Guide to Preventing *Clostridium difficile* Infections

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Table of Contents

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Introduction

Preventing *Clostridium difficile* transmission and infection continues to represent a serious and difficult challenge in infection prevention and patient safety. The average total cost for a single inpatient *C. difficile* infection (CDI) is more than $35,000, and the estimated annual cost burden for the healthcare system exceeds $3 billion.[1] The epidemiology of this infection is changing, and its presence in healthcare settings as well as the community has caused personnel across the entire healthcare continuum to re-evaluate approaches and perspectives. Acknowledging this, the U.S. Department of Health and Human Services (HHS) convened the Federal Steering Committee for the Prevention of Healthcare-Associated Infections. Members of the steering committee include clinicians, scientists, and public health leaders. In April 2012, the steering committee, along with scientists and program officials across HHS, released the *National Action Plan to Prevent Healthcare-Associated Infections: Roadmap to Elimination,*[2] a healthcare-associated infection (HAI) action plan providing a roadmap for preventing HAIs in acute care hospitals, ambulatory surgical centers, and other facilities. In the first phase, the HAI action plan focused on acute care hospitals where the scientific information on prevention and the capacity to measure improvement was most complete and where the associated morbidity and mortality was greatest. In phase 1, CDIs were specifically targeted because CDI rates have been increasing in recent years. Prevention strategies primarily focus on judicious antimicrobial use, environmental cleaning, and preventing transmission using basic infection prevention isolation precautions.

Much needs to be done, but there has been a new level of collaboration and partnership to focus on prevention. Patients, long-term care residents,[a] and families have been increasingly included in care and care decisions. Patient and resident education and healthcare professional training continue to expand and evolve, producing new ways of addressing the problem. There has been collaboration between environmental services professionals and infection preventionists that has produced innovation in environmental assessment, cleaning, disinfection, monitoring, and evaluation. And, there has been an increased understanding of the need to use antimicrobials wisely. Clearly, prevention of CDI requires a team approach. (See Appendix 1 for a diagrammatic overview of the prevention of CDI.)

This document is an update to the 2008 Elimination Guide and contains both new material and revised content that reflect the evolving practices and new discoveries.

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[a]The authors realize that there are different terms used when referring to persons in facilities. These include, but are not limited to, patient, resident, and client. For the purpose of this guide, the term *patient* will be used in order to avoid sentence structure that detracts from the information being conveyed.

Section 1: Pathogenesis and Changing Epidemiology of *Clostridium difficile* Infection (CDI)

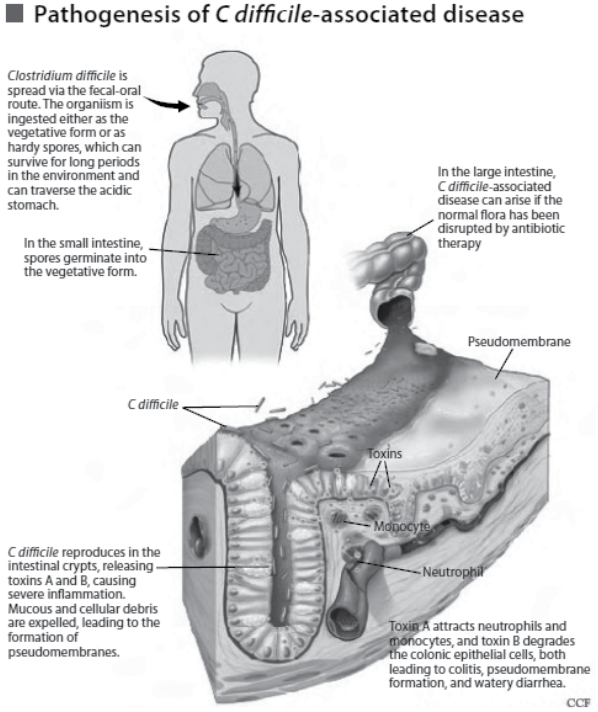
Background

Clostridium difficile, an anaerobic, Gram-positive, spore-forming bacillus, was first detected in 1935 in lower intestinal microbiota of healthy newborns.[1] *C. difficile* was thought to be nonpathogenic for nearly four decades after its initial isolation. It was only in 1978 that *C. difficile* was identified as the primary cause of pseudomembranous colitis in patients treated with antibiotics.[2,3]

Pseudomembranous colitis is an inflammatory condition of the colon that develops in response to toxins produced by microorganisms. This process occurs when the normal microbiota of the intestinal tract are disrupted, which usually happens as a result of antibiotic treatment. This allows organisms not affected by the particular antibiotic(s) to proliferate.[4] 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 1.1 provides graphic demonstration of the transmission and impact of *C. difficile*.

C. difficile infection (CDI) is the leading cause of antibiotic-associated diarrhea and a highly problematic healthcare-associated infection (HAI).[5] The development of CDI most commonly has two essential requirements: (1) exposure to antibiotics and (2) new acquisition of *C. difficile* such as that occurring via fecal–oral transmission. Although some people exposed to these two factors will develop CDI, others may only become asymptomatically colonized. A third factor, possibly related to host susceptibility or bacterial virulence, is thought to be an important determinant for developing disease.[6] In contrast

Figure 1.1. Transmission and impact of *C. difficile*.



Modified from: Sunenshine RH, McDonald LC. *Clostridium difficile*-associated disease: new challenges from an established pathogen. *Cleve Clin J Med* 2006;73:187-197.

to many other HAIs, people who are colonized (asymptomatic) with *C. difficile* appear to be at decreased risk of developing CDI.[7]

Acquisition of *C. difficile* occurs by ingestion of spores, usually transmitted from other patients. This may occur as a result of contamination of the patient environment, of shared equipment, or via the hands of healthcare personnel (HCP).[8,9] The spores resist the acidity of the stomach and germinate into vegetative bacteria in the small intestine. Alteration of the normal lower intestinal microbiota by exposure to antibiotics provides an environment that allows *C. difficile* to multiply, flourish, and produce toxins that cause colitis. The virulence of *C. difficile* is caused primarily by two large exotoxins, toxins A and B, which 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. Toxin-negative *C. difficile* strains are considered nonpathogenic. Recent studies suggest that toxin B, not toxin A as previously thought, is the major toxin responsible for *C. difficile* virulence.[10,11]

The major risk factors for CDI are exposure to antibiotics, hospitalization, and advanced age.[12] Nearly all antibiotics have been implicated in CDI, but certain antibiotic classes, such as cephalosporins, clindamycin, and fluoroquinolones, seem to have a higher risk for causing disease. This may be related to those antibiotics' ability to disrupt normal lower intestinal microbiota in addition to the antibiotic resistance patterns of prevalent *C. difficile* strains. In recent CDI outbreaks, fluoroquinolones have been the major class of antibiotics implicated in CDI,[13–15] an association that has been attributed to high-level resistance to fluoroquinolones of the current epidemic strain, BI/NAP1/027.[16]

Despite the fact that exposure to multiple antibiotic classes and longer courses of therapy appear to increase an individual's risk of CDI, exposure to even a single dose of antibiotic given for preoperative prophylaxis has been associated with CDI.[17–19] Several studies suggest restriction of certain antibiotic classes or changes to the formulary that promote the use of narrow-spectrum antibiotics will reduce the incidence of CDI and control outbreaks.[20–22] These activities form the basis for antimicrobial stewardship programs.

In some studies, proton pump inhibitors (PPIs), a group of drugs whose main action is reduction of gastric acid production, have shown a tendency to increase the risk of both community- and healthcare-associated CDI. The U.S. Food and Drug Administration (FDA) issued a communication (February 8, 2012) advising physicians to consider the diagnosis of CDI in patients taking PPI.[23–25] However, no data are currently available suggesting that restriction of PPI use will decrease CDI incidence. Although the mechanism by which PPI increases the risk of CDI is not understood, it has been suggested that PPI may play a more important role in patients with minimal or no antibiotic exposure.[26]

Available evidence suggests that the incubation period of *C. difficile* following acquisition is short (median of 2–3 days).[9,27] Acquisition of *C. difficile* is more likely to occur in the setting where patients become symptomatic and CDI is diagnosed.[28] In contrast, the effect of antibiotics on the lower intestinal microbiota is much longer lasting. Recent epidemiologic evidence indicates patients remain at elevated risk for CDI for 3 or more months after they have stopped antibiotic treatment.[29,30]

Changing epidemiology

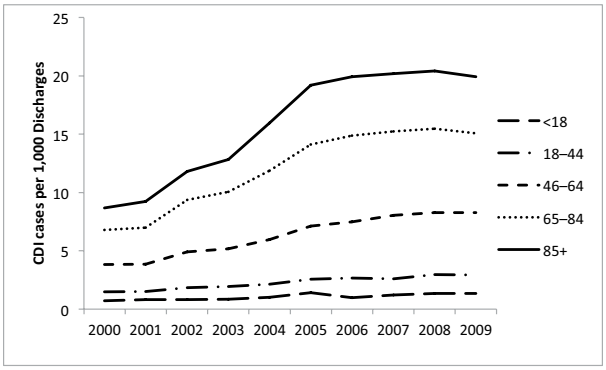
In recent years, the epidemiology of CDI has changed dramatically, with increases in incidence and severity of cases being reported across the United States, Canada, and Europe.[31–34] In at least one U.S. region, *C. difficile* has replaced methicillin-resistant *Staphylococcus aureus* (MRSA) as the most common cause of HAI.[35] In the United States, the rate of hospital discharges

with CDI listed as any diagnosis increased from 3.82 per 1,000 discharges in 2000 to 8.75 per 1,000 discharges in 2008; with a disproportionate increase among persons 65 years of age and older. In 2009 the rate of CDI-related hospital discharges seems to have leveled off compared to 2008 (Figure 1.2).[36,37]

A total of 336,600 CDI-related hospital stays were documented in 2009; representing 0.9 percent of all U.S. hospital stays. In 67 percent of these hospital stays, CDI was listed as a secondary diagnosis. The highest rate of CDI-related hospital stays were in the Northeast, followed by the Midwest, South, and West regions. Persons 65 years of age or older have been most affected, representing over two-thirds of patients with CDI. Finally, females had higher rates of CDI hospital stays compared to males.[36]

The recently changing epidemiology has also involved emergence of CDI in populations previously thought to be at low risk, including severe cases among healthy peripartum women. There are also increasing reports of CDI in children and healthy people who have had minimal or no recent exposure to healthcare settings.[38]

Figure 1.2. Discharge rate for CDI from U.S. short-stay hospitals by age, Nationwide Inpatient Sample, United States, 2000–2009.



Source: Healthcare Cost and Utilization Project. NIS summary statistics. Available at: http://www.hcup-us.ahrq.gov/db/nation/nis/nissummstats.jsp. Accessed March 23, 2012.

During this period of rising incidence of CDI, there were many indications of increasing severity, with greater frequency of reported complications and mortality related to CDI. In reports of CDI outbreaks in hospitals in Quebec, Canada, and subsequently in the United States, a greater number of severe cases associated with higher numbers of colectomies, treatment failures, and deaths were reported than ever before.[13,16,39] In 2004, the 30-day attributable mortality rate of healthcare-associated CDI in Quebec hospitals was 6.9 percent.[39] This was a fourfold increase compared to the Canadian national average of 1.5 percent in 1997.[40] Attributable mortality is the amount or proportion of death that can be attributed to CDI. In the United States, data from vital records showed that the number of death certificates with enterocolitis due to *C. difficile* listed as the primary cause of death increased almost 10-fold between 1999 and 2008 from 793 in 1999 to 7,483 deaths due to CDI in 2008. In 2009, the numbers of deaths decreased slightly to 7,285 similar to the slight (but nonsignificant) decrease seen in rates of hospitalizations in which CDI was listed as a discharge diagnosis. The age-adjusted death rate for *C. difficile* decreased from 2.3 deaths per 100,000 population in 2008 to 2.2 deaths per 100,000 population in 2009, representing a 4 percent decrease. In 2009, 92 percent of deaths from *C. difficile* occurred among persons 65 years of age or older, and *C. difficile* was the nineteenth leading cause of death in this age group.[41]

Part of this change in *C. difficile* epidemiology has been attributed to the emergence of a hypervirulent epidemic strain of *C. difficile.* This strain was found to be associated with outbreaks in Canada, the United States, and Europe.[16,39,42] This epidemic strain has been designated restriction endonuclease analysis type BI, North American pulsed-field gel electrophoresis type 1 (NAP1), polymerase chain ribotype 027 (BI/NAP1/027). Several characteristics found in BI/NAP1/027 may contribute to its hypervirulence and rapid spread. First, the epidemic strain has a mutation in a negative regulator of toxin production, *tcd*C,

leading to higher toxin production compared to other strains.[43] Second, there is the presence of a third toxin called binary toxin.[16] The role of binary toxin is not completely understood yet; however, it is postulated that the binary toxin acts together with toxin A and B causing more severe disease.[44] Third, the resistance to the fluoroquinolone class of antibiotics likely contributed to the successful spread of this strain in healthcare settings.[16] Although BI/NAP1/027 isolates existed previously, historic strains were less resistant to fluoroquinolones, and they were not associated with outbreaks of disease. Although hypersporulation of BI/NAP1/027 strains has been suggested to explain its spread in the environment,[45] more recent data have shown that the sporulation rate of BI/NAP1/027strains does not appear to be higher than non-BI/NAP1/027strains.[46] The BI/NAP1/027 strain has been reported to the U.S. Centers for Disease Control and Prevention (CDC) from at least 41 states as of February 2012. Because CDI is not nationally reportable and cultures are often not performed to allow characterization of isolates, there is reason to believe that BI/NAP1/027 has spread nationwide.

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Section 2: Diagnosis

CDI should be suspected in any patient with diarrhea or abdominal pain and a recent history of antibiotic use, healthcare exposures, or in patients with unexplained leukocytosis.[1,2] Severe CDI has also recently been reported in low risk populations—that is, people without recent antibiotic or healthcare facility exposures—therefore, CDI should be considered in any patient who has diarrhea lasting longer than 3 days and has a fever or abdominal pain.[3] CDI is most commonly confirmed with a laboratory-based assay, but there are advantages and disadvantages for all laboratory-based methods for detecting *C. difficile* or its toxins. Because of the different targets and combinations that can be measured when detecting *C. difficile* (bacterium, glutamate dehydrogenase, toxins, and toxin genes), the measured incidence of infection may vary according to the methods used by the laboratory. [4] Therefore, it is essential to understand the method used in the assay.

Who should be tested and how frequently

It is recommended to test for *C. difficile* only in patients experiencing diarrhea, unless ileus is suspected. It is recommended to NOT screen asymptomatic patients or perform a "test of cure" in patients who have responded to therapy.[1,2] There are several reasons for these recommendations. All nonculture laboratory-based assays for detecting *C. difficile* or its toxins have been developed and validated to diagnose CDI only in symptomatic patients. The sensitivity (the likelihood that someone with the disease or condition will have a positive test result), specificity (the likelihood that someone that 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 for that population of patients. In addition, this information provides no clinically useful information and may result in patient harm and unnecessary antimicrobial use due to an inaccurate test result. Although asymptomatic patients colonized with *C. difficile* have been implicated as a potential driver of *C. difficile* transmission in healthcare settings,[5] current guidelines recommend against routine surveillance for or treatment of asymptomatic carriers.[1] Persistently positive test results at the end of treatment are not predictive of *C. difficile* relapse, and a "test of cure" at the end of therapy should not be performed.[1]

A common question is how often a patient with diarrhea should be tested if the initial tests are negative because of concerns of low sensitivity of the tests. This practice was encouraged when there was a heavy reliance on enzyme immunoassays (EIA) using a single *C. difficile* toxin for diagnostic testing.[6] These tests have poor sensitivity for diagnosis of CDI.[7] Several recent publications have demonstrated that repeat testing within a 7-day window does not substantially improve sensitivity and comes with an increased risk of a false-positive result.[8–11]

Therefore, due to the relatively small increase in diagnostic sensitivity combined with an increased likelihood of a false-positive result, routine use of repeat testing is discouraged.[1]

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, leak-proof container, and should be transported to the laboratory as soon as possible. Although *C. difficile* spore viability is largely unaffected by routine storage conditions, toxin activity is widely believed to decrease during storage, especially if subjected to multiple freeze–thaw cycles.[12] If testing cannot be performed immediately, it is recommended stool specimens be stored at 2° to 8°C for up to 24 hours, or frozen at –70°C for longer storage.[13]

Laboratory tests for diagnosing CDI

Because 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* toxins A and B. There are numerous assays available for diagnosis of CDI, and these vary widely in characteristics such as test performance, cost, complexity, and turnaround time (Table 2.1).

Cytotoxic culture, requiring culture of the organism and demonstration of toxin production by the methods described below, is the most sensitive assay for diagnosis of CDI. However, this assay requires up to 4 days to complete, making it impractical for clinical use. Furthermore, *C. difficile* culture also requires specialized media, experience with anaerobic culture, and the ability to recognize the organism. Because of this, cytotoxic culture is used as the gold standard for evaluation of new test methods, and in support of epidemiologic and outbreak investigations.[1,2,14]

The cell cytotoxicity assay, which detects toxin B-specific cytopathic effects on cultured cell lines, is considered the reference clinical laboratory assay for the diagnosis of CDI even though it is less sensitive than toxigenic culture.[2,15]

Advantages of this assay are that it is more sensitive than immunoassays for toxin A and/or B, is relatively inexpensive, and it has a faster turnaround time than toxigenic culture. Disadvantages include a longer turnaround time than EIAs of 48 to 72 hours and the complex nature of the testing.[14,15]

EIAs for toxins A and/or B have become the most widely used laboratory-based method for diagnosing CDI in the United States because of their low cost, ease of use, and rapid turnaround time. Most assays

Table 2.1. Comparison of laboratory-based diagnostic tests for CDI.

Diagnostic test	Advantages	Disadvantages
Toxin enzyme immunoassay (EIA)	Inexpensive Rapid	Very poor sensitivity Poor specificity
Glutamate dehydrogenase	Inexpensive Rapid Good sensitivity Good negative predictive value	Very poor specificity Requires use of a second-line test for toxin detection
Toxigenic (cytotoxic) culture	Excellent sensitivity Good specificity	Requires second-line test for toxin detection 3- to 4-day turnaround time Requires expertise in culturing *C. difficile*
Cell cytotoxicity	Good sensitivity	2-day turnaround time Requires tissue culture capacity
Nucleic acid amplification (including polymerase chain reaction [PCR])	Excellent sensitivity Excellent specificity Rapid	Expensive

in use today target both toxin A and toxin B, because some fully virulent strains do not produce toxin A.[16] Although there are several advantages of EIA compared to cell cytotoxicity assays, the sensitivity of these assays range from 60 to 81 percent with a specificity of 91 to 99 percent compared to toxigenic culture.[17,18] The poor performance of EIAs in terms of both sensitivity and specificity results in repeat testing, inefficient use of laboratory resources, and overuse of Contact Precautions and antibiotics. Many now view standalone toxin EIA tests as inadequate for clinical diagnosis of CDI.[19–22]

Glutamate dehydrogenase (GDH) is a protein produced by all *C. difficile* strains; EIA tests are available to detect GDH in stool. EIA tests targeting GDH have better sensitivity for detection of *C. difficile* than EIA tests directed at toxins,[19,21] and are relatively low cost and rapid. GDH assays do not distinguish between toxigenic and nontoxigenic *C. difficile* strains and must be used in combination with toxin-detection assays for CDI diagnosis. However, the GDH assays have high negative predictive values as a rule-out test for CDI. Several two- and three-step algorithms using GDH assays as the first step in the testing process have been recommended in the literature. By pairing the quick and inexpensive GDH rule-out test with more sensitive tests that are more expensive or have longer turnaround times, testing laboratories can maximize clinical utility and optimize use of laboratory resources.[2,23,24]

In addition, there are EIAs that test for both GDH and *C. difficile* toxins in a single assay. These assays have the advantages of low price, quick turnaround, and sensitivity of the GDH component. They remain limited by the poor sensitivity of the toxin detection component of the assay.[25]

The relatively recent introduction of nucleic acid amplification tests (NAATs), including polymerase chain reaction (PCR), for CDI diagnosis has had an impact on both laboratory detection of *C. difficile* and perceived infection rates in healthcare facilities.[26] Numerous FDA-approved and laboratory-developed NAAT for CDI diagnosis have been described in the literature, nearly all of which demonstrate diagnostic sensitivity and specificity equivalent to toxigenic culture, but with a turnaround time of 1 to 3 hours rather than days.[20,27] One objection to widespread implementation of NAAT has been the high cost of these assays compared to EIA; however, several studies have suggested that use of NAATs as either a standalone assay or as part of a multistep algorithm may actually be more cost-effective because it facilitates better use of laboratory resources, appropriate infection prevention precautions, and treatment.[28–31]

Others have suggested that NAAT may be too sensitive for *C. difficile* detection, with the potential for overinterpreting asymptomatic colonization as CDI. This concern has not been borne out in clinical evaluations of NAAT, but it does reinforce the importance of performing testing only on symptomatic patients. Finally, it is important to keep in mind that the increased sensitivity of NAAT compared to EIA and cell cytotoxicity will impact perceived and reported rates of CDI once NAATs are implemented for routine diagnosis, and it will be important to communicate this to infection preventionists and clinicians at the impacted healthcare facilities. Even with the relatively high price per test of NAATs compared to other methods, the sensitivity and specificity of these assays, combined with rapid turnaround time, makes it clear that NAATs are the future of CDI diagnostic assays.

