



**FIGURE 347-9** Endoscopic appearance of (A) peptic esophagitis, (B) a peptic stricture, (C) Barrett's metaplasia, and (D) adenocarcinoma developing within an area of Barrett's esophagus.

esophagus during swallow-related LES relaxation, a phenomenon that does not normally occur.

Inherent in the pathophysiologic model of GERD is that gastric juice is harmful to the esophageal epithelium. However, gastric acid hypersecretion is usually not a dominant factor in the development of esophagitis. An obvious exception is with Zollinger-Ellison syndrome, which is associated with severe esophagitis in about 50% of patients. Another caveat is with chronic *Helicobacter pylori* gastritis, which may have a protective effect by inducing atrophic gastritis with concomitant hypoacidity. Pepsin, bile, and pancreatic enzymes within gastric secretions can also injure the esophageal epithelium, but their noxious properties are either lessened without an acidic environment or dependent on acidity for activation. Bile warrants attention because it persists in refluxate despite acid-suppressing medications. Bile can transverse the cell membrane, imparting severe cellular injury in a weakly acidic environment, and has also been invoked as a cofactor in the pathogenesis of Barrett's metaplasia and adenocarcinoma. Hence, the causticity of gastric refluxate extends beyond hydrochloric acid.

### SYMPTOMS

Heartburn and regurgitation are the typical symptoms of GERD. Somewhat less common are dysphagia and chest pain. In each case, multiple potential mechanisms for symptom genesis operate that extend beyond the basic concepts of mucosal erosion and activation of afferent sensory nerves. Specifically, hypersensitivity and functional pain are increasingly recognized as cofactors. Nonetheless, the dominant clinical strategy is empirical treatment with acid inhibitors, reserving further evaluation for those who fail to respond. Important exceptions to this are patients with chest pain or persistent dysphagia, each of which may be indicative of more morbid conditions. With chest pain, cardiac disease must be carefully considered. In the case of persistent dysphagia, chronic reflux can lead to the development of

a peptic stricture or adenocarcinoma, each of which benefits from early detection and/or specific therapy.

Extraesophageal syndromes with an established association to GERD include chronic cough, laryngitis, asthma, and dental erosions. A multitude of other conditions including pharyngitis, chronic bronchitis, pulmonary fibrosis, chronic sinusitis, cardiac arrhythmias, sleep apnea, and recurrent aspiration pneumonia have proposed associations with GERD. However, in both cases, it is important to emphasize the word *association* as opposed to *causation*. In many instances, the disorders likely coexist because of shared pathogenetic mechanisms rather than strict causality. Potential mechanisms for extraesophageal GERD manifestations are either regurgitation with direct contact between the refluxate and supraesophageal structures or via a vagovagal reflex wherein reflux activation of esophageal afferent nerves triggers efferent vagal reflexes such as bronchospasm, cough, or arrhythmias.

### DIFFERENTIAL DIAGNOSIS

Although generally quite characteristic, symptoms from GERD need to be distinguished from symptoms related to infectious, pill, or eosinophilic esophagitis, peptic ulcer disease, dyspepsia, biliary colic, coronary artery disease, and esophageal motility disorders. It is especially important that coronary artery disease be given early consideration because of its potentially lethal implications. The remaining elements of the differential diagnosis can be addressed by endoscopy, upper gastrointestinal series, or biliary tract ultrasonography as appropriate. The distinction among etiologies of esophagitis is usually easily made by endoscopy with mucosal biopsies, which are necessary to evaluate for infection or eosinophilic inflammation. In terms of endoscopic appearance, infectious esophagitis is diffuse and tends to involve the proximal esophagus far more frequently than does reflux esophagitis. The ulcerations seen in peptic esophagitis are usually solitary and distal, whereas infectious ulcerations are punctate and diffuse. Eosinophilic esophagitis characteristically exhibits multiple esophageal rings, linear furrows, or white punctate exudate. Esophageal ulcerations from pill esophagitis are usually singular and deep at points of luminal narrowing, especially near the carina, with sparing of the distal esophagus.

### COMPLICATIONS

The complications of GERD are related to chronic esophagitis (bleeding and stricture) and the relationship between GERD and esophageal adenocarcinoma. However, both esophagitis and peptic strictures have become increasingly rare in the era of potent antisecretory medications. Conversely, the most severe histologic consequence of GERD is Barrett's metaplasia with the associated risk of esophageal adenocarcinoma, and the incidence of these lesions has increased, not decreased, in the era of potent acid suppression. Barrett's metaplasia, endoscopically recognized by tongues of reddish mucosa extending proximally from the gastroesophageal junction (Fig. 347-9) or histopathologically by the finding of specialized columnar metaplasia, is associated with a substantially increased risk for development of esophageal adenocarcinoma.

Barrett's metaplasia can progress to adenocarcinoma through the intermediate stages of low- and high-grade dysplasia (Fig. 347-10). Owing to this risk, areas of Barrett's and especially any included areas of mucosal irregularity should be extensively biopsied. The rate of cancer development is estimated at 0.1–0.3% per year, but vagaries in definitional criteria and of the extent of Barrett's metaplasia requisite to establish the diagnosis have contributed to variability and inconsistency in this risk assessment. The group at greatest risk is obese white males in their sixth decade of life. However, despite common practice, the utility of endoscopic screening and surveillance programs intended