

## ***Clostridium difficile* (C. diff) Fact Sheet**

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### **Overview**

*Clostridium difficile* (C. diff) is a potentially life-threatening, spore-forming bacterium that causes intestinal disease. The risk of contracting CDI increases with age, antibiotic treatment and time spent in hospitals or nursing homes, where multiple cases can lead to outbreaks. While most types of healthcare-associated infections (HAIs) are declining, C. diff is emerging as a leading cause of life-threatening, HAIs worldwide.<sup>1, 2</sup>

According to the Centers for Disease Control and Prevention (CDC), approximately 500,000 Americans are infected with C. diff,<sup>3</sup> and at least 14,000 fatalities are attributed to C. diff each year.<sup>1</sup> Globally, there has been an increase in the incidence and severity of C. diff infection (CDI) reported in many European and Asian countries, possibly due to the emergence of hyper-virulent strains.<sup>4</sup> Deaths related to C. diff increased 400 percent between 2000 and 2007.<sup>5</sup> With the emergence of difficult-to-manage strains of C. diff (such as BI/NAP1/027), CDI has become more frequent, more severe and more difficult to treat in recent years, raising concerns about how to both control and prevent transmission of the disease.<sup>2</sup>

### **Cause**

A main source of C. diff is infected patients who release spores into the environment that can then infect other patients. When antibiotics disrupt the gut's normal flora and a person has ingested C. diff spores, the C. diff bacteria multiply and release potent toxins that can damage a patient's intestinal lining and cause C. diff disease.<sup>6</sup> The susceptibility for infection generally increases with age.<sup>5</sup>

### **Risk Factors**

CDI symptoms typically manifest in hospital patients (25 percent) and in people recently cared for in nursing homes, doctors' offices and clinics (75 percent).<sup>5</sup>

- **Highest Risk:** older adults in hospitals or long-term care facilities who take broad-spectrum antibiotics; advanced age correlates with severity of disease, likelihood of recurrence and CDI-associated death.<sup>2</sup>
- **Age Demographics:** almost half of infections occur in people younger than 65; more than 90 percent of CDI-related deaths occur in people 65 and older.<sup>5</sup>
- **Contributing Factors:** antibiotic exposure, proton pump inhibitors, gastrointestinal surgery/manipulation, serious underlying illness and/or immune-compromising conditions.<sup>2</sup>

### **Symptoms and Impact on the Patient**

C. diff toxins cause gastrointestinal disease that can lead to death in approximately eight to 15 percent of patients.<sup>7</sup>

- **Symptoms:** range from mild diarrhea to life-threatening pseudomembranous colitis and often include dehydration, abdominal pain and spasms.<sup>2</sup>
- **Complications:** bowel paralysis and toxic megacolon, a lethal condition.<sup>2</sup>
- **Recurrence:** 20 to 30 percent of patients experience recurrences of CDI, which result in re-hospitalizations and longer hospital stays.<sup>8</sup>

### **Associated Costs**

- Combined data from the U.S. and European Union (EU) indicate that healthcare systems spend more than \$7 billion annually on CDI acute care.
  - *Regional Breakdown:* U.S. (\$4.8 billion)<sup>9</sup>, EU (€3 billion)<sup>10</sup>
- Costs are expected to almost double over the next four decades.<sup>10</sup>

- Estimates of the cost of infection range from £10,000 per case in the United Kingdom (U.K.) to \$12,000 per case in the U.S.<sup>2,11</sup>
- On average, CDI patients in the U.S. spend an additional three<sup>12</sup> to six<sup>13</sup> days in the hospital. In Europe, CDI can extend hospitalization by 13 (Spain) to 30 days (U.K.).<sup>14</sup>

### **Current Treatments**

- Totally eliminating *C. diff* spores is extremely difficult because they can survive routine environmental cleaning with detergents, as well as hand sanitization with alcohol-based gels.<sup>2</sup>
- CDI can be treated with an appropriate course (approximately 10 days) of antibiotics.<sup>2</sup>
- Fecal microbiota transplantation (FMT) has been used as a treatment modality in patients with severe, recurrent CDI because it has the potential to restore natural colonic bacteria.<sup>3</sup>
- In some cases, removing the colon may be required as the risk of perforation increases due to the high fatality rate associated with ruptures.<sup>2</sup>

### **Current Methods of Prevention**

There is currently no vaccine or antibiotic with an indication for the prevention of CDI approved on the market.

