Guide to the Elimination of Clostridium difficile in Healthcare Settings

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Cover photo courtesy of CDC.
Micrograph of the bacterium Clostridium difficile made from an impression smear of 72hr anaerobe blood agar (1980).
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Acknowledgments

The challenges posed by *Clostridium difficile* represent some of the most difficult and alarming issues confronting infection prevention and control. The elements involved in addressing this problem, as well as the changing epidemiology of *C. difficile*, have collided, resulting in a prevention and control “perfect storm.” This has already impacted the health and safety of patients, regardless of whether they receive care in a hospital, long-term care facility, outpatient setting, ambulatory care setting, or a physician’s office.

The difficulties presented by this organism serve as a catalyst for increasing collaboration among healthcare personnel and providers as we work together to minimize the impact of *C. difficile* and maximize patient safety. The prevalence of this organism highlights the need to continue strong relationships between infection prevention, the microbiology laboratory, and pharmacy.

This guide provides current information regarding *C. difficile* and its impact on the patient and the care environment, and introduces a tiered approach that infection preventionists can use in their own facilities. Specific tools have been included to enable the preventionist to address the problem within the realm of a particular setting. The Association for Professionals in Infection Control and Epidemiology (APIC) acknowledges the valuable contributions from the following individuals:

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Special thanks to Julia J. Fauerbach, interior designer, Shands Healthcare business associate, M. Arch and Health candidate, Clemson University 2009, for her artistry and knowledge regarding physical elements and design of the patient room.
Guide Overview

The impact of *Clostridium difficile* Infection (CDI) has been felt across the entire spectrum of healthcare and is now recognized as a pathogen capable of causing human suffering to a degree matching that of Methicillin-resistant *Staphylococcus aureus*. The severity of disease is increasing and has affected children, adults, and the elderly. CDI is associated with an increased length of stay in healthcare facilities by 2.6 to 4.5 days and attributable costs for inpatient care have been estimated to be $2,500 to $3,500 per episode, excluding costs associated with surgical interventions. In the United States, the economic consequences related to management of this infection exceeds $3.2 billion annually. Sadly, CDI has been associated with an attributable mortality rate of 6.9% at 30 days and 16.7% at one year.\(^1\)\(^-\)\(^6\) Clearly, preventing the development and transmission of CDI should be a top priority for infection preventionists in all healthcare settings.

As rates of CDI continue to increase nationally and internationally, it is important that information provided in this guide start at the beginning in its description of the problem, include incremental steps that identify targeted areas for intervention, and provide clear guidance for implementation.

The concepts of intervention “bundling” and use of a tiered approach represent an organized approach to address prevention of *C. difficile* transmission applicable in all healthcare settings. The use of a tiered approach is consistent with the recommendations from the Healthcare Infection Control Practices Advisory Committee (HICPAC) and the Centers for Disease Control and Prevention (CDC) regarding prevention of multidrug-resistant organisms (MDROs).\(^7\)

Consider the following examples of CDI among patients across the spectrum of healthcare:

- 48-year-old male, treated with antibiotics for healthcare-associated infection, develops CDI while an inpatient in an acute care facility
- 25-year-old female, given a single dose of antibiotics as surgical prophylaxis, develops CDI within days after returning home, following a surgical procedure in an outpatient surgical setting
- 62-year-old male, develops CDI while a resident in a long-term care facility
- 51-year-old female, develops CDI after taking a course of antibiotics prescribed by her primary care provider
- 12-year-old female, develops CDI following a course of antibiotics prescribed during treatment for a chronic medical condition

Before the incidence of *C. difficile* increased and more virulent strains emerged, healthcare teams often considered diarrhea associated with antimicrobial therapy a nuisance, and perhaps even an accepted outcome for patients receiving antibiotics. Complacency toward this healthcare-associated complication can no longer exist at any point in the healthcare spectrum, including ambulatory care, acute care, long-term care and home care. The severe morbidity and mortality associated with *C. difficile* provides the impetus for healthcare providers to intensify efforts toward developing prevention strategies that can be consistently applied across the continuum of healthcare. Although it is recognized that few “one size fits all” initiatives work, the goal of this guide is to build on evidence that “bundling” of activities has been effective in addressing other healthcare-associated infections, as has use of a tiered approach for interventions guided by outcomes in the specific healthcare setting.

A bundled approach to *C. difficile* prevention and control at the University of Pittsburgh included education, enhanced case finding, expanded infection control measures, the formation of a *C. difficile* management team,
and implementation of an antimicrobial stewardship program. McDonald analyzed the Muto and colleagues’ report and concluded that the bundled approach reflected successive, tiered interventions based on data from their surveillance. This highlights the importance of using local data to drive priority setting, and choice and timing of interventions. As an organization focuses on CDI prevention, healthcare facilities should evaluate their local surveillance data and select appropriate interventions that address their particular situation. Elements of a CDI bundle include activities such as the following:

- Early recognition of CDI, through appropriate surveillance case-finding methods and microbiologic identification
- Implementation of contact precautions, in addition to standard precautions and patient placement
- Establishment and monitoring of adherence with environmental controls
- Hand hygiene measures
- Patient and family education
- Evidence-based methods for patient treatment and management of disease
- Antimicrobial stewardship
- Education of healthcare workers
- Administrative support

In the sections that follow, these elements will be discussed at length, following a review of the pathogenesis of CDI, its changing epidemiology and modes of transmission. Bundle elements are organized in the sections outlining routine and heightened infection prevention and control responses.
Pathogenesis and Changing Epidemiology of Clostridium difficile Infection (CDI)

To understand the chain of events involved in CDI, it is helpful to begin with an overview of the organism and how it affects an individual. A review of the pathogenesis and the changing epidemiology of C. difficile provide insight into points where preventive interventions can best be targeted.

Clostridium is an anaerobic, gram-positive, spore-forming bacillus. Within the genus Clostridium, there are a number of species, including C. tetani, C. botulinum, C. perfringens and C. difficile. All of these organisms are associated with significant disease in humans, but the focus of this guide involves illness associated with C. difficile. Some produce no toxin, some produce low levels of toxin, and some are highly toxigenic.

Prior to the mid-1970s, development of pseudomembranous colitis was recognized to occur following the use of some antibiotics, especially clindamycin and lincomycin. Pseudomembranous colitis is an inflammatory condition of the colon that develops in response to toxins that have been produced by microorganisms. This process occurs when the normal flora of the intestinal tract is disrupted (for example, from the use of antibiotics) and the remaining flora provides an opportunity for organisms not impacted by the particular antibiotic(s) to proliferate. In the case of C. difficile, this process enables C. difficile to attach to the mucosa of the colon and sets the stage for toxin production and resultant mucosal disease. Toxin-producing strains of C. difficile can cause illness ranging from mild or moderate diarrhea to pseudomembranous colitis, which can lead to toxic dilatation of the colon (megacolon), sepsis, and death. Figure 3.1 provides graphic demonstration of the transmission and impact of C. difficile.

The first reports establishing Clostridium difficile as the cause of antibiotic-induced pseudomembranous colitis were published in 1978.\textsuperscript{10,11} Since then, CDI has emerged as the most common cause of antibiotic-associated diarrhea and a highly problematic healthcare-associated infection. The development of CDI most commonly has two essential requirements: (1) exposure to antimicrobial agents and (2) new acquisition of C. difficile such as that occurring via fecal-oral transmission. While some people exposed to these two factors will develop CDI, others will instead become asymptomatically colonized. Thus, a third factor, possibly related to host susceptibility or bacterial virulence, is thought to be another important determinant for developing disease.\textsuperscript{12}

Acquisition of C. difficile occurs by oral ingestion of spores that resist the acidity of the stomach. These spores germinate into vegetative bacteria in the small intestine. Alteration of the normal colonic flora by exposure to antimicrobials provides an environment in which C. difficile is able to multiply, flourish and produce toxins that cause colitis. The primary toxins are toxin A and B, two large exotoxins that cause inflammation and mucosal damage. An exotoxin is a protein produced by a bacterium and released into its environment, causing damage to the host by destroying other cells or disrupting cellular metabolism. Although evidence has suggested that toxin A is the major toxin, C. difficile strains that produce only toxin B have been shown to cause the same spectrum of disease as strains that produce both toxins.\textsuperscript{13}

The major risk factors for CDI are exposure to antimicrobials, hospitalization, and advanced age.\textsuperscript{14} Nearly all antimicrobials have been implicated in CDI, but certain antimicrobial classes, such as cephalosporins, clindamycin, and fluoroquinolones, seem to cause higher risk for disease. This is probably related to those antimicrobials’ propensity for disrupting normal colonic flora in addition to the antimicrobial resistance patterns of prevalent C. difficile strains. In recent CDI outbreaks, fluoroquinolones have been the major class of antimicrobials implicated in CDI,\textsuperscript{15-17} an association that has been attributed to high-level resistance to fluoroquinolones of the current epidemic strain.\textsuperscript{18}
Despite the fact that exposure to multiple antimicrobial agents and longer courses of therapy appear to increase an individual’s risk of CDI, exposure to even a single dose of antimicrobials given for preoperative prophylaxis has been associated with CDI. Several studies support restriction of certain antimicrobial agents or formulary changes promoting the use of narrow-spectrum antimicrobials to reduce the incidence of CDI and to control outbreaks. These activities form a basis for antimicrobial stewardship programs.

The incubation period of *C. difficile* following acquisition has not been clearly defined. Although one study suggested a short incubation period of less than seven days, the interval between exposure and onset of symptoms may be longer. Thus, many cases of healthcare-associated CDI may have their onset in the community after hospitalization. According to CDI definitions developed for the purposes of surveillance, community-onset cases with symptom onset occurring within four weeks of discharge from a healthcare facility (acute or long-term) should be attributed to that facility. Specific surveillance definitions will be reviewed later in this guide.

### Changing Epidemiology

In recent years, the epidemiology of CDI has changed dramatically, with increases noted in the incidence of disease internationally, and reports of CDI outbreaks within healthcare facilities in North America and Europe involving more severe disease than previously described. In the United States, national surveillance data indicate
that the number of hospital discharges with CDI listed as any diagnosis doubled between 2000 and 2003, with a disproportionate increase for persons older than 64 years of age (Figure 3.2). More recent statistics have shown a more than doubling of the number of hospital discharges with CDI from 2001-2005, increasing from approximately 149,000 cases in 2001 to over 300,000 cases in 2005. Similar increases in rates of CDI per 10,000 discharges were also noted, indicating that the steep rise in CDI discharges was not simply due to an increase in number of hospital discharges. Cases of CDI in the U.S. were geographically distributed, with the highest rates in the Northeast, followed by the Midwest and Southern regions. Persons older than 65 years of age have been most affected, with the highest increases in discharge rates with CDI, representing over two-thirds of patients with CDI. However, the recent changing epidemiology has also involved emerging reports of CDI occurring in populations previously at low risk, including severe cases among healthy peripartum women, and increasing reports in children and other healthy people in the community with no recent healthcare contact or antimicrobial exposure.

During this time period of rising incidence of CDI, there were many indications of increasing severity, with greater numbers of complications and mortality related to CDI. Reports of CDI outbreaks in hospitals in Quebec, Canada, and subsequently in the U.S., emerged, describing severe cases associated with higher numbers of colectomies, treatment failures, and deaths than were ever before reported. In 2004, the 30-day attributable mortality rate of nosocomial CDI in Quebec hospitals was 6.9%, compared to 1.5% among Canadian hospitals in 1997. Attributable mortality is the amount or proportion of death that can be attributed to CDI. In the U.S., death certificate data showed that mortality rates from CDI increased from 5.7 per million population in 1999 to 23.7 per million in 2004 (Figure 3.3).

A hypervirulent epidemic strain of C. difficile was found to be associated with the outbreaks in Quebec and at least eight hospitals in six U.S. states, and subsequently with outbreaks in Europe. This epidemic strain has been named BI/NAP1/027 and produces a type of toxin not previously seen in hospital strains. The BI/NAP1/027/toxinotype III strain has been found to produce 16-fold higher concentrations of toxin A and 23-fold higher concentrations of toxin B in vitro than toxinotype 0 strains. Another feature of this strain is the production of a toxin called binary toxin, the role of which is not yet defined; however, strains that produce binary toxin may be associated with more severe diarrhea. The cause of the extreme virulence of the BI/NAP1/027 strain may be a combination of increased toxin A and B production, binary toxin, or other unknown factors.
Aside from its increased virulence, another feature that may account for the proliferation of this strain is its high-level resistance to the fluoroquinolone class of antimicrobials. Although BI/NAP1/027 isolates existed previously, historic strains were less resistant to fluoroquinolones, and they were not associated with outbreaks of disease. The BI/NAP1/027 strain had been detected in at least 38 U.S. states as of November 2007 (see www.cdc.gov/ncidod/dhqp/id_Cdiff_data.html) (Figure 3.4), in seven Canadian provinces, and has led to outbreaks in the United Kingdom and other parts of Europe.

Figure 3.3. Yearly *C. difficile*-related mortality rates per million population in the U.S. 1999 to 2004.

Figure 3.4. States with BI/NAP1/027 strain of *C. difficile* (n = 38), November 2007.
Source: CDC, (www.cdc.gov/ncidod/dhqp/id_Cdiff_data.html).
CDI in the Pediatric Population

At present, there is much we do not know about CDI in children, but we do know that CDI is much less common in children than in adults, and that from 2% to 70% of infants may be asymptptomatically colonized with *C. difficile*, including colonization with toxigenic strains.\(^{40,41}\) Rates of colonization decrease with age, falling to about 6% at age two years, while in children older than two, colonization rates are similar to those in adults (approximately 3%).

Infants may acquire colonization early in the first week of life.\(^{42}\) Studies examining risk factors for *C. difficile* have failed to show a consistent association between mode of delivery or receipt of formula versus breast milk. However, nosocomial acquisition of the organism is well-described in Neonatal Intensive Care Units (NICU), and *C. difficile* contamination of the NICU environment has been demonstrated.\(^{43}\)

Most studies have failed to show an epidemiologic association between colonization and disease in infants less than one year of age. For example, in one Swedish study, *C. difficile* was isolated with equal frequency in healthy children one week to one year of age (17%) and in children less than six years with diarrhea (18%).\(^{44}\) In a study of outpatient children, *C. difficile* was isolated from 7% of patients with diarrhea and 15% of healthy controls. Children with *C. difficile* were younger than children without the organism (mean age 8.2 to 9.8 months); prior antibiotic exposure was noted in only 22%.\(^{39}\) In another study, toxin B was identified in 4.2% of 618 children with diarrhea and in an equivalent number of healthy controls.\(^{46}\)

Similar findings have been noted in most controlled studies of NICU patients. *C. difficile* toxin was recovered from the stools of 55% of patients in one NICU, but signs of enteric disease, including necrotizing enterocolitis, occurred with equal frequency in both toxin-positive and toxin-negative infants.\(^{47}\) Sporadic case reports suggest that severe CDI occasionally occurs in infants, especially those with underlying intestinal pathology.

The accurate diagnosis of CDI in young children is complicated by the fact that commonly used tests such as the enzyme immunoassay (EIA) for toxin A and B may lack specificity in this age group. Between 2004 and 2006, a hospital in Georgia noted an increase in *C. difficile* toxin-positive stools in premature infants. Five infants were diagnosed with necrotizing enterocolitis. Retesting of 26 frozen stool specimens by EIA at the Centers for Disease Control and Prevention (CDC) confirmed toxin in only five specimens. *C. difficile* could not be isolated in culture in any specimen, although other *Clostridia* species were found in 50% of samples. (L. Clifford McDonald, CDC, personal communication).

Young children who are colonized with *C. difficile* without symptoms nevertheless represent a reservoir for transmission of disease to others. A 19-year-old woman developed CDI in the immediate post-partum period. Although her symptoms resolved with metronidazole treatment, she developed three recurrences. Her asymptomatic infant was a carrier of the identical strain of *C. difficile* isolated from the mother, suggesting the infant was the source of the mother’s recurrent disease.\(^{48}\)

The emergence of B1/NAP1/027 may be changing the epidemiology of CDI in children. B1/NAP1/027 has been associated with severe disease in both adult and pediatric patients without recent exposure to healthcare facilities, and in some cases, without recent antimicrobial use. In 2005, the CDC reported cases of severe CDI in populations previously at low risk for disease, including healthy children with no recent antibiotic use.\(^{32}\) A five-year retrospective study performed at a tertiary care children’s hospital revealed an increase in the number of children seen in the Emergency Department with community-associated CDI; 43% lacked a history of recent antibiotic use.\(^{49}\)
There remain gaps in our knowledge about the pathogenicity of *Clostridium difficile* in infants, the spectrum of disease in children due to the epidemic strain B1/NAP1/027, and the most appropriate diagnostic tools to confirm CDI in pediatric patients. Judicious testing and prospective surveillance using consistent definitions is essential to better understanding the disease in this population.

