COURSE #94614 — 5 CONTACT HOURS/CREDITS RELEASE DATE: 10/01/23 EXPIRATION DATE: 09/30/26

Clostridioides difficile Infection

HOW TO RECEIVE CREDIT

- Read the enclosed course.
- Complete the questions at the end of the course.
- Return your completed Evaluation to NetCE by mail or fax, or complete online at www.NetCE.com. (If you are a physician or Florida nurse, please return the included Answer Sheet/Evaluation.) Your postmark or facsimile date will be used as your completion date.
- Receive your Certificate(s) of Completion by mail, fax, or email.

Faculty

Carol Shenold, RN, ICP, graduated from St. Paul's Nursing School, Dallas, Texas, achieving her diploma in nursing. Over the past thirty years she has worked in hospital nursing in various states in the areas of obstetrics, orthopedics, intensive care, surgery and general medicine.

Mrs. Shenold served as the Continuum of Care Manager for Vencor Oklahoma City, coordinating quality review, utilization review, Case Management, Infection Control, and Quality Management. During that time, the hospital achieved Accreditation with Commendation with the Joint Commission, with a score of 100.

Mrs. Shenold was previously the Infection Control Nurse for Deaconess Hospital, a 300-bed acute care facility in Oklahoma City. She is an active member of the Association for Professionals in Infection Control and Epidemiology (APIC). She worked for the Oklahoma Foundation for Medical Quality for six years.

John M. Leonard, MD, Professor of Medicine Emeritus, Vanderbilt University School of Medicine, completed his post-graduate clinical training at the Yale and Vanderbilt University Medical Centers before joining the Vanderbilt faculty in 1974. He is a clinician-educator and for many years served as director of residency training and student educational programs for the Vanderbilt University Department of Medicine. Over a career span of 40 years, Dr. Leonard conducted an active practice of general internal medicine and an inpatient consulting practice of infectious diseases.

Faculty Disclosure

Contributing faculty, Carol Shenold, RN, ICP, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Contributing faculty, John M. Leonard, MD, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

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The division planners and director have disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Audience

This course is designed for physicians, physician assistants, nurses, pharmacists, and allied health professionals in all settings, especially direct care, who may intervene to prevent or appropriately treat *Clostridioides difficile* infections in their patients.

Accreditations & Approvals

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A complete Works Cited list begins on page 27.

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This activity has been designated for 5 Lifelong Learning (Part II) credits for the American Board of Pathology Continuing Certification Program.

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NetCE designates this continuing education activity for 5 ANCC contact hours.

IPCE CREDIT™

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NetCE designates this continuing education activity for 6 hours for Alabama nurses.

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AACN Synergy CERP Category A.

NetCE designates this activity for 5 hours ACPE credit(s). ACPE Universal Activity Numbers: JA4008164-0000-23-022-H01-P and JA4008164-0000-23-022-H01-T.

Individual State Nursing Approvals

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The purpose of NetCE is to provide challenging curricula to assist healthcare professionals to raise their levels of expertise while fulfilling their continuing education requirements, thereby improving the quality of healthcare.

Our contributing faculty members have taken care to ensure that the information and recommendations are accurate and compatible with the standards generally accepted at the time of publication. The publisher disclaims any liability, loss or damage incurred as a consequence, directly or indirectly, of the use and application of any of the contents. Participants are cautioned about the potential risk of using limited knowledge when integrating new techniques into practice.

Disclosure Statement

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Course Objective

Clostridioides difficile infection (CDI) continues to be a challenging clinical and infection control issue for hospitals and other healthcare facilities. It has now passed methicillin-resistant *Staphylococcus aureus* (MRSA) to become the most prevalent hospital-associated infection. The purpose of this course is to provide a practical review of the epidemiology, pathogenesis, clinical features, and management of CDI, with an emphasis on prevention and infection control measures required to limit transmission and reduce the incidence of disease.

Learning Objectives

Upon completion of this course, you should be able to:

1. Discuss the pathogenesis, clinical features, and current trends in virulence and prevalence of *Clostridioides difficile* and C. *difficile* diseases.
2. Identify populations at increased risk for C. *difficile* infection.
3. Describe ways C. *difficile* can be transmitted.
4. Cite methods of testing for C. *difficile* colonization and infection.
5. Select an appropriate C. *difficile* treatment option based on severity of disease.
6. Apply key principles and develop a specific strategy for infection control and prevention of C. *difficile* infection within healthcare facilities, including contact precautions, environmental cleaning, and antimicrobial stewardship.

Pharmacy Technician Learning Objectives

Upon completion of this course, you should be able to:

1. Outline the epidemiology and presentation of *Clostridioides difficile* infection.
2. Describe methods to detect, treat, and prevent C. *difficile* infection.

EVIDENCE-BASED PRACTICE RECOMMENDATION

Sections marked with this symbol include evidence-based practice recommendations. The level of evidence and/or strength of recommendation, as provided by the evidence-based source, are also included so you may determine the validity or relevance of the information. These sections may be used in conjunction with the course material for better application to your daily practice.

INTRODUCTION

The bacterium *Clostridioides difficile* can cause severe colitis and life-threatening diarrhea. Most infections occur in persons who have recently taken antibiotics for other conditions. Before the incidence of C. *difficile* increased and more virulent strains were identified, diarrhea associated with antibiotic therapy was often considered nothing more than a nuisance, sometimes even an acceptable risk of taking antibiotics. However, complacency toward this healthcare-associated complication is no longer an option in any setting.

According to 2019 statistics, hospital-onset, healthcare-associated C. *difficile* infection (CDI) has increased in frequency, surpassing methicillin-resistant *Staphylococcus aureus* (MRSA) infections to become the most prevalent hospital-acquired infection [1; 2]. In 2019, an estimated 323,700 infections and 10,600 deaths were caused by MRSA, compared with 223,900 infections and 12,800 deaths caused by CDI [1]. Although MRSA is still a major patient threat, hospital-related infections declined 21% between 2013 and 2017, whereas those related to CDI remained relatively stable (244,400 cases in 2013 and 223,900 cases in 2017) [2]. As of 2017, the Centers for Disease Control and Prevention (CDC) estimates there are 223,900 cases of CDI in hospitalized patients each year leading to 12,800 deaths, with an attributable healthcare cost of $1 billion [3]. The CDC has assigned a threat level of "urgent" to C. *difficile*, meaning these bacteria are immediate public health threats that require urgent and aggressive action [1; 3].

C. *difficile* bacteria form spores that are shed in the stool and are able to survive on environmental surfaces for months. The usual preventive measures and precautions that are effective in reducing acquisition of MRSA have proved to be much less effective for C. *difficile*. Moreover, there is concern that the prevalence of CDI may be considerably greater than indicated by clinical publications, which are often based on hospital surveillance and do not account for cases of CDI that develop after discharge or arise in the community [4].

AN OVERVIEW OF THE *C. DIFFICILE* PROBLEM

Compounding *C. difficile* issues in hospitals is the fact that variant strains of the pathogen have emerged in response to antimicrobial pressure, strains with heightened virulence and diminished responsiveness to metronidazole therapy. This trend, which is not confined to healthcare facilities, is now evident in the community, where cases have appeared in previously unaffected populations [1]. Even more significant, a number of these cases have been observed in patients with no recent hospitalization or antibiotic use, according to a study based on the Rochester Epidemiological Project [5]. Probable causes for this change include an aging population, broader use of antibiotics, widespread resistance to fluoroquinolones, and a new, more virulent strain of *C. difficile* [1; 5].

Some CDI cases are also proving more difficult to treat, with the emergence of resistant strains and increasing number of community-acquired cases [1]. As a result, the pathogenesis of CDI is not always clear-cut; it could be attributed to overuse of antibiotics, undertreatment (i.e., patients not completing a full course of antibiotics), or even a novel change in the bacteria.

Within hospitals and long-term care facilities there exists an undetected reservoir of asymptomatic patients who are "carriers" of *C. difficile* [4]. Many studies indicate that noncompliance with preventive measures designed to limit transmission, such as proper cleaning of infected patients' rooms, play a role in this problem. One key to controlling CDI may lie in the practice of cleaning all surfaces as if they are contaminated with *C. difficile* rather than only the surfaces in rooms of patients known to be infected [4]. Another study described a targeted strategy to eliminate *C. difficile* using ultra-germicidal bleach wipes for cleaning. Before the intervention, the incidence of CDI was 18.4 per 10,000 patient-days. After the intervention, the incidence decreased to 3.76 per 10,000 patient-days [4].

Complicating this difficult issue is the fact that common hand-hygiene products are often ineffective at eliminating *C. difficile*, perhaps because the bacteria have "sticky" properties, similar to anthrax. *C. difficile* spores have an exosporium that confers a particulate adherence—sticky chains of protein-containing substances that stick on hands. This reinforces the need for Contact Precautions, including gloves, for the care of these patients [6].

A survey conducted by the Association for Professionals in Infection Control and Epidemiology (APIC) found that, of the hospitals that participated, most are using multiple strategies to address CDI [7]. This included:

- 70% adopting additional interventions since the previous survey (but only 42% have seen a decline in CDI)
- 77% having hand hygiene initiatives (promoting soap and water handwashing but also having alcohol-based hand rubs available)
- 75% conducting surveillance or other methods and activities to promptly identify CDI cases (before the Centers for Medicare and Medicaid Services [CMS] reporting requirements went into effect)
- 42% always placing CDI patients on Contact Precautions, using gowns and gloves when caring for them
- 92% increasing their emphasis on environmental cleaning

Although CDI rates are at historic highs, only one in five survey respondents (21%) have been able to add more infection prevention staff since 2010 [7].

