Clostridium difficile is quickly surpassing methicillin-resistant Staphylococcus aureus (MRSA) as the most problematic pathogen in healthcare institutions. While prevention methods appear to be helping to lower hospital infection rates from MRSA, C. difficile, a deadly antibiotic-resistant bacterium, is on the rise.

By Kelly M. Pyrek
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Activities to stop the spread of the intestinal superbug *Clostridium difficile* are on the rise, but they are not yielding large improvements, according to a nationwide survey of infection preventionists released in March by the Association for Professionals in Infection Control and Epidemiology (APIC).

According to the new survey, 70 percent of infection preventionists have adopted additional interventions in their healthcare facilities to address *C. difficile* infection (CDI) since March of 2010, but only 42 percent have seen a decline in their healthcare facility-associated CDI rates during that time period; 43 percent have not seen a decline. While CDI rates have climbed to all-time highs in recent years, few facilities (21 percent of respondents) have added more infection prevention staff to address the problem.

APIC conducted the 2013 CDI Pace of Progress survey in January 2013 to assess activities that have been implemented in U.S. healthcare facilities in the last three years to prevent and control CDI, a healthcare-associated infection that kills 14,000 Americans each year. A total of 1,087 APIC members completed the survey which was intended to provide a general overview of trends and indicate areas where more in-depth research might be beneficial. The findings were presented today at APIC’s *Clostridium difficile* Educational and Consensus Conference in Baltimore, Md.

“We are encouraged that many institutions have adopted stronger measures to prevent CDI, but as our survey indicates, more needs to be done to reduce the spread of this infection,” says Jennie Mayfield, BSN, MPH, CIC, APIC president-elect and clinical epidemiologist at Barnes-Jewish Hospital. “We are concerned that staffing levels are not adequate to address the scope of the problem.”

The Pace of Progress survey also noted an inconsistency between cleaning efforts and monitoring. More than 9 in 10 respondents (92 percent) have increased the emphasis on environmental cleaning and equipment decontamination practices since March 2010, but...
64 percent said they rely on observation, versus more accurate and reliable monitoring technologies to assess cleaning effectiveness. Fourteen percent said that nothing was being done to monitor room cleaning.

“Because C. difficile spores can survive in the environment for many months, environmental cleaning and disinfection are critical to prevent the transmission of CDI,” says Mayfield. “Environmental services must take the lead in developing aggressive programs to monitor cleaning practices and then ensure that the results are shared with front-line staff. Without that buy-in, practices are unlikely to improve.”

According to the survey, antimicrobial stewardship programs are slowly increasing. Sixty percent of respondents have antimicrobial stewardship programs at their facilities, compared with 52 percent in 2010. Because antimicrobial use is one of the most important risk factors for CDI, stewardship programs that promote judicious use of antimicrobials should be encouraged.

Nearly 4 out of 5 respondents have used the APIC Implementation Guide on CDI to help identify or guide improvements. APIC has released a second, expanded edition that showcases tools and resources for prevention programs.

“We look forward to the dialogue at our conference among government leaders, clinical experts, public health professionals, and infection preventionists,” says Katrina Crist, APIC CEO. “Working together we will identify knowledge gaps and research needs so that we can chart the steps toward stopping transmission of this infection.”

According to APIC’s 2010 survey on C. difficile, 53 percent of respondents reported adopting additional measures to control the spread of CDI. Less than a quarter, however, have been able to add more infection prevention staff. APIC conducted the 2010 CDI Pace of Progress poll to determine if hospitals have increased interventions to prevent CDI in the 18 months since the 2008 APIC CDI prevalence study revealed CDI rates to be six to 20 times greater than previous estimates. According to the 2010 Pace of Progress survey, institutions that have not added interventions believe their rates of CDI are under control: 45 percent said CDI was not identified as a high-priority problem for their facility, 34 percent have an infection control plan to increase interventions in the event of an outbreak, and 30 percent said that CDI rates were declining with current practices.

APIC’s 2010 CDI Pace of Progress poll indicated that institutions are using multiple strategies, as recommended, to address CDI:

- 83 percent of respondents currently have hospital-wide hand hygiene initiatives
- 90 percent perform surveillance or conduct activities to promptly identify CDI cases
- 94 percent always place patients with CDI on Contact Precautions, meaning they isolate patients suspected of having CDI, and healthcare professionals use gowns and gloves when caring for them
- 86 percent have increased their emphasis on environmental cleaning

According to the Centers for Disease Control and Prevention, deaths related to CDI increased 400 percent between 2000 and 2007, due in part to a stronger germ strain. CDI is estimated to add at least $1 billion annually to U.S. healthcare costs.
Clostridium difficile is quickly surpassing methicillin-resistant Staphylococcus aureus (MRSA) as the most problematic pathogen in healthcare institutions. While prevention methods appear to be helping to lower hospital infection rates from MRSA, C. difficile, a deadly antibiotic-resistant bacterium, is on the rise, confirms research from the Duke Infection Control Outreach Network (DICON).

“We found that MRSA infections have declined steadily since 2005, but C. difficile infections have increased since 2007,” says Becky Miller, MD, an infectious diseases fellow at Duke University Medical Center. C. difficile is a multidrug-resistant bacterium that causes diarrhea and in some cases life-threatening inflammation of the colon. The infections are currently treated with one of two antibiotics. But relapses are common and occur in one-quarter of patients despite treatment, according to Miller.

“This is not a nuisance disease,” says Daniel Sexton, MD, director of DICON. “A small percentage of patients with C. difficile may die, despite treatment. Also, it is likely that the routine use of alcohol-containing hand cleansers to prevent infections from MRSA does not simultaneously prevent infections due to C. difficile.”

Miller and her team evaluated data from 28 hospitals in DICON, a collaboration between Duke and 39 community hospitals located in Georgia, North Carolina, South Carolina, and Virginia. The group tries to improve infection control programs by compiling data on infections occurring at member hospitals, identifying trends and areas for improvement, and providing ongoing education and leadership to community providers. During a 24-month period, there were 847 cases of C. difficile infections in the 28 hospitals and the rate of C. difficile infection was 25 percent higher than the rate of infection due to MRSA. Miller presented her findings at the Fifth Decennial International Conference on Healthcare-Associated Infections in 2010 in Atlanta.

“C. difficile is very common and deserves more attention,” Miller says. “Most people continue to think of MRSA as the big, bad superbug. Based on our data, we can see that this thinking, along with prevention methods, will need to change.”

In the past, hospitals were focused on MRSA and developed their prevention methods on MRSA as the issue, Sexton says. “I have always thought that we need to be looking more globally at all the problems and this new information about C. difficile provides more data to support that,” he says.

C. difficile has been a low priority for hospitals, but now it is a relatively important priority, Sexton adds.

“The key is to develop prevention methods aimed at C. difficile while still maintaining the success we have had with MRSA,” Miller says.
Compounding C. difficile issues in hospitals is the fact that new variants and strains of CDI have increased in virulence, decreased in their response to metronidazole therapy. This is not only happening in hospital settings, but in the community where cases are showing up in nonelderly populations. Even more significant, a number of these cases occurred in patients with no recent hospitalization or antibiotic use, according to a study based on the Rochester Epidemiological Project, released in a presentation for the American College of Gastroenterology 2009 annual scientific meeting. Probable causes for this change may include an older population, broader use of antibiotics and a new, more virulent strain of CDI, according to Darrell S. Pardi at the Mayo Clinic in Rochester, Minn., senior author on the study.

Some cases are proving more difficult to treat with the resistant strains that are emerging and where they’re coming from is not always clear-cut, as it could be overuse of antibiotics or under treatment, where patients aren’t taking their full course of antibiotics or even a novel change of the bacteria that is occurring.

Carlene A. Muto, MD, medical director for infection control at the University of Pittsburgh School of Medicine, noted that there is a large undetected reservoir in patients who asymptotically carry CDI. Many studies have cited non-compliance with patient room cleaning but one key to controlling CDI may lie in the practice of cleaning all surfaces this way rather than only the ones in rooms of patients known to be infected.

Compounding this difficult picture is the fact that common hand hygiene products are often ineffective at killing CDI as the bacteria is sticky, similar to anthrax. The C. difficile spores have an exosporium that confers a particulate adherence-sticky chains of protein containing substances that stick on hands says Dale Gerding, MD, associate chief of staff, research and development coordinator for Edward Hines Jr. VA Hospital. These results reinforce the need for contact precautions, complete with gloves, for the care of these patients.

Studies are indicating that due to an increased number of C. diff cases, infectious diarrhea is on the rise in U.S. healthcare facilities. The Society for Healthcare Epidemiology of America (SHEA) recommends increasing prevention efforts aimed at controlling the spread of C. difficile—including good hand hygiene and antimicrobial stewardship. Unnecessary antibiotic use can create an environment for C. difficile to grow and create serious health issues. To help eliminate inappropriate use of these drugs, antimicrobial stewardship programs and interventions help guide prescribers’ understanding of when antibiotics are needed and what the best treatment choices are for a particular patient.

“Nearly 50 percent of antibiotics are inappropriately prescribed, killing off the natural protective bacteria in our gut,” says Jan E. Patterson, MD, MS, past-president of SHEA. “The increased prevalence in C. difficile demonstrates the need for better control and use of antibiotics, not only to preserve the efficacy of these life saving drugs, but to prevent adverse events like C. difficile infection.”

C. difficile can spread from person-to-person on contaminated equipment and on the hands of healthcare professionals and visitors. But C. difficile infections can be prevented. In the Compendium of Strategies to Prevent Healthcare-Associated Infections, SHEA recommends that health professionals clean hands with soap and water during outbreaks to
prevent transmission of C. difficile infections. Evidence shows that soap and water is superior to alcohol-based sanitizers for removing C. difficile spores. Healthcare professionals should also follow contact precautions and wear gloves when entering the room of a patient with C. difficile.

