Clostridioides difficile Infection

Summary

Clostridioides difficile (or *C. diff*) is a spore-forming bacterium that can result in asymptomatic colonization or clinical infection. *Clostridium difficile* infection (CDI) causes diarrhea that can range from mild to severe and can even be life-threatening. Signs and symptoms can include watery diarrhea, fever, abdominal pain/tenderness, nausea, and loss of appetite. Serious sequelae, such as pseudomembranous colitis, toxic megacolon, perforations of the colon, sepsis, and death may result from CDI. It is also possible for a person to be colonized with *C. difficile*, and thus not exhibit any clinical signs or symptoms; studies have shown approximately 5% of the general population, and 50% or more of other populations, such as hospitalized patients, residents of long-term care facilities and infants under one year of age, are colonized with *C. difficile*. After treatment for CDI, repeat testing ("test of cure") is not recommended if signs and symptoms have resolved, as some persons may remain colonized for an undetermined period, perhaps weeks to months.

Risk for CDI is increased in persons with recent or prolonged antibiotic exposure, long length of stay in healthcare settings, gastrointestinal surgery and/or manipulation, serious underlying chronic health conditions, immunocompromised status, advanced age, and proton pump inhibitor use. Although CDI remains primarily associated with healthcare exposure, recently infections have been more commonly reported in traditionally 'low risk' individuals, such as healthy persons in the community and peripartum women. Changes to the prevalence of CDI may be in part due to the emergence of a more virulent strain of *C. difficile*, known as the restriction enzyme analysis type BI, North American Pulsed Field type 1 (NAP1), or PCR ribotype 027 (BI/NAP1/027). Judicious use of antibiotics, proper contact precautions, and environmental cleaning and disinfection are important prevention strategies for CDI.

Agent

Clostridium difficile is a Gram-positive, spore-forming, anaerobic bacillus that produces two exotoxins: toxin A and toxin B. The epidemic BI/NAP1/027 strain appears to be more virulent due to increased production of toxins A & B, production of a third toxin called binary toxin, as well as other factors currently being studied. In addition, BI/NAP1/027 is resistant to fluoroquinolones.

Transmission

Reservoir:

> Humans are the most important reservoir, though it is also found in many domestic and food animal species. Can be isolated from soil; however, any surface, device, or material (e.g., electronic rectal thermometers, commodes, bathing tubs, remote controls) that becomes contaminated with feces may serve as a reservoir for *C. difficile* spores.

Mode of Transmission:

> *C. difficile* is spread through the fecal-oral route. *C. difficile* spores may also be transferred to patients via the hands of healthcare personnel who have touched a contaminated item or surface.

Period of communicability:

Person-to-person spread occurs from both symptomatic patients and asymptomatic carriers. *C. difficile* spores are highly resistant to desiccation, killing by alcohol and standard EPA-registered hospital disinfectants, and can survive in the environment (such as on surfaces or contaminated items) for months or years.

Clinical Disease

Incubation Period:

The incubation period of CDI following medical interventions or organism acquisition has not been clearly defined. Although one study suggested a short incubation period of less than 7 days, others supported a time frame of up to 3 months after completion of antibiotic therapy. Thus, many cases of healthcare-associated CDI may have their onset in the community after hospitalization or medical care.

Illness:

Symptomatic *Clostridium difficile* infection causes inflammation of the colon, or colitis. Symptoms may include mild-to- severe watery diarrhea, fever, abdominal pain/tenderness, nausea, and loss of appetite. In severe cases, pseudomembranous colitis, toxic megacolon, perforations of the colon, sepsis, and/or death may occur. However, many studies show that over half of hospital patients and up to 80% of infants under one year of age are asymptomatically colonized. *C. difficile* accounts for 20–30% of antibiotic-associated diarrhea.

