the biliary system can lead to emphysematous cholecystitis, especially in diabetic patients. *C. perfringens* in association with mixed aerobic and anaerobic microbes can cause aggressive life-threatening type I necrotizing fasciitis or Fournier's gangrene.

The treatment of mixed aerobic/anaerobic infection of the abdomen, perineum, or gynecologic organs should be based on Gram's staining, culture, and antibiotic sensitivity information. Reasonable empirical treatment consists of ampicillin or ampicillin/sulbactam combined with either clindamycin or metronidazole (Table 179-1). Broader gram-negative coverage may be necessary if the patient has recently been hospitalized or treated with antibiotics. Such coverage can be obtained by substituting ticarcillin/clavulanic acid, piperacillin/sulbactam, or a penem antibiotic for ampicillin or by adding a fluoroquinolone or an aminoglycoside to the regimen. Empirical treatment should be given for 10–14 days or until the patient's clinical condition improves.

ENTERIC CLOSTRIDIAL INFECTIONS

C. perfringens type A is one of the most common bacterial causes of food-borne illness in the United States and Canada. The foods typically implicated include improperly cooked meat and meat products (e.g., gravy) in which residual spores germinate and proliferate during slow cooling or insufficient reheating. Illness results from the ingestion of food containing at least ~10^8 viable vegetative cells, which sporulate in the alkaline environment of the small intestine, producing *C. perfringens* enterotoxin in the process. The diarrhea that develops within 7–30 h of ingestion of contaminated food is generally mild and self-limiting; however, in the very young, the elderly, and the immunocompromised, symptoms are more severe and occasionally fatal. Enterotoxin-producing *C. perfringens* has been implicated as an etiologic agent of persistent diarrhea in elderly patients in nursing homes and tertiary-care institutions and has been considered to play a role in antibiotic-associated diarrhea without pseudomembranous colitis.

C. perfringens strains associated with food poisoning possess the gene (*cpe*) coding for enterotoxin, which acts by forming pores in host cell membranes. *C. perfringens* strains isolated from non-food-borne diseases, such as antibiotic-associated and sporadic diarrhea, carry *cpe* on a plasmid that may be transmitted to other strains. Several methods have been described for the detection of *C. perfringens* enterotoxin in feces, including cell culture assay (Vero cells), enzyme-linked immunosorbent assay, reversed-phase latex agglutination, and polymerase chain reaction (PCR) amplification of *cpe*. Each method has its advantages and limitations.

Enteritis necroticans (gas gangrene of the bowel) is a fulminating clinical illness characterized by extensive necrosis of the intestinal mucosa and wall. Cases can occur sporadically in adults or as epidemics in people of all ages. Enteritis necroticans is caused by α toxin– and β toxin–producing strains of *C. perfringens* type C; β toxin is located on a plasmid and is mainly responsible for pathogenesis. This life-threatening infection causes ischemic necrosis of the jejunum. In Papua New Guinea during the 1960s, enteritis necroticans (known in that locale as *pigbel*) was found to be the most common cause of death in childhood; it was associated with pig feasts and occurred both sporadically and in outbreaks. Intramuscular immunization against the β toxin resulted in a decreased incidence of the disease in Papua New Guinea, although the condition remains common. Enteritis necroticans has also been recognized in the United States, the United Kingdom, Germany (where it is known as *darmbrand*), and other developed nations; especially affected are adults who are malnourished or who have diabetes, alcoholic liver disease, or neutropenia.

Necrotizing enterocolitis, a disease resembling enteritis necroticans but associated with *C. perfringens* type A, has been found in North America in previously healthy adults. It is also a serious gastrointestinal disease of low-birth-weight (premature) infants hospitalized in neonatal intensive care units. The etiology and pathogenesis of this disease have remained enigmatic for more than four decades. Pathologic similarities between necrotizing enterocolitis and enteritis necroticans include the pattern of small-bowel necrosis involving the submucosa, mucosa, and muscularis; the presence of gas dissecting the tissue planes; and the degree of inflammation. In contrast to enteritis necroticans, which most commonly involves the jejunum, necrotizing enterocolitis affects the ileum and frequently the ileocecal valve. Both diseases may manifest as intestinal gas cysts, although this feature is more common in necrotizing enterocolitis. The sources of the gas, which contains hydrogen, methane, and carbon dioxide, are probably the fermentative activities of intestinal bacteria, including clostridia. Epidemiologic data support an important role for *C. perfringens* or other gas-producing microorganisms (e.g., *C. neonatale*, certain other clostridia, or *Klebsiella* species) in the pathogenesis of necrotizing enterocolitis.

Patients with suspected clostridial enteric infection should undergo nasogastric suction and receive IV fluids. Pyrantel is given by mouth, and the bowel is rested by fasting. Benzylpenicillin (1 mU) is given IV every 4 h, and the patient is observed for complications requiring surgery. Patients with mild cases recover without surgical intervention. If surgical indications are present (gas in the peritoneal cavity, absent bowel sounds, rebound tenderness, abdominal rigidity), however, the mortality rate ranges from 35% to 100%; a fatal outcome is due in part to perforation of the intestine.

As pigbel continues to be a common disease in Papua New Guinea, consideration should be given to the use of a *C. perfringens*

TABLE 179-1 TREATMENT OF CLOSTRIDIAL INFECTIONS

Condition	Antibiotic Treatment	Penicillin Allergy	Adjunctive Treatment/Note
Wound contamination	None	—	Treatment should be based on clinical signs and symptoms as listed below and not solely on bacteriologic findings.
Polymicrobial anaerobic infections involving clostridia (e.g., abdominal wall, gynecologic)	Ampicillin (2 g IV q4h) ***plus*** Clindamycin (600–900 mg IV q6–8h) ***plus*** Ciprofloxacin (400 mg IV q6–8 h)	Vancomycin (1 g IV q12h) ***plus*** Metronidazole (500 mg IV q6h) ***plus*** Ciprofloxacin (400 mg IV q6–8h)	Empirical therapy should be initiated. Therapy should be based on Gram's stain and culture results and on sensitivity data when available. Add gram-negative coverage if indicated (see text).
Clostridial sepsis	Penicillin, 3–4 mU IV q4–6h ***plus*** Clindamycin (600–900 mg IV q6–8h)	Clindamycin alone ***or*** Metronidazole (as above) ***or*** Vancomycin (as above)	Transient bacteremia without signs of systemic toxicity may be clinically insignificant.
Gas gangrene	Penicillin G (4 mU IV q4–6 h) ***plus*** Clindamycin (600–900 mg IV q6–8h)	Cefoxitin (2 g IV q6h) ***plus*** Clindamycin (600–900 mg IV q6–8h)	Emergent surgical exploration and thorough debridement are extremely important. Hyperbaric oxygen therapy may be considered after surgery and antibiotic initiation.