CDC’s 2012 Vital Signs report found that 337,000 cases of C. difficile occur annually in the U.S. and are linked with about 14,000 deaths, adding at least $1 billion in healthcare costs. Patterson notes, “It is important to create a public dialogue about infections such as C. difficile – what they are, where they are most likely to occur and how they spread. This is a critical component of increasing our understanding of these infections and ultimately reducing rates of them.”

Let's take a closer look at these issues.

The Challenge of Clostridium difficile

A 2012 Vital Signs report from the Centers for Disease Control and Prevention (CDC) says that C. difficile infections are at an all-time high, and are linked to 14,000 deaths in the U.S. annually. Deaths related to C. difficile increased 400 percent between 2000 and 2007, due in part to a stronger pathogen strain. Almost half of infections occur in people younger than 65, but more than 90 percent of deaths occur in people 65 and older.

Most C. difficile infections are connected with receiving medical care — about 25 percent of C. difficile infections first show symptoms in hospital patients; 75 percent first show in nursing home patients or in people recently cared for in doctors’ offices and clinics.

Infections from Clostridium difficile is a patient safety concern in all types of medical facilities, not just hospitals as traditionally thought, according to the 2012 Vital Signs report. While many healthcare-associated infections, such as bloodstream infections, declined in the past decade, C. difficile infection rates and deaths climbed to historic highs.

“C. difficile harms patients just about everywhere medical care is given,” says CDC director Thomas R. Frieden, MD, MPH. “Illness and death linked to this deadly disease do not have to happen. Patient lives can be saved when healthcare providers follow the 6 Steps to Prevention, which include key infection control and smart antibiotic prescribing recommendations.”
C. difficile is linked to about 14,000 U.S. deaths every year. Those most at risk are people who take antibiotics and also receive care in any medical setting. Almost half of infections occur in people younger than 65, but more than 90 percent of deaths occur in people 65 and older. Previously released estimates based on billing data show that the number of U.S. hospital stays related to C. difficile remains at historically high levels of about 337,000 annually, adding at least $1 billion in extra costs to the healthcare system. However, the Vital Signs report shows that these hospital estimates may only represent one part of C. difficile’s overall impact.

Deaths Caused by C. difficile Infections*

* Age-adjusted rate of C. difficile as the primary (underlying) cause of death
Source: CDC National Center for Health Statistics, 2012

According to the 2012 Vital Signs report, 94 percent of C. difficile infections are related to medical care. About 25 percent of C. difficile infections first show symptoms in hospital patients; 75 percent first show in nursing home patients or in people recently cared for in doctor’s offices and clinics. Although the proportion of infection onset is lower in hospitals, these facilities remain at the core of prevention since many patients with C. difficile infections are transferred to hospitals for care, raising risk of spread within the facility. The 2012 Vital Signs report shows that half of C. difficile infections diagnosed at hospitals were already present at the time the patient was admitted (present on admission), usually after getting care in other facilities. The other half were related to care given in the hospital where the infection was diagnosed.

Researchers have been able to track the emergence of the global spread of Clostridium difficile. In a recent study (He, et al., 2012), they show that the global epidemic of Clostridium difficile 027/NAP1/BI in the early to mid-2000s was caused by the spread of two different but highly related strains of the bacterium rather than one as was previously thought. The spread and persistence of both epidemics were driven by the acquisition of resistance to a frontline antibiotic. Unlike many other healthcare-associated bacteria, C. difficile produces highly resistant and infectious spores. These spores can promote the transmission of C. difficile and potentially facilitates its spread over greater geographical distances, even across continents.
This study highlights the ease and rapidity with which the hospital bacterium, *C. difficile*, can spread throughout the world, emphasizing the interconnectedness of the global healthcare system.

“Between 2002 and 2006, we saw highly publicized outbreaks of *C. difficile* in hospitals across the UK, U.S., Canada and Europe,” says Dr. Miao He, first author from the Wellcome Trust Sanger Institute. “We used advanced DNA sequencing to determine the evolutionary history of this epidemic and the subsequent pattern of global spread. We found that this outbreak came from two separate epidemic strains or lineages of *C. difficile*, FQR1 and FQR2, both emerging from North America over a very short period and rapidly spread between hospitals around the world.”

The team used the genetic history to map both epidemic strains of *C. difficile* using a global collection of samples from hospital patients between 1985 and 2010. They demonstrated that the two *C. difficile* strains acquired resistance to this antibiotic, fluoroquinolone, separately, a key genetic change that may have instigated the epidemics in the early 2000s.

“Up until the early 2000s, fluoroquinolone was an effective treatment for *C. difficile* infection,” says professor Brendan Wren, author from the London School of Hygiene and Tropical Medicine. “We’ve seen that since these strains acquired resistance to this frontline antibiotic, not only is it now virtually useless against this organism, but resistance seems to have been a major factor in the continued evolution and persistence of these strains in hospitals and clinical settings.”

The team found the first outbreak strain of *C. difficile*, FQR1 originated in the U.S. and spread across the country. They also saw sporadic cases of this strain of *C. difficile* in Switzerland and South Korea. They found that the second strain of *C. difficile*, FQR2, originated in Canada and spread rapidly over a much wider area, spreading throughout North America, Australia and Europe.

The team showed that the spread of *C. difficile* into the UK was frequently caused by long-range geographical transmission event and then spread extensively within the UK. They confirmed separate transmission events to Exeter, Ayrshire and Birmingham from North America and a transmission event from continental Europe to Maidstone. These events triggered large-scale *C. difficile* outbreaks in many hospitals across the UK in the mid-2000s.

“We have exposed the ease and rapidity with which these fluoroquinolone-resistant *C. difficile* strains have transmitted across the world,” says Dr. Trevor Lawley, lead author from the Wellcome Trust Sanger Institute. “Our research highlights how the global healthcare system is interconnected and how we all need to work together when an outbreak such as this occurs. Our study heralds a new era of forensic microbiology for the transmission tracking of this major global pathogen and will now help us understand at the genetic level how and why this pathogen has become so aggressive and transmissible worldwide. This research will act as a database for clinical researchers to track the genomic changes in *C. difficile* outbreaks.”
The Epidemiology of Clostridium difficile

Clostridium difficile is a spore-forming, Gram-positive anaerobic bacillus that produces two exotoxins: toxin A and toxin B. It is a common cause of antibiotic-associated diarrhea (AAD). It accounts for 15 percent to 25 percent of all episodes of AAD.

There are a handful of diseases that result from Clostridium difficile infection, including:
- Pseudomembranous colitis (PMC)
- Toxic megacolon
- Perforations of the colon
- Sepsis
- Death (rarely)

The main clinical symptoms of Clostridium difficile infection include:
- Watery diarrhea
- Fever
- Loss of appetite
- Nausea
- Abdominal pain/tenderness

There are certain patients who are at increased risk for Clostridium difficile infection; risk increases for patients with the following:
- Antibiotic exposure
- Proton pump inhibitors
- Gastrointestinal surgery/manipulation
- Long length of stay in healthcare settings
- A serious, underlying illness
- Immunocompromising conditions
- Advanced age

Clinicians should understand the differences between Clostridium difficile colonization and Clostridium difficile infection:

Clostridium difficile colonization:
- Patient exhibits NO clinical symptoms
- Patient tests positive for Clostridium difficile organism and/or its toxin
- More common than Clostridium difficile infection

Clostridium difficile infection:
- Patient exhibits clinical symptoms
- Patient tests positive for the Clostridium difficile organism and/or its toxin

Clostridium difficile is the most frequent etiologic agent for healthcare-associated diarrhea. In one hospital, 30 percent of adults who developed healthcare-associated diarrhea were positive for C. difficile. One recent study employing PCR-ribotyping techniques demonstrated that cases of C. difficile-acquired diarrhea occurring in the hospital included patients whose infections were attributed to endogenous C. difficile strains and patients whose illnesses were considered to be healthcare-associated infections. Most patients remain asymptomatic after infection, but the organism continues to be shed in their stools.
Risk factors for acquiring C. difficile-associated infection include:

- Exposure to antibiotic therapy, particularly with beta-lactam agents
- Gastrointestinal procedures and surgery
- Advanced age
- Indiscriminate use of antibiotics. Of all the measures that have been used to prevent the spread of C. difficile-associated diarrhea, the most successful has been the restriction of the use of antimicrobial agents.

**Diagnosis of Clostridium difficile**

There are a number of laboratory tests are commonly used to diagnose Clostridium difficile infection:

- **Stool culture for Clostridium difficile**: While this is the most sensitive test available, it is the one most often associated with false-positive results due to presence nontoxigenic Clostridium difficile strains. However, this can be overcome by testing isolates for toxin production (i.e. “toxigenic culture”). Nonetheless, stool cultures for Clostridium difficile are labor intensive, require an appropriate culture environment to grow anaerobic microorganisms, and have a relatively slow turn-around time (i.e., results available in 48 to 96 hours) making them overall less clinically useful. Results of toxigenic cultures do serve as a gold-standard against which other test modalities are compared in clinical trials of performance.

- **Molecular tests**: FDA-approved PCR assays, which test for the gene encoding toxin B, are highly sensitive and specific for the presence of a toxin-producing Clostridium difficile organism.

- **Antigen detection for Clostridium difficile**: These are rapid tests (<1 hour) that detect the presence of Clostridium difficile antigen by latex agglutination or immunochromatographic assays. Because results of antigen testing alone are non-specific, antigen assays have been employed in combination with tests for toxin detection, PCR, or toxigenic culture in two-step testing algorithms.

- **Toxin testing for Clostridium difficile**: Tissue culture cytotoxicity assay detects toxin B only. This assay requires technical expertise to perform, is costly, and requires 24 to 48 hours for a final result. It does provide specific and sensitive results for Clostridium difficile infection. While it served as a historical gold standard for diagnosing clinical significant disease caused by Clostridium difficile, it is recognized as less sensitive than PCR or toxigenic culture for detecting the organism in patients with diarrhea. Enzyme immunoassay detects toxin A, toxin B, or both A and B. Due to concerns over toxin A-negative, B-positive strains causing disease, most laboratories employ a toxin B-only or A and B assay. Because these are same-day assays that are relatively inexpensive and easy to perform, they are popular with clinical laboratories. However, there are increasing concerns about their relative insensitivity (less than tissue culture cytotoxicity and much less than PCR or toxigenic culture).

