



PIC QUESTION OF THE WEEK: 11/10/06

Q: What are the treatment approaches for recurrent *Clostridium difficile*-associated disease?

A: *Clostridium difficile* (*C. difficile*) is a gram-positive, spore-forming anaerobic bacillus that is responsible for about 25% of cases of antibiotic-associated diarrhea and approximately 50-75% of cases of antibiotic-related colitis. Antibiotic therapy, which disrupts the normal colonic flora, facilitates the colonization of *C. difficile*. As the organism multiplies, toxins are released with subsequent activation of pro-inflammatory cytokines. Symptoms of *C. difficile*-associated disease (CDAD) may begin as early as the first day of therapy or up to six weeks after discontinuation of antibiotics. It is estimated that 10-25% of patients will have a recurrence of disease after treatment of the initial episode. Additionally, nearly 65% of these patients will have multiple recurrences of CDAD. Although the exact mechanism of recurrence is not completely understood, it is thought to develop as a result of reinfection with the same or a different strain of *C. difficile* rather than to antimicrobial resistance. This may occur from re-ingestion of spores from the environment or from activation of spores remaining in the gastrointestinal tract. People at high risk include the elderly, those with underlying comorbidities, and exposure to other antimicrobials after initial CDAD therapy. For initial recurrences confirmed with stool toxin assay, healthy individuals with mild disease should discontinue any causative antimicrobials and be managed supportively. For most elderly patients with moderate to severe symptoms, a repeat 14-day course of therapy is indicated. Second recurrences are typically treated with tapering dosage regimens of vancomycin or metronidazole; however, vancomycin appears to be the preferred agent. This method of tapering and pulsing the antimicrobial allows spores to vegetate on *off* days and consequently be killed on days of therapy. This tapering regimen consists of vancomycin 125 mg four times daily for one week; twice daily for one week; once daily for one week; every other day for a week; and, lastly, every three days for two weeks. Restoration of colonic flora with probiotics such as *Saccharomyces boulardii* (Florastor®) and *Lactobacillus* may also be beneficial. Cholestyramine, an anion-binding resin, may enhance the efficacy of antibiotics, but administration must be separated by at least three hours, otherwise antibiotic absorption may be decreased. Intravenous gamma globulin, rifaximin, and nitazoxanide have also been used successfully in some patients with recurrent CDAD. Hospital staff members and patients must take appropriate measures to prevent and reduce the spread of *C. difficile*.

References:

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- Malnick S, Zimhony O. Treatment of *Clostridium difficile*-associated diarrhea. *Ann Pharmacother* 2002;36:1767-75.
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Jennifer M. Cersosimo and Tina M. Pezzella, Pharmacy Clerkship Students

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