Both trophozoites (Fig. 247-1) and cysts (Fig. 247-2) are found in the intestinal lumen, but only trophozoites of *E. histolytica* invade tissue. The trophozoite is 20–60 μm in diameter and contains vacuoles and a nucleus with a characteristic central nucleolus. In animals, depletion of intestinal mucus, diffuse inflammation, and disruption of the epithelial barrier precede trophozoite contact with the colonic mucosa. Trophozoites attach to colonic mucus and epithelial cells by their Gal/GalNAc lectin. The earliest intestinal lesions are microulcerations of the mucosa of the cecum, sigmoid colon, or rectum that release erythrocytes, inflammatory cells, and epithelial cells. Proctoscopy reveals small ulcers with heaped-up margins and normal intervening mucosa (Fig. 247-3*A*). Submucosal extension of ulcerations under viable-appearing surface mucosa causes the classic "flask-shaped" ulcer containing trophozoites at the margins of dead and viable tissues. Although neutrophilic infiltrates may accompany the early lesions in animals, human intestinal infection is marked by a paucity of inflammatory cells, probably in part because of the killing of neutrophils by trophozoites (Fig. 247-3*B*). Treated ulcers characteristically heal with little or no scarring. Occasionally, however, full-thickness necrosis and perforation occur.

Rarely, intestinal infection results in the formation of a mass lesion, or *ameboma*, in the bowel lumen. The overlying mucosa is usually thin and ulcerated, while other layers of the wall are thickened, edematous, and hemorrhagic; this condition results in exuberant formation of granulation tissue with little fibrous-tissue response.

A number of virulence factors have been linked to the ability of *E. histolytica* to invade through the interglandular epithelium. One factor consists of the extracellular cysteine proteinases that degrade collagen, elastin, IgA, IgG, and the anaphylatoxins C3a and C5a. Other enzymes may disrupt glycoprotein bonds between mucosal epithelial cells in the gut. Amebas can lyse neutrophils, monocytes, lymphocytes, and cells of colonic and hepatic lines. The cytolytic effect of amebas appears to require direct contact with target cells and may be linked to the release of phospholipase A and pore-forming peptides. *E. histolytica* trophozoites also cause apoptosis of human cells. Phagocytosis is a virulence factor that leads to defective parasite proliferation if inhibited. This process is potentially modulated by calmodulin-like calcium-binding protein 3, which pairs with actin and myosin during initiation and formation of phagosomes. Another virulence factor is the ability to resist reactive oxygen species, reactive nitrogen species such as nitric oxide, or S-nitrosothiols such as S-nitrosoglutathione (GSNO) and S-nitrosocysteine (CySNO). *E. histolytica* trophozoites are constantly exposed to reactive oxygen and nitrogen species from their own metabolism and host defenses during tissue invasion. Overexpression of hydrogen peroxide regulatory motif–binding protein appears to increase *E. histolytica* cytotoxicity. Since *E. histolytica* lacks glutathione and glutathione reductase, it relies on its thioredoxin/thioredoxin reductase system to prevent, regulate, and repair the damage caused by oxidative stress. This antioxidant system is versatile in that it can reduce

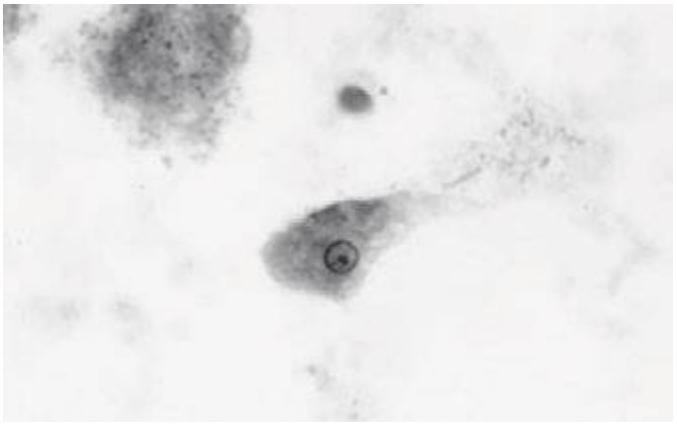


FIGURE 247-1 Trophozoite of *E. histolytica*. A single nucleus with a central, dot-like nucleolus is seen (trichrome stain).