- **Clostridium difficile toxin is very unstable. The toxin degrades at room temperature and may be undetectable within two hours after collection of a stool specimen. False-negative results occur when specimens are not promptly tested or kept refrigerated until testing can be done.
Treatment of Clostridium difficile Infection

In about 20 percent of patients, Clostridium difficile infection will resolve within two to three days of discontinuing the antibiotic to which the patient was previously exposed. The infection can usually be treated with an appropriate course (about 10 days) of antibiotics, including metronidazole, vancomycin (administered orally), or recently approved fidaxomicin. After treatment, repeat Clostridium difficile testing is not recommended if the patients’ symptoms have resolved, as patients may remain colonized.

Over the past several years nationwide, states have reported increased rates of C. difficile infection, noting more severe disease and an associated increase in mortality. C. diffic infection remains a disease mostly associated with healthcare (at least 80 percent). Patients most at risk remain the elderly, especially those using antibiotics. Although the elderly are still most affected, more disease has been reported in traditionally ‘low risk’ persons such as healthy persons in the community, and peripartum women. These changes may be largely due to the new emergence of the current epidemic strain of C. difficile, known by its names assigned by various typing schemes as restriction enzyme analysis type BI, North American Pulsed Field type 1 (NAP1), or PCR ribotype 027. BI/NAP1/027 has spread widely after first being found responsible for outbreaks in Pittsburgh (2000), Atlanta (2001-2), and Montreal (2003). This strain appears more virulent possibly due to its increased production of toxins A and B and its production of an additional toxin known as binary toxin, as well as other factors still under study. In addition to being more virulent, it is more resistant to a commonly-used class of antimicrobials known as the fluoroquinolones.

Like other strains of C. difficile, BI/NAP1/027 can be detected in the stool of infected patients by using laboratory tests that are commonly available in most hospitals. However, none of the FDA-approved tests differentiate between the various strains of C. difficile. Fortunately, because the control measures for outbreaks of any strain of C. difficile are similar, identification of the specific strain is not imperative for controlling outbreaks.

The usual treatment for C. difficile infection includes, if possible, stopping antibiotics being given for other purposes and/or treatment with metronidazole or vancomycin. In order to reduce selective pressure for vancomycin resistance in Enterococci, current guidelines recommend the first-line use of metronidazole over vancomycin.

Recent reports suggest that BI/NAP1/027 may not respond as well to treatment with metronidazole despite the absence of laboratory evidence of metronidazole resistance. Evidence suggests that more severe disease should be treated with vancomycin, over metronidazole.

Increased fluoroquinolone resistance does not affect the management of infections caused by this strain. Fluoroquinolones have never been recommended for treatment of C. difficile infection and susceptibility testing is performed only as a part of an epidemiological investigation. However, resistance to fluoroquinolones may provide the new strain with an advantage over susceptible strains to spread within healthcare facilities where these antibiotics are commonly used.

Healthcare facilities should monitor the number of C. difficile infections and, especially if rates at the facility increase, the severity of disease and patient outcomes. If an increase in rates or severity is observed, healthcare facilities should reassess compliance with core recommended practices as outlined in the CDC Toolkit for Evaluation of Environmental Cleaning for known cases of C. diff infection.
Antimicrobial stewardship is a key component to CDI control and prevention. In the Clinical Practice Guidelines for Clostridium difficile Infection in Adults, Cohen, et al. (2010) emphasize antimicrobial-use restrictions: “Minimize the frequency and duration of antimicrobial therapy and the number of antimicrobial agents prescribed, to reduce CDI risk. Implement an antimicrobial stewardship program. Antimicrobials to be targeted should be based on the local epidemiology and the C. difficile strains present, but restricting the use of cephalosporin and clindamycin (except for surgical antibiotic prophylaxis) may be particularly useful.”

The importance of antimicrobial and antibiotic stewardship becomes clear in an era when Clostridium difficile infections are becoming more common and more severe in vulnerable patient populations — hospitalized children and the elderly — in large part due to greater use of antibiotics. Mayo Clinic researchers reported on studies presented at a recent American College of Gastroenterology annual meeting, including one Mayo study that analyzed five years of data from the National Hospital Discharge Survey and found that of an estimated 13.7 million hospitalized children, the 46,176 with C. diff infections had significantly longer hospital stays, more instances of colectomy, increased admission to long- or short-term care facilities, and higher risk of death.

“Despite increased awareness of C. difficile in children, and advancements in management and prevention, this remains a major problem in hospitalized children,” says Sahil Khanna, MBBS, a Mayo Clinic gastroenterologist. Elderly patients also have a greater risk of complications from C. difficile and dying from the infection. In a separate study of 1.3 million adult patients hospitalized with C. diff, patients over 65 were in the hospital longer, sent to nursing homes more frequently and had a greater risk of death. That suggests being over age 65 is an independent risk factor for adverse outcomes associated with the infection.

Researchers say increased use of antibiotics is a main reason for the increasing infection rates. When a person takes antibiotics, good bacteria or flora that protect against infection are destroyed. When these bacteria are destroyed, patients are vulnerable to C. difficile picked up from contaminated surfaces or spread from a healthcare provider’s hands.

Treatments depend on the severity and number of times a patient has had a C. diff infection. Typically, physicians will treat it with the antibiotic metronidazole or oral vancomycin. For severe cases and patients with recurrent C. diff, fecal transplants are an option. Stool transplant restores healthy intestinal bacteria by placing donor stool in the colon.

Recurrent C. difficile is a major problem with the risk of recurrence being 20 percent after a first infection and as much as 60 percent after multiple infections. People who have had C. difficile are twice as likely to get it again. Other known risk factors include proton-pump inhibitors for gastric reflux, immunosuppression, and long hospital stays.
Transmission of Clostridium difficile

Cohen, et al. (2010) explain that the primary mode of C. difficile transmission resulting in disease is person-to-person spread through the fecal-oral route, principally within inpatient healthcare facilities: “Studies have found that the prevalence of asymptomatic colonization with C. difficile is 7 percent to 26 percent among adult inpatients in acute care facilities and is 5 percent to 7 percent among elderly patients in long-term care facilities. Other studies, however, indicate that the prevalence of asymptomatic colonization may be more on the order of 20 percent to 50 percent in facilities where CDI is endemic. The risk of colonization increases at a steady rate during hospitalization, suggesting a cumulative daily risk of exposure to C. difficile spores in the healthcare setting. Other data suggest that the prevalence of C. difficile in the stool among asymptomatic adults without recent healthcare facility exposure is less than 2 percent.”

According to Cohen, et al. (2010), the usual incubation period from exposure to onset of CDI symptoms is not known with certainty; however, “in contrast to the situation with other multidrug-resistant pathogens that cause healthcare-associated infections, persons who remain asymptptomatically colonized with C. difficile over longer periods of time appear to be at decreased, rather than increased, risk for development of CDI.” The researchers note further that the period between exposure to C. difficile and the occurrence of CDI has been estimated in several studies to be a median of two to three days: “This is to be distinguished from the increased risk of CDI that can persist for many weeks after cessation of antimicrobial therapy and which results from prolonged perturbation of the normal intestinal flora. However, recent evidence suggests that CDI resulting from exposure to C. difficile in a healthcare facility can have onset after discharge. The hands of healthcare workers, transiently contaminated with C. difficile spores, are probably the main means by which the organism is spread during non-outbreak periods.”

So as we have seen, transfer of the pathogen to the patient via the hands of healthcare workers is thought to be the most likely mechanism of exposure. Standard isolation techniques intended to minimize enteric contamination

HOW C. DIFFICILE SPREADS

George, a 68-year-old man, goes to the doctor’s office and is diagnosed with pneumonia. He is prescribed antibiotics, drugs that put him at risk for C. difficile infection for several months.

ONE MONTH LATER

George breaks his leg and goes to a hospital. A healthcare worker spreads C. difficile to him after forgetting to wear gloves when treating a C. difficile-infected patient in the next room.

TWO DAYS LATER

George transfers to a rehabilitation facility for his leg and gets diarrhea. He is not tested for C. difficile. The healthcare worker doesn’t wear gloves and infects other patients.

THREE DAYS LATER

George goes back to the hospital for treatment of diarrhea and tests positive for C. difficile. The healthcare worker doesn’t wear gloves and infects other patients.

Source: CDC, 2012
of patients, healthcare workers’ hands, patient-care items, and environmental surfaces have been published. Handwashing remains the most effective means of reducing hand contamination. Proper use of gloves is an ancillary measure that helps to further minimize transfer of these pathogens from one surface to another.

Clostridium difficile is shed in feces. Any surface, device, or material (e.g., commodes, bathing tubs, and electronic rectal thermometers) that becomes contaminated with feces may serve as a reservoir for the Clostridium difficile spores. Clostridium difficile spores are transferred to patients mainly via the hands of healthcare personnel who have touched a contaminated surface or item.

C. difficile moves with patients from one healthcare facility to another, infecting other patients. Remember, the 2012 Vital Signs report found that half of all hospital patients with C. difficile infections have the infection when admitted and may spread it within the facility. The most dangerous source of spread to others is patients with diarrhea.

Unnecessary antibiotic use in patients at one facility may increase the spread of C. difficile in another facility when patients transfer. When a patient transfers, healthcare providers are not always told that the patient has or recently had a C. difficile infection, so they may not take the right actions to prevent spread.

