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Role of the hospital environment in disease transmission, with a focus on *Clostridium difficile*

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Abstract. Contamination of the surface environment in hospital rooms plays an important role in the transmission of several key healthcare-associated pathogens including *Clostridium difficile*, methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococcus* spp. (VRE), *Acinetobacter* spp. and norovirus. *Clostridium difficile* is especially important as it is now the most common healthcare-associated pathogen in the United States. It may cause serious disease, especially in older individuals, it may survive for long periods of time in the environment and it is relatively resistant to many commonly used antiseptics and disinfectants.

Evidence that the contaminated surface environment is important in the transmission of *C. difficile* includes the following: (1) environmental contamination is frequent in the rooms of patients with *C. difficile* infection (CDI), (2) the hands/gloves of healthcare personnel are as likely to become contaminated from contact with the environment as from direct contact with the patient, (3) the higher the frequency of environmental contamination, the more frequent the contamination of the hands/gloves of healthcare providers, (4) patients admitted to a room previously occupied by a patient with CDI have an increased risk of developing *C. difficile* infection, and (5) improved cleaning/disinfection of the environment has led to a decrease in the incidence of *C. difficile* transmission.

Key measures to prevent *C. difficile* transmission and infection include antibiotic stewardship (minimising antibiotic use), placing patients with CDI on contact precautions, and proper cleaning and disinfection of the surfaces in hospital rooms daily and at discharge using a sporicidal disinfectant or a 'no-touch' method (e.g. ultraviolet light).

Additional keywords: environmental surfaces, disinfection, noncritical items.

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Introduction

Healthcare-associated infections remain an important source of morbidity and mortality with an estimated 1.7 million infections and 99 000 deaths annually in the United States. The major source of nosocomial pathogens is thought to be the patient's endogenous flora, but an estimated 20–40% of healthcare-associated infections have been attributed to cross-infection via the contaminated hands of healthcare personnel.[1] Contamination of the hands of healthcare personnel could in turn result from either direct patient contact or indirectly from touching contaminated environmental surfaces. Healthcare personnel have frequent contact with the environmental surfaces in patients' rooms, providing ample opportunity for contamination of gloves and/or hands.[2] Two recent studies demonstrated that contact with the environment was just as likely to contaminate the hands of healthcare workers as was direct contact with the patient.[3,4] Further, it has been observed that there is lower compliance with hand hygiene by healthcare personnel following contact with the patient's environment than directly with the patient.[5]

There is excellent evidence in the scientific literature that environmental contamination plays an important role in the transmission of several key healthcare-associated pathogens including methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococcus* (VRE), *Acinetobacter*, norovirus, and *Clostridium difficile*.[6–9] All these pathogens have been demonstrated to persist in the environment for hours to days (in some cases months),[10] to frequently contaminate the environmental surfaces in rooms of colonised or infected patients, to transiently colonise the hands of healthcare personnel, to be transmitted by healthcare personnel, and to cause outbreaks in which environmental

Implications

- *Clostridium difficile* infection (CDI) is a growing problem in many countries as it can cause serious and even life-threatening infection, especially in the elderly.
- There is growing scientific evidence that contamination of surfaces in rooms that house patients with CDI plays an important role in the transmission of CDI in healthcare facilities.
- Improved infection prevention strategies including antibiotic stewardship, appropriate contact precautions, hand hygiene and improved cleaning with a sporicidal agent will decrease the risk of *C. difficile* transmission.

transmission was deemed to play a role. Further, admission to a room in which the previous patient had been colonised or infected with MRSA, VRE, *Acinetobacter* or *C. difficile* has been shown to be a risk factor for the newly admitted patient to develop colonisation or infection.[11–13] This paper will review the scientific evidence demonstrating that the contaminated environment plays an important role in the transmission of pathogens with a focus on *C. difficile*. We will also review currently recommended methods to reduce the risk of environmentally mediated transmission of *C. difficile* and discuss products, practices and technologies to disinfect hospital room surfaces and equipment. This paper will expand and update recent publications of this same topic.[8,14]

