# *Clostridium difficile*

**For Healthcare Providers: Risks, Testing and Treatment, and Infection Prevention**

## What is *Clostridium difficile*?

*Clostridium difficile*, a toxin-producing, spore-forming, anaerobic gram-positive bacillus, is a significant cause of infectious diarrhea, called *C. difficile* infection (CDI).

## Who gets CDI?

Persons 65 years of age and older as well as those with multiple medical co-morbidities are at increased risk for CDI. People with some conditions, including inflammatory bowel disease and Crohn's Disease, often have a higher rate of CDI. This may be due to a combination of colonic disruption and use of immunosuppressive medications to control those conditions. It is suspected that proton pump inhibitors (PPIs) are also associated with an increase in the risk of CDI, presumably due to inhibition of gastric acid, the body's natural defense against *C. difficile* spores. Other events that impair the normal colonic mucosa may also precipitate CDI, including gastrointestinal surgery, colitis, chemotherapy, and treatment with stool softeners and laxatives. There are also cases of community acquired CDI, often in younger patients, where common risk factors are absent.

Antibiotic exposure is the most important modifiable risk for acquisition of CDI. The risk varies depending on the antibiotic's ability to disrupt normal intestinal flora, enabling *C. difficile* to establish in the bowel. There is a well-defined dose-dependent increase in the risk of CDI with increasing dose and days of antibiotic exposure. In a recent study, patients who received two antibiotics compared to those receiving only one had a 2.5-fold increased risk of CDI.

**Table 1. Classification of Antibiotics Relative to Risk of Contribution to CDI**

| High Risk |
|---|
| Fluoroquinolones |
| Carbapenem |
| Cephalosporins (2nd, 3rd, and 4th generation) |
| Clindamycin |
| **Medium Risk** |
| Penicillins |
| Penicillin + β-lactamase inhibitors (i.e., amoxicillin/clavulanate, piperacillin/tazobactam) |
| 1st generation cephalosporin |
| Macrolides (i.e., azithromycin, clarithromycin) |
| **Low Risk** |
| Tetracyclines |
| Sulfamethoxazole/Trimethoprim |
| Aminoglycosides |
| Fosfomycin |
| Rifampin |
| Linezolid |
| Nitrofurantoin |

Table 1 highlights common antibiotic classes and their potential for contributing to CDI. The ability of clindamycin and cephalosporin to induce CDI is well known. Recently, fluoroquinolones have emerged as a significant risk factor. Widespread use of these broad agents over the last decade directly influenced the development of the highly fluoroquinolone resistant (NAP1) strain of *C. difficile***.**

## How is *C. difficile* spread?

*C. difficile* is not part of the normal fecal flora in most people. Infection is most often acquired in a medical setting, such as a long-term care environment, hospital, or clinic, from a contaminated surface or a healthcare provider's hands.

## What are the symptoms of CDI?

Clinically significant diarrhea (≥ 3 watery stools/day) following recent antibiotic exposure and/or hospitalization should prompt evaluation. Fever, leukocytosis, and abdominal pain combined with any of the above should raise suspicion for CDI. It is important to note that presentation can occur weeks or even months after exposure to an antibiotic and can be triggered by as little as one dose of medication.

## What is the appropriate testing for CDI?

***NOTE:*** Only watery, unformed stool samples should be sent for analysis; *C. difficile* detected in formed stool likely indicates asymptomatic carriage and should **not** be treated.

The most frequently used diagnostic test for CDI is enzyme immunoassay (EIA) to detect toxins A and B. It is a quick and easy test to perform and inexpensive. The sensitivity of the test is relatively low; however, false negative results are common. **High clinical suspicion of CDI should override a negative EIA.**

PCR (polymerase chain reaction) is a more expensive but far more sensitive test than EIA, virtually eliminating false negative results. By detecting the organism, however, and not the active disease, false positive results and detection of asymptomatic carriage are common.

Diagnostic tests, such as PCR and EIA, should **not** be repeated after a course of therapy to assess for clearance of *C. difficile*. The spores continue to persist for weeks, even months, after an effective course of antibiotic therapy and do not represent true disease in the absence of symptoms.

## Does having CDI once make a person immune to later infection with *C. difficile*?

No. People can contract CDI repeatedly.

## What are the complications associated with CDI?

Illness can range from mild gastrointestinal symptoms to life-threatening toxic megacolon and death. Since 2002, an increase in the severity of CDI has been seen, and in the United States CDI-associated deaths increased 400% between 2000 and 2007. CDI is now linked to ~14,000 deaths per year, mostly in people 65 and over. *C. difficile* infections result in at least $1 billion in extra healthcare costs annually.

