

## FIVE THINGS TO KNOW ABOUT ...

Treating *Clostridium difficile* infection

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**First-line treatment for mild or moderate *Clostridium difficile* infection is metronidazole; vancomycin is first-line treatment for severe infection**

A randomized controlled trial (RCT) showed that metronidazole was as effective as vancomycin taken orally for the treatment of mild *Clostridium difficile* infection. However, in cases of severe infection, 97% of patients given vancomycin had clinical resolution compared with only 76% of those given metronidazole.<sup>1</sup> The Society for Healthcare Epidemiology of America and the Infectious Diseases Society of America recommend metronidazole as first-line therapy for mild or moderate *C. difficile* infection and vancomycin for severe infection (Box 1).<sup>2</sup> Although criteria for severe infection differ between guideline and trial, both include a leukocyte count greater than  $15 \times 10^9$  cells/L.

**Box 1: Classification of the severity of *Clostridium difficile* infection<sup>1,2</sup>**

Severity	Guidelines <sup>1</sup>	Randomized controlled trial <sup>2</sup>
Mild–moderate	<ul style="list-style-type: none"> <li>• <math>&lt; 15 \times 10^9</math> leukocytes/L and</li> <li>• Serum creatinine <math>&lt; 1.5</math> times premorbid level</li> </ul>	<ul style="list-style-type: none"> <li>• Infections that do not satisfy the criteria for severe infection</li> </ul>
Severe	<ul style="list-style-type: none"> <li>• <math>\geq 15 \times 10^9</math> leukocytes /L or</li> <li>• Serum creatinine <math>\geq 1.5</math> times premorbid level</li> </ul>	Two of: <ul style="list-style-type: none"> <li>• Age <math>&gt; 60</math> years</li> <li>• Temperature <math>&gt; 38.3^\circ\text{C}</math></li> <li>• Albumin <math>&lt; 25</math> g/L</li> <li>• <math>&gt; 15 \times 10^9</math> leukocytes/L</li> </ul> or one of: <ul style="list-style-type: none"> <li>• Colonoscopic evidence of pseudo-membranous colitis</li> <li>• Treatment in intensive care unit</li> </ul>

**Fidaxomicin is as effective as vancomycin for treatment of *C. difficile* infection and results in fewer relapses**

In a phase 3 controlled clinical trial, fidaxomicin was noninferior to vancomycin in achieving clinical resolution of *C. difficile* infection.<sup>3</sup> Of note, 13.3% of patients given fidaxomicin had recurrent infection within four weeks, compared with 24.0% of patients given vancomycin.<sup>3</sup>

**Duodenal infusion of donor feces is more effective than vancomycin for recurrent infection**

In an RCT comparing treatment of recurrent *C. difficile* infection with vancomycin or duodenal infusion of donor feces, 81% of patients in the fecal infusion group had resolution of the infection, compared with 31% of patients given vancomycin alone.<sup>4</sup>

**Probiotics have no role in the treatment of *C. difficile* infection, and their role in prophylaxis is unclear**

The latest guidelines do not recommend the use of probiotics for prophylaxis or treatment of *C. difficile* infection.<sup>2</sup> A systematic review and meta-analysis of 20 RCTs found moderate-quality evidence suggesting a 34% risk reduction of *C. difficile* infection with the use of probiotics for prevention, with no increase in adverse events; this finding was limited by the variability of probiotic regimens and missing data in 13 studies.<sup>5</sup> However, a recent high-quality RCT found no evidence that a multistrain probiotic preparation prevented infection.<sup>6</sup>

For references, please see Appendix 1, available at [www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.131315/-/DC1](http://www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.131315/-/DC1)

**Phase 3 clinical trials of *C. difficile* vaccines are underway**

The *Cdiffense* study is a phase 3 RCT that will evaluate the efficacy of inactivated *C. difficile* toxoids A and B in preventing *C. difficile* infection. Phase 1 trials showed development of an immune response in humans.<sup>7</sup> Phase 2 results are forthcoming.

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