“C. difficile infections are usually a regional problem since patients transfer back and forth between facilities, allowing the disease to spread,” says L. Clifford McDonald, MD, CDC medical epidemiologist and lead author of the Vital Signs study. “Health departments have the ability to work with many types of healthcare facilities, and have a unique opportunity to coordinate local, comprehensive prevention programs to reduce the occurrence of these infections.”

**FAST FACTS**

**WHAT PATIENTS CAN DO**

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<tr>
<th>Patients Can:</th>
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<tbody>
<tr>
<td>- Take antibiotics only as prescribed by your doctor.</td>
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<tr>
<td>Antibiotics can be lifesaving medicines.</td>
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<tr>
<td>- Tell their doctor if they have been on antibiotics and get diarrhea within a few months.</td>
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<tr>
<td>- Wash their hands after using the bathroom.</td>
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<tr>
<td>- Try to use a separate bathroom if you have diarrhea, or be sure the bathroom is cleaned well if someone with diarrhea has used it.</td>
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Prevention of Clostridium difficile Infection: Hand Hygiene, Contact Precautions and Environmental Cleaning

The Health and Human Services Department (HHS)'s National Action Plan to Prevent Healthcare-Associated Infections addresses Clostridium difficile infections. The 2013 National Prevention Target is a 30 percent reduction in facility-wide healthcare facility-onset C. difficile or 0.70 SIR. According to data from the CDC’s National Healthcare Safety Network, the preliminary 2012 Assessment is 1.28 SIR; 28 percent increase from baseline (2010-2011 is the baseline period).

The summary of progress toward the 30-percent reduction goal for Clostridium difficile (hospitalizations) has been as follows:

- 2013 National Prevention Target: 30 percent reduction in hospitalizations with C. difficile
- 2012 Assessment Projection: 12.9 hospitalizations per 1,000 discharges; 11.2 percent increase from baseline
- 2011 Assessment Projection: 12.4 hospitalizations per 1,000 discharges; 6.9 percent increase from baseline

According to the HHS and to AHRQ’s Healthcare Cost and Utilization Project, the 2013 target is unlikely to be met on schedule.

The 2012 Vital Signs report says that despite the numerous challenges, C. difficile infections can be prevented. Early results from hospital prevention projects show 20 percent fewer C. difficile infections in less than two years with infection prevention and control measures.

Clostridium difficile infection be prevented in healthcare settings through the following strategies:

- Use antibiotics judiciously
- Use Contact Precautions: for patients with known or suspected Clostridium difficile infection:
  - Place these patients in private rooms. If private rooms are not available, these patients can be placed in rooms (cohorted) with other patients with Clostridium difficile infection.
  - Use gloves when entering patients’ rooms and during patient care.
  - Perform hand hygiene after removing gloves. Because alcohol does not kill Clostridium difficile spores, use of soap and water is more efficacious than alcohol-based handrubs. However, early experimental data suggest that, even using soap and water, the removal of C. difficile spores is more challenging than the removal or inactivation of other common pathogens. Preventing contamination of the hands via glove use remains the cornerstone for preventing Clostridium difficile transmission via the hands of healthcare workers; any theoretical benefit from instituting soap and water must be balanced against the potential for decreased compliance resulting from a more complex hand hygiene message. If your institution experiences an outbreak, consider using only soap and water for hand hygiene when caring for patients with Clostridium difficile infection (see sidebar on page 20).
  - Use gowns when entering patients’ rooms and during patient care.
  - Dedicate or perform cleaning of any shared medical equipment.
• Continue these precautions until diarrhea ceases. Because Clostridium difficile-infected patients continue to shed organism for a number of days following cessation of diarrhea, some institutions routinely continue isolation 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.
  • Consider using an Environmental Protection Agency (EPA)-registered disinfectant with a sporicidal claim for environmental surface disinfection after cleaning in accordance with label instructions; generic sources of hypochlorite (e.g., household chlorine bleach) also may be appropriately diluted and used. (Note: Standard EPA-registered hospital disinfectants are not effective against Clostridium difficile spores.) Hypochlorite-based disinfectants may be most effective in preventing Clostridium difficile transmission in units with high endemic rates of Clostridium difficile infection.
  • Follow the manufacturer’s instructions for disinfection of endoscopes and other devices.

In the Clinical Practice Guidelines for Clostridium difficile Infection in Adults, Cohen, et al. (2010) address environmental cleaning and disinfection: “Identification and removal of environmental sources of C. difficile, including replacement of electronic rectal thermometers with disposables, can reduce the incidence of CDI. Use chlorine-containing cleaning agents or other sporicidal agents to address environmental contamination in areas associated with increased rates of CDI. Routine environmental screening for C. difficile is not recommended.”

**FAST FACTS**

**WHAT ADMINISTRATORS CAN DO**

Health Care Facility Administrators Can:
- Support better testing, tracking, and reporting of infections and prevention efforts.
- Make sure cleaning staff follows CDC recommendations, using an EPA-approved spore-killing disinfectant in rooms where C. difficile patients are treated.
- Notify other healthcare facilities about infectious diseases when patients transfer, especially between hospitals and nursing homes.
- Participate in a regional C. difficile prevention effort.
As Cohen, et al. (2010) note, “The true extent of the contribution of the healthcare environment to infection transmission remains controversial. However, for bacteria that resist desiccation, there is much evidence that the environment is an important source of nosocomial infection. C. difficile spores can survive in the environment for months or years and can be found on multiple surfaces in the healthcare setting.”

To help control Clostridium difficile, environmental surfaces should be kept clean, and body substance spills should be managed promptly as outlined in CDC’s Guidelines for Environmental Infection Control in Health-Care Facilities. Routine cleaning should be performed prior to disinfection. EPA-registered disinfectants with a sporicidal claim have been used with success for environmental surface disinfection in those patient-care areas where surveillance and epidemiology indicate ongoing transmission of Clostridium difficile.

Note: EPA-registered disinfectants are recommended for use in patient-care areas. When choosing a disinfectant, check product labels for inactivation claims, indications for use, and instructions.

In a section for special pathogens, the Guidelines for Environmental Infection Control in Health-Care Facilities, 2003 emphasizes the challenge of dealing with C. diff spores: “Normally fastidious in its vegetative state, it is capable of sporulating when environmental conditions no longer support its continued growth. The capacity to form spores enables the organism to persist in the environment (e.g., in soil and on dry surfaces) for extended periods of time. Environmental contamination by this microorganism is well known, especially in places where fecal contamination may occur. The environment (especially housekeeping surfaces) rarely serves as a direct source of infection for patients. However, direct exposure to contaminated patient-care items (e.g., rectal thermometers) and high-touch surfaces in patients’ bathrooms (e.g., light switches) have been implicated as sources of infection.”

**FAST FACTS**

**WHAT COMMUNITIES CAN DO**

Communities and states can:
- Encourage healthcare facilities to track and share data using CDC’s National Healthcare Safety Network.
- Develop regional C. difficile prevention projects with many types of facilities.
- Help healthcare facilities in their prevention efforts.
- Provide a standardized form for facilities to use during patient transfers, especially between hospitals and nursing homes.
The guideline adds, “The degree to which the environment becomes contaminated with C. difficile spores is proportional to the number of patients with C. difficile-associated diarrhea, although asymptomatic, colonized patients may also serve as a source of contamination. Few studies have examined the use of specific chemical germicides for the inactivation of C. difficile spores, and no well-controlled trials have been conducted to determine efficacy of surface disinfection and its impact on healthcare-associated diarrhea. Some investigators have evaluated the use of chlorine-containing chemicals (e.g., 1,000 ppm hypochlorite at recommended use-dilution, 5,000 ppm sodium hypochlorite [1:10 v/v dilution], 1:100 v/v dilutions of unbuffered hypochlorite, and phosphate-buffered hypochlorite [1,600 ppm]). One of the studies demonstrated that the number of contaminated environmental sites was reduced by half, whereas another two studies demonstrated declines in healthcare-associated C. difficile infections in a HSCT unit and in two geriatric medical units during a period of hypochlorite use. The presence of confounding factors, however, was acknowledged in one of these studies. The recommended approach to environmental infection control with respect to C. difficile is meticulous cleaning followed by disinfection using hypochlorite-based germicides as appropriate. However, because no EPA-registered surface disinfectants with label claims for inactivation of C. difficile spores are available, the recommendation is based on the best available evidence from the scientific literature.” Since the writing of this guideline, a number of products with C. diff claims have emerged; infection preventionists are encouraged to investigate manufacturers’ product information and read product labels carefully.

As Cohen, et al. (2010) observe, “A wide range of disinfectants suitable for decontamination of instruments (e.g., endoscopes) or the environment have in vitro activity against C. difficile spores. With [some] exceptions, comparative data on the in situ efficacy of these disinfection options are lacking. The efficacy of cleaning is critical to the success of decontamination in general, and thus user acceptability of disinfection regimens is a key issue.”

**FAST FACTS**

**WHAT THE FEDERAL GOVERNMENT CAN DO**

Federal Government Is:
- Tracking and reporting national progress toward preventing C. difficile infections in many types of healthcare facilities. These programs help track the size of the problem, antibiotics used, and people at risk.
- Providing prevention expertise, as well as outbreak and laboratory support to health departments and facilities.
Guidelines emphasize the care that must be taken when using disinfectants, as they can be a double-edged sword. As Cohen, et al. (2010) note, “A study found that working-strength concentrations of five different cleaning agents inhibited growth of C. difficile cultures in vitro. However, only chlorine-based cleaning agents used at the recommended working concentrations were able to inactivate C. difficile spores. Also, in vitro exposure of epidemic C. difficile strains, including NAP1/BI/027, to subinhibitory concentrations of non–chlorine-based cleaning agents (detergent or hydrogen peroxide) significantly increased sporulation capacity; this effect was generally not seen with chlorine-based cleaning agents. These observations suggest the possibility that some cleaning agents, if allowed to come into contact with C. difficile in low concentrations, could promote sporulation and, therefore, the persistence of the bacterium in the environment. Use of chlorine-containing cleaning products presents health and safety concerns, as well as compatibility challenges that need to be assessed for risk. However, current evidence supports the use of chlorine-containing cleaning agents (with at least 1,000 ppm available chlorine), particularly to address environmental contamination in areas associated with endemic or epidemic CDI. Routine bacteriological surveillance of the environment is generally unhelpful, largely because it has not been possible to establish threshold levels associated with increased risk of clinical infection, but it may be useful for ascertaining whether cleaning standards are suboptimal, notably in a setting experiencing an outbreak or where C. difficile is hyperendemic.”