Guidelines published by the Society for Healthcare Epidemiology of America (SHEA) in 1995 discouraged testing of stools from infants less than one year of age for *Clostridium difficile*. The National Healthcare Safety Network (NHSN) surveillance definition for CDI does not discriminate between adult and pediatric patients except to exclude NICU patients. Other patients less than one year of age are not specifically excluded, although it remains difficult to differentiate incidental colonization from true CDI in this population. Given the changing epidemiology of disease in other populations previously at low risk for disease, additional guidance for clinicians is warranted. Systematic evaluation of CDI in young children, including NICU patients, is essential to better understanding the epidemiology of disease in this population.

Guidelines for the diagnostic evaluation for CDI in children have been proposed (L. Clifford McDonald, Ad Hoc *Clostridium-difficile* Surveillance Working Group, personal communication). Pending additional information, it seems prudent to restrict routine testing for *C. difficile* in children less than one year of age. When testing is performed, more than one diagnostic approach should be utilized. For example, a culture and/or toxin testing should be performed in addition to other tests. Retention of microbiological, surgical and autopsy specimens for additional testing by public health authorities or centers with special expertise may be useful for confirming the diagnosis, or detecting epidemic strains. Investigation of suspected clusters of infections is essential.

Because asymptomatic colonization decreases with age, testing for *C. difficile* should be considered in children one to two years of age with diarrhea and recent antibiotic exposure, especially after more common pathogens have been excluded.

Children older than two years of age with diarrhea and a history of recent antimicrobial use may be tested in the same manner as older children and adults. Because disease has been confirmed in healthy children without recent antibiotic exposure, testing for *C. difficile* may be considered, but other diagnoses are more likely.
Modes of Transmission

When considering the modes of transmission for *C. difficile*, it is important to note these key concepts:

- *C. difficile* can survive in the hospital environment and on hospital surfaces. As the organism strives to protect itself from undesirable environmental conditions, it assumes its spore form.
- Patients and/or healthcare workers can transmit and/or acquire *C. difficile* from contact with contaminated surfaces, including contamination with both vegetative cells and spores.
- Transmission occurs via a fecal-oral route, so any activity that may result in movement of the organism into the mouth must be addressed as part of prevention activities.

**Survival of *C. difficile* in the Healthcare Environment**

*Clostridium difficile* is a fastidious anaerobe and the vegetative cell dies rapidly, generally within 24 hours, outside the colon.\(^50,51\) This would lead one to believe that *C. difficile* is not a highly transmissible organism. However, *C. difficile* produces spores that can persist in the environment for many months and are highly resistant to cleaning and disinfection measures.\(^50,51\) The spores make it possible for the organism to survive passage through the stomach, resisting the killing effect of gastric acid, when ingested. After ingestion, the spores can germinate, produce toxins and cause disease. Therefore, both the vegetative and spore forms of *C. difficile* are important in terms of environmental cleaning and disinfection.

**Transmission of *C. difficile* to Patients from the Healthcare Environment**

The two major reservoirs of *C. difficile* in healthcare settings are infected humans (symptomatic or asymptomatic) and inanimate objects. Patients with symptomatic intestinal infection are thought to be the major reservoir.\(^52\)

The level to which the environment becomes contaminated with *C. difficile* spores is proportional to the severity of disease in the patient.\(^6\) However, asymptomatic colonized patients should also be considered as a potential source of contamination.\(^56\) Patient care items such as electronic thermometers and contaminated commodes have also been implicated in the transmission of CDI.\(^53\)

Transmission of *C. difficile* to the patient via transient hand carriage on healthcare workers’ hands is thought to be the most likely mode of transmission. Reduction of CDI rates associated with the use of gloves provides strong support for the importance of hand carriage.\(^54\) Alcohol is not effective in killing *C. difficile* spores, but CDI rates have not been found to increase as use of alcohol-based hand rubs (ABHR) increase. If a hospital is experiencing an outbreak or increasing infection rates with *C. difficile*, it can be beneficial for healthcare workers to wash their hands with soap and water exclusively when caring for patients with known CDI.\(^55\)

**Transmission Via Patient Care Activities**

There are a number of patient care activities that provide an opportunity for fecal-oral transmission of *C. difficile*. Some of these activities include:

- Sharing of electronic thermometers that have been used for obtaining rectal temperatures (handles may be contaminated with *C. difficile* even through probes are changed and probe covers used)
- Oral care or oral suctioning when hands or items are contaminated
- Administration of feedings or medication with contaminated hands, food or medication
- Emergency procedures such as intubation
- Poor hand hygiene practices
- Ineffective or inconsistent disinfection of patient care equipment
- Sharing of patient care items without appropriate disinfection
- Ineffective environmental cleaning

These examples serve to identify the broad array of activities that could result in fecal-oral transmission of *Clostridium difficile*. Therefore, when prevention strategies are designed, it is important that transmission opportunities such as these be considered and observation of patient care activities be performed, in an effort to identify previously unrecognized or unsuspected potential modes of transmission.
**Diagnosis**

*Clostridium difficile* infection (CDI) should be suspected in any patient with diarrhea or abdominal pain with recent antibiotic or healthcare exposures. \(^{32}\) Severe CDI has also recently been reported in “low-risk” populations, for example, people without recent antibiotic or healthcare facility exposures, and CDI should be considered in any patient with diarrhea lasting longer than three days with fever or abdominal pain. \(^{32}\) Review the surveillance definitions provided later in this guide. CDI is most commonly confirmed with a laboratory-based assay, and there are advantages and disadvantages for all laboratory-based methods for detecting *C. difficile* or its toxins. Therefore, it is essential to be familiar with the method used at your facility.

**Who Should be Tested and How Frequently?**

It is recommended to only test for *C. difficile* in patients who are suspected of having CDI, for example, patients experiencing diarrhea. \(^{52,57}\) It is recommended to NOT screen asymptomatic patients or perform a “test of cure” in patients who have responded to therapy. \(^{52,57}\) There are several reasons for these recommendations. All non-culture laboratory-based assays for detecting *C. difficile* or its toxins have been developed and validated to diagnose CDI only in symptomatic patients. There are numerous reasons to believe the sensitivity (the likelihood that someone with the disease or condition will have a positive test result), specificity (the likelihood that someone who does not have the disease or condition will have a negative test result), and positive predictive value (the likelihood that someone who tests positive actually has the disease or condition) of these assays are lower in asymptomatic patients, resulting in more false-positive and false-negative results. In addition, this information provides no clinically useful information and may result in patient harm.

It is not recommended to place asymptomatic patients colonized with *C. difficile* in Contact Precautions. This can lead to decreased patient satisfaction as well as an increase in healthcare costs associated with placing the patient in a private room and the unnecessary use of gowns and gloves. Some reports question the impact of isolation on patient safety, due to other adverse events such as falls, decreased monitoring, and medical error.

Persistently positive test results at the end of treatment are not predictive of a *C. difficile* relapse, and a positive test result in an asymptomatic patient may result in unnecessary treatment with antimicrobials, which can increase the patient’s risk of developing CDI in the future. \(^{59}\) Testing asymptomatic patients also takes nursing and microbiology time to collect and test the stool, plus the cost of the test itself.

A common question is how often a patient with diarrhea should be tested if the initial tests are negative, due to concerns of low sensitivity of the tests. Some studies have demonstrated that an additional 10% of patients will have a positive test if repeat testing is performed. \(^{52}\) It is important to note that the prevalence of CDI is lower in patients with a previous negative test. When the prevalence of CDI decreases, the positive predictive value of the test decreases as well, increasing the likelihood that a positive test will be a false-positive test. The increase in false-positive tests and low yield of additional testing does not support the routine use of repeat testing as a cost-effective measure. \(^{52}\)

**Collection and Transport of Stool for *C. difficile* Testing**

Only watery or loose stool should be collected and tested to establish the diagnosis of CDI. Specimens should be submitted in a clean, watertight container. Transport media is not necessary, and may increase the false positive rate of some tests. \(^{59}\) Specimens should be transported as soon as possible and stored at 2˚ to 8˚C until tested.
Storage at room temperature decreases the sensitivity of some tests, presumably due to toxin inactivation. Repeat freezing and thawing of the specimen should also be avoided for the same reason.

**Laboratory Tests for Diagnosing CDI**

As CDI is a toxin mediated disease and only *C. difficile* isolates capable of producing toxin are able to cause CDI, most diagnostic tests involve the detection of *C. difficile* toxin A and/or toxin B (Table 6.1). The cell cytotoxicity assay, which detects the cytopathic effect of toxin B on cultured cell lines, is considered the gold-standard clinical laboratory assay for the diagnosis of CDI. However, some have reported a sensitivity of this assay as low as 67% compared to culture for *C. difficile*. The primary advantage of this assay is it is more sensitive than immunoassays for toxin A and/or B. Disadvantages of this assay include a prolonged turn-around time of 48 to 72 hours, and that it is necessary to be able to maintain cell cultures in order for a laboratory to perform this assay.

Enzyme immunoassays (EIA) for toxins A and/or B have become the most widely used laboratory-based methods for diagnosing CDI in the United States because of their low cost, ease of use, and rapid turn-around time. Some assays detect only toxin A, whereas others detect both toxins A and B. This is an important distinction. There are some strains of *C. difficile* that produce only toxin B. These strains are capable of producing the same spectrum of illness as strains that produce both toxins A and B. These strains are missed by EIAs that only detect toxin A. Although there are several advantages of EIAs compared to cell cytotoxicity assays as mentioned above (lower cost, ease of use, and rapid turn-around time), the sensitivity of these assays range from 63% to 94%, with a specificity of 75% to 100% compared to cell cytotoxicity assays.

Glutamate dehydrogenase (GDH) is a protein produced by *C. difficile*, and assays are available to detect GDH in stool. Initially, it was thought that this assay was specific for *C. difficile*, but it was subsequently demonstrated that other bacterial strains can cross-react with this assay. These assays are relatively low-cost and rapid. Newer assays for GDH have a sensitivity of 85-95% and specificity of 89-99%. This assay is not specific for *C. difficile* and

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<td>Less sensitive than cell cytotoxicity assay. Some only test for toxin A.</td>
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<tr>
<td>Cell cytotoxicity assay</td>
<td>More sensitive than toxin EIA assays.</td>
<td>Not all laboratories able to perform the test. 48-72 hours for results.</td>
</tr>
<tr>
<td>Stool culture for <em>C. difficile</em></td>
<td>Most sensitive test. Provides <em>C. difficile</em> isolates.</td>
<td>Not specific (detects non-toxigenic <em>C. difficile</em>). Labor intensive. Can take more than 72 hours for results.</td>
</tr>
</tbody>
</table>
detects some strains of \textit{C. difficile} that do not produce toxin (and are unable to cause disease); therefore this assay should not be used alone to diagnose CDI.\textsuperscript{52}

Because of the high negative predictive value of GDH assays, several investigators have studied the GDH assay as a screening test.\textsuperscript{61,62,63} Stool with a negative GDH assay is reported as such and no further testing is performed. Stool positive for GDH is then tested for toxin with a cell cytotoxicity assay. Stool positive by the cell cytotoxicity assay is diagnostic for CDI; stool negative by the cell cytotoxicity assay is reported as negative. The two-step approach is able to rapidly identify patients without CDI (negative GDH assay), while utilizing the more sensitive cell cytotoxicity assay to identify patients with CDI. This approach may also be more cost-effective than use of the cell cytotoxicity assay alone.\textsuperscript{63}

Under the proper conditions, stool culture is the most sensitive laboratory method for detecting \textit{C. difficile}. However, because of the expense and time required for culture, it is rarely performed in the U.S. Characteristic colony morphology and gram stain appearance are often sufficient for identifying \textit{C. difficile}. \textit{C. difficile} isolates should be tested for toxin production to establish the diagnosis of CDI because as many as 25\% of \textit{C. difficile} isolates do not produce toxin and are incapable of causing CDI.\textsuperscript{52} Stool culture is necessary to perform molecular fingerprinting, and is therefore a useful tool in evaluating outbreaks, sources of infection and control measures.

\textbf{Molecular Typing}

There are several molecular typing techniques for \textit{C. difficile}, but these are not routinely available outside of research laboratories. Due to the reliance on toxin assays, cultures for \textit{C. difficile} are not routinely performed to diagnose CDI, and isolates are infrequently available for molecular typing. While molecular typing is necessary for in-depth epidemiological studies of \textit{C. difficile} and is helpful when changes in CDI epidemiology occur, it is not necessary for routine patient care.

\textbf{Non-laboratory Based Tests}

CDI is the cause of more than 90\% of cases of pseudomembranous colitis (PMC) and can be diagnosed with direct visualization of pseudomembranes by sigmoidoscopy or colonoscopy. Some patients may not have PMC identified by direct visualization, but have evidence of PMC on histopathology. Although considered diagnostic for CDI, PMC is identified in only 50\% of cases of CDI.\textsuperscript{64}

Abdominal CT scans are helpful to suggest the diagnosis of CDI if colitis is identified in a patient with abdominal pain or ileus. However, these scans should not be relied upon to rule in or rule out the diagnosis of CDI due to their poor sensitivity and specificity.\textsuperscript{65,66} Abdominal CT scan findings alone also do not correlate with severity of CDI.\textsuperscript{65,66}
Surveillance

Surveillance is defined as the ongoing, systematic collection, analysis, interpretation and dissemination of data regarding a health-related event, used to reduce morbidity and mortality and to improve health. Surveillance may involve process measures (e.g., hand hygiene, adherence rates to specific protocols, etc.) or outcome measures such as infection rates, death rates, lengths of stay, or costs of care. Outcome measures are particularly important to evaluate the effectiveness of infection prevention efforts and identifying indications for change.

The essential components of a healthcare surveillance system are:

- Standardized definitions
- Identification and monitoring of populations at risk for infection
- Statistical analysis (calculation of rates using appropriate numerators and denominators, trend analysis using control charts to identify high-incidence areas and to monitor trends)
- Feedback of results to the primary care givers
- Feedback to managers, directors, and to senior leadership, including administrators and even the board of directors or trustees

At a minimum, every healthcare facility should have the ability to identify clusters of infections, know how to conduct a systematic epidemiologic investigation to determine commonalities in persons, places and time, and develop, implement and evaluate prevention measures. For *C. difficile*, this can be accomplished through monitoring of clinical disease, or by using a proxy measure, laboratory-based surveillance indicator.

Case Definitions for Clinical CDI Surveillance

Standardized case definitions are critical if the information is going to be used to compare one unit or facility with another, to monitor trends over time, or to evaluate the effectiveness of interventions to reduce infections. The definitions proposed by McDonald et al. are summarized here and recommended for surveillance purposes. It is important to remember that surveillance definitions are not necessarily the same as clinical definitions and may not be appropriate for clinical decision-making and treatment.

A case of CDI is defined as an individual patient with the symptom of diarrhea (unformed stool that conforms to the shape of a specimen collection container) or toxic megacolon (abnormal dilation of the large intestine documented radiologically) without other known etiology in which:

1. the patient has a diarrheal stool sample positive for *C. difficile* toxin A and/or B, or a toxin-producing *C. difficile*
   OR
2. pseudomembranous colitis is found during surgery or endoscopically
   OR
3. pseudomembranous colitis is seen during histopathological examination.

Healthcare Facility-onset, Healthcare Facility-associated CDI

A healthcare facility is defined as any acute care, long-term acute care or other facility in which skilled nursing care is provided and patients are admitted at least overnight.
A patient classified as having healthcare facility-onset, healthcare facility-associated CDI is defined as a patient who develops diarrhea or CDI symptoms more than 48 hours after admission to a healthcare facility and fulfills criterion 1, 2, or 3 defined above. The National Healthcare Safety Network (NHSN) has further clarified this to be the third calendar day after admission.

Healthcare facility-onset, healthcare facility-associated CDI is also defined as a patient who develops diarrhea or CDI symptoms less than 48 hours after discharge from a healthcare facility and fulfills criterion 1, 2, or 3 defined above.

Community-onset, Healthcare Facility-associated CDI

A patient classified as having community-onset, healthcare-facility associated CDI is defined as a patient with CDI symptom onset in the community or 48 hours or less after admission to a healthcare facility, provided that symptom onset was less than four weeks after the last discharge from a healthcare facility.

Community-associated CDI

A patient classified as having community-associated CDI is defined as a patient with CDI symptoms onset in the community, or 48 hours or less after admission to a healthcare facility, provided that symptom onset was more than 12 weeks after the last discharge from a healthcare facility.

Indeterminate or Unknown CDI

A patient who does not fit any of the above criteria would be defined as having indeterminate or unknown CDI.

Recurrent CDI

A patient with recurrent CDI is defined as one with an episode of C. difficile that occurs eight weeks or less after the onset of a previous episode that resolved with or without therapy. Table 7.1 shows these organized definitions.

Table 7.1. Surveillance definitions for C. difficile infection.

<table>
<thead>
<tr>
<th>Case Type</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthcare facility-onset, Healthcare facility-associated (HO-HCFA)</td>
<td>CDI symptom onset more than 48 hours after admission (third calendar day).</td>
</tr>
<tr>
<td>Community-onset, healthcare facility-associated (CO-HCFA)</td>
<td>CDI symptom onset in the community, or within 48 hours from admission, provided symptom onset was less than four weeks after the last discharge from a healthcare facility.</td>
</tr>
<tr>
<td>Community-associated (CA-CDI)</td>
<td>CDI symptom onset in the community, or within 48 hours after admission to a healthcare facility, provided symptom onset was more than 12 weeks after the last discharge from a healthcare facility.</td>
</tr>
<tr>
<td>Indeterminate or unknown onset</td>
<td>CDI case patient who does not fit any of the above criteria.</td>
</tr>
<tr>
<td>Recurrent CDI</td>
<td>Episode of CDI that occurs eight weeks or less after the onset of a previous episode, provided the symptoms from the prior episode resolved.</td>
</tr>
</tbody>
</table>
Figure 7.1 provides a visual timeline that may be of assistance in applying the definitions. Case patients with symptom onset during the window of hospitalization marked by an asterisk (*) would be classified as having community-onset, healthcare facility–associated disease (CO-HCFA), if patient was discharged from a healthcare facility within the previous 4 weeks; would be classified as having indeterminate disease, if the patient was discharged from a healthcare facility between the previous 4-12 weeks; would be classified as having community-associated CDI (CA-CDI), if the patient was not discharged from a healthcare facility in the previous 12 weeks; if symptom onset more than 48 hours after admission; would be classified as having, healthcare facility–onset, healthcare facility–associated CDI (HO-HCFA).  

For surveillance purposes:

1. A symptomatic patient with an additional positive toxin assay within two weeks or less after the last specimen tested positive is a continuation of the same CDI case AND not a new case.
2. A symptomatic patient with an additional positive toxin assay within two to eight weeks after the last specimen tested positive is a recurrent CDI case AND not a new case.
3. A symptomatic patient with an additional positive toxin assay more than eight weeks after the last specimen tested positive is a new CDI case.

Conducting Surveillance

Depending on the purposes of surveillance, all or only some of the above CDI case definitions may be appropriate for use. Because inpatient stay in a healthcare facility is a recognized risk factor for CDI, the initial purpose of surveillance in a healthcare facility should be to first track and compare healthcare facility–onset, healthcare facility–associated CDI.

Surveillance should be facility-wide and a line list maintained in a retrievable database file, such as Microsoft Excel, Microsoft Access, SPSS (Statistical Package for the Social Sciences), or another such electronic means. The database should include at least the following:

- Patient identification (name or unique identifier, such as medical record number)
- Date of birth
- Admission date
- Patient location (unit and room) at the time of stool collection
- CDI symptom onset date (e.g. diarrhea)
- Stool collection date
- Discharge date

Other information may also be collected, including elements such as underlying diagnosis, treatment (e.g. antibiotics), procedures (e.g. endoscopy, surgical interventions), or additional circumstances that may have led
to exposure or acquisition risks. In addition, it may be helpful to note if/when a previous admission took place, residence or location prior to admission (transfer from another healthcare facility, including long-term care facility), and discharge status (death, discharge to extended/long-term care, residence, etc.).

**CDI Rates**

**Denominator for Calculation of CDI Rates**

- Rates should be expressed as number of case patients per reporting period (usually per month) per 10,000 patient days.
- The calculation of this rate is (number of CDI case patients per month/number of inpatient days per month) x 10,000 = rate per 10,000 inpatient days.
- This rate reflects the per-day patient risk for CDI and is useful across different types of healthcare facilities with varying lengths of patient stay.
- This rate can be used for comparing facility-wide CDI rates with other organizations as well as for comparing different units, wards and/or services within a given healthcare facility in which unit-specific/ward-specific/service-specific denominators are available.

**Expression of CDI Rates for Feedback to Caregivers and Comparative Purposes**

**Control charts**

Control charts may be created to display the number of CDI cases or rates for the entire healthcare facility, and/or by unit/ward/service.

- The X-axis is the surveillance time period (month).
- The Y-axis is the number of CDI cases or CDI rate.
- Control charts are useful to determine if the rate of a healthcare facility and/or unit/ward/service is out of range, and to monitor trends.
- Control charts can be used to demonstrate different aspects of surveillance, using a separate chart for each of the following: healthcare facility-onset, healthcare facility-associated; community-onset, healthcare facility-associated; community-associated; indeterminate; or recurrent CDI. The emphasis should be on providing information and the monitoring of outcomes relevant to the facility and the community.
- Control charts can be posted on individual patient-care units and used during educational in-services so staff can understand what the charts reflect and also see the results of interventions put into place to reduce CDI rates. An example of a control chart is provided in Figure 7.2.
- The use of control charts is a valuable tool in monitoring rates of CDI as well as providing visual representation of when rates are in or out of statistical control.

Using the control chart shown in Figure 7.2, when the rate of CDI exceeds three standard deviations, this can be a trigger for implementation of heightened interventions using a tiered approach. The appropriate use of control charts and identification of triggers to guide interventions is an important topic of discussion in the infection prevention and control committee. For example, an initial use of three standard deviations from the mean may be the place to start with regard to that trigger. As time goes on and rates move closer to zero, the committee may choose to adjust the triggers or elect to explore other rules for special cause monitoring.

For more information regarding control charts, refer to the work done by J.C. Benneyan in *ICHE* and a review of statistical process control by Amin in *Quality Management in Health Care*.57-69
Other monitoring tools

The infection preventionist may also find other types of charts or figures to be helpful when monitoring rates as well as temporal documenting of interventions. Figure 7.3 demonstrates a run chart developed using EpiGraphics (available from APIC).

Run charts show the rate over time, and enable the infection preventionist to add text boxes describing specific interventions and when they were performed. Charts such as this can be of help when providing a comprehensive overview of activities and outcomes to groups such as medical staff, administration, and accreditation surveyors.

An epidemic curve (epi curve) can be used to present a graphic depiction of the number of cases of illness by the date of illness onset. An epi curve can provide information on the pattern of spread, magnitude of the event, outlier cases, and time trend.

Laboratory-based Surveillance for C. difficile

Laboratory-based surveillance may also be considered as a simplified option or proxy measure rather than conducting surveillance for clinical disease with chart review. This should be performed solely in conjunction with laboratories that only test unformed stool samples and laboratories that do not perform screening cultures or toxin assays for colonization with C. difficile, all of which are discouraged.
Laboratory-based surveillance can be conducted for the entire facility or by specific unit/location. The denominator should be patient days for the entire facility or by specific unit/location, respectively.

In an effort to ensure that a patient has been in the facility for a minimum of 48 hours, without reviewing the medical record for the exact time of admission and date and time of onset (as is done for clinical disease surveillance), a case of laboratory-based healthcare facility-onset disease should be limited to those patients with *C. difficile* first detected on or after calendar day three after admission (more than 48 hours after admission).

By maintaining an ongoing line list of positive patients, incident or recurrent disease can also be ascertained. A new or incident case is defined as a new patient with *C. difficile* or one in whom the last positive specimen was obtained more than eight weeks after a previous positive. A recurrent case is defined as a patient with a positive specimen obtained more than two weeks, but less than or equal to eight weeks after a previous positive specimen. If a patient has another positive specimen within two weeks, this is considered a continuation of the infection and should not be counted again.

Incident cases of CDI should be monitored for the entire facility or by specific locations to detect trends and possible outbreaks. Recurrent disease should be monitored to evaluate the effectiveness of treatment. Control charts can be created in the same manner as described above for clinical CDI, but should be clearly titled to reflect that the information is based upon laboratory-based surveillance data.

The Centers for Disease Control and Prevention will be incorporating a laboratory-based *C. difficile* module into the National Healthcare Safety Network for hospitals wanting to monitor and compare their *C. difficile* rates.
Focusing on Prevention: Contact Precautions

Early recognition of patients who are suspected to have, or who are diagnosed with, CDI is the first step in preventing the spread of this epidemiologically significant organism. *C. difficile* can be spread by direct and indirect contact with the patient or the patient’s environment, and therefore, patients with this organism should be placed on Contact Precautions as recommended in the HICPAC/CDC Guideline for Isolation Precautions.\(^7\) Adherence to the components of Contact Precautions will help to break the chain of infection. Fecal incontinence and an increased potential for extensive and prolonged environmental contamination make patients with CDI a significant threat for dissemination and transmission of the disease. The following components of Contact Precautions should be observed for all patients suspected of, or diagnosed with, CDI.

1. **Patient Placement**

Patients should be assigned to a private room with a bathroom that is solely for use by that patient. When private rooms are of limited availability, patients who are fecally incontinent should preferentially be assigned to those private rooms. If a private room is not available, the infection control team should assess the risks and work with the patient care team to determine the best patient placement options (e.g., cohort with another patient diagnosed with CDI and no other discordant organisms, or keeping the patient with an existing roommate). If both patients have CDI and are cohorted, once the diarrhea stops for one person, that patient, if possible, should be transferred to a clean room.\(^70\)

In many care settings, such as rehabilitation programs, long-term care institutions or residential settings, private rooms may not be available. The care team needs to determine if a room should be closed off to other patients. The team should have administrative support to take this additional precautionary step. In the multi-patient room setting where isolation in a single patient room is not possible, other activities may be considered, including the use of at least a three-foot spatial separation between beds to reduce the opportunities for inadvertent sharing of items between the infected/colonized patient and other patients. It may be prudent to draw a privacy curtain between patients to promote separation. Some facilities use a visual queue, such as colored tape placed on the floor, in order to identify areas where restricted access and use of additional precautions are needed.

2. **Personal Protective Equipment (PPE)**

Barrier precautions are critical to prevent transmission from the patient to the healthcare worker and then to another patient. PPE must be donned before going into the room or cubicle and discarded before exiting the patient’s room/cubicle. Visit the CDC web site (www.cdc.gov/ncidod/dhqp/ppe.html) for a video and posters illustrating proper PPE donning and removal procedures, entitled “Guidance for the Selection and Use of Personal Protective Equipment (PPE) in Healthcare Settings.”

   a. **Gloves**

   Gloves must be donned before entering the room and worn by all healthcare providers during patient care and when in contact with the patient’s environment. Gloves should also be changed according to standard recommendations for gloves utilization (e.g., if heavily contaminated or torn), and removed/discarded as the healthcare provider leaves the room. Contact with the patient and the patient’s environment can expose the healthcare worker to vegetative *Clostridium difficile* and its spores.

   High-touch surfaces (e.g., bedrails, light switches, faucets) are a known source of *C. difficile* spores. *C. difficile* may also be found at multiple skin sites of patients with CDI, including groin, chest, abdomen, forearm, and hands, and could be transferred to the care provider’s hands. This colonization can persist after the cessation of diarrhea.\(^71\)

   b. **Gowns**

   Healthcare workers should don and wear gowns and gloves when entering a room to provide care to a person on Contact Precautions. The use of gloves alone may be as effective in preventing transmission
as the use of gloves and gowns together. However, until conclusive data is generated, gowns should continue to be worn with gloves for all interactions that may involve contact with the patient, contaminated equipment, or potentially contaminated areas within the patient’s environment.

Protective equipment and personal items such as clothing and uniforms may become contaminated after care of a patient colonized or infected with an infectious agent such as *C. difficile*. Although contaminated clothing has not been implicated directly in transmission, the potential exists for soiled garments to transfer infectious agents to successive patients, and in light of the severity of CDI, liberal use of PPE is appropriate.

3. Patient Transport
When a patient has CDI, patient transportation and movement outside the room or cubicle should be limited to medically necessary purposes. Patients should be taught to perform hand hygiene prior to movement from their room. These strategies can help contain and limit shedding into the environment. According to the HICPAC Isolation Guideline, the transporter should remove and discard contaminated PPE and perform hand hygiene prior to transporting patients on Contact Precautions. Clean PPE should be donned to handle the patient at the transport destination. The patient’s isolation status should be communicated to the receiving unit prior to transport, so that unit personnel are able to accommodate the special needs of that patient.

4. Patient Care Equipment, Instruments, Devices and the Environment
*C. difficile* contaminates patient care equipment and devices through fecal shedding or through the contaminated hands of patient or healthcare provider. The ability of *C. difficile* to survive on environmental surfaces demands adherence to recommended measures to prevent cross-contamination. Ongoing transmission of *C. difficile* may be a marker for poor adherence to environmental decontamination and other infection prevention measures. The infection control team should observe personnel and measure adherence to appropriate healthcare practices, especially when ongoing transmission occurs, in order to identify any breaches in infection prevention practice.

*C. difficile* spores can persist for months in the healthcare environment and be transmitted to patients during this time. Fecal contamination of surfaces, devices, and materials (e.g., commodes, bathing tubs, and electronic rectal thermometers) may provide a reservoir for the *C. difficile* spores, which leads to transmission. High-touch surfaces and equipment must be thoroughly cleaned and disinfected to remove and/or kill spores. Use of an individual bedside commode for each patient reduces the risk of transmission of infectious agents. When a bedside commode is used, the staff must use appropriate PPE and empty waste in a manner that prevents splashing. The commode must also be cleaned and disinfected after waste is discarded.

Each healthcare care setting should have a plan to clean and disinfect surfaces when fecal contamination (e.g., uncontrolled diarrhea) has occurred. Personnel should be sure to clean and disinfect all patient care equipment that has been contaminated. Reusable equipment must be cleaned and disinfected between patients. Whenever possible, each patient should be assigned his or her own equipment to minimize cross-contamination.

5. Discontinuing Contact Precautions
It is currently recommended that Contact Precautions may be discontinued when the patient no longer has diarrhea. Because of continued environmental contamination and patient skin colonization, some experts recommend continuing contact precautions for two days after diarrhea stops. This is one example of heightened response activities and will be discussed in more detail in the section addressing a tiered approach to CDI transmission prevention.

6. Assessing Adherence to Isolation Precautions
Assessing adherence with isolation precautions is an important element in prevention. Figure 8.1 provides an example of a tool used to monitor adherence. This tool is also available at www.apic.org/eliminationguides.
Infection Prevention and Control Isolation Compliance Checklist

<table>
<thead>
<tr>
<th>Unit</th>
<th>Room #</th>
<th>Compliance with Hand Hygiene Practices</th>
<th>Person Observed (HCW or visitor)</th>
<th>100% Compliant with isolation? Yes or No</th>
<th>Identify variance by PPE or Signage</th>
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<tr>
<td></td>
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<td></td>
<td>Person Observed (HCW or visitor)</td>
<td>100% Compliant with isolation? Yes or No</td>
<td>Identify variance by PPE or Signage</td>
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<td>1 = Physician</td>
<td>7 = Rehab</td>
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<td>2 = RN</td>
<td>8 = Lab</td>
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<td>3 = Transporter</td>
<td>9 = Dietary</td>
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<td>4 = PA</td>
<td>10 = Housekeeping</td>
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<td>5 = Respiratory RX</td>
<td>11 = Other HCW</td>
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<td></td>
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<td>6 = Nursing assistant</td>
<td>12 = Visitor</td>
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</table>

ABHR | Soap + H₂O | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 1 | 1 | 1 | 2 |
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Figure 8.1. Infection Prevention and Control Isolation Compliance Checklist. Source: Loretta Litz Fauerbach, Shands at the University of Florida.
Focusing on Prevention: Hand Hygiene

Prevention of CDI demands measurement, assessment, and evaluation of current hand hygiene practices. *C. difficile* trumps all other healthcare-associated infections for the polarized approaches regarding the best hand hygiene practices to prevent transmission. Understanding of the incidence of CDI in your setting, barriers to performance of hand hygiene, and environmental cleanliness will help your team select the right epidemiologically-driven interventions to prevent transmission of this organism.

According to the CDC HICPAC hand hygiene guidelines, healthcare provider hands are frequently contaminated with *C. difficile* following patient contact. Wearing gloves can significantly reduce the spread of *C. difficile* in hospitals. Current information on the need to use traditional hand washing, as compared to using alcohol hand rubs, is conflicting. Common antimicrobial agents (including alcohols, chlorhexidine, hexachlorophene, iodophors, PCMX, and triclosan) for hand washing are not active against spores. The benefit of hand washing with soap and water is the physical removal and dilution of spores from the hands, rather than the killing of spores.\(^{54}\)

After gloves are removed, healthcare providers’ hands should be washed with a non-antimicrobial or an antimicrobial soap and water, or disinfected with an alcohol-based hand rub.\(^{76}\) Hospitals using alcohol-based hand rubs as their primary means of hand hygiene have not seen increases in the incidence of CDI associated with their introduction. The increased incidence of CDI noted in numerous hospitals has been attributed to the introduction of the epidemic *C. difficile* strain NAP1 and not due to increased use of alcohol based hand rubs.\(^{77}\) However, during outbreaks or evidence of on-going transmission of *C. difficile*-related infections in an institution, washing hands with a non-antimicrobial or antimicrobial soap and water after removing gloves and other personal protective equipment (PPE) is prudent.