Six in ten respondents did not have an antimicrobial stewardship program, which is a vital strategy, as 90% of patients with CDI have previously received antibiotics [7]. The variation in some of the practices identified in the CDI Pace of Progress survey indicate a need to improve standardization of prevention measures and guide future practices [7].

Two large population studies have modified understanding of the epidemiology and prevention of CDI, emphasizing the value of tight control over antimicrobial usage in hospitals. The first is a CDC analysis of 10,342 cases of CDI, collected from 111 hospitals and 316 nursing homes [8]. Although 94% of cases were healthcare associated, only 25% resulted from acquisition of *C. difficile* in the hospital where illness was observed. In 75% of cases, *C. difficile* (colonization or active infection) had been acquired prior to hospitalization.

A second study, conducted by the British health system in response to a growing epidemic of CDI throughout the United Kingdom, showed [9]:

- Using molecular chain-sequencing to track acquisition and transmission of strains within the hospital environment, only 25% of cases resulted from person-to-person transmission within the hospital.
- The majority of patients were already colonized at the time of admission.
- Tight control of antimicrobial usage, including a restriction on the use of fluoroquinolones and cephalosporins, resulted in a 60% reduction in the CDI case rate.

These studies demonstrate that a significant proportion of CDI cases occurring within healthcare facilities, especially hospitals, are the result of antimicrobial therapy in patients colonized prior to admission. Moreover, the targeted control of antibiotic usage (i.e., an antimicrobial stewardship program) is seen to be as important as the usual infection control measures for reducing the number of cases and limiting transmission.

THE CURRENT ENVIRONMENT

Most anaerobic infections arise from sources indigenous to the patient. However, there are circumstances in which infection develops after acquisition of dormant bacteria from an exogenous source. The ability of organisms like *C. difficile* to produce spores makes them easily acquired from the environment. *C. difficile* is the main pathogen implicated in antibiotic-associated colitis and is the causative pathogen for 15% to 25% of nosocomial antibiotic-associated diarrhea [10].

As discussed, current strains of *C. difficile* may be less susceptible to available treatments, making its growing prevalence an even greater concern. One study noted the emergence and increasing prevalence of *C. difficile* strains with reduced susceptibility to both metronidazole and vancomycin [11].

PREVALENCE AND BURDEN OF CDI

C. difficile accounts for 20% to 30% of all antibiotic-associated diarrhea and is the most commonly identified reason for infectious diarrhea in hospital settings [10]. Because CDI is not a reportable disease in the United States, data are sparse. Only 20 states mandate hospital reporting either under state law or by incorporating the federal reporting requirements of the CMS. While state laws are more common, incorporation of federal reporting requirements is increasing. State surveillance activities have been heavily influenced by the CMS reporting requirements, which became mandatory in 2013. States that have not mandated reporting have taken other actions to reduce CDIs by implementing prevention collaboratives offered by the CDC [12].

The CDC Emerging Infections Program (EIP) was established in 2011 to monitor the incidence *C. difficile* infection and the burden of CDI in communities and hospitals within the United States. The EIP network consists of 35 counties in 10 states, with a surveillance population in excess of 12 million persons [13]. In 2021, 13,348 cases of CDI were reported to EIP. Of these, 49.3% were healthcare-associated and 51.0% were community-associated cases. The

estimated incidence nationally was 55.9 per 100,000 population for community-associated CDI and 54.3 per 100,000 population for healthcare-associated CDI. Incidence rates were higher among female patients than male patients, among White patients than non-White patients, and among persons younger than 65 years of age than those older than 65 years of age [13]. Adjusting EIP data for enhanced sensitivity of diagnostic testing in the past decade, the estimated national burden of CDI decreased 24% from 2012 to 2017 [14]. This improvement was driven by a 36% decline in reported cases of healthcare-associated CDI. Although hospitalizations for CDI also declined by 24%, the number of first recurrences and in-hospital deaths did not change significantly. The estimated incidence of community-associated CDI was unchanged from 2011 to 2017 and accounted for almost 50% of the national burden of CDI in 2017. These data demonstrate the need for continued efforts to improve infection prevention and antibiotic stewardship in both inpatient and outpatient settings [14].

It is believed that long-term care facilities may be at the greatest risk for outbreaks. Because many of the patients in these settings are elderly and have been exposed to multiple antimicrobials, it has been suggested that the disease and colonization rates may be high [10]. An analysis of acute care hospital discharges in the United States found the discharge diagnoses of CDI doubled between 2000 and 2003. In 2003, close to 2% of patients discharged from acute care to long-term care carried the diagnosis of CDI [10].

CDI-associated medical costs also have reached historic highs. In 2015, the average cost for CDI case management and CDI-attributable costs per case were $42,316 and $21,448, respectively [15]. Hospital-onset CDI-attributable cost per case was $34,157, which was approximately 1.5 times the cost of community-onset CDI ($20,095). The average length of stay for inpatient treatment was 11.1 days. The total cost attributable to CDI in the United States is estimated to be $6.3 billion each year. Total annual CDI hospital management required nearly 2.4 million days of inpatient stay [15].

MORTALITY

Historically, the mortality associated with CDI has been low. Death as a direct or indirect result of CDI occurred in between 2% and 9% of cases [10; 13]. However, the mortality rate associated with CDI varies according to the patient variables and disease. While many patients with *C. difficile*-associated diarrhea recover without specific therapy, symptoms may be prolonged and debilitating. Progression to *C. difficile* colitis is a serious matter and carries a mortality rate as high as 25% in elderly patients who are frail [10]. Reports focusing on patients who are more seriously ill indicate mortality rates of between 10% and 30%. As incidence rates have risen over the past decade, so too have mortality rates, and both reflect, in part, an increase in the virulence of *C. difficile* strains. Several hypervirulent outbreaks have been caused by the North American Pulsed Field type 1 and polymerase chain reaction (PCR) ribotype 027 (BI/NAP1/027) strain [5; 16]. This virulent strain has been associated with increased production of toxins A and B, fluoroquinolone resistance, and the production of binary toxin. The role of binary toxin is not clear, but it may synergistically increase the virulence of toxins A and B. The virulent strain BI/NAP1/027 has been reported in most states throughout the United States and in several countries in Europe [16]. Preventive strategies for BI/NAP1/027 are similar to those taken for other strains, including barrier methods, use of disposable equipment, handwashing (with soap and water), environmental disinfection techniques, and antimicrobial stewardship. Vaccines are under development to target the toxins, and a novel drug (SYN-004 [ribaxamase]) for preventing *C. difficile* is under investigation [17].

PATHOGENESIS

C. difficile is an anaerobic, gram-positive, spore-forming bacillus within the genus *Clostridioides*. Also in this genus is *C. mangenotii*. *C. mangenotii* has been found in human feces, marine sediment, and soil [18].

C. difficile was first described in 1935 as a component of the fecal flora of healthy newborns and was initially not thought to be a pathogen. It was named *C. difficile* (the Latin word for difficult) because it grows slowly and is difficult to culture. While early investigators noted that the bacterium produced a potent toxin, the role of *C. difficile* in antibiotic-associated diarrhea and pseudomembranous colitis was not determined until the 1970s [18; 19].

In a given patient, the administration of broad-spectrum antimicrobials causes, to some degree, an alteration in the normal bacterial ecosystem of the intestinal tract. Such an alteration facilitates acquisition (colonization) and adversely affects the natural history of CDI. *C. difficile* spores tend to remain dormant within the colon of a colonized patient until disruption of the normal bacterial flora, as with antibiotics, permits activation, proliferation, and toxin production. When this occurs, the toxins produced by *C. difficile* cause progressive inflammation and damage to the colonic mucosa (colitis). The severity of the colitis is variable, determined in part by the virulence of the infecting strain, the degree of toxin production, and the duration of exposure. In severe cases, there is extensive colonic inflammation combined with patchy zones of mucosal erosion and focal necrosis with admixed leukocytes and cellular debris. On colonoscopy, this has the appearance of white, membranous patches, hence the term "pseudomembranous colitis."

Not everyone infected with *C. difficile* develops diarrhea or colitis. Many infants, young children, and some adults become carriers of the pathogen yet have no symptoms, even under circumstances of altered intestinal flora. In these patients, *C. difficile* most likely does not progress to colitis due to:

- Low levels of bacteria in the colon maintained as non-active spores
- Acquired antibodies against low levels of the *C. difficile* toxin

Prior to the mid-1970s, pseudomembranous colitis was encountered frequently following a course of certain antibiotics, especially clindamycin and lincomycin. After the first reports established *C. difficile* as the cause of antibiotic-induced pseudomembranous colitis in 1978, CDI emerged as the principal form of the disease. The development of CDI typically has two essential requirements: acquisition of a toxin-producing strain by fecal-oral transmission and exposure to antimicrobial agents that have a significant impact on intestinal flora [9]. According to one report, 96% of patients with symptomatic *C. difficile* had received antimicrobials in the 14 days before the onset of diarrhea and all had received an antimicrobial within the previous three months [20]. Upon exposure to antibiotic pressure, infected patients develop symptoms of CDI usually within days, with a median time of two to three days to onset of symptoms [10].