Clostridium difficile

Clostridium difficile, a Gram-positive, anaerobic bacteria, was first isolated from stool in 1935. It is part of the normal intestinal flora in humans and is carried by ~3% of healthy adults and 20% to 30% of hospitalised adults. *C. difficile* exists in both vegetative and spore forms; in the colon, it exists as a vegetative cell, whereas, outside the colon, it survives in spore form.[8,15] It is now recognised as the major cause of antibiotic-associated colitis. Colonisation of the intestinal tract occurs via the fecal–oral route. *C. difficile* infection (CDI) occurs in a colonised patient when antibiotic therapy disrupts the colonic microflora leading to proliferation of *C. difficile* with release of toxin A (enterotoxin) and/or toxin B (cytotoxin), which results in mucosal injury and inflammation. Antibiotic use is the most commonly recognised risk factor for CDI. The risk factors for CDI are well understood and include older age and the receipt of certain drugs especially antibiotics. Therefore, an important preventive method is antibiotic stewardship, limiting antibiotics to appropriate clinical situations and, when feasible, choosing antibiotics with a lower potential to precipitate CDI[15–17].

Over the past decade, an increasing incidence has been recognised both for *C. difficile* infection (CDI) and severe or fatal CDI.[16–20] *USA Today* reported that *C. difficile* caused 346 800 hospitalisations and more than 30 000 deaths in the United States in 2010 which represented a greater than four-fold increase in hospitalisations from 1993.[21] A recent study conducted among 10 community hospitals in the south-eastern United States reported that healthcare-associated CDI was 25% more common than MRSA infection.[22] Associated with the increase in CDI has been the spread of a new *C. difficile* strain throughout the United States that is characterised as restriction endonuclease analysis group B1, North American pulsed-field gel electrophoresis type 1 (NAP 1), ribotype 027, and toxinotype III. This strain is also characterised by increased production of toxins A and B, production of a binary toxin and fluoroquinolone resistance. It particularly impacts patients greater than 65 years of age with healthcare exposure such as residence in a nursing home.[15]

C. difficile is acquired by fecal–oral transmission. In the healthcare setting, three mechanisms of transfer of *C. difficile* are possible: (1) direct transfer of *C. difficile* from a colonised or infected patient to the environment (e.g. rectal thermometer, commode, over-the-bed-table) and contact by another patient with inoculation into the mouth or directly into the colon; (2) direct transfer from a colonised or infected patient to a healthcare worker via contact and transfer via hands to a noncolonised or noninfected patient; and (3) indirect transfer via healthcare worker contact (or any other person) with the contaminated environment or equipment, and transfer to a noncolonised or noninfected patient.

Evidence that the contaminated environment plays a role in transmission of *Clostridium difficile*

Several microbiological features of *C. difficile* promote environmental survival and transmission of this pathogen. These include prolonged environmental survival of spores, low inoculating dose (based on animal studies),[23] frequent environmental contamination, continued environmental contamination despite treatment of symptomatic patients, transmission via contaminated medical devices, and relative resistance to germicides. In recent years there has been growing evidence that contamination of room surfaces and equipment plays an important role in the transmission of *C. difficile* between patients (Box 1).

Environmental survival

Vegetative *C. difficile* bacilli survive for only a short time on hospital surfaces. While vegetative bacilli die rapidly on dry surfaces, they remain viable for up to 6 h on moist surfaces at room temperature.[24] On the other hand, bacterial spores are highly resistant to drying, heat, and chemical agents.[25] Kim and colleagues reported that *C. difficile* inoculated onto a floor persisted for 5 months.[26]

Frequency and level of environmental contamination

In 1989, McFarland and colleagues reported that 49% of rooms occupied by symptomatic patients with *C. difficile* were contaminated and 29% of rooms occupied by

Box 1. Evidence of the role of environmental contamination in patient-to-patient transmission