**HAND HYGIENE AND C. DIFFICILE PREVENTION**

In a special addendum to the Compendium of Strategies to Prevent Healthcare-Associated Infections in Acute Care Hospitals, “Rationale for Hand Hygiene Recommendations after Caring for a Patient with Clostridium difficile Infection,” Erik R. Dubberke, MD, MSPH and Dale N. Gerding, MD, acknowledge that questions arise in regard to the recommended method of hand hygiene after caring for patients with Clostridium difficile infection (CDI). The CDI component of the SHEA/IDSA Compendium of Practice Recommendations to Prevent Healthcare-Associated Infections and the SHEA/IDSA Clinical Practice Guidelines for CDI recommend preferential use of soap and water for hand hygiene over alcohol-based hand hygiene products only in outbreak settings. As Dubberke and Gerding note, “Some have found the recommendation to preferentially perform hand hygiene with soap and water after caring for a patient with CDI only during outbreaks, and not in non-outbreak settings, confusing. Alcohol does not kill C. difficile spores. In addition, several studies have found handwashing with soap and water, or with an antimicrobial soap and water, to be more effective at removing C. difficile spores than alcohol-based hand hygiene products from the hands of volunteers inoculated with a known number of C. difficile spores.”
They add further, “The primary reason hand hygiene with soap and water is not recommended for CDI prevention in non-outbreak settings is 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 of the 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. The combination of these findings, lack of change in CDI but decreases in other non-spore forming, multidrug-resistant pathogens, with the use of alcohol-based hand hygiene products are the basis behind not recommending preferential use of soap and water for CDI prevention in non-outbreak settings. However because of the theoretical increase in risk of C. difficile transmission based on the volunteer hand contamination studies, the experts who wrote the CDI component of the SHEA/IDSA Compendium and the SHEA/IDSA Clinical Practice Guidelines for CDI felt it was prudent to recommend preferential use of soap and water after caring for a patient with CDI in outbreak settings.”

Dubberke and Gerding continue, “There are several potential explanations for the lack of an association between CDI incidence and method of hand hygiene. One is healthcare workers may have continued to use soap and water after caring for patients with CDI during periods when alcohol-based hand hygiene products were the preferred method for hand hygiene. We feel this is an unlikely explanation since hand hygiene compliance is typically ≤ 40% with the use of soap and water. A more likely explanation is it is recommended to don gloves prior to entering the room of a patient with CDI. Glove use is the only CDI prevention recommendation with the highest strength of recommendation and quality of evidence rating of “AI”. Gloves decrease risk of C. difficile transmission by preventing the contamination of healthcare worker hands with C. difficile spores. If gloves are removed properly to prevent hand contamination in the removal process, any potential benefit of using soap and water over alcohol-based hand hygiene products is likely negated. In conclusion, although soap and water is superior to removing C. difficile spores from hands of volunteers compared to alcohol-based hand hygiene products, there have been no studies in acute care settings that have demonstrated an increase in CDI with alcohol-based hand hygiene products or a decrease in CDI with soap and water. This is why preferential use of soap and water for hand hygiene after caring for a patient with CDI is not recommended in non-outbreak settings. 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.”

Gloves decrease risk of C. difficile transmission by preventing the contamination of healthcare worker hands with C. difficile spores.
What the Literature Says About Clostridium difficile

Let’s take a look at some of what has been published in the medical literature regarding various aspects of Clostridium difficile:

_C. difficile increases hospital length of stay._

Hospital-onset Clostridium difficile-associated diarrhea (HO-CDAD) has been associated with longer length of stay (LOS) and higher hospital costs among patients in general. The burden of HO-CDAD is unknown among patients who may be at particular risk of poor outcomes: older patients, those with complex or chronic conditions (renal disease, cancer, inflammatory bowel disease [IBD]), and those with concomitant antibiotic (CAbx) use during treatment for CDAD. Campbell, et al. (2013) conducted a retrospective analysis (2005-2011) of the Health Facts® database (Cerner Corp., Kansas City, MO) containing comprehensive clinical records from 186 US hospitals identified hospitalized adult patients with HO-CDAD based on a positive C. difficile toxin collected ≥48 hours after admission. Control patients were required to have total hospital LOS ≥2 days. Separate logistic regression models to estimate propensities were developed for each study group, with HO-CDAD vs controls as the outcome. Differences in LOS and costs were calculated between cases and controls for each group. Results: A total of 4521 patients with HO-CDAD were identified. Mean age was 70 years, 54 percent were female, and 13 percent died. After matching, LOS was significantly greater among HO-CDAD patients (vs controls) in each group except IBD. The significant difference in LOS ranged from 3.0 (95% CI = 1.4-4.6) additional days in older patients to 7.8 (95% CI = 5.7-9.9) days in patients with CAbx exposure. HO-CDAD was associated with significantly higher costs among older patients (p < 0.001) and among those with renal impairment (p = 0.012) or CAbx use (p < 0.001). Limitations: Missing cost data and potential misclassification of colonized patients as infected. Conclusions: Renal impairment, advanced age, cancer, and CAbx use are associated with significantly longer LOS among HO-CDAD patients, with CAbx users being the most resource intensive. Early identification and aggressive treatment of HO-CDAD in these groups may be warranted.

Mitchell and Gardner (2012) used an integrative review method to understand the impact that CDI has on length of stay (LOS). Papers were reviewed and analyzed individually and themes were combined using integrative methods. They report that findings from all studies suggested that CDI contributes to a longer LOS in hospital. In studies that compared persons with and without CDI, the difference in the LOS between the two groups ranged from 2.8 days to 16.1 days. Potential limitations with data analysis were identified, given that no study fully addressed the issue of a time-dependent bias when examining the LOS. Recent literature suggests that a multi-state model should be used to manage the issue of time-dependent bias. The researchers conclude that studies examining LOS attributed to CDI varied considerably in design and data collected. Future studies examining LOS related to CDI and other healthcare-associated infections should consider capturing the timing of infection in order to be able to employ a multi-state model for data analysis. Their research was published in Antimicrobial Resistance and Infection Control.
Forster, et al. (2011) determined the independent impact of hospital-acquired infection with C. difficile on length of stay in hospital by conducting a retrospective observational cohort study of admissions to hospital between July 1, 2002, and Mar. 31, 2009, at a single academic hospital. They measured the association between infection with hospital-acquired C. difficile and time to discharge from hospital using Kaplan-Meier methods and a Cox multivariable proportional hazards regression model. They controlled for baseline risk of death and accounted for C. difficile as a time-varying effect. Hospital-acquired infection with C. difficile was identified in 1,393 of 136,877 admissions to hospital (overall risk 1.02 percent. The median length of stay in hospital was greater for patients with hospital-acquired C. difficile than for those without C. difficile. Survival analysis showed that hospital-acquired infection with C. difficile increased the median length of stay in hospital by six days. In adjusted analyses, hospital-acquired C. difficile was significantly associated with time to discharge, modified by baseline risk of death and time to acquisition of C. difficile. The hazard ratio for discharge by day 7 among patients with hospital-acquired C. difficile was 0.55 for patients in the lowest decile of baseline risk of death and 0.45 for those in the highest decile; for discharge by day 28, the corresponding hazard ratios were 0.74 and 0.61. The researchers conclude that hospital-acquired infection with C. difficile significantly prolonged length of stay in hospital independent of baseline risk of death.

Unnecessary antibiotic administration exacerbates the C. difficile problem.

Shaughnessy, et al. (2013) sought to determine the fraction of unnecessary antimicrobial use among patients with current and/or recent Clostridium difficile infection (CDI). The study was a retrospective review from January 2004 through December 2006 at Minneapolis Veterans Affairs Medical Center (MVAMC). Study participants were patients with new-onset CDI diagnosed at the MVAMC without another CDI diagnosis in the prior 30 days. Pharmacy and medical records were reviewed to identify incident CDI cases, non-CDI antimicrobial use during and up to 30 days after completion of CDI treatment, and patient characteristics. Two infectious disease physicians independently assessed non-CDI antimicrobial use, which was classified as unnecessary if not fully indicated. Factors associated with only unnecessary use were identified through univariable and multivariable analysis. Of 246 patients with new-onset CDI, 141 (57 percent) received non-CDI antimicrobials during and/or after their CDI treatment, totaling 2,147 antimicrobial days and 445 antimicrobial courses. The two reviewers agreed regarding the necessity of antimicrobials in more than 99 percent of antimicrobial courses (85 percent initially, 14 percent after discussion). Seventy-seven percent of patients received at least one unnecessary antimicrobial dose, 26 percent of patients received only unnecessary antimicrobials, and 45 percent of total non-CDI antimicrobial days included unnecessary antimicrobials. The leading indications for unnecessary antimicrobial use were putative urinary tract infection and pneumonia. Drug classes frequently used unnecessarily were fluoroquinolones and β-lactams. The researchers conclude that 26 percent of patients with recent CDI received only unnecessary (and therefore potentially avoidable) antimicrobials. Heightened awareness and caution are needed when antimicrobial therapy is contemplated for patients with recent CDI.
Diligence is needed to identify recurrence of Clostridium difficile infection. Kelly (2012) notes that although most patients with Clostridium difficile infection (CDI) can be managed effectively with discontinuation of prescribed antibiotics and additional treatment with oral metronidazole or vancomycin, up to 25 percent experience disease recurrence, usually within 30 days of treatment. Failure to mount a systemic anti-toxin antibody response differentiates patients with CDI and recurrent CDI from symptomless carriers of toxinogenic C. difficile. The immunological senescence that accompanies ageing may lead to impaired immune responses to C. difficile and contribute to the significant association between advancing age and increased risk of CDI recurrence. Inadequate immunity may also explain why previous episodes of recurrence constitute a significant risk factor for further CDI recurrences. Other risk factors for recurrent CDI include concurrent use of antibiotics for non-C. difficile infections (which perpetuate the loss of colonization resistance), proton-pump inhibitors, and other gastric acid anti-secretory medications, prolonged hospitalization, and severe underlying illness (as reflected by a high Horn index score). Prominent risk factors have been examined to develop and validate a clinical prediction tool for recurrent CDI, with three factors (age >65 years, severe underlying disease (by the Horn index score), and continued use of antibiotics for non-CDI infections) being highly predictive of CDI recurrence. Such simple clinical prediction rules have the potential to identify patients at high risk of recurrent CDI, and can alert the treating physician to the need for prompt recognition, confirmatory diagnosis and treatment with regimens ideally designed to mitigate the risk of subsequent recurrences.