C. DIFFICILE DISEASES

As noted, pseudomembranous colitis is an inflammatory condition that develops in response to toxins produced by *C. difficile* organisms in the colon. This process is triggered by certain antibiotics that alter the normal intestinal flora in such a way as to permit activation and proliferation of *C. difficile*. This, in turn, leads to overproduction of toxin and injury to the colonic mucosa. The resulting illness, ranging from mild-to-moderate diarrhea to pseudomembranous colitis, may lead to serious complications such as toxic dilatation of the colon, perforation, sepsis, and even death [21].

C. difficile-associated diarrhea may be accompanied by the passage of mucus or occult blood in the stool, but melena or hematochezia is rare. Fever, cramping, abdominal discomfort, and a peripheral leukocytosis are relatively common, but are found in fewer than half the patients [10]. Extraintestinal manifestations, such as arthritis and bacteremia, occur but are very rare. *C. difficile* ileitis or pouchitis may be seen, rarely, in patients who have had a total colectomy for complicated CDI or some other

indication [10]. Patients with severe disease have the potential for developing colonic ileus or dilatation (toxic megacolon). On occasion, the atypical case presents with abdominal pain and distention accompanied by leukocytosis but having minimal or no diarrhea. Other features of CDI include volume depletion and dehydration, electrolyte disturbances, azotemia, and hypoalbuminemia—all markers of severity. Serious complications include toxic megacolon, bowel perforation, hypotension, renal failure, systemic inflammatory response syndrome, sepsis, and/or death within 30 days of diagnosis [10; 22].

AT-RISK POPULATIONS

Three populations at highest risk of acquiring *C. difficile* are the elderly, patients receiving antibiotics, and those with long hospital stays. However, other groups, including surgery patients and the immunocompromised, are also at risk for CDI. It is important that steps be taken to prevent infection in these patients, when possible.

OLDER ADULTS

Advanced age is considered a risk factor for CDI, as evidence by the higher age adjusted incidence of CDI [23]. Age older than 65 years is considered a risk factor both for acquisition of *C. difficile* and for the development of *C. difficile*-associated diarrhea [23; 24]. This difference in prevalence is not attributable to a greater exposure to antibiotics among older adults. The Society for Healthcare Epidemiology of America (SHEA) suggests that the greater morbidity and mortality of CDI in elderly populations may be due to age-related changes in fecal flora, immunosenescence, or the presence of other underlying diseases [23]. Frequent interactions with healthcare systems also may place the older adults at greater risk for CDI. Data from the EIP show that in 2010, exposure to health care preceded 94% of CDI. Of those, 75% were inpatient exposures, with the remaining 25% associated with long-term care facilities and outpatient care settings [25; 26].

PATIENTS TAKING ANTIBIOTICS

The most modifiable risk factor for the development of CDI is exposure to antibiotic agents. The antibiotics most frequently implicated in cases of CDI are clindamycin, cephalosporins, fluoroquinolones, and penicillins. However, virtually every antibiotic has been associated with CDI through the years. Even very limited exposure, such as single-dose surgical antibiotic prophylaxis, increases a patient's risk of both *C. difficile* colonization and symptomatic disease [10].

LONG HOSPITAL STAYS

Healthcare workers are the most common hand carriers of *C. difficile* due to breaks in hand washing technique, actively caring for infected patients, and the existence of *C. difficile* spores on surfaces commonly touched by patients and workers alike. As such, longer hospital or facility stays increase the probability of contact. The risk of acquiring the disease during an admission increases with time and can be as high as 40% during longer hospitalizations [10].

IMMUNOCOMPROMISED PATIENTS

A compromised immune system can allow *C. difficile* to proliferate, and immunocompromised patients are at an increased risk for CDI and poorer outcomes. For example, cancer chemotherapy often leads to immunosuppression, neutropenia, intercurrent infection, and prolonged hospital stays—all of which are associated with increased risk for CDI. Furthermore, evidence also suggests that *C. difficile* has become the most important pathogen causing bacterial diarrhea in patients with human immunodeficiency virus (HIV) in the United States [27]. Immunosuppression, either as a result of chemotherapy or disease process, can increase the probability of developing CDI; this risk may be compounded by concurrent use of antimicrobials or prolonged hospitalization [10].

GASTROINTESTINAL SURGERY

Another risk factor for C. *difficile* is gastrointestinal surgery or manipulation of the gastrointestinal tract, including tube feedings [10]. It has also been hypothesized that the use of acid-suppressing medications, such as histamine-2 receptor antagonists and proton pump inhibitors (PPIs), may lead to CDI [28; 29; 30]. Although many studies suggest an association between using these medications and the acquisition of CDI, other well-controlled studies have suggested that the association is the result of prolonged hospital stays, prolonged use of PPI therapy, and underlying disease severity [10; 30]. Additionally, a system review of observational studies suggests that patients who receive acid-suppressing medications may be at increased risk for recurrent CDI [31].

PEDIATRIC PATIENTS

CDI is much less common in children than in adults. However, 2% to 70% of young children, depending on age and other factors, may be asymptomatically colonized with C. *difficile*, including toxigenic strains [21; 32; 33]. Colonization rates decrease as infants age, falling to about 6% by 2 years of age and down to 2% by 3 years of age [21]. Although infants may acquire colonization in the first week of life, no studies have shown a consistent association between mode of feeding (i.e., formula instead of breast milk) as viable factors. Colonization of infants younger than 1 year of age has failed to show an epidemiologic association with the development of disease. At the same time, nosocomial transmission in the neonatal intensive care unit (NICU) has been well documented, as has C. *difficile* contamination of the NICU environment [21]. In predominantly healthy infants without significant healthcare exposure, C. *difficile* colonization and acquisition reflect environmental exposure, with pet dogs identified as a novel risk factor [32].

One complication in the accurate diagnosis of CDI in young children is the lack of specific tests for this age group (such as the enzyme immunoassay [EIA]). However, it is important to remember that children who are colonized with C. *difficile* do represent a reservoir for disease transmission, even if they are asymptomatic. This returns to the issue of environmental cleaning, which has been recognized as a key factor in transmission prevention for many organisms [21; 34].

The epidemiology of CDI in children may be changing with the emergence of BI/NAP1/027. Because this strain has been associated with severe disease in both adult and pediatric patients without recent exposure to healthcare facilities, testing for C. *difficile* should be considered in children 1 to 2 years of age with diarrhea and recent antibiotic exposure, especially when more common causes have been excluded. Children older than 2 years of age with diarrhea and a history of recent antimicrobial use may be tested with the same techniques used for older children or adults. Because the disease has been confirmed in asymptomatic children without recent antibiotic exposure, testing for C. *difficile* may be considered for these patients, but other diagnoses are more likely [21].

POPULATIONS PREVIOUSLY AT LOW RISK

It is vital to remain vigilant regarding CDI even among populations previously believed to be at low risk for the disease, as virulence and infection patterns are changing [35]. Statistics indicate that CDI is occurring among healthy peripartum women, who have been previously at very low risk for the disease [33; 36]. The frequency of the disease also seems to be increasing among persons living in the community, including, but not limited to, healthy persons with no recent healthcare contact. But, there are limited historical data against which to compare these statistics [10].

TRANSMISSION

The cycle of transmission for C. *difficile* consists of the following steps:

- Spore ingestion
- Germination
- Colonization in the bowel
- Asymptomatic carriage
- Flora disruption
- Diarrhea
- Hand and environmental contamination
- Spore ingestion

This cycle can be broken with antibiotic stewardship, hand hygiene, and environmental decontamination.

PERSON TO PERSON

The primary mode of C. *difficile* transmission is person-to-person spread through the fecal-oral route, principally within healthcare facilities [10]. Asymptomatic patients (carriers) colonized with C. *difficile* may be shedding spores, a source of environmental contamination that facilitates transmission of infection to more vulnerable patients within the facility. Person-to-person contact permits C. *difficile* spores to pass readily from carriers and their bedding to the hands and clothing of healthcare workers. The hands of healthcare workers, transiently contaminated with C. *difficile* spores, are probably the main means by which the organism is spread during non-outbreak periods [10]. Studies have found a prevalence of asymptomatic colonization with C. *difficile* of 7% to 26% in acute care facilities and 5% to 7% in long-term care facilities, although other studies indicate the prevalence of asymptomatic colonization may be closer to 20% to 50% in facilities where CDI is endemic [37]. In a prospective, blinded cohort study in two university hospitals, the rate of hospital-acquired CDI among patients admitted to the same ward as an asymptomatic carrier was 4.6%, compared with 2.6% among patients residing in a ward having no asymptomatic carrier [38]. The risk of acquiring CDI correlated with the amount of exposure and length of stay.

As discussed, the longer a person remains hospitalized, the greater the exposure risk, which indicates a cumulative daily risk of exposure to C. *difficile* spores in the healthcare setting. In most cases, the period between exposure to C. *difficile* and the development of infection has been estimated to be a median of two to three days [10]. CDI resulting from exposure to C. *difficile* in a healthcare facility can also have onset after discharge [10].

ENVIRONMENTAL CONTAMINATION

Environmental contamination also has an important role in transmission of C. *difficile* in healthcare settings. Aside from transmission on healthcare professionals' hands and clothing, there have also been outbreaks traced back to electronic rectal thermometers, inadequately cleaned commodes, and bedpans shared between patients [10]. Environmental samples of C. *difficile* also have been obtained from homes, parks, chain stores, fast food restaurants, and other commercial sites [39; 40; 41; 42].

The environment must be accepted as a critical source of contamination as it plays an important role in supporting the spread of infection. Because C. *difficile* is shed in feces, any surface, item, or medical device that becomes contaminated with feces is a potential source for the spores and can become involved in infection transmission. C. *difficile* spores can exist for five months on hard surfaces without adequate cleaning. In one study, spores were found in 49% of rooms occupied by patients with CDI and in 29% of the rooms with asymptomatic carriers [21].

