

## Spectrum of *Clostridium difficile* infections outside health care facilities

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∞ See related research paper by Dial and colleagues, page 767

**C***lostridium difficile* is mainly known as a hospital-acquired, nosocomial infection. The hospital environment is considered an ideal place for *C. difficile* to persist, infect susceptible elderly patients and spread among vulnerable patients. However, there are several reports of *C. difficile* infection acquired in the community. This is not surprising, since *C. difficile* has been cultured from the stool of 3% of healthy adults and up to 80% of healthy newborns and infants.<sup>1</sup> In addition, the emergence of new strains of *C. difficile* that cause large outbreaks in hospitals and nursing homes will promote the carriage and circulation of such strains in the general population. This will first and foremost affect admitted patients, not all of whom will have symptoms of *C. difficile*-associated diarrhea during their hospital stay. Eventually, such carriage, even if transient, will increase the incidence and spread of *C. difficile* infection outside well-known risk groups that currently share the characteristic of prior hospital admission.

Host factors and the normal colonic flora are assumed to be of specific importance in containing *C. difficile* colonization. Risk factors associated with *C. difficile* infection are increased age, recent hospital admission, previous use of antibiotics and conditions that may affect the colonic flora. In this issue of *CMAJ*, Dial and colleagues<sup>2</sup> report from their matched, nested case-control study that about half of the patients admitted to hospital because of community-acquired *C. difficile* infection had no recent antibiotic exposure. Clearly, this observation is of interest. However, the authors restricted the study population to patients 65 years of age and older who had severe *C. difficile* infection and at least 1 prior hospital stay during the 8-year study period. The question remains whether community-acquired *C. difficile* infection occurs among younger individuals without any predisposing condition or hospital stay.

When studying *C. difficile* infection with an apparent onset in the community, it is important to have a consensus on an appropriate definition. This is especially relevant when one wants to determine whether community-acquired *C. difficile* infection is associated with use of a health care facility. The European Centre for Disease Prevention and Control and the US Centers for Disease Control and Prevention have proposed similar definitions for community-acquired *C. difficile* infection: the onset of symptoms occurred while the patient was outside a health care facility and the patient had not been discharged from a health care facility within

### Key points

- Reports from Canada, the United States and Europe indicate that the rate of community-acquired *Clostridium difficile* infection may be increasing.
- A large proportion of cases of community-acquired *C. difficile* infection are not linked to recent antibiotic therapy, increased age, comorbidity or prior hospital admission.
- Because the absence of classic risk factors is unreliable for ruling out community-acquired *C. difficile* infection, it is worthwhile to test for *C. difficile* even in patients with diarrhea who have no known risk factors.
- Further research to identify risk factors for community-acquired *C. difficile* infection is urgently needed.

12 weeks before symptom onset (community onset, community acquired); or the onset of symptoms occurred within 48 hours after admission to a health care facility and the patient had no prior stay in a health care facility within the 12 weeks before symptom onset (health-care-facility onset, community acquired).<sup>1,3</sup>

Using these definitions, Kutty and colleagues<sup>4</sup> found that 34% of 604 patients in North Carolina with community-onset *C. difficile* infection truly had community-acquired infection. Most of the cases acquired in health care facilities that had a community onset occurred within 4 weeks after discharge. Community-acquired *C. difficile* infection has also been reported in otherwise healthy children, pregnant women and adults without known risk factors. Klein and colleagues<sup>5</sup> found an unexpectedly high rate of *C. difficile* infection of 6.7% among children with diarrhea who presented to a pediatric emergency department. Roupahel and coauthors<sup>6</sup> described 10 previously healthy women who had severe *C. difficile* infection during pregnancy. Only 3 of the women had a history of hospital admission and had used antibiotics within the 3 months before symptom onset. The US Centers for Disease Control and Prevention reported an increase in severe community-acquired *C. difficile* infection in populations previously considered to be at low risk.<sup>7</sup> Of 33 patients in whom *C. difficile* infection developed, 8 (24%) reported no direct exposure to antimicrobial agents within the 3 months before symptom onset, but 3 of them reported having had close con-

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tact with an individual who had diarrhea. Finally, a surveillance study of community-acquired *C. difficile* infection in Connecticut revealed an incidence of 6.9 per 100 000 inhabitants.<sup>8</sup> Of 241 patients, 36% had no history of antibiotic use within 3 months before symptom onset, and 25% had no underlying medical condition or recent hospital admission and, moreover, were younger than 45.

Community-acquired *C. difficile* infection is almost certainly underdiagnosed. However, there is an increasing interest worldwide in recognition of this new disease entity. In a well-designed prospective study in Germany, Weil and colleagues<sup>9</sup> found that immunoassay results were positive for *C. difficile* toxins A and B in 66 (9.4%) of the stool samples submitted by general practitioners of 703 patients with diarrhea. Of these 66 patients, 35 (53%) truly had community-acquired infection. Recent use of antibiotics was reported by 52% of the 66 patients, most frequently cephalosporins (33%) and fluoroquinolones (33%). In a prospective surveillance study in the United Kingdom, Wilcox and colleagues<sup>10</sup> found that 2.1% of 2000 randomly selected fecal samples were positive for *C. difficile* cytotoxin. Although exposure to antibiotics in the 4 weeks before symptom onset and hospital admission in the 6 months before onset were significantly associated with *C. difficile* infection, about one-third of cases had neither risk factor. In a third, recently completed study, in the Netherlands, Bauer and colleagues<sup>11</sup> identified *C. difficile* infection in 37 (1.5%) of 2423 patients with diarrhea attending general practitioners. Of the patients with *C. difficile* infection, 65% had not been admitted to a health care institution in the year before symptom onset, 42% had not used antibiotics during the 6 months before symptom onset, and 23% had neither risk factor.

The results of these studies indicate that it is worthwhile to test for community-acquired *C. difficile* infection in patients with diarrhea who have no known risk factors. Practitioners cannot rely on classic risk factors such as recent antibiotic use, prior hospital stays, comorbidity and age of 65 years or more.<sup>12</sup> There is an urgent need to identify and better characterize potential risk factors for community-acquired *C. difficile* infection to explain the large proportion of cases not linked to recent antibiotic therapy or hospital stays. Moreover, the role of animal reservoirs should be explored in this respect, since *C. difficile* strains from humans and animals of-

ten belong to similar polymerase chain reaction (PCR) ribotypes and have identical virulence factors.<sup>13,14</sup>

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