Effective communication is needed in the prevention of Clostridium difficile.

Clostridium difficile is the most common healthcare-associated infection and a major cause of death and increased morbidity. It is vital that patients and the public are provided with the right information and communication to assist them to understand their role in preventive measures. Successful implementation of communication and management strategies hinges on individuals’ risk perceptions. Burnett, et al. (2012) performed a structured literature review to examine the evidence regarding public and patients’ risk perceptions and responses toward Clostridium difficile and other healthcare-associated infections (HAIs). Fourteen studies were included. Only one study was specific to Clostridium difficile, and seven were related to other HAIs. Many reported limited understanding of the technical issues of the infection, concerns of transmission to family and friends, inadequate information available, and distrust. The media were one of the main sources of information. Both emotional and physical responses highlighted the level of confusion, fear, anxiety and anger. The researchers conclude that empirical research of risk perceptions toward Clostridium difficile is limited. Without well-researched studies examining risk perceptions and responses, there is a danger of developing and implementing communication and management strategies that do not meet the needs of our patients or the public.
Strategies abound for prevention of Clostridium difficile infection.

Dubberke (2012) says that 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.

Clostridium difficile-associated diarrhea (CDAD) presents mainly as a nosocomial infection, usually after antimicrobial therapy. Many outbreaks have been attributed to C. difficile, some due to a new hyper-virulent strain that may cause more severe disease and a worse patient outcome. As a result of CDAD, large numbers of C. difficile spores may be excreted by affected patients. Spores then survive for months in the environment; they cannot be destroyed by standard alcohol-based hand disinfection, and persist despite usual environmental cleaning agents. All these factors increase the risk of C. difficile transmission. Once CDAD is diagnosed in a patient, immediate implementation of appropriate infection control measures is mandatory in order to prevent further spread within the hospital. The quality and quantity of antibiotic prescribing should be reviewed to minimize the selective pressure for CDAD. Vonberg, et al. (2008) provide a review of the literature that can be used for evidence-based guidelines to limit the spread of C. difficile. These include early diagnosis of CDAD, surveillance of CDAD cases, education of staff, appropriate use of isolation precautions, hand hygiene, protective clothing, environmental cleaning and cleaning of medical equipment, good antibiotic stewardship, and specific measures during outbreaks. Existing local protocols and practices for the control of C. difficile should be carefully reviewed and modified if necessary.

Gerding, et al. (2008) say that Control of Clostridium difficile infection (CDI) outbreaks in healthcare facilities presents significant challenges to infection control specialists and other healthcare workers. C. difficile spores survive routine environmental cleaning with detergents and hand hygiene with alcohol-based gels. Enhanced cleaning of all potentially contaminated surfaces with 10 percent sodium hypochlorite reduces the environmental burden of C. difficile, and use of barrier precautions reduces C. difficile transmission. Thorough handwashing with chlorhexidine or with soap and water has been shown to be effective in removing C. difficile spores from hands. Achieving high-level compliance with these measures is a major challenge for infection control programs. Good antimicrobial stewardship complements infection control efforts and environmental interventions to provide a comprehensive strategy to prevent and control outbreaks of CDI. The efficacy of metronidazole or vancomycin prophylaxis to prevent CDI in patients who are receiving other antimicrobials is unproven, and treatment with these agents is ineffective against C. difficile in asymptomatic carriers.
Environmental surfaces play a role in the transmission of pathogens such as Clostridium difficile.

In a 2011 commentary in *Infection Control and Hospital Epidemiology*, David J. Weber, MD, MPH, of the Department of Medicine, University of North Carolina at Chapel Hill and William A. Rutala, PhD, MPH, of the Department of Hospital Epidemiology at UNC Health Care in Chapel Hill, N.C. note that, “The epidemiologic evidence strongly supports an important role for environmental contamination in the acquisition of C. difficile infection in healthcare facilities” even though in the past “The major mechanism of transmission of healthcare-associated pathogens among patients has been thought to be patient-to-patient transmission via the hands of healthcare providers.”

Weber and Rutala add, “Over the past decade, there has been a growing appreciation that environmental contamination makes an important contribution to hospital-acquired infection with MRSA and vancomycin-resistant enterococcus (VRE). More recently, environmental contamination has been demonstrated to play an important role in acquisition of infection with C. difficile, norovirus and Acinetobacter species.” The researchers point to various new technologies currently in the marketplace (such as vaporized hydrogen peroxide and ultraviolet light) and say that the best method for environmental control of multidrug-resistant organisms has not been determined. They add, “Specifically, whether the use of a sporicidal agent for daily room disinfection or at terminal cleaning would reduce CDI incidence in hospitals has not been evaluated. New technologies... hold promise in reducing the incidence of CDI, but additional studies are warranted.”

Weber, et al. (2010) say that healthcare-associated infections (HAI) remain a major cause of patient morbidity and mortality. Although the main source of nosocomial pathogens is likely the patient’s endogenous flora, an estimated 20 percent to 40 percent of HAIs have been attributed to cross infection via the hands of healthcare personnel, who have become contaminated from direct contact with the patient or indirectly by touching contaminated environmental surfaces. Multiple studies strongly suggest that environmental contamination plays an important role in the transmission of methicillin-resistant Staphylococcus aureus and vancomycin-resistant Enterococcus spp. More recently, evidence suggests that environmental contamination also plays a role in the nosocomial transmission of norovirus, Clostridium difficile, and Acinetobacter spp. All three pathogens survive for prolonged periods of time in the environment, and infections have been associated with frequent surface contamination in hospital rooms and healthcare worker hands. In some cases, the extent of patient-to-patient transmission has been found to be directly proportional to the level of environmental contamination. Improved cleaning/disinfection of environmental surfaces and hand hygiene have been shown to reduce the spread of all of these pathogens. Importantly, norovirus and C. difficile are relatively resistant to the most common surface disinfectants and waterless alcohol-based antiseptics. Current hand hygiene guidelines and recommendations for surface cleaning/disinfection should be followed in managing outbreaks because of these emerging pathogens.
It has been found that MRSA and C. difficile are identified from a variety of surfaces in the general hospital environment. Faires, et al. (2012) conducted sampling of environmental surfaces distributed over the medicine and surgical wards at each hospital once a week for four consecutive weeks. Sterile electrostatic cloths were used for environmental sampling and information regarding the surface sampled was recorded. For MRSA, air sampling was also conducted. Enrichment culture was performed and spa typing was performed for all MRSA isolates. For C. difficile, isolates were characterized by ribotyping and investigated for the presence of toxin genes by PCR. Using logistic regression, the following risk factors were examined for MRSA or C. difficile contamination: type of surface sampled, surface material, surface location, and the presence/absence of the other HA pathogen under investigation. Overall, 11.8 percent (n=612) and 2.4 percent (n=552) of surfaces were positive for MRSA and C. difficile, respectively. Based on molecular typing, five different MRSA strains and eight different C. difficile ribotypes, including ribotypes 027 (15.4 percent) and 078 (7.7 percent), were identified in the hospital environment. Results from the logistic regression model indicate that compared to computer keyboards, the following surfaces had increased odds of being contaminated with MRSA: chair backs, hand rails, isolation carts, and sofas. MRSA and C. difficile were identified from a variety of surfaces in the general hospital environment; the researchers conclude that several surfaces had an increased risk of being contaminated with MRSA but further studies regarding contact rates, type of surface material, and the populations using these surfaces are warranted. Their research is published in BMC Infectious Diseases.

