

# ***Clostridium difficile***

## **Introduction and Epidemiology**

*Clostridium difficile* is the most common non-epidemic cause of acute diarrhea in the long-term care setting. Long-term care settings, because of high rates of antibiotic use and close resident proximity, are particularly prone to high disease incidence and outbreaks of disease. Because long-term care residents often are older and have co-morbid medical conditions, they are more likely to experience poor outcomes from *Clostridium difficile* disease.

*Clostridium difficile* is estimated to be the cause of 15-25% of the 3 million annual cases of antibiotic-associated diarrhea. It has a mortality rate of between 1 and 2.5 percent, and is responsible for 5000-6000 annual deaths in the United States. Analysis of hospital discharge data shows a significant increase in the proportion of patients discharged from acute care hospitalization with a diagnosis of *Clostridium difficile* from 2000 to 2003. This increase occurred primarily in patients over the age of 65 years, many of who transfer to long-term care facilities. In 2003, 57,000 patients transferred from acute care to long-term care had *C. difficile* associated diarrhea at the time of transfer.<sup>1</sup>

## **New Epidemic Strain**

Over the past several years, an increase in the severity of disease caused by *Clostridium difficile* has been well described. A case series from Pittsburgh described an increased incidence of life-threatening symptoms,<sup>2</sup> and a New Jersey survey demonstrated increases in disease incidence, complications, and outbreaks.<sup>3</sup>

Research has demonstrated the emergence of a new epidemic strain in the United States, Canada, and Europe. This strain (NAP-1/BI) is associated with increased disease severity and worsened clinical outcomes. It is characterized by increased production of toxins A and B<sup>4</sup> and production of a binary toxin; the significance of the latter is unclear. This strain also shows increased resistance to the fluoroquinolone class of antibiotics,<sup>5</sup> making it more likely to survive in the GI tract when other bacteria are killed during a course of fluoroquinolone therapy.

## **Pathogenesis**

Rates of colonization with *Clostridium difficile* are much higher than rates of disease caused by the organism. Approximately 4-20% of long-term care residents are colonized with *Clostridium difficile*, with higher rates during outbreaks. Colonization rates range from 3% in healthy adults to 70% in newborns. It is hypothesized that colonization may be protective against diarrheal disease by stimulating an appropriate immune response.

In order for *Clostridium difficile* to cause symptomatic disease, two processes must occur: acquisition of the organism and disruption of normal gastrointestinal flora (usually by antibiotics). These two events generally occur in close temporal proximity to each other. Chronic colonization is not felt to be a major risk factor for development of disease, and may be protective against the development of clinical symptoms.<sup>6</sup>

Acquisition of *Clostridium difficile* usually occurs via fecal-oral contamination. Persons with active diarrhea caused by the organism are highly infectious. *Clostridium difficile* spores are able to survive for months in the environment, and decontamination of contaminated surfaces usually requires the use of bleach-containing products. Transmission usually occurs via contaminated objects such as commodes, telephones, or door handles) or via the hands of healthcare workers who touch contaminated objects or infected patients.

## **Risk Factors**

The most important risk factor for *Clostridium difficile* disease is prior antibiotic use. Over 90% of cases of disease occur during or soon after antibiotic therapy. While essentially all antibiotic classes increase the risk of disease, broad spectrum agents are more likely to be associated with disease. The fluoroquinolone class of antibiotics, due to high rates of usage, is in some studies the class of antibiotic most likely to be associated with disease.<sup>7</sup>

Other potential risk factors for *Clostridium difficile* disease include older age, use of feeding tubes, prolonged hospitalization, severe underlying medical problems, and possibly the use of anti-ulcer medications such as proton pump inhibitors. Long-term care residents often have many of these risk factors, in addition to high rates of antibiotic use.

## **Clinical Manifestations**

Infection with *Clostridium difficile* can produce a spectrum of clinical manifestations, ranging from none in the case of asymptomatic colonization to severe infection resulting in death. Diarrhea is the most common symptom of *Clostridium difficile* disease. It is usually characterized by frequent, loose, watery bowel movements. Other common accompanying symptoms include fever and cramping abdominal pain. In severe disease, patients can develop toxic megacolon and pseudomembranous colitis. Such patients often present in shock with findings of an acute abdomen on exam, and are at high risk of death from the infection. Leukocytosis is common with more severe infection, and may be an early warning sign for fulminant infection even in the absence of other symptoms.



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## **Diagnosis**

A number of tests are available for the diagnosis of infection with *Clostridium difficile*. The most commonly used test is enzyme immunoassay for toxin A production. This test has an estimated sensitivity of 63-99%.<sup>8</sup> Culture of the organism is a more sensitive test, but is more expensive and not available everywhere. The diagnosis of *Clostridium difficile* is sometimes made on lower endoscopy, but this is an invasive test, has lower sensitivity, and should not be relied on routinely in the initial diagnostic approach.

When testing stool samples for *Clostridium difficile*, loose watery stools should be sent. Multiple stool samples may increase the diagnostic yield of the enzyme immunoassay test. Asymptomatic patients should not be tested, nor should toxin testing or culture be used as a test of cure in patients without diarrhea.

## **Treatment**

Diarrheal illness caused by *Clostridium difficile* is usually treated with metronidazole (oral or intravenous) or oral vancomycin. Intravenous vancomycin is ineffective as it does not penetrate into the gastrointestinal system. Metronidazole is generally preferred for most cases of mild to moderate disease, though vancomycin may be preferred for severe infection.

In addition to specific antibiotic therapy against *Clostridium difficile*, any inciting antibiotics should be stopped if at all possible. The use of opiates or other anti-peristaltic agents should generally be avoided. Supportive care, with fluid and electrolyte replenishment, is often required. In cases of severe disease, surgical intervention is often required.

Persons with asymptomatic colonization should not be treated with antibiotics. There is no role for routine screening for asymptomatic colonization, and no proven benefit of pre-emptive treatment, even in outbreak situations.<sup>9</sup>

## **Prevention**

There are two aspects to the prevention of *Clostridium difficile* associated disease: preventing acquisition of the organism and preventing disruption of normal flora which leads to disease. Good infection control practices (hand hygiene, cleaning potentially contaminated surfaces, and contact isolation of patients with fecal incontinence) are important in preventing the transmission of *Clostridium difficile*. As alcohol-based hand rubs are not as effective at killing spores as soap and water, using soap and water for hand-hygiene may be preferred when caring for patients with *Clostridium difficile*.

Appropriate and judicious use of antibiotics is the second key facet in preventing disease caused by *Clostridium difficile*. In long-term care, as is true for all healthcare settings, antibiotics are often prescribed when not indicated, for conditions such as

asymptomatic bacteriuria or viral upper respiratory infection. Using antibiotics judiciously, for only the minimum duration required, would be expected to decrease the risk of disease caused by *Clostridium difficile*.

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