Molecular typing

Although molecular typing is necessary for in-depth epidemiological studies of *C. difficile* and helpful when changes in CDI epidemiology occur, molecular strain characterization is not necessary for routine patient treatment or infection prevention. There are several molecular typing techniques for *C. difficile*, but these are not routinely available outside of research laboratories. Due to the reliance on toxin assays, cultures for *C. difficile* are not routinely performed to diagnose CDI and isolates are infrequently available for molecular typing.

Table 2.2. Common typing methods for characterizing *C. difficile* strains.

Acronym	Method title	Description
MLVA	Multilocus variable-number tandem-repeat analysis	DNA is extracted from an organism and amplified (increased in quantity) using a PCR.[a] MLVA is based on fragment analysis of five repeat nucleic acid loci. It provides results that are comparable across institutions and that are not dependent on interpretation. MLVA has the advantages of typing methods based on PCR (low cost, short time, and easy to perform) that are independent of equipment and yield unambiguous typing data, which are critical in both detecting outbreaks and determining their source.
AFLP	Amplified fragment length polymorphism	AFLP uses enzymes to digest cellular DNA to produce fragments. Some of the fragments are then selected to be amplified using a PCR. The amplified fragments are separated using electrophoresis, then visualized on polyacrylamide gels, either through autoradiography or fluorescence methodologies.
slpAST	Surface layer protein A gene sequence typing	In this assay, the nucleotides that make up a variable area on the gene (surface layer protein A) are identified (sequenced) in order to identify the specific strain of *C. difficile*. Sequence typing has the advantage of allowing easy comparison of typing results among multiple laboratories without the need to exchange reference strains.
PCR-ribotyping	Polymerase chain reaction ribotyping	Nucleic acid sequences from genes for coding ribosomal RNA are extracted. These sequences are amplified (increased in quantity) using the PCR. The products of this amplification are then analyzed by electrophoresis.[b] Strains can be differentiated by comparing to electrophoresis patterns of related organisms.
REA	Restriction endonuclease analysis	Enzymes are mixed with the nucleic acid that cleave (cut) it at particular places in the sequence. These fragments are separated using electrophoresis and compared to others and known reference materials.
MLST	Multilocus sequence typing	This technique involves PCR amplification followed by DNA sequencing. Nucleotide differences between strains can be checked at a variable number of genes depending on the degree of discrimination desired.
PFGE	Pulsed field gel electrophoresis	Similar to electrophoresis as described, although in PFGE, the current is passed through the medium in alternating directions. PFGE allows for better separation of very large DNA fragments, whereas normal electrophoresis does not.

a) PCR is a method of copying chemical material. On its most basic level, the PCR is a biologic copier. A small amount of material is combined with the individual building blocks that make up that material and an enzyme. Under the right conditions, the result is a much larger amount of the original material. In this way, a very small amount of material can be increased to an amount suitable for chemical testing.

b) Electrophoresis is a method of separating components of a mixture. The chemical is placed on a medium, such as agarose, and an electric current is conducted through the medium (positive at one end, negative at the other). Depending on the positive or negative charges on the components to be separated, as well as their size, some will move farther than others on the medium. Standard current and time are used to allow for comparison to known references. After the electrophoresis has been completed, the medium is treated and stained to allow visualization of the result.

Nonlaboratory–based tests

CDI is the cause of over 90 percent of cases of pseudomembranous colitis (PMC). PMC 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 histopathologic examination. PMC is identified in only 50 percent of cases of CDI[32]; however, when it occurs, it is diagnostic for CDI.

Abdominal computed tomography (CT) scans are helpful to suggest the diagnosis of CDI if colitis is identified in a patient with abdominal pain or ileus. Abdominal CT scans should not be relied upon to make or rule out the diagnosis of CDI due to poor sensitivity and specificity, and these scans do not necessarily correlate with severity of illness, although such testing may assist with some prognostic indicators.[33–35]

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Section 3: Modes of Transmission

To understand the transmission of *C. difficile*, the following key facts are important to remember:

- *C. difficile* can survive in the hospital environment including on hard surfaces, equipment, and patient items. The vegetative stage does not last long, but the spores can persist in the environment for many months.
- Patients and/or HCP can transmit and/or acquire *C. difficile* from contact with contaminated surfaces, including contamination with both vegetative cells and spores.
- Transmission occurs via the 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

C. difficile is a fastidious anaerobe and the vegetative cell dies rapidly, generally within 24 hours, outside the colon.[1,2] However, *C. difficile* produces spores that can persist in the environment for many months and are highly resistant to cleaning and disinfection measures.[1,2] 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. 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.[3]

The level of environmental contamination with *C. difficile* spores increases with increasing severity of disease in the patient.[4] However, asymptomatic colonized patients should also be considered as a potential source of contamination.[5] Patient care items such as electronic thermometers and contaminated commodes have been implicated in the transmission of CDI.[6]

Transmission of *C. difficile* to the patient on HCPs' 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 this.[7] Alcohol is not effective in killing *C. difficile* spores, but use of alcohol-based hand rubs (ABHR) has not shown an increase in CDI rates over hand washing. However, if a facility is experiencing an outbreak or increased infection rates with *C. difficile*, it can be beneficial for HCP to wash their hands with soap and water exclusively when caring for patients with known CDI.[8]

Transmission of disease from contaminated cellular, or mobile, telephones may also occur.[9] A study of bacterial contamination from cell phones showed that after using alcohol-based hand sanitizer to clean their hands, 30 of 32 clinicians

had contaminated hands after making a short call using their cellular telephone. In the study, contamination included *Klebsiella pneumoniae*, *Bacillus anthracis*, and coagulase negative *Staphylococcus* species; however, the study shows the potential for transmission of *C. difficile* from cellular telephones.[9]

Transmission via patient care activities

There are a number of patient care activities that provide an opportunity for 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
- Emergency procedures such as intubation
- Poor hand hygiene practices
- Sharing of patient care items without appropriate disinfection
- Ineffective environmental cleaning

These examples serve to identify some of the many activities that could result in fecal–oral transmission of *C. difficile*. When prevention strategies are designed, it is important that transmission opportunities such as these be considered. Patient care observation can identify other activities that may be potential modes of transmission.

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Section 4: Surveillance

Surveillance is the ongoing, systematic collection, analysis, interpretation, and dissemination of data regarding a health-related event to reduce morbidity and mortality and to improve health. Surveillance of both process measures and the infection rates to which the processes are linked are important for evaluating the effectiveness of infection prevention efforts and for identifying indications for change.[1]

The essential components of a surveillance system are:

1. Standardized definitions
2. Identification of patient populations at risk for infection
3. Statistical analysis (calculation of rates using appropriate denominators, trend analysis using control charts to identify high incidence areas and to monitor trends)
4. Feedback of results to all stakeholders (managers, directors, primary caregivers, senior leadership including administrators, governing boards, trustees, etc.)[1]

Identification of clusters or outbreaks of CDIs should be studied using a systematic epidemiologic investigation to determine whether there are common people, places, or times. The findings can then guide interventions and evaluation of the effectiveness of the interventions.[1,2] The first step to properly evaluate the effectiveness of any process implemented to reduce CDI or any other HAI is to develop a standardized case definition.[2]

Case definitions

Standardized case definitions are critical if the information is going to be used to compare one unit or facility with another (benchmarking), to monitor trends over time, or to evaluate the effectiveness of interventions to reduce infections. A surveillance case definition can be defined as a standard set of criteria to identify whether a person has a disease or condition. It is important to remember that surveillance definitions are used to trend the frequency of a disease or condition among specified populations over time. This is not the same as a clinical diagnosis, which is used to identify and treat individual patients.

Although surveillance definitions may include patients with a clinical diagnosis of the same disease as the surveillance definition, oftentimes these definitions do not identify the same patients. For the purposes of infection prevention, it is critical to follow surveillance definitions, not clinical definitions, so that standardized, methodological data collection is performed. Only through this process can trends be established, risk factors identified, and prevention interventions be successfully evaluated.

At this time, there are two nationally acceptable definitions for CDI surveillance in the acute care setting. The first is from the National Health Safety Network (NHSN), a division of the CDC,[3] and the second is from the Society for Healthcare Epidemiology of America (SHEA) and the Infectious Disease Society of America (IDSA) Clinical Practice Guidelines.[4] It is important to remember that whichever surveillance definition is used, comparisons can only be done with facilities using the same surveillance definitions.

For national comparison or benchmarking, federal agencies such as the CDC, HHS, and Centers for Medicare & Medicaid Services (CMS) focus mainly upon the NHSN definitions. In addition, NHSN surveillance methods have been recognized by many professional organizations as the recommended approach for infection prevention program surveillance. Training programs, such as the APIC EPI courses, focus on use of those methods and definitions as critical elements in a surveillance process.

According to the CDC, cases of CDI can be identified through two main methods:

I) Infection surveillance
II) Laboratory identification (considered a proxy, or substitute, measure).

The infection preventionist usually conducts infection surveillance, and each patient is evaluated by case review to determine if he or she meets the specified case definition. On the other hand, laboratory identification permits diagnostic data to be used without clinical evaluation of the patient. This substitute, or proxy, method provides for a much less labor-intensive method to track CDI.

NHSN surveillance case definition for *C. difficile* [3]

I. Infection Surveillance Method: NHSN uses two surveillance and reporting classifications for *C. difficile* infections: gastroenteritis or gastrointestinal tract infection.

GI-GASTROINTESTINAL SYSTEM INFECTION

- GE-Gastroenteritis

  Gastroenteritis must meet at least one of the following criteria:

  1. Patient has an acute onset of diarrhea (liquid stools for more than 12 hours) with or without vomiting or fever (>38°C) with no likely noninfectious cause (e.g., diagnostic tests, therapeutic regimen other than antimicrobial agents, acute exacerbation of a chronic condition, or psychological stress) or
  2. Patient has at least two of the following signs or symptoms with no other recognized cause: nausea, vomiting, abdominal pain, fever (>38°C), or headache

     and

     The identification of ***C. difficile*** disease by at least one of the following methods:

     a. *C. difficile* is cultured from stool or rectal swab
     b. *C. difficile* is detected by routine or electron microscopy
     c. *C. difficile* is detected by antigen or antibody assay on blood or feces
     d. Evidence of *C. difficile* is detected by cytopathic changes in tissue culture (toxin assay)
     e. Diagnostic single antibody titer (immunoglobulin [Ig]M) or fourfold increase in paired sera (IgG) for *C. difficile*.

- GIT-Gastrointestinal tract

  Gastrointestinal tract infections, excluding gastroenteritis and appendicitis, must meet at least one of the following criteria:

  1. Patient has an abscess or other evidence of infection seen during a surgical operation or histopathologic examination, or
  2. Patient has at least two of the following signs or symptoms with no other recognized cause and compatible with infection of the organ or tissue involved: fever (38°C), nausea, vomiting, abdominal pain, or tenderness,

and

At least one of the following:

a. *C. difficile* cultured from drainage or tissue obtained during a surgical operation or endoscopy or from a surgically placed drain

b. *C. difficile* seen on Gram or potassium hydroxide (KOH) stain or multinucleated giant cells seen on microscopic examination of drainage or tissue obtained during a surgical operation or endoscopy or from a surgically placed drain

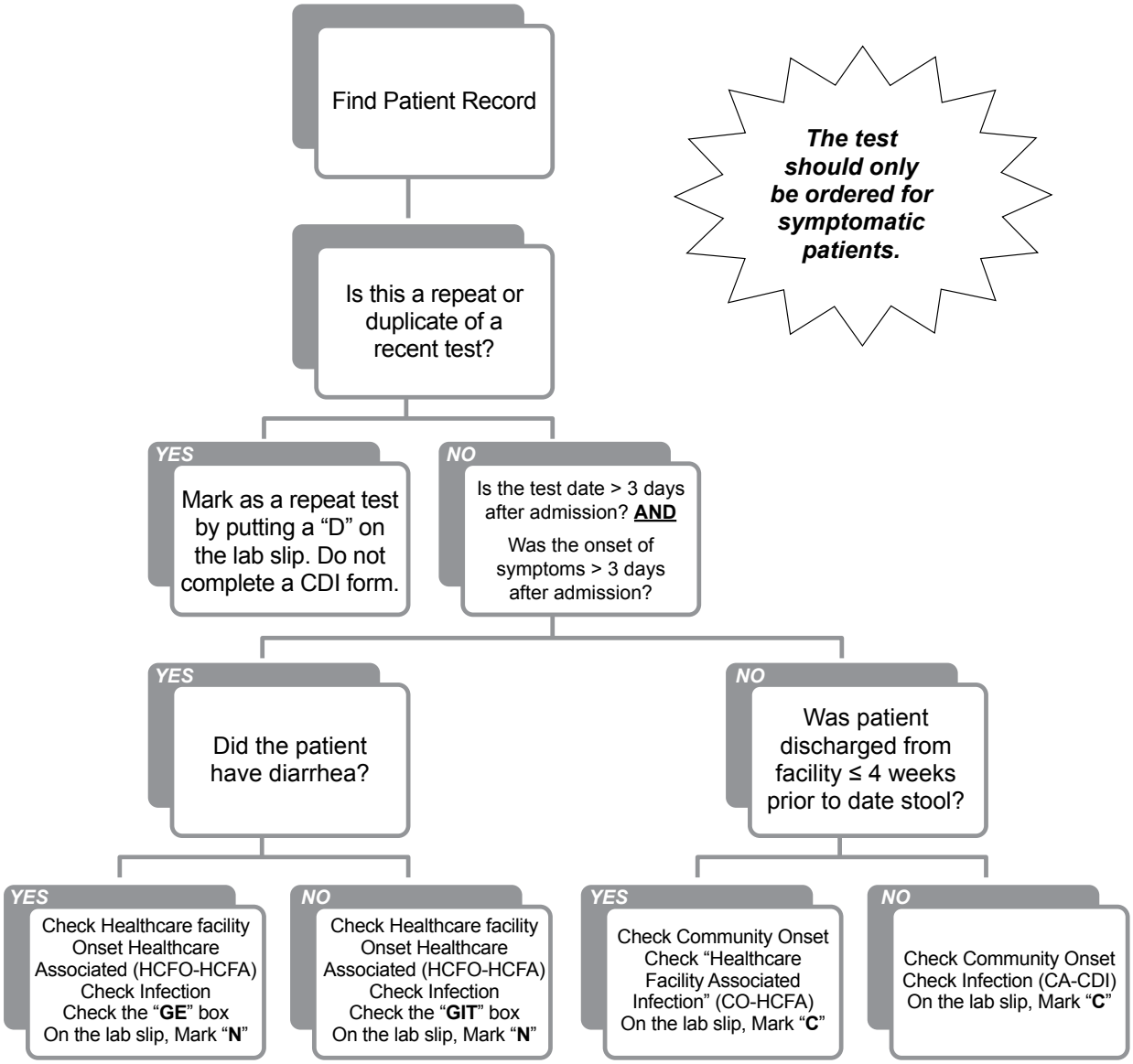
c. *C. difficile* cultured from blood, or

d. Evidence of pathologic findings on endoscopic examination constant with *C. difficile* disease.

Figure 4.1 depicts a CDI surveillance diagram.

Laboratory Identified (LabID Event) Method: A case of CDI is defined as a positive laboratory

Figure 4.1. CDI surveillance algorithm. (Courtesy of the Arizona Department of Health Services.)



test result (nonduplicative) for *C. difficile* toxin A and/or B, or a toxin-producing *C. difficile* organism detected by culture or other laboratory means performed on a stool sample. A duplicate positive test is any *C. difficile* toxin-positive laboratory result from the same patient and location, following a previous *C. difficile* toxin-positive laboratory result within the past 2 weeks (14 days). LabID Events can include specimens collected during emergency department or other outpatient clinic visit, if collected on the same day as the patient admission. Figure 4.2 depicts the LabID Event algorithm for *C. difficile* from the NHSN manual.

Further classification of Lab ID Event data is stratified by time, incident or recurrent, and location.

- Time: Stratified by month, quarter, annual, etc.
- Location: Facility-wide or stratified by patient care location.
- Incident (new case) CDI Assay: Any LabID Event from a specimen obtained >8 weeks after the most recent LabID Event (or with no previous LabID Event documented) for that patient.
- Recurrent CDI Assay: Any LabID Event from a specimen obtained >2 weeks and ≤8 weeks after the most recent LabID Event for that patient.

The incident and recurrent CDI events are further categorized within NHSN. These categories are based on the timing of admission to facility and/or location and specimen collection, location where specimen was collected, and previous discharge. Figure 4.3 displays a timeline for NHSN surveillance of healthcare facility–onset, community-onset, and community-onset healthcare facility–associated CDI.

Figure 4.2. Laboratory identification algorithm for *C. difficile*.[3]

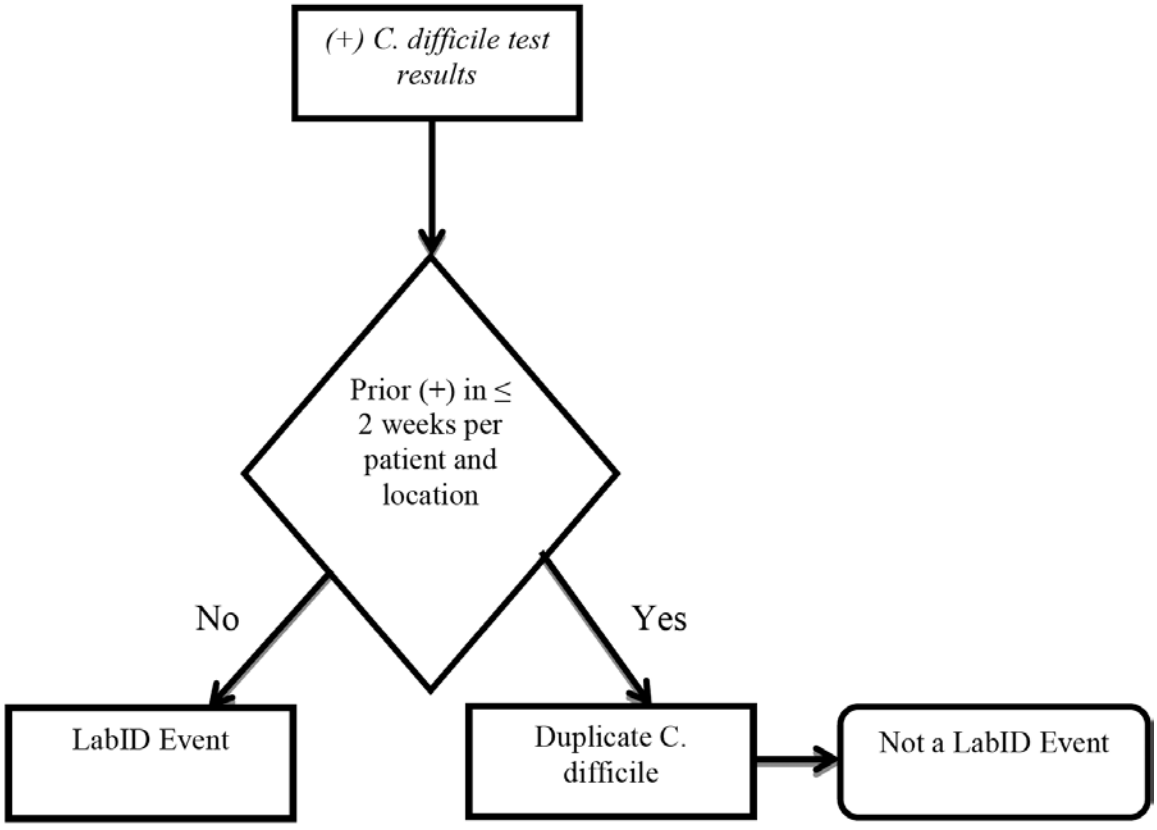
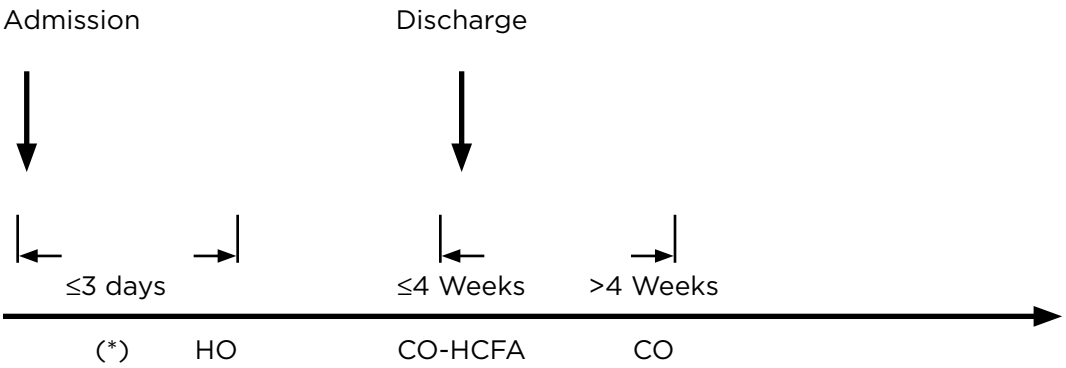


Figure 4.3. Timeline for NHSN surveillance of *C. difficile*.



- Healthcare Facility–Onset (HO): CDI identified >3 days after admission to the facility (i.e., on or after day 4).
- Community-Onset (CO): CDI identified as an outpatient or an inpatient ≤3 days after admission to the facility (i.e., before or on days 1, 2, or 3 of admission).
- Community-Onset Healthcare Facility–Associated (CO-HCFA): Community onset CDI identified from a patient who was discharged from the facility ≤4 weeks prior to current date of stool specimen collection.