The heaviest contamination is present on floors, in bathrooms, and on any surfaces commonly touched by hands, such as light switches, bed rails, and tabletops. Other potential contamination sites include thermometers, blood pressure cuffs, and call buttons [21].

FOOD CONTAMINATION

One study noted that in samples of cooked and uncooked meat products, 42% contained toxigenic *C. difficile* strains. These findings indicate that food products may play a role in *C. difficile* transmission [41; 43]. However, foodborne transmission is not considered a major part of the usual transmission cycle so far [44].

DIAGNOSIS

As previously discussed, patients admitted to a healthcare facility are often colonized with *C. difficile*, in the absence of diarrheal disease. Others become colonized after admission as the result of environmental contamination and person-to-person transmission. In either case, CDI then develops in association with underlying host factors and altered intestinal flora caused by broad-spectrum antimicrobial therapy. The antibiotic choice, susceptibility pattern, route of administration, mode of elimination, and presence of antibiotic metabolites in the gut all impact the risk for antibiotic-associated collateral damage [9].

In 2017, the SHEA and the Infectious Diseases Society of America (IDSA) updated clinical practice guidelines for CDI in adults [10]. The guideline is designed to improve the diagnosis and management of CDI. In addition, recommended methods of infection control and environmental management of the pathogen are presented. Recommendations are based on the best available evidence and practices as determined by a joint expert panel appointed by the SHEA and the IDSA [10]. In 2021, the SHEA and the IDSA published a focused update of these guidelines, with new recommendations for antibiotic therapy [24].

SIGNS AND SYMPTOMS

A case definition of CDI should include symptoms (usually diarrhea) and either a stool test result positive for *C. difficile* toxins, or detection of toxigenic *C. difficile*, or colonoscopic findings demonstrating pseudomembranous colitis. Clinical manifestations of infection with toxin-producing strains of *C. difficile* can be as varied as nonsymptomatic carriage, mild-to-moderate diarrhea, or a fulminant pseudomembranous colitis. A history of antimicrobial use within three months of the onset of diarrhea is characteristic. The most common symptoms of mild-to-moderate *C. difficile* disease are [10]:

- Watery diarrhea three or more times per day for two or more days
- Mild abdominal cramping and tenderness
- Fever

Signs and symptoms of severe infection include:

- Watery diarrhea 10 to 15 times a day
- Moderate-to-severe abdominal cramping and pain
- Fever
- Blood or pus in the stool
- Leukocytosis
- Nausea, vomiting
- Signs of hypovolemia
- Weight loss

As noted, fever, cramping, abdominal discomfort, and a peripheral leukocytosis are found in fewer than half of CDI patients [10].

DIAGNOSTIC TESTING

Hospitalized patients and persons residing in long-term care facilities should be tested for CDI whenever they develop unexplained and new-onset diarrhea, defined as three or more unformed stools in 24 hours [10]. The diagnosis of CDI is made in one of two ways: a stool positive for *C. difficile* toxins or toxigenic strain of the organism, or endoscopic/histologic findings of pseudomembranous colitis.

Testing of stool from asymptomatic patients is not clinically useful, even when used as a test of cure, and is not recommended except in epidemiologic studies [10]. Diagnostic stool evaluation should be considered in the patient with clinically significant diarrhea (i.e., three or more loose stools for at least two days), or performed immediately in the patient with severe diarrhea (10 to 15 stools in a 24-hour period), especially if combined with fever or recent antibiotic usage.

EVIDENCE-BASED PRACTICE RECOMMENDATION

According to the Infectious Diseases Society of America (IDSA) and the Society for Healthcare Epidemiology of America (SHEA), patients with at least three unexplained and new-onset unformed stools in 24 hours are the preferred target population for testing for *Clostridioides difficile* infection (CDI).

(https://www.idsociety.org/practice-guideline/clostridium-difficile. Last accessed September 11, 2023.)

Strength of Recommendation/Level of Evidence: Weak recommendation, very low quality of evidence

Specimen Collection

The proper specimen for the diagnosis of CDI is a watery, loose, or semi-formed stool promptly submitted to the laboratory. Rectal swab specimens are generally unreliable and should not be utilized unless the patient has ileus without diarrhea. Because 10% or more of hospitalized patients may be colonized with *C. difficile*, diagnostic testing on formed stool from an asymptomatic patient lacks specificity and is not indicated. Routine testing of multiple specimens from the same patient is not recommended due to the low yield and possibility of false-positive results [10].

Laboratory Testing

A number of tests are used for the detection of toxins or toxigenic strains in stool, and the results can be available in hours [10]. The two most commonly employed by clinical laboratories are the enzyme immunoassay (EIA) and the PCR. Two additional tests—a selective anaerobic culture and the cell culture cytotoxicity assay—are highly sensitive and specific but are labor-intensive and too slow (two days or more) for clinical use.

EIA testing for *C. difficile* toxin A and B is rapid and specific, but less sensitive than PCR or the cell cytotoxin assay. The relatively low sensitivity (about 75%) is because detection requires that a threshold level of toxin be present in the sample.

EIA for glucose dehydrogenase (GDH) antigen is a rapid and highly sensitive way to detect the presence of *C. difficile* in stool but cannot distinguish between toxigenic and non-toxigenic strains. This assay is useful as an initial screening test but requires an additional step (e.g. PCR or specific culture) for confirmation.

PCR testing for the detection of toxin A and toxin B genes is highly sensitive and specific, and results can be available within one to two hours [10]. The disadvantage is that the test is so sensitive that false positives may occur if the patient is simply a carrier of *C. difficile*. About half of the hospital laboratories in the country now employ PCR, either alone or as part of a multi-step protocol that begins with EA screening for GDH or toxin.

Imaging

Pseudomembranous colitis can only be diagnosed with certainty by direct visualization via colonoscopy and/or by histopathology via mucosal biopsy. Unfortunately, visualization only detects pseudomembranes in 51% to 55% of cases that are diagnosed by combined clinical and laboratory criteria [45]. The American College of Radiology recommends abdominal computed tomography scanning as the imaging modality of choice for *C. difficile* when pseudomembranous colitis, other complications of CDI, or other intra-abdominal pathology is suspected [46]. Marked colonic wall thickening is the most common finding. Other features may include ascites, irregularity of the bowel wall, and pericolonic stranding.

MOLECULAR TYPING

One important tool for understanding CDI epidemiology is molecular typing. In order to gain an accurate understanding of transmission and the settings for transmission, molecular characterization of isolates is necessary. Molecular typing can confirm a shift in epidemiology and allow tracking of certain strains. The BI/NAP1/027 epidemic strain of *C. difficile* was identified and distinguished from other strains using the PCR method of typing [10].

However, typing requires access to a stool sample, which may be difficult given the preference for nonculture diagnosis methods [10]. If a culture is obtained, molecular typing may be completed by examining polymorphisms after restriction endonuclease digestion of chromosomal DNA, PCR-based methods, or sequence-based methods. PCR testing is rapid and is the most commonly recommended method. The information gained from typing the *C. difficile* strain can assist in treatment decisions and determining prognosis. However, the SHEA/IDSA guidelines indicate that more data on utility are necessary before this methodology can be recommended for routine testing.

TREATMENT

INITIAL EPISODE

The important principles for effective management of CDI are as follows [10]:

- Immediate cessation of the inciting antibiotic when possible. If continued treatment of a serious systemic infection is necessary, one should consider alternative agents with narrow spectrum and less impact on bowel flora.
- Implementation of infection control measures, including contact precautions and hand-washing with soap and water before and after contact with the patient.
- Initiation of antibiotic therapy for CDI should be started empirically for situations where a substantial delay in laboratory confirmation is expected, or for fulminant CDI.

When managing CDI there are important clinical and laboratory features to consider in assessing severity, choosing therapy, and judging prognosis. These include age older than 65 years, general debility, immunodeficiency status, renal function, and leukocytosis. A peripheral leukocytosis greater than 15,000 cells/mcL is indicative of severe colitis. Leukemoid reactions in the range of 30,000–50,000 cells/mcL are sometimes seen and may be a herald sign of toxic megacolon or impending bowel perforation [10].

Mild-to-Moderate Disease

Mild-to-moderate illness is defined in the IDSA guidelines as CDI in the presence of a white blood cell count ≤15,000/mcL and serum creatinine <1.5 mg/dL [10]. In order to reduce selective pressure for vancomycin resistance in enterococci, previous recommendations were to initiate treatment with metronidazole for cases of mild-to-moderate illness. The 2021 focused guideline update recommends fidaxomicin over metronidazole for treatment of an initial or first recurrent episode of CDI [24]. The dosage is 200 mg twice daily for 10 days. Fidaxomicin is a first-in-class oral macrocyclic antibiotic with potent bactericidal activity against *C. difficile* [47; 48]. Unlike vancomycin and metronidazole, fidaxomicin has a narrow spectrum of activity against normal gut flora. In settings in which access to fidaxomicin is limited, it is suggested to use vancomycin or metronidazole if the episode of CDI is not severe [24]. The suggested regimen is metronidazole 500 mg orally three times daily for 10 days, while the vancomycin dose is 125 mg orally four times per day for 10 days. The response to treatment is usually prompt, with a significant reduction in the rate of stooling within 24 to 48 hours. There are reports indicating that some patients infected with the BI/NAP1/027 strain respond more slowly, even unsatisfactorily, to metronidazole [16; 49].