## What are the recommended treatments/interventions for CDI?

**Cessation of Precipitating Antibiotic:**
Cessation of antibiotic therapy should occur in all patients with CDI when feasible. If antibiotic therapy must be continued, it should be narrowed when possible to antimicrobials less likely to exacerbate CDI *(see Table 1).*

**For Asymptomatic Colonization:**
Only symptomatic patients with diarrhea significantly different from baseline should be tested and treated. PCR can too easily detect asymptomatic *C. difficile* colonization, a condition which should **not** be treated. Treating a colonized patient offers no benefit and actually increases the risk of developing active CDI.

**For Mild-to-Moderate Disease:**
For younger patients with mild-to-moderate diarrhea, fecal leukocytosis and no fever, simply discontinuing the offending antibiotic will result in resolution of symptoms in about 25% of patients and reduce the likelihood of recurrence. For those whose inciting antibiotic therapy cannot be stopped, or who have symptomatic mild-to-moderate disease requiring treatment, metronidazole, 500 mg PO every eight hours for 10-14 days, is the treatment of choice due to its low cost and efficacy.

**For Severe Disease:**
Vancomycin has been proven more effective than metronidazole in severe CDI and is the agent of choice. Table 2 summarizes the criteria for distinguishing mild-to-moderate from severe CDI. Any patient scoring two or more points based on the criteria should receive Vancomycin, 125 mg PO QID, as initial therapy.

**For Recurrent Disease**
Despite optimal first-line therapy, 20% of patients will have recurrent CDI, which usually develops one to two weeks after completing initial therapy, but which can be delayed by up to two months. A first recurrence should be treated with the same regimen as for the initial episode, based on severity of disease. Subsequent recurrences are treated with longer tapers of oral Vancomycin.

With severe or recurrent disease, fecal microbiota transplantation may be an option to consider and should be discussed with your healthcare provider.

**Table 2. Criteria for Severe CDI**

| Two Points Each |
|---|
| • ICU Admission<br>• Pseudomembranous colitis |
| **One Point Each** |
| • Age > 60 years<br>• WBC > 15,000 cells/mm3<br>• Fever ≥ 38.4°C<br>• Hypoalbuminemia (<2.5 mg/dL) |

## What can be done to prevent the spread of CDI?

In addition to early identification, accurate interpretation of diagnostic tests, and appropriate therapy for CDI, it is essential that measures be implemented to reduce *C. difficile* transmission**.**

**Core Prevention Measures:**

- Evaluate and optimize testing for CDI
- Institute a laboratory-based alert system for immediate notification of positive test results
- Use Contact Precautions for duration of diarrhea –wear gloves and gowns whenever working with patients with CDI, even during short visits
- Clean and disinfect equipment and the environment with bleach***** or another EPA-approved, spore-killing disinfectant
- Perform hand hygiene in compliance with the Society for Healthcare Epidemiology of America (SHEA) /Infectious Disease Society of America (IDSA) guidelines******
- Educate other healthcare providers, housekeeping, administration, patients, and families about CDI
- When a patient transfers, notify the receiving facility if the patient has CDI
- Cohort patients being treated for CDI whenever possible, and provide a dedicated commode for each patient

**Supplemental Prevention Strategies:**

- Extend use of Contact Precautions beyond duration of diarrhea (e.g., 48 hours)*****
- Presumptively isolate symptomatic patients pending confirmation of CDI
- Implement use of soap and water for hand hygiene before exiting the room of a patient with CDI******
- Implement universal glove use on units with high CDI rates
- Ensure that environmental cleaning is adequate and that high-touch surfaces are not being overlooked
- Identify and remove environmental sources of C. difficile, including replacement of electronic rectal thermometers with disposables
- Assign patients with CDI to private rooms when possible
- During an outbreak of CDI, instruct visitors to wash their hands with soap and water after caring for or contact with patients with CDI

*****Bleach can kill spores, but other standard disinfectants cannot. Limited data suggest cleaning with bleach (1:10 dilution prepared fresh daily) reduces *C. difficile* transmission; bleach may be most effective in reducing burden where CDI is highly endemic.

******Alcohol-based hand sanitizers are not effective in eradicating *C. difficile* spores, and spores may be difficult to eradicate even with hand washing. For these reasons, adherence to glove use and Contact Precautions should be emphasized for preventing *C. difficile* transmission via the hands of healthcare personnel.

[The primary reason hand hygiene with soap and water is not recommended for CDI prevention in non-outbreak settings is that there are no studies that have found an increase in CDI with the use of alcohol-based hand hygiene products or a decrease in CDI with the use of soap and water. Conversely, several studies did identify decreases in methicillin-resistant *Staphylococcus aureus* (MRSA) or vancomycin resistant enterococcus (VRE) associated with the use of alcohol-based hand hygiene products. However, because of the theoretical increase in risk of *C. difficile* transmission the authors of the SHEA/IDSA Clinical Practice Guidelines for CDI felt it was prudent to recommend *preferential use of soap and water when caring for a patient with CDI in an outbreak setting*.]

## For more information:

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