Clostridioides difficile infection: Prevention and control

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INTRODUCTION

Clostridioides difficile is the causative organism of antibiotic-associated colitis. It is the most common infectious cause of health care-associated diarrhea and a significant cause of morbidity and mortality among hospitalized patients [1]. Most cases of *C. difficile* infection (CDI) in the United States are associated with inpatient or outpatient contact with a health care setting [2-4].

Development of CDI usually requires two events: disruption of the fecal microbiota (typically via exposure to antibiotics) and ingestion of spores via the fecal-oral route. *C. difficile* may be shed into the environment by individuals who are infected or colonized. High colonization rates may occur among hospitalized adults, nursing home residents, and healthy infants [5-7].

C. difficile spores can be transmitted between patients via environmental surfaces and contaminated hands of health care personnel [8]. Thus, efforts to prevent CDI must focus on two goals: reducing patient susceptibility to CDI and preventing organism transmission [9]. Prevention of *C. difficile* transmission is especially challenging because the organism forms spores that can persist on environmental surfaces for months and are resistant to commonly used cleaning agents and alcohol-based hand gels [10].

Issues related to prevention of CDI in health care and community settings are discussed here. Issues related to prevention of CDI in individual patients are discussed separately. (See "*Clostridioides difficile* infection in adults: Treatment and prevention".)

The pathophysiology, epidemiology, clinical manifestations, diagnosis, and treatment of CDI are discussed separately. (See related topics.)

INPATIENT CARE SETTINGS

Infection control and antibiotic stewardship are critical for reducing the incidence of CDI in health care settings [11-13]. Appropriate testing is an important step to prevent unnecessary antibiotic prescribing [9,14,15]. There have been reports of severe CDI in some settings and waves of the COVID-19 pandemic, highlighting the importance of both antibiotic stewardship and avoiding delays in diagnosis during a pandemic [16].

Infection control — Guidance for prevention of CDI in acute-care hospital settings was published in 2018 by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America [9]; the recommendations are summarized briefly here.

Surveillance — Standardized case definitions for *C. difficile* surveillance are as follows [9]:

- Health care facility onset (HO) – CDI case established based on laboratory test collected >3 days after admission to the facility (ie, on or after day 4). The rate of HO-CDI should be expressed as the number of cases per 10,000 patient-days.
- Community onset, health care facility associated (CO-HCFA) – CDI case occurring within 28 days after discharge from a health care facility. The CO-HCFA prevalence rate should be expressed as the number of cases per 1000 patient admissions.
- Community associated (CA) – CDI case occurring in the absence of health care facility admission or CDI case occurring ≥28 days following discharge.

At a minimum, inpatient health care facilities should conduct surveillance (among patients ≥2 years of age) for HO-CDI to detect elevated rates or outbreaks. When CDI incidence is above goals or in outbreak settings, data should be stratified by patient location to target control measures.

In the United States, reporting of facility-wide CDI events using the National Healthcare Safety Network (NHSN) [17] is required in acute-care hospitals, long-term acute-care facilities, and inpatient rehabilitation facilities [18-20].

The United States Centers for Disease Control and Prevention developed a strategy known as the Targeted Assessment for Prevention (TAP), which includes a CDI assessment tool that can help identify and address specific gaps in infection prevention in a unit or facility [21]. In

addition, the strategies to prevent *CDI* in acute care facilities have been created to facilitate CDI-prevention efforts [14].

Prevention strategies

Early detection and isolation — Early detection of CDI with rapid implementation of contact precautions is essential for preventing transmission; it requires vigilant screening for new-onset diarrhea in patients at risk and rapid, accurate testing. (See "*Clostridioides difficile* infection in adults: Clinical manifestations and diagnosis", section on 'Diagnosis' and "*Clostridioides difficile* infection in children: Clinical features and diagnosis", section on 'Approach to diagnosis'.)

Issues related to transmission of CDI are discussed further separately. (See "*Clostridioides difficile* infection in adults: Epidemiology, microbiology, and pathophysiology".)

Contact precautions — Patients with suspected or proven CDI should be placed on contact precautions, including assignment to a private room with dedicated toileting facilities. If the number of such rooms is limited, patients with stool incontinence should be prioritized [9]. Gloves and gowns should be donned upon room entry and removed prior to exiting the room [9].