EVIDENCE-BASED PRACTICE RECOMMENDATION

For patients with an initial CDI episode, the IDSA and the SHEA suggest using fidaxomicin rather than a standard course of vancomycin. This recommendation places a high value in the beneficial effects and safety of fidaxomicin, but its implementation depends upon available resources. Vancomycin remains an acceptable alternative.

(https://www.idsociety.org/practice-guideline/clostridioides-difficile-2021-focused-update. Last accessed September 11, 2023.)

Strength of Recommendation/Level of Evidence: Conditional recommendation, moderate certainty of evidence

The 2021 focused guideline update also recommends coadministration of bezlotoxumab along with antibiotic therapy for patients with a recurrent CDI episode within the last six months [24]. Bezlotoxumab is a monoclonal antibody targeting toxin B produced by C. *difficile* and may be helpful in preventing recurrence in at-risk individuals.

Severe Disease

Vancomycin is the initial oral drug of choice for patients with moderate-to-severe illness or complicated infection and for less severe patients not showing satisfactory response to fidaxomicin or metronidazole within 48 to 72 hours. As noted, cases may be classified as severe with any combination of the following: age older than 65 years, fever and abdominal pain, leukocytosis >15,000/mcL, and/or serum creatinine greater than 1.5 times the premorbid level. Fulminant CDI is severe illness complicated by hypotension, ileus, or megacolon. The SHEA/IDSA guidelines recommend an initial vancomycin dosage regimen of 250–500 mg orally every six hours for severe disease without complications [10]. In high-risk patients (such as the elderly) and cases with evidence of impending complications, the dose of vancomycin should be increased to 500 mg every six hours and combined with intravenous metronidazole (500 mg every eight hours) until a satisfactory response has been achieved [10]. Patients should be followed closely for response to therapy, time to symptom resolution, signs of recurrence after initial symptom resolution, and development of complications. Major complications include hypovolemic or septic shock, megacolon, and colonic perforation.

CDI with Complications

For patients with severe CDI and signs of ileus, vancomycin can also be administered per rectum. The recommended regimen is vancomycin 500 mg in approximately 100 mL normal saline per rectum every six hours as a retention enema [10]. This is in addition to the oral vancomycin and IV metronidazole therapy described for severe CDI cases. Ileus may impair the delivery of orally administered vancomycin to the colon, but intravenous metronidazole is excreted into the biliary tract, diffuses readily into other body fluids and tissue departments, and thus is likely to yield therapeutic levels within the bowel lumen. Although vancomycin retention enemas may not achieve effective drug levels in the right and transverse colon, they have proved to be useful in some cases and are considered safe in patients with no signs of colonic perforation.

A colectomy can be life-saving for patients with megacolon, colonic perforation, acute abdomen, and potentially with septic shock. However, such patients are often elderly and, in the presence of elevated serum lactate levels and other markers of sepsis, are at risk for high operative mortality and postoperative complications. Surgery consultation should be requested early for severely ill patients, especially when there is marked leukocytosis or signs of megacolon. If surgery is necessary, subtotal colectomy with preservation of the rectum is the preferred approach [10].

Due to the limited number of approved therapies for CDIs, new treatments are needed to decrease recurrence rates. Several novel antibiotics (e.g., ramoplanin, cadazolid, ridinilazole, surotomycin) are in development to treat CDI [50; 51; 52; 53].

Alternative Approaches

Studies of the use of probiotic *Saccharomyces boulardii* to treat or prevent CDI have been inconclusive. A controlled trial of the probiotic in combination with high-dose vancomycin did appear to decrease the number of recurrences; however, it has been associated with fungemia in immunocompromised patients with central venous lines and should be avoided in critically ill patients [10]. A systematic review that included *S. boulardii* and three additional probiotics found that they significantly improved primary CDI prevention but none improved secondary prevention of CDI. Additional trials are needed [54].

Fecal microbiota transplantation has been explored as a treatment option for recurrent CDI or CDI in patients with immunocompromise, but availability is limited [55]. In 2018, the IDSA and SHEA recommended fecal microbiota transplantation for patients with multiple recurrences of CDI who failed appropriate antibiotic treatments [10]. The IDSA/SHEA 2021 focused update also recommends fecal microbiota transplantation (in addition to fidaxomicin) as a treatment option for recurrent CDI [24].

RECURRENCE OF DISEASE

The recurrence of symptoms following a successful course of therapy, and necessitating further treatment, remains a challenging problem. Up to 25% of patients treated for CDI have already experienced at least one previous episode [10]. In most cases, the recurrence of diarrhea represents relapse of the initial infection and is thought to be caused by residual vegetative spores that once again proliferate after therapy is lifted. The SHEA/IDSA guidelines list three options for re-treatment of a first recurrence of CDI [24]:

- Preferred: Fidaxomicin, 200 mg twice daily for 10 days, OR twice daily for 5 days followed by once every other day for 20 days
- Alternative: Use a prolonged tapered and pulsed vancomycin regimen if a standard regimen was used for the initial episode (e.g., 125 mg four times daily for 10 to 14 days, two times per day for a week, once a day for a week, and then every 2 to 3 days for 2 to 8 weeks)
- Vancomycin 125 mg four times daily for 10 days if metronidazole was used for the initial episode
- Adjunctive treatment: Bezlotoxumab 10 mg/kg IV once during administration of antibiotics

Options for treatment of a second or subsequent CDI recurrence include [24]:

- Fidaxomicin 200 mg twice daily for 10 days, OR twice daily for 5 days followed by once every other day for 20 days
- Vancomycin by mouth in a tapered/pulsed regimen, 125 mg 4 times daily for 10 days, followed by rifaximin 400 mg 3 times daily for 20 days
- Fecal microbiota transplantation. Appropriate antibiotic treatments for at least two recurrences (i.e., three CDI episodes) should be tried prior to fecal microbiota transplantation
- Adjunctive treatment: Bezlotoxumab 10 mg/kg IV once during administration of antibiotics

In a randomized trial, oral fidaxomicin was found to be superior to vancomycin in preventing a second relapse in patients with a single recurrence of prior CDI. At 28-day follow-up, the relapse rate in the group treated with fidaxomicin was 20%, compared to 36% in the group receiving oral vancomycin [47]. Fidaxomicin appears to be an important therapeutic option for treating relapses and limiting recurrent disease.

Because disruption of the indigenous bowel flora is a major component of symptomatic infection and relapse, selected patients with multiple relapses have been treated by the instillation of stool (fecal microbiota transplantation) from a healthy donor. The rationale is to restore normal flora, and success has been reported in several uncontrolled case series. As stated, fecal microbiota transplantation is recommended for patients with multiple recurrences of CDI who have failed appropriate antibiotic treatments [10]. However, the use of this technique is limited by availability and logistics, expense, lack of health insurance coverage, and the need to screen the donor for potentially transmissible infections.

In 2023, the U.S. Food and Drug Administration approved the first fecal microbiota product that is taken orally [87]. This product, sold under the brand name Vowst, is approved for individuals 18 years of age and older, following antibacterial treatment for recurrent CDI. The dosing regimen is four capsules taken once a day, orally, for three consecutive days. The agent contains live bacteria and is manufactured from human fecal matter that has been donated by qualified individuals. Although the donors and donated stool are tested for a panel of transmissible pathogens, it may carry a risk of transmitting infectious agents and/or containing food allergens [87].

Fulminant CDI should be treated with vancomycin 500 mg four times daily orally or by nasogastric tube. Consider adding rectal instillation of vancomycin for ileus. IV metronidazole (500 mg every eight hours) should be administered together with oral or rectal vancomycin, particularly if ileus is present [24].

PREVENTIVE MEASURES

A patient can be exposed to *C. difficile* through contact with a healthcare worker with transient hand colonization, a patient with CDI or colonization, and/or the contaminated environment. In order to be efficient, facilities often must adopt an infection control/prevention program that utilizes more than one method for minimizing exposure to *C. difficile*, including emphases on [56; 57]:

- Early detection
- Contact Precautions (e.g., gowns and gloves for contact with all patients with *C. difficile*)
- Strict hand hygiene with soap and water
- Controlling the number of patients per room
- Cleaning the area with 1:10 hypochlorite solution
- Disposable equipment
- Antibiotic stewardship

Institutions with high rates of CDI have found that they also have a high rate of asymptomatic *C. difficile*-colonized inpatients. Therefore, it is important to identify and treat these asymptomatic patients, as they potentially serve as a reservoir for horizontal spread of CDI to other patients, either by the environment or on the hands of medical personnel. Vancomycin has been found effective in the treatment of asymptomatic *C. difficile* but is associated with an increased risk for re-infection or prolonged carriage after treatment is stopped [10].

Hand hygiene is considered to be one of the cornerstones of the prevention of nosocomial transmission of *C. difficile*, as it is for many healthcare-acquired infections. Studies have confirmed that hand washing will reduce infections, but studies have also revealed that healthcare compliance with hand hygiene is poor [58]. Alcohol hand hygiene products have been viewed as a breakthrough for compliance and ease of hand hygiene [59; 60]. Unfortunately, the *C. difficile* spore is highly resistant to killing by alcohol. Mechanically washing with soap and water is much more effective, but even then only removes 90% of the pathogen load [61].

Contact Precautions, private rooms, and cohorting of patients with active CDI have had varied success. The use of gloves is essential in the control of the spread of the disease due to the difficulty of removing the spores from hands without the use of heavy-duty hand cleaners, which cannot be routinely used in healthcare settings.