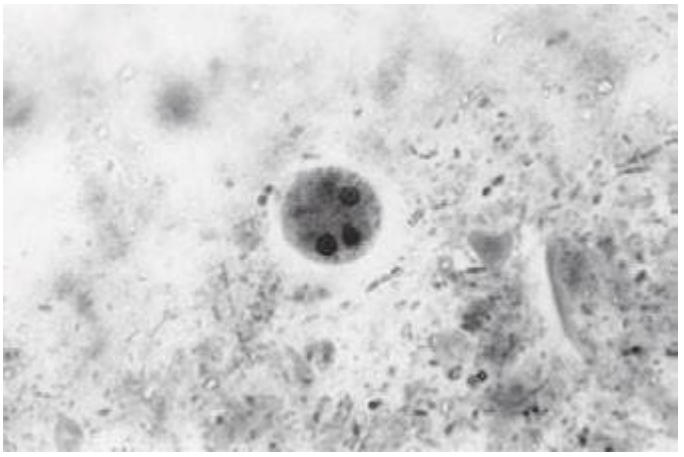
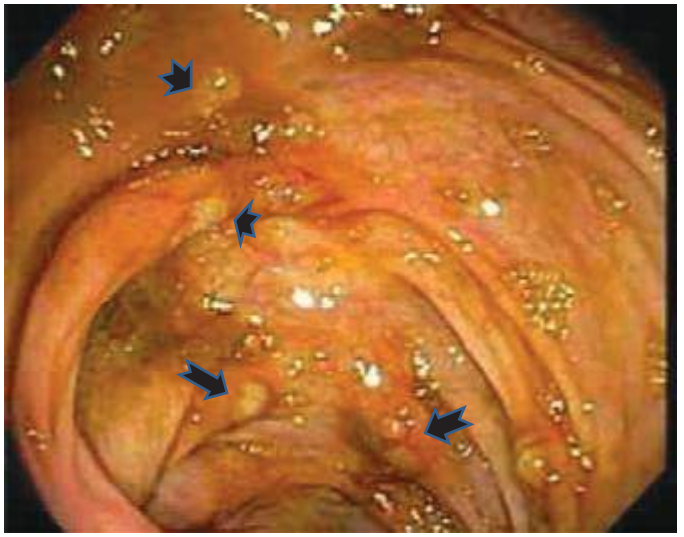
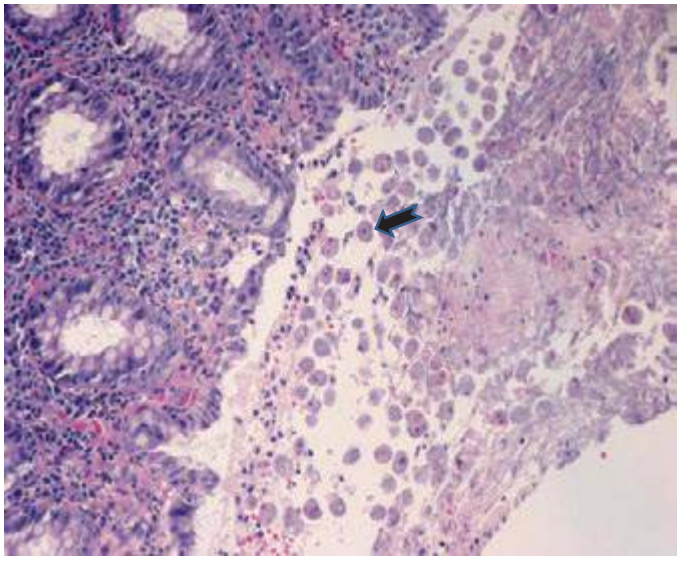


FIGURE 247-2 Cyst of *E. histolytica*. Three of the four nuclei are visible (trichrome stain).



A



B

FIGURE 247-3 Endoscopic and histopathologic features of intestinal amebiasis. *A.* Appearance of ulcers on colonoscopy (*arrows*). ***B.*** Inflammatory infiltrate and *E. histolytica* trophozoites (*arrow*) in invasive amebic colitis (hematoxylin and eosin). *(Courtesy of the Department of Pathology and Gastroenterology, VA San Diego Medical Center.)*