While no simple bundle for eliminating *Clostridium difficile* infection exists, prevention is possible through implementing comprehensive steps across the continuum of care.

By David J. Witt, MD, and Sue Barnes, RN, BSN, CIC

Each year, more than 14,000 Americans die of *Clostridium difficile* (C. difficile) infection (CDI) according to the Centers for Disease Control and Prevention (CDC). Furthermore, CDI costs at least $1 billion in extra healthcare costs annually, as reported in the March 2012 CDC *Vital Signs* report. While significant progress has been made in the prevention of central line-associated bloodstream infections, invasive MRSA infections, and surgical site infections—as per the U.S. Department of Health and Human Services’ (HHS) National HAI Action Plan to Eliminate Healthcare-Associated Infections—in the United States, CDI remains at historically high levels. HHS has set a goal for a 30 percent reduction in *C. difficile* infections and hospitalizations; however, preliminary data from the first half of 2012 have shown an increase in CDI.
These alarming statistics make the need for an increased emphasis on CDI prevention strategies clear; this comes as no surprise to healthcare professionals working in the infection prevention field. While we have witnessed widespread efforts to address these CDI prevention gaps across the continuum of care, more must be done to prevent these deadly infections. Healthcare personnel (HCP) at all levels—physicians, infection preventionists (IPs), pharmacists, nurses, laboratory professionals, environmental services professionals, and others—must effectively communicate and work in concert in order to move the needle toward progress of CDI prevention. Key areas of effort include hand hygiene, contact precautions, environmental cleaning, rapid diagnostics, antimicrobial stewardship, and fecal bacteriotherapy. While no simple solution exists for eliminating CDI, prevention is possible through teamwork, education, and open communication at all levels in multiple care settings.

HEALTHCARE PROVIDER AND PATIENT HAND HYGIENE

Hand hygiene is the cornerstone of any successful CDI prevention program, due in part to the small infectious dose required to transmit *C. difficile* from patient to patient. As recommended in the National HAI Action Plan, one area of research is focused on identifying the best method for hand hygiene for those who care for CDI patients. Wearing gloves can significantly reduce the spread of CDI by providing a physical barrier that decreases, if not prevents, hand contamination with spores. There is no increase in CDI with alcohol-based hand rub and no decrease in CDI with hand washing compared to the use of alcohol-based hand rub. The recommendation to use soap and water preferentially in outbreak settings after caring for a patient with CDI is based on expert opinion, as there are no data that demonstrate preferential use of soap and water for hand hygiene after caring for a patient with CDI in an outbreak setting is effective at preventing CDI. To ensure optimal hand hygiene is performed, the IP may wish to institute a hand hygiene monitoring program.

One of the newest tools for optimizing hand hygiene is automated compliance monitoring. These systems are designed to track hand hygiene compliance using one of several technologies including radio frequency identification sensors. There are numerous systems on the market, most designed to sense the proximity of employees to soap and degermer dispensers and other key patient zone locations and to register the use of degermer and soap. The resulting compliance data provides immediate feedback, printed reports, and (in some cases) can interface with infection prevention software programs to overlay compliance rates on infection rate graphs. One study suggests this type of technology not only improves compliance with
hand hygiene, but can reduce overall healthcare-associated infection (HAI) rates.5 6 Dr. Maryanne McGuckin has published a guide for evaluation of automated hand hygiene compliance monitoring systems.7

Experts have also recommended extending hand hygiene programs to include patient participation to further reduce the risk of infection transmission.8 And beyond hands, as an adjunct to patient bathing, chlorhexidine gluconate-impregnated cloths has been used to reduce the rate and risk of device-associated infections as well as pathogens of interest, including MRSA, vancomycin-resistant enterococci, and CDI.7 This additional prevention measure might be one to consider if other standard prevention efforts are not successful in achieving a zero rate.