Environmental Protection Agency (EPA)-registered products specific for inactivating C. *difficile* spores, should be used in units with high C. *difficile* rates. Combined use of appropriate hand hygiene, barrier precautions, and meticulous environmental cleaning, including use of an EPA-registered disinfectant appropriate for the level of risk, should effectively prevent spread of the organism [57; 62].

HAND HYGIENE

Although hand washing has been acknowledged as a clear necessity in the healthcare fields, consistent compliance with hand hygiene standards continues to be suboptimal. Despite the simplicity of the intervention, its substantial impact, and wide dissemination of the CDC guideline for hand hygiene, compliance with recommended hand hygiene has ranged from 16% to 81%, with an average of 30% to 50% [58; 61; 63; 64; 65]. Among the reasons given for the lack of compliance are inconvenience, understaffing, and damage to skin [61; 64]. Across facility systems and organizations, consistent hand hygiene performance is an ongoing issue requiring continual attention.

Hand hygiene is a simple and effective way to prevent healthcare-acquired infections, especially C. *difficile*. Several studies have documented the reduction of healthcare-associated infections by improving hand hygiene compliance among healthcare workers between episodes of patient contact, but barriers to effective hand washing persist. The development of effective alcohol-based handrub solutions addresses these concerns, and studies have demonstrated that these solutions have increased compliance [59; 60; 65]. Unfortunately, it was discovered that C. *difficile*, in its spore form, is highly resistant to killing by alcohol. Healthcare professionals who attempt to decontaminate their hands with alcohol-based products may simply displace spores over the skin surface, without much reduction in the risk of transmission to other patients under their care. Residual spores are readily transferred by a handshake after use of an alcohol-based handrub [66]. Studies have shown that although the implementation of alcohol-based products has decreased the rates of MRSA and vancomycin-resistant *Enterococcus* (VRE), the rates of CDI do not change [10; 66]. What does work is mechanical hand washing with soap and water after each contact with an infected patient. This practice physically removes the spores and reduces the likelihood of transmission. Therefore, hand hygiene should be performed with soap (or antimicrobial soap) and water before and after every contact with CDI patients, and gloves should be used and disposed of properly.

EDUCATION

Staff, patient, and visitor education can be key to hand hygiene compliance as well as compliance with all measures to prevent and control CDI. Staff education must include all staff, not simply medical, nursing, or healthcare staff. Housekeeping staff must know how to protect themselves and how to adequately disinfect surfaces, especially those most likely to be contaminated, such as floors, light switches, bedside rails, call buttons, and tables.

Frequent in-services on patient care units as well as during orientation can ensure that all staff members are reminded frequently about the necessary precautions to prevent CDI. Signs posted on alcohol handrub can remind staff that hand washing with soap and water is required in a room with a CDI patient. Another key to compliance with hand hygiene and any infection control measures is monitoring and feedback to staff regarding compliance.

Patients and visitors should also be instructed that hand washing is an essential practice, and instructions on proper hand hygiene should be provided. Although most individuals know to wash their hands before eating and after using the restroom, few do little more than remove obvious dirt. Good hand washing involves removing the skin oils where organisms can remain even when the hands look clean. A quick pass under the water faucet and fast dry with a towel removes visible dirt, but the oils and organisms remain.

To effectively remove the oils and organisms, the process should take at least 20 seconds—the amount of time it takes to sing the song "Happy Birthday." The hands should be soaped and rubbed vigorously for 15 seconds to create a good lather and to assure that all parts of each hand are soaped and rubbed well. Then the hands should be rinsed thoroughly and dried, preferably with a paper towel. The towel should be used to turn off the water and then properly thrown away. Such hand washing removes the oils that harbor the organisms. Some mistakenly think that hot water must be used to kill the organisms. Water hot enough to kill organisms would be too hot to touch. Warm water mainly adds to comfort and encourages better washing technique.

Considerations for Health Literacy and Non-English-Proficient Patients

In order to comply with hand washing and other prevention recommendations, patients require a clear understanding of the processes as well as expected infection control steps. The ability to understand health information and make informed health decisions, known as health literacy, is integral to good health outcomes [67]. Yet, the National Assessment of Adult Literacy estimated that only 12% of adults have "proficient" health literacy and 14% have "below basic" health literacy [68]. Rates of health literacy are especially low among ethnic minority populations and individuals older than 60 years of age [67]. Compounding the issue of health literacy is the high rate of individuals with limited English proficiency. According to U.S. Census Bureau data from 2021, more than 44.8 million Americans are foreign-born, and more than 25.5 million (8.2% of the population) speak English less than "very well" [69].

Clinicians should assess their patients' literacy level and understanding and implement interventions as appropriate. Healthcare professionals should use plain language in their discussions with patients who have low literacy or limited English proficiency. They should ask them to repeat pertinent information in their own words to confirm understanding, and reinforcement with the use of low-literacy or translated educational materials may be helpful.

Translation services should be provided for patients who do not understand the clinician's language. "Ad hoc" interpreters (family members, friends, bilingual staff members) are often used instead of professional interpreters for a variety of reasons, including convenience and cost. However, this should be avoided, as it impedes communication and compliance. Clinicians should also check with their state's health officials about the use of ad hoc interpreters, as several states have laws about who can interpret medical information for a patient [70]. Children should especially be avoided as interpreters, as their understanding of medical language is limited and they may filter information to protect their parents or other adult family members [70].

CONTACT PRECAUTIONS

The use of additional isolation techniques, such as Contact Precautions in addition to Standard Precautions, with patients with active CDI has been employed during breakouts with varied success. This addresses the transmission of *C. difficile* via patients with active CDI, but healthcare professionals' hands and the environment are equally efficient modes of disease transmission. Therefore, adhering to hand hygiene standards and stringent surface decontamination are equally important. The following descriptions of Contact Precautions are summarized from the 2007 Standard Precautions guideline and the 2017 SHEA/IDSA *C. difficile* guidelines [10; 56]. The CDC website also provides updated guidance for clinicians and healthcare facilities on prevention of CDI, including isolation precautions, disinfection and sterilization, and hand hygiene [71].

Patient Placement

When possible, patients with CDI should be accommodated in a private room with a dedicated toilet. When a private room is not available, place the patient in a room with a patient(s) who has active infection with the same micro-organism but with no other infection (cohorting). When a private room is not available and cohorting is not achievable, consider the epidemiology of the micro-organism and the patient population when determining patient placement. Consultation with infection control professionals is advised before patient placement.

Gloves and Handwashing

In addition to wearing gloves in accordance with Standard Precautions (when touching blood, body fluids, secretions, excretions, and contaminated items), wear gloves (clean, nonsterile gloves are adequate) when entering the room. During the course of providing care for a patient, change gloves after having contact with infective material that may contain high concentrations of microorganisms (e.g., fecal material and wound drainage). Remove gloves before leaving the patient's room, and wash hands immediately with an antimicrobial agent, preferably soap and water. After glove removal and hand washing, ensure that hands do not touch potentially contaminated environmental surfaces or items in the patient's room, to avoid transfer of microorganisms to other patients or environments.

Gown

In addition to wearing a gown as outlined under Standard Precautions (during procedures and patient-care activities likely to generate splashes or sprays), wear a gown (a clean, non-sterile gown is adequate) when entering the room if you anticipate that your clothing will have substantial contact with the patient, environmental surfaces, or items in the patient's room, or if the patient is incontinent or has diarrhea, an ileostomy, a colostomy, or wound drainage not contained by a dressing. Remove the gown before leaving the patient's environment. After gown removal, ensure that clothing does not contact potentially contaminated environmental surfaces, to avoid transfer of microorganisms to other patients or environments.

Patient Transport

Limit the movement and transport of the patient from the room to essential purposes only. If the patient is transported out of the room, ensure that precautions are maintained to minimize the risk of transmission of microorganisms to other patients and contamination of environmental surfaces or equipment.

Patient-Care Equipment

When possible, dedicate the use of noncritical patient-care equipment to a single patient (or cohort of patients infected or colonized with *C. difficile*) to avoid sharing between patients. If use of common equipment or items is unavoidable, then adequately clean and disinfect equipment with a sporicidal disinfectant that is equipment-compatible before use for another patient.

ENVIRONMENTAL SERVICES

Because *C. difficile* spore production can increase when exposed to nonchlorine-based cleaning agents and the spores are more resistant to commonly used surface disinfectants than vegetative cells, some investigators have recommended the use of dilute solutions of hypochlorite (1,600 ppm available chlorine) for routine environmental disinfection of rooms of patients with *C. difficile*-associated diarrhea or colitis, to reduce the incidence of *C. difficile* diarrhea, or in units with high *C. difficile* rates [57]. Acidified nitrite and preacetyl ions have also been found to effectively and safely destroy *C. difficile* spores [56].

Cleaning, Disinfecting, and Reprocessing Equipment

The guideline on disinfection and sterilization published by the CDC includes updated evidence-based recommendations on preferred methods for cleaning, disinfecting, and sterilizing medical devices and for cleaning and disinfecting the healthcare environment [57]. The guideline also addresses several new topics, including inactivation of antibiotic-resistant bacteria, bioterrorist agents, emerging pathogens, and bloodborne pathogens; disinfection of patient-care equipment used in ambulatory settings and home care; and new sterilization processes, such as hydrogen peroxide gas plasma and liquid peracetic acid [57].