In an intensive care unit study that characterized healthcare workers’ (HCW) encounters with patients and correlated that to their hand hygiene compliance, it was noted that hand hygiene compliance was the lowest after brief encounters of less than two minutes. The observers noted that brief encounters made up a substantial portion of the contact and healthcare workers had opportunities for hand hygiene during all brief encounters. The authors concluded that HCW education and training should include special emphasis on the potential for hand contamination even during brief encounters, and should stress the importance of hand hygiene. In light of hypervirulent strains and the increasing incidence of CDI and other epidemiologically-significant organisms, those missed opportunities present a real risk of transmission.\(^{77}\)

- Several resources for hand hygiene educational materials are provided in Table 9.1. An example provided by APIC is shown in Figure 9.1. (These materials are also available at www.apic.org/eliminationguides).

Teaching patient hygiene including hand hygiene and bathing

Families, visitors and patients should be partners in preventing CDI. There have been several national initiatives encouraging patients to take an active role in their care. An informed patient promotes understanding of their care. Education should include:

- Explanation of the infection caused by *C. difficile*
- Review of the spectrum of disease and re-occurrences
- Discussion of how the organism is spread
- Description of what the patient can do to help reduce the spread of the disease
- Education of patients and their families about visitors who may be at high risk for acquiring *C. difficile*, such as individuals on antibiotics, or who are immunosuppressed, and helping them decide about their visitations
Table 9.1. Resources for hand hygiene educational materials.

<table>
<thead>
<tr>
<th>Resource</th>
<th>Description</th>
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<tbody>
<tr>
<td><strong>IHI How-to Guide: Improving Hand Hygiene “A Guide for Improving Practices among Health Care Workers.”</strong></td>
<td>This guide was a collaborative effort between the Centers for Disease Control and Prevention (CDC), the Association for Professionals in Infection Control and Epidemiology (APIC), and the Society of Healthcare Epidemiology of America (SHEA), and has been endorsed by APIC and SHEA. Valuable input also was provided by the World Health Organization's World Alliance for Patient Safety through the Global Patient Safety Challenge. (This document is in the public domain and is available on <a href="http://www.IHI.org">www.IHI.org</a>. It may be used or reprinted without permission provided appropriate reference is made to the Institute for Healthcare Improvement).</td>
</tr>
<tr>
<td><strong>Hand Hygiene for Health Care Settings.</strong></td>
<td>Ontario Ministry of Health and Long-Term Care/Public Health Division/Provincial Infectious Diseases Advisory Committee; May 2008. To review the Hand Hygiene Fact Sheet with supporting evidence go to: <a href="http://www.health.gov.on.ca/english/providers/program/infectious/pidac/fact_sheet/fs_handwash_010107.pdf">http://www.health.gov.on.ca/english/providers/program/infectious/pidac/fact_sheet/fs_handwash_010107.pdf</a></td>
</tr>
<tr>
<td><strong>The Joint Commission</strong></td>
<td>has been working with leading infection prevention and control organizations and hand hygiene experts to develop an educational monograph to guide the field in measuring adherence to hand hygiene guidelines. The monograph will offer guidance on setting measurement goals and will explore the pros and cons of the three major approaches to measuring hand hygiene. The monograph will contain extensive resources, including organization-specific examples of measurement tools and links to helpful web sites. The monograph is expected to be available in fall of 2008 and will be posted on the APIC web site.</td>
</tr>
<tr>
<td><strong>CDC’s Hand Hygiene</strong></td>
<td>site contains posters and educational programs as well as an interactive educational program. <a href="http://www.cdc.gov/Handhygiene/">http://www.cdc.gov/Handhygiene/</a></td>
</tr>
<tr>
<td><strong>John Boyce and St. Raphael’s</strong></td>
<td>site provides a PowerPoint presentation for educating staff and hand hygiene monitoring tools. <a href="http://www.handhygiene.org/">http://www.handhygiene.org/</a></td>
</tr>
<tr>
<td><strong>Henry the Hand</strong></td>
<td>provides campaign slides and programs to use in developing a local hand hygiene campaign and increasing compliance. <a href="http://www.henrythehand.com/">http://www.henrythehand.com/</a></td>
</tr>
<tr>
<td><strong>Soap and Detergent Association</strong></td>
<td>Educational materials are presented on this site. <a href="http://www.cleaning101.com/newsroom/2005_survey/handhygiene/">http://www.cleaning101.com/newsroom/2005_survey/handhygiene/</a></td>
</tr>
</tbody>
</table>
Wash Your Hands: *The Right Way!*

**Alcohol Based Hand Rubs***

Procedure for using Alcohol Based Hand Rubs:

1. Apply product to the palm of one hand using the following approximate amounts:
   - **Gel:** dime-sized amount
   - **Foam:** egg-sized amount

2. Rub hands together until hands are dry, water is not required

*Alcohol-based products are preferred in all cases except for visibly dirty hands, during an outbreak of *C. difficile*, or after exposure to *Bacillus anthracis.*

**Handwashing**

Procedure for Handwashing:

1. Wet your hands with clean running water and apply soap
2. Rub hands together to make lather and scrub for 15-20 seconds
3. Rinse hands well under running water
4. Dry your hands with a paper towel or air dryer
5. If possible, use your paper towel to turn off the faucet and open bathroom door

With either method, be sure to cover all surfaces of the hands and fingers including:

- Under your nails
- Around your wrists
- In between your fingers

*Figure 9.1.* Sample hand hygiene educational material. Source: APIC.
• Description of how to prevent transmission of *C. difficile*, including Contact Precautions, Standard Precautions, and hand hygiene
• Identifying steps that patients and family can take to clean their environment at home

A successful patient and family education program can gain cooperation with following Contact Precautions while in the hospital.79 Hand hygiene, especially hand washing, will be critical in minimizing the spread. Nursing staff should assist the patient in hand hygiene if the patient cannot do it, especially after toileting and before eating. Nursing staff should educate the family about the risk factors for transmission.

Patient education should include the importance of both hand hygiene and showering to reduce the bioburden of *C. difficile* on their skin. If a patient is unable to shower, bed baths should be performed, with the staff assisting as needed. A clean hospital gown/clothing should be donned after bathing or showering. Fresh bed linens are also important, since the patient may continually shed the bacteria and its spores, creating heavier contamination on used linens.

Table 9.2 is a sample handout that can be used for patient/family education regarding *C. difficile*. (This table is also available at www.apic.org/eliminationguides).

### Table 9.2. Patient and family education.

**Patient and Family Education Regarding Clostridium difficile Infection (CDI)**

**What is Clostridium difficile?**
*Clostridium difficile* is a bacterium that causes diarrhea as well as more serious intestinal conditions such as colitis, an inflammation of the bowel.

**What is Clostridium difficile infection?**
*Clostridium difficile* is the most common cause of infectious diarrhea in healthcare facilities. The main symptoms include watery diarrhea, fever, and abdominal pain or tenderness. *Clostridium difficile* infection may occur as an undesirable consequence when antibiotics are taken to treat an infection. When treating that infection, some of your good bowel bacteria are also killed thereby allowing the bacteria that are not killed by the antibiotics to grow. One of these bacteria that are resistant to many antibiotics is *Clostridium difficile*. When *Clostridium difficile* multiplies, it produces toxins or substances that can damage the bowel and cause diarrhea. *Clostridium difficile* infection results in diarrhea requiring specific treatment and it can sometimes be quite severe. In severe cases, surgery resulting in removal of a portion of the intestines may be needed.

**Who can develop *Clostridium difficile* infection?**
*Clostridium difficile* infection, also known as CDI, usually occurs during or after the use of antibiotics. Those individuals having serious illness, the elderly, or those in poor general health are at increased risk of developing CDI.

**How is *Clostridium difficile* infection diagnosed?**
If you are on antibiotics, or have recently taken antibiotics, and you develop watery diarrhea and fever, your doctor may suspect *Clostridium difficile* as a cause of those symptoms. A sample of your stool (feces) will be collected and sent to the laboratory for analysis. The laboratory will test the stool to see if *Clostridium difficile* toxins are present. One or more stool samples may be collected.

**How is *Clostridium difficile* infection treated?**
Your doctor may prescribe a specific type of antibiotic that targets and kills *Clostridium difficile*. Treatment usually consists of antibiotics taken for about 10 days.

**How do people get *Clostridium difficile* infection?**
People in good health usually don’t get *C. difficile* infection. People who have other illnesses or conditions requiring prolonged use of antibiotics and the elderly are at greater risk of acquiring this disease. When a person has *Clostridium difficile* infection,
the germs in the stool can soil surfaces such as toilets, handles, bedpans, or commode chairs. When touching these items, the hands of the patient as well as the hands of healthcare workers and family members can become soiled with *Clostridium difficile*. These soiled items and hands can be involved in moving the organism to other surfaces and other people. This is why an individual with *Clostridium difficile* infection is placed in isolation when in a healthcare setting.

What type of isolation is used for *Clostridium difficile* infection?  
If you have *Clostridium difficile* diarrhea, you will be moved to a private room until you are free from diarrhea. Your activities outside the room will be restricted. Everyone who enters your room must wear gown and gloves. Everyone MUST clean their hands after providing care to you or touching your environment. You should also pay attention to cleaning your hands regularly and showering or bathing to reduce the amount of bacteria on your skin. Your room will also be cleaned regularly and all equipment disinfected before it is removed from your room.

What should I do to prevent the spread of *C. difficile* to others?  
If you are infected you can spread the disease to others. However, only people that are hospitalized or on antibiotics are likely to become ill. For safety precautions you may do the following to reduce the chance of spread to others:

- wash hands with soap and water, especially after using the restroom and before eating;
- clean surfaces in bathrooms, kitchens and other areas on a regular basis with household detergent/disinfectants

Should special practices be done when I go home?  
Healthy people like your family and friends who are not taking antibiotics are at very low risk of developing *Clostridium difficile infection*. However, it is prudent for everyone to clean their hands regularly and maintain a hygienic environment, especially the bathroom area. Cleaning of the environment can be done using your regular germicide or you can use a solution of chlorine bleach and water. If you use this solution, mix 1 part chlorine bleach (unscented) with 9 parts tap water. Change the solution daily and be sure to protect yourself from splashes or sprays of the solution into your face and eyes. You might want to wear protective gloves so the bleach solution does not come into contact with your skin.

What else should I know about cleaning the house environment?  
Use a clean cloth and saturate it with the germicide or bleach solution. Use friction when cleaning surfaces then allow the surface to air dry. If there is soil on the surface, remove it then use a new cloth saturated with the germicide in order to disinfect the surface. Pay special attention to areas that may have some in contact with feces such as the commode and sink. When laundering items, rinse clothing or fabric that has been soiled with stool, then use your regular laundry processes. Use the hot water cycle and detergent. If you want to add some chlorine bleach, that will assist with killing of the germs. Dry the items in the dryer. There is no need to initiate special precautions with dishes and eating utensils.

What about cleaning of hands?  
Having clean hands is the most important thing any of us can do to prevent illness. When performing hand hygiene (another term for cleaning hands), it can be done using traditional soap and water hand washing or using an alcohol-based solution. Since *Clostridium difficile* is an organism found in feces, use of traditional hand washing is preferred.

When washing your hands, first wet your hands with water than apply soap in the palm. Rub hands together taking care to cover all surfaces of the hands as well as between the fingers. Rub for at least 15 seconds, then rinse with water. Pat hands dry instead of rubbing as this may prevent damage to the skin of the hands and chapping. If alcohol-based hand rubs are used, put a small amount of the solution (about the size of a nickel) in the palm of one hand then rub the solution over both hands and between fingers until the solution dries. There is no need to rinse hands afterward.

Perform hand hygiene after using the toilet, after touching dirty surfaces or items, before eating, before preparing meals, and any time your hands are visibly soiled or “feel” dirty. Teach this important practice to others including children.

What other information is important for me to know?  
It is very important that you take all your medication as prescribed by your doctor. You should not use any drugs from the drugstore that will stop your diarrhea (e.g., Imodium) as this may result in the *Clostridium difficile* toxins staying inside your colon and causing more severe illness. **If your diarrhea persists or comes back, contact your doctor.**

For more information on *Clostridium difficile* infection, go to the Centers for Disease Control and Prevention website www.cdc.gov/ncidod/dhqp/id_CdiffFAQ_general.
Focusing on Prevention: Environmental Control

The environment must be recognized as a critical source of contamination, and it plays a significant role in supporting the spread of infection. Because *Clostridium difficile* is shed in feces, any surface, item, or medical device that becomes contaminated with feces can act as a source for the spores and, therefore, be involved in infection transmission.\(^{50,51}\)

*C. difficile* spores can exist for five months on hard surfaces.\(^{50,51}\) In one study, spores were found in 49% of the rooms occupied by patients with CDI and 29% of the time in rooms of asymptomatic carriers.\(^{80}\) The heaviest contamination is on floors and in bathrooms.\(^{74}\)

Other sites that can be contaminated include electronic thermometers, blood pressure cuffs, bedrails, call buttons, tube feedings, flow-control devices for IVs and tube feedings, bed sheets, commodes, toilets, scales, telephones, TV controls, light controls, and window sills in the patient room. As levels of environmental contamination increase, the level of hand contamination of healthcare personnel also increases. The greater the incidence of CDI, the greater the opportunity for transmission, so interventions should be tied to surveillance results.

Disinfectants commonly used in healthcare settings include quaternary ammoniums and phenolics, neither of which are sporicidal\(^{81,82}\) Some disinfectants may actually encourage sporulation (the changing of the organism from the vegetative state to the protected spore state). The term hypersporulation has been used to denote the propensity of the bacterium to move from the vegetative form to the spore form with increased rapidity. The term has also been used to note that contact with some germicides stress the bacterium, so it more readily transitions to the spore form. Therefore, the term hypersporulation may be understood as the propensity of the organism to more readily move from the vegetative form to the spore than occurs under usual conditions. Although many EPA-registered germicides kill the vegetative *C. difficile*, only chlorine-based disinfectants and high-concentration, vaporized hydrogen peroxide kill spores. Currently, there are no EPA-registered sporicidal agents acceptable for use as a general surface disinfectant.\(^{83-85}\)

This information might lead one to believe that the environments of all patients with CDI must or should be cleaned with a hypochlorite solution. But there are a number of problems associated with use of a sodium hypochlorite solution (hereafter referred to as bleach), including corrosion and pitting of equipment and other surfaces over time, and employee-related concerns such as the triggering of respiratory difficulties in workers using the solutions. Therefore, the use of bleach should be limited to outbreak situations as recommended by the CDC. Cleaning and disinfection activities using the physical motions of cleaning and use of the routine germicide removes and dilutes spore concentration and is acceptable in the absence of an outbreak.

In general, 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.”\(^{86}\) This document can be accessed at the web site www.cdc.gov/ncidod/hip/enviro/guide.htm. Disinfectant products with EPA registration can be used for routine cleaning in healthcare settings. Active cleaning involves the removal and dilution of dirt and contamination. Cleaning is critical for optimal disinfection to occur.

As the CDC environmental guideline indicates, hypochlorite-based disinfectants have been used with some success for environmental surface disinfection in those patient-care areas where surveillance and epidemiology indicate ongoing transmission of *C. difficile*. The use of a 10% sodium hypochlorite solution mixed fresh daily (one part household chlorine bleach mixed with nine parts tap water) has been associated with a reduction in CDI in
some settings. Communication from the Environmental Protection Agency (EPA) has suggested that use of a pH-adjusted bleach solution made by mixing one part household bleach (5.25%-6%), nine parts water and one part vinegar (5% acetic acid), may provide an even greater impact on C. difficile (J. Kempter, Environmental Protection Agency, 2008, personal communication).

A word of caution to the infection-prevention team when they evaluate a disinfectant’s claims of efficacy; be sure to clarify what the claims mean. For example, a product may claim to kill C. difficile and be referring to the vegetative cells, not the spores. Vegetative cells are readily killed by most disinfectants. Cleaning and disinfecting agents should be reviewed and approved by infection prevention and control committees to assure the chemicals meet the standards and are effective for the intended use.

If using a 10% sodium hypochlorite solution, there are several key points to remember:

- Commercially available solutions contain a detergent base, which is helpful in cleaning as well as disinfecting.
- Evaluate the use of commercially available solutions within your facility. Some hypochlorite products are available in a ready to use solution. This may be a time-saving process that minimizes dilution error, but it may also be a challenge for storage and prove to be more costly.
- Making a mixture of bleach and water will provide only the disinfectant, not the detergent base. Therefore, a two-step process may be needed if cleaning is to be performed prior to disinfection.
- If a bleach and water mixture is made, use only chlorine bleach without the scent additive, as this reduces the resultant parts per million (ppm) of available chlorine.
- A bleach and water solution should provide at least 4,800 ppm of available chlorine.
- There is a difference between a germicidal bleach (6.15% hypochlorite), a laundry bleach (6.0% hypochlorite), and a discounted bleach (5.25% or less hypochlorite).
- A contact time of one minute for the hypochlorite (bleach and water) solution should provide adequate disinfection for non-porous surfaces. This is accomplished by a thorough wetting of the surface with the hypochlorite solution, then allowing it to air dry. (Rutala, APIC 2008).

**Contact Time**

Contact time refers to the amount of time necessary for the germicide to come into contact with the organism and result in a significant reduction in the number of micro-organisms. This usually means a 3 logarithmic (3 log) reduction in the number of organisms. It is this kill claim that must be submitted to the EPA in order for a germicide to receive approval as acceptable for use in healthcare settings.

When applying the concept of contact time in the healthcare environment, it is vital for the infection preventionist to know the contact time of the selected germicide and how to apply this knowledge. Germicides commonly used in the healthcare setting have a contact time of 10 minutes, although some have a shorter contact time. This means that the surface being disinfected should come into contact with the germicide (stay wet after cleaning) for 10 minutes (or less according to the specifics of the germicide) in order to reduce the amount of organisms by 3 logs (99%). This can best be accomplished by using the bucket method of cleaning, where the germicide is mixed with the appropriate amount of water in accordance with manufacturer’s recommendations and placed in a clean bucket or container. A clean cloth is used during cleaning, and the cleaning process prohibits the dirty cloth from returning to the bucket or container of clean germicide. The germicide solution must be changed periodically to ensure its effectiveness, and buckets or containers are washed and disinfected regularly, in addition to being inspected for cracks. The practices used during cleaning and disinfection should be clearly outlined in policy format and observation used to evaluate adherence.
Germicidal wipes have become an important addition to environmental cleaning, but they must be used appropriately to be effective. Wipes are made of a material, or substrate, that lets them absorb the germicide in which they are packaged and allows that germicide to be distributed onto the surface during the cleaning and disinfection process.

Germicidal wipes are registered with the EPA and the germicide has a specific contact time as part of that EPA approval process. This means that the wipe must enable the user to wet the surface being disinfected for the contact time noted on the label in order to destroy the organisms on the surface being cleaned. Therefore, it is important to use wipes for the right type of job. For example, one currently available germicidal wipe has a contact time of 30 seconds for some bacteria (including *C. difficile*) and one minute for some viruses. To maintain a wet surface for that contact time, that wipe is appropriate for disinfecting 20 square feet. For infection preventionists, it is important to know the contact time for the germicide, as well as the ability of the wipe to maintain contact time for the task in which it will be used. If wipes are used to clean the high-touch surfaces in a patient room, multiple wipes will likely need to be used to accomplish that task, due to the number of surfaces to be disinfected. Healthcare personnel, including environmental services staff, must be trained to use the wipes appropriately. The infection preventionist must be involved in selection of the right type of wipe to perform the desired jobs.

**Monitoring Environmental Cleaning**

Consistency with recommended cleaning and disinfection procedures should be routinely monitored. All surfaces and items near the patient should be included in this process. A checklist will help the worker to confirm that each critical area has been cleaned and disinfected—however, the worker must follow the list and check off each item as the cleaning and disinfection process is completed.

- Checklists that delineate recommended practices for a facility and routine rounds to evaluate practices will assist the care team in identifying opportunities for improvement. Working with unit and specialty specific groups to develop checklists and measures to support adherence with environmental cleaning activities will help improve adherence. Table 10.1 shows a checklist used among healthcare facilities in New York to assess environmental cleaning. Table 10.2 shows a checklist used when *C. difficile* is involved and environmental cleaning practices have been altered. Figure 10.1 depicts a patient room that has not yet had high-touch surfaces identified. Figure 10.2 depicts a patient room and identifies high-touch surfaces that need to be targeted for specific patient environments. (These checklists and figures are also available at http://www.apic.org/eliminationguides)

Note that in some settings, some patient care equipment such as infusion pumps and ventilators are cleaned by nurses or special equipment technicians. Adaptation of these examples should include local practices.

There is no need for routine environmental biological sampling for *C. difficile*. It is important for the team to select the appropriate environmental disinfectant. Non-compliance with protocols will usually be detected by ongoing transmission of the organism. If ongoing transmission is noted, then a thorough cleaning and disinfection of the environment must be done.
Table 10.1. Environmental checklist using sodium hypochlorite for daily cleaning.

**ENVIRONMENTAL CHECKLIST -**

**FOR DAILY CLEANING - ROOM OBSERVATIONS:** Please review a sample of 5 patients per week (1 patient per day)

**Hospital:** ____________________________  
**Date:** ____________________________  
**Unit:** ____________________________  
**Room:** ____________________________  
**Time:** ____________________________

<table>
<thead>
<tr>
<th>Instruction</th>
<th>Component</th>
<th>Yes</th>
<th>No</th>
<th>N/A</th>
</tr>
</thead>
<tbody>
<tr>
<td>At start, perform hand hygiene.</td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>Put on PPE.</td>
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<td></td>
<td></td>
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<tr>
<td><strong>Disinfect high-touch surfaces:</strong></td>
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<tr>
<td>Door knobs/handles</td>
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<tr>
<td>Door surface</td>
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</tr>
<tr>
<td>Bed rails</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Call button</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Phone</td>
<td></td>
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</tr>
<tr>
<td>Overbed table &amp; drawer</td>
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</tr>
<tr>
<td>Countertop</td>
<td></td>
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<tr>
<td>Light switches</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Furniture</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Arms of patient chair</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Seat of patient chair</td>
<td></td>
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<td></td>
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<tr>
<td>All other miscellaneous horizontal surfaces</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Window sills</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Bedside commode</td>
<td></td>
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<tr>
<td>Medical equipment (e.g., IV controls)</td>
<td></td>
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<tr>
<td>Spot clean walls with disinfectant cloth</td>
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<td></td>
</tr>
<tr>
<td><strong>Disinfect:</strong></td>
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<tr>
<td>BATHROOM, including:</td>
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<tr>
<td>Bathroom door knob</td>
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<tr>
<td>Toilet horizontal surface/seat</td>
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<tr>
<td>Toilet lever/flush</td>
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<tr>
<td>Faucets (at sink)</td>
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<td></td>
</tr>
<tr>
<td>Bathroom handrails</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Sink</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Tub/shower</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Mirror</td>
<td></td>
<td></td>
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</tr>
<tr>
<td><strong>Damp dust:</strong></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Overhead light (if the bed is empty)</td>
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<td></td>
</tr>
<tr>
<td>TV &amp; stand</td>
<td></td>
<td></td>
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</tr>
<tr>
<td><strong>Clean:</strong></td>
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<td></td>
</tr>
<tr>
<td>Lights</td>
<td></td>
<td></td>
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</tr>
<tr>
<td><strong>Clean floor:</strong></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dust mop tile</td>
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<tr>
<td>Wet mop tile</td>
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<tr>
<td><strong>Replace as needed:</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Hand sanitizer</td>
<td></td>
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</tr>
<tr>
<td>Paper towels</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Soiled curtains</td>
<td></td>
<td></td>
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<tr>
<td><strong>For terminal cleaning, damp dust:</strong></td>
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<td></td>
</tr>
<tr>
<td>Bed frame</td>
<td></td>
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</tr>
<tr>
<td>Mattress</td>
<td></td>
<td></td>
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<tr>
<td>Remake bed with clean linen</td>
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<tr>
<td>Replace as needed: Pillows, mattresses, pillow covers, mattress covers</td>
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<tr>
<td><strong>Other:</strong></td>
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<tr>
<td>Empty trash &amp; replace liner</td>
<td></td>
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<tr>
<td><strong>Discard dust cloths:</strong></td>
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<tr>
<td>Change mop heads after each isolation room.</td>
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</tr>
<tr>
<td>Remove PPE before exit.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perform hand hygiene.</td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

Any significant areas not mentioned above (please describe):

This room looks clean and ready for use:  
Sign-off by environmental services employee cleaning the room: ____________________________

Sign-off by TBD, based on your hospital process for cleaning room: ____________________________
Table 10.2. Environmental checklist using sodium hypochlorite for daily cleaning when *C. difficile* is involved.

*Clostridium difficile* ENVIRONMENTAL CHECKLIST USING SODIUM HYPOCHLORITE

FOR DAILY CLEANING - ROOM OBSERVATIONS: Please review a sample of 5 patients per week (1 patient per day) with known or suspected *C. difficile*.

**Hospital:**

**Date:**

**Unit:**

**Room:**

**Time:**

<table>
<thead>
<tr>
<th>Instruction</th>
<th>Component</th>
<th>Yes</th>
<th>No</th>
<th>N/A</th>
</tr>
</thead>
<tbody>
<tr>
<td>At start, perform hand hygiene</td>
<td>N/A</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Put on PPE</td>
<td>N/A</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disinfect w/ hypochlorite-based disinfectant, high-touch surfaces</td>
<td>Door knobs/handles</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Door surface</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bed rails</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Call button</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Phone</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Overbed table &amp; drawer</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Countertop</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Light switches</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Furniture</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Arms of patient chair</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Seat of patient chair</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>All other miscellaneous horizontal surfaces</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Window sills</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bedside commode</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Medical equipment (e.g., IV controls)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Spot clean walls with disinfectant cloth</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Disinfect w/ hypochlorite-based disinfectant:</strong></td>
<td><strong>BATHROOM,</strong> including:</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Bathroom door knob</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Toilet horizontal surface/seat</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Toilet lever/flush</strong></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td><strong>Faucets (at sink)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Bathroom handrails</strong></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td><strong>Sink</strong></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td><strong>Tub/shower</strong></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td><strong>Mirror</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Damp dust:</strong></td>
<td>Overhead light (if the bed is empty)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>TV &amp; stand</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Clean:</strong></td>
<td>Lights</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Clean floor:</strong></td>
<td>Dust mop tile</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Wet mop tile</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Replace as needed:</strong></td>
<td>Hand sanitizer</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Paper towels</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Soiled curtains</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Per terminal cleaning, damp dust:</strong></td>
<td>Bed frame</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mattress</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Remake bed with clean linen</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Replace as needed: Pillows, mattresses, pillow covers, mattress covers</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Other:</strong></td>
<td>Empty trash &amp; replace liner</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Discard dust cloths:</strong></td>
<td>N/A</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Change mop heads after each hospitalization room:</strong></td>
<td>N/A</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Remove PPE before exit:</strong></td>
<td>N/A</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Perform hand hygiene:</strong></td>
<td>N/A</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Any significant areas not mentioned above (please describe):

This room looks clean and ready for use:

Sign-off by Environmental Services employee cleaning the room: ________________________________

Sign-off by TBD, based on your hospital process for cleaning room: ________________________________
Figure 10.1. Picture of a patient’s room for use in training individuals regarding room cleaning.

Figure 10.2. Picture of room noting some high touch surfaces and items.
Tiered Approach to CDI Transmission Prevention

The prior sections have focused on expanding knowledge regarding CDI and the many questions as to the most effective and efficient way to eliminate transmission while continuing to provide care for all patients in a complex healthcare environment. Understanding those challenges and constraints, the CDC first introduced the idea of a tiered approach to address the unique aspects of multidrug-resistant organisms as part of the 2006 guidelines for preventing transmission of MDROs.

Following that lead, this guide outlines some of the transmission-prevention activities that should be undertaken as part of routine infection prevention and control responses to C. difficile. In the pages that immediately follow these routine activities, the next tier of heightened activities are provided. Routine and heightened activities have been separated so they clearly demonstrate when and how to initiate a more intense response to patient outcomes specific to a single healthcare setting. These tiered activities are relevant to a variety of healthcare settings and stress the use of local data to guide decision-making.

Summary of C. difficile Transmission Prevention Activities During Routine Infection Prevention and Control Responses

Early Recognition of CDI

**Surveillance**

- Perform facility-wide surveillance for CDI.
- Calculate healthcare-onset/healthcare-associated CDI rates for each patient care area as well as an aggregate organization-wide rate.
- Provide CDI data and interventions to key individuals and groups such as the infection control committee, administration, medical staff, nursing staff, and pharmacy and therapeutics committee.
- Monitor for an increased rate of colectomies.
- Network with other area infection preventionists as a means of assessing the impact of CDI across the community.
- Communicate openly with local health department regarding CDI rates.

**Microbiologic identification**

- Work with microbiology lab to ensure rapid reporting of test results for CDI, including weekends and holidays.
- Ensure there is a process for providing results to the patient care area so isolation precautions can be initiated promptly.

**Implementation of Contact Precautions for Patients with CDI**

- Use Standard Precautions for all patients, regardless of diagnosis.
- Place patients with CDI on Contact Precautions in private rooms when available. Preference for private rooms should be given to patients who have fecal incontinence.
- If a private room is not available, cohort patients with CDI; however, patients infected with other organisms of significance (i.e., MRSA, VRE, Acinetobacter) should not be housed with patients who are not.
- Use dedicated equipment (i.e., blood pressure cuff, thermometer, stethoscope).
- Put on gown and gloves upon entry to the patient’s room.
• Change gloves immediately if visibly soiled, and after touching or handling surfaces or materials contaminated with feces.
• Remove gown and gloves before exiting the room.
• If cohorting is used, change gown and gloves and perform hand hygiene prior to touching the next patient.
• Routinely check available supplies for Contact Precautions to ensure that adequate selection and amounts are readily available. This may best occur by assigning specific responsibility for the task of checking and restocking supplies on a regular basis.
• Discontinue Contact Precautions when diarrhea resolves. Consider increasing the duration of Isolation Precautions in epidemic situations, or when ongoing transmission is suspected. Refer to the section outlining Summary of Additional C. difficile Transmission Prevention Activities During Heightened Infection Prevention and Control Responses.
• Do not isolate asymptomatic carriers of C. difficile.

Environmental Controls

• Use EPA-approved germicide for routine disinfection during non-outbreak situations.
• Ensure that personnel allow appropriate germicide contact time.
• Ensure that personnel responsible for environmental cleaning and disinfection have been appropriately trained.
• For routine daily cleaning of all patient rooms, address at least the following items:
  o Bed, including bedrails and patient furniture (i.e., bedside and over-the-bed tables and chairs)
  o Bedside commodes
  o Bathrooms, including sink, floor, tub/shower, toilet
  o Frequently touched or high-touch surfaces such as light switches, door knobs, call bell, monitor cables, computer touchpads, monitors, and medical equipment (e.g., intravenous fluid pumps)
• Disinfect all items that are shared between patients (e.g., glucose meters, infusion pumps, feeding pumps).
• Monitor adherence to cleaning and disinfection processes by personnel responsible for environmental cleaning.

Hand Hygiene

• Perform hand hygiene upon removal of gown and gloves and exiting the patient’s room.
• Use alcohol-based hand rubs for hand hygiene during routine infection prevention and control responses to C. difficile.
• Hand washing is the preferred method for hand hygiene when hands are visibly soiled.
• Assess hand hygiene compliance to address obstacles to performance.

Antimicrobial Stewardship

• Implement a program that supports the judicious use of antimicrobial agents.
• The program should incorporate a process that monitors and evaluates antimicrobial use and provides feedback to medical staff and facility leadership.

Patient Education

• Share information regarding C. difficile and its transmission with patients and their families.
• Instruct patients and families on hand hygiene and personal hygiene.
• Instruct patients and families regarding the importance of daily bathing and provide assistance as needed.

Healthcare Workers Education

• Provide ongoing education regarding modes of infection transmission, rates of CDI, and infection prevention interventions with patient care staff.
• Expand capacity through development of infection control liaison or links with patient care staff and utilize their assistance in monitoring adherence to preventive practices such as isolation, hand hygiene, and environmental cleanliness.

**Administrative Support**

• Share rates and infection prevention interventions with senior leadership.
• Include senior leadership in communications regarding adherence monitoring.
• Communicate expectation of support and accountability regarding prevention activities to key leadership and provide concrete examples of ways they can support infection prevention and control.

**Summary of Additional *C. difficile* Transmission Prevention Activities During Heightened Infection Prevention and Control Responses**

A heightened level of interventions should be implemented when there is evidence of ongoing transmission of *C. difficile*, an increase in CDI rates, and/or evidence of change in the pathogenesis of CDI (e.g., increased morbidity/mortality among patients with CDI), despite routine preventive activities.

**Early Recognition of CDI**

**Surveillance**

• Perform patient care rounds to identify patients who have diarrhea that may be related to CDI.
• Initiate Contact Precautions for all symptomatic patients in whom CDI is suspected (e.g., patients with diarrhea of unknown origin). If initial testing is negative for *C. difficile*, discontinue isolation.
• Consider expanding surveillance to include other categories of CDI patients, such as community-onset, healthcare-associated.
• Increase active communication with the local health department and other infection preventionists in your community.

