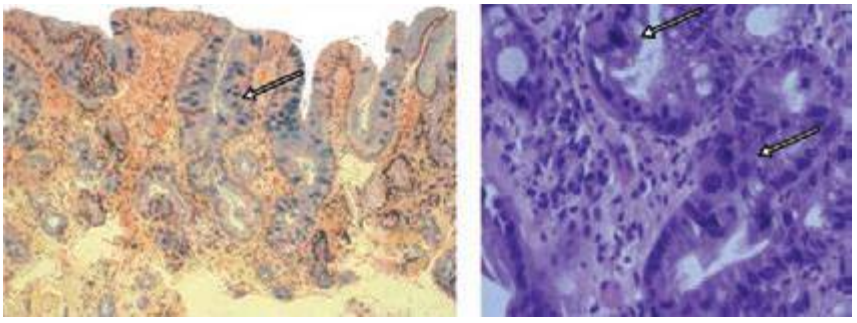

FIGURE 347-10 Histopathology of Barrett's metaplasia and Barrett's with high-grade dysplasia. H&E, hematoxylin and eosin.

to control the adenocarcinoma risk has not been established. Also of note, no high-level evidence confirms that aggressive antisecretory therapy or antireflux surgery causes regression of Barrett's esophagus or prevents adenocarcinoma.

Although the management of Barrett's esophagus remains controversial, the finding of dysplasia in Barrett's, particularly high-grade dysplasia, mandates further intervention. In addition to the high rate of progression to adenocarcinoma, there is also a high prevalence of unrecognized coexisting cancer with high-grade dysplasia. Nonetheless, treatment remains controversial. Esophagectomy, intensive endoscopic surveillance, and mucosal ablation have all been advocated. Currently, esophagectomy is the gold standard treatment for high-grade dysplasia in an otherwise healthy patient with minimal surgical risk. However, esophagectomy has a mortality ranging from 3–10%, along with substantial morbidity. That, along with increasing evidence of the effectiveness of endoscopic therapy with purpose-built radiofrequency ablation devices, has led many to favor this therapy as a preferable management strategy.

TREATMENT GASTROESOPHAGEAL REFLUX DISEASE (GERD)

Lifestyle modifications are routinely advocated as GERD therapy. Broadly speaking, these fall into three categories: (1) avoidance of foods that reduce LES pressure, making them "refluxogenic" (these commonly include fatty foods, alcohol, spearmint, peppermint, tomato-based foods, and possibly coffee and tea); (2) avoidance of acidic foods that are inherently irritating; and (3) adoption of behaviors to minimize reflux and/or heartburn. In general, minimal evidence supports the efficacy of these measures. However, clinical experience dictates that subsets of patients are benefitted by specific recommendations, based on their unique history and symptom profile. A patient with sleep disturbance from nighttime heartburn is likely to benefit from elevation of the head of the bed and avoidance of eating before retiring, but those recommendations are superfluous for a patient without nighttime symptoms. The most broadly applicable recommendation is for weight reduction. Even though the benefit with respect to reflux cannot be assured, the strong epidemiologic relationship between body mass index and GERD and the secondary health gains of weight reduction are beyond dispute.

The dominant pharmacologic approach to GERD management is with inhibitors of gastric acid secretion, and abundant data support the effectiveness of this approach. Pharmacologically reducing the acidity of gastric juice does not prevent reflux, but it ameliorates reflux symptoms and allows esophagitis to heal. The hierarchy of effectiveness among pharmaceuticals parallels their antisecretory potency. Proton pump inhibitors (PPIs) are more efficacious than histamine$_2$ receptor antagonists (H_2RAs), and both are superior to placebo. No major differences exist among PPIs, and only modest gain is achieved by increased dosage.

Paradoxically, the perceived frequency and severity of heartburn correlate poorly with the presence or severity of esophagitis. When GERD treatments are assessed in terms of resolving heartburn, both efficacy and differences among pharmaceuticals are less clear-cut than with the objective of healing esophagitis. Although the same overall hierarchy of effectiveness exists, observed efficacy rates are lower and vary widely, likely reflecting patient heterogeneity.

Reflux symptoms tend to be chronic, irrespective of esophagitis. Thus, a common management strategy is indefinite treatment with PPIs or H_2RAs as necessary for symptom control. The side effects of PPI therapy are generally minimal. Vitamin B_{12} and iron absorption may be compromised and susceptibility to enteric infections, particularly *Clostridium difficile* colitis, increased with treatment. Population studies have also suggested a slight increased risk of bone fracture with chronic PPI use suggesting an impairment of calcium absorption, but prospective studies have failed to corroborate this. Nonetheless, as with any medication, PPI dosage should be minimized to that necessary for the clinical indication.

Laparoscopic Nissen fundoplication, wherein the proximal stomach is wrapped around the distal esophagus to create an antireflux barrier, is a surgical alternative to the management of chronic GERD. Just as with PPI therapy, evidence on the utility of fundoplication is strongest for treating esophagitis, and controlled trials suggest similar efficacy to PPI therapy. However, the benefits of fundoplication must be weighed against potential deleterious effects, including surgical morbidity and mortality, postoperative dysphagia, failure or breakdown requiring reoperation, an inability to belch, and increased bloating, flatulence, and bowel symptoms after surgery.

EOSINOPHILIC ESOPHAGITIS

Eosinophilic esophagitis (EoE) is increasingly recognized in adults and children around the world. Current prevalence estimates identified 4–6 cases per 10,000 with a predilection for white males. The increasing prevalence of EoE is attributable to a combination of an increasing incidence and a growing recognition of the condition. There is also an incompletely understood, but important, overlap between EoE and GERD that confuses diagnosis of the disease.

EoE is diagnosed based on the combination of typical esophageal symptoms and esophageal mucosal biopsies demonstrating squamous epithelial eosinophil-predominant inflammation. Alternative etiologies of esophageal eosinophilia include GERD, drug hypersensitivity, connective tissue disorders, hypereosinophilic syndrome, and infection. Current evidence indicates that EoE is an immunologic disorder induced by antigen sensitization in susceptible individuals. Dietary factors play an important role in both the pathogenesis and treatment of EoE. Aeroallergens may also contribute, but the evidence is weaker. The natural history of EoE is unclear, but an increased risk of esophageal stricture development paralleling the duration of untreated disease has been noted.