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<sup>1</sup> Centers for Disease Control and Prevention. Clostridium difficile Infection. Centers for Disease Control and Prevention. [http://www.cdc.gov/hai/organisms/cdiff/cdiff\\_infect.html](http://www.cdc.gov/hai/organisms/cdiff/cdiff_infect.html). Last Updated March 1, 2013. Accessed May 30, 2013.

<sup>2</sup> Centers for Disease Control and Prevention. Frequently Asked Questions about Clostridium difficile for Healthcare Providers. Centers for Disease Control and Prevention. [http://www.cdc.gov/HAI/organisms/cdiff/Cdiff\\_faqs\\_HCP.html](http://www.cdc.gov/HAI/organisms/cdiff/Cdiff_faqs_HCP.html). Last Updated March 6, 2013. Accessed May 30, 2013.

<sup>3</sup> Rohlke F and Stollman N. Fecal microbiota transplantation in relapsing Clostridium difficile infection. *Therap Adv Gastroenterol*. 2012 November; 5(6): 403–420. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3491681/#bibr37-1756283X12453637>. Accessed May 30, 2013.

<sup>4</sup> Jones AM, Kuijper EJ and Wilcox MH. Clostridium difficile: A European perspective. *Journal of Infection* 2013; 66(2): 115-128. <http://www.sciencedirect.com/science/article/pii/S0163445312003052>. Accessed May 30, 2013

<sup>5</sup> Centers for Disease Control and Prevention. Making Health Care Safer: Stopping *C. difficile* Infections. Centers for Disease Control and Prevention. <http://www.cdc.gov/VitalSigns/HAI/index.html>. Last Updated August 21, 2012. Accessed May 30, 2013.

<sup>6</sup> Delmee M and Warny M. (1995). Clostridium difficile colitis: recent therapeutical and immunological considerations. *Acta Gastroenterol Belg*, 58 (3-4), p.313-317.

<sup>7</sup> Mitchell BG and Gardner A. (2012) Mortality and Clostridium difficile infection: a review. *Aric journal*.

<sup>8</sup> Garey KW, et al. (2008) Meta-analysis to assess risk factors for recurrent Clostridium difficile infection. *Journal Hospital Infection*, 70, p. 298-304.

<sup>9</sup> Dubberke ER and Olsen MA. Burden of Clostridium Difficile on the Healthcare System. *Clinical Infectious Diseases* 55, no. suppl 2 (2012): S88–S92. doi:10.1093/cid/cis335.

<sup>10</sup> European CDC, Clostridium Difficile basic facts. Accessed May 20, 2013. [http://www.ecdc.europa.eu/EN/HEALTHTOPICS/CLOSTRIDIUM\\_DIFFICILE\\_INFECTIO/BASIC\\_FACTS/Pages/basic\\_facts.aspx](http://www.ecdc.europa.eu/EN/HEALTHTOPICS/CLOSTRIDIUM_DIFFICILE_INFECTIO/BASIC_FACTS/Pages/basic_facts.aspx)

<sup>11</sup> O'Brien J, et al. (2007) The Emerging Infectious Challenge of Clostridium difficile-Associated Disease in Massachusetts Hospitals: Clinical and Economic Consequences. *Infect Control and Hospital Epidemiology*, 28 (11).

<sup>12</sup> Dubberke ER, Butler AM, Reske KA, et al. Attributable outcomes of endemic Clostridium difficile-associated disease in nonsurgical patients. *Emerg Infect Dis*. 2008b; 14(7):1031-8.

<sup>13</sup> Zilberberg MD, Nathanson BH, Sadigov S, et al. Epidemiology and outcomes of clostridium difficile-associated disease among patients on prolonged acute mechanical ventilation. *Chest*. 2009 Sep;136(3):752-8.

<sup>14</sup> Eckmann, et al. (2013) Increased hospital length of stay attributable to Clostridium difficile infection in patients with four co-morbidities: an analysis of hospital episode statistics in four European countries. Manuscript submitted to *European Journal of Health Economics*.