#### **REVIEWS**

### Strategies for Prevention of Clostridium difficile Infection

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Infection control is the most essential component of an effective overall management strategy for prevention of nosocomial *Clostridium difficile* infection (CDI). The cornerstones of CDI prevention are appropriate contact precautions and strict hand hygiene. Other important tactics are effective environmental cleaning, identification and removal of environmental sources of *C. difficile*, and antibiotic stewardship. Hospitalists, as coordinators of care for each patient and advocates for quality care, can spearhead these efforts. *Journal of Hospital Medicine* 2012;7:S14–S17. © 2012 Society of Hospital Medicine

Infection control is a critical component of an overall management strategy for *Clostridium difficile* infection (CDI). In fact, preventing patients from acquiring this nosocomial condition in the healthcare setting has been identified as the most essential component. In 2008, the Society for Healthcare Epidemiology of America/Infectious Diseases Society of America (SHEA/IDSA) published a compendium of strategies to prevent healthcare-associated infections, including CDI. This guideline includes graded recommendations and provides helpful strategies for applying them in a healthcare facility. An effective and comprehensive preventive program to reduce the incidence and impact of CDI requires several key components:<sup>2</sup>

- 1. Communication of responsibilities and accountability.
- 2. Application of "basic" recommendations (Table 1).<sup>2</sup>
- 3. Application of "special" recommendations if the incidence of CDI is not adequately controlled with the basic recommendations (Table 2).<sup>2</sup>

Many healthcare providers are involved in patient care, and therefore each of these departments—including administration, the medical staff, the infection control department, nursing, pharmacy, the clinical laboratory, and environmental control—must be supportive of, and accountable for, implementing strategies to prevent CDI. Hospital administration must ensure that nursing, environmental services, and infection prevention and control have adequate support. The department of infection prevention and control should take the lead role in designing, implementing,

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and monitoring the CDI prevention program, including the education of hospital staff.

Clinical staff must comply with infection prevention and control policies, and have a high index of suspicion for rapid identification of patients with CDI, so they can be placed under contact precautions and started on treatment quickly. Nursing and physician leaders must hold personnel accountable for adhering to infection prevention and control policies. Finally, environmental services play a key role and must ensure that housekeeping personnel are appropriately trained and monitored to ensure they are following effective cleaning policies and procedures.

#### TRANSMISSION OF CDI

Healthcare workers are a primary mode of C. difficile transmission. C. difficile spores end up on multiple hospital surfaces and contaminate healthcare worker hands and medical devices (stethoscopes, thermometers, etc) used on multiple patients. One study found that after caring for a patient with CDI, 59% of healthcare workers had hand contamination regardless of whether or not they actually touched the patient.<sup>3</sup> Many studies have shown that patients in adjacent rooms are at equal or higher risk of acquiring CDI as patients admitted to the same room. 4,5 Although a recent study found that admission to an intensive care unit room that previously housed a patient for CDI was a risk factor for developing CDI, 89% of patients who actually developed CDI did not have this risk factor.6 This indicates that most C. difficile acquisitions came from healthcare workers.

# CONTACT PRECAUTIONS AND STRICT HAND HYGIENE ARE KEY

The combination of appropriate contact precautions and strict hand hygiene has been reported to reduce the incidence of CDI by as much as 80%. <sup>1,7,8</sup> The CDI prevention recommendation with the strongest level of evidence is the donning of gloves when caring for a patient with CDI (Table 1).<sup>9</sup>

The optimal method of hand hygiene after caring for a patient with CDI is a matter of some confusion.

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TABLE 1. Preventing CDI: Basic Recommendations

Recommendation	Grade*
Contact precautions for patients with CDI until 48 hr	A-I for gloves
after diarrhea resolves	A-II for hand hygiene
	B-III for gowns
	B-III for single-patient room
Ensure adequate disinfection of equipment and environment	B-II for environment
	B-III for equipment
Laboratory-based alert system to notify clinical and infection prevention and control personnel if patient diagnosed with CDI	B-III for alert system
Conduct CDI surveillance and feedback data to units and	B-III for CDI surveillance
hospital administrators	
Educate healthcare personnel, housekeeping personnel, and hospital administration about CDI	B-III for hospital staff education
Educate patients and their families about CDI, as appropriate	B-III for patient education
Measure hand hygiene and contact precaution compliance	B-III for monitoring compliance

NOTE: See Dubberke et al.2

Abbreviations: CDI, Clostridium difficile infection.