If cohorting is required, patients infected or colonized with the same organism(s) should be cohorted (ie, patients with CDI who are discordant for other multidrug-resistant organisms should not be cohorted together). In cohort rooms, gowns and gloves should be removed, and hand hygiene should be performed between patients [9,22,23].

General principles regarding contact precautions and attire of health care personnel are discussed further elsewhere. (See "Infection prevention: Precautions for preventing transmission of infection", section on 'Contact precautions' and "Infection prevention: Precautions for preventing transmission of infection", section on 'Attire for health care personnel'.)

The optimal approach for discontinuation of contact precautions for CDI is uncertain. We are in agreement with guidelines regarding the duration of contact precautions for acute care settings that were published in 2018 by the Society for Healthcare Epidemiology of America and Infectious Disease Society of America [9,24]. These guidelines favor continuation of contact precautions for at least 48 hours after resolution of diarrhea. Continuation of contact precautions beyond resolution of diarrhea is reasonable since persistent stool shedding of *C. difficile* spores is common [9,25]. In acute care settings with elevated CDI rates despite

appropriate infection prevention and control measures, continuation of contact precautions until discharge is reasonable.

Hand hygiene — Prior to contact with a patient with CDI, health care personnel should perform hand hygiene then don gloves. Following contact with a patient with CDI, health care personnel should remove gloves then perform hand hygiene.

In routine settings, hand hygiene may be performed with soap and water or an alcohol-based hand rub (ABHR) [9]. In outbreak settings, hand hygiene should be performed preferentially with soap and water before and after caring for patients with suspected or proven CDI; use of ABHR is not adequate because ABHR does **not** eradicate *C. difficile* spores [9,26-30]. In addition, hand hygiene with soap and water is preferred if there is direct content with feces or an area where fecal contamination is likely (eg, the perineal region).

Hand washing with soap and water involves vigorous mechanical scrubbing and rinsing, so it is more effective than ABHR for physical removal of bacterial spores. However, hand washing with soap and water is less effective than ABHR for inactivation of vegetative (ie, non-spore-forming) bacteria [31]. (See "Infection prevention: Precautions for preventing transmission of infection", section on 'Hand hygiene'.)

Patients with CDI should wash hands with soap and water after using the bathroom, before eating or food preparation, and when hands are visibly soiled.

Environmental cleaning and disinfection — Careful attention to environmental cleaning of clinical areas where patients with CDI are treated is critical; this includes daily cleaning and cleaning following discharge.

C. difficile spores can survive on dry surfaces for up to several months, and routine disinfection with standard quaternary ammonium-based chemicals does not eliminate *C. difficile* spores [5,6,32-38]. Disinfection of clinical areas where patients with CDI are treated requires use of a sporicidal agent (such as bleach or an alternative agent with a *C. difficile* sporicidal label claim; in the United States, a list of these is available on the Environmental Protection Agency website). Some sporicidal agents can cause caustic damage to equipment surfaces and cause skin irritation for patients and health care personnel; these issues should be considered in the agent selection [38-40]. (See "Infection prevention: General principles", section on 'Health care environment: Cleaning and disinfection'.)

However, interventions that focus only on improving cleaning may not be sufficient to control health care-associated CDI. In one randomized trial including 16 hospitals in Ohio, an

environmental disinfection intervention improved the thoroughness and effectiveness of cleaning but did not reduce the incidence of health care-associated CDI [41].

When possible, disposable medical equipment should be used, since multiuse equipment (such as blood pressure cuffs, stethoscopes, and thermometers) can serve as fomites for *C. difficile* transmission [9,42-44]. If use of disposable equipment is not possible, equipment should be dedicated to a single patient with CDI. Equipment that must be shared between patients should be cleaned and disinfected with a sporicidal agent between uses [9]. (See "Infection prevention: General principles", section on 'Medical equipment: Disinfection and sterilization'.)

