

Table 3 Treatment of Recurrent *Clostridium difficile* Diarrhea

-
1. Consider conservative therapy if symptoms are mild
 2. Second course of therapy with metronidazole or vancomycin
 3. Tapered antibiotic course
 4. Other options:
 - Combined therapy with antibiotic and cholestiramine
 - Therapy with microorganisms
 - Bacteriotherapy with enteric flora
 - Saccharomyces boulardii*
 - Lactobacillus GG*
 - Intravenous immunoglobulin treatment
-

cause of the relapse.

Although symptoms of the relapse respond promptly to the antibiotic therapy, new episodes of diarrhea are common after antibiotics are discontinued and these patients may experience numerous episodes of diarrhea. Various approaches have been suggested for the management of repeated relapses such as slow tapering of antibiotic therapy,⁴² use of cholestyramine,⁴³ bacteriotherapy with fecal enemas and oral administration of nontoxicogenic *C. difficile*.⁷ In early clinical trials the administration of *Saccharomyces boulardii*, a non-pathogenic yeast, in combination with metronidazole was shown to reduce the rate of recurrence in patients with multiple recurrences.⁴⁴ The rationale of this treatment is that the yeast competes with *C. difficile* for a metabolically favored niche in the colonic microflora and possibly releases factor(s) that reduce the enterotoxic effects of *C. difficile* toxins.⁴⁵ The yeast itself does not colonize the bowel chronically and is eliminated spontaneously after treatment is discontinued.

References

1. McFarland LV, Mulligan ME, Kwok RY, Stamm WE: Nosocomial acquisition of *Clostridium difficile* infection. *N Engl J Med* 1989; 320: 204-210
2. Hall IC, O'Toole E: Intestinal flora in newborn infants, with description of a new pathogenic anaerobe *Bacillus difficilis*. *Am J Dis Child* 1935; 49: 390-402
3. Bartlett JG, Moon N, Chang TW, Taylor N, Onderdonk AB: Role of *Clostridium difficile* in antibiotic-associated pseudomembranous colitis. *Gastroenterology* 1978; 75: 778-782
4. McFarland LV, Elmer GW, Stamm WE, Mulligan ME: Correlation of immunoblot type, enterotoxin production, and cytotoxin production with clinical manifestations of *Clostridium difficile* infection in a cohort of hospitalized patients. *Infect Immun* 1991; 59: 2456-2462
5. Tabaqchali S: Epidemiologic markers of *Clostridium difficile*. *Rev Infect Dis* 1990; 12(Suppl 2): S192-S199
6. Borriello SP: The influence of the normal flora on *Clostridium difficile* colonisation of the gut. *Ann Med* 1990; 22: 61-67
7. Tvede M, Rask-Madsen J: Bacteriotherapy for chronic relapsing *Clostridium difficile* diarrhoea in six patients. *Lancet* 1989; 1: 1156-1160
8. Kelly CP, Pothoulakis C, LaMont JT: *Clostridium difficile* colitis. *N Engl J Med* 1994; 330: 257-262
9. Anand A, Glatt AE: *Clostridium difficile* infection associated with antineoplastic chemotherapy: a review. *Clin Infect Dis* 1993; 17: 109-113
10. Tedesco FJ, Barton RW, Alpers DH: Clindamycin-associated colitis. A prospective study. *Ann Intern Med* 1974; 81: 429-433
11. Triadafilopoulos G, Pothoulakis C, O'Brien MJ, LaMont JT: Differential effects of *Clostridium difficile* toxins A and B on rabbit ileum. *Gastroenterology* 1987; 93: 273-279
12. Sears CL, Kaper JB: Enteric bacterial toxins: mechanisms of action and linkage to intestinal secretion. *Microbiol Rev* 1996; 60: 167-215
13. Hecht G, Pothoulakis C, LaMont JT, Madara JL: *Clostridium difficile* toxin A perturbs cytoskeletal structure and tight junction permeability of cultured human intestinal epithelial monolayers. *J Clin Invest* 1988; 82: 1516-1524
14. Just I, Wilm M, Selzer J, Rex G, von Eichel-Streiber C, Mann M, Aktories K: The enterotoxin from *Clostridium difficile* (ToxA) monoglucosylates the Rho proteins. *J Biol Chem* 1995; 270: 13932-13936
15. Pothoulakis C, Gilbert RJ, Cladaras C, Castagliuolo I, Semenza G, Hitti Y, Moncrief JS, Linevsky J, Kelly CP, Nikulasson S, Desai HP, Wilkins TD, LaMont JT: Rabbit sucrose-isomaltase contains a functional intestinal receptor for *Clostridium difficile* toxin A. *J Clin Invest* 1996; 98: 641-649
16. Castagliuolo I, LaMont JT, Letourneau R, Kelly C, O'Keane JC, Jaffer A, Theoharides TC, Pothoulakis C: Neuronal involvement in the intestinal effects of *Clostridium difficile* toxin A and *Vibrio cholerae* enterotoxin in rat ileum. *Gastroenterology* 1994; 107: 657-665
17. Pothoulakis C, Castagliuolo I, LaMont JT, Jaffer A, O'Keane JC, Snider RM, Leeman SE: CP-96, 345, a substance P antagonist inhibits rat intestinal responses to *Clostridium difficile* toxin A but not cholera toxin. *Proc Natl Acad Sci USA* 1994; 91: 947-951
18. Castagliuolo I, Riegler M, Pasha A, Nikulasson S, Lu B, Gerard C, Gerard NP, Pothoulakis C: Neurokinin-1 (NK-1) receptor is required in *Clostridium difficile*-induced enteritis. *J Clin Invest* 1998; 101: 1547-1550
19. Kelly CP, Becker S, Linevsky JK, Joshi MA, O'Keane JC, Dickey BF, LaMont JT, Pothoulakis C: Neutrophil recruitment in *Clostridium difficile* toxin A enteritis in the rabbit. *J Clin Invest* 1994; 93: 1257-1265
20. Riegler M, Sedivy R, Pothoulakis C, Hamilton G, Zacherl J, Bischof G, Cosentini E, Feil W, Schiessel R, LaMont JT, Wenzl E: *Clostridium difficile* toxin B is more potent than toxin A in damaging human colonic epithelium in vitro. *J Clin Invest* 1995; 95: 2004-2011
21. McFarland LV: Epidemiology, risk factors and treatments for antibiotic-associated diarrhea. *Dig Dis* 1998; 16: 292-307
22. Hirschhorn LR, Trnka Y, Onderdonk A, Lee ML, Platt R: Epidemiology of community-acquired *Clostridium difficile*-associated diarrhea. *J Infect Dis* 1994; 169: 127-133
23. Kim KH, Fekety R, Batts DH, Brown D, Cudmore M, Silva J Jr, Waters D: Isolation of *Clostridium difficile* from the environment and contacts of patients with antibiotic-associated colitis. *J Infect Dis* 1981; 143: 42-50
24. Bliss DZ, Johnson S, Savik K, Clabots CR, Willard K, Gerding DN: Acquisition of *Clostridium difficile* and *Clostridium difficile*-associated diarrhea in hospitalized patients receiving tube feeding. *Ann Intern Med* 1998; 129: 1012-1019
25. Leung DY, Kelly CP, Boguniewicz M, Pothoulakis C, LaMont JT, Flores A: Treatment with intravenously administered gamma globulin of chronic relapsing colitis induced by *Clostridium difficile* toxin. *J Pediatr* 1991; 118: 633-637
26. Johnson S, Clabots CR, Linn FV, Olson MM, Peterson LR, Gerding DN: Nosocomial *Clostridium difficile* colonisation and