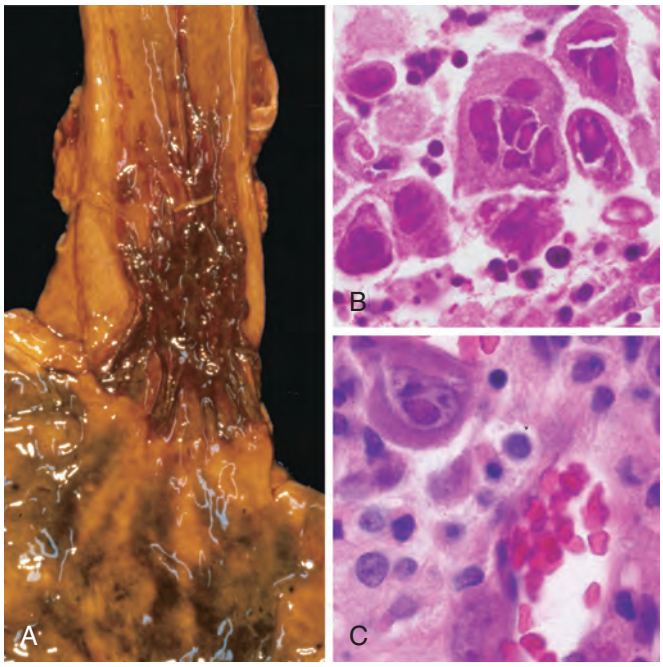

Figure 17-4 Viral esophagitis. **A,** Postmortem specimen with multiple, overlapping herpetic ulcers in the distal esophagus. **B,** Multinucleate squamous cells containing herpesvirus nuclear inclusions. **C,** Cytomegalovirus-infected endothelial cells with nuclear and cytoplasmic inclusions.

of densely matted fungal hyphae and inflammatory cells covering the esophageal mucosa.

The endoscopic appearance often provides a clue as to the infectious agent in viral esophagitis. Herpes viruses typically cause punched-out ulcers (Fig. 17-4*A*). Biopsy specimens demonstrate nuclear viral inclusions within a rim of degenerating epithelial cells at the margin of the ulcer (Fig. 17-4*B*). In contrast, CMV causes shallower ulcerations and characteristic nuclear and cytoplasmic inclusions within capillary endothelium and stromal cells (Fig. 17-4*C*). Although the histologic appearance is characteristic, immunohistochemical stains for virus-specific antigens are sensitive and specific ancillary diagnostic tools.

Histologic features of esophageal **graft-versus-host disease** are similar to those in the skin and include basal epithelial cell apoptosis, mucosal atrophy, and submucosal fibrosis without significant acute inflammatory infiltrates. The microscopic appearances of esophageal involvement in bullous pemphigoid, epidermolysis bullosa, and Crohn disease are also similar to those in the skin (Chapter 25).

Reflux Esophagitis

The stratified squamous epithelium of the esophagus is resistant to abrasion from foods but is sensitive to acid. Submucosal glands, which are most abundant in the proximal and distal esophagus, contribute to mucosal protection by secreting mucin and bicarbonate. More importantly, the tone of the lower esophageal sphincter prevents reflux of acidic gastric contents, which are under positive pressure and would otherwise enter the esophagus. Reflux of gastric contents into the lower esophagus is the most frequent cause of esophagitis and the most common outpatient GI diagnosis in the United States. The associated clinical condition is termed *gastroesophageal reflux disease (GERD)*.

Pathogenesis. The most common cause of gastroesophageal reflux is transient lower esophageal sphincter relaxation. This is thought to be mediated via vagal pathways, and can be triggered by gastric distention, by gas or food, mild pharyngeal stimulation that does not trigger swallowing, and stress. Gastroesophageal reflux can also occur following swallow-induced lower esophageal sphincter relaxations or due to forceful opening of a relatively hypotensive lower esophageal sphincter by an abrupt increase in intraabdominal pressure, such as that due to coughing, straining, or bending. Other conditions that decrease lower esophageal sphincter tone or increase abdominal pressure and contribute to GERD include alcohol and tobacco use, obesity, central nervous system depressants, pregnancy, hiatal hernia (discussed later), delayed gastric emptying, and increased gastric volume. In many cases, no definitive cause is identified. Reflux of gastric juices is central to the development of mucosal injury in GERD. In severe cases, reflux of bile from the duodenum may exacerbate the damage.

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Simple hyperemia, evident to the endoscopist as redness, may be the only alteration. In mild GERD the mucosal histology is often unremarkable. With more significant disease, eosinophils are recruited into the squamous mucosa followed by neutrophils, which are usually associated with more severe injury (Fig. 17-5*A*). Basal zone hyperplasia exceeding 20% of the total epithelial thickness and elongation of lamina propria papillae, such that they extend into the upper third of the epithelium, may also be present.

Clinical Features. GERD is most common in individuals older than age 40 but also occurs in infants and children. The most frequent clinical symptoms are heartburn, dysphagia, and regurgitation of sour-tasting gastric contents.

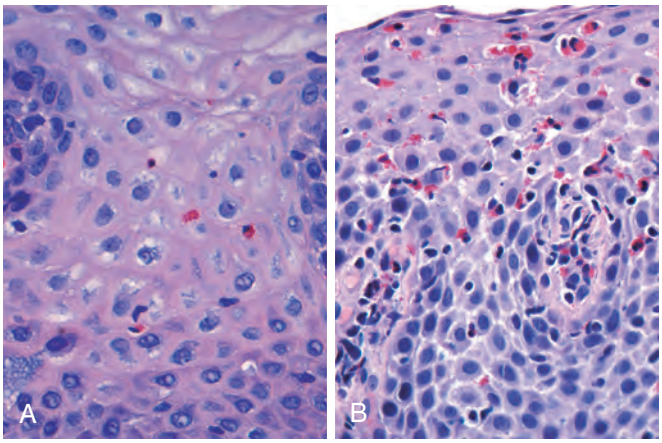

Figure 17-5 Esophagitis. **A,** Reflux esophagitis with scattered intraepithelial eosinophils and mild basal zone expansion. **B,** Eosinophilic esophagitis is characterized by numerous intraepithelial eosinophils. Abnormal squamous maturation is also apparent.