The impact of ultraviolet (UV) light for disinfection on the incidence of CDI is uncertain. One report that evaluated the impact UV irradiation following 542 patient discharges noted a reduction in CDI incidence by 25 percent compared with a preintervention baseline period [45]. In contrast, in another study that included 21,395 patients (in the intention-to-treat analysis) admitted to rooms from which a patient on contact precautions was discharged, no substantial decrease in CDI was observed in patients who subsequently occupied the same room, despite the addition of UV light to bleach disinfection (versus bleach alone) for room cleaning [46]. However, a secondary analysis of these data noted a broader effect, with declines in facility-wide incidence of both *C. difficile* and vancomycin-resistant enterococci infection or colonization, which were associated with enhanced terminal disinfection involving UV light [47].

Patient bathing — Patients should be encouraged to wash hands and shower to reduce the burden of spores on the skin [9].

Based on available data, the role for routine chlorhexidine (CHG) bathing for prevention of CDI is uncertain [48,49]. In one study including administration of more than 68,000 CHG baths, the incidence of CDI decreased with bathing daily (relative risk [RR] 0.41, 95% CI 0.29-0.59) or three times weekly (RR 0.71, 95% CI 0.57-0.89) [48]. However, another trial including 9340 adults in intensive care units noted that daily CHG bathing demonstrated no impact on CDI incidence [49].

Asymptomatic carriers — Asymptomatic carriers appear to play a role in *C. difficile* transmission. Data suggest that many new CDI cases are not molecularly linked to symptomatic CDI cases [50-52]. In one study including 1200 cases of CDI, patients with symptomatic infection served as the likely source for no more than 35 percent of new cases, suggesting an important role for asymptomatic carriers [50].

There is no clear role for routine implementation of precautions for asymptomatic carriers although benefits have been observed in some studies [9]. Use of precautions may be beneficial in selected circumstances; further study is needed [14,53,54]. Benefit associated with use of

precautions for asymptomatic carriers has been observed in some studies. In one study including more than 360 asymptomatic carriers identified and placed on precautions, the incidence of health care-associated CDI decreased from 6.9 to 3.0 per 10,000 patient-days over a two-year period [55]. Similar studies in oncology and bone marrow transplant units have also observed decreases in the incidence of health care-associated CDI [56,57].

Antibiotic stewardship — Antibiotic stewardship to reduce the unnecessary use of antibiotics plays an important role in controlling CDI rates [9]. Administration of antibiotics disrupts the intestinal microbiota and has been linked to *C. difficile* colonization [58], increasing the likelihood of a colonized patient contaminating their immediate environment [59]. Antibiotic use also increases risk for developing infection by 7- to 10-fold during and up to one month after treatment and by approximately threefold for two months thereafter [3,54]. In addition, antibiotic use has been shown to be a risk factor for recurrent CDI [60]. (See "*Clostridioides difficile* infection in adults: Epidemiology, microbiology, and pathophysiology", section on 'Antibiotic use' and "*Clostridioides difficile* infection in children: Microbiology, pathogenesis, and epidemiology", section on 'Antibiotic exposure'.)

Antibiotic stewardship programs can significantly aid in the reduction of CDI incidence [61]. Targeted restriction of a particular antibiotic agent or class of agents can facilitate control of hospital outbreaks and reduce CDI rates in the community and in health care settings [62-67]. (See "Antimicrobial stewardship in hospital settings", section on 'Reducing the incidence of C. difficile infection'.)

Antibiotics frequently associated with increased CDI risk include clindamycin, fluoroquinolones, cephalosporins, carbapenems, and penicillins (table 1):

- Clindamycin restriction has been followed by rapid reductions in CDI cases in several outbreaks [65,68]. Similar findings have been observed in outbreaks caused by the highly clindamycin-resistant J strain [64]. In one study, for example, a policy requiring infectious disease physician approval for clindamycin use led to reduction in CDI cases (from 11.5 to 3.3 cases per month) [68].

- Fluoroquinolone use has been associated with outbreaks caused by the highly fluoroquinolone-resistant PCR ribotype 027 strain [69-71]. Restriction of all fluoroquinolones may be required for effective control in such circumstances [67,72,73]. In one study, elimination of fluoroquinolone use was associated with a reduction in CDI cases and in the proportion of cases due to the 027 strain [74]. In another study, reduction in fluoroquinolone use across England was primarily responsible for reduction in CDI

incidence [67]. (See "*Clostridioides difficile* infection in adults: Epidemiology, microbiology, and pathophysiology", section on 'PCR ribotype 027 strain'.)