- Frequent contamination of surfaces in rooms of patients with CDI
- Frequent contamination of equipment in rooms of patients with CDI
- Contamination may be found in hospital rooms of patients without CDI
- Frequent contamination of hands or gloves of healthcare providers caring for patients with CDI
- Frequency of hand contamination of healthcare providers correlated with frequency of environmental contamination
- Frequency of CDI correlates with frequency of environmental contamination
- Person-to-person transmission of *C. difficile* demonstrated using molecular typing in clusters and outbreaks
- Being admitted to room whose previous occupant had CDI is a risk factor for development of CDI
- Enhanced environmental disinfection (with hypochlorites) has been part of interventions that control *C. difficile* outbreaks
- Improved room disinfection had been demonstrated to lead to decreased rates of CDI

asymptomatic patients were contaminated.[27] Since that study, numerous other studies have demonstrated widespread and frequent contamination on hospital surfaces and equipment in the rooms of patients with CDI.[26,28–33] In these reports, the frequency of *C. difficile* recovered from environmental surfaces in the rooms of patients with *C. difficile* was as follows: Kim *et al.*, 9.3%;[26] Kaatz, 31.4%;[28] Samore, 58%;[29] Pulvirenti *et al.*, 14.7%, 2.9%;[30] McCourbrey, 14%;[31] Martirosian, 12.2%;[32] and Dubberke *et al.*, 27%.[33] Moreover, *C. difficile* has been isolated from surfaces in rooms of patients not colonised or infected with *C. difficile*, although with a lower frequency.[26,33–35] Other studies have also demonstrated a high frequency of environmental contamination but did not specify whether samples were collected from rooms of colonised or infected patients.[36–44] The frequency of environmental contamination has been associated with the time-course and treatment status of patients with CDI. Sethi and co-workers demonstrated that the frequency of environmental contamination was highest before treatment, remained high at the time of resolution of diarrhoea (37%), was lower at the end of treatment (14%), but again increased 1–4 weeks after treatment (50%).[45] Contamination of such rooms is likely a result of the prolonged survival of *C. difficile* spores coupled with inadequate terminal room cleaning and disinfection. In addition to hospital rooms, *C. difficile* has been recovered from physician and nurse work areas including telephones and computer keyboards.[46] As *C. difficile* spores have been isolated from the air, aerial disseminating of spores may in part account for widespread environmental contamination in work areas and rooms not occupied by colonised or infected patients.[47,48]

Most studies that evaluated the level of microbial contamination of the environment reported that surfaces were contaminated with <1–2-$\log_{10}$*C. difficile*.[26,28,29,34,49] However, two studies have demonstrated somewhat higher levels of contamination.[50,51] One study reported 1 to >200 *C. difficile* colonies,[50] while a second study that sampled several sites with a sponge found up to 1300 colonies.[51] Importantly, the frequency of acquisition of *C. difficile* has been linked with the level of environmental contamination.[29,44,52] For example, Fawley and colleagues reported that in a ward with endemic *C. difficile*, the incidence of CDI correlated significantly with the prevalence of environmental *C. difficile* in ward areas closely associated with patients and healthcare personnel.[52]

C. difficile has also been isolated from medical devices such as ultrasound machines, ECG machines, pulse oximeters and blood pressure cuffs[30,46,53] and personal equipment such as stethoscopes and flashlights.[34,54] McFarland demonstrated in 1981 that a contaminated portable commode chair was responsible for secondary spread to eight other patients on the ward within the span of one week.[27] A before-and-after study[55] and a crossover study[56] have demonstrated that switching from electronic rectal thermometers to either tympanic or disposable thermometers, respectively, resulted in a decreased incidence of CDI.

Frequency of hand contamination of patients and healthcare personnel

Clostridium difficile has commonly been isolated from the skin and hands of infected patients.[35,45,57] Sethi and colleagues demonstrated that the frequency of skin contamination of patients with CDI was similar to the frequency of stool detection.[45]

C. difficile has also been frequently isolated from the hands of healthcare personnel providing care to patients with CDI.[26,29,35,36] The frequency of positive hand cultures for healthcare personnel has been shown to be strongly correlated with the intensity of environmental contamination.[29,35,44] For example, hand contamination was 0% when environmental contamination was 0–25%, 8% when environmental contamination was 26–50% and 36% when environmental contamination was greater than 50%.[29] Bobulsky demonstrated that contact with the skin of a patient with CDI would lead to 1 to >100 colonies on the gloves of an investigator; contact with the skin yielded the highest number of colonies.[57] In a recent study, Guerrero and colleagues reported that acquisition of *C. difficile* spores on gloved

hands was as likely after contact with commonly touched environmental surfaces (e.g. bed rails, bedside table) as after contact with commonly examined skin sites (i.e. chest, arm, hand).[4] Importantly, *C. difficile* has been isolated from the hands of healