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Treatment of *Clostridium Difficile* Colitis in the Critical Care Setting

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Clostridium difficile has emerged as an important cause of infection during the past 10 to 15 years [1]. This organism causes an acute inflammation of the colon, largely attributable to its release of toxins A and B into the lumen. A syndrome of acute diarrheal disease follows, which is debilitating and not infrequently lethal. Some authorities continue to use the phrase "*C difficile*–associated diarrhea" or "*C difficile*–associated disease" to describe this disease, but those terms are left over from the late 1970s when the cause was still uncertain. A better descriptive term is "*C difficile* colitis" (CDC).

CDC was originally recognized exclusively as a nosocomial infection and, subsequently, as a problem in extended care facilities [2]. Infection tends to occur in bedridden patients, especially those who have underlying diseases including malnutrition and other common debilitating conditions [3]. Early reports suggested that nearly all patients received antibiotics before infection. Subsequently, it was shown that chemotherapy and the use of drugs that inhibit gastric acidity strongly increase the risk of CDC [4]. In the past few years, an increasing number of community-acquired cases have been reported [5,6]; many of the patients who acquire this infection in the community have not received antibiotics in the preceding 90 days [6,7].

In the epidemiologic setting of a hospitalized patient who has received prior antimicrobial therapy or chemotherapy, the clinical syndrome of CDC is usually easy to recognize. Abdominal discomfort and diarrhea,

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generally more than three loose or watery bowel movements per day, develop over a period of a few days. Fever is present in about half of patients during the first few days of symptoms but, interestingly, may abate by the time the diagnosis is considered, a stool sample is submitted, and results of *C difficile* toxin are positive. About 40% of hospitalized patients have leukocytosis (white blood cell $>12{,}500/mm^3$); in the authors' medical center, 25% of all patients who have peripheral white blood cell counts greater than $30{,}000/mm^3$ have CDC [8]. Because this infection occurs in patients who already have severe underlying diseases complicated by infection and antibiotic treatment, or malignancy and chemotherapy [3], the diarrhea itself contributes to further debilitation. As a result, CDC is associated with substantial mortality, nearly 20% in the first month after diagnosis and 27% in 3 months after diagnosis [9].

As with nearly every disease, the best approach is preventive. This article emphasizes treatment of CDC, considers diagnostic techniques, and describes means for preventing the spread of this infection in the intensive care setting.

Treatment

Stopping the antibiotic

In early reports [10–12], 15% to 23% of patients with CDC had spontaneous resolution of symptoms within 48 to 72 hours of stopping the offending antibiotic and without specific antimicrobial therapy. This approach is not recommended, except perhaps in outpatients who have very mild disease, certainly not in an intensive care setting. One cannot predict which patients will clear the infection spontaneously, and it is often not feasible to discontinue antibiotics. Furthermore, diarrhea contributes to contagion [13] and, in the hospital setting, delaying initial therapy prolongs the period of contagion. Finally, persons who develop CDC tend to be more debilitated and to have received more intensive antibiotic treatment than in the past, suggesting that an even smaller proportion than originally reported might respond to simple cessation of antibiotics.

Specific therapy

Vancomycin

In vitro, *C difficile* is susceptible to vancomycin (minimum inhibitory concentration $[MIC]_{90}$, 1 μg/mL; range, 0.06–4 μg/mL) [14]. Oral vancomycin was used to treat staphylococcal enterocolitis and clindamycin-associated diarrhea before the discovery that *C difficile* was responsible for the disease [15–17]. Recognition of the role of *Clostridium* was followed by additional studies using vancomycin for treatment [11,18–21]; doses ranging from 125 to 500 mg four times daily were found to be equally effective