Laboratory Diagnosis

Most diagnostic testing for *C. difficile* is based on detection of toxin B and/or toxin A in a diarrheal stool specimen or detection of the genes encoding for toxin production. Testing should be performed only on unformed stool unless ileus (i.e., blockage of the intestines caused by a lack of peristalsis) is suspected. Testing for cure and testing on asymptomatic patients is not clinically useful and thus not recommended except for epidemiological studies. Enzyme immunoassay (EIA) tests, which detect toxins A and B, offer rapid turn-around time but have a relatively low sensitivity. A two-step algorithm testing approach, using the more sensitive but nonspecific EIA test for glutamate dehydrogenase (GDH) combined with toxin testing, is often used. A more sensitive and specific approach which has become more widely available is molecular assay testing using nucleic acid amplification tests (NAATs) (e.g., PCR). NAAT may be used as a stand-alone test or as confirmatory testing for discrepant toxin/GDH tests. Stool culture for *C. difficile*, though the most sensitive test available, is labor intensive and has a relatively slow turn-around time and is therefore less clinically useful. *Clostridium difficile* toxin degrades at room temperature and can be undetectable within 2 hours of stool specimen collection. Specimens should be promptly tested and kept refrigerated at 4°C to minimize the occurrence of false-negative results.

Treatment

Discontinuation of the potentially precipitating antimicrobial therapy should occur as soon as possible. In approximately 20% of patients, symptomatic CDI will resolve within 2–3 days of discontinuation of antibiotic exposure for patients with an initial *Clostridioides difficile* infection (CDI) episode, Infectious Diseases Society of America (IDSA) and the Society for Healthcare

Epidemiology of America (SHEA) suggests using fidaxomicin rather than a standard course of vancomycin (conditional recommendation, moderate certainty of evidence).

In patients with recurrent CDI episodes, we suggest fidaxomicin (standard or extended-pulsed regimen) rather than a standard course of vancomycin (conditional recommendation, low certainty evidence.

For patients with a recurrent CDI episode within the last 6 months, we suggest using bezlotoxumab as a co-intervention along with standard-of-care (SOC) antibiotics rather than SOC antibiotics alone (conditional recommendation, very low certainty of evidence).

Dosing guidelines in Table 1 of 2021 IDSA and SHEA

As a reminder, FMT (fecal microbiota transplantation) is recommended only for patients with multiple recurrences of CDI who have failed appropriate antibiotic treatments and where appropriate screening of donor and donor fecal specimens has been performed, in accordance with these newer FDA recommendations.

Surveillance

Case definition:

The Centers for Disease Control and Prevention (CDC) and the Council of State and Territorial Epidemiologists (CSTE) have not developed case definitions for CDI. The New Mexico Department of Health currently conducts two types of CDI surveillance: 1) statewide CDI laboratory surveillance through hospitals that identify cases through positive *C. difficile* toxin assays or positive *C. difficile* molecular assays (e.g., PCR) on stool specimens following National Health Safety Network (NHSN) LabID event protocols; and 2) population-based surveillance in Bernalillo County only through the New Mexico Department of Health Emerging Infections Program (NM EIP) following national EIP surveillance protocols.

Reporting:

Report all suspected or confirmed cases of CDI to the Epidemiology and Response Division (ERD). Information needed includes patient's name, age, date of birth, sex, race, ethnicity, home address, home phone number, occupation, specimen collection date, and health care provider.

Steps to Prevent Spread:

If a patient has had ≥ 3 stools in 24 hours:

Order a C. diff test if other etiologies of diarrhea (e.g., stool softener or laxative use) are considered unlikely.

Isolate patients with possible C. diff immediately, even if you only suspect CDI.

Wear gloves and a gown when treating patients with C. diff, even during short visits. Gloves are important because hand sanitizer doesn't kill C. diff and handwashing might not be sufficient alone to eliminate all C. diff spores.

In patient being evaluated for C. diff, reassess appropriateness of antibiotics. Order a C. diff test if other etiologies of diarrhea (e.g., stool softener or laxative use) are considered unlikely.

Isolate patients with possible C. diff immediately, even if you only suspect CDI.

Wear gloves and a gown when treating patients with C. diff, even during short visits. Gloves are important because hand sanitizer doesn't kill C. diff and handwashing might not be sufficient alone to eliminate all C. diff spores.

In patient being evaluated for C. diff, reassess appropriateness of antibiotics.

How can CDI be prevented in hospitals and other healthcare settings?

Use contact precautions for patients with known or suspected CDI:

Place these patients in private rooms. If private rooms are not available, they can be placed in rooms (cohorted) with other CDI patients.

Wear gloves and a gown when entering CDI patient rooms and during their care.

As no single method of hand hygiene will eliminate all C. diff spores, using gloves to prevent hand contamination remains the cornerstone for preventing C. diff transmission via the hands of healthcare personnel.

Always perform hand hygiene after removing gloves.

If your institution experiences an outbreak, consider using soap and water instead of alcohol-based hand sanitizers for hand hygiene after removing gloves while caring for patients with CDI.

Dedicate or perform cleaning and disinfection of any shared medical equipment between patients.

Continue CDI precautions at least until diarrhea ceases.

Because CDI patients continue to shed the organism for a number of days following cessation of diarrhea, some institutions routinely continue isolation and contact precautions for either several days beyond symptom resolution or until discharge, depending upon the type of setting and average length of stay.

Implement an environmental cleaning and disinfection strategy.

Ensure adequate cleaning and disinfection of environmental surfaces and reusable devices, especially items likely to be contaminated with feces and surfaces that are touched frequently.

Ensure daily and terminal cleaning of patient rooms.

Use an Environmental Protection Agency (EPA)-registered disinfectant with a sporicidal claim for environmental surface disinfection after cleaning in accordance with label instructions. (Note: Only hospital surface disinfectants listed on EPA's List K are registered as effective against C. diff spores).

Follow the manufacturer's instructions for disinfection of endoscopes and other devices.

Management of CDI in Child Care Centers and Long-Term Care Facilities

Children with *C. difficile* diarrhea should be excluded from childcare settings for the duration of the diarrhea.

Long-term care facility residents with suspect or confirmed CDI should be under appropriate contact precautions, using the least restrictive approach possible that offers adequate protection but does not adversely affect psychosocial well-being. Residents with the ability to maintain adequate personal hygiene should be allowed to participate in group activities, when possible, after performing hand hygiene, disinfecting assistive devices (walkers, canes, wheelchairs), before leaving their room. Residents unable to comply with good hygiene may benefit from a 1:1 caregiver. Guidelines for room assignment strategies can be found in the 2013 APIC Guide to Eliminating *Clostridium difficile* Infections.

Healthcare workers should use contact precautions when in the resident's room and maintain meticulous hand hygiene. Medical devices and equipment should be dedicated to single resident use or be disinfected between uses; rectal thermometers should not be used. The CDC NHSN offers a free, voluntary, internet-based surveillance system to allow long-term care facilities to enter data and compare infection rates.

Contact the Epidemiology and Response Division at 505-827-0006 for further recommendations.

References

American Academy of Pediatrics. In: Kimberlin, DW, et al eds. Red Book: 2018 Report of the Committee on Infectious Diseases. 31st ed. Itasca, IL: American Academy of Pediatrics; 2018.

Centers for Disease Control and Prevention (CDC). "Frequently Asked Questions about *Clostridium difficile* Information for Healthcare Providers", http://www.cdc.gov/HAI/organisms/cdiff/Cdiff_faqs_HCP.html#a1, Last reviewed 10/25/2022.

Centers for Disease Control and Prevention (CDC). "CDI Prevention Strategies", https://www.cdc.gov/cdiff/clinicians/cdi-prevention-strategies.html. Last reviewed December 17, 2021.

Clinical Practice Guidelines by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA): 2021 Focused Update Guidelines on Management of Clostridioides difficile Infection in Adults. *Clinical Infectious Diseases*, Volume 73, Issue 5, 1 September 2021, Pages e1029–e1044, https://doi.org/10.1093/cid/ciab549

See *Clostridium difficile* Fact Sheets (English) (Spanish).