**Microbiologic identification**

• Discuss a CDI rate increase with microbiology staff, and evaluate alterations in testing methods that may have impacted results.

**Implementation of Contact Precautions for Patients with CDI**

• Consider the utility of an additional CDI sign in order to ensure awareness of all staff, including personnel responsible for cleaning the environment, as they will need to use an alternative cleaning solution and process. If used, the sign must protect the privacy of the patient and not reveal the diagnosis.
• Evaluate the current system for patient placement.
• Consider placing all patients with diarrhea in Contact Isolation until CDI is ruled out (as opposed to waiting for positive test results to initiate isolation).
• Increase monitoring of adherence to isolation precautions and hand hygiene.
• Hold an open forum with patient care staff to identify barriers to infection prevention practices (e.g., interruption in isolation supplies, lack of private rooms).
• Continue Contact Precautions even when diarrhea resolves. Consider extending isolation until patient discharge.
Environmental Controls

- Use 10% sodium hypochlorite for disinfecting the patient’s room and all equipment used in that room. Verify compatibility of the equipment with the bleach solution.
- Use 10% sodium hypochlorite for daily disinfection as well as discharge disinfection for the room of the patient with CDI.
- If there is evidence of ongoing transmission, consider expanding the use of 10% sodium hypochlorite for disinfection of all patient rooms and equipment.
- Ensure that staff members understand how to use the sodium hypochlorite (bleach) solution and allow adequate contact time.
- Ensure that personnel responsible for environmental cleaning and disinfection have been appropriately trained and are using the correct PPE.
- Use bleach wipes as an adjunct to environmental cleaning and disinfection; train staff on their use, including instruction on how large an area can be disinfected with a single wipe and potential adverse effects of the product, such as staining, corrosion, and damage to equipment.
- Monitor and enforce adherence to cleaning and disinfection processes by personnel responsible for environmental cleaning.

Hand Hygiene

- Ensure compliance with appropriate hand hygiene upon removal of gown and gloves and exiting the patient's room.
- Enforce hand washing as the preferred method for hand hygiene during this heightened response.
- Assess hand hygiene compliance to address obstacles to performance.
- Ensure that alcohol-based hand rubs are available for use as part of a comprehensive hand hygiene program.

Antimicrobial Stewardship

- A program that supports the judicious use of antimicrobial agents should be in place.
- Evaluate the use of antimicrobials among patients identified with CDI and provide feedback to medical staff and facility leadership.

Patient Education

- Share information regarding *Clostridium difficile* and its transmission with patients and their families.
- Instruct them regarding hand hygiene, and monitor for adherence.

Education of Healthcare Workers

- Provide ongoing education to clinicians, healthcare providers and ancillary personnel (e.g., environmental services) regarding CDI rates and their changing responsibilities in light of the increased rates.

Administrative Support

- Share rates and interventions with senior leadership and clearly outline the activities needed to demonstrate administrative support.
- Share costs associated with CDI and the financial impact on the facility.
Other Preventive Measures

Despite the myriad of published data on the increasing morbidity and mortality rates associated with *C. difficile* transmission in U.S. healthcare institutions, and the importance of hand washing and basic infection control practices in preventing this adverse event, national data published by the CDC indicate increasing secular trends of *C. difficile* infection and disease in U.S. healthcare institutions over the past decade. This reality has brought to the forefront the quandary of whether other preventive efforts are required in addition to existing infection control practices and procedures. In the current era of managed care, additional preventive efforts need to be focused on areas where there is at least a modicum of evidence of potential effectiveness.

There are data on three additional areas of prevention:

1. **Antimicrobial Stewardship**
   Because any antimicrobial can potentially induce *C. difficile* disease, stewardship programs that promote judicious use of antimicrobials should be encouraged and complement infection control efforts and environmental interventions.\(^{87,88}\) In terms of CDI prevention, antimicrobial stewardship can involve restriction of antibiotics associated with CDI at that institution(s) and/or decreasing unnecessary antimicrobial use and is discussed elsewhere in this guide.

2. **Probiotics**
   These are naturally occurring, live bacteria that are largely non-pathogenic. The rationale for their use in preventing *C. difficile* disease is based on the hypothesis that they would restore equilibrium to the gastrointestinal flora that have been altered by prior antimicrobial exposure and thus protect against colonization or overgrowth with *C. difficile*. Probiotics that have been considered for prevention of *C. difficile* disease include various bacteria (*Bifidobacterium*, a gram-positive anaerobe that is commonly found in the colon; *Lactobacillus* spp., *Enteroccus faecium*), and yeasts (*Saccharomyces boulardii*, *S. cerevisiae*). They are commonly available as lyophilized capsules or in the form of a fermented drink. Sullivan and Nord\(^{89}\) have suggested that *S. boulardii* was somewhat effective in preventing recurrent *C. difficile* infection. However, studies of the utility of probiotics in preventing *C. difficile* disease in patients receiving antimicrobial agents have shown no reductions in the incidence of *C. difficile* disease. To date, there is insufficient evidence-based data to support routine clinical use of probiotics to prevent or treat *C. difficile* disease.

3. **Decolonization**
   To date, there are no data that support the use of vancomycin or metronidazole in asymptomatic individuals who are colonized with *C. difficile* in an attempt to rid the patient of the organism; such use of these antimicrobials does not work. Moreover, the effectiveness of vancomycin and metronidazole in preventing *C. difficile* disease in patients who are receiving other antimicrobials has not been shown.

In conclusion, until there is further published evidence on the utility of probiotics, vaccines, and decolonization modalities, the basis of effective prevention of *C. difficile* infection and disease, for the time being, will rest largely on an integrated infection control program that includes the following: (a) enforcement of hand hygiene, (b) appropriate use of standard and contact precautions, (c) maintenance of a high standard of environmental cleanliness, and (d) an antimicrobial stewardship program.
Antimicrobial Stewardship and Clostridium difficile Infection: A Primer for the Infection Preventionist

Antimicrobial stewardship is an aspect of infection prevention and control that may be a new addition to the job responsibilities of the infection preventionist. The discussion of antimicrobial use and its impact on patients in all healthcare settings and antimicrobial stewardship programs will be solely within the context of C. difficile infection (CDI). The term “antimicrobial stewardship” is used in place of “antibiotic stewardship,” since development of a stewardship program ideally includes antiviral and antifungal agents in addition to antibiotics; hence use of the broader term. The term “antibiotics” is used most often in this discussion, whereas those are the agents most relevant when addressing C. difficile infection.

Role of Antibiotic Use in the Occurrence of CDI

Since CDI is seen almost exclusively as a complication of antibiotic use, the development of a healthcare facility program to ensure appropriate antibiotic use is considered an important intervention for the control of CDI. Figure 13.1 represents the different phases of C. difficile infection of the colon, starting with a normal colonic environment (phase A), through the development of pseudomembranous colitis (phase D). To understand the critical role that antibiotic use plays in the development of pseudomembranous colitis, the different steps in the pathogenesis of CDI will be reviewed.

Normal Colonic Flora

The normal gastrointestinal flora is an important defense mechanism against intestinal pathogens. Some of the normal flora is attached to receptors in the colonic epithelial cells, while other bacteria are present in the lumen of

![Figure 13.1. Phases of the pathogenesis of C. difficile colitis.](image)
the gut (Figure 13.1, phase A). In order for \textit{C. difficile} to colonize the gut, the normal flora needs to be disrupted. Due to the diverse number of bacterial species in the human colon, it has been difficult to identify which particular organisms are responsible for the protective effect against \textit{C. difficile}. The exact manner by which an intact gut flora protects against \textit{C. difficile} colonization is not completely understood, but several mechanisms have been proposed. \textit{C. difficile} needs to attach to receptors in the human gut cells, but as long as the receptors are occupied by normal gut flora, \textit{C. difficile} strains reaching the gut mucosa will have no place for attachment.

Besides preventing colonization by competing for attachment sites, the normal flora may prevent colonization by depriving \textit{C. difficile} from essential nutrients. The normal flora may also antagonize \textit{C. difficile} through production of substances that inhibit or kill \textit{C. difficile}. Antibiotics may favor \textit{C. difficile} not only by altering the colonic flora, but also by altering the colonic microenvironment by changing the local protein composition or amount of local mucus production.

\textbf{\textit{C. difficile} Colonization}

Patients admitted to a healthcare facility are likely to come in contact with facility strains of \textit{C. difficile}. Even though \textit{C. difficile} may reach the colonic environment, it will not be able to become established as part of the intestinal flora and colonize the intestines as long as the patient has a normal flora. The patient with a normal gut flora is generally resistant to \textit{C. difficile} colonization. It is considered that \textit{C. difficile} does not have an advantage over susceptible organisms in regard to survival mechanisms in the patient’s colonic microflora environment. Once the microflora environment is disrupted by antibiotic use, the patient is placed at risk for colonization (Figure 13.1, phase B).

The propensity of a particular antibiotic to alter the gut flora is defined as antibiotic collateral damage. The extent of collateral damage depends upon a series of antibiotic factors such as the spectrum of activity, the amount of the antibiotic that reaches the colonic environment, and the bactericidal activity of the antibiotic under the anaerobic conditions of the colon. Other considerations that will affect the extent of collateral damage include the antibiotic dose, the route of administration, elimination by the bile, and the presence of antibiotic metabolites in the gut. Antibiotic collateral damage is for the most part due to the killing of normal colonic flora, but antibiotics may cause collateral damage by altering other colonic factors beyond bacteria that may play an important role in local defense mechanisms against \textit{C. difficile}.

\textbf{\textit{C. difficile} Toxin Production}

Not all strains of \textit{C. difficile} produce toxins. The toxigenic strains primarily produce two types of toxins: A and B. The toxins need to attach to receptors in the epithelial cells to be able to penetrate the cells (Figure 13.1, phase C). The absence of intestinal receptors for toxins A and B in neonates may explain why neonates are protected against CDI.

Both toxins possess cytotoxic activity. Recent outbreaks of severe CDI in U.S. hospitals have been caused by a highly toxigenic strain that produces about 15 to 20 times the amount of toxins A and B as usual strains. The strain was characterized by molecular techniques as toxino type III, North American PFGE type 1 (NAP1).

\textbf{\textit{C. difficile} Colitis}

After colonization and development of toxins, the toxins attach to cell receptors and penetrate the cells in the colon. \textit{C. difficile} toxins induce cell death by promoting cell apoptosis. Apoptosis is a natural process of self-destruction in certain cells that are genetically programmed to have a limited life span or are damaged. Epithelial cells are shed from the basement membrane into the lumen, leaving a shallow colonic ulcer. White blood cells and other inflammatory cells, as well as serum proteins and mucus, flow outward from the ulcer, creating the typical \textit{C. difficile}-associated colonic pseudomembrane (Figure 13.1, phase D).
Antimicrobial Stewardship as a Component of C. difficile Prevention Activities

The worst possible clinical scenario for healthcare-associated, healthcare-onset CDI would be represented by a patient who is admitted to the hospital without an infection, with normal gastrointestinal flora, who after several days of hospitalization dies due to intra-abdominal sepsis as a consequence of C. difficile fulminant colitis. Figure 13.2 depicts the different steps in the clinical course of this type of patient from the time of hospitalization until the patient death. The figure also depicts an organized and systematic approach to the strategies that can be applied for the prevention, control, and treatment of healthcare-associated, healthcare-onset CDI. Improving the use of antibiotics in the healthcare setting by developing and implementing a local antimicrobial stewardship program is a critical component in several steps in the processes involving C. difficile prevention activities.

Role of Antimicrobial Stewardship in Prevention of Colonization

All antibiotics produce disruption of the colonic flora, but antibiotics are not equal in their capability of causing collateral damage of the patient’s gastrointestinal flora. Two elements need to be considered when evaluating the risk for CDI produced by a particular antibiotic (Figure 13.3). One is the level of risk produced by a particular antibiotic. In this regard, some antibiotics will place the patient at low, intermediate, or high risk for development of CDI. The other is the number of days that the patient will be at risk for development of CDI. Days at risk for colonization occur during the time that the patient is receiving antibiotic therapy, and up to five to 10 days after discontinuation of antibiotics.

For example, a patient who receives a narrow spectrum antibiotic for less than one day, such as one dose of a first-generation cephalosporin for surgical prophylaxis, will be considered to have a low level of risk and a short duration of risk (Figure 13.3, point A). If the same patient is given surgical prophylaxis with an unnecessary broad spectrum antibiotic, the level of risk can move from low to high without any additional clinical benefit from that unnecessary antibiotic (Figure 13.3, point B). Extension of surgical prophylaxis with a first generation cephalosporin for
multiple doses that continue beyond the day of surgery will also increase the risk of CDI by extending the number of days that the patient will be at risk (Figure 13.3, point C).

Even though all antibiotic therapy, appropriate or inappropriate, will produce collateral damage and place the patient at risk for CDI, the prolonged inappropriate use of broad-spectrum antibiotics is a critical determinant of collateral damage that should be prevented. This type of collateral damage will place the patient at high risk for a long duration of time (Figure 13.3, point D).

The most common inappropriate antibiotic use that will place a patient at a high level and prolonged duration of risk is the continuation of broad-spectrum antibiotics after the etiology of infection has been identified and the pathogen is susceptible to a narrower spectrum antibiotic. For example, in a patient with a prolonged ICU stay who developed a ventilator-associated pneumonia (VAP), it would be appropriate to start empiric therapy with a broad-spectrum regimen to cover the possibility of resistant gram-positive as well as gram-negative bacteria.

If respiratory or blood cultures identify a Methicillin-susceptible Staphylococcus aureus (MSSA) as the etiology of VAP, the continuation of the initial broad-spectrum coverage should be considered inappropriate. In this clinical scenario, antibiotic therapy should be de-escalated to a regimen that targets MSSA, such as nafcillin or cefazolin. Initial empiric broad-spectrum therapy in hospitalized patients at risk of infections due to resistant organisms should always be followed by de-escalation of therapy if resistant organisms are not identified as the etiology of infection. Since lack of de-escalation is a common reason for inappropriate antibiotic use, the antibiotic stewardship program should develop strategies to prevent the collateral damage associated with lack of appropriate de-escalation of antibiotic therapy.

The antibiotic program should intervene to correct other poor antibiotic practices that are associated with collateral damage, such as the use of antibiotics directed to treat bacterial colonization or contamination, as well as the use of antibiotics in patients without documented infections.

**Role of Antimicrobial Stewardship in Prevention of Infection**

Once a patient is colonized with *C. difficile*, the patient may progress to develop *C. difficile* colitis, or may remain colonized without developing disease. Lack of disease may be due to colonization with a *C. difficile* strain that does not produce toxins. In this clinical scenario, once the patient is colonized with a non-toxigenic strain, the
patient will be protected from colonization with a toxigenic strain. It is considered that the initial strain may occupy receptors that become unavailable to the new strain. The use of metronidazole in a patient colonized with a non-toxigenic \textit{C. difficile} strain may favor development of \textit{C. difficile} colitis by killing the non-toxigenic strain and allowing colonization and infection due to a toxigenic strain.

It has been suggested that \textit{C. difficile} may change its ability to produce toxins when it is in contact with certain antibiotics. In vitro experiments indicate that \textit{C. difficile} in contact with antibiotics may be able to express more toxins. In theory, a patient already colonized with \textit{C. difficile} who is started on antibiotics may be at increased risk of disease by the direct effect of the antibiotic on \textit{C. difficile}. This has implications for the antibiotic stewardship program, since avoidance of unnecessary antibiotic use may be an important strategy to prevent \textit{C. difficile} infection once a patient is already colonized.

Not all strains of \textit{C. difficile} have the same capabilities to produce toxins and colitis. Fulminant colitis is more frequent when a patient is infected with the hypervirulent NAP 1 strain. Since this particular \textit{C. difficile} strain is resistant to fluoroquinolones, the use of fluoroquinolones may alter gut flora and produce selective pressure in favor of the NAP 1 strain. Antimicrobial stewardship regarding fluoroquinolones is important in areas where the NAP 1 strain is present.

A positive test for \textit{C. difficile} toxin in the stool is not by itself indication for antibiotic therapy. A patient who is asymptomatic but has a positive \textit{C. difficile} test should be considered a carrier, and antibiotic therapy is not indicated. The inappropriate use of metronidazole or vancomycin may favor development of disease in a patient who is only a carrier. Since the presence of normal gut flora may inhibit toxin production by \textit{C. difficile}, the inappropriate use of broad-spectrum antibiotics may favor toxin production and development of disease in a patient who is only colonized with \textit{C. difficile}.

