Clinical Features. The clinical manifestations of Crohn disease are extremely variable. In most patients disease begins with intermittent attacks of relatively mild diarrhea, fever, and abdominal pain. Approximately 20% of patients present acutely with right lower quadrant pain, fever, and bloody diarrhea that may mimic acute appendicitis or bowel perforation. Periods of active disease are typically interrupted by asymptomatic periods that last for weeks to many months. Disease re-activation can be associated with a variety of external triggers, including physical or emotional stress, specific dietary items, and cigarette smoking. The latter is a strong exogenous risk factor for development of Crohn disease and, in some cases, disease onset is associated with initiation of smoking. Unfortunately, smoking cessation does not result in disease remission.

Iron-deficiency anemia may develop in individuals with colonic disease, while extensive small bowel disease may result in serum protein loss and hypoalbuminemia, generalized nutrient malabsorption, or malabsorption of vitamin B_{12} and bile salts. *Fibrosing strictures,* particularly of the terminal ileum, are common and require surgical resection. Disease often recurs at the site of anastomosis, and as many as 40% of patients require additional resections within 10 years. *Fistulae* develop between loops of bowel and may also involve the urinary bladder, vagina, and abdominal or perianal skin. *Perforations* and peritoneal abscesses are common. Anti-TNF antibodies have revolutionized treatment of Crohn disease, and other biologic therapies are becoming available.

Extraintestinal manifestations of Crohn disease include uveitis, migratory polyarthritis, sacroiliitis, ankylosing spondylitis, erythema nodosum, and clubbing of the fingertips, any of which may develop before intestinal disease is recognized. Pericholangitis and primary sclerosing cholangitis occur in Crohn disease with a higher frequency than in those without Crohn disease, but are even more common in those who have ulcerative colitis (see below and Chapter 18). As discussed later, risk of colonic adenocarcinoma is increased in patients with long-standing IBD affecting the colon.

Ulcerative Colitis

Ulcerative colitis is closely related to Crohn disease. However, the disease in ulcerative colitis is limited to the colon and rectum. Common extraintestinal manifestations of ulcerative colitis overlap with those of Crohn disease and include migratory polyarthritis, sacroiliitis, ankylosing spondylitis, uveitis, and skin lesions. Approximately 2.5% to 7.5% of individuals with ulcerative colitis also have primary sclerosis cholangitis (Chapter 18). The long-term outlook for ulcerative colitis patients depends on the severity of active disease and disease duration.

MORPHOLOGY

Grossly, ulcerative colitis always involves the rectum and extends proximally in a continuous fashion to involve part or all of the colon. Disease of the entire colon is termed pancolitis (Fig. 17-36*A*), while left-sided disease extends no farther than the transverse colon. Limited distal disease may be referred to descriptively as ulcerative proctitis or ulcerative proctosigmoiditis. The small intestine is normal, although mild mucosal inflammation of the distal ileum, termed backwash ileitis, may be present in severe cases of pancolitis. Skip lesions are not seen (although focal appendiceal or cecal inflammation may occasionally be present in left-sided ulcerative colitis).

Grossly, involved colonic mucosa may be slightly red and granular or have extensive, **broad-based ulcers**. There can be an abrupt transition between diseased and uninvolved colon (Fig. 17-36*B*). Ulcers are aligned along the long axis of the colon but do not typically replicate the serpentine ulcers of Crohn disease. Isolated islands of regenerating mucosa often bulge into the lumen to create **pseudopolyps** (Fig. 17-36*C*), and the tips of these polyps may fuse to create **mucosal bridges** (Fig. 17-36*D*). Chronic disease may lead to **mucosal atrophy** with a flat and smooth mucosal surface that lacks normal folds. Unlike Crohn disease, **mural thickening is not present, the serosal surface is normal, and strictures do not occur**. However, inflammation and inflammatory mediators can damage the muscularis propria and disturb neuromuscular function leading to colonic dilation and **toxic megacolon**, which carries a significant risk of perforation.

Histologic features of mucosal disease in ulcerative colitis are similar to colonic Crohn disease and include inflammatory infiltrates, crypt abscesses (Fig. 17-37*A*), crypt distortion, and pseudopyloric epithelial metaplasia (Fig. 17-37*B*). However, **the inflammatory process is diffuse and generally limited to the mucosa and superficial submucosa** (Fig. 17-37*C*). In severe cases, extensive mucosal destruction may be accompanied by ulcers that extend more deeply into the submucosa, but the muscularis propria is rarely involved. Submucosal fibrosis, mucosal atrophy, and distorted mucosal architecture remain as residua of healed disease but histology may also revert to near normal after prolonged remission. **Granulomas are not present** in ulcerative colitis.

Clinical Features. Ulcerative colitis is a relapsing disorder characterized by attacks of bloody diarrhea with stringy, mucoid material, lower abdominal pain, and cramps that are temporarily relieved by defecation. These symptoms may persist for days, weeks, or months before they subside. The initial attack may, in some cases, be severe enough to constitute a medical or surgical emergency. More than half of patients have clinically mild disease, although almost all experience at least one relapse during a 10-year period, and up to 30% require colectomy within the first 3 years after presentation because of uncontrollable symptoms. Colectomy effectively cures intestinal disease in ulcerative colitis, but extraintestinal manifestations may persist.

The factors that trigger ulcerative colitis are not known, but infectious enteritis precedes disease onset in some cases. In other cases the first attack is preceded by psychologic stress, which may also be linked to relapse during remission. The initial onset of symptoms has also been reported to occur shortly after smoking cessation in some patients, and smoking may partially relieve symptoms. Unfortunately, studies of nicotine as a therapeutic agent have been disappointing.

Indeterminate Colitis

Because of the extensive pathologic and clinical overlap between ulcerative colitis and Crohn disease (Table 17-9),