A case patient who had symptom onset or LabID Event during the window of hospitalization marked by an (*) would be classified as having community-onset healthcare facility–associated (CO-HCFA), if the patient had been discharged from the healthcare facility within the previous 4 weeks; or would be classified as having community onset (CO) if the patient had not been in a healthcare facility in the past 4 weeks.

Conducting surveillance

In January 2013, CMS began requiring acute care hospitals that participate in the CMS Inpatient Prospective Payment System (IPPS) to report laboratory-identified *C. difficile* infections via the NHSN. (For additional information, see the CDC NHSN website at http://www.cdc.gov/nhsn/.)

Depending on the purposes of surveillance, all or only some of the above CDI case definitions may be appropriate for use by a healthcare facility.[2] 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 CDI.

Surveillance should be facility-wide and a line list may be maintained in an electronic spreadsheet or database file such as in Microsoft Excel, Microsoft Access, SPSS (Statistical Package for the Social Sciences), or another such electronic means. Small facilities may not require an electronic system. The file should include at least the following:

- Patient identification (name or unique identifier such as medical record number)
- Patient age
- Patient gender
- Admission date
- Patient location (unit and room, outpatient, or home)
- Service (medicine, surgery, OB/GYN, etc.)
- CDI symptom onset date
- CDI test date
- Discharge date
- Other known risk factors for CDI obtained from the scientific literature

CDI rates

1. **Denominator** for Calculation of CDI Rates[2]

   - Rates should be expressed as number of patients per reporting period (usually per month) per 1,000 patient-days or resident days.[(a)]
   - The calculation of this rate is (number of CDI case patients per month / number of inpatient days per month) × 1,000 = rate per 1,000 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 as well as comparing different units, wards, and/or services within a healthcare facility in which unit-/ward-/service-specific denominators are available.

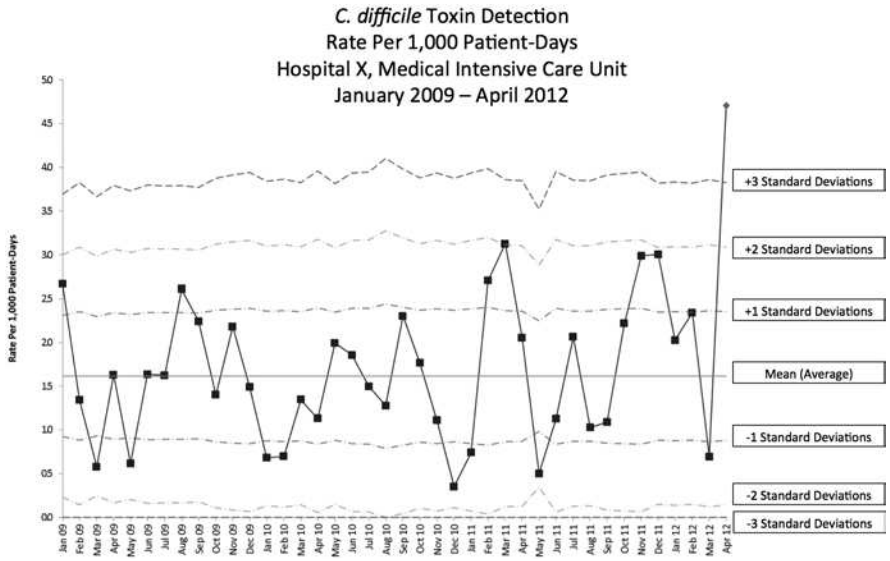
2. Expression of CDI Rates for Feedback to Caregivers and Comparative Purposes

   - **Control charts** (Figure 4.4) should be created to display CDI cases and rates for the entire healthcare facility and/or by unit/ward/service.
   - The *X axis* is the surveillance time period (month, quarter, year).
   - The *Y axis* is the CDI rate per 1,000 patient-days.
   - Control charts are useful to determine if a healthcare facility's and/or unit's, ward's, or service's rate is out of range compared to what is "normal" or "expected" for the facility and to monitor trends.
   - Control charts should be posted on individual patient care units and used during educational in-services so staff can understand what the charts reflect and also to see results of processes put into place to reduce CDI rates.

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

[(a)] Units used vary by facility, with 1,000 and 10,000 commonly used , although 100; 100,000; and 1,000,000 are also used.

Figure 4.4. Example of a statistical process control chart.

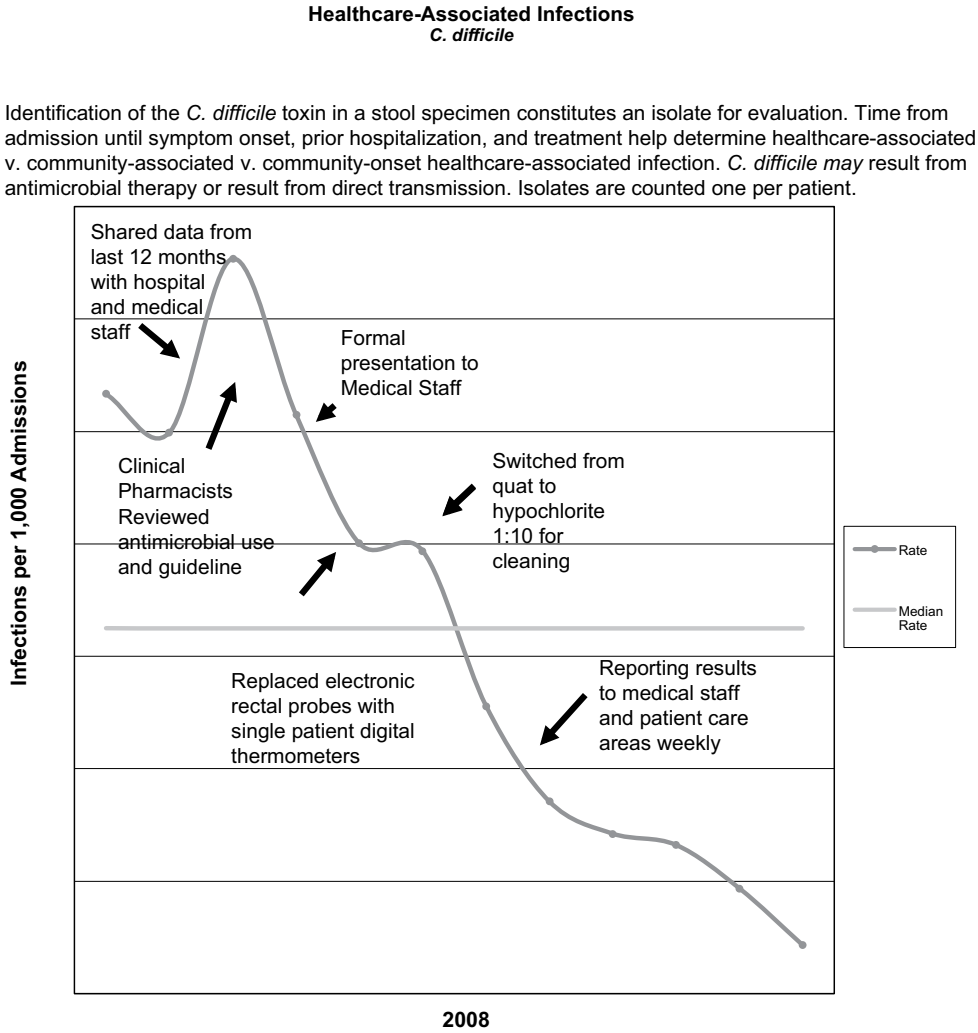


of statistical control. Using the control chart shown in Figure 4.4, the rate of CDI exceeds +3 standard deviations from the mean in April 2012, which is an indicator for when expanded interventions using a tiered approach might be necessary. For more information regarding control charts, refer to the work done by JC Benneyan in *Infection Control and Hospital Epidemiology.*[5,6] It is very important to ensure that enough data points (months, quarters, years) are available for the control chart prior to creation of the chart. Too few data points (fewer than 25) can limit the ability to identify points above the upper control limit (+3 standard deviations from the mean). Too many data points (more than 50) will begin to identify false-positives (points above +3 standard deviations from the mean that are due to chance and not abnormal events).

For more information on how to choose the appropriate control chart, see the chapter on statistical process control in the *APIC Text of Infection Control and Epidemiology*.[7]

The infection preventionist (IP) may also find other types of charts to be of help when monitoring rates as well as interventions, particularly if not enough data points are available to construct a control chart. Figure 4.5 demonstrates a run chart developed using EpiGraphics (available from APIC). This chart shows the rate over time and enables the IP to add

Figure 4.5. Run chart with examples of interventions.



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. It is not necessary to have 25 data points to begin to construct these charts, but they cannot detect significantly abnormal data points.

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Section 5: Focusing on Prevention: Hand Hygiene

Prevention of all HAIs requires strict adherence to hand hygiene. This is particularly true in the prevention of CDI, and IPs should assess compliance with hand hygiene practices if the rate of CDI increases. Knowing the incidence of CDI in your setting, knowing barriers to compliance with hand hygiene standards, and ensuring environmental cleanliness will help your team select interventions to prevent transmission of this organism.

Current opinions regarding the use of traditional hand washing instead of ABHR are conflicting. Neither kills the *C. difficile* spores. Common antimicrobial agents for hand washing (including alcohols, chlorhexidine, hexachlorophene, iodophors, PCMX, and triclosan) are not active against spores; however, soap and water hand washing removes *C. difficile* spores from hands of volunteers when compared to ABHRs.[1,2] There have been no studies in acute care settings that demonstrate an increase in CDI with ABHRs or a decrease in CDI with traditional hand washing with soap and water. The use of soap and water for hand hygiene over the use of ABHRs after caring for a patient with CDI is not recommended in nonoutbreak settings. The recommendation to use soap and water preferentially in outbreak settings after caring for a patient with CDI is recommended based on the theoretical benefit of the physical removal and dilution of spores from the hands by washing, rather than killing the spores.[1]

According to the CDC Healthcare Infection Control Practices Advisory Committee (HICPAC) hand hygiene guideline,[3] HCPs' hands are frequently contaminated with *C. difficile* following patient contact. Wearing gloves can significantly reduce the spread of *C. difficile* by providing a physical barrier that decreases, if not prevents, hand contamination with spores.[4] Gloves should be removed if the integrity is compromised. The gloves should be removed properly to prevent hand contamination. After gloves are removed, the HCP's hands should be washed with a nonantimicrobial or an antimicrobial soap and water or disinfected with an ABHR.[3]

Although some facilities remove ABHR from a patient's room if the patient has CDI, removing ABHRs may increase the risk of other infections. The use of ABHRs has been shown to improve compliance and reduce the risk of multidrug-resistant organisms (MDROs) such as vancomycin-resistant *Enterococcus* and MRSA. When providing device-related care where there is a need to decontaminate hands and don clean gloves, ABHRs may improve compliance, minimize the time for cleaning hands, and reduce the risk of device-related infections.

In an intensive care unit (ICU) study that characterized the HCP encounter with patients and correlated that to their hand hygiene compliance, it was noted that hand hygiene compliance was the lowest after brief encounters that lasted less than 2 minutes. The observers noted that brief encounters made up a substantial portion of the contact and HCP had opportunities for hand hygiene during all brief encounters. Because of the potential for hand contamination even during brief encounters, IPs should stress that improving adherence with hand hygiene after brief encounters may have an important overall impact on disease transmission.[5]

Advanced technologies to monitor hand hygiene electronically may serve as a reminder to perform hand hygiene any time a provider enters the room. Electronic devices provide useful information on frequency, time, and location of its use, and also reveal trends in hand disinfection events over time, while direct observations offer essential data on compliance with the hand hygiene protocols. Data generated by the electronic devices can be used as a supplementary source of information to evaluate the effectiveness of hand hygiene promotion campaigns.[6] A hand hygiene monitoring tool is shown in Figure 5.1.

Teaching patient hygiene including hand hygiene and bathing

Families, visitors, and patients should be partners in preventing CDI.[7] There have been several national initiatives encouraging patients to take an active role in their care. The HHS Partnership for Patients created "Do the Wave"[8] to teach families and patients how to protect themselves when they are in the hospital. This message provides helpful teaching points that can relate to *C. difficile* prevention. The "WAVE" reminds families to wash hands to protect against germs; to ask questions to improve quality of care; to vaccinate against flu and pneumonia; and finally to ensure safety by making sure medical devices are clean and used properly.

Information provided to patients promotes understanding of their care and should include:

1. Explanation of the infection caused by *C. difficile.*
2. Review the spectrum of disease and reoccurrences.
3. Discuss how the organism is spread, including skin contamination, colonization, shedding, and environmental contamination.
4. Describe what the patient can do to help reduce the spread of the disease, including performance of patient hand hygiene.[9]
5. Educate the patient and their family about visitors who may be at high risk for acquiring *C. difficile,* such as individuals on antibiotics or who are immunosuppressed, and help them make a decision about their visitation.
6. Describe how to prevent transmission of *C. difficile* including Contact Precautions, Standard Precautions, and hand hygiene, especially while in any healthcare settings.
7. Identify steps that patients and family can do to clean their environment at home including not sharing towels or hygiene products, cleaning, and laundry practices.

A patient and family education program can promote cooperation with adherence to prevention strategies including the use of Contact Precautions and the importance of hand hygiene[7] (see Figure 5.2).

The family should understand that items that have been in the patient's room should not be taken to common waiting room areas because they may be contaminated with spores.

Hand hygiene is critical in minimizing the spread of infections. Nursing staff should assist the patient if the patient is unable to perform hand hygiene. This is especially important after toileting and before eating to minimize reinoculation. Nursing staff should educate the family about the risk factors for transmission of CDI.

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 or clothing should be donned after bathing or showering. Assessment and preplanning for this situation is advised. In one

SINAI HEALTH SYSTEM
INFECTION CONTROL DEPARTMENT
HAND HYGIENE MONITORING TOOL

UNT_______________MONTH_____________________YEAR___________

DATE/ TIME	NAME	JOB CATEGORY	BEFORE PATIENT CARE	AFTER PATIENT CARE	SUPPLIES AVAILABLE	FOLLOW UP
		MD MS RN/LPN CNA/ERT RT LAB REHAB RAD EVSOTHER______	HH DONE? Y N IF YES, HW ABHR IF HW, 15 SEC? Y N	GLOVES WORN? Y N HH DONE? Y N IF YES, HW ABHR IF HW, 15 SEC? Y N	SINK WORKING? Y N HAND SOAP AVAIL? Y N PAPER TOWELS AVAIL? Y N ABHR AVAIL? Y N	STAFF MEMBER COUNSELED MANAGER NOTIFIED EVS NOTIFIED FET NOTIFIED
		MD MS RN/LPN CNA/ERT RT LAB REHAB RAD EVSOTHER______	HH DONE? Y N IF YES, HW ABHR IF HW, 15 SEC? Y N	GLOVES WORN? Y N HH DONE? Y N IF YES, HW ABHR IF HW, 15 SEC? Y N	SINK WORKING? Y N HAND SOAP AVAIL? Y N PAPER TOWELS AVAIL? Y N ABHR AVAIL? Y N	STAFF MEMBER COUNSELED MANAGER NOTIFIED EVS NOTIFIED FET NOTIFIED
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		MD MS RN/LPN CNA/ERT RT LAB REHAB RAD EVSOTHER______	HH DONE? Y N IF YES, HW ABHR IF HW, 15 SEC? Y N	GLOVES WORN? Y N HH DONE? Y N IF YES, HW ABHR IF HW, 15 SEC? Y N	SINK WORKING? Y N HAND SOAP AVAIL? Y N PAPER TOWELS AVAIL? Y N ABHR AVAIL? Y N	STAFF MEMBER COUNSELED MANAGER NOTIFIED EVS NOTIFIED FET NOTIFIED
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		MD MS RN/LPN CNA/ERT RT LAB REHAB RAD EVSOTHER______	HH DONE? Y N IF YES, HW ABHR IF HW, 15 SEC? Y N	GLOVES WORN? Y N HH DONE? Y N IF YES, HW ABHR IF HW, 15 SEC? Y N	SINK WORKING? Y N HAND SOAP AVAIL? Y N PAPER TOWELS AVAIL? Y N ABHR AVAIL? Y N	STAFF MEMBER COUNSELED MANAGER NOTIFIED EVS NOTIFIED FET NOTIFIED
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		MD MS RN/LPN CNA/ERT RT LAB REHAB RAD EVSOTHER______	HH DONE? Y N IF YES, HW ABHR IF HW, 15 SEC? Y N	GLOVES WORN? Y N HH DONE? Y N IF YES, HW ABHR IF HW, 15 SEC? Y N	SINK WORKING? Y N HAND SOAP AVAIL? Y N PAPER TOWELS AVAIL? Y N ABHR AVAIL? Y N	STAFF MEMBER COUNSELED MANAGER NOTIFIED EVS NOTIFIED FET NOTIFIED

HW - Hand Washing HH - Hand Hygiene ABHR - Alcohol Based Hand Rub

Figure 5.1. Sample hand hygiene monitoring tool (Courtesy of Sinai Health System, Chicago, IL).

Figure 5.2. Sample hand hygiene poster. (Courtesy of the Minnesota Department of Health)

study, chlorhexidine gluconate (CHG) baths (4% liquid formulation) were used in a three-pronged design. It was found that there was a decrease in central line–associated blood stream infections (CLABSIs) and a decrease in MDROs including *C. difficile*. The antimicrobial CHG soap kills the vegetative cells, and the soap and water removes the spores.[10]

Resources

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Section 6: Focusing on Prevention: Contact/Isolation Precautions

Early identification of patients who are being investigated for, or diagnosed with, CDI is the first step in preventing the spread of the disease. *C. difficile* can be spread by direct and indirect contact with the patient or the patient's environment. Placement of patients on appropriate Contact Precautions is recommended.[1–5] Prevention of transmission may be assisted by application of Contact Precautions for patients with diarrhea.[5] Placing patients on Contact Precautions as recommended in the HICPAC/CDC Guideline for Isolation Precautions is a critical step in preventing the spread of CDI.[5]

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 by the organism[6] make patients with CDI a significant threat for dissemination and transmission of the disease. The use of presumptive isolation and Contact Precautions have been recommended while awaiting the results of screening for patients who develop healthcare-associated diarrhea.[7–9] The following components of Contact Precautions should be observed for all patients suspected of, or diagnosed with, CDI.

Patient placement

If at all possible, patients should be assigned to a private room with a bathroom that is only for use by that patient.[5] If a private room is not available, the infection prevention team should work with the patient care team to determine the best patient placement options. This includes placement with other patients diagnosed with CDI, which is known as cohorting (in the absence of any other condition that would preclude cohorting). A patient who is cohorted for CDI may be moved to a clean room once diarrhea resolves to prevent reinfection.[10]

In some care settings (e.g., rehabilitation programs, long-term care institutions, or residential settings), private rooms may not be available. The care team should decide what precautions need to be taken, including closing a room off to other patients. If this is deemed necessary, the team should have administrative support and a process in place to take this precautionary step. In the multipatient room setting where isolation in a single patient room is not possible, other actions may be considered, including the use of spatial separation (a 3-foot distance between beds is recommended) to reduce the possibility of sharing of items between the "isolated" patient and others. Privacy curtains drawn between patients may also promote separation. Some facilities use a visual cue, such as colored tape placed on the floor, in order to identify areas where restricted access and use of additional precautions are needed.

Personal protective equipment (PPE)

PPE refers to a variety of special clothing or equipment (such as masks) used alone or in combination to protect mucous membranes,

Table 6.1. Recommendations for application of Standard Precautions for the care of all patients in all healthcare settings[5]

COMPONENT	RECOMMENDATIONS
Hand hygiene	After touching blood, body fluids, secretions, excretions, contaminated items; immediately after removing gloves; between patient contacts
Gloves	For touching blood, body fluids, secretions, excretions, contaminated items; for touching mucous membranes and nonintact skin
Gown	During procedures and patient care activities when contact of clothing/exposed skin with blood/body fluids, secretions, and excretions is anticipated
Mask, eye protection (goggles), face shield*	During procedures and patient care activities likely to generate splashes or sprays of blood, body fluids, secretions, especially suctioning, endotracheal intubation
Soiled patient care equipment	Handle in a manner that prevents transfer of microorganisms to others and to the environment; wear gloves if visibly contaminated; perform hand hygiene
Environmental control	Develop procedures for routine care, cleaning, and disinfection of environmental surfaces with an EPA-registered sporicidal disinfectant, especially frequently touched surfaces in patient care areas
Textiles and laundry	Handle in a manner that prevents transfer of microorganisms to others and to the environment
Needles and other sharps	Do not recap, bend, break, or hand-manipulate used needles; if recapping is required, use a one-handed scoop technique only; use safety features when available; place used sharps in puncture-resistant container
Patient resuscitation	Use mouthpiece, resuscitation bag, other ventilation devices to prevent contact with mouth and oral secretions
Patient placement	Prioritize for single-patient room if patient is at increased risk of transmission, is likely to contaminate the environment, does not maintain appropriate hygiene, or is at increased risk of acquiring infection or developing adverse outcome following infection
Respiratory hygiene/cough etiquette (source containment of infectious respiratory secretions in symptomatic patients, beginning at initial point of encounter [e.g., triage and reception areas in emergency departments and physician offices])	Instruct symptomatic persons to cover mouth/nose when sneezing/coughing; use tissues and dispose in no-touch receptacle; observe hand hygiene after soiling of hands with respiratory secretions; wear surgical mask if tolerated or maintain spatial separation, >3 feet if possible.