- Restriction of third- and fourth-generation cephalosporins has been successful in reducing CDI rates [62,63,75-77]. Other studies have noted associations between formulary restrictions and reduced CDI rates by limiting antibiotics to penicillin, trimethoprim-sulfamethoxazole, and aminoglycosides in the setting of an outbreak [63].

- With increased use and reliance on carbapenems to address resistance caused by extended-spectrum beta-lactamases, there may be an increasing role for this class in driving facility CDI rates [78].

Even reducing the duration of broad-spectrum antibiotics might have a role in decreasing CDI rates. In a retrospective cohort study of 808 patients with Enterobacteriaceae bloodstream infections, receipt of empiric antipseudomonal beta-lactam therapy for <48 hours was independently associated with a lower 90-day risk of CDI compared with continued antipseudomonal beta-lactam use beyond 48 hours [79]. Further study is needed to determine if systematic early de-escalation of antibiotics can result in decreased incidence of CDI.

OUTPATIENT CARE SETTINGS

Patients may present to an outpatient setting if they acquired the infection in the community, after discharge from a health care setting where they received antibiotics, or as a follow-up from a hospital admission related to CDI or exposure to an outpatient setting [2,80].

In general, outpatient care settings should follow the same prevention strategy guidelines as inpatient care setting, such as developing an IPC program, providing education and training to all health care personnel on the basic principles and practices for preventing the spread of CDI, performance of hand hygiene by both the patient and health care personnel, and contact precautions for all health care personnel who enter the examination room or are in contact with the infected patient [81,82]. (See 'Contact precautions' above and 'Hand hygiene' above.)

Whenever possible, disposable medical equipment should be used (eg, stethoscopes, blood pressure cuffs, thermometers), especially when evaluating a patient with diarrhea. When possible, a patient with diarrhea should be placed in a private room. Meticulous cleaning should be performed with an EPA-registered sporicidal disinfectant (List K) for environmental disinfection.

While preventing transmission in outpatient as well as inpatient settings is important, antibiotic stewardship is imperative for reducing unnecessary antibiotic use that increases patient susceptibility to *C. difficile* infection [83-85].

COMMUNITY SETTINGS

Outpatient antibiotic use is a risk factor for developing CDI [4]. In addition, emergency departments may serve as an environmental reservoir [4].

Households — *C. difficile* can spread among household contacts; however, it is rare for otherwise healthy individuals to develop CDI in the absence of antibiotic use.

Patients with CDI should wash hands with soap and water after using the bathroom, before eating or food preparation, and when hands are visibly soiled. If possible, patients with diarrhea should avoid using the same toilet as other family members. In addition, bathroom and kitchen areas (including toilet seats, toilet bowl, flush handle, sink faucet handles, and countertops) may be cleaned with a mixture of bleach and water (1 part bleach to every 10 parts water) to help prevent spread of infection. More information can be found on the CDC website.

Childcare settings — Children with diarrhea due to CDI should be excluded from childcare settings for the duration of diarrhea [86]. Diaper changing surfaces in childcare settings where children with CDI have been cared for may be sanitized with a disinfectant with sporicidal activity (eg, hypochlorite) [86].

Neonates and infants frequently are colonized with toxigenic *C. difficile*. They rarely develop symptomatic disease but can serve as a reservoir of infection for others. (See "*Clostridioides difficile* infection in children: Microbiology, pathogenesis, and epidemiology", section on 'Neonates and infants'.)

