# Community-acquired Clostridium difficile infection

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he Gram-positive anaerobic bacterium *Clostridium difficile* is transmitted by the fecal-oral route.<sup>1,2</sup> *Clostridium diffi*cile infection (CDI) can cause illness ranging from diarrhea to colitis, toxic megacolon, and death. The incidence in the United States has doubled since the 1990s, to 95.3 cases per 100000 in acute care settings.34 The classic risk factors include recent antibiotic use, recent hospitalization, and old age. Clostridium difficile is responsible for 15% to 25% of antibiotic-associated diarrhea.<sup>2</sup> Recent studies have suggested dramatic changes in the epidemiology of CDI.<sup>3-6</sup> Members of community populations are acquiring CDI who were previously thought to be at low risk. Community-acquired CDI is defined as the onset of symptoms within 48 hours of admission to hospital or more than 12 weeks after discharge. This case report presents an important paradigm shift: C difficile can no longer be viewed solely as a hospital-acquired infection.

## Case

A 45-year-old woman with no relevant past medical history presented to her family physician's office complaining of foul-smelling, watery diarrhea for 3 days. She had been having 4 to 5 nonbloody bowel movements per day. She was afebrile and otherwise well. She reported no travel, no sick contacts at home, and had not eaten anything unusual. She denied any recent hospitalizations or antibiotic use. Her physician assumed she had viral gastroenteritis; she was instructed to drink lots of fluids and was sent home. She returned 4 days later with the same pattern of bowel movements. She was now also experiencing lower abdominal pain. A stool sample was sent for immunoassay for glutamate dehydrogenase antigen and for C difficile toxins. Results were positive for both. The patient was treated with a 10-day course of metronidazole and made a full recovery.

## **EDITOR'S KEY POINTS**

- Recent epidemiologic studies have challenged the belief that Clostridium difficile infection (CDI) is a purely hospital-acquired infection. Further, communityacquired CDI is now known to affect individuals who were previously thought to be at low risk. Primary care physicians should be aware of the changing epidemiology of CDI.
- Asymptomatic carriers could have a role in disseminating the bacteria in the community. When considering C difficile-associated diarrhea, it is not only important to inquire about any recent hospitalizations but also about any recent health care exposure. The emergence of new virulent strains in recent years has been associated with increasing severity of CDI.
- Primary care physicians need to maintain a high index of suspicion in patients with diarrhea lasting longer than 24 hours, even in the absence of classic risk factors.



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#### Discussion

Clostridium difficile infection has historically been considered a hospital-acquired infection. However, a recent population-based study found 41% of CDIs were actually community acquired.5 This is a substantial proportion of CDIs and these results have been replicated in other surveillance studies.<sup>3,6</sup> It is becoming apparent that communityacquired CDI affects populations previously thought to be at low risk: younger patients and patients who had no exposure to antibiotics in the 12 weeks before infection.<sup>5,6</sup> This suggests additional factors might play a role in communityacquired CDI. First, asymptomatic carriers could have a role in disseminating the bacteria in the community. Previous studies have shown that asymptomatic carriers of C difficile far outnumber patients with CDI at a ratio as high as 7 to 1.7 It is also known that infants younger than 2 years of age can be asymptomatic carriers of C difficile, with colonization rates of up to 70%.6 Contact with children younger than 2 years of age has been associated with an increased risk of community-acquired CDI.6,8 Second, it was found that 82% of patients with community-acquired CDI had some form of health care exposure other than hospitalization (eg, family physician's office, dental clinic, dialysis clinic, emergency department).6 When considering C difficile-associated diarrhea, it is not only important to inquire about any recent hospitalizations but also about any recent health care exposure. Finally, the emergence of new virulent strains in recent years has been associated with increasing severity of CDI. The most common strain is North American pulsed-field gel electrophoresis (NAP) type 1, which

is characterized by higher toxin production, an increased mortality rate, and substantial fluoroquinolone resistance.1 Population-based studies have shown the incidence of NAP1 in the community to be approximately 20%.<sup>1,3</sup> Other common strains include NAP4 and NAP11.<sup>3</sup>

The diagnosis and treatment of CDI is the same regardless of where it is acquired. The American Academy of Family Physicians recommends testing for C difficile if a patient has 3 or more unformed bowel movements in 24 hours.<sup>2</sup> Testing includes enzyme immunoassay (EIA) for the glutamate dehydrogenase antigen and for C difficile toxins A and B. Clostridium difficile infection is present if EIAs reveal positive results for both the antigen and the toxins. If there is discordance between the EIA results, polymerase chain reaction should be performed for C difficile toxigenic genes. Stool testing should not be repeated after treatment in patients who are asymptomatic.9

Initial treatment of CDI requires discontinuing the offending antibiotic if it is no longer indicated. Choice of treatment then depends on the severity of infection. A randomized, placebo-controlled trial found that metronidazole and vancomycin were equally effective for mild infection but vancomycin was superior for severe infection.<sup>10</sup> Severe infection was defined as the presence of 2 of the following: age older than 60 years, temperature greater than 38.3°C, albumin level less than 25 g/L, and white blood cell count greater than 15×10<sup>9</sup>/L.<sup>10</sup> Evidence of pseudomembranous colitis or admission to an intensive care unit were also considered to indicate severe infection. 10 In 2012, fidaxomicin was approved by Health Canada for the treatment of CDI.11 Fidaxomicin has been shown to be noninferior to vancomycin in clinical cure after treatment and was also associated with a lower rate of recurrence. 12 However, the substantially higher cost of fidaxomicin compared with vancomycin or metronidazole currently limits its use.

Probiotics given for the duration of antibiotic therapy might be beneficial in preventing CDI.13 In a metaanalysis of 20 randomized controlled trials, which included 3818 mostly adult inpatients, probiotics reduced the incidence of C difficile-associated diarrhea by 66%.14 However, the PLACIDE (Probiotic Lactic Acid Bacteria and Antibiotic-associated and C difficile Diarrhoea in the Elderly) trial, a recent multicentre randomized controlled trial of 2941 inpatients 65 years of age and older, compared a preparation of lactobacilli and bifidobacteria with placebo and found no difference between the groups in antibiotic-associated diarrhea, including C difficile–associated diarrhea. 15 Therefore, it appears that probiotics reduce CDI in younger patients taking antibiotics but might not be as beneficial in elderly patients.

Although community-acquired CDI is generally less severe than hospital-acquired CDI, it is still important to identify patients at high risk early to direct appropriate therapy and improve outcomes. A 2012 study of community-acquired CDI found that 40% of patients

required hospitalization, 20% had severe infection, 20% had treatment failure, and 28% had recurrence.16 Hospitalization was associated with significant morbidity (P=.001) by predisposing patients to other hospitalacquired infections and venous thromboembolism. These authors also found that patients who were older, had more severe disease, and had more comorbid conditions were more likely to require hospitalization. There is a paucity of Canadian literature on this topic. Most studies dealt with communities exclusively in the United States. This highlights the need for an epidemiologic study in Canada.

## Conclusion

Recent epidemiologic studies have challenged the belief that CDI is a purely hospital-acquired infection. Further, community-acquired CDI is now known to affect individuals who were previously thought to be at low risk (younger and without recent exposure to antibiotics). Therefore, it is prudent for primary care physicians to be aware of the changing epidemiology of CDI. They will need to maintain a high index of suspicion in patients with diarrhea lasting longer than 24 hours, even in the absence of classic risk factors.

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### Competing interests

None declared

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