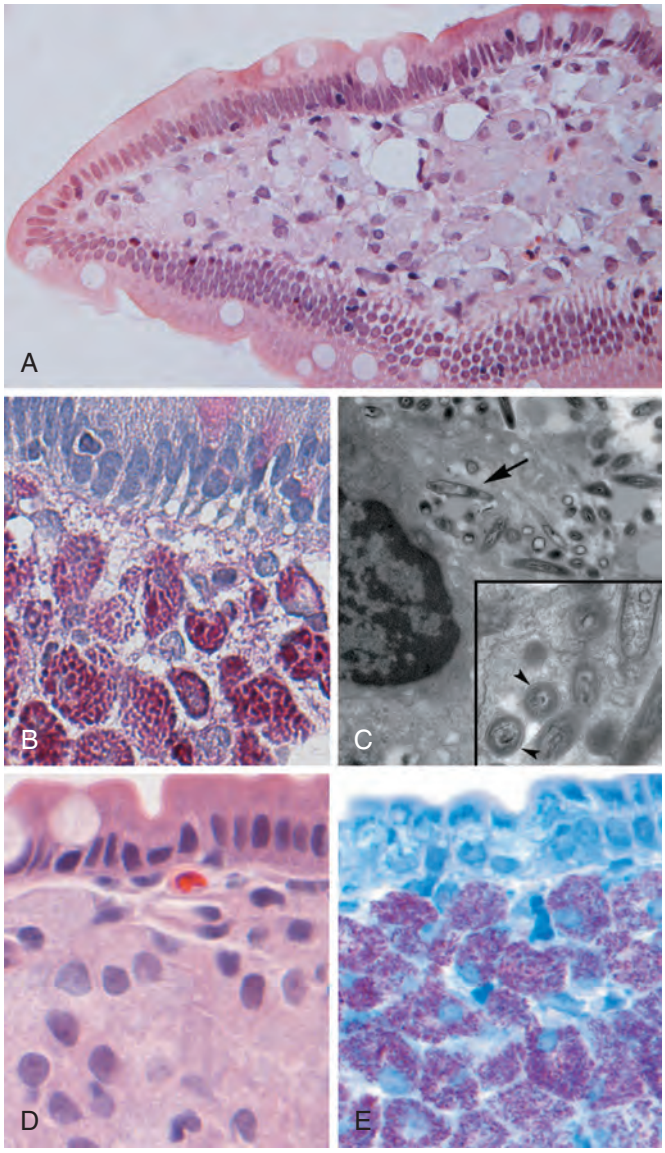

Figure 17-30 Whipple disease and mycobacterial infection. **A,** hematoxylin and eosin staining shows effacement of normal lamina propria by a sheet of swollen macrophages. **B,** PAS stain highlights macrophage lysosomes full of bacilli. Note the positive staining of mucous vacuoles in the overlying goblet cells. **C,** An electron micrograph of part of a macrophage shows bacilli within the cell (top arrow); also seen at higher magnification (inset). **D,** The morphology of mycobacterial infection can be similar to Whipple disease, particularly in the immunocompromised host. Compare with **A**. **E,** Mycobacteria are positive with stains for for acid-fast bacteria. (**C,** Courtesy George Kasnic and Dr. William Clapp, University of Florida, Gainesville, Fla.)

MORPHOLOGY

The morphologic hallmark of Whipple disease is a **dense accumulation of distended, foamy macrophages in the small intestinal lamina propria** (Fig. 17-30*A*). The macrophages contain periodic acid–Schiff (PAS)-positive, diastase-resistant granules that represent lysosomes stuffed with partially digested bacteria (Fig. 17-30*B*). Intact rod-shaped bacilli can also be identified by electron microscopy (Fig. 17-30*C*). A similar infiltrate of foamy macrophages is present in intestinal tuberculosis (Fig. 17-30*D*), and the organisms are PAS-positive in both diseases. The acid-fast stain can be helpful, since mycobacteria stain positively (Fig. 17-30*E*) while *T. whippelii* do not.

The **villous expansion** caused by the dense macrophage infiltrate imparts a shaggy gross appearance to the mucosal surface. Lymphatic dilatation and mucosal lipid deposition account for the common endoscopic detection of white to yellow mucosal plaques. In Whipple disease, bacteria-laden macrophages can accumulate within **mesenteric lymph nodes, synovial membranes of affected joints, cardiac valves, the brain,** and other sites.

Whipple disease is most common in Caucasian men, particularly farmers and others with occupational exposure to soil or animals. While there is no consistent familial clustering, the rarity of infection despite a large number of healthy carriers suggests that genetic risk factors may exist.

The clinical presentation of Whipple disease is usually a triad of diarrhea, weight loss, and arthralgia. Extraintestinal symptoms, which can exist for months or years before malabsorption, include arthritis, arthralgia, fever, lymphadenopathy, and neurologic, cardiac, or pulmonary disease.

Mycobacterial infections are considered in detail in Chapter 8.

Viral Gastroenteritis

Symptomatic human infection is caused by several distinct groups of viruses. The most common are discussed here.

Norovirus. This was previously known as Norwalk-like virus and is a common cause of nonbacterial gastroenteritis. These are small icosahedral viruses with a single-stranded RNA genome that forms a genus within the Caliciviridae family. **Norovirus causes approximately half of all gastroenteritis outbreaks worldwide and is a common cause of sporadic gastroenteritis in developed countries.** In the United States, noroviruses are the most common cause of acute gastroenteritis requiring medical attention and are second only to rotavirus as a cause of severe diarrhea in infants and young children. In developing countries, noroviruses cause more than 200,000 childhood deaths annually. Norovirus is expected to become the most common cause of diarrhea worldwide in all age groups as rotavirus vaccination becomes widespread.

Local norovirus outbreaks are usually related to contaminated food or water, but person-to-person transmission underlies most sporadic cases. Infections spread easily within schools, hospitals, nursing homes, and other large groups in close quarters, such as those on cruise ships. In these environments, vehicles of infection include airborne droplets, environmental surfaces and fomites.

Following a short incubation period, affected individuals develop nausea, vomiting, watery diarrhea, and abdominal pain. Biopsy morphology is nonspecific. When present, abnormalities are most evident in the small intestine and include mild villous shortening, epithelial vacuolization, loss of the microvillus brush border, crypt hypertrophy, and lamina propria infiltration by lymphocytes (Fig. 17-31*A*). The disease is self-limited in immunocompetent hosts.