* During aerosol-generating procedures on patients with suspected or proven infections transmitted by respiratory aerosols (e.g., severe acute respiratory syndrome [SARS]), wear a fit-tested N95 or higher respirator in addition to gloves, gown, and face/eye protection.

** Information provided is for guidance only; personnel should consult their facility's procedures.

airways, skin, and clothing from contact with infectious agents. The selection of PPE is based on the nature of patient care and/or the likely mode(s) of transmission.[5] Barrier precautions are critical to prevent transmission from the patient to the healthcare worker and patient to patient. PPE must be donned before going into the room or cubicle and discarded before exiting the patient's room/cubicle. The CDC website has a video ("Guidance for the Selection and Use of Personal Protective Equipment [PPE] in Healthcare Settings," www.cdc.gov/HAI/ppt/ppe/

ppeslides6-29-04.ppt) and posters illustrating proper PPE donning and removal procedures. Designated containers for used disposable or reusable PPE should be placed in a location that is convenient to the site of removal to facilitate disposal and containment of contaminated materials. Hand hygiene is always the final step after removing and disposing of PPE.[5]

a. **Gloves**

Gloves must be donned before entering the room and worn by all HCP during patient care and when in contact with the patient's environment. Gloves should also be changed according to standard recommendations for glove use (e.g., if heavily contaminated or torn), and removed and discarded as the HCP leaves the room. Contact with the patient and the patient's environment can expose the healthcare worker to vegetative *C. difficile* and its spores. Nonsterile disposable medical gloves made of a variety of materials (e.g., latex, vinyl, nitrile) are available for routine patient care.[5]

High-touch surfaces, such as bedrails, light switches, and faucets, are a known repository of *C. difficile* spores. *C. difficile* may also be found at multiple skin sites of patients with CDI, including the groin, chest, abdomen, forearm, and hands. Colonization can persist after the cessation of diarrhea.[11] Because of this, proper use of gloves and hand hygiene after every patient interaction (Standard Precautions) is needed to keep the organism from being transferred to the care provider's hands.

b. **Gowns**

Contact Precautions includes the wearing of gowns as well as gloves when entering a room to provide care. The use of gloves alone may be as effective in preventing transmission as the use of gloves and gowns together.[12] However, until conclusive data are 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 recommended.[13]

Patient transport

When a patient has CDI, patient transportation and movement outside the room or cubicle should be limited to medically necessary purposes, such as diagnostic and therapeutic procedures that cannot be performed in the patient's room. Patients should perform hand hygiene prior to leaving their room, and the patient should use appropriate barriers. These strategies can help contain and limit shedding into the environment. According to the HICPAC Isolation Guideline[5] 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 the receiving unit personnel are able to prepare appropriately. If the receiving unit does not routinely treat patients requiring Contact Precautions, it may be prudent to inquire and offer education on the handling of patients requiring Contact Precautions, as needed. (Education programs for HCP have been associated with sustained improvement in adherence to best practices and a related decrease in device-associated HAIs in teaching and nonteaching settings and in medical and surgical ICUs.[5])

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 HCP. 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 an indicator of poor adherence to environmental decontamination and other infection prevention measures. The infection prevention team should observe personnel performing 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 can be transmitted to patients during this time.[6] Fecal contamination of surfaces, devices, and materials (e.g., commodes, bathing tubs, and electronic rectal thermometers) with *C. difficile* spores may lead to transmission.[14] The cleaning and disinfection of all frequently touched surfaces in all patient care areas is important. Special attention should be paid to those areas closest to the patient, including bedrails, bedside tables, commodes, doorknobs, sinks, surfaces, and equipment in close proximity to the patient, because these are most likely to be contaminated. The frequency or intensity of cleaning may need to change based on the patient's level of hygiene and the degree of environmental contamination. This may be especially true in long-term care facilities and pediatric facilities where patients with stool and urine incontinence are encountered more frequently.[5]

Use of an individual bedside commode for each patient with CDI who cannot be placed into a private room may reduce the risk of transmission of infectious agents because it eliminates the sharing of a toilet. 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.

Family members

In some healthcare settings, family members may request to stay in the patient's room. This is most common in pediatric units. Assessment and preplanning for this situation is advised. Wearing the PPE (gown and gloves) associated with Contact Precautions for a long time or during sleep can be very uncomfortable. It is important that family members understand the risks and prevention strategies for CDI.

Hospitals should develop a plan for these situations. The family member may be contaminated with spores on their clothing and other belongings. Some personal items can be put into a plastic bag while in the room. If the family member leaves the room for coffee or other refreshments, they could be asked to wash hands prior to leaving the room to prevent spreading the bacteria. Gloves may be donned based on a standard approach which takes into account the epidemiologic data for the unit. If the transmission data shows minimal risk, the hospital may choose not to use the "reverse isolation" approach. By developing a policy that includes all stakeholders, the staff will be able to respond appropriately when requests are made. This also allows development of educational resources for the staff, patient, and family.

Patients may be involved in transmission in

four ways: transfer of pathogens within the environment, direct spread to other patients, spread to other patients or the environment via contact with HCP, and direct contact producing illness in themselves.[15] Hand hygiene is one of the most important ways of preventing transmission and infection. A successful patient hand hygiene program should be developed that provides resources, education, monitoring, and feedback.[15]

Discontinuing Contact Precautions

It is currently recommended that Contact Precautions may be discontinued when the patient no longer has diarrhea.[5] Because of continued environmental contamination and patient skin colonization, some experts recommend continuing Contact Precautions for 2 days after diarrhea stops.[16] In addition, if the rates of CDI remain high, Contact Precautions may be continued until hospital discharge.[17] Up to 70 percent of patients may have skin contamination with *C. difficile* 6 days after the resolution of diarrhea and 40 percent may have skin contamination up to 9 days after the resolution of diarrhea.[18] This is one example of heightened response activities used in outbreak conditions and is discussed in more detail in the following section, which addresses a tiered approach to CDI transmission prevention.

Assessing adherence to isolation precautions

Assessing adherence with isolation precautions is an important element in prevention. Figure 6.2 provides an example of a tool used to monitor adherence. This tool is also available at http://www.apic.org/implementationguides. Figures 6.3 and 6.4 are examples of signs for contact and special enteric Contact Precautions.

Tiered approach to CDI transmission prevention

Coordination of efforts is required to prevent or eliminate CDI. Departments have to work together. It is not enough for Environmental Services to perform frequent, extensive cleaning if Contact Precautions are not in place, or if the antibiotics that produced the CDI are not discontinued. In addition to departments and teams working together, the CDC introduced the idea of a tiered approach to address the unique aspects of MDROs as part of the 2006 guidelines for preventing transmission of MDROs.

This guide outlines some of the transmission prevention activities that should be undertaken as part of routine infection prevention responses to *C. difficile*. In the pages that immediately follow these routine activities, the next tier of heightened activities follows. 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; however, the activities are not exclusive. Moving to the next tier does not mean that ALL the activities need to be added. Many components of routine activities remain important in CDI precautions. Those in the heightened category are added to the routine, as necessary. 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 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.

Figure 6.2. Infection prevention and control isolation compliance checklist. (Courtesy of Shands at the University of Florida, 2008)

Date and Time of Observation_____ Observer_____

Precaution/Isolation Type _____

Unit	Room #	Compliance with Hand Hygiene Practices		Person Observed (HCW or visitor) Please check appropriate box. KEY: 1 = Physician; 2 = RN; 3 =Transporter; 4 = PA; 5 = Respiratory RX; 6 = Nursing assistant; 7= Rehab; 8 = Lab; 9 = Dietary; 10 = Housekeeping; 11 = Other HCW; 12 = Visitor												100% Compliant with isolation? Yes or No Identify variance by PPE or Signage				
																YES	NO Check Observed Variance			
		ABHR	Soap + H_20	1	2	3	4	5	6	7	8	9	10	11	12		Gloves	Gown	Mask	Signs

Courtesy of Shands at the University of Florida, 2008

Figure 6.3. Contact Precautions sign.

(Courtesy of the University of North Carolina.)

Figure 6.4. Contact Precautions sign.

(Courtesy of the University of North Carolina.)

- Provide CDI data and interventions to key individuals and groups such as the infection prevention committee, administration, medical staff, nursing staff, and pharmacy and therapeutics committee.
- Monitor for an increased incidence in colectomies.
- Network with other area IPs 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 (e.g., MRSA, VRE, *Acinetobacter*) should not be housed with patients who are not colonized with the same microbe.
- Use dedicated equipment (blood pressure cuff, thermometer, and stethoscope).
- Put on gown and gloves before 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 the gown and gloves and perform hand hygiene after caring for one patient and prior to providing care for the next patient.
- Routinely check available supplies for Contact Precautions to ensure that adequate selection and amounts are readily available. Consider 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 the "Summary of additional *C. difficile* transmission prevention activities during heightened infection prevention responses."
- Do not isolate asymptomatic carriers of *C. difficile.*

Environmental controls

- Use EPA-approved germicide for routine disinfection during nonoutbreak 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:
  - Bed, including bedrails and patient furniture (including the bedside and over-the-bed tables and chairs)
  - Bedside commodes
  - Bathrooms, including sink, floor, tub/shower, toilet

    - Frequently touched or high-touch surfaces such as light switches, doorknobs, 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. (Remove the gown prior to removing the gloves.)
- Use ABHRs for hand hygiene during routine infection prevention 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 personnel 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 prevention 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.

Summary of additional *C. difficile* transmission prevention activities during heightened infection prevention responses

An increased 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.

In addition to the interventions listed here, additional interventions may be used if they are applicable to the particular environment. These may include cohorting staff as well as patients,

closing the affected unit to new admissions, tighter visitation rules and requirements for visitation (e.g., mandated gloves and gowns for visitors) in affected units, increased use of dedicated or disposable equipment, and the use of alternate methods of disinfection (e.g., ultraviolet light or vaporized hydrogen peroxide).

Use the risk assessment to determine which additional interventions should be implemented and when, while keeping others in reserve.

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 (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 IPs in your community.

Microbiologic identification

- Discuss a CDI rate increase with microbiology staff, and evaluate alterations in testing methods that may impact 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, because 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.
- Consider placing all patients with diarrhea in contact isolation until CDI is ruled out.
- Increase monitoring of adherence to isolation precautions and hand hygiene.
- Ask patient care staff to identify barriers to infection prevention practices (interruption in isolation supplies, lack of private rooms).
- Continue Contact Precautions even when diarrhea resolves. Consider extending isolation until patient discharge.

Environmental controls

- Use a 1:10 dilution of 5.25% 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 a 1:10 dilution of 5.25% sodium hypochlorite for daily disinfection of the patient's room as well as discharge cleaning for the patient with CDI.
- If there is evidence of ongoing transmission, consider expanding the use of a 1:10 dilution of 5.25% 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 of 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.
- Consider use of other products and technologies such as vaporized hydrogen peroxide and ultraviolet light aimed at environmental disinfection as individual national guidelines and recommendations are updated.

Hand hygiene

- Ensure compliance with appropriate hand hygiene upon removal of gown and gloves and exiting the patient's room.
- Consider using hand washing as the preferred method for hand hygiene during this heightened response.
- Assess hand hygiene compliance to address obstacles to performance.

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 *C. difficile* and its transmission with patients and their families.
- Instruct the patients and their families regarding hand hygiene, and monitor for adherence.

Education of healthcare personnel

- Provide ongoing education to clinicians, HCP, 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.

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Section 7: Focusing on Prevention: Environmental Infection Prevention

The environment plays a significant role in the spread of CDI.[1–7] Because *C. difficile* is shed in feces, any surface, item, or medical device that becomes contaminated with feces can act as a source for spores and, therefore, be involved in infection transmission.[8,9] *C. difficile* spores can exist for 5 months on hard surfaces.[8,9] In one study, spores were found in 49 percent of the rooms occupied by patients with CDI and 29 percent of the time in rooms of asymptomatic carriers.[10] The heaviest contamination is on floors and in bathrooms.[11] Facility policies should address strategies to prevent contamination from spreading from isolation rooms to other places. For example, consider the use of shoe covers and disposable mop heads in isolation rooms. 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 windowsills in the patient room. Even stethoscopes have been implicated as vectors of CDI.[12] As levels of environmental contamination increase, the level of hand contamination of HCP also increases. The greater the incidence of CDI, the greater the opportunity for transmission. Interventions should be linked to surveillance results.

Disinfectants commonly used in healthcare settings include quaternary ammoniums and phenolics, neither of which is sporicidal.[13,14] Some disinfectants may actually encourage sporulation (the changing of the organism from the vegetative state to the protected spore state). Hypersporulation has been used to denote the tendency of the bacterium to move from the vegetative form to the spore form with increased rapidity when in contact with some germicides, compared to normal. Although many EPA-registered germicides kill the vegetative *C. difficile*, only chlorine-based disinfectants and high-concentration hydrogen peroxide formulations kill spores.

Industry has responded to the need for alternatives to cleaning and disinfection when spores are involved, and there are now a few EPA-registered sporicidal agents containing chlorine or hydrogen peroxide formulations that are acceptable for use as general surface disinfectants.[15–17] The new products are able to be used on hard, nonporous surfaces, can be used while rooms are occupied (suitable for frequent, everyday use), allow for rapid room turnover because they can be used to do terminal cleaning and disinfection, require minimal training, are relatively inexpensive, require shorter exposure times, combine cleaner and disinfectant together, and are available in concentrates or ready-to-use sprays and wipes.

The environments of all patients with CDI do not require cleaning with a hypochlorite solution or a highly concentrated hydrogen peroxide solution. The problems associated with use of a sodium hypochlorite solution (also known as bleach) include corrosion and pitting of equipment and other surfaces over time, and may be greater if solutions are mixed at the individual facility and are not those that are commercially prepared. There are employee-related concerns such as the triggering of respiratory difficulties in workers using the solutions. Because of these problems and concerns, care should be

taken when bleach is used.[17] Although some of the newer formulations decrease some of the negative effects, these new formulations, like the previous formulations, may not be appropriate for use on fabrics. Users are urged to check the label for specific product warnings.

Cleaning requires physical action along with the use of a germicide, and rinsing helps to lower the spore concentration by removal and dilution. Individuals who are responsible for cleaning should be taught proper cleaning technique. They should be required to show understanding and competency by demonstration. In nonoutbreak settings, continued use of the cleaner routinely used may be acceptable. It is important to know the facility's epidemiology when assessing the routine cleaning process and when determining the need to escalate to the next level of interventions if evidence of ongoing transmission is found.

In general, surfaces should be kept clean and body substance spills should be managed promptly.[17] EPA-registered disinfectant products 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. It may be that physical cleaning is more important than the disinfectant used.[18] 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.[19–21]

The infection prevention team should verify any disinfectant's claims of efficacy. 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 environmental services, materials management, and infection prevention to ensure the chemicals meet standards and are effective and easy to use. The infection prevention team, along with other stakeholders (environmental services, purchasing, etc.) should review both chlorine bleach–based products and high concentrate hydrogen peroxide products to determine the best product for the planned use.

If using a 10% sodium hypochlorite solution (one part household chlorine bleach mixed with nine parts tap water), there are several points to remember:

- There are commercially available bleach solutions that also contain a detergent base which is helpful in cleaning as well as disinfecting. The detergent base breaks up grease, oils, and proteinaceous material.
- Evaluate the use of commercially available solutions within your facility. Some hypochlorite products are available in a ready-to-use solution, which may save time and minimize dilution errors. However, storage of the ready-to-use container and the cost may be important issues at the facility.
- Making a mixture of bleach and water will provide only the disinfectant, not the detergent base. Cleaning will be required prior to disinfection.
- If a bleach and water mixture is made at the facility, use chlorine bleach without a scent additive. (The scent additive reduces the parts per million [ppm] of available chlorine.)
- The chlorine bleach and water solution should provide at least 4800 ppm of available chlorine. (This is typically equivalent to a 1:10 dilution, although some highly concentrated bleach products are also available, which may require alternate dilutions. Always refer to manufacturer labels for the exact dilutions required.)

- The IP should be aware that there is a difference between a germicidal bleach (6.15% or more hypochlorite), a laundry bleach (6.0% hypochlorite), and a discounted bleach (5.25% or less hypochlorite).

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 microorganisms. This usually means a 3 logarithmic (3 log or 99%) reduction in the number of organisms. This is known as the kill claim and is submitted to the EPA in order to receive approval as a germicide acceptable for use in healthcare settings.

It is vital for the IP to know the contact time of the selected germicide. Germicides commonly used in the healthcare setting have a contact time of 10 minutes. This means 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 process used for cleaning 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. Buckets or containers should be washed and disinfected regularly in addition to being inspected for cracks and stored dry. The practices used during cleaning and disinfection should be clearly outlined in policy. Some recently developed germicides have shorter contact times than 10 minutes.

A contact time of 1 minute for the hypochlorite (bleach and water) solution should provide adequate disinfection for nonporous surfaces. This is accomplished by a thorough wetting of the surface with the hypochlorite solution then allowing it to air dry. (Rutala, "Disinfection and Sterilization: Current Issues and New Technologies," APIC Annual Conference, 2008).

Germicidal wipes have become an important addition to environmental cleaning but they must be used appropriately in order to be effective. Wipes are made of a material, or substrate, that enables them to absorb the germicide and enables 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 specified in the EPA approval process. The wipe must allow the user to wet the surface being disinfected for the contact time as noted on the label in order to destroy the organisms. 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 1 minute for some viruses. In order to maintain a wet surface for that contact time, that wipe is appropriate for disinfecting 20 square feet. It is important for IPs to know the contact time for the germicide as well as the area the wipe can disinfect. If wipes are used to clean the high touch surfaces in a patient room, multiple wipes will likely need to be used because of the number of surfaces to be disinfected. Environmental services staff must be trained to use the wipes appropriately.

Manufacturers' recommendations for contact times are governed by the tests submitted to the EPA during their approval process. Although evidence of shorter, more practical exposure times is available, APIC supports the following of disinfectant label instructions until updated guidance is released from the EPA.

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 if they follow the list and check off each item as the cleaning and disinfection process is completed.

Checklists that delineate recommended practice for a facility and routine rounds to evaluate practices will assist the care team in identifying opportunities for improvement. Working with unit and specialty groups to develop checklists and measures to support adherence with environmental cleaning activities will help improve adherence. Example 7.1 shows a CDC checklist to assess environmental cleaning. Example 7.2 shows a checklist used when CDI has necessitated altered environmental cleaning practices.

Figure 7.3 depicts a patient room that has not yet had high touch surfaces identified. Figure 7.4 shows the same patient room identifying high touch surfaces that have been targeted for specific patient environments. Although it is important to ensure cleaning of high touch surfaces, it is also important to note that all surfaces within the patient environment, not just high touch surfaces, are important when cleaning and disinfection is performed. Focusing on high touch surfaces alone may interfere with consistent environmental cleaning and disinfection and may enable ongoing transmission.

There are five monitoring processes that are commonly used today.[20]

1. Direct Observation. Direct monitoring of cleaning can provide objective assessment of individual staff performance. Logistical issues related to maintaining such a program may limit the ability to use this process. This process may also be difficult to employ without the evaluator being recognized.
2. Swab Cultures. Swab cultures are easy to use; however, the cost of processing, the delay in analyzing results (24–72 hours), the need to determine precleaning levels, and the limited practicality of swabbing multiple surfaces in multiple patient rooms limit the ability to use this method widely.
3. Agar Slide Cultures. Agar-coated glass slides with finger holds were developed for use in environmental surface monitoring in healthcare settings; they quantify aerobic colony counts (ACCs) per cm. Some difficulties have been encountered in using the agar slide cultures on other than large, flat surfaces. However, they provide an easy method for quantifying viable microbial surface contamination. Precleaning levels of contamination need to be determined for each object evaluated in order to accurately assess cleaning practice.
4. Fluorescent Markers. Powder and lotion have been used as part of educational interventions. Their overt visibility, ease with which they can be disturbed (powder), and difficulty with easy removal (e.g., lotion if allowed to air dry) may limit their use in a monitoring system. The fluorescent gel dries transparent on surfaces, resists abrasion, and there are several studies demonstrating the accuracy of the system in objectively evaluating cleaning practice.[22,23] This is done by applying fluorescent dyes to surfaces and then asking the staff to clean the area. The results are immediate and allow for timely feedback. However, the fluorescent markers cannot provide a colony count or a log reduction of bacteria. This method cannot identify the organisms that are present after the surfaces have been cleaned. Because these fluorescent markers are all designed to indicate physical removal of an applied substance, surfaces that are effectively disinfected but less effectively cleaned may be more likely flagged as failing to meet a quality standard using one of these markers than one of the culture techniques.
5. ATP Bioluminescence. This involves the measurement of organic ATP on surfaces using a specialized swab to sample a

Example 7.1. CDC environmental checklist for monitoring terminal cleaning.

CDC Environmental Checklist for Monitoring Terminal Cleaning[1]

Date:	
Unit:	
Room Number:	
Initials of ES staff (optional):[2]	

Evaluate the following priority sites for each patient room:

High-touch Room Surfaces[3]	Cleaned	Not Cleaned	Not Present in Room
Bed rails / controls			
Tray table			
IV pole (grab area)			
Call box / button			
Telephone			
Bedside table handle			
Chair			
Room sink			
Room light switch			
Room inner doorknob			
Bathroom inner doorknob / plate			
Bathroom light switch			
Bathroom handrails by toilet			
Bathroom sink			
Toilet seat			
Toilet flush handle			
Toilet bedpan cleaner			

Evaluate the following additional sites if these equipment are present in the room:

High-touch Room Surfaces[3]	Cleaned	Not Cleaned	Not Present in Room
IV pump control			
Multi-module monitor controls			
Multi-module monitor touch screen			
Multi-module monitor cables			
Ventilator control panel			

Mark the monitoring method used:

☐ Direct observation ☐ Fluorescent gel
☐ Swab cultures ☐ ATP system ☐ Agar slide cultures

_____

[1]Selection of detergents and disinfectants should be according to institutional policies and procedures.
[2]Hospitals may choose to include identifiers of individual environmental services staff for feedback purposes.
[3]Sites most frequently contaminated and touched by patients and/or healthcare workers

National Center for Emerging and Zoonotic Infectious Diseases
Division of Healthcare Quality Promotion

Example 7.2. Terminal cleaning checklist.

