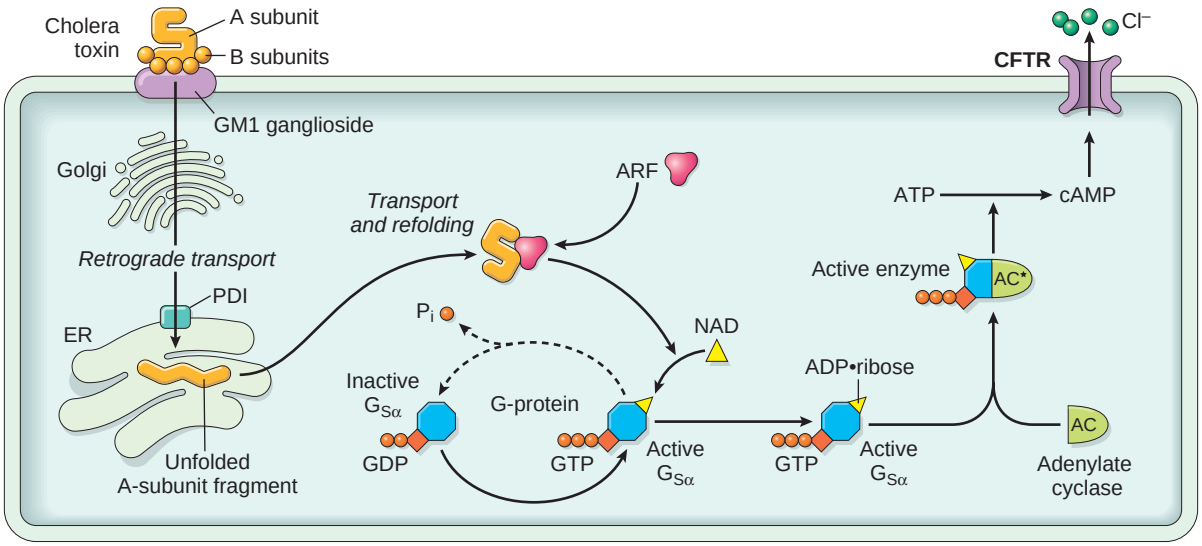

Figure 17-27 Cholera toxin transport and signaling. After retrograde toxin transport to the endoplasmic reticulum (ER), the A subunit is released by the action of protein disulfide isomerase (PDI) and is then able to access the epithelial cell cytoplasm. In concert with an ADP-ribosylation factor (ARF), the A subunit then ADP-ribosylates $G_s\alpha$, which locks it in the active, GTP-bound state. This leads to adenylate cyclase (AC) activation, and the cAMP produced opens CFTR to drive chloride secretion and diarrhea.

Pathogenesis. The pathogenesis of *Campylobacter* infection remains poorly defined, but the four major properties that contribute to virulence are: motility, adherence, toxin production, and invasion. Flagella allow *Campylobacter* to be motile. This facilitates adherence and colonization, which are necessary for mucosal invasion. Cytotoxins that cause epithelial damage and a cholera toxin-like enterotoxin are also released by some *C. jejuni* isolates. Dysentery, i.e. bloody diarrhea, is generally associated with invasion and only occurs with a small minority of *Campylobacter* strains. Enteric fever occurs when bacteria proliferate within the lamina propria and mesenteric lymph nodes.

Campylobacter infection can result in reactive arthritis, primarily in patients with HLA-B27. Other extraintestinal complications, including erythema nodosum and Guillain-Barré syndrome, a flaccid paralysis caused by immunologically mediated inflammation of peripheral nerves, are not HLA-linked (Chapter 27). Molecular mimicry has been implicated in the pathogenesis of Guillain-Barré syndrome, as serum antibodies to *C. jejuni* lipopolysaccharide cross-react with peripheral and central nervous system gangliosides. Up to 40% of Guillain-Barré syndrome cases are associated with *Campylobacter* infection in the preceding 1 to 2 weeks and up to 50% have positive stool cultures or circulating antibodies to *Campylobacter*. Guillain-Barré syndrome develops in 0.1% or less of those infected with *Campylobacter*.

MORPHOLOGY

Campylobacter are comma-shaped, flagellated, gram-negative organisms. Diagnosis is primarily by stool culture, since biopsy findings are nonspecific, and reveal acute self-limited colitis with features common to many forms of infectious colitis. Mucosal and intraepithelial neutrophil infiltrates are prominent, particularly within the superficial mucosa (Fig. 17-28*A*); cryptitis (neutrophil infiltration of the crypts) and crypt abscesses (crypts with accumulations of luminal neutrophils) may also be present. Importantly, crypt architecture is preserved (Fig. 17-28*D*), although this can be difficult to assess in cases with severe mucosal damage.

Clinical Features. Ingestion of as few as 500 *C. jejuni* organisms can cause disease after an incubation period of up to 8 days. Watery diarrhea, either acute or following an influenza-like prodrome, is the primary symptom, but dysentery develops in 15% of adults and more than 50% of children. Patients may shed bacteria for 1 month or more after clinical resolution. Antibiotic therapy is generally not required.

Shigellosis

Shigella are gram-negative unencapsulated, nonmotile, facultative anaerobes that belong to the Enterobacteriaceae family and are closely related to enteroinvasive E. coli. Although humans are the only known reservoir, *Shigella* spp. remain one of the most common causes of bloody diarrhea. It is estimated that 165 million cases occur worldwide each year. Given the infective dose of fewer than several hundred organisms and the presence of as many as 10^9 organisms in each gram of stool during acute disease, *Shigella* are highly transmissible by the fecal-oral route or via contaminated water and food.

In the United States and Europe, children in daycare centers, migrant workers, travelers to developing countries, and those in nursing homes are most commonly affected. Most *Shigella* infections and deaths occur in children younger than 5 years of age. In countries where *Shigella* is endemic it is responsible for approximately 10% of pediatric diarrheal disease and as many as 75% of diarrheal deaths.