



*Lymphocytic gastritis* is characterized by a mononuclear infiltration of T cells, usually antral predominant, and is often associated with celiac disease, collagenous and lymphocytic colitis, and Ménétrier disease. *Eosinophilic gastritis* is characterized by an eosinophilic infiltration of the stomach, especially the antrum. All layers of the gastric wall may be affected, but selective predominance of eosinophilic infiltrates may be found in the submucosa, muscle layers, or subserosa, making biopsy diagnosis difficult. Clinical manifestations include delayed gastric emptying or manifestations of anemia from chronic blood loss caused by associated mucosal ulceration. Corticosteroids are used to control symptoms.

*Ménétrier disease* is a rare disease characterized by giant gastric folds in the fundus and the body of the stomach. Histologically, increased mucosal thickness, glandular atrophy, and an increase in the size of the gastric pits are characteristic findings. Hypochlorhydria and hypoalbuminemia are commonly seen. In children, Ménétrier disease is thought to be caused by cytomegalovirus (CMV), whereas overexpression of a tissue growth factor has been implicated in the adult form of the disease.

In addition to *H. pylori*, a variety of infectious pathogens may involve the stomach. Gastric infections are typically seen in patients who are immunocompromised in the settings of HIV infection, chemotherapy, and organ transplantation. Bacterial infections such as tuberculosis and syphilis rarely involve the stomach. CMV and herpesvirus infection, as well as fungal (e.g., *Candida*, histoplasmosis, mucormycosis, cryptococcosis, aspergillosis), and parasitic infections (e.g., *Cryptosporidium*, *Strongyloides*) are also possible. Other diseases such as sarcoidosis and Crohn disease may involve the stomach. The presence of granulomas on histologic specimens, along with systemic manifestations of the disease, confirms the diagnosis.

The stomach is occasionally involved by acute *graft-versus-host* disease. Gastric erosions or ulcers may be encountered in the investigation of bone marrow transplantation patients with abdominal pain or GI bleeding. Biopsy specimens should be obtained to rule out opportunistic infections (e.g., CMV).

Alcohol, drugs (e.g., cocaine, iron, potassium chloride), and physical agents (nasogastric tubes) are also associated with non-specific forms of gastritis. Similarly, ischemia as a result of vascular injuries, embolization, vasculitis, and amyloidosis has been described as a cause of gastritis.

### NONULCER DYSPEPSIA

Dyspepsia, defined as pain or discomfort in the upper abdomen, is a common clinical problem and may be seen at some time in 25% to 40% of adults. Though dyspepsia is a classic manifestation of PUD, only 15% to 25% of patients with dyspepsia are found to have a gastric or duodenal ulcer. The remainder of patients have nonulcer or functional dyspepsia, a condition most likely related to an abnormal perception of events in the stomach caused by afferent visceral hypersensitivity. Abnormal gastric motility may also play a role in nonulcer dyspepsia (NUD), and recent evidence suggests that about 40% of patients with NUD have impairment in the fundic accommodation response of the stomach. Dyspeptic symptoms may be chronic, recurrent, or of new onset. The diagnostic evaluation should focus on excluding other causes of dyspepsia such as gastroparesis and gastric cancer.

### Management

Three possible strategies for managing patients with NUD have been formulated (see Fig. 36-6). Immediate endoscopic evaluation is indicated for individuals older than 45 years and persons exhibiting alarm features (*red flags*) such as weight loss, recurrent vomiting, dysphagia, GI bleeding, anemia, a strong family history of GI cancer, or an abdominal mass. Urgent endoscopic examination is indicated to exclude a serious underlying disease process, particularly gastric and esophageal carcinoma. If a gastric ulcer is found during endoscopic examination, multiple biopsies and cytologic analysis should be obtained to exclude malignancy. Ulcer treatment is subsequently employed, and ulcer healing should be confirmed with a follow-up endoscopic examination because nonhealing ulcers can occasionally be a manifestation of gastric carcinoma. Barium radiography offers poor sensitivity and specificity and is thus no longer recommended in the evaluation of dyspepsia.

The second option when treating patients younger than 45 years with NUD but without alarm features is an empirical trial of antisecretory therapy for 1 to 2 months. Endoscopy is indicated in patients who fail to respond to this regimen. Avoiding the introduction of long-term drug use in this situation is important, particularly because of the considerable benefit of placebo in such individuals.

The third strategy for managing NUD involves initial noninvasive testing for *H. pylori* followed by antimicrobial therapy in patients with positive tests. This strategy is presumed to heal ulcers if present, eliminate the ulcer diathesis, and save on resources, particularly in patients younger than 45 years without alarm symptoms. The frequency of *H. pylori* infection in the community should also be taken into account because noninvasive tests show decreased accuracy when the prevalence of *H. pylori* is less than 10%. This approach, although advocated by some physicians, has shown variable effectiveness in relieving NUD. Moreover, indiscriminate use of antimicrobial therapy may be associated with altering normal intestinal flora, increasing resistance of *H. pylori* and other bacteria that are not a target of therapy, and producing a series of adverse events such as antibiotic-associated and *Clostridium difficile* colitis.

### ZOLLINGER-ELLISON SYNDROME

Zollinger-Ellison Syndrome (ZES) is characterized by elevated levels of serum gastrin produced by gastrin-secreting tumors that are most often located in the pancreas and duodenum. Hypergastrinemia stimulates hypersecretion of gastric acid and pepsin, which may produce peptic ulcers, duodenojejunitis, esophagitis, and diarrhea. ZES is an uncommon cause of PUD, accounting for less than 1% of the instances. The gastrin-secreting tumor in ZES, referred to as a *gastrinoma*, is frequently located in the *gastrinoma triangle*, an area encompassed by the second and third portions of the duodenum, the junction of the head and neck of the pancreas, and the cystic duct. Seventy-five percent of all gastrinomas are sporadic; the remaining 25% are part of the type I multiple endocrine neoplasia (MEN-I) syndrome, an autosomal-dominant condition with a locus on chromosome 11, typically associated with hyperparathyroidism and pituitary tumors. All patients with sporadic gastrinomas without evidence of liver