TERMINAL CLEANING

Record results of evaluation for each surface on the checklist for every room monitored. Use the following symbols for marking:
O = NOT CLEAN, X = CLEAN, LEAVE BLANK = NOT EVALUABLE NOTE - USE CAP LETTERS “X” AND “O”

				High Touch I			High Touch II			High Touch III			
Unit	Rm No.	Date of Marking (If applicable)	Date of Evaluation	Bed rails	Tray table	IV pole	Call box / button	Telephone	Bedside table handle	Chair	Rm sink	Rm light switch	Rm inner doorknob

Figure 7.3. Sample patient room.

surface area. The swab is taken by a portable handheld luminometer. The total amount of ATP, both microbial and nonmicrobial, is quantified. This method measures organic debris and has been used in the food industry for years. Feedback is immediate and provides insight into residual organic matter. However, it does not identify a pathogen nor provide a colony count. It does serve as a surrogate marker for biological contamination.

Routine environmental biological sampling for *C. difficile* is not required. It is important for the team to select the appropriate environmental disinfectant when concerned about *C. difficile*. Noncompliance with cleaning protocols will usually be detected by ongoing transmission of the organism.

Environmental service workers are rarely assigned the responsibility of cleaning ventilators, IV pumps, and other critical patient care equipment. These types of patient care equipment are typically cleaned by nurses or by special equipment technicians. However, to ensure that these high touch/high risk devices are cleaned, a listing of who is responsible for what surface or device, as well as what disinfectant should be used to clean a device, should be developed with agreement by each group involved so there is no confusion.

Cleaning and disinfection of the environment is crucial in the limitation and elimination of CDI. One way to lessen the bio load is containment of the patient's diarrhea. Simple diapering can help but quite often in the case of severe CDI this approach is inadequate. The use of a bedside commode may help. However, the commode still provides a potential reservoir for contaminating the environment and the HCP. HCP should research newer products that are being met with positive reviews, especially in the long-term care environment, where private rooms may not be available. There are several new devices, such as disposable commode liners and bowel catheters, that are designed to contain fecal incontinence

Figure 7.4. Sample patient room identifying high touch surfaces.

and may contribute an overall effort to minimize spore contamination in the environment.

Other patient care areas and strategies to prevent spread of *C. difficile*

Preventing the spread of *C. difficile* in the patient care unit has been the primary focus of many institutions' control efforts. Because of extensive procedural areas for inpatient and outpatient care, both areas need to be included. Staff need to be included in developing strategies to manage the patient with CDI while providing the diagnostic and treatment services the patient needs.

Procedure area containment strategies

1. Communicate with the area supervisor (or other designated healthcare worker) when scheduling and prior to sending patient to the procedure suite. The area should plan for continuation of Contact Precautions and have supplies available, such as disinfectants that contain bleach or high concentrations of hydrogen peroxide.
2. The receiving unit should ensure that appropriate PPE is available when receiving the patient. The transporter will need to be provided with PPE if assisting with the transfer of the patient. It will be important to provide training if the area has not provided care to a CDI patient recently.
3. Schedule time for preparing the room and for cleaning and disinfection after the patient has left. After exposure to a patient with *C. difficile*, the cleaning and disinfecting process is critical and cannot be cut short without negative consequences.
4. The procedure room should be prepared prior to receiving the patient.

a. Consider having the patient circumvent the preprocedural area and have the patient taken directly to the procedure room. Consider having the patient recovered in the procedure room as well.
b. Cover or remove unnecessary supplies and equipment from the procedural room. Disposable drapes or plastic sheeting as used in the operating room or endoscopy suites may be used. These covers can be discarded when the room is cleaned. Preplanning and action can help decrease the cleanup time post procedure.
c. Plan for management of stool while the patient is in the area. Is there a bathroom attached to the procedure room? Is the patient capable of using it? Does the patient need a bedpan or a bedside commode? Having the right equipment on hand may prevent unnecessary cleanup and disinfection. Disposal of excreta and cleaning of the bedpan or commode should be preplanned.
d. When covering or removing equipment, the computer on wheels (COW) or workstations on wheels (WOW) should not be overlooked. These units can become heavily contaminated especially when they are located close to the patient and the procedural field. It is prudent to cover with plastic if possible and to know how the monitor can be cleaned without impacting the screen. See upcoming section that addresses WOWs.

5. Clean and thoroughly disinfect patient care area. Be sure to discard covers and other items that may be contaminated.

Prevention strategies in the operating room

1. Communication is crucial when planning to take a patient to the operating room. When the patient is scheduled, the need for Contact Precautions related to *C. difficile* should be clearly explained. Due to the preparation time and post procedure cleanup, the patient may be scheduled later in the day, or as the last case, so the overall schedule and efficiency is not impacted as greatly.
2. Consider transporting the patient directly to the operating room and bypass the preoperative holding area.
3. Removing unnecessary equipment and devices will help prevent contamination requiring additional cleanup. If a machine or piece of equipment may be needed, it should be covered until used, to limit exposure if not used.
4. A refresher on Contact Precautions and *C. difficile* will assist the staff in compliance and ensure appropriate precautions are used. Everyone in the room needs to be gowned (no need for sterile gowns if not at the sterile field) and gloved to limit their exposure. When preparing the room, surgical technicians should include nonsterile gowns and gloves for anesthesiology personnel and the circulating nurse.
5. Routine hand hygiene is challenging in this setting. The use of gloves followed by hand hygiene is important, as with all patients. It is important for everyone to remember that the need for hand hygiene when moving from a contaminated area to a clean area requires hand hygiene and changing of gloves.
6. Consider having the patient recover in the operating room and then taken back to their inpatient room as appropriate. This strategy may help to limit exposure and cleanup of multiple areas. This should be coordinated with the operating room staff in advance.
7. Finally, the operating room should be thoroughly cleaned and drapes and other protective covers discarded. Depending

on the institution's risk assessment and policies, the operating room may not require a bleach-based disinfectant, if in nonoutbreak settings. If prevention strategies have been escalated, obtaining a *C. difficile* disinfectant may be critical to ensure standardization of practice.

Prevention strategies for workstations on wheels

Cleaning and disinfection of computers, including keyboards, should be a normal part of the daily routine. Healthcare providers should not touch the computer keyboard with contaminated hands. Remove gloves and clean hands prior to using the keyboard or touch screen. When investing in WOWs, cleanable keyboards or keyboard protection should be evaluated. Mobil computers used by patients during their stay should be disinfected between patients. If a patient is on isolation, the computer should be left in the room, if possible, and then disinfected before assigning to another patient. Routine disinfection can be performed safely using a quaternary ammonium compound or hydrogen peroxide wipes. Check the computer manufacturer's recommendations for acceptable products. Exposure to an environment or patient with CDI can create a challenge especially when there is a highly virulent strain. The use of some of the bleach-containing disinfectants may not be possible due to potential damage. Protecting the unit from contamination by using disposable covers can help limit contamination to the electronics.

HCP should use alcohol hand gel or wash hands prior to computer use and prior to touching the patient. No gloves should be worn when using the computer unless in an isolation room that requires gloves. Clean gloves should be donned before using the computer. Hands must be cleaned after accessing the computer and before touching patients in multibed rooms. Roving computers must be cleaned before moving from one patient's room or bed space to the next patient or area. Touch screen computer monitors should be cleaned and disinfected the same as other horizontal surfaces and equipment in patient's room—at least daily and when soiled. Nontouch screen monitors should be cleaned per manufacturer's instructions and/or when visibly soiled. Inclusion of these steps in policy format may be useful in training staff and monitoring adherence.

Preventing contamination of the WOW or even a stationary computer is recommended. The following recommendations should be part of the basic infection prevention program to prevent waterborne contamination. Whenever possible install or place computer at least 3 feet away from sink. If space is limited and that spatial separation is not possible, then a splash guard can be used between computer and sink. Splash guards should be made of clear plastic and a material that is compatible with the hospital approved disinfectants that will be used on the guard. Splash guards should be cleaned with the same frequency and process as other horizontal surfaces in the patient care environment.

Privacy curtains

Privacy curtains have received little scientific attention. The few studies available indicate that privacy curtains are frequently and rapidly contaminated with pathogenic organisms.[24–26] Spraying with 3% hydrogen peroxide has been effective against Gram-positive organisms in the laboratory,[27] as has the use of antimicrobial complex element compounds incorporated into the material.[24] Privacy curtains should be changed during terminal cleaning at a minimum, and shorter intervals should be considered with longer term patients. Written policies and procedures should reflect the decisions made by the stakeholders with regard to changing privacy curtains. IPs should be aware of the recommendations made by the Association for the Healthcare Environment (AHE), the professional association for environmental services personnel, in their practice guidance documents.

Toilets

There is currently no research that indicates that common tools for cleaning toilets in rooms

occupied by patients with CDI contribute to the spread or transmission of CDI. However, some facilities have decided to maintain dedicated toilet cleaning tools and materials in rooms where these patients reside. The tools and materials are then disposed of when the patient is discharged.

Laundry

According to the CDC, the risk of disease transmission from soiled linen is negligible, and common sense hygienic practices for processing and storage of linen are recommended.[28]

Policies and procedures should be in place to ensure that soiled linen is handled as little as possible to prevent microbial contamination of the air and of persons handling the linen. Soiled linen should be bagged or placed in containers at the location where it was used and should not be sorted or rinsed at that location. Heavily soiled or contaminated linen should be placed into containers that will prevent leakage. Soiled linen is usually sorted in the laundry before washing. Policies and procedures for appropriate protective apparel to be worn by laundry personnel should be in place and enforced at the laundering facility.[28] The soiled textiles area must be functionally separated from the clean textiles processing area. Functional separation may be obtained by any one or more of the following methods: a physical barrier, negative air pressure in the soiled textiles area, and/or positive air flow from the clean textiles area through the soiled textiles area with venting directly to the outside.[29]

To remove significant quantities of microorganisms from grossly contaminated linen commercial laundry facilities, use water temperatures of at least 160°F, and may use 50 to 150 ppm of chlorine bleach as well. Satisfactory reduction of microbial contamination can be achieved at water temperatures lower than 160°F if chemicals suitable for low temperature washing are used. In the home, normal washing and drying cycles including "hot" or "cold" cycles are adequate to ensure patient safety. Commercial dry cleaning of fabrics soiled with blood provides safety from the risk of pathogen transmission.[28]

Clean linen should be handled, transported, and stored properly to ensure its cleanliness is maintained. If storage of clean, unwrapped textiles is indicated, these items must be stored in clean areas, free of vermin, devoid of lint, temperatures ranging from 68° to 78°F, properly ventilated (i.e., positive air exchange rate of 6–10 per hour), positive air pressure relative to adjacent spaces, and no drains or hot water pipes placed in this area. Shelves for storing clean textiles shall be placed as per the ANSI/AAMI standards. Shelves will be approximately 1 to 2 inches from the wall for accessible cleaning. The bottom shelf shall be 6 to 8 inches from the floor; and the top shelf shall be 12 to 18 inches below the ceiling. Routine microbiologic testing of reusable textiles is not recommended.[30,31]

Administrative issues

Administrative leadership is critical in managing outbreak situations. The administrator must act as a leader to delineate responsibilities. Having a clear understanding of who is responsible to clean, disinfect, stock supplies, and communicate information during a time of increased interventions is critical to promote teamwork and ensure all responsibilities are carried out.

One role of the administrator is to ensure that staff have sufficient time to provide a thorough and complete cleaning and apply disinfectant with sufficient contact time. Appropriate removal and dilution of spores and other pathogens by vigorous cleaning and disinfection with the appropriate disinfecting agent is the basic foundation for prevention. All administrators and managers should acknowledge that effective cleaning and disinfection are crucial to the limitation and reduction of CDI and that cleaning and disinfection take time.

Often environmental service staff are evaluated on room turnaround time, but when dealing with *C. difficile* thoroughly wiping all surfaces with a disinfectant requires time. Environmental services leaders and IPs must be aligned with respect to the importance of effective cleaning and disinfection

practices. The increased workload for environmental services must not compromise infection prevention activities.

It is critical, especially in the midst of an outbreak or cluster, that cleaning and disinfection practices be validated. A monitoring method must be developed to provide desired information and timely feedback. Administration, environmental services, and infection prevention must collaborate in the development of a monitoring program that provides the necessary information and is acceptable to all involved. In addition to routine monitoring, enhanced monitoring, either on a random basis or during special circumstances (e.g., a CDI outbreak), can be used to ensure the important task of environmental services is being performed. Monitoring should not be presented as punitive or as an issue of trust, but as an opportunity for education.

Assessing the cleaning process is important. If the prevention strategies are not working it is important to know whether the continued incidence of infection is a result of poor implementation.

Newer methods of decontamination

Other than in outbreak situations, solutions used for routine cleaning are sufficient to provide disinfection. When outbreaks occur, sodium hypochlorite has been the mainstay of environmental disinfection.[19–21] Newer products and technologies are also improving the ability to adequately address the environment. Formulating a plan and a process that maximizes the benefits, considering costs and minimizes risks, is a critical part of CDI prevention.

If surveillance data indicates an increase in cross contamination or untoward outcomes in a specific population, such as bone marrow transplant patients, administration and infection prevention teams should evaluate the potential benefit of using one of the newer technologies that provides so-called "no touch" decontamination. These new technologies are effective at killing organisms within their range without having to touch the surfaces. However, to work efficiently, surfaces need to be thoroughly cleaned before these "no-touch" methods can be used. Two of these technologies are ultraviolet light disinfection and vaporized hydrogen peroxide decontamination. Both technologies are successful in reducing the bio burden of a room and have been shown to stop outbreaks associated with environmental contamination. Although there are some general characteristics for all ultraviolet light units or vaporized hydrogen peroxide systems, each brand and system must be evaluated for its own effectiveness and ability to meet the facility's requirements.[32,33]

Mobile, fully automated room decontamination technology using ultraviolet–C radiation to kill pathogens is also available. After 45 minutes of use, *C. difficile* spores were reduced by up to 99 percent. Ultraviolet radiation cannot be used when the room is occupied, and precautions must be taken to prevent anyone from entering the room while the device is operating. Effective killing of the organism requires cleaning of surfaces prior to the use of the ultraviolet radiation.[33]

Hydrogen peroxide vapor, or airborne hydrogen peroxide, has also been studied as a method of disinfecting patient rooms. CDC and HICPAC made recommendations in both the *2003 Guidelines for Environmental Infection Control in Health-Care Facilities* and the *2008 Guideline for Disinfection and Sterilization in Healthcare Facilities* that the CDC does not support disinfectant fogging. These recommendations refer to the spraying or fogging of chemicals (e.g., formaldehyde, phenol-based agents, or quaternary ammonium compounds) as a way to decontaminate environmental surfaces or disinfect the air in patient rooms. These recommendations do not apply to technologies, such as hydrogen peroxide vapor, that became available since the 2003 and 2008 recommendations. Newer technologies use ozone mists or vaporized hydrogen peroxide (fogging) for room decontamination, and the CDC/HICPAC recommendations do not preclude their use.[34]

Use of these newer fogging systems reduced the risk of infection to the occupant of a room previously occupied by a patient with an MDRO[19] and was associated with a significant reduction in the incidence of CDI in one hospital.[35–37] Airborne hydrogen peroxide, whether in the form of vapor or dry mist, can be an effective method of disinfection of the hospital environment. As with ultraviolet radiation, the room cannot be occupied during treatment. Effective killing of the organism requires cleaning of surfaces prior to the use of this method.[37] In addition, stabilized hydrogen peroxide cleaner (0.05%) and accelerated hydrogen peroxide cleaner (0.5%) have been shown to be effective in reducing *C. difficile* spores when used for toilet cleaning during nonoutbreak situations.[38]

Other newer commercial methods of disinfection include portable saturated steam,[39] ozone, chlorine dioxide,[35] and sodium dichloroisocyanurate (NaDCC), with or without added detergent.[40] Chlorine releasing agents have been found to be superior in reducing *C. difficile* spore counts, although products with the same active ingredients performed at different levels of effectiveness, and proper dilution was critical to performance.[41,42] It is important for the facility IP to be involved in the selection of products to be sure that the disinfectant chosen is effective when used.

Microfiber cloths have been used to remove surface microorganisms, including *C. difficile*. Laboratory research conducted using 10 commercial cloths showed that performance varies greatly between cloths and with the organism tested.[43] According to one study, disposable cloths demonstrated a smaller reduction in microorganisms than the reusable cloths (1.41 log reduction compared to 2.75 for one of the reusable cloths). Reusable cloths showed improved performance after approximately 75 washings; however, performance started to decrease after approximately 150 washings.[43]

Although ultraviolet irradiation and vaporized hydrogen peroxide have been shown to perform well, some of the newer products and technologies require further evaluation under clinical conditions. When a facility is evaluating the best technology for their situation, a team including administration, engineering, medical staff, nursing, and infection prevention should work together to evaluate what they expect to achieve from the device. Questions to be answered will include which device best meets their specific situation, whether they want to purchase or lease, where the device will be used, how the device will improve infection rates, and the anticipated cost. Figure 7.5 lists some of the basic questions for evaluating new technologies and how they will meet the facility's needs.

Self-disinfecting surfaces

The idea of a self-disinfecting surface has great appeal. The use of such surfaces would mean that incomplete cleaning of surfaces by HCP would not result in disease transmission to others. However, any potentially bioactive-coated surface needs to be durable enough to withstand regular healthcare cleaning without a reduction in activity. In addition, any such surface needs to be economically reasonable for mass production and use.

Copper has been shown to reduce surface microorganisms when used in alloys with 58 percent or more copper. But, although using copper on door push plates, pull handles, levers, and other high-touch areas may decrease VRE, methicillin-sensitive *S. aureus* (MSSA), MRSA, and coliforms on surfaces, similar decreases have not been seen with *C. difficile*, especially spores.[44–46]

Silver is another metal that is toxic to microorganisms at low levels. It can be applied to surfaces as a water-soluble silver iodide coating. Although silver has been successful in the laboratory against organisms such as *S. aureus* and *Pseudomonas aeruginosa*, studies on its effectiveness on *C. difficile* have not been published. In addition, the effectiveness of silver nanoparticles incorporated into environmental surfaces has not been studied in actual hospital environments under working conditions, and the durability of the coating has yet to be determined under those conditions. Finally, even if shown to be effective, and used only where

Figure 7.5.

Questions to Ask about The "No Touch" New Disinfecting Technologies

- What is the cost to purchase? Can it be leased?
- What is the cost for a single disinfecting cycle?
- What replacement equipment or supplies are needed, how often will that replacement need to occur and what is the cost?
- Is it sporicidal; bactericidal?
- Is there residual toxic chemical left after the process?
- How long does a cycle take? Is there aeration time required? Does the cycle vary depending on the organism?
- Who can run the machine?
- Does it require extensive training and expertise?
- Does the company provide onsite training?
- What is the active ingredient? Or how does it decontaminate an area?
- Does it penetrate or fill an entire space with the active ingredient?
- Does it need to have direct contact with areas in order for it to function?
- What is the log reduction after a cycle? Is a biological monitor used to verify kill?
- Is it fully automated and how is it calibrated?
- Can it be run with the patient in the room?
- Does room ventilation need to be shut down in order for the system to work?
- What is the expected life of the equipment?
- Can your biomedical engineers provide support and preventive maintenance for the unit or must it be sent to the manufacturer?
- How many machines will be needed to address the intervention plan outlined by infection prevention?
- How long is the warranty and what is included/excluded?
- Are there peer-reviewed articles demonstrating the effectiveness of the machine?
- Will the manufacturer provide a list of current customers who would be willing to discuss their experience with the machine?
- What is the expected delivery time after order is placed?

necessary, the cost involved with using silver in this way may be prohibitive.[46,47]

Triclosan is a nonionic, colorless material that has antimicrobial activity at concentrations of 0.2% to 2%. It has a broad range of activity, but is frequently bacteriostatic rather than bactericidal. Triclosan has been effective at reducing bacteria such as *S. aureus, Salmonella, Escherichia coli,* and *Serratia* species when incorporated into home and personal care items; however, laboratory studies have shown that bacteria with reduced susceptibility can develop relatively quickly.[47]

Quaternary ammonium salts used in a carrier test demonstrated bactericidal effects against *P.*

aeruginosa and *E. coli* on some surfaces, but after 4 days, a rechallenge did not produce inactivation on these treated surfaces. Engineered microtopology has shown limited inhibition of urogenic *E. coli* in the laboratory, but no studies have been found studying this on hospital environmental surfaces.

Finally, light-activated antimicrobial coatings have been studied. Pure colonies of *S. aureus* were reduced by up to 99 percent, but when the bacteria were suspended in saliva or serum, activity was greatly decreased. Under clinical conditions, a 63 percent reduction of aerobes and an 81 percent reduction in anaerobes have been reported.[46]

The development of self-disinfecting surfaces holds tantalizing promise. However, most of these surfaces have limited or no effectiveness against all microorganisms, especially *C. difficile* spores. Before any of these surfaces are produced and used commercially, questions regarding durability, effectiveness, cost, and development of resistance will need to be answered. Development of new technologies and refinement of existing technologies continue to bring new products and methods to the market continually. IPs should investigate and evaluate these new technologies to determine whether any provide significant improvement over those currently used. At this time, research has shown that traditional methods, using chlorine-releasing agents, have proven as effective and more cost-effective as the newer technologies.[48]

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Additional resources

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Section 8: Special Considerations in Skilled Nursing Facilities

Risk factors for developing CDI are often present in residents of skilled nursing facilities.[1] The typical skilled nursing facility provides healthcare to short-term residents who have been recently discharged from the hospital for rehabilitation following surgery, a stroke, or other acute medical condition or to long-term residents with chronic medical needs that cannot be provided at home, but do not require admission to an acute care hospital.[2] The term "resident" is used in skilled nursing to create the perception that the resident's room and the facility are the resident's space and serve as a "home away from home." This concept is important to keep in mind when implementing infection prevention measures. The length of stay for about 75 percent of residents in a skilled nursing facility is less than 3 months.[3] Only about 10.5 percent of residents will stay in the facility for 1 year or longer.[3]

Transmission-based precautions

Use Contact Precautions for residents with suspect or confirmed CDI. The 2009 CMS F441 interpretive guidelines states, *"Transmission-based precautions are maintained for as long as necessary to prevent the transmission of infection. It is appropriate to use the least restrictive approach possible that adequately protects the resident and others. Maintaining isolation longer than necessary may adversely affect psychosocial well-being. The facility should document in the medical record the rationale for the selected transmission-based precautions."*[4] Two common therapeutic objectives in skilled nursing are to promote independence and to preserve dignity[3]; therefore, a balance between infection prevention safety and maximizing the resident's rehabilitation goals must be addressed in the nursing care plan.

Ambulation and socialization while in Contact Precautions

Assess the resident's ability to contain body fluids and the resident's personal hygiene.[5] Allow the resident to participate in group activities when possible.[5] Assess bowel control before ambulating the resident outside of the room. Have the resident perform hand hygiene, place a clean gown over the resident's clothing, and disinfect assistive devices (walkers, canes, wheelchairs) before leaving the room. Consider using a gait belt that can be disinfected after each use or dedicate the gait belt to a single resident.

The healthcare worker who assists with ambulation may need to wear gloves while walking with the resident. If gloves are worn, the healthcare worker should not touch items outside the room without first removing the gloves and performing hand hygiene. The healthcare worker should review the facility's policies and procedures to determine whether donning a gown is necessary for walking with the resident or transporting the resident outside of the resident's room. This may depend on the severity of the disease and whether contamination may be expected during ambulation or transport.

In some populations it may be difficult to monitor and control behavior. Residents with chronic

mental illness or dementia may not be able to comply with good personal hygiene. Under these conditions, it may be decided to staff these residents with a 1:1 caregiver.

Living arrangements

Although a private room with attached bathroom is ideal, this arrangement is not common in most skilled nursing facilities. When considering potential roommates, select someone who is not taking antibiotics and is not compromised to the point of being susceptible to infections in general. In addition, some facilities may be challenged by having multiple-bed rooms with a shared bathroom. Managing the resident's diarrhea can be difficult in a semi-private room with a shared bathroom. Alternatives include cohorting residents with CDI in the same room; assigning the CDI resident with a roommate that does not use the bathroom; assigning the CDI resident in a room closest to the bathroom; and having the non-CDI resident roommate use a bedside commode. If the CDI resident must use a bedside commode, line the commode with a plastic bag and absorbent material to reduce healthcare worker exposure to fecal material. An adult brief, sanitary pad, or other absorbent material can be used. The plastic bag can be discarded as regular trash. If a bedpan is needed, provide a one-time use, disposable bedpan if possible. An alternate is to use a single patient–use bedpan that can be cleaned with a bleach-based disinfectant after each use; however, logistics of disinfection and storage makes this option difficult to accomplish.

Equipment, supplies, and the environment

Discontinue use of rectal thermometers. Medical devices and equipment should be dedicated to single resident use or be disinfected between uses. Personal clothing, linens, and towels can be washed in the usual manner and do not require special handling.[5] Used dishware, cups, and utensils can be handled and sanitized in the usual manner.[5]

Surveillance

The CDC offers skilled nursing and assisted living facilities the opportunity to enter data and compare infection rates through a free, voluntary, Internet-based surveillance system called the NHSN. Laboratory based reporting for *Clostridium difficile* began in September 2012 and is available at http://www.cdc.gov/nhsn/LTC/index.html. NHSN offers standardized definitions and case finding methods for CDI.

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Section 9: CDI in Special Populations

Clostridium difficile and pregnancy

CDI during pregnancy and the peripartum period is similar to CDI in other groups, except for age.[1] Prior antibiotic use is associated with most cases (92 percent), as is healthcare facility admission (67 percent), although infection with hypervirulent *C. difficile* without further risk factors was noted in two (2/14) cases.[1] CDI following cesarian delivery (2.2/1,000 live births) was more common than following vaginal delivery (0.2/1,000 live births).[2]

Treatment for CDI during pregnancy generally parallels treatment in other populations and should be guided by the clinician treating the patient. Clinicians should entertain the diagnosis of CDI in these patients with severe diarrhea, even in the absence of traditional risk factors such as antibiotic use or concurrent hospitalizations.[2] Cesarian section may increase the risk of CDI.[1]

Infection prevention measures especially during outbreaks may include education and training of staff, Contact Precautions for all suspected and documented cases of CDI, thorough hand hygiene, gowns and gloves for contact with any suspected or documented cases of CDI, extensive environmental cleaning and disinfecting of the unit, replacement of carpets with more easily cleaned flooring, and antimicrobial stewardship.[3]

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CDI in the pediatric population

Although CDIs have historically been less common and less severe in children than adults, recent studies suggest that pediatric rates of CDI have increased in both hospitals[1–3] and the community[4] over the last decade. Risk factors for CDI in children are similar to those in adults and include antibiotic use, cancer and other conditions associated with immune suppression, and inflammatory bowel disease.[5] CDI has also been reported in children previously thought to be at low risk for the disease, including those without prior antibiotic or hospital exposure.[6]

In a study conducted between 2001 and 2006 at 21 free-standing children's hospitals, CDI increased 53 percent in hospitalized children, from 2.6 cases to 4.0 per 1,000 admissions.[1] A separate study that analyzed two large administrative databases demonstrated a nearly twofold increase in CDI-associated hospitalization between 1997 and 2006.[3] Both of these studies included cases

in children younger than 1 year of age, a group in whom asymptomatic *C. difficile* colonization is well-recognized. Nevertheless, significant increases in CDI in hospitalized children have been documented, even when children younger than 1 year of age are excluded.[2]

Although severe CDI has occasionally been reported in young infants, especially those with underlying gastrointestinal disease such as Hirschsprung disease, true CDI in this population is still believed to be rare.[7] Conversely, asymptomatic colonization is common. Forty to 70 percent of asymptomatic, healthy newborns may be colonized with *C. difficile* in the first 10 to 28 days of life; colonization rates decrease to 3 to 10 percent by the second year of life.[8] Rates of *C. difficile* colonization in children older than 2 years of age approximate those in healthy adults and may be as low as 2 to 3 percent.[9–11]

Infants may be colonized with both toxin-producing and nontoxigenic strains.[12] A long duration of hospitalization, hospitalization in an intensive care setting, low birth weight, and formula feeding have all been associated with increased rates of *C. difficile* colonization.[8] However, when large numbers of toxigenic *C. difficile* bacteria and high levels of toxin A and B are present, young children usually remain asymptomatic,[13] and most studies have failed to show an epidemiologic association between colonization and disease in infants younger than 1 year of age. For example, in one Swedish study, *C. difficile* was isolated with equal frequency in healthy children 1 week to 1 year of age (17 percent) and children younger than 6 years with diarrhea (18 percent).[14] In a study of outpatient children, *C. difficile* was isolated from 7 percent of patients with diarrhea and 14.8 percent of healthy controls. Children with *C. difficile* were younger than children without the organism; prior antibiotic exposure was noted in only 22 percent.[15] In a recent study of children presenting to an emergency department, *C. difficile* cytotoxin positivity was similar in children younger than 36 months of age with diarrhea and healthy, age-matched controls (5.2 percent versus 8.8 percent).[16] Similar findings have been noted in most controlled studies of neonatal intensive care unit (NICU) patients. *C. difficile* toxin was recovered from the stools of 55 percent 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.[17]

Why young infants are frequently colonized with toxin-producing *C. difficile* strains yet rarely have symptoms is poorly understood. Interestingly, asymptomatic infants may have *C. difficile* colony counts similar to those observed adults with pseudomembranous colitis (as high as $10^{8.1}$ bacteria per gram of feces), suggesting that reduced bacterial density is not the mitigating factor.[8] Experiments in newborn rabbits suggested that protection against disease may result from lack of receptors for toxin A.[18] However, more recent data suggest the numbers of toxin A receptors present on the enterocytes of neonatal pigs are adequate to cause disease, suggesting that differences in the appearance of receptors with age may be a species-specific phenomenon.[19] It has also been proposed that immaturity of the toxin receptor sites may play a role in the absence of disease in neonates.[20]

Although *C. difficile* rarely causes disease in young children, those 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 postpartum 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.[21]

Although the epidemic North American pulsed-field type 1 (NAP 1) strain of *C. difficile* has been isolated in children with diarrhea, it is not clear whether it is associated with more severe disease

in children, as it is in adults.[22–24] In a report that included hospitalized children with CDI identified through the Canadian Nosocomial Infections Surveillance Program, children with NAP1 were more likely to suffer complications from CDI than were children with other strains (29 percent versus 6 percent; relative risk [RR], 4.6; 95 percent confidence interval [CI], 1.1–17.2; $P = 0.04$).[23] However, in a prospective study of children with CDI at U.S. hospitals, infection with NAP1 was not associated with increased disease severity.[22]

The diagnosis of CDI in young children remains challenging. According to the American Academy of Pediatrics, the positive predictive value of a positive *C. difficile* test in children younger than 5 years is unknown because of the high rates of asymptomatic carriage in this population.[25,26] Some positive tests are likely to simply reflect colonization. Enzyme immunoassays (EIA) tests commonly used to diagnose CDI in adults may lack both sensitivity and specificity in children.[27,28] In one study of hospitalized children, one third of all EIA tests performed to identify CDI were ultimately found to be falsely positive.[28] Additionally, most *C. difficile* diagnostic assays have not been validated for use in young children.

Pending additional information, it seems prudent to restrict routine testing for *C. difficile* in children younger than 1 year of age. Other causes of diarrhea should always be sought in young children.[26] When true CDI is suspected in this population, 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.

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Section 10: Antimicrobial Stewardship and *Clostridium difficile* Infection: A Primer for the Infection Preventionist

Antimicrobial stewardship may be a relatively new addition to the job responsibilities of the IP. The discussion of antimicrobial use and its impact on patients in all healthcare settings in this section is focused solely within the context of *C. difficile*. The broad term "antimicrobial stewardship" is used in place of "antibiotic stewardship," as development of a stewardship program ideally includes all antiviral and antifungal agents as well as antibiotics. As antibiotics are the antimicrobial agents effective against bacteria, the term antibiotic is used most often in the discussion of *C. difficile* infection.

Role of antibiotic use in the occurrence of CDI

Because CDI is nearly always a complication of antibiotic use, the development of a healthcare facility program to ensure appropriate antibiotic use is considered an important prevention intervention.[1-4] Figure 10.1 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).

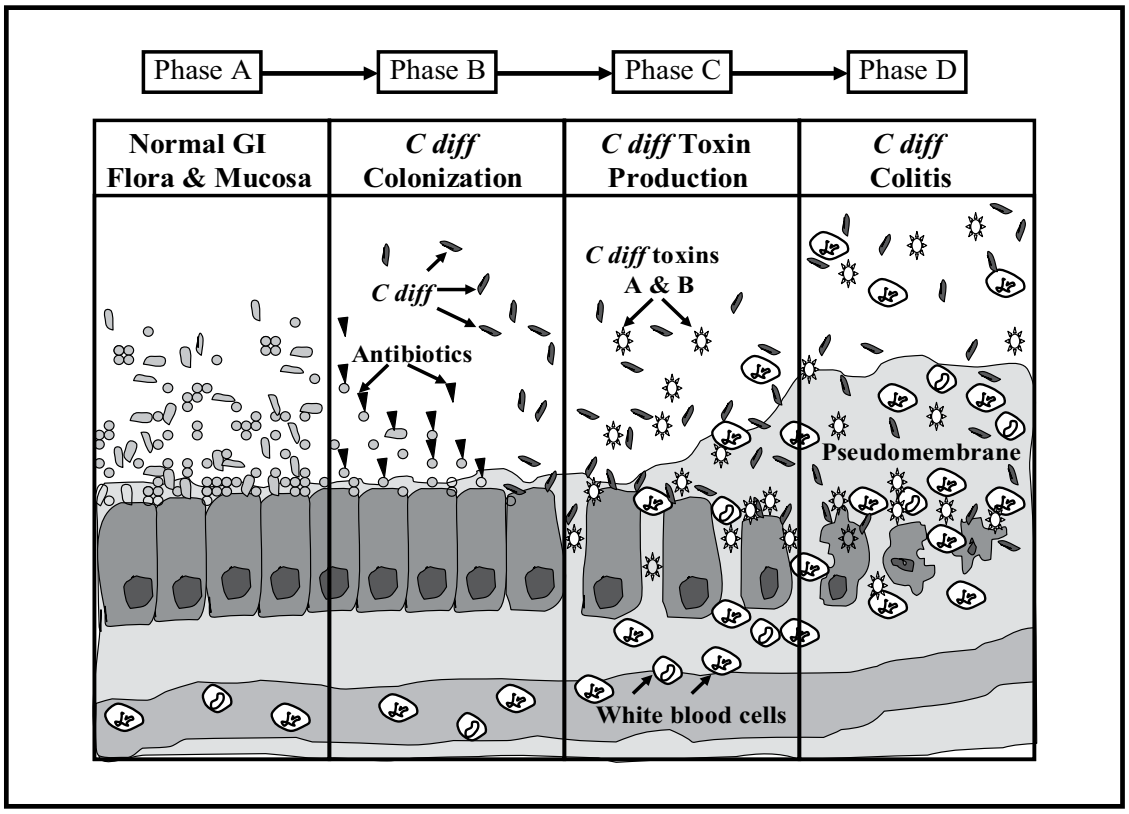
The most important protection mechanism against CDI in humans is the normal gut flora. These bacteria reside in the gastrointestinal tract and prevent pathogens from attaching, multiplying, and producing disease.[5,6]

Normal colonic flora

The hundreds of trillions of bacteria that make up our normal gastrointestinal flora are an important defense mechanism against intestinal pathogens.[5,6] This ecosystem of bacteria is called the human gastrointestinal microbiome. Some of the normal bacterial flora is attached to receptors on the epithelial cells in the colon, whereas other bacteria are present in the lumen of the gastrointestinal tract (Figure 10.1, phase A). In order for *C. difficile* to maintain a presence, the normal flora must be depleted. Due to the diverse bacterial species in the human colon, it has been difficult to identify which particular organisms are responsible for the protective effect against *C. difficile*. The exact mechanism by which an intact gastrointestinal flora protects against *C. difficile* colonization is not completely understood, but several mechanisms have been proposed. To cause colonization or an infection, *C. difficile* needs to attach to receptors in the human gastrointestinal cells. If these receptors are occupied by organisms of the normal gastrointestinal flora, *C. difficile* strains reaching the gut mucosa will have no place for attachment and will not be able to survive.

In addition to preventing colonization by competing for attachment sites, the normal flora may prevent colonization by depriving *C. difficile* of essential nutrients. The normal flora may also antagonize *C. difficile* through the production of substances that inhibit or kill *C. difficile*. Antibiotics may also alter the colonic microenvironment by changing the local protein composition or amount of local mucus production, which may aid the survival of *C. difficile*.

Figure 10.1. Phases of pathogenesis of *C. difficile* colitis.



Antibiotic collateral damage

As mentioned previously, the normal gastrointestinal flora are the main protection mechanism of the host to prevent colonization and infection with pathogens such as *C. difficile*. If this microbiome is disrupted (Figure 10.1, phase B), *C. difficile* can attach to the gastrointestinal epithelial cells, produce toxin (Figure 10.1, phase C), and cause disease (Figure 10.1, phase D). Because antibiotics kill bacteria and are not specific to one particular bacterium, they all have the ability to disrupt the balance of bacteria in the microbiome. The propensity of a particular antibiotic to alter the gastrointestinal flora can be defined as antibiotic "collateral damage."[7]

The extent of damage depends upon a number of antibiotic-specific factors such as: 1) the spectrum of activity, 2) duration of therapy, 3) the amount of the antibiotic that reaches the colonic environment, 4) the activity of the antibiotic under the anaerobic conditions of the colon, 5) antibiotic dose, 6) the route of administration, and 7) antibiotic excretion in the bile. Antibiotic collateral damage is largely 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 *C. difficile*. In the next sections, we review the major factors of antibiotics that play a role in the disruption of the normal colonic flora, leading to colonization and/or infection with this pathogen.

Antibiotic spectrum of activity and duration of therapy

All antibiotics produce disruption of the colonic flora, but they are not equal in their capability to cause collateral damage. The first two elements that need to be considered when evaluating the risk for CDI produced by a particular antibiotic

include antibiotic spectrum and duration.[8] The first is the level of risk produced by a particular antibiotic, defined by the antibiotic spectrum of activity. As the titles suggest, broad-spectrum antibiotics kill a variety of different bacteria, whereas narrow-spectrum antibiotics kill a much smaller variety. In this regard some antibiotics will place the patient at low, intermediate, or high risk for development of CDI.

The second factor to be considered is the number of days that the patient will be at risk for development of CDI. Greatest days at risk for colonization occur during the time that the patient is receiving antibiotic therapy and up to 5 to 10 days after discontinuation of antibiotics, although the risk may extend for 3 months or more. The longer a patient is treated with an antibiotic, the more normal flora will be killed.[8]

These two factors combined are critical in the pathogenesis of *C. difficile*. For example, a patient who receives a narrow-spectrum antibiotic for less than 1 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. If the same patient is given surgical prophylaxis with an unnecessarily broad-spectrum antibiotic (e.g., a carbapenem), the level of risk can move from low to high without any additional clinical benefit from that broad-spectrum antibiotic. 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 increasing the number of days that the patient will be at risk. Even though all antibiotic therapy, appropriate or inappropriate, will place the patient at risk for CDI, the prolonged use of broad-spectrum antibiotics is an unnecessary additional risk factor that may be prevented.

The most common inappropriate antibiotic use that places a patient at increased risk is the continuation of broad-spectrum antibiotics after the etiology of infection has been identified, and the pathogen is found to be susceptible to a narrower-spectrum antibiotic. For example, in a patient with a prolonged ICU stay that 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 (e.g., vancomycin plus piperacillin/tazobactam). If respiratory or blood cultures identify an 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. Because 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 (versus infection) or contamination (e.g., blood cultures) as well as the use of antibiotics in patients without documented infections.

Antibiotic uptake in the colon

Different antibiotics have a varied uptake in different areas of the body. For example, oral vancomycin is not absorbed systemically and will therefore only kill bacteria in the gut. Intravenous vancomycin, on the other hand, by definition of the route of administration, is systemically available. However, IV vancomycin does not reach adequate concentrations in the gastrointestinal tract and consequently may not be able to kill a significant amount of the normal gastrointestinal flora. The availability of different antibiotics to

different body sites is an important consideration for antimicrobial stewardship activities, as availability in the colon provides more disruption of the normal flora.

Activity of antibiotics under anaerobic conditions

A very limited amount of oxygen is available to organisms living in the colon. Because of this, organisms living primarily in the colon, such as *C. difficile,* are only capable of surviving in anaerobic conditions. This is a critical factor for the treatment of CDI, as only antibiotics with activity against anaerobic organisms are able to kill *C. difficile*. Additionally, this is an important factor for antimicrobial stewardship programs. Antibiotics that have anaerobic activity will kill more of the normal colonic flora (as most are anaerobic), leaving room for attachment and growth of *C. difficile*. As before, it is important to consider the spectrum of activity and duration of treatment in conjunction with this factor. A narrow-spectrum antibiotic with good anaerobic coverage will be less of an issue than a broad-spectrum antibiotic with limited anaerobic coverage. Although the narrow-spectrum antibiotic will kill anaerobes, it will only kill a limited variety. The broad-spectrum antibiotic will kill the anaerobes as well, but it will kill a wide variety, leaving the colonic environment more hospitable for *C. difficile.*

Antibiotic dose

The dose of antibiotic administered is another important consideration for antimicrobial stewardship programs. Over- or underdosing may be considered inappropriate in many situations. A dose greater than necessary may kill a greater number of normal flora, whereas a lower dose may not appropriately kill the bacteria causing the infection. This cycle may lead to the switching to or addition of a new antibiotic, or the need for a longer duration of therapy. Each of these factors may contribute to CDI.

Antibiotic routes of administration

As mentioned previously, the route (typically intravenous versus oral) of administration of antibiotics may confer a different risk to the normal flora. Oral antibiotics may pose a greater risk to the normal gastrointestinal flora, as incompletely absorbed oral antibiotics may have direct access to these bacteria.[9] Members of antimicrobial stewardship programs should be aware of these risks to ensure the most effective and least detrimental route of antibiotic administration is utilized.