**Rigorous, enhanced cleaning has an impact on Clostridium difficile.**

Manian, et al. (2012) say that implementation of a hospital-wide program of terminal cleaning of patient rooms revolving around hydrogen peroxide vapor (HPV) technology and evaluation of its impact on endemic nosocomial Clostridium difficile-associated diarrhea (CDAD) have not been previously reported. This retrospective quasi-experimental study involving a 900-bed community hospital. During the preintervention period (January 2007-November 2008), rooms vacated by patients with CDAD or on contact precautions for other targeted pathogens underwent one or more rounds of cleaning with bleach. During the intervention period (January-December 2009), targeted newly evacuated rooms underwent “enhanced cleaning” consisting of use of bleach followed by HPV decontamination utilizing a priority scale based on the pathogen and room location. Rooms vacated by patients with CDAD but for which HPV decontamination was not possible the same day underwent 4 rounds of cleaning with bleach instead. During the intervention period, 1,123 HPV decontamination rounds were performed involving 96.7 percent of hospital rooms. Of 334 rooms vacated by patients with CDAD (May-December 2009), 180 (54%) underwent HPV decontamination. The rate of nosocomial CDAD rate dropped significantly from 0.88 cases/1,000 patient-days to 0.55 cases/1,000 patient-days (rate ratio, 0.63; 95% confidence interval: 0.50-0.79, P < .0001). The researchers conclude that a hospital-wide program of enhanced terminal cleaning of targeted patient rooms revolving around HPV technology was practical and was associated with a significant reduction in CDAD rates.
C. difficile spores in the environment of patients with C. difficile associated disease (CDAD) are difficult to eliminate. Bleach (5,000 ppm) has been advocated as an effective disinfectant for the environmental surfaces of patients with CDAD. Few alternatives to bleach for non-outbreak conditions have been evaluated in controlled healthcare studies. Alfa, et al. (2010) conducted a prospective clinical comparison during non-outbreak conditions of the efficacy of an accelerated hydrogen peroxide cleaner (0.5 percent AHP) to the currently used stabilized hydrogen peroxide cleaner (0.05 percent SHP at manufacturer recommended use-dilution) with respect to spore removal from toilets in a tertiary care facility. The toilets used by patients who had diarrhea with and without C. difficile associated disease (CDAD) were cultured for C. difficile and were monitored using an ultraviolet mark (UVM) to assess cleaning compliance on a daily basis five days per week. A total of 243 patients and 714 samples were analyzed. The culture results were included in the analysis only if the UVM audit from the same day confirmed that the toilet had been cleaned. The data demonstrated that the efficacy of spore killing is formulation specific and cannot be generalized. The OxivirTB AHP formulation resulted in statistically significantly ($p = 0.0023$) lower levels of toxigenic C. difficile spores in toilets of patients with CDAD compared to the SHP formulation that was routinely being used (28 percent versus 45 percent culture positive). The background level of toxigenic C. difficile spores was 10 percent in toilets of patients with diarrhea not due to CDAD. The UVM audit indicated that despite the enhanced twice-daily cleaning protocol for CDAD patients cleaning was not achieved on approximately 30 percent to 40 percent of the days tested. The researchers conclude that their data indicate that the AHP formulation evaluated that has some sporicidal activity was significantly better than the currently used SHP formulation. This AHP formulation provides a one-step process that significantly lowers the C. difficile spore level in toilets during non-outbreak conditions without the workplace safety concerns associated with 5000 ppm bleach.

Hacek, et al. (2010) report on increased rates of Clostridium difficile-positive tests at three hospitals in a healthcare system. In response, an intervention of terminal room cleaning with dilute bleach was instituted to decrease the amount of C difficile environmental spore contamination from patients with C difficile infection. The intervention consisted of replacing quaternary ammonium compound as a room cleaning agent with dilute bleach to disinfect rooms of patients with CDI upon discharge. All surfaces, floor to ceiling were wiped with dilute bleach applied with towels to thoroughly wet the surfaces. Daily room cleaning remained unchanged. Patients remained on C difficile contact isolation precautions until discharge. To determine the effectiveness of this program, rates of nosocomial CDI for all three hospitals were determined using the MedMined Virtual Surveillance Interface for 10 months prior to and two years after the cleaning intervention. Statistical significance was determined using Poisson regression analysis. There was a 48 percent reduction in the prevalence density of C difficile after the bleaching intervention. The researchers conclude that the implementation of a thorough, all-surface terminal bleach cleaning program in the rooms of patients with CDI has made a sustained, significant impact on reducing the rate of nosocomial CDI in a healthcare system.
Salgado, et al. (2009) describe the outbreak, the relationship between antibiotic use and CDI, and the effect of enhanced infection control measures (EICM) on CDI. Rates were calculated as positive C. difficile toxin A or B tests among patients with nosocomial diarrhea per 1,000 patient-days (duplicates removed). Antibiotic use was calculated as defined daily dose per 1,000 patient-days. EICM consisted of (1) placing patients with diarrhea into empiric Contact Precautions, (2) cleaning with a bleach product in areas with CDI patients, and (3) requiring soap and water hand hygiene when caring for CDI patients. CDI rates were analyzed by chi(2) for trend. Time series methodology was used to examine the association between CDI and antibiotic use. During the outbreak (October 2004-May 2005), the researchers observed 144 excess cases of CDI. The CDI rate decreased after EICM were implemented and was maintained for 36 months beyond the outbreak. Multivariate analysis revealed positive associations between CDI rates and cefazolin use (P = .008) and levofloxacin/gatifloxacin use (P = .015). Despite an association between some antibiotic use and CDI rates, the researchers achieved sustained control of an outbreak using EICM without formulary changes or new antibiotic control policies; they say this suggests that patient-to-patient spread may be a more important cause of increased CDI.

Wipes can be effective tools against Clostridium difficile.

Rutala, et al. (2012) tested the effectiveness of disinfectants and wipe methods against Clostridium difficile spores. Wiping with nonsporicidal agents (physical removal) was effective in removing more than 2.9 log(10) C. difficile spores. Wiping with sporicidal agents eliminated more than 3.90 log(10) C. difficile spores (physical removal and/or inactivation). Spraying with a sporicide eliminated more than 3.44 log(10) C. difficile spores but would not remove debris.

Aronhalt, et al. (2012) notes that more healthcare institutions are using bleach products which are sporicidal to reduce Clostridium difficile infection (CDI). There may be patient and employee concerns about the appearance of bleach residue left on surfaces, odors, and respiratory tract irritation. The intervention used bleach wipes for daily and terminal patient room cleaning to reduce transmission of CDI and was implemented on patient care units with a relatively high incidence of CDI. Both patients and Environmental Services (ES) staff were surveyed to assess their satisfaction of the bleach wipe product used during room cleaning. Patients (n = 94) (91 percent) continued to be very satisfied with how well their rooms were cleaned every day. Bleach wipes were well tolerated by patients (n = 44) (100 percent) surveyed on the medical units and less tolerated by patients (n = 50) (22 percent) on the hematology-oncology units. ES staff (6) reported less satisfaction and more respiratory irritation from using the bleach wipes; however, later their satisfaction improved.

Orenstein, et al. (2011) evaluated daily cleaning with germicidal bleach wipes on wards with a high incidence of hospital-acquired Clostridium difficile infection (CDI). The intervention reduced hospital-acquired CDI incidence by 85 percent, from 24.2 to 3.6 cases per 10,000 patient-days, and prolonged the median time between hospital-acquired CDI cases from eight to 80 days.
Chlorine-based cleaning products are often used in acute settings for high-level disinfection of the environment to help control C. difficile. However, these products must be used at high concentrations, making them irritant, toxic and corrosive. This means they are inappropriate for the near-patient environment, and can lead to user resistance and non-compliance. More recently, products using peracetic acid and hydrogen peroxide have become available, which are highly effective even under conditions of heavy soiling. Carter and Barry (2011) sought to determine whether peracetic acid sporicidal wipes could help reduce rates of C. difficile at a London hospital. An observational study of C. difficile rates was carried out at an acute London trust between 2006 and 2010. All inpatients aged two years and over were monitored. Chlorine-based cleaning regimens and products were changed to peracetic acid sporicidal wipes in April 2008 and monitored for 18 months. Inpatient bed days were also monitored to ensure findings were not affected by changing patient numbers. The mean C. difficile rate per 1,000 patients fell from six to two following the 2008 introduction of the sporicidal wipes. In the first half of 2009, this rate dropped to below two. The overall rate of C. difficile infection was reduced by 72 percent following the introduction of the wipes. The researchers conclude that the introduction of sporicidal wipes resulted in a significant reduction in C. difficile rates. This supports the need to review and enhance traditional environmental cleaning regimens for preventing and controlling C. difficile in acute settings.

Smith, et al. (2011) investigated the ability of 10 different microfiber cloths to remove microbial contamination from three surfaces commonly found in hospital settings (stainless steel, furniture laminate and ceramic tile), under controlled laboratory conditions. Tests were conducted using organisms known to cause healthcare-associated infections, i.e., methicillin-resistant Staphylococcus aureus (MRSA), Clostridium difficile (in spore form) and Escherichia coli. For all the cloths tested, there was significant statistical evidence to suggest a difference in cleaning performance between them on first and single use. However, the overall performance of the nine re-useable cloths did not differ in practice with differences in log_{10} reductions of <1. The performance of the disposable microfiber cloth was notably worse. The performance of all cloths decreased with repeated use on a succession of contaminated surfaces. After repeated washing, re-usable cloth performance improved at 75 washes, and reduced after 150 washes, although, in most instances, performance after 150 washes was better than at first wash. For all cloths, price was not an indication of performance. Based on these laboratory findings, it is concluded that use of the microfiber cloths investigated is an effective way to reduce the levels of MRSA, E. coli and C. difficile (in spore form) on a range of surfaces found in the clinical environment and could therefore be of benefit to these environments.
Newer technologies can serve as an adjunct to manual environmental disinfection.

Admission to a room previously occupied by a patient with certain multidrug-resistant organisms (MDROs) increases the risk of acquisition. Traditional cleaning strategies do not remove all environmental MDROs. We evaluated the environmental and clinical impact of hydrogen peroxide vapor (HPV) room disinfection. Passaretti, et al. (2013) performed a 30-month prospective cohort intervention study on six high-risk units in a 994-bed tertiary care hospital. Following a 12-month preintervention phase, HPV was implemented on three units to decontaminate the rooms of patients known to be infected or colonized with epidemiologically important MDROs, following their discharge. Monthly environmental samples for MDROs were collected on all study units for three preintervention and six intervention months. The risk of MDRO acquisition in patients admitted to rooms decontaminated using HPV was compared with rooms disinfected using standard methods. The prior room occupant was known to be infected or colonized with an MDRO in 22 percent of 6,350 admissions. Patients admitted to rooms decontaminated using HPV were 64 percent less likely to acquire any MDRO and 80 percent less likely to acquire VRE after adjusting for other factors. The risk of acquiring Clostridium difficile, methicillin-resistant Staphylococcus aureus, and multidrug-resistant gram-negative rods individually was reduced, but not significantly. The proportion of rooms environmentally contaminated with MDROs was reduced significantly on the HPV units, but not on non-HPV units. The researchers conclude that HPV decontamination reduced environmental contamination and the risk of acquiring MDROs compared with standard cleaning protocols.