CONTACT PRECAUTIONS
Any successful CDI prevention program includes contact precautions directing the use of gowns and gloves to create a barrier to contamination of HCP hands and clothing.9 The term “contact plus” precautions is sometimes used for CDI patients to reference the addition of bleach for environmental disinfection, and soap and water for cleaning hands. Removal of personal protective equipment (PPE) at point of use is critical to ensure these items do not become fomites for transmission of infection. Furthermore, HCP must remove PPE in a manner to prevent contamination of hands and clothing.10 Healthcare organizations have successfully used simulation to support more deliberate and correct performance of basic healthcare protocols, which include contact precautions and hand hygiene processes.12

ENVIRONMENTAL CLEANING
A patient’s risk of acquiring CDI is increased when placed in a room recently occupied by a patient with CDI.13 Environmental cleaning and disinfection is critical to any successful CDI prevention program to prevent transmission to new admissions. Healthcare product manufacturers continue to introduce improved environmental disinfection products that are more effective against spore-forming organisms such as C. difficile and

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that also have a shorter required contact time. The three most effective solutions for elimination of *C. difficile* spores are bleach, hydrogen peroxide, and peracetic acid.14 Cubicle curtains and hard surfaces are a concern for transmission of CDI. Strategies proposed to address contaminated cubicle curtains during recent APIC Annual Conference poster presentations have included the following: using disposable or antimicrobial impregnated curtains; increasing curtain inventory to permit changing at discharge for all contact isolation rooms; using specialized curtains that permit quick switching without a ladder; utilizing a disposable plastic adhesive shield that can be applied to the grab area of the curtain and changed between patients; and spraying HP disinfectant solution on the grab area of the privacy curtain during daily room cleaning and at time of discharge.15

Quality tools have been introduced in recent years for the assessment of environmental cleanliness resulting in improved cleaning and disinfection and increased engagement of environmental services departments. They include fluorescing marker solution that glows under ultra violet light and adenosine triphosphate (ATP).16-18

Automated cleaning technologies have been introduced as a means for eliminating environmental contamination of CDI. Perfect environmental cleaning is not possible due to human factors; therefore, it is necessary to closely scrutinize the evolving evidence relative to automated cleaning technologies. These technologies are designed for use in addition to manual cleaning and include ultra violet light, hydrogen peroxide vapor, steam cleaning, and active ionized water.19-22

RAPID DIAGNOSTICS

Rapid diagnosis of CDI is vital for appropriate isolation. Early termination of unnecessary isolation will permit effective use of limited isolation resources and avoid the well-delineated adverse consequences of isolation for the patient.

Several tests and test strategies are available for the diagnosis of CDI. Suspecting CDI is the most vital part of diagnosis. Clinical suspicion is required in any patient with diarrhea and recent antibiotic use. However, antibiotic use is not a prerequisite, as patients who are immunocompromised, receiving chemotherapeutic agents and even, on occasion, healthy persons, may all have *C. difficile* diarrhea. Additionally, patients with severe disease may present with sepsis and abdominal pain without diarrhea.

A nurse’s clinical identification of *C. difficile* stools is surprisingly accurate and has a sensitivity of 55 percent and specificity of 83 percent—decent, but not adequate to discriminate those who may or may not have *C. difficile* diarrhea. Several laboratory tests are used for *C. difficile* identification. The enzyme immunoassay (EIA) test for glutamate dehydrogenase

This photograph depicts *C. difficile* colonies after 48-hour growth on a blood agar plate; magnified 4.8X.

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(GDH), an enzyme that C. difficile produces constitutively, is 96 to 100 percent sensitive for the presence of the organism; however, because it does not test for toxin, it cannot distinguish between pathogenic and non-pathogenic strains. EIA tests for both toxin A and B are only 70 to 80 percent sensitive, but do identify pathogenic strains. EIA tests for toxin A alone are also available, but even less sensitive. These tests are inexpensive but are limited by their low sensitivity for pathogenic strains. Polymerase Chain Reaction (PCR) tests are now commercially available and have excellent sensitivity and specificity, 93 and 97 percent respectively, but are relatively expensive and require enhanced laboratory support. Some PCR tests can detect the epidemic strain, 027/NAP1/B1, responsible for the more aggressive CDI strains, which adds some epidemiologic value. Two-step tests combine speed and specificity using the sensitive GDH EIA with testing of positive samples with either PCR or toxin EIA for confirmation. Cytotoxin assays are 94 to 100 percent sensitive but are slow and expensive and, therefore, not commonly utilized. Culture is slow, expensive, and cannot distinguish pathogenic from non-pathogenic strains, and is also not often utilized clinically.