\*Strength of recommendation and quality of evidence identified by letter and Roman numeral, respectively. Definitions for strength of recommendation are: A for good evidence to support a recommendation for use; and B for moderate evidence to support a recommendation for use. Definitions for quality of evidence are: I for evidence from >1 properly randomized, controlled trial: II for evidence from >1 well-designed clinical trial without randomization, from cohort or case-control analytic studies (preferably from >1 center), from multiple time series, or from dramatic results from uncontrolled experiments; III for evidence from opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

Alcohol-based hand sanitizers did not reduce the amount of C. difficile spores on the hands of volunteers contaminated with a known quantity of C. difficile spores. 10 However, studies have not found an increase in CDI with use of alcohol-based hand sanitizers or a decrease in CDI with use of soap and water. 11 In addition, several of these studies have found the use of alcohol-based hand hygiene products to be associated with decreases in methicillin-resistant Staphylococcus aureus or vancomycin-resistant enterococcus. For these reasons, in non-outbreak settings, hand hygiene with alcohol-based hand sanitizers, in addition to wearing gloves as a component of contact precautions, is considered an acceptable method of hand hygiene after caring for a patient with CDI. 11 In outbreak settings, however, preferential use of soap and water is recommended after caring for a patient with CDI because of the theoretical increase in risk of C. difficile transmission based on the volunteer hand contamination studies.<sup>2,11,12</sup>

### **DISINFECTION OF EQUIPMENT AND ENVIRONMENT**

Environmental services staff must be educated about the incidence, transmission of, and impact of CDI, as well as strategies effective for C. difficile spores, which are resistant to standard cleaning products and may persist in patient rooms for many months. During CDI outbreaks, rooms should be cleaned with a chlorine-based disinfectant (either an Environmental Protection Agency-approved disinfectant with known sporicidal activity or a 1:10 dilution of household bleach), which rapidly destroys C. difficile spores.<sup>1</sup> The sporicidal solution should have a contact time of

**TABLE 2.** Reducing the Incidence of CDI: Special Recommendations

Recommendations	Grade*
Initiate an antimicrobial stewardship program	A-II
Use diluted sodium hypochlorite for environmental disinfection if current practices deemed adequate	B-II
Intensify efforts at hand hygiene and contact precaution compliance	B-III
Preferentially use soap and water when performing hand hygiene after caring for a patient with CDI	B-III
Place patients in contact precautions while <i>C. difficile</i> testing is pending	B-III
Prolong contact precautions until discharge	B-III
Assess the adequacy of room cleaning	B-III

Abbreviations: CDI, Clostridium difficile infection.

Strength of recommendation and quality of evidence identified by letter and Roman numeral, respectively. Definitions for strength of recommendation are: A for good evidence to support a recommendation for use; and B for moderate evidence to support a recommendation for use. Definitions for quality of evidence are: for evidence from ≥1 properly randomized, controlled trial; II for evidence from ≥1 well-designed clinical trial without randomization, from cohort or case-control analytic studies (preferably from >1 center), from multiple time series, or from dramatic results from uncontrolled experiments; III for evidence from opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

at least 10 minutes.<sup>2</sup> Efforts to control spores in the environment and prevent transmission are even more important considering recent data demonstrating that hypervirulent C. difficile strains may have increased sporulation, which in combination with increased toxin production, pose a major management challenge. 13 Identification and removal of other sources of C. difficile, including replacement of electronic rectal thermometers with disposable thermometers, can also reduce the incidence of CDI.12

#### ANTIMICROBIAL STEWARDSHIP AND RESTRICTION

Interventions to ensure appropriate use of antibiotics, including antimicrobial stewardship programs and antibiotic restriction programs, are also effective. A study during an outbreak of a hypervirulent strain of C. difficile showed that an antimicrobial stewardship program reduced the incidence of CDI by 60%. 14 In this study, the antimicrobial stewardship program focused on shifting antimicrobial selection to antimicrobials that were associated with a lower risk of CDI at their institution whenever possible. Reducing unnecessary antimicrobial use was stressed as well. Formal restrictions were not instituted; rather, clinicians received education and pocket guides to assist in antimicrobial selection.

Several studies have found respiratory fluoroquinolones, such as gatifloxacin or moxifloxacin, to be associated with the highest risk of CDI during outbreaks due to the BI/NAP1/027 strain. 15,16 Interestingly, this antimicrobial stewardship program recommended respiratory fluoroquinolones over cephalosporins for community-acquired pneumonia, as cephalosporins historically have been strongly associated with CDI. Nevertheless, the incidence of CDI decreased after initiation of the antimicrobial stewardship program, despite increased use of respiratory fluoroquinolones.