Antibiotic excretion in the bile

Antibiotics excreted in the bile at a high concentration have been shown to deplete more of the normal flora than those that are not. This is due to high intraintestinal concentrations of these drugs. Antibiotic excretion in the bile may be considered a higher priority than oral versus intravenous administration as well. Intravenous antibiotics excreted in the bile at high concentrations may kill more of the normal flora than incompletely absorbed oral antibiotics.[10,11]

Role of antimicrobial stewardship in prevention of colonization and infection

Colonization with *C. difficile* may occur when the normal flora is depleted and the organism is introduced into the gastrointestinal tract. Interventions to improve the practice with regard to the previously mentioned factors will help to reduce the excessive depletion of the normal flora. However, antimicrobial stewardship practices will not prevent introduction of the organism into the gastrointestinal tract. Basic infection prevention practices are necessary for this essential component of *C. difficile* prevention.

Once a patient is colonized with *C. difficile*, the patient may progress to develop *C. difficile* colitis

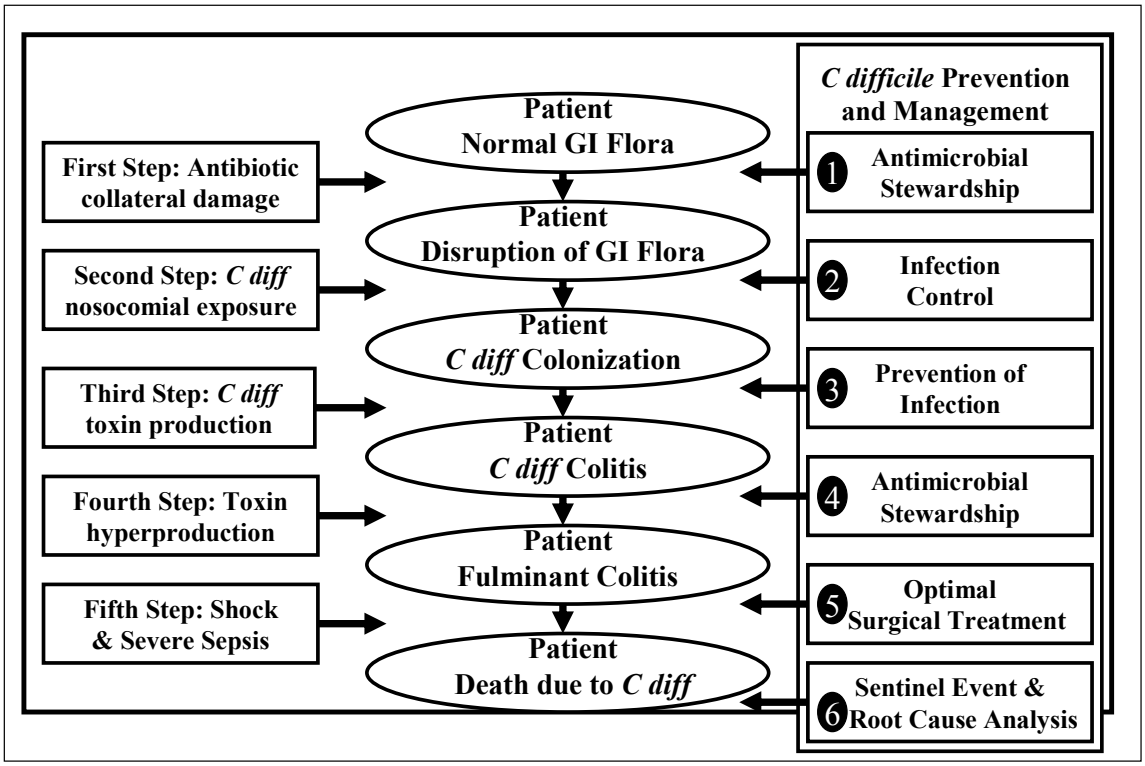
or may remain colonized without developing disease. Lack of disease may be due to colonization with a *C. difficile* strain that does not produce toxins.[12] Once the patient is colonized with a nontoxigenic strain, the patient may be less likely to be colonized with another strain—one that may be toxigenic. It is considered that the initial strain may occupy receptors than become unavailable to a new strain. The use of metronidazole in a patient colonized with a nontoxigenic *C. difficile* strain may favor development of *C. difficile* colitis by killing the nontoxigenic strain and allowing colonization and infection due to a toxigenic strain. This is the reason behind laboratory testing for *C. difficile* toxins as opposed to solely testing for *C. difficile* antigens (e.g., glutamate dehydrogenase). Antigen testing does not differentiate between toxigenic and nontoxigenic strains.[13] Identification of the organism through antigen testing alone will provide clinicians with unnecessary data and may result in unnecessary antimicrobial treatment. However, a positive test for *C. difficile* toxin in the stool is not by itself indication for antibiotic therapy. A patient who is asymptomatic but has a positive *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 or MDROs in a patient who is only a carrier.

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 *C. difficile* prevention activities (Figure 10.1) as the fourth level of intervention. There are three strategies that can be considered for the management of a patient with *C. difficile* colitis: 1) killing of *C. difficile*, 2) blocking toxin, and 3) restoring normal flora.

Killing of *C. difficile* in the colon can be achieved with the use of a number of antibiotics, most

Figure 10.2. Activities to prevent and manage *C. difficile* infection in healthcare settings.



commonly oral metronidazole or oral 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 because 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 *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 percent of the patients. A relatively new agent, fidaxomicin, is also available for the treatment of *C. difficile* infections. This agent has been shown to be as effective as the other available agents, but may improve patient outcomes through decreasing the likelihood of disease relapse.[14]

Blocking *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 because commercially available intravenous formulations contain antibodies to toxin A and B. This approach is sometimes 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 an 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 the 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 to block receptors for *C. difficile* binding, improvement of intestinal barrier function, and favorable modulation of the local immune system. Because 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.[15] 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 largely limited to case series, the fecal transplant has been shown to be more than 90 percent successful at treating relapsing CDI.[16]

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, at the right dose, 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. Thorough discussions of the key elements of an antimicrobial stewardship program can be found in other sources.[17,18] 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.

Infections due to *C. difficile* are increasing in incidence and severity in healthcare settings. These infections are associated with increased patient morbidity and mortality. It is concerning that patients admitted to a healthcare facility for noninfectious diseases 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 all healthcare facilities and practitioners to implement an antimicrobial stewardship program with a focus on CDI prevention, control, and treatment. A combination of optimal infection prevention 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 IP understands the components of an antimicrobial stewardship program and the organizational support necessary for its success.

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Section 11: Fecal Bacteriotherapy

Introduction

Transplantation of enteric bacteria from one host to another was first described in the seventeenth century as a therapy for animals to correct issues with rumination.[1] Since this time, there has been an increasing interest in the potential use of beneficial bacteria to correct human gastrointestinal disease. Probiotics, or medications containing live "beneficial bacteria," have been widely studied for this use but have had varying success to correct various human diseases.[2,3] The issues with probiotics likely lie in the fact that the human microflora is incredibly diverse and it is currently impossible to create a medication containing all of these normal bacteria contained within our bodies. The FDA does not endorse the use of probiotics for CDI prevention because they are considered nutritional supplements and there is a risk of fungemia associated with the use of probiotics, particularly in immunocompromised individuals.[4]

Recently, there has been resurgence in the potential therapeutic use of fecal bacteriotherapy (also known as fecal transplant, stool transplant, fecal microbiota transplantation), which allows the instillation of nearly a complete microflora from one host to another.[5] This therapy includes collection of feces from a healthy donor, which is then transplanted into the gastrointestinal tract of the ill host. Fecal bacteriotherapy is becoming more common with the increase in severe and recurrent CDI. This therapy has been shown to be very successful in eliminating CDI and preventing recurrence.[5] The following section describes the relationship of the human microflora to CDI, fecal bacteriotherapy as a therapeutic remedy for this disease, and provides example protocols for collection, preparation, and transplantation of feces from a healthy host to the ill host.

Definitions

Some terms common to fecal bacteriotherapy are defined here.

- Fecal bacteriotherapy – the transplantation of human feces from a donor to a recipient. Also known as: stool transplant, fecal microbiota transplantation, and fecal transplant
- Microbiome/Microbiota/Microflora – the bacterial communities residing inside or on the human body
- Metagenomics – the study of bacterial genes in the microbiota
- Retention enema – instillation of a product into the colon of a recipient and held in place for a designated period of time

Normal human microflora

Humans are born with a sterile gastrointestinal tract.[6] During the first years of life, we become colonized with various microbes that develop into a stable microbiome. The human microbiome is relatively stable over time, but may change based on our genetic composition, changes in our diet, comorbidities, and medication/antimicrobial use.[7] By the time our microbiome is developed, we are colonized with many more bacteria than there are cells that comprise what we know as our body.[6] These bacteria play critical roles in the support of human health. For example, some of these bacteria help us to degrade and digest starches and other nondigestible carbohydrates, lactose, absorb amino acids and B vitamins, and extract energy from various food sources.[6] The microbiome is also increasingly recognized for its critical role in immune function.[8,9]

Moreover, these bacteria help to prevent colonization and infection with pathogenic microorganisms in the gastrointestinal tract. The trillions of normal bacteria in the gut serve to outcompete pathogens by taking up receptor sites and food sources. Disruption of the microflora can lead to harmful effects on the host through elimination of their supporting roles in human health.

Disruption of the microflora and CDI

Once the microflora is disrupted, pathogens such as *C. difficile* are able to flourish and cause disease. There are many factors that can disrupt the microflora but it is still unclear as to how much flora must be disrupted to be problematic. Three important factors that can disrupt the normal microflora include: 1) advanced age, 2) gastric acid modifying agents, and 3) antimicrobials.

Advanced Age

Although it is not possible to intervene on the aging process, it is important to understand the process of the microflora development and degradation with respect to age. As mentioned previously, humans are born with a sterile gastrointestinal tract. The normal flora is built during the first years of life and becomes stable during adulthood. As humans age, the microflora becomes altered via processes that are not well understood. However, it is critical to understand that advanced age is a clear a risk factor for CDI. The rationale behind advanced age as a risk factor likely involves that natural disruption of the normal microflora as we age.

Gastric Acid Modifying Agents

Recent studies have linked the use of gastric acid modifying agents such as proton pump inhibitors (PPIs) and H_2-blockers to an increased risk of CDI.[10–13] An acidic stomach environment has been shown to kill *C. difficile* and prevent *C. difficile* toxin activity.[14] Utilization of PPIs will increase the gastric acid pH and reduce this beneficial host protective mechanism. The acidity of the stomach also helps to eliminate pathogens that may be ingested.[15] Therefore, the pressure of pathogenic microorganisms in the gastrointestinal tract will be much higher if medications are taken to increase the pH of the stomach. However, the evidence is still inconclusive. If gastric acid modification does increase the risk of CDI, further work is necessary to understand the importance of the duration of therapy, dose, and medication that increase these risks.

Antimicrobial Use

Antimicrobial use is the most studied and conclusive risk factor for CDI. Because antimicrobials are not selective for one particular organism, there are disruptive effects on the gastrointestinal microflora when these agents are administered.[16,17] The more broad spectrum the antimicrobial agent used, the higher the risk of CDI.[18] Fluoroquinolones, cephalosporins, and clindamycin have all been implicated as antimicrobials that increase the risk for *C. difficile* infection.[19–22] Misuse, prolonged use, and the use of multiple antimicrobials at the same time increase the damage to the microflora and provide a higher risk of CDI.[23]

Fecal bacteriotherapy

Once the normal fecal microflora is disrupted, it is critical to restore the balance of these beneficial bacteria. For *C. difficile*, it is important to eliminate the inciting antibiotic or reduce the dose or spectrum of the antibiotic. Some physicians have also used probiotics to attempt to restore the normal flora. However, fecal bacteriotherapy is the only therapy that will restore balance to the normal flora, as it is the only mechanism currently available to harvest most of the entire healthy normal flora and transplant it to a host with a disrupted flora. Fecal bacteriotherapy includes the following steps:

1) Identification of a healthy stool donor
2) Obtaining the healthy stool specimen
3) Screening the healthy stool for infectious diseases
4) Identifying the route of transplantation
5) Preparing the recipient for transplantation
6) Preparing the stool specimen for transplantation
7) Transplanting the specimen
8) Patient education (follows along with each step of the process)
9) Follow-up

Identification of the healthy stool donor

The healthy donor is typically identified as someone without any gastrointestinal symptoms or diseases, is not currently on any medication that is known to disrupt the normal flora, has not been on such medications in the prior 6 months, and is a relative of the recipient but does not necessarily live with them. Gastrointestinal symptoms or diseases include a wide array including diarrhea, Crohn disease, irritable bowel syndrome, and others. Medications that disrupt the normal microflora include antibiotics, gastric acid modifying agents, and chemotherapy. It may be prudent to select donors who do not take any medications, as it is unclear as to how any drugs affect the normal microflora. Selection of a relative of the donor provides a higher likelihood that the normal flora is similar. However, selecting a donor who does not live with the recipient may be judicious because there is less likelihood that the donor is colonized with *C. difficile*. Siblings, children, and close friends who do not live with the recipient may be good considerations for donors.

Obtaining the healthy stool specimen

Stool can be obtained by the donor in the home environment. A 24-hour stool container, a toilet hat, gloves, and tongue depressors should be provided to the donor, and they should be instructed to obtain as much stool as possible to fill the stool container. The stool should be collected directly into the stool hat and transferred to the container, and not collected from the toilet water. If the donor is worried about not being able to pass stool in the night before the transplant, they can be provided laxatives. Stool should be placed in a biohazard bag and placed in the refrigerator after collection. Stool maintained at room temperature may allow for overgrowth of certain bacteria and will decrease the likelihood of treatment success.

Screening the stool for infectious diseases

It is critical to screen the stool for infectious diseases prior to transplantation to ensure that pathogens are not transplanted into the already ill host. Common screening tests for the donor stool include: *C. difficile* culture (or antigen), ova and parasites, RPR (for syphilis), hepatitis A virus, hepatitis B virus surface antigen, hepatitis C virus, and HIV-1/2. Other considerations include stool culture for foodborne pathogens (*Salmonella, Shigella, E. coli, Vibrio,* etc.), *Helicobacter* pylori, and other viruses such as cytomegalovirus and Epstein-Barr virus.[1]

Identifying the route for transplantation

Three major routes of transplantation have been described in the literature. These include 1) retention enema, 2) instillation via colonoscopy, and 3) instillation via nasogastric tube. It is not clear which, if any, of these routes are superior. Many patients may prefer colonoscopy because they will be sedated and will not be conscious during the process. Retention enemas may be able to be performed at home, which is potentially a great benefit to patients.[24] Nasogastric instillation may represent a risk of aspiration either during the procedure or upon removal of the nasogastric tube.

Preparing the recipient for transplantation

The recipient should be discontinued from any agents that modify the gastrointestinal microflora for as long as possible prior to the transplant. However, this may not be possible as many patients are being treated for other diseases that necessitate these agents. A thorough examination should be performed to determine if any medications being administered might be discontinued without harming the patient. If the patient will be transplanted via colonoscopy, traditional preparation for this procedure should be followed.

Preparing the stool specimen for transplantation

The stool specimen must be suspended and filtered prior to transplantation. Many methods are currently used for this process and nothing has been standardized to date. Commonly used processes include adding the stool (5–300 grams) to a 1-liter sterile bottle with 300 to 600 mL of nonbacteriostatic saline.[1] This bottle is closed and agitated to suspend the stool. It has been suggested that an appropriately sterilized blender can be used for this process to better suspend the stool. If this process is utilized, care must be taken to ensure proper sterilization of the blender after use. It may also be considered to dispose of the blender after use and purchase a new blender for each patient. If a retention enema will be used, the stool may be mixed within the enema bag. This suspension must then be filtered to remove large portions of unsuspended stool. This process can be slow and tedious. Suggested mechanisms for filtering include sterile metal coffee filters, paper coffee filters, or sterile washcloths.[1] Stool preparation should be completed 10 minutes to 2 hours prior to transplantation to ensure that overgrowth of certain bacterial species does not occur.[1]

Transplanting the specimen

There is currently no standardization of procedures for fecal transplantation. During a colonoscopic instillation, 50 to 60 mL of the processed stool may be drawn into 5 to 10 syringes and injected into various areas of the colon. For a retention enema, processed stool should be instilled into the colon, the patient instructed to lie on their left side and hold the contents as long as possible.[24] If diarrhea ensues within 1 to 2 hours, another specimen may be transplanted.[24] There is no consensus as to how much stool or supernatant should be used, or how many times per day or on how many consecutive days enemas should be provided. However, a systematic review showed that multiple transplants, larger volumes of processed stool, and a higher number of grams of stool showed more treatment success.[5]

Patient education

Patient education is critical throughout this process so they understand the importance of maintaining the protocol. Some physicians recommend nutritional consultation to ensure an appropriate diet is followed after transplantation. This will help maintain the appropriate food sources for the newly transplanted microflora.

Follow-up

Follow-up is critical in all patients who undergo fecal bacteriotherapy. It is not well understood as to how many times patients may need to undergo therapy or after how many failures it is prudent to consider alternative therapies. However, long-term follow-up of colonoscopic bacteriotherapy has shown excellent results with relatively high patient satisfaction.[25]

Infection prevention issues with fecal bacteriotherapy

There are two major infection prevention issues with respect to fecal bacteriotherapy. These include appropriate screening of donor stool and appropriate disinfection of equipment after stool preparation and transplantation. Many of the currently published studies regarding fecal

bacteriotherapy do not describe the screening of donor stool, which may lead to beliefs that donor screening is not important.[1] Clearly, this is not the case, as therapeutic transplantation of human feces may transmit a variety of viral, fungal, bacterial, or parasitic agents. A clear protocol should be developed to ensure that appropriate testing for pathogens is completed prior to transplantation.

Appropriate disinfection of products used in the preparation and transplant of feces is also a critical aspect of fecal bacteriotherapy. Although instruments such as endoscopes can be processed in the usual manner, other instruments such as metal filters and blenders may or may not have a clear process for sterilization. In fact, many of these products may not be able to be sterilized with other instruments without being degraded or destroyed. This has led many programs to consider these products disposable after one use.

Successes of fecal bacteriotherapy in curing CDI

With traditional antimicrobial therapy, failure rates for the treatment of CDI are around 25 percent.[26,27] Furthermore, one quarter to one third of patients will have a relapse after treatment. Success rates of fecal bacteriotherapy in systematic reviews have been found to be upward of 92 percent, with minimal to no relapse.[5,27] Success is likely based on the route of administration, the donor, the number of transplants, and the amount of stool transplanted.

Fecal bacteriotherapy is becoming a more common therapy for refractory and recurrent CDI. Infection prevention issues with fecal bacteriotherapy include the screening of donor stool for various infectious diseases as well as appropriate disinfection of nontraditional equipment that may be used during transplantation. With the extremely high success rates related to appropriate bacteriotherapy, this mechanism of CDI treatment can be a successful part of any infection prevention program.

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Section 12: Glossary of Terms

Acute Care Transfer-Long-term Care Facility-onset (ACT-LO) – LTCF-onset (LO) LabID Event with date specimen collected ≤ 4 weeks following date of last transfer from an Acute Care Facility (Hospital, Long-term acute care hospital, or acute inpatient rehabilitation facility only). NHSN definition.

BI/NAP1/027 strain – Hypervirulent epidemic strain of *C. difficile* found to be associated with the outbreaks in Quebec, the United States, 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 as of yet unknown factors.

CDAD – *Clostridium difficile*-associated disease - term less commonly used than the term *Clostridium difficile* infection (CDI) as CDI describes presence of the organism with symptoms of infection such as diarrhea.

CDI – *Clostridium difficile* infection – symptomatic disease caused by the toxins produced by the organism *Clostridium difficile*.

Cleaning – Physical removal of organisms on a surface and the step that should precede disinfection.

Clostridium difficile – An anaerobic, Gram-positive spore-forming bacillus.

Colonization – Occurs when a patient carries a microorganism, but has no signs or symptoms of infection. However, it is important to note that a colonized person may have the potential to infect others without clinical signs or symptoms.

Community-onset (CO) – CDI identified as an outpatient or an inpatient ≤3 days after admission to the facility (i.e., before or on days 1, 2, or 3 of admission). NHSN definition.

Community-onset Healthcare Facility–associated (CO-HCFA) – Community-onset CDI identified from a patient who was discharged from the facility ≤4 weeks prior to current date of stool specimen collection. NHSN definition.

Diarrhea – Passage of three or more unformed stools in 24 or fewer consecutive hours.

Disinfection – Process used to kill or render pathogenic organisms inert. The disinfection process does not result in sterilization. An important factor in the efficacy of the disinfection process involves the time the disinfectant spends on the surface being disinfected (contact time).

Exotoxin – Protein produced by a bacterium and released into its environment causing damage to the host by destroying other cells or disrupting cellular metabolism.

Fecal bacteriotherapy – Procedure used to treat patients with *C. difficile* by transplanting fecal material from a healthy donor patient, in order to restore healthy bacterial flora in the ill patient. This procedure is also known as fecal transfusion, fecal transplant, stool transplant, fecal enema, and human probiotic infusion.

Healthcare Facility–onset (HO) – CDI identified >3 days after admission to the facility (i.e., on or after day 4). NHSN definition.

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 – Solution capable of killing the bacterial spores of *C. difficile* in concentrations larger than 4800 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.

Ileus – Partial or complete obstruction of the small or large intestine that occurs when the contractions of the intestine stop. These contractions are necessary to assist with the movement of feces through the bowel.