Recent scientific literature suggests that portable steam vapor systems are capable of rapid, chemical-free surface disinfection in controlled laboratory studies. Sexton, et al. (2011) evaluated the efficacy of a portable steam vapor system in a hospital setting. The study was carried out in eight occupied rooms of a long-term care wing of a hospital. Six surfaces per room were swabbed before and after steam treatment and analyzed for heterotrophic plate count (HPC), total coliforms, methicillin-intermediate and -resistant Staphylococcus aureus (MISA and MRSA), and Clostridium difficile. The steam vapor device consistently reduced total microbial and pathogen loads on hospital surfaces, to below detection in most instances. Treatment reduced the presence of total coliforms on surfaces from 83 percent (40/48) to 13 percent (6/48). Treatment reduced presumptive MISA (12/48) and MRSA (3/48) to below detection after cleaning, except for one post-treatment isolation of MISA (1/48). A single C difficile colony was isolated from a door push panel before treatment, but no C difficile was detected after treatment. The researchers conclude that the steam vapor system reduced bacterial levels by >90 percent and reduced pathogen levels on most surfaces to below the detection limit. The steam vapor system provides a means to reduce levels of microorganisms on hospital surfaces without the drawbacks associated with chemicals, and may decrease the risk of cross-contamination.
Falagas, et al. (2011) reviewed the effectiveness of airborne hydrogen peroxide as an environmental disinfectant and infection control measure in clinical settings. Systematic review identified 10 studies as eligible for inclusion. Hydrogen peroxide was delivered in the form of vapor and dry mist in seven and three studies, respectively. Pathogens evaluated included methicillin-resistant Staphylococcus aureus (MRSA), Clostridium difficile and multiple bacterial types, in five, three, and two studies, respectively. Before the application of any cleaning intervention, 187/480 of all sampled environmental sites were found to be contaminated by the studied pathogens in nine studies that reported specific relevant data. After application of terminal cleaning and airborne hydrogen peroxide, 178/630 of the sampled sites in six studies and 15/682 of the sampled sites in 10 studies, respectively, remained contaminated. Four studies evaluated the use of hydrogen peroxide vapor for infection control. This was associated with control of a nosocomial outbreak in two studies, eradication of persistent environmental contamination with MRSA and decrease in C. difficile infection in each of the remaining two studies.

Nerandzic, et al. (2010) examined the efficacy of environmental disinfection using an environmental disinfection system in the laboratory and in rooms of hospitalized patients. Cultures for C. difficile, methicillin-resistant Staphylococcus aureus (MRSA), and vancomycin-resistant Enterococcus (VRE) were collected from commonly touched surfaces before and after use of the environmental disinfection system. On inoculated surfaces, application of the environmental disinfection system at a reflected dose of 22,000 microWs/cm(2) for approximately 45 minutes consistently reduced recovery of C. difficile spores and MRSA by >2-3 log10 colony forming units (CFU)/cm2 and of VRE by >3-4 log10 CFU/cm(2). Similar killing of MRSA and VRE was achieved in approximately 20 minutes at a reflected dose of 12,000 microWs/cm(2), but killing of C. difficile spores was reduced. Disinfection of hospital rooms with the environmental disinfection system reduced the frequency of positive MRSA and VRE cultures by 93 percent and of C. difficile cultures by 80 percent. After routine hospital cleaning of the rooms of MRSA carriers, 18 percent of sites under the edges of bedside tables (i.e., a frequently touched site not easily amenable to manual application of disinfectant) were contaminated with MRSA, versus 0% after use of the environmental disinfection system. The system required <5 minutes to set up and did not require continuous monitoring. The researchers conclude that an environmental disinfection system is an efficient environmental disinfection technology that significantly reduces C. difficile, VRE and MRSA contamination on commonly touched hospital surfaces.
Disinfectants must be chosen with care.

Clostridium difficile spores can survive in the environment for months or years, and contaminated environmental surfaces are important sources of nosocomial C. difficile transmission. Doan, et al. (2012) sought to compare the clinical and cost effectiveness of eight C. difficile environmental disinfection methods for the terminal cleaning of hospital rooms contaminated with C. difficile spores. This was a novel randomized prospective study undertaken in three phases. Each empty hospital room was disinfected, then contaminated with C. difficile spores and disinfected with one of eight disinfection products: hydrogen peroxide vapor 350-700 parts per million (ppm); dry ozone at 25 ppm; 1,000 ppm chlorine-releasing agent; microfiber cloths used in combination with and without a chlorine-releasing agent; high temperature over heated dry atomized steam cleaning in combination with a sanitizing solution; steam cleaning; and peracetic acid wipes. Swabs were inoculated on C. difficile-selective agar and colony counts were performed pre and post disinfection for each method. A cost-effectiveness analysis was also undertaken comparing all methods to the current method of 1,000 ppm chlorine-releasing agent. Products were ranked according to the log(10) reduction in colony count from contamination phase to disinfection. The three statistically significant most effective products were hydrogen peroxide (2.303); 1,000 ppm chlorine-releasing agent (2.223) and peracetic acid wipes (2.134). The researchers conclude that the cheaper traditional method of using a chlorine-releasing agent for disinfection was as effective as modern methods.

Decontamination of surfaces and medical equipment is integral to the control of Clostridium difficile transmission, and many products claim to inactivate this bacterium effectively.

Decontamination of surfaces and medical equipment is integral to the control of Clostridium difficile transmission, and many products claim to inactivate this bacterium effectively. Speight, et al. (2011) tested 32 disinfectants were tested against spores of C. difficile in a suspension test based on European Standard BS EN 13704:2002, with contact times of 1 and 60 minutes in simulations of clean (0.3 percent albumin) and dirty (3 percent albumin) conditions. The addition of a 1-minute contact time was chosen as a more realistic simulation of probable real-life exposures in the situation being modeled than the 60 minutes specified by the Standard. The manufacturer's lowest recommended concentrations for use were tested. Sixteen products achieved >10(3) reduction in viability after 60 minutes (the pass criterion for the Standard) under both clean and dirty conditions. However, only eight products achieved >10(3) reduction in viability within 1 minute under dirty conditions. Three products failed to reduce the viability of the C. difficile spores by a factor of 10(3) in any of the test conditions. This study highlights that the application of disinfectants claiming to be sporicidal is not, in itself, a panacea in the environmental control of C. difficile, but that carefully chosen environmental disinfectants could form part of a wider raft of control measures that include a range of selected cleaning strategies.
Macleod-Glover, et al. (2010) reviewed the evidence for the efficacy of products used for environmental or hand cleaning on the rates of Clostridium difficile-associated diarrhea (CDAD). MEDLINE, EMBASE, and the Cochrane Database of Systematic Reviews were searched for articles pertinent to the efficacy of cleaning products against C. difficile or studies with outcomes related to rates of CDAD. Evidence was level II. Minimizing the incidence of CDAD in geriatric rehabilitation units is essential to achieving the goals of increasing patient function and independence for discharge into the community. Attention to environmental control of C. difficile and its spores by health care workers and patient visitors is an important secondary prevention strategy. The researchers found in their review that chlorine-releasing agents are more effective than detergents for killing spores produced by C. difficile. No level I evidence is available to determine if the use of chlorine-releasing agents has an effect on rates of CDAD. Handwashing is currently the recommended strategy for reducing transmission of C. difficile. Alcohol gels do not inactivate C. difficile spores; however, increased use of alcohol hand gel has not been associated with higher rates of CDAD.

**Monitoring of cleaning performance is important.**

Alfa, et al. (2008) describe a study in which an ultraviolet visible marker (UVM) was used to assess the cleaning compliance of housekeeping staff for toilets in a tertiary healthcare setting. The UVM was applied to the toilets of patients who were on isolation precautions due to Clostridium difficile-associated diarrhea (CDAD) as well as for patients who were not on isolation precautions. Cleaning was visually scored using a numeric system where 0, 1, 2, and 3 represented; no, light, moderate or heavy residual UVM. Rodac plates containing CDMN selective agar were used to test for the presence of C. difficile on the surfaces of patient’s toilets. Despite twice daily cleaning for the toilets of patients who were on CDAD isolation precautions, the average cleaning score was 1.23 whereas the average cleaning score for toilets of patients not on isolation precautions was 0.9. Even with optimal cleaning (UVM score of 0) C. difficile was detected from 33 percent of the samples taken from toilets of patients with CDAD (4 percent detection in toilet samples from patients who had diarrhea not due to CDAD). The researchers conclude that their data demonstrated the value of UVM for monitoring the compliance of housekeeping staff with the facility's toilet cleaning protocol. In addition to providing good physical cleaning action, agents with some sporicidal activity against C. difficile may be needed to effectively reduce the environmental reservoir.
If all else fails, hire a C. diff-detecting dog.

A study conducted by investigators at two large hospitals in The Netherlands shows that a trained dog was able to detect Clostridium difficile with high estimated sensitivity and specificity, both in stool samples and in hospital patients infected with C. difficile. Bomers, et al. (2012) conducted this proof of principle study using a case-control design. A 2-year-old beagle was trained to identify the smell of C difficile and tested on 300 patients (30 with C difficile infection and 270 controls). According to the researchers, the dog was guided along the wards by its trainer, who was blinded to the participants’ infection status. Each detection round concerned 10 patients (one case and nine controls). The dog was trained to sit or lie down when C. difficile was detected. Main outcome measures were sensitivity and specificity for detection of C difficile in stool samples and in patients. The dog’s sensitivity and specificity for identifying C difficile in stool samples were both 100 percent (95 percent confidence interval 91 percent to 100 percent). During the detection rounds, the dog correctly identified 25 of the 30 cases (sensitivity 83 percent, 65 percent to 94 percent) and 265 of the 270 controls (specificity 98 percent, 95 percent to 99 percent).

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