DEFINITIONS OF LEVELS OF CLEANING AND DISINFECTION	
Level	**Definition**
Decontamination	Use of a 0.5% chlorine solution to reduce the number of pathogenic organisms on the device
Cleaning	Use of soap and water to remove all visible dust, soil, blood, or other body fluids
Low-level disinfection	Use of disinfectant to destroy pathogenic organisms (may not eliminate resistant bacteria or most viruses or fungi)
Intermediate-level disinfection	Use of disinfectant to destroy pathogenic organisms (eliminates most bacteria, viruses, and fungi)
High-level disinfection	Use of chemical disinfectants, boiling, or steaming to destroy all micro-organisms
Sterilization	Use of high-pressure steam (autoclave), dry heat (oven), chemical sterilants, or radiation to eliminate all forms of viable micro-organisms
Reprocessing	A multistep procedure that consists of meticulous cleaning, high-level disinfection with a liquid chemical sterilant or disinfectant, and proper drying
Source: [57; 72; 74]	*Table 1*

Various levels of cleaning and disinfection have been defined, and decontamination and cleaning must be carried out before any of the higher level processes (***Table 1***) [57; 72; 73; 74]. The cleaning and disinfection of devices varies according to the Spaulding classification, with critical devices requiring sterilization and semi-critical devices requiring high-level disinfection; noncritical devices may be cleaned with low-level disinfection [72; 73; 74; 75].

Endoscopic instruments present a challenge to proper reprocessing because of the complex internal design and long, narrow channels [72]. Trained and accredited personnel should carry out the reprocessing procedure according to the manufacturer's recommendations, and the process should be monitored regularly for quality control [76]. Guidelines and recommendations for reprocessing of gastrointestinal endoscopes have been developed by several federal agencies, such as the U.S. Food and Drug Administration and the CDC, as well as many professional organizations [72; 73; 76; 77; 78; 79]. The reprocessing procedure should begin immediately after use to prevent secretions from drying [57; 72; 78; 79].

Some inconsistencies across reprocessing guidelines and manufacturer recommendations have been found, primarily with regard to drying [78]. Also, various steps in the procedure have been emphasized as being the most critical. For example, one report notes that meticulous mechanical cleaning is the most important step because it removes the majority of the contaminating bacteria [76]. Some formulations based on peracetic acid are recommended by manufacturers for the cleaning step. However, one report notes that disinfection using peracetic acid may be insufficient if the preceding cleaning step is not performed adequately [80]. As stated, decontamination and cleaning must be carried out before any of the higher level processes.

Cleaning the Environment

Every healthcare facility should have a written housekeeping schedule for the routine cleaning of the environment. Routine cleaning removes so-called visible dirt, which can harbor micro-organisms. Soap and water can be used to remove visible dirt from most surfaces, such as walls, doors, ceilings, and floors. A disinfectant should be used when there are signs of contamination. The level of asepsis in cleaning depends on the likelihood of contamination. The World Health Organization suggests classifying areas within a healthcare facility into four zones [72]:

- Zone A: No patient contact
- Zone B: Care of patients who are not infected and are not highly susceptible
- Zone C: Infected patients (isolation units)
- Zone D: Highly susceptible patients (protective isolation) or protected areas, such as operating suites, delivery rooms, intensive care units, NICUs, transplant units, oncology units, and hemodialysis units

Cleaning according to this classification should be as follows [72]:

- Zone A: Normal cleaning
- Zone B: Cleaning procedures that do not raise dust. (Dry sweeping or vacuum cleaners are not recommended.) Use of a detergent solution and disinfection of any areas with visible contamination with blood or body fluids before cleaning.
- Zones C and D: Cleaning with a detergent/disinfectant solution, with separate cleaning equipment for each room

Written policies should specify how frequently each area should be cleaned and should note the cleaning agents used for various surfaces and items such as beds, curtains, screens, fixtures, and furniture. In general, all surfaces in the environment (e.g., walls, doors, floors) must be cleaned daily to remove soil. Sinks, toilets, and baths should be scrubbed daily, or more often if needed, with a disinfectant cleaning solution using a separate mop, brush, or cloth. Patient rooms should also be cleaned daily and after each patient is discharged. Surfaces and countertops in procedure rooms, examination rooms, and the laboratory must be cleaned with a disinfectant solution after any activity.

Spills of blood or other body fluid should be removed and cleaned immediately. The area should first be cleaned with a 0.5% chlorine solution and then washed clean with a disinfectant solution. Gloves should be worn while cleaning.

Managing Waste

Management of waste is a concern in healthcare facilities, but 75% to 90% of waste poses no risk of infection. The following types of waste are considered to be hazardous [72]:

- Infection-associated waste (from isolation units, laboratory cultures, tissue swabs)
- Pathologic waste (blood, body fluids, human tissue)
- Sharps (needles, scalpels, blades, knives)
- Pharmaceutical waste (expired pharmaceutical agents)
- Chemical waste (laboratory reagents, solvents)
- Heavy metal waste (broken blood pressure gauges, batteries)
- Radioactive waste

As with cleaning, written policies should document the appropriate handling, storage, and transportation of all types of waste.

FACILITY LAYOUT

Improving hospital layout can have a markedly positive effect on the transmission of *C. difficile* from patient to patient [81]. In a cohort study of nosocomial acquisition of CDI, it was noted that double rooms had a higher rate of acquisition than single rooms, as did the exposure of a patient to a roommate with a positive *C. difficile* culture [10]. Another study example compared an older hospital with fewer single beds, higher bed occupancy, a low use of broad-spectrum antibiotics, and no antibiotic stewardship program to a newer facility with these programs. The more modern hospital with more private rooms had a lower rate of CDI; however, it was impossible to elucidate causation [10]. The difficulty comes in finding studies that provide enough quality, evidence-based information that bears out the theory of hospital layout affecting the CDI rate [10].

EVIDENCE-BASED PRACTICE RECOMMENDATION

The IDSA and the SHEA recommend accommodating patients with CDI in a private room with a dedicated toilet to decrease transmission to other patients. If there is a limited number of private single rooms, prioritize patients with stool incontinence for placement in private rooms.

(https://www.idsociety.org/practice-guideline/clostridium-difficile. Last accessed September 11, 2023.)

Strength of Recommendation/Level of Evidence: Strong recommendation, moderate quality of evidence

ANTIMICROBIAL STEWARDSHIP

Research supports the fact that the great majority of patients with CDI have been recently administered antibiotics of some kind. However, antibiotic risk studies and prescribing intervention studies do not always consider exposure to *C. difficile* when assessing outcomes. In order to achieve a significant reduction in the incidence of CDI, it is necessary to limit the use of antibiotics known to increase risk for CDI. Antibiotics to be targeted should be based on the local epidemiology and the *C. difficile* strains present. Inpatient facilities should consider placing some restriction on use of fluoroquinolones, clindamycin, and cephalosporins (except for surgical antibiotic prophylaxis) [10]. The development of a healthcare facility program for appropriate antibiotic use is an important aspect of the control of *C. difficile*. Simply making lower risk agents available on the formulary is not sufficient; an antimicrobial stewardship program should be established [10].

Antimicrobial stewardship programs are interventions designed to ensure that hospitalized patients receive the right antibiotic, at the right dose, at the right time, and for the right duration [82]. These programs have been proven to improve patient outcomes, decrease length of hospital stays, and lower healthcare costs. Furthermore, research indicates that antimicrobial stewardship is one of two practices with good evidence of efficacy in preventing CDI [83]. As such, it is an essential aspect of preventing CDI in all healthcare settings. The core elements of a successful stewardship program are hospital leadership commitment, accountability, pharmacy expertise, implementation of interventions, tracking, reporting, and education [71; 82].

Despite this proven efficacy, antimicrobial stewardship remains underutilized throughout the United States. The CDC has recommended the integration of stewardship programs at all facilities with the expectation that this one intervention would effectively prevent CDI and save lives [82]. A stewardship program assessment tool from the CDC is available online at https://www.cdc.gov/antibiotic-use/healthcare/pdfs/assessment-tool-P.pdf.

PROBIOTICS

In the past, the administration of probiotics was thought to be an effective CDI preventive measure for patients receiving antibiotics. However, studies have not definitively shown them to be useful, although research has been difficult considering the diversity of probiotics used [84; 85]. Additional problems include the lack of standardization, variations in bacterial counts in the products due to duration of storage, and potential for bacteremia or fungemia induction.

One randomized trial showed that drinking a probiotic drink with specific lactobacillus strains twice daily reduced the risk of CDI in patients older than 50 years of age taking antibiotics [86]. The study, however, was limited to a small number of patients in a selected population and excluded those receiving high-risk antibiotics. Larger, more diverse studies are needed before this practice can be recommended.

SURVEILLANCE

All surveillance programs, whether or not an outbreak is present, must have a standard definition of infection; use lab-based data, if possible; and track epidemiologically important variables, depending upon the organism(s) in question. The data must be analyzed and the analysis results communicated to all pertinent departments [56].

If an outbreak of *C. difficile* is identified, action must be taken to contain and alleviate the infection. If breaks in technique are tied to the outbreak or transmission, steps must be taken to correct the behavior, including the initiation of education interventions [56].

ESTABLISHING A PREVENTION PLAN

Every facility should have a plan for both prevention and control of CDI. Many of the transmission/prevention activities are in place as routine infection control measures. The hospital risk assessment for CDI can provide the framework for a prevention plan, as it identifies the unique needs of a specific facility and individual units. A pediatric or day surgery unit might have a lower risk of CDI than the long-term geriatric unit [9]. It is essential to perform facility-wide surveillance for CDI, including nosocomial rates, and report the data to the infection control committee. Information and interventions should be shared with all units, and open communication with other preventionists and local health departments can allow for early identification of CDI arising in the community.

