug therapy and provides a rationale to proceed to surgery. Poor esophageal body peristalsis raises concern about postoperative dysphagia and directs the choice of surgical technique. Nonacidic reflux may be detected by combined esophageal impedance-pH testing in medication-unresponsive patients.

Upper endoscopy is recommended as the initial test in patients with unexplained dyspepsia who are >55 years old or who have alarm factors because of the purported elevated risks of malignancy and ulcer in these groups. However, endoscopic findings in unexplained dyspepsia include erosive esophagitis in 13%, peptic ulcer in 8%, and gastric or esophageal malignancy in only 0.3%. Management of patients <55 years old without alarm factors depends on the local prevalence of *H. pylori* infection. In regions with low *H. pylori* prevalence (<10%), a 4-week trial of an acid-suppressing medication such as a proton pump inhibitor (PPI) is recommended. If this fails, a "test and treat" approach is most commonly applied. *H. pylori* status is determined with urea breath testing, stool antigen measurement, or blood serology testing. Those who are *H. pylori* positive are given therapy to eradicate the infection. If symptoms resolve on either regimen, no further intervention is required. For patients in areas with high *H. pylori* prevalence (>10%), an initial test and treat approach is advocated, with a subsequent trial of an acid-suppressing regimen offered for those in whom *H. pylori* treatment fails or for those who are negative for the infection. In each of these patient subsets, upper endoscopy is reserved for those whose symptoms fail to respond to therapy.

Further testing is indicated in some settings. If bleeding is noted, a blood count can exclude anemia. Thyroid chemistries or calcium levels screen for metabolic disease, whereas specific serologies may