Incident CDI LabID Event – The first LabID Event ever entered or a subsequent LabID Event entered > 8 weeks after the most recent LabID Event reported for an individual resident. NHSN definition.

Long-term Care Facility Onset (LO) – Date specimen collected > 3 calendar days after current admission to facility (i.e., on or after day 4). LO can be subclassified as ACT-LO (see definition above). NHSN definition.

Metabolomics – Chemical fingerprinting of organisms.

Metagenomics – Whole genomic sequencing of microbiota.

Microbiota – Resident microbial communities. In the case of CDI, these are resident microbial communities living in the intestines.

Microbiome – The collective genome of microbial communities.

Phenolic – EPA-registered disinfectant used in healthcare settings. This disinfectant is used less commonly than quaternary ammoniums.

Prebiotics – Nondigestible food elements that stimulate growth and/or activity of bacteria in the digestive tract that are beneficial to overall health. Although there is not significant evidence to support the benefit of prebiotics in preventing and treating *C. difficile*, the hypothesis is that prebiotics are beneficial because they help stimulate the growth of probiotics and lower pH levels.

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 have been altered by prior antimicrobial exposure and thus protect against colonization or overgrowth with *C. difficile.* To date, there is insufficient evidence-based data to support routine clinical use of probiotics to prevent or treat *C. difficile* disease.

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 CDI.

Quaternary ammonium – A class of disinfectants commonly used to control bacterial growth in clinical settings because of their broad spectrum antimicrobial activity.

Recurrent CDI – Any LabID Event entered > 2 weeks and ≤ 8 weeks after the most recent LabID Event reported for an individual resident. NHSN definition.

Refractory *Clostridium difficile* disease – Situations where patients with CDI fail to respond to traditional therapies.

Retention enema – The process of slowly infusing liquid into the rectum, which then allows the liquid to be absorbed without activating the nerves commonly responsible for elimination of waste.

Spore – The dormant stage some bacteria will enter when environmental conditions cause stress to the organism or no longer support its continued growth. *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.

Systems engineering – The interdisciplinary field of engineering that incorporates design, implementation, and control of interacting components or subsystems, with the goal being to produce a system that meets the needs of users.

Toxic megacolon – A life-threatening complication of intestinal conditions, characterized by a dilated colon with severe colitis and systemic symptoms such as fever, abdominal pain, or shock.

Toxigenic – Producing a toxin or toxic effect.

Universal gloving – The practice of a healthcare worker wearing gloves for all patient care interactions and activities.

Vegetative *C. difficile* – The actively growing and metabolizing state of the bacteria. When *C. difficile* in the vegetative phase is not sufficiently killed by cleaning, the bacterium may form a spore that protects the organism from unfavorable environmental conditions.

Section 13: Frequently Asked Questions

1. Is antibiotic therapy the only risk factor for CDI?
Patients who receive any medical care in any medical setting, patients with nasogastric tubes, prolonged hospital stays, gastric suppression with PPIs and hydrogen pump blockers, steroids, other immunosuppressors, and antibiotic therapies have increased risk of developing CDI. Advanced age is also a risk factor.

2. Which antibiotics are most frequently implicated in causing CDI?
Antibiotic therapy alters the normal gut flora. Although ampicillin, amoxicillin, cephalosporins, clindamycin, and fluoroquinolones are most frequently linked to CDI, most antibiotics predispose patients to CDI.

3. What is the incubation period for CDI?
The incubation period of CDI following medical interventions or organism acquisition has not been clearly defined. Although one study suggested a short incubation period of less than 7 days, others supported a time frame of up to 3 months after completion of antibiotic therapy. Thus, many cases of healthcare-associated CDI may have their onset in the community after hospitalization or medical care.

4. What are hypervirulent strains of *C. difficile*?
Hypervirulent strains of *C. difficile* produce more toxins and cause severe disease or death. The North American pulsed-field type 1, restriction-endonuclease analysis type BI, polymerase chain reaction ribotype 027 (NAP1/BI/027) strain produces binary toxin, and more toxin A and toxin B than other strains.

5. 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* infection. The most effective prevention activity is through antimicrobial stewardship programs that target the antimicrobial to the specific organism(s), quickly de-escalate therapy (narrow the spectrum), and promote the shortest duration of therapy while adequately treating the infection.

6. When should a patient with *C. difficile* be removed from contact isolation?
In normal situations, a patient with CDI can be removed from contact isolation when diarrhea resolves; however, some organizations recommend continuing Contact Precautions for at least 48 hours after diarrhea resolves. If there is an outbreak or evidence of ongoing *C. difficile* transmission, consider extending contact isolation until the patient is discharged, or extending isolation until the patient is without diarrhea for 2 days.

7. 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 protect itself and transform into a spore. This

spore 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 routine activities indicate that any germicide can be used during nonoutbreak 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 which should include changing the germicide to one part EPA-registered hospital disinfectant sodium hypochlorite (5.25–6.15%) to nine parts water until the outbreak or transmission is under control.

8. Can bleach wipes be used to effectively clean frequently touched surfaces in rooms of patients suspected or diagnosed with *C. difficile* infection? If so, what criteria should be used to select the product?

EPA-registered hospital grade disinfectant germicidal wipes providing a 1:10 dilution of EPA registered hospital disinfectant sodium hypochlorite (5.25–6.15%) are good adjuncts to cleaning when it has been determined that the routine EPA-registered hospital disinfectant is no longer adequate for the circumstances. Product labeling, cost, ease of use, contact time, hazards to humans, precautions, and packaging are usually the biggest issues when deciding to use a germicidal wipe. Review product warnings to ensure the safety of your employees and patients. Be sure to include the size of the wipes and surface area contact time in your evaluation, as well as input from your front-line end user.

9. How do we determine if diarrhea is due to *C. difficile* or from some other cause of diarrhea?

The best way to rule out *C. difficile* as a cause for diarrhea is to perform appropriate testing on nonformed stool. Several tests are available to identify *C. difficile*. These include: tissue culture cytotoxicity assay, enzyme-linked immuno-absorbant assay (ELIZA), polymerase chain reaction (PCR), and glutamate dehydrogenase (GDH) testing. Each method varies based on cost, sensitivity, specificity, and technical expertise. It is important to understand the type of test being used and the risk of false-positive and false-negative results as this information may influence a clinician's diagnosis.

10. Can bleach be used in the pediatric setting?

Yes; a 1:10 dilution of EPA-registered hospital disinfectant sodium hypochlorite (5.25–6.15%) can be used in the pediatric setting but, as with all settings, bleach is malodorous and may induce respiratory issues in those using the bleach to clean and the patients in the area during product use. 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, bleach must be stored in a secure manner so children or other unauthorized personnel cannot access the products.

11. Can bleach be used to clean the OR setting?

Yes; a 1:10 dilution of EPA-registered hospital sodium hypochlorite (5.25–6.15%) can be used but care must be taken to avoid contact with items that may be damaged following long-term use. Some commercially available preparations have been formulated to minimize the corrosive effect of bleach. Check with the equipment/instrument manufacturers and product label to identify appropriate use of the product.

12. Is there a benefit to mixing our own bleach solution over purchasing one that is premixed?

Although mixing your own bleach solution sounds like a good and cost-effective idea, there are a number of drawbacks to this pathway. First, not all bleach is the same and not all bleach is EPA approved for eradicating *C. difficile* spores. In addition, bleach does not have a detergent base that promotes the

removal of organic and inorganic matter needed for cleaning the patient environment. Finally, diluted bleach is not stable and must be mixed daily to maintain the appropriate chloride part per million when not in premixed form.

13. We do not restrict use of alcohol-based hand rubs for HCP providing care for patients with CDI. Is this incorrect?

Many recommendations support this strategy unless an outbreak or evidence of ongoing patient-to-patient transmission of *C. difficile* supports a policy of heightened prevention interventions of hand washing with soap and water. Alcohol-based hand rubs (ABHRs) do not kill the *C. difficile* spores. Hand washing provides a theoretical advantage of physical removal of spores with rinsing. There have been no studies that show increased CDI over hand washing when ABHR is used instead of hand washing, and there have been no studies that show a decrease in CDI when hand washing is compared to ABHR use. During normal circumstances, following direct patient care hygiene activities, hand washing makes sense to remove spores and debris but use of ABHRs should also be available for HCP and family members. The few simple rules for this complex situation include:

1) Hand hygiene between all patient contact and immediately after removal of PPE

2) Wash with soap and water as the preferred hand hygiene method if hands are visibly soiled

3) Provide ABHRs as an additional method to perform hand hygiene for HCP

14. 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 for that patient. The most appropriate use for loperamide, opiates, or other therapies that serve to minimize diarrhea is after the cause has been identified and the desire is to minimize dehydration. Although dehydration may certainly occur with CDI, the most important thing for these patients is to start on appropriate treatment and resolve the infection causing the diarrhea.

15. 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 does the use of bedpans that are disinfected between patients or between uses. Contact Precautions supports dedicating equipment for sole use by the patient with CDI. Bedpans or commodes must be dedicated to the patient. After that patient no longer needs the item, it should be disposed of (if disposable) or, if reusable, cleaned/disinfected per CDC guidelines. Handling of contaminated items, including bedpans, presents the likelihood of hand contamination by the HCP and the patient so hand hygiene and environmental cleaning remain critical interventions.

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

During an outbreak or evidence of ongoing patient-to-patient transmission, tracing a patient's movement may be an element used during an epidemiology study. During normal circumstances, your organization should have established policies and protocols for maintaining a clean environment for all patient care areas and throughout your facility. Routine cleaning methods should impact the burden of *C. difficile* and terminal cleaning should move closer toward eradication of the organism in the environment. The term "terminal cleaning" is used to describe the 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 (i.e., 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 using EPA-registered hospital-grade disinfectants.

17. What is the risk of transmission within the environment in long-term care facilities?
The risk of transmission within a specific environment such as long-term care has not been quantified but the risk factors involved in CDI development and transmission are largely the same no matter the setting. In the long-term care setting, emphasis would be placed on antimicrobial stewardship, hand hygiene, Standard and Contact Precautions, and environmental cleaning.

18. What is the impact of ventilation and air pressure gradients on control of CDI?
There is no evidence that CDI is airborne, therefore ventilation and air pressure gradients are not important prevention measures. Aerosolization of spores or vegetative bacterium during patient care activities that come into contact with the mouth or contaminates hands that touch the mouth may act as a fecal–oral mode of transmission. Contact Precautions are appropriate to prevent transmission.

19. 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 for all patients with CDI. If the patient has a colostomy, the stool draining into the colostomy bag should be considered to be 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.

20. What is the risk of transmission by asymptomatic carriers?
An individual without symptoms (i.e., diarrhea) is not thought to be a likely transmitter of *C. difficile.* At this time there is no support for testing of patients because not all carriers develop CDI and there are no recommended prophylaxis or decolonization methods. Remember that not all *C. difficile* is alike in that some are not 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. This is a basis for the recommendation that a "test of cure" not be done.

21. What are the benefits of single rooms with their own toilets for the prevention of *C. difficile*?
Contact Precautions support placing the patient in a private room with their own toilet. Separating the patient having diarrhea from others and providing them with a toilet that will not be used by others are two vital interventions that disable the chain of transmission.

22. Do hyperspreaders exist and, if so, who are they?
There is currently no evidence regarding hyperspreaders but if we look at the concept within the presentations and transmission of other infections, such as SARS, the idea that there are individuals who are seriously ill and presenting with pronounced clinical symptoms, it is conceivable that individuals with profound diarrhea may contaminate the environment to 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 and rapid and early implementation of Contact Precautions.

23. Is there a relationship between CDI rates and nurse–patient ratios?
At this point, 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 low 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 the 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 transmission and not one single process or interaction can be entirely responsible for prevention.

24. How many stool specimens should be sent for *C. difficile* diagnosis?
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. Determining the approach for testing should occur as a collaborative discussion between clinicians, microbiologists, and IPs and be based on available laboratory technology. Several tests are available to identify *C. difficile*. These include: tissue culture cytotoxicity assay, enzyme-linked immuno-absorbant assay (ELIZA), PCR, and GDH testing. Each method varies based on cost, sensitivity, specificity, and technical expertise. It is important to understand the type of test being used and the risk of false-positive and false-negative results as this information may influence a clinician's diagnosis. Developing sequenced testing optimizes the specificity of diagnosis and is cost effective.

25. Should I handle an endoscope differently after it is 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 2011, as well as information provided in the HICPAC Sterilization and Disinfection guideline (December 2009), can serve as two of your resources. Certainly, errors in reprocessing of semicritical items place patients at risk so your process should include steps to monitor and evaluate adherence to the process.

26. What is the role of probiotics in treatment of CDI?
Several studies support use of probiotic (normal colonic microbes) to help restore normal intestinal microflora in cases of recurrent CDI. Clinicians should consider all treatment options when developing a plan for patients with recurrent CDI.

27. What is fecal transplantation?
Fecal transplantation, fecal microbiota transplantation (FMT), or fecal bacteriotherapy is a treatment option to consider for patients with recurrent CDI. CDI disrupts the normal colonic microbe balance. FMT introduces normal colonic microbes via donor feces to reestablish normal balance. Currently, there is no consensus of opinion on the technique necessary to perform FMT at this time.

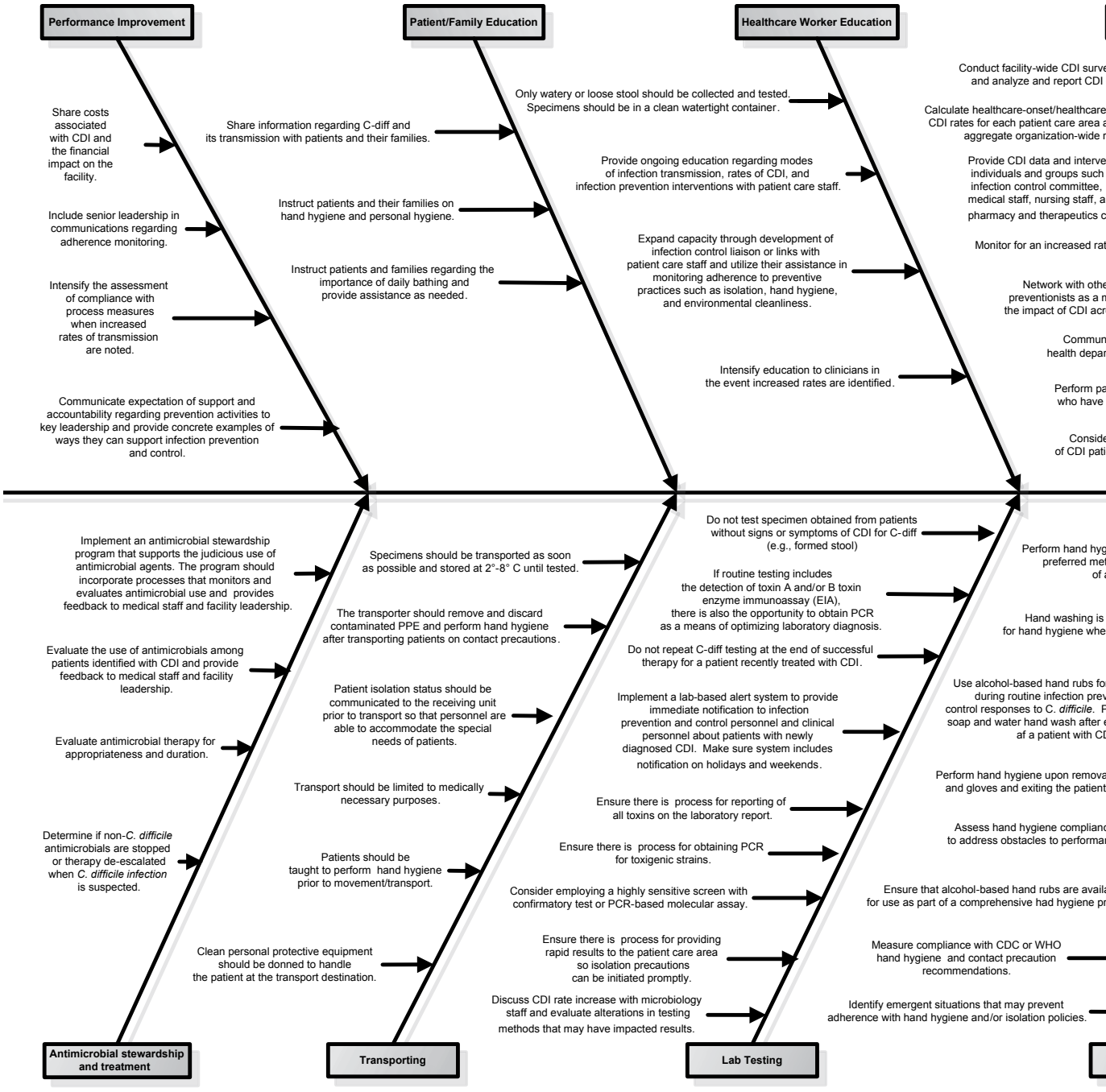
28. When caring for a patient with CDI how can I protect my family?
HCP can protect themselves, their patients, and their families from spreading *C. difficile* by strict compliance with Contact Precautions that includes protective PPE use and removal, hand washing with soap and water, and cleaning of environment and equipment.

29. How do we prevent the spread of *C. difficile* from ambulating patients and their families?
Engage your patients and their families in education about the transmission and prevention of *C. difficile* through hand hygiene, environmental cleaning, PPE, and containing or minimizing diarrhea and loose stools. Encourage them to comply with Contact Precautions by limiting their movement until their diarrhea has subsided.

30. I have seen a number of skin care items and fecal management systems. Do they have a role in 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 and care of the skin may be a primary nursing care goal. Use of a system that serves to minimize environmental and hand contamination may have a role in preventing transmission of *C. difficile* in healthcare settings.

Appendix

Preventing Transmission of *Clostridium d*



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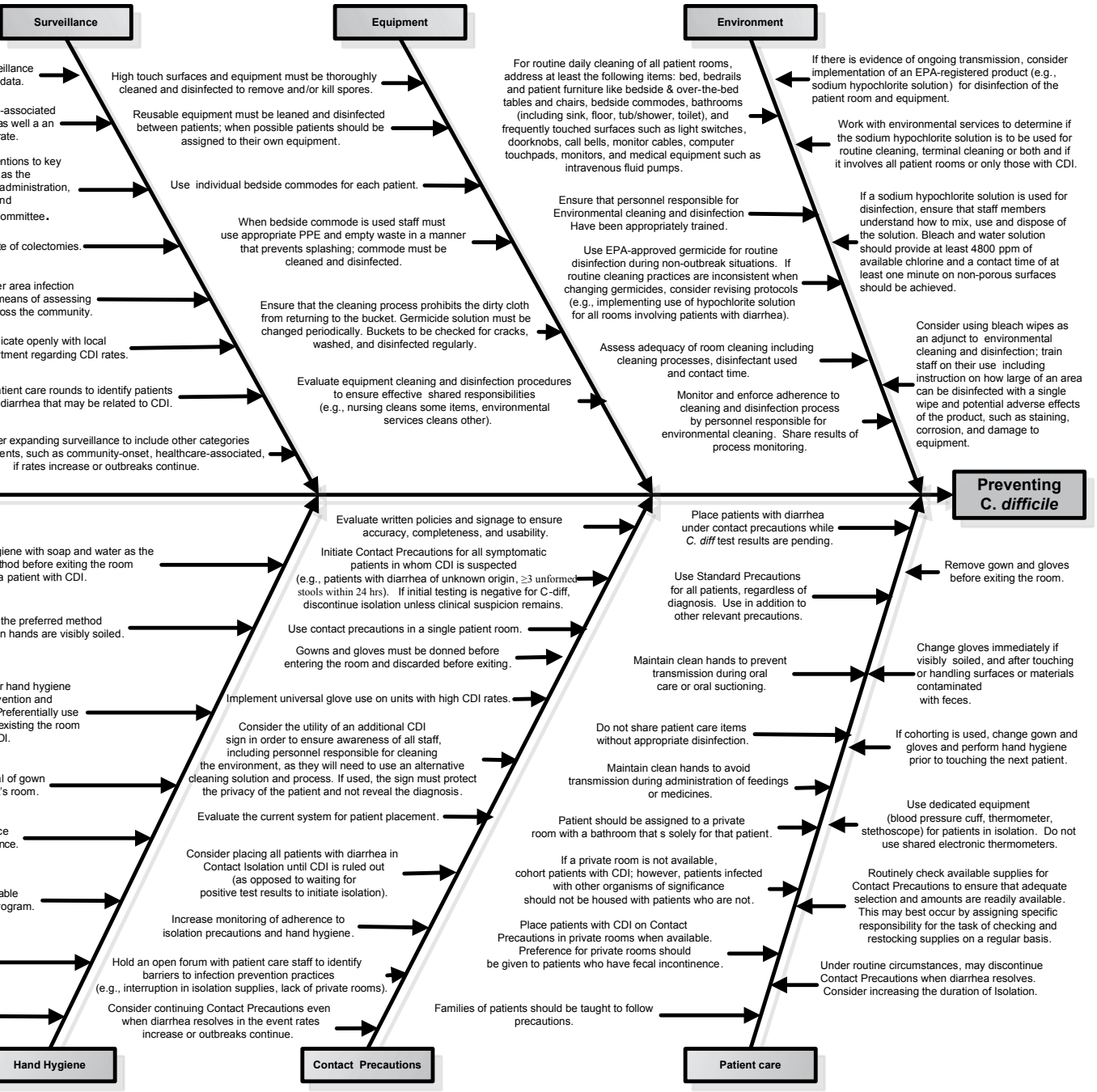

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