PRACTICE

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# Protecting against *Clostridium difficile* illness

***Background and epidemiology:*** A gram-positive, anaerobic bacterium that is common in the environment, *Clostridium difficile* is transmitted by the fecal–oral route. Its resistant spores are ingested, survive passage through the stomach and ultimately reside in the colon.[1] Antimicrobial therapy disrupts the ecosystem of stool flora, which fosters *C. difficile* overgrowth.

Clinical symptoms range from none (asymptomatic carriage) to watery diarrhea to life-threatening pseudomembranous colitis. The incidence of *C. difficile* carriage, about 1%–3% among healthy adults, is higher among hospital employees and those working with susceptible patients. The rate increases to about 20% with antibiotic use. As many as 31% of high-risk patients in hospital are colonized with *C. difficile*, with only a subset becoming symptomatic.[1]

*C. difficile*–associated diarrhea tends to become a problem in hospitals, nursing homes and other long-term care facilities. Disease severity depends on the pathogenicity of the strain as well as the individual patient's risk factors: use of antibiotic therapy (particularly macrolides, third- and second-generation cephalosporins, clindamycin and quinolones, but also including flagyl and vancomycin),[2] advanced age, underlying illness (especially inflammatory bowel disease), institutional setting; and immunodeficiency due to HIV infection or chemotherapy. Recent outbreaks in Canada, the United Kingdom and the United States suggest that infections are more common than had been suspected, or that new strains have emerged that are more invasive or pathogenic.[3]

Various strains of *C. difficile* possess multiple virulence factors that aid in adherence and colonization, such as flagellar proteins, surface-layer proteins and surface-exposed adhesion proteins. Pathogenic strains of *C. difficile* express 1 or 2 large exotoxins, conventionally identified as A and B — although emerging epidemiologic data also point to a bivalent protein, yet to be fully characterized, that is associated with more severe forms of the illness.

Oligosaccharide receptors for toxin A are expressed on the apical membranes on intestinal epithelia; a toxin B receptor has yet to be identified. Purified toxin A shows enterotoxic and proinflammatory activity. The A and B toxins appear to act synergistically when together: toxin A degrades the integrity of epithelial cells, allowing entry of the more potent cytotoxin B.[1] The magnitude and kinetics of the host's IgG response to toxin A appears to have an important role in the clinical outcome of *C. difficile* infection. Individuals in whom the development of circulating antitoxin A IgG antibodies after primary infection is not prompt are likelier to experience more severe symptoms and recurrent diarrhea.[1]

***Clinical management:*** Diagnosis is generally based on the detection of toxin A or B in stool filtrates. Because of its quick turnaround and ease of use, a toxin-specific enzyme-linked immunosorbent assay (ELISA) is often useful. Detecting cytotoxin B in diarrheal stool filtrates by means of tissue-culture cytotoxicity assay is considered the "gold standard" for diagnosis, but results for such tests may take up to 3 days.

Treatment typically involves cessation of the offending antibiotic, initiation of oral metronidazole or vancomycin therapy, and fluid replacement.[1] In severe cases the colon may perforate, necessitating colectomy. In a recently published series of cases from Quebec,[2] 25.4% of patients with *C. difficile* (68/298) who had an elevated leukocyte count or creatinine level experienced complications (megacolon, perforation, shock or colectomy); of these, 19% died within 30 days of diagnosis.

***Prevention:*** Active and passive immunization (with intravenous immune globulin therapy) is undergoing evaluation for use in the treatment of relapsing cases of *C. difficile*.[1]

Preventing nosocomial transmission of *C. difficile* depends on careful attention to isolation and barrier precautions, cleaning of the physical environment all through the symptomatic period of the disease, and handwashing.[4] Correct handwashing involves a 2-minute scrub with soap to remove the surface layer of skin oil (which holds spores), followed by hand-drying with a disposable paper towel.

After a series of *C. difficile*–associated deaths in Quebec, the provincial government responded by introducing more intensive surveillance, and the Public Health Agency of Canada (see www.phac-aspc.gc.ca/c-difficile) initiated a 6-month surveillance study in teaching hospitals across the country.

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## References

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