Standard Precautions are essential for all patients, but CDI patients must also have Contact Precautions. Dedicated equipment, gowns, and gloves upon entrance to the patient room are essential. In addition, an intensive hand hygiene program and strict antimicrobial stewardship have been crucial for a comprehensive CDI prevention program. Comprehensive education for visitors, patients, and healthcare workers must be maintained. Senior leadership should be aware of the CDI rates and resources needed to implement and maintain all measures for both prevention and control of CDI.

In the case of an outbreak, basic measures should be implemented immediately if they are not already in place [10]:

- Use of gowns and gloves on entry to the room of a patient with CDI
- Hand hygiene compliance increased
- Visitors and healthcare workers to wash hands with soap and water after caring for or contacting patients with CDI
- Patients with CDI placed in a private room. If a private room is not available, patients should be cohorted, providing a dedicated commode for each patient.
- Contact Precautions maintained for the duration of diarrhea

Routine identification of asymptomatic carriers is not recommended for infection control [10].

INFECTION CONTROL MEASURES

Basic infection control measures apply to all communicable diseases, including *C. difficile*. The most basic programs for prevention of the spread of infectious diseases include:

- Making infection prevention a priority for the facility
- Establishing a culture of infection prevention
- Utilizing specialists in infection control, establishing full-time equivalent physicians based on the needs of the patient population
- Allowing infection control practitioners the ability to initiate isolation and oversee patient placement without a physician order
- Including infection preventionists in the facility construction planning (e.g., to determine sink placement, hand hygiene availability, air handling and intake)
- Including infection preventionists in the acquisition of equipment
- Providing policies and procedures regarding visitor limitation if a patient is infected

Although these measures are not *C. difficile* specific, they are important for the prevention of its transmission [56].

PERFORMANCE MEASURES

Performance measures are often developed according to the researched risk for *C. difficile* occurrence in a specific facility. No matter the level of assessed risk, standard performance measures are necessary. They include [10]:

- Infection control practices that are consistent with guideline recommendations, including compliance with isolation precautions and adequacy of environmental cleaning
- Treatment of the initial CDI episode consistent with guidelines
- Appropriate testing for CDI, including submitting samples of only unformed stool

SUSTAINING QUALITY

One of the many issues affecting a facility's ability to attain quality measures and sustain them is the failure of healthcare providers to acknowledge the problem and commit to necessary changes. After performance improvement measures have been identified, they must be tailored to the practitioners and integrated into practice while building organization commitment. A practice that works in one system may require rearranging in order to work in another and be successfully sustained. It is essential to be inventive and adaptable to ensure that a change goes beyond current practice to sustained practice.

CASE STUDY

Patient P, a woman 50 years of age, has a history of rheumatoid arthritis and complicated diverticulitis. She had previously undergone a temporary colostomy and has now returned for reversal surgery. Her bowel surgery is uneventful. Because Patient P is a nurse and quite knowledgeable about the healthcare system, she is diligent in reminding staff to wash hands with soap and water, or use a hand sanitizer, before having contact with her or handling the equipment in her room.

After recovery and subsequent return to normal dietary activity, Patient P continues to have some discomfort in the lower abdomen, fails to gain weight, and develops a watery diarrhea. This persists despite multiple return visits to the surgeon's office. Eventually, the surgeon informs her that everything appears to be progressing satisfactorily from his perspective and that she should see her primary care physician or consider counseling for the symptoms. Unhappy with this assessment, she consults the infection control practitioner at the facility where she works and requests a test for *C. difficile*. The test is positive for *C. difficile* infection. Patient P is afebrile, having minimal pain, and estimates her diarrhea at 8 to 10 loose or watery stools per 24 hours. She is treated initially with metronidazole, 500 mg every eight hours for 10 days. She improves rapidly, and after one week of therapy, is now having one to 2 formed stools per 24 hours and notes improving appetite and sense of well-being. However, two weeks after the conclusion of therapy, at about the time she had planned to resume working, her diarrhea recurs and is rapidly approaching the original level of severity. She is retreated, but this time with vancomycin, 125 mg every six hours for 14 days, followed by a slow tapered dose over the subsequent three weeks. At six-weeks follow-up, she feels much improved. Her stool is formed, her bowel habits have returned to normal, and she has regained much of her lost weight. The patient and her physician are unsure whether she had been an asymptomatic carrier prior to admission (as a byproduct of her work exposure) or had acquired the infection due to hand carriage while in the hospital recovering from surgery. She wonders if earlier recognition, diagnostic consideration, and treatment might have led to a more rapid and satisfactory response to treatment, hastening her recovery and permitting a more rapid return to work.

CONCLUSION

With the 2017 and 2021 updates of the SHEA and IDSA guidelines for *C. difficile* infection, progress has been made in the standardization of diagnosis as well as identification of preventive methods to control the spread of CDI. However, in the past decade infecting strains have become more virulent, and symptomatic infection has spread to populations previously at low risk for CDI, such as healthy peripartum women. In addition to consistent implementation of infection control measures that limit transmission, the tight control of antimicrobial usage within hospitals has now been shown to be an important means for reducing the incidence of CDI.

At present, *C. difficile* transmission occurs primarily in healthcare facilities, but community-associated CDI also appears to be increasing [39; 40; 41]. This complicates prevention efforts, as sources of *C. difficile* in community settings are not always known [21]. Continued, diligent surveillance and the broader application of molecular epidemiologic techniques will be key strategies in the ongoing effort to monitor changes in the prevalent strain of *C. difficile* and to further clarify emerging epidemiologic trends in the incidence and transmission of infection.

Public awareness of resistant organisms, or "superbugs," is at an all-time high and affords healthcare professionals the opportunity to extend education to the general public, including visitors and discharged patients. Public visibility of the issue provides opportunities to slow the spread of the disease. Techniques that are tested and implemented now will be available to help combat any future contenders for "superbugs."

APPENDIX A

SAMPLE PATIENT/FAMILY EDUCATION REGARDING *CLOSTRIDIOIDES DIFFICILE*

What is *Clostridioides difficile*?

Clostridioides difficile is a bacterium that occasionally inhabits the bowel of normal, healthy people without causing problems. Under certain circumstances, this bacterium may begin to grow at a rapid rate and produce a toxin that causes diarrhea and potentially a serious form of bowel inflammation (colitis).

What is *C. difficile* infection?

Symptomatic *Clostridioides difficile* infection, or CDI, is the most common cause of infectious diarrhea in healthcare facilities. Symptoms include diarrhea, fever, and abdominal discomfort or tenderness. The condition arises as a complication of antibiotic use in sick or unhealthy persons. This is because the usage of certain antibiotics can alter the diversity and balance of (normal) bacterial populations within the bowel, allowing *C. difficile* to grow. When *C. difficile* multiplies, toxins are produced that can cause damage to the bowel. Fortunately, the great majority of patients receiving antibiotics do not develop this infection, even if ill from other conditions,

Who can develop *C. difficile* infection?

This infection is encountered most often in hospitals and nursing homes, but is being seen more frequently in the community, as a complication of antibiotic use in relatively healthy persons. The most vulnerable are the elderly, persons with chronic disease and impaired immunity, and those with ongoing serious illness.

How is this disease diagnosed?

There are many causes for diarrhea, and even among persons with diarrhea who are receiving antibiotics, only about 25% are caused by *C. difficile*. If you are currently on antibiotics or recently discontinued antibiotics and develop diarrhea, contact your doctor promptly. If symptoms persist, or worsen, after one to two days, the doctor can have a sample of your stool collected and sent to the lab for analysis for *C. difficile* toxins.

How is CDI treated?

Your doctor may prescribe a specific antibiotic, taken by mouth, that targets and kills *C. difficile*.

What can I do to help prevent *C. difficile* infection?

If you or a family member have CDI, remind all healthcare providers (including doctors and nurses) to wash their hands with soap and water, using proper handwashing technique, after having contact or being in the room with you. Wash your own hands after using the bathroom and before eating. Take antibiotics only as prescribed by your doctor.

Will I give *C. difficile* to my friends and family?

Visitors are not likely to get *C. difficile*, but they should wash their hands when entering and leaving the room.

What do I need to do when I go home from the hospital?

If you are given a prescription to treat *C. difficile*, take the medicine exactly as prescribed.

Wash your hands often, and instruct people who live with you to wash their hands often as well. If diarrhea recurs after completing a course of treatment, notify your doctor promptly.

Implicit Bias in Health Care

The role of implicit biases on healthcare outcomes has become a concern, as there is some evidence that implicit biases contribute to health disparities, professionals' attitudes toward and interactions with patients, quality of care, diagnoses, and treatment decisions. This may produce differences in help-seeking, diagnoses, and ultimately treatments and interventions. Implicit biases may also unwittingly produce professional behaviors, attitudes, and interactions that reduce patients' trust and comfort with their provider, leading to earlier termination of visits and/or reduced adherence and follow-up. Disadvantaged groups are marginalized in the healthcare system and vulnerable on multiple levels; health professionals' implicit biases can further exacerbate these existing disadvantages.

Interventions or strategies designed to reduce implicit bias may be categorized as change-based or control-based. Change-based interventions focus on reducing or changing cognitive associations underlying implicit biases. These interventions might include challenging stereotypes. Conversely, control-based interventions involve reducing the effects of the implicit bias on the individual's behaviors. These strategies include increasing awareness of biased thoughts and responses. The two types of interventions are not mutually exclusive and may be used synergistically.

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