\textbf{Role of Antimicrobial Stewardship in Treatment of Infection}

Once a patient is diagnosed as having CDI, antimicrobial stewardship is important to achieve optimal medical therapy. This is represented in the \textit{C. difficile} Prevention Activities (Figure 13.2) as the fourth level of intervention. There are three strategies that can be considered for the management of a patient with \textit{C. difficile} colitis: 1) killing of \textit{C. difficile}, 2) blocking toxin, and 3) restoring normal flora.

Killing of \textit{C. difficile} in the colon can be achieved with the use of oral metronidazole or vancomycin. In patients treated with oral metronidazole, the stool metronidazole levels decrease as colonic inflammation improves, when the patient moves from liquid stools to more formed stools. Oral vancomycin maintains similar concentrations throughout therapy. In patients with an ileus, a significant delay in the passage of antibiotics from the stomach to the colon may occur. When intravenous therapy is necessary, metronidazole can be used since it is excreted by the bile and by the inflamed colonic mucosa, achieving fecal levels sufficient to treat CDI. On the other hand, intravenous vancomycin is not excreted into the colon and cannot be used to treat CDI. If oral vancomycin cannot be used, vancomycin enemas are an alternative to kill \textit{C. difficile} in the colon. Even when appropriate metronidazole or vancomycin therapy is used, relapse of CDI is expected to occur in 10% to 25% of patients.

Blocking \textit{C. difficile} toxin in the colon with the anion-binding resins colestipol and cholestyramine has been investigated, but this strategy is not effective as primary therapy for CDI. The toxins may be blocked by administration of intravenous immunoglobulin, since commercially available intravenous formulation contains antibodies to toxin A and B. This approach is considered for patients with severe disease.

Restoration of the normal colonic microenvironment is of paramount importance in the management of CDI. A critical step in the restoration of normal colonic flora is an evaluation of the patient to determine if current antibiotic
therapy could be discontinued. In some patients, continuation of antibiotic therapy will be necessary to complete treatment of a defined infection. In these cases, the antimicrobial team, considering the type of infection, can suggest continuation of therapy with an antibiotic that produces minimal collateral damage of the gastrointestinal flora.

In an attempt to restore colonic microenvironment, the oral administration of microorganisms with beneficial properties, or probiotics, has been investigated in patients with CDI. The theoretical benefits of probiotics in patients with CDI may include the suppression of *C. difficile* growth, the binding of probiotics to epithelial cells with no receptors available for *C. difficile* binding, improvement of intestinal barrier function, and favorable modulation of the local immune system. Since the data from clinical studies of probiotics in patients with CDI is inconclusive, probiotics are not considered current standard of care in the management of patients with CDI.

In an effort to restore normal colonic flora, the administration of the entire fecal flora from a healthy individual, an approach referred to as fecal transplant, has been investigated. Although the data are limited to case series, fecal transplant has been used successfully to treat relapsing CDI.

**Elements of an Antimicrobial Stewardship Program**

The goal of an antimicrobial stewardship program is to optimize the use of the right drug, for the right purpose, and for the right duration in an effort to promote judicious use of the antimicrobial agent. Discussion of what constitutes an effective stewardship program is beyond the scope of this document, but the basics include elements such as:

1. written guidelines for use of specific antimicrobials that have been developed using evidence as a basis and involve input from clinicians
2. accurate microbiologic results and prompt reporting of those results
3. antibiograms compiled and disseminated in a manner that enables clinicians to select the appropriate agent(s) for empiric therapy
4. systems that minimize opportunities for inappropriate duration of therapy
5. processes that actively support de-escalation of therapy to a more narrow spectrum agent
6. feedback on adherence to guidelines, and
7. monitoring of systems that support the total program

These examples are but a few of the important elements for an effective antimicrobial stewardship program and serve to demonstrate the scope of activities and depth of administrative support necessary for success.

**Conclusions**

CDI is increasing in incidence and severity in healthcare settings. Infections due to *C. difficile* are associated with increased patient morbidity and mortality. It is deeply disturbing that patients admitted to a healthcare facility for a non-infectious disease can die during hospitalization due to an infection produced by *C. difficile*. Considering the critical role that antibiotic use plays in the pathogenesis of CDI, it is important for hospitals to implement an antimicrobial stewardship program with a focus on CDI prevention, control, and treatment. A combination of optimal infection prevention and control activities and antibiotic control is necessary to prevent the transmission of *C. difficile* and development of CDI.

To maintain a comprehensive approach to optimizing use of antimicrobial agents, it is important that the infection preventionist understands the components of an antimicrobial stewardship program and the organizational support necessary for its success.
Using a Systems Approach to Eliminate *Clostridium difficile* Infection

As healthcare knowledge increased exponentially over the past 50 years, healthcare delivery in the U.S. evolved into silos of care, with groups of specialized workers providing highly specialized services and information systems. Many of these systems could not communicate or share data with one another, increasing the paperwork burden and adding more tasks for already over-burdened healthcare workers (HCW).

Healthcare has traditionally lacked standardized performance measures, and activities to improve quality and efficiency are frequently isolated within a larger system. In situations where performance goals are established, a goal of 80% compliance is often considered acceptable. Compared to non-healthcare industries, however, healthcare goals appear woefully inadequate—a performance level of 80% in other industries would mean that 36 million checks would be drawn on the wrong account every day; 9 million credit card transactions would contain errors, and there would be a 1,000-fold increase in aviation deaths.

One factor complicating the healthcare system in the U.S. is that it is event-based. In other words, the occurrence of an event (e.g., a positive stool toxin assay for *C. difficile*) triggers other work actions (e.g., the initiation of Contact Precautions). These events are frequently disconnected from the triggering event and from one another.

The Institute of Medicine (IOM) identified serious and widespread problems throughout the U.S. healthcare system almost 10 years ago. In its landmark report, *To Err is Human: Building a Safer Health System*, the IOM noted that as many as 98,000 patients die every year as a result of medical errors. The majority of these errors do not result from individual or even a group’s carelessness, but rather from faulty systems, processes, and conditions that either fail to prevent mistakes or lead people to make them.

The IOM recognized that building a safer healthcare system meant designing processes of care so that patients are safe from accidental injury. It also recognized that the work of other high-risk industries has provided experience and tools which can be used to improve healthcare systems.

In 2005, the IOM published another seminal report, *Building a Better Delivery System: A New Engineering/Health Care Partnership*. This report noted that systems engineering tools have been used to revolutionize the quality and performance of large-scale industries like telecommunications, transportation, and manufacturing companies, and suggested that these tools can also be used to improve the healthcare system.

**A Review of Systems Engineering**

Systems engineering is the design, implementation, and control of interacting components or subsystems to produce a system that meets the needs of users and participants. All systems consist of interrelated, interdependent parts, or subsystems. These subsystems are a set of interacting objects or people that behave in ways individuals would not, and the interaction of these subsystems is responsible for the system’s characteristics.

A system’s goal is to meet specific performance objectives. The two broad categories of performance objectives are service (availability, reliability, quality, etc.) and cost (the degree to which costs can be controlled or reduced). Mathematical and analytical methods allow measurement of system performance and can also improve the operation of existing systems and their sub-systems. The 2005 IOM report reviews and discusses systems design
and analysis tools which may be useful in measuring healthcare system performance, including concurrent engineering and quality function deployment, queuing methods, discrete-event simulation, supply-chain management, and others.  

One frequently used method for developing streamlined and efficient subsystems is the process flow model. Process flow identifies all the steps and tasks in the ideal state; these are then compared to the existing process. A gap analysis enables identification of potential bottlenecks and encourages the consideration of every improvement opportunity. The work team, composed of representatives from all disciplines involved in the process, visualizes the ideal process and works to turn that vision into a reality. One of the most important questions to ask when performing process evaluation is “why?” In other words, why do we do this the way we do? This question helps identify steps necessary to the task, versus those that are done because they’ve always been done that way.

The following sections review key processes in eliminating *C. difficile* from a systems perspective, and identify issues to consider when mapping the ideal process flow.

**Using a Process Flow Model to Eliminate *Clostridium difficile* Infection Transmission**

The system in this case is comprised of all of the work tasks and resources required to prevent, control, and eliminate the transmission of *C. difficile*. The desired performance threshold is that no cases of hospital-acquired CDI will occur. However, preventing *C. difficile* requires several subsystems, or processes, including surveillance, prompt diagnosis and treatment, initiation and maintenance of Contact Precautions, and environmental cleaning and disinfection.

**Surveillance**

If the medical record is electronic, it may be possible to work with IT/IS to develop an automated *C. difficile* query using recently published surveillance definitions.  

The surveillance definitions provide the programming rules for the query. If room or ward data from previous admissions is in the hospital database, an automated query would enable surveillance for community-onset, healthcare facility-associated (CO-HCFA) cases as well as healthcare facility onset, healthcare facility-associated (HCFO-HCFA) cases. Developing an automated query would allow more time to be allocated to prevention efforts and less time spent reviewing and collecting data.

**Prompt Diagnosis and Treatment of High-risk Patients**

What triggers *C. difficile* testing?

Having a high index of suspicion in patients with risk factors for CDI (prior use of antimicrobials or antineoplastic agents which impact gut flora; increasing age; previous hospitalization within 30 days; resident of a long-term care facility) is essential for early detection.

1. If antibiotics are ordered, give thought to activities that enhance the index of suspicion. Once such method might be to place a sticker at the front of the chart with the message: “Antibiotics are a risk factor for the development of *Clostridium difficile* infection (CDI). Consider evaluating for CDI if patient develops diarrhea while receiving antibiotics or has received antibiotics within the past 60 days.”

   a. If the medical record is electronic, the above message could be automatically generated at the time the antibiotic is entered into the computerized order entry system (COE) and sent to the attending or treating physician’s e-mail or computerized task list. Entry into the COE could also trigger a flag on the nursing care plan to remind staff to evaluate the patient for diarrhea.
b. An order for antibiotics could trigger a search of the microbiology database; if the patient has a previous positive toxin assay, an electronic message notifying of the CDI history and recommending repeat testing if the patient has new onset of diarrhea is automatically sent to physicians and the nursing care plan.

2. A field in the computerized I&O sheet could be dedicated to liquid stool output. If the patient is receiving antibiotics and a number other than 0 is entered into the diarrhea field, a message is automatically triggered to encourage the physician to consider C. difficile testing.

**How often does the microbiology or reference laboratory perform C. difficile toxin assays?**

Many laboratories batch tests and run them once or twice a week. Depending on the volume of assays, it may be feasible to increase the frequency of toxin assay testing.

**If the toxin assay is positive, are appropriate staff members notified immediately (infection prevention, treating physician, nursing staff)? Is the microbiology laboratory able to call in the results if positive? Who should be called? Can that person be reached 24/7/365?**

1. If the record is electronic, an automated message could be sent to the attending/treating physician, infection preventionist, and nursing staff at the time the microbiology laboratory enters a positive result into the computer.
2. Have a designated field in the record for isolation category and flag all isolation patients. Make the flag visible to other patient care departments so that the isolation category is known at the time of scheduling procedures and tests.

**How much time elapses from when the result of the toxin assay is available to when the physician writes an order for metronidazole? How much time elapses from when the order is written to when the patient receives the first dose of metronidazole?**

1. If the notification system is automated, the automated message could contain a field for the medication order, e.g., “Patient having diarrhea and stool is positive for C. difficile. Do you want to order metronidazole now?”
2. If the physician clicks yes, the order would be automatically entered into the COE, triggering other messages.

**Initiation and Maintenance of Contact Precautions**

**Who initiates Contact Precautions, and why?**

Requiring a physician order was necessary when pay-for-performance was the standard for reimbursement. Today, healthcare facilities negotiate reimbursement schedules based on DRG, and a physician’s order may not be necessary. Authorizing staff caring for patients with CDI to initiate isolation should shorten the time required to isolate that patient.

**How much times elapses from when the test result is available to when the isolation sign is placed on the door?**

If CDI is strongly suspected (prior antibiotic use, liquid stools, etc.) or if the unit has more than one HCFO/HCFA case at a time, nursing staff may want to initiate Contact Precautions when the stool is sent for toxin assay, rather than wait for the result.
How are isolation supplies obtained?

1. If an isolation cart system is used, necessary supplies (gowns, disposable stethoscope, disposable BP cuff, thermometer, disinfectant wipes) are delivered with the cart.
2. If electronic, an automated order for isolation supplies is sent to Central Supply (CS) when a positive test result is entered by microbiology.

Are isolation supplies (gowns, gloves, etc.) readily available? Who is responsible for re-filling isolation carts or wall-mounted racks with necessary supplies? If isolation supplies are needed, can they be obtained in a timely manner?

1. Verify that re-stocking supplies on a regular schedule is included in the task list of the individual assigned to do it.
2. Use a visual cue, e.g., a red arrow at a designated level on the wall-mounted isolation rack, to help staff easily recognize when supplies are getting low. When the level of gowns falls below the red arrow, the rack should be re-stocked.
3. If a particular item, such as gowns, for example, is frequently in short supply, the nursing unit and CS should evaluate unit par levels for that item.
4. If shortages occur on more than one unit, CS may need to evaluate par levels house-wide.
5. Determine an average number of isolation gowns used per patient, per day. Notify CS daily of the number of isolation patients on the unit. An automated report with numbers of isolation patients per unit, per day should be possible if isolation status can be flagged in the patient’s record. Send the automated report daily, so that CS can restock based on the actual number of isolation patients rather than a fixed par level.
6. Keep extra “isolation packs” containing isolation sign, gowns, stethoscope, etc., in the clean supply room.
7. Keep extra gowns in the clean supply room.

If the facility requires hand hygiene with soap and water following contact with a CDI patient, how is staff from other units or departments notified of the patient’s CDI status?

1. A picture of a bleach bottle on the door could be used to indicate that soap and water must be used for hand hygiene.
2. A word of caution: Bleach should not be used on the hands, so recognize the potential for access to bleach and misinterpretation of the bleach bottle sign, and build in appropriate training and monitoring.

Environmental Cleaning and Disinfection

If bleach is used to clean the rooms of C. difficile patients, how is housekeeping notified?

a. Have the housekeepers check daily with the charge nurse for the list of rooms needing bleach or place a picture of a bleach bottle on the door.

To ensure efficient and effective cleaning and disinfection, there are other questions that needed to be addressed as well.

- Are cleaning supplies (prepackaged wipes, spray bottles and cloths, impregnated cloths, etc.) readily available to staff for cleaning equipment that cannot be dedicated?
- Who is responsible for maintaining the supply?
- Who is responsible for monitoring and replacing dated supplies, e.g., pre-mixed quaternary ammonium?
• Are cleaning supplies kept with portable equipment (bed scales, EKG machines, x-ray, ultrasound, etc.) so that staff can easily clean and disinfect between patients?
• Who is responsible for maintaining the supply?
• Who is responsible for monitoring and replacing dated or pre-mixed supplies?

Eliminating the spread of CDI requires the efforts of a wide range of healthcare departments and personnel. Systems engineering provides tools which will allow the development of efficient processes and communication of information for its control. Systems engineering will also enable ongoing evaluation of those processes, while continually looking for ways to improve them. Having efficient care models and automating processes that integrate isolation tasks whenever possible will eliminate some of the added-on steps that isolating patients requires. This in turn will decrease the likelihood that a particular step in the process is over-looked or forgotten. Ultimately, healthcare workers will have more time to do what they want and do best—spend time with their patients.
Glossary of Terms

BI/NAP1/027 Strain: A hypervirulent epidemic strain of C. difficile found to be associated with the outbreaks in Quebec, the U.S., and Europe. The BI/NAP1/027 strain has been found to produce 16-fold higher concentrations of toxin A and 23-fold higher concentrations of toxin B in vitro. Another feature of this strain is the production of a toxin called binary toxin, the role of which is not yet defined; however, strains that produce binary toxin may be associated with more severe diarrhea. The cause of the extreme virulence of the BI/NAP1/027 strain may be a combination of increased toxin A and B production, binary toxin, or other unknown factors.

CDAD: Clostridium difficile-associated disease. This term is being replaced by the term Clostridium difficile Infection (CDI).

CDI: Clostridium difficile Infection.

Clostridium difficile: An anaerobic, gram-positive, spore-forming bacillus.

Community-associated CDI: CDI symptom onset in the community, or 48 hours or less after admission to a healthcare facility, provided that symptom onset was more than 12 weeks after the last discharge from a healthcare facility.

Community-onset, healthcare facility-associated CDI: CDI symptom onset in the community, or 48 hours or less after admission to a healthcare facility, provided that symptom onset was less than four weeks after the last discharge from a healthcare facility.

Exotoxin: A protein produced by a bacterium and released into its environment, causing damage to the host by destroying other cells or disrupting cellular metabolism.

Fecal transplantation/fecal slurry: A somewhat controversial procedure using a slurry of human feces and saline solution to regrow healthy bacteria in the intestinal tract of an individual experiencing CDI that has been refractory to traditional therapy. The process involves obtaining donor feces from another family member, usually a spouse, and transplanting it into the ill individual via nasogastric tube.