The antimicrobial stewardship program was implemented prior to the identification of the fluoroquinolone-resistant epidemic strain. This shows that herd protection against CDI can occur by improvements in overall antimicrobial prescribing practices by decreasing the total number of patients at risk for CDI. This, in turn, will decrease the number of patients who develop CDI and contribute to the spread of *C. difficile*. In addition to using education to improve antimicrobial prescribing, several studies have found that restriction of specific antimicrobials associated with CDI (for example, clindamycin or fluoroquinolones) can result in a decrease in CDI.<sup>1,17–20</sup>

## INSIGHTS ABOUT OPPORTUNITIES FOR IMPROVEMENT

Results of a recent point prevalence survey conducted by the Association for Professionals in Infection Control and Epidemiology, Inc (APIC) provide important insights into knowledge and clinical practice gaps related to early diagnosis and prevention of CDI.<sup>21</sup> More than 12,000 APIC members were asked to provide a 1-day snapshot of patients identified with CDI or colonization at their institutions. Responses from 648 (12.5%) acute care hospitals in the United States, representing 47 states, indicate a clear need to improve infection control practices.<sup>21</sup> The following recommendations are based on recent evidence:

- Patients should be placed in contact isolation at the first suspicion of CDI, and kept in isolation for up to 2 days after diarrhea resolves because contamination persists in the environment that long.<sup>2</sup> Of note, this differs from the SHEA/IDSA Clinical Practice Guidelines for *Clostridium difficile* Infection in Adults, which state: "Maintain contact precautions for the duration of diarrhea." The Centers for Disease Control and Prevention (CDC) currently recommends contact precautions for the duration of illness when caring for patients with CDI.<sup>22</sup>
- Bleach solution should be used for routine and terminal cleaning during CDI outbreaks, as recommended by SHEA/IDSA and the CDC.
- Hand washing with soap and water is more effective than alcohol-based hand sanitizers for removal of spores. However, appropriate donning and removal of gloves prevents hand contamination with *C. difficile* spores, likely explaining why hand washing with soap and water has not been associated with a decrease in CDI compared with alcohol-based products.
- A formal program to educate environmental services personnel should be implemented to ensure they understand their critical role on the infection control team and effective strategies for cleaning.

#### SPECIAL APPROACHES

When basic approaches are not effective to reduce the incidence of CDI, the SHEA has recommendations for special approaches, which should be implemented

as appropriate for each institution (summarized in Table 2).<sup>2</sup> Strategies for prevention of CDI are also available from the CDC and the Institute for Healthcare Improvement (IHI).<sup>23,24</sup>

#### **SUMMARY**

Effective management and prevention of CDI requires a multidisciplinary approach that includes leaders in hospital administration, clinicians, the infection control department, nursing, pharmacy, and the clinical laboratory, as well as environmental services. All of these professionals must be accountable and take an active role in implementing and complying with evidence-based strategies to ensure that patients at risk are identified early and managed appropriately, and that effective strategies for prevention are in place. Hospitalists, as front-line caregivers, physician leaders in their hospitals, and coordinators of patient care, can play a key role in these regards. Care when deciding when and which antimicrobial to use to treat non-CDI infections; being attuned to symptoms that may be due to CDI, and prompt diagnosis and treatment of CDI; adhering to infection control policies; awareness of cleaning practices; and also being an active member of the infection control committee are all ways that hospitalists may take active roles in preventing CDI.

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#### References

- Riddle DJ, Dubberke ER. Clostridium difficile infection in the intensive care unit. *Infect Dis Clin North Am.* 2009;23(3):727–743.
- Dubberke ER, Gerding DM, Classen D. Strategies to prevent Clostridium difficile infections in acute care hospitals. *Infect Control Hosp Epidemiol*. 2008;29(suppl 1):S81–S92.
   McFarland LV, Mulligan ME, Kwok RY, Stamm WE. Nosocomial
- McFarland LV, Mulligan ME, Kwok RY, Stamm WE. Nosocomial acquisition of Clostridium difficile infection. N Engl J Med. 1989; 320(4):204–210
- Clabots CR, Johnson S, Olson MM, et al. Acquisition of Clostridium difficile by hospitalized patients: evidence for colonized new admissions as a source of infection. *J Infect Dis*. 1992;166:561–567.
- Chang VT, Nelson K. The role of physical proximity in nosocomial diarrhea. Clin Infect Dis. 2000;31(3):717–722.
- Shaughnessy MK, Micielli RL, DePestel DD, et al. Evaluation of hospital room assignment and acquisition of Clostridium difficile infection. *Infect Control Hosp Epidemiol*. 2011;32(3):201–206.
- Zafar AB, Gaydos LA, Furlong WB, Nguyen MH, Mennonna PA. Effectiveness of infection control program in controlling nosocomial Clostridium difficile. *Am J Infect Control*. 1998;26(6):588–593.
- Muto CA, Blank MK, Marsh JW, et al. Control of an outbreak of infection with the hypervirulent Clostridium difficile BI strain in a university hospital using a comprehensive "bundle" approach. Clin Infect Dis. 2007;45(10):1266–1273.
- Johnson S, Samore MH, Farrow KA, et al. Epidemics of diarrhea caused by a clindamycin-resistant strain of Clostridium difficile in four hospitals. N Engl J Med. 1999;341(22):1645–1651.
- four hospitals. N Engl J Med. 1999;341(22):1645–1651.
  Oughton MT, Loo VG, Dendukuri N, Fenn S, Libman MD. Hand hygiene with soap and water is superior to alcohol rub and antiseptic wipes for removal of Clostridium difficile. Infect Control Hosp Epidemiol. 2009;30(10):939–944.
- Gerding DM, Muto CA, Owens RC. Measures to control and prevent Clostridium difficile infection. Clin Infect Dis. 2008;46(suppl 1):S43–S49.
- Cohen SH, Gerding DN, Johnson S, et al. Clinical practice guidelines for Clostridium difficile infection in adults: 2010 update by the Society for Healthcare Epidemiology of America (SHEA) and the Infectious Diseases Society of America (IDSA). *Infect Control Hosp Epidemiol*. 2010;31(5):431–455.

- 13. Merrigan M, Venugopal A, Mallozzi M, et al. Human hypervirulent Clostridium difficile strains exhibit increased sporulation as well as robust toxin production. *J Bacteriol*. 2010;192(19):4904-4911.

  14. Valiquette L, Cossette B, Garant MP, Diab H, Pépin J. Impact of a
- reduction in the use of high-risk antibiotics on the course of an epidemic of Clostridium difficile-associated disease caused by the hypervirulent NAP1/027 strain. *Clin Infect Dis*. 2007;45(suppl 2):S112–S121.

  15. Pépin J, Saheb N, Coulombe MA, et al. Emergence of fluoroquinolones as the predominant risk factor for Clostridium difficile-association.
- ated diarrhea: a cohort study during an epidemic in Quebec, Canada.
- Clin Infect Dis. 2005;41(9):1254–1260.

  16. Loo VG, Poirier L, Miller MA, Oughton M, et al. A predominantly clonal multi-institutional outbreak of Clostridium difficile-associated diarrhea with high morbidity and mortality. N Engl J Med. 2005;
- 353:2442–2449.
  17. Climo MW, Israel DS, Wong ES, et al. Hospital-wide restriction of clindamycin: effect on the incidence of Clostridium difficile-associated diarrhea and cost. Ann Intern Med. 1998;128:989-995.
- 18. Davey P, Brown E, Fenelon L, et al. Interventions to improve antibiotic prescribing practices for hospital inpatients. Cochrane Database Syst Rev. 2005CD003543.

- 19. Khan R, Cheesbrough J. Impact of changes in antibiotic policy on Clostridium difficile-associated diarrhoea (CDAD) over a five-year period in a district general hospital. J Hosp Infect. 2003;54:104–108. O'Connor KA, Kingston M, O'Donovan M, et al. Antibiotic prescrib-
- ing policy and Clostridium difficile diarrhoea. *Q J Med.* 2004;97: 423–429.
- 21. Association for Professionals in Infection Control and Epidemiology (APIC). Guide to the elimination of Clostridium difficile in healthcare settings. Available at: http://www.apic.org/Content/Navigation-Menu/PracticeGuidance/APICEliminationGuides/C.diff\_Elimination\_ guide\_logo.pdf. Accessed August 9, 2011. 22. Centers for Disease Control and Prevention. Frequently asked ques-
- tions about Clostridium difficile for healthcare providers. Available at: http://www.cdc.gov/HAI/organisms/cdiff/Cdiff\_faqs\_HCP.html. Accessed August 9, 2011.
- 23. Centers for Disease Control and Prevention. Information about the current strain of Clostridium difficile. Available at: http://www. cdc.gov/HAI/organisms/cdiff/Cdiff-current-strain.html. Accessed June
- 24. Institute for Healthcare Improvement. Available at: http://www. ihi.org. Accessed July 26, 2011.