The selection of testing strategy varies according to hospital resources and testing volume. If an effective testing strategy is not adopted by one’s healthcare facility, it is vital for the Infection Prevention Committee to mandate availability of appropriate testing.

**ANTIBIOTIC STEWARDSHIP AND ACID BLOCKERS**

The use of antibiotics has been highly associated with the risk for CDI, dating to the original recognition of “Antibiotic Associated Colitis,” long before the identification of C. difficile as the etiology. Antibiotics are not all equally at risk, but in general, the more antibiotic exposure, the higher the risk. The antibiotics with the highest possibility of causing CDI in susceptible patients include fluoroquinolones, clindamycin, and third-generation cephalosporins. Antibiotics with the lowest risk of causing CDI are tetracyclines.

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Access peer-reviewed articles about Clostridium difficile in the American Journal of Infection Control


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and metronidazole. Combinations of antibiotics increase the possibility of CDI, as does an increased duration of exposure. However, fatal CDI has been identified with even prophylactic doses of first generation cephalosporins.27

Restriction of total and broad-spectrum antibiotic use has demonstrated to be an effective intervention to control outbreaks of C. difficile. Experts believe that an antibiotic stewardship program is one of the critical interventions to prevent CDI, but this has been hard to prove as a specific intervention, as the factors related to the spread of C. difficile are multifaceted and include adequacy of environmental cleaning, adherence to isolation requirements, severity of illness, obesity, and others.

Furthermore, reducing unnecessary proton pump inhibitor (PPI) use may potentially be an effective intervention to decrease CDI incidence. Stomach-acid suppression is highly associated with CDI, with PPIs being a more significant risk than histamine blockers. Research has shown that the risk is increased over three-fold with PPIs and approximately half of that with histamine blockers. Interestingly enough, this is on par with antibiotics in the higher-risk categories. Studies have documented that a large proportion of PPI use in hospitals is without an appropriate indication.

FECAL BACTEROThERAPY

Treatments available for CDI are less than optimal. Although the majority of patients are effectively treated with currently available medications, a significant percentage of patients still have treatment failures. Of these failures, a disturbing number have repeated treatment failures leading to severe ongoing morbidity. Attempts to restore the normal bowel flora have been performed for years, albeit infrequently, despite the fact that this may be the most effective treatment for refractory disease. The reluctance to pursue this therapy for aesthetic reasons is apparent and the lack of protocols for donor screening, processing, and administration of the therapy has worsened the problem.

The mechanism of action of this therapy is not totally clear. While restoration of normal bowel flora may be the mechanism, other theories besides restoration of the intestinal microbiome include: addition of flora that inhibit C. difficile growth; stimulation of immune responses of the host by changes in the microbiome; and, even changes induced by the cathartic prep for the installation procedure itself.28

The procedure itself is relatively simple and has reportedly been performed at home with clear instruction (anecdotal). A sample of stool from a donor screened for potentially contagious diseases is suspended in saline and infused by enema, colonoscopic, enteroscopic, or nasogastric tube. Efficacy rates in refractory cases range from 70 to 100 percent, depending on route, preparation, and even the source of the donor.29 The optimal process remains to be delineated, but even the least effective route cures cases refractory to all other available therapy the vast majority of the time.

CONCLUSION

Healthcare professionals across the continuum of care should...
actively pursue opportunities to improve CDI prevention via hand hygiene, contact precautions, environmental cleaning, rapid diagnostics, antimicrobial stewardship, and fecal bacteriotherapy. Utilizing teamwork and research, prevention of CDI is possible with a multifaceted approach to aim toward elimination. Research will continue to best direct efforts relative to promising new technologies including automated room disinfection, automated hand hygiene compliance monitoring, and more universal employment of fecal transplant.

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