Healthcare facility-onset, healthcare facility-associated CDI: Development of diarrhea or CDI symptoms more than 48 hours after admission to a healthcare facility and fulfills criterion for the case definition of CDI.

Hypersporulation: The propensity of the bacterium to move more readily from the vegetative form to the spore than occurs under normal circumstances. Hypersporulation can be induced by contact with some germicides.

Hypochlorite solution: A solution capable of killing the bacterial spores of C. difficile in concentrations larger than 4,800 parts per million (ppm) available chlorine. This is typically a solution of one part unscented chlorine bleach and nine parts water, yielding a 10% hypochlorite solution. These solutions are commercially available and contain a detergent, in addition to the hypochlorite solution.

Probiotics: Naturally-occurring, live microorganisms that are administered to confer a health benefit to a host. The rationale for their use in preventing C. difficile disease is based on the hypothesis that they would restore equilibrium to the gastrointestinal flora that has been altered by prior antimicrobial exposure and thus protect.
against colonization or overgrowth with \textit{C. difficile}. To date, there is insufficient evidence-based data to support routine clinical use of probiotics to prevent or treat \textit{C. difficile} disease.

\textbf{Pseudomembranous colitis}: An inflammatory condition of the colon consisting of a characteristic membrane with adherent plaques associated with severe symptoms, including profuse watery diarrhea and abdominal pain. The condition is considered pathognomonic for \textit{Clostridium difficile} infection.

\textbf{Recurrent CDI}: An episode of CDI that occurs eight weeks or less after the onset of a previous episode that resolved with or without therapy.

\textbf{Spore}: The dormant stage some bacteria will enter when environmental conditions cause stress to the organism or no longer support its continued growth. \textit{C. difficile} spores are highly resistant to cleaning and disinfection measures, and the spores also make it possible for the organism to survive passage through the stomach, resisting the killing effect of gastric acid.

\textbf{Systems engineering}: The design, implementation, and control of interacting components or subsystems, with the goal being to produce a system that meets the needs of users and participants.

\textbf{Toxic megacolon}: A life-threatening complication of intestinal conditions, characterized by a dilated colon with severe colitis and systemic symptoms such as fever, tachycardia, or shock.

\textbf{Vegetative \textit{C. difficile}}: The actively growing and metabolizing state of the bacteria.
Frequently Asked Questions

1. What is the incubation period for *C. difficile*?
The incubation period for *C. difficile* following acquisition has not been clearly defined. Although one study suggested a short incubation period of less than seven days, the interval between exposure and onset of symptoms may be longer. Thus, many cases of healthcare-associated CDI may have their onset in the community after hospitalization.

2. If the patient is on antibiotics, is there a way to prevent them from developing *C. difficile* colitis?
At present, there is no prophylaxis for *C. difficile*. The most effective prevention activity is through antimicrobial stewardship programs targeted to the specific organism(s), and to quickly de-escalate therapy (narrow the spectrum) and promote the shortest duration of therapy while adequately treating the infection.

3. When should a patient with *C. difficile* be removed from contact isolation?
Under routine circumstances, a patient with CDI can be removed from isolation when the diarrhea resolves. If there is an outbreak or evidence of ongoing *C. difficile* transmission, the infection preventionist recognizes that even after the diarrhea resolves, the patient may continue to shed *C. difficile*, so the preventionist may consider extending contact isolation until the patient is discharged. A heightened response might also include another method for extending isolation, such as continuing Contact Precautions, until the patient is without diarrhea for two days, followed by showering or bathing of the patient, provision of clean linen, then thorough cleaning of the room.

4. We are currently using a germicide that kills *C. difficile* in the vegetative state. Is that good enough?
*C. difficile* is a spore-former, and even though it may initially be in the vegetative state in the stool, soon after it encounters stressful environmental conditions, it will try to protect itself and transform into a spore which remains in the environment until it is removed or dies, and may or may not return to a vegetative state at any time. Many germicides kill the vegetative form of *C. difficile*, and are suitable for use during non-outbreak times. Some germicides induce hypersporulation, resulting in an increased spore burden in the environment, so if an outbreak occurs and/or there is evidence of ongoing patient-to-patient transmission, heightened responses are necessary. They should include changing the germicide to a 10% sodium hypochlorite solution until the outbreak or transmission is under control.

5. Can bleach wipes be used to effectively clean frequently touched surfaces in rooms of patients suspected of having, or diagnosed with, *C. difficile* Infection? If so, what criteria should be used to select the product?
Germicidal wipes providing a 10% sodium hypochlorite solution providing at least 5000 parts per million of chlorine are good adjuncts to cleaning when it has been determined that the routine germicide is no longer adequate for the circumstances. Effectiveness, cost, and ease of use are usually the biggest issues when deciding to use a germicidal wipe. Look at how the wipes are packaged (individually or in a pop-up container). Are they big enough for the job? Read the directions and look at the size and wetness of the wipe, and do a test to check contact time and the number of surfaces that need to be wiped. This can help you decide if a wipe will meet your needs, and if so, how many are needed for each task. Once you have an idea of use, you can calculate costs. Check other aspects of the wipes that may impact how they are used. For example, if the user cannot tolerate or does not like the smell, he or she may be less inclined to use it. When you are testing your germicidal wipe, leave the room, returning shortly after to determine whether a residual odor may negatively impact use. Involve those who will be using the wipes in these tests as well.

6. How do we determine if diarrhea is due to *C. difficile* or from another cause?
The best way to rule out *C. difficile* as a cause for diarrhea is to perform an appropriate test. If diarrhea continues and there is still concern that *C. difficile* may be the cause, it is up to the ordering clinician to use his or her best judgment as to whether or not the patient should be assumed to have CDI, and to implement isolation and treatment.
7. Can bleach be used in the pediatric setting?
Yes, a hypochlorite solution can be used in the pediatric setting but, as in all settings, bleach has a characteristic odor, but this odor is generally innocuous and bleach vapors alone generally do not cause irritation. (Direct exposure to sprays or mists of bleach products is a different issue and potentially can cause irritation.) However, during use, bleach can interact with soils to form malodorous vapors that people might find objectionable or possibly irritating. People with preexisting compromised lung function may be particularly sensitive to such vapors (e.g. asthma, obstructive lung disease, heart conditions). Bleach should not be mixed with other cleaning products since mixing with certain types of products can form irritating or harmful vapors. Exposure to fumes from improper mixing is infrequent and rarely produces serious health effects, in part because the fumes compel people to leave the area preventing significant exposure. Exposure might be more serious if a person is unable to leave the area if improper mixing occurs. Care should be taken to allow for adequate ventilation, regardless of the setting. Commercial formulations may ease some of the odor issues, but those using the products should be involved in determining the effect of the odor and its impact on both user and patient. As with all chemicals, hypochlorite solutions must be stored in a secure manner so children or other unauthorized personnel cannot access the product.

8. Can bleach be used to clean the OR setting?
Yes, but care must be taken to avoid contact with items such as surgical instruments, whereas corrosion and damage may occur following long-term use. Some commercially available preparations have been formulated to minimize this corrosive effect.

9. Is there a benefit to mixing a bleach solution over purchasing one pre-mixed?
Only EPA registered products are reviewed for efficacy, purity and shelf life. EPA review establishes standards for product manufacturing and distributing to better ensure product quality, concentration and efficacy.

When you want to clean with a germicide, it is important that the germicide have a detergent base that promotes the removal of organic and inorganic matter. Mixing sodium hypochlorite with water does not provide that detergent. If it is desired to combine additional cleaning agents or detergents with the germicide, a pre-mixed product should be used. Detergent should not be added to sodium hypochlorite diluted in water to avoid the potential release of hazardous fumes (see question 7). In addition, some detergents will destroy all or part of the hypochlorite so that the desired antimicrobial benefit will not be achieved. Instead one should purchase a properly formulated product that has been approved by the EPA for product safety and efficacy. These products can reduce the time required for cleaning and disinfecting by combining both activities into one step and reduce the overall cost by reducing the amount of labor required.

10. We do not restrict use of alcohol-based hand rubs for healthcare workers providing care for patients with CDI. Is this incorrect?
This is a satisfactory strategy to use unless you have been unable to control your cases of CDI. We know that alcohol-based hand rubs do not kill the *Clostridium difficile* spores and that hand washing serves to physically remove then wash away spores. When a patient has CDI, they have diarrhea for some time until treatment helps resolve the infection. Therefore, it can be reasonably anticipated that feces will have contaminated the environment, and it is likely that the healthcare worker will come into contact with feces while caring for the patient. Consequently, hand washing makes sense, but use of alcohol-based hand rubs should also be available during routine care of patients with CDI. We also know that hand hygiene compliance goes down if alcohol-based hand rubs are removed, making it counterproductive to what we wish to accomplish. To that end, the few simple rules for this complex situation include:

- perform hand hygiene between all patient contact and immediately after removal of PPE
- wash with soap and water as the preferred hand hygiene method if hands are visibly soiled
- provide alcohol-based hand rubs as an additional method to perform hand hygiene for healthcare personnel
11. What are the potential benefits and risks of the use of loperamide and opiates in the control of diarrhea in patients?

In terms of diarrhea caused by *C. difficile*, it is important to remember that there is a toxin involved and use of antimotility agents may be harmful to the patient. The most appropriate use for loperamide, opiates, or other therapies that serve to minimize diarrhea comes after the cause has been identified, and the desire is to now minimize dehydration. Although dehydration may certainly occur with CDI, the most important thing for these patients is to start on appropriate treatment and correct the infection. When infection is corrected, the diarrhea will resolve.

12. Is there a benefit to the use of disposable bedpans?

This question implies that use of disposable bedpans may be of greater benefit in preventing transmission than is the use of bedpans that are disinfected between patients or between uses. Bedpans or commodes must be designated for sole use by the patient with CDI. Once that patient no longer needs this item, it should be disposed of (if disposable) or cleaned, then disinfected if it is made of material designed to be reused. The simple use of a disposable bedpan does not imply increased patient safety. The systems and processes of care that make it difficult for contaminated equipment to be shared between patients represent the greater opportunity for patient safety. Handling the bedpan presents the likelihood of hand contamination by the healthcare personnel and the patient, so hand hygiene remains a critical intervention.

13. Is there value in tracing previous locations of patients with CDI in the facility and then terminally cleaning the area?

Although tracing a patient’s movement may be an element used during an epidemiologic study, when considering this question in the context of CDI, the more useful approach is to ensure that there are systems in place for consistent environmental cleaning throughout the facility. The term “terminal cleaning” seems to have many definitions, but when we hear that term, it is generally used to describe the more in-depth cleaning that is done following patient discharge if it involves a patient room, or cleaning done at the end of the day or end of a procedure in areas such as the operating suite. Terminal cleaning should involve the cleaning and disinfection of all items and surfaces in the room and may also include the changing of items that may remain in the room (e.g., cubicle curtains) if they are soiled. Therefore, there should already be a system in place that supports consistent terminal cleaning by personnel who have been trained in the process and have been deemed competent to perform that process. The idea that terminal cleaning would be part of a patient tracing system is counterintuitive to the systems approach. Routine cleaning methods should impact the burden of *C. difficile*, and terminal cleaning should move closer toward eradication of the organism in the environment.

14. What is the environmental transmission risk of CDI in long-term care facilities?

The risk of transmission within a specific environment such as a long-term care facility has not been quantified, but the risk factors involved in CDI development and transmission are largely the same, regardless of the setting. In the long-term care setting, emphasis would certainly be placed on antimicrobial stewardship, hand hygiene, and standard and contact precautions. These are the same elements emphasized in most settings. Although there is no “one size fits all” for a CDI prevention program, the elements in all such programs should be fairly consistent.

15. What is the impact of ventilation and air pressure gradients on control of CDI?

There is no evidence that *C. difficile* spores are airborne, therefore ventilation and air pressure gradients are not elements requiring specific actions. Inhalation of *C. difficile* spores is unlikely to cause infection. However, aerosolization of spores or vegetative bacterium that comes into contact with the mouth or contaminates hands that touch the mouth may act as a mode of transmission. This further supports the concepts of Standard Precautions and use of personal protective equipment and practices that prevent contact with patient body fluids. Airborne or droplet precautions are not indicated. Contact precautions and standard precautions are the appropriate activities to prevent transmission.
16. What is the infectious potential of patients who have had interventions such as colectomy?
Following colectomy, the area of pseudomembranous colitis has been removed but the organisms continue to be present in the remaining areas of the colon. Therefore, precautions should continue as for all patients with CDI. If the patient has a colostomy, the stool draining into the colostomy bag should be considered a source of contamination. Contact Precautions should continue until the diarrhea resolves or until stool consistency that can be expected via a colostomy has resumed. In addition, if the patient has rectal drainage via a mucous fistula, precautions should continue until that drainage has stopped.

17. What is the risk of transmission by asymptomatic carriers?
Surveillance testing, or a “test of cure,” should not be done on asymptomatic patients. Not all C. difficile is alike in that some are non-toxin producers, and some produce the hypervirulent toxin. If asymptomatic individuals are tested, not only are they subject to the sensitivity and specificity constraints of the testing, we are left not knowing what the results mean. An individual without symptoms (i.e., diarrhea) is not thought to be a likely transmitter of C. difficile.

18. What are the benefits of single rooms with their own toilets for the prevention and control of C. difficile?
A private room and toilet are two of the most critical actions that should be taken as part of the CDI transmission prevention program. Separating diarrhea patients from others and providing them with the sole use of a toilet are two vital interventions that disable the chain of CDI transmission.

19. Do hyper-spreaders exist, and if so, who are they?
There is currently no evidence regarding hyper-spreaders. However, if we look at the concept within the presentations and transmission of other infections, such as SARS, the idea is that there are individuals who are seriously ill and present with pronounced clinical symptoms. This makes it conceivable that individuals with profound diarrhea may contaminate the environment at a greater degree than others. It is also important to recognize that the hypervirulent strains of C. difficile are not more transmissible; therefore, an important element in transmission prevention involves early recognition of individuals with CDI, followed by rapid and early implementation of Contact Precautions.

20. Is there a relationship between CDI rates and nurse-patient ratios?
There is no specific evidence of a relationship between CDI rates and nurse-patient ratios, although we can learn from prior research that demonstrates the effect of staffing and the resultant decline in adherence with basic infection prevention measures, such as hand hygiene and environmental cleanliness. Because the development of CDI is multifaceted and involves a number of different components, including antimicrobial usage, hand hygiene, environmental cleanliness, and Contact Precautions, it is easy to see that nurse-patient ratio is not the only concern. Preventing the development and transmission of CDI is an excellent representation of the need for a systems approach. Not one single process is responsible for the transmission, and therefore no single process or interaction can be entirely responsible for prevention.

21. How many stool specimens should be sent for C. difficile diagnosis?
Determining the approach for testing ideally occurs as a collaborative discussion between clinicians, microbiologists and infection preventionists. There are currently no data to guide the establishment of a set number of stool samples that should be sent for testing on any given patient. Therefore, establishment of local policy should be made using the best available information and within the supporting systems and capabilities of the facility. Despite the lack of data to guide decision-making surrounding this issue, some facilities have implemented the following steps as a means of developing policy development:

- When testing a patient for C. difficile, only loose, watery stool specimens will be evaluated by microbiology. Formed stool samples will be discarded and not evaluated.
- Only one stool sample for C. difficile will be evaluated by microbiology during a 24-hour period. Additional samples will be discarded and not evaluated.
• Testing for *C. difficile* consists of one sample sent each day for two consecutive days. If both specimens are negative, no further testing will be conducted unless the clinical course of the patient changes. If the first test is positive for *C. difficile*, no further testing will be done.

• Tests of cure will not be performed.

These are not hard and fast rules, but are simply a combination of activities used at some facilities. The infection preventionist is encouraged to discuss this issue with the infection prevention and control committee to determine local strategy.

22. **Should I handle endoscopes differently after being used on a patient with CDI?**

   There is no need to alter your methods for reprocessing of endoscopes if your processes are consistent with current recommendations. The Multi-society Guideline for Reprocessing Flexible Gastrointestinal Endoscopes, published in 2003, as well as information provided in the HICPAC Sterilization and Disinfection guideline, can serve as resources. Certainly errors in reprocessing of semi-critical items place patients at risk, so your process should include steps to monitor and evaluate adherence to the process.

23. **I have seen a number of skin care items and fecal management systems. Do they have a role in the prevention of *C. difficile* transmission?**

   Maintaining the integrity of the patient’s skin is always a patient care goal. Patients with CDI will have liquid stools, so skin care may be a primary nursing care goal. Use of a system that serves to minimize environmental and hand contamination may also have a role in preventing transmission of *C. difficile* in healthcare settings.
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**Additional Resources**


For links to references and resources, please visit www.apic.org/EliminationGuides.