Antibiotic stewardship — Antibiotic stewardship plays an important role in controlling CDI rates [9]. (See 'Antibiotic stewardship' above and "Antimicrobial stewardship in outpatient settings".)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: *Clostridioides difficile* infection".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "Patient education: *C. difficile* infection (The Basics)")
- Beyond the Basics topics (see "Patient education: Antibiotic-associated diarrhea caused by *Clostridioides difficile* (Beyond the Basics)")

SUMMARY

- **Overview** – *Clostridioides difficile* is the causative organism of antibiotic-associated colitis. It is the most common infectious cause of health care-associated diarrhea and a significant cause of morbidity and mortality among hospitalized patients. (See 'Introduction' above.)
- **Hand hygiene** – Hand hygiene is an important factor in reducing the spread of CDI. Gloves should be donned by health care personnel prior to caring for individuals with suspected or proven CDI. All health care personnel, patients, caretakers, and household members should perform hand hygiene by washing hands with soap and water following care of individuals with suspected or proven CDI; use of alcohol-based hand rub (ABHR) is not adequate because ABHR does **not** eradicate *C. difficile* spores. Hand washing with soap and water involves vigorous mechanical scrubbing and rinsing, so it is more effective than ABHR for physical removal of bacterial spores. (See 'Hand hygiene' above and 'Households' above and 'Childcare settings' above.)
- **Prevention strategies for health care settings** – Prevention and control of *C. difficile* infection (CDI) in health care settings require early detection and isolation with contact

precautions, careful attention to hand hygiene, and effective environmental cleaning. (See 'Infection control' above.)

- **Contact precautions** – Patients with suspected or proven CDI should be placed on contact precautions, including assignment to a single room with dedicated toileting facilities or cohorting with other patients who have CDI. Gloves and gowns should be donned upon room entry and removed prior to exiting the room. (See 'Contact precautions' above.)

- **Environmental cleaning and disinfection** – Careful attention to environmental cleaning of clinical areas where patients with CDI are treated is critical. *C. difficile* spores can survive on dry surfaces for up to several months, and routine disinfection with standard quaternary ammonium-based chemicals does not eliminate *C. difficile* spores. Disinfection of clinical areas where patients with CDI are treated requires use of a sporicidal agent (such as bleach or an alternative agent with a *C. difficile* sporicidal label). (See 'Environmental cleaning and disinfection' above.)

- **Use of medical equipment** – When possible, disposable medical equipment should be used, since multiuse equipment (such as blood pressure cuffs, stethoscopes, and thermometers) can serve as fomites for *C. difficile* transmission. If use of disposable equipment is not possible, equipment should be dedicated to a single patient with CDI. Equipment that must be shared between patients should be cleaned and disinfected with a sporicidal agent between uses. (See 'Environmental cleaning and disinfection' above.)

- **Antibiotic stewardship** – Administration of antibiotics disrupts the intestinal microbiota and has been linked to *C. difficile* colonization and disease. Targeted restriction of a particular antibiotic agent or class of agents can facilitate control of hospital outbreaks and reduce CDI rates in the community and in health care settings. Antibiotics frequently associated with increased CDI risk include clindamycin, fluoroquinolones, cephalosporins, and penicillins (table 1). (See 'Antibiotic stewardship' above.)

- **Prevention strategies for community settings** – *C. difficile* can spread among household contacts, although it is rare for otherwise healthy individuals to develop CDI in the absence of antibiotic use. Patients and household members should be counseled to wash their hands frequently, especially after the use of the bathroom, before preparation of or contact with food, and when hands are visibly soiled. Children with diarrhea due to CDI

should be excluded from childcare settings for the duration of diarrhea. (See 'Community settings' above.)

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GRAPHICS

Antimicrobial agents that may induce *Clostridioides difficile* diarrhea and colitis

Frequently associated	Occasionally associated	Rarely associated
▪ Fluoroquinolones ▪ Clindamycin ▪ Penicillins and combinations (broad spectrum) ▪ Cephalosporins (2nd/3rd/4th generation)* ▪ Carbapenems	▪ Macrolides ▪ Penicillins (narrow spectrum) ▪ Cephalosporins (1st generation) ▪ Trimethoprim-sulfamethoxazole ▪ Sulfonamides	▪ Aminoglycosides ▪ Tetracyclines ▪ Tigecycline ▪ Chloramphenicol ▪ Metronidazole ▪ Vancomycin ▪ Nitrofurantoin

* Use of 1 to 2 doses of a first-generation cephalosporin for surgical antibiotic prophylaxis does not confer significant risk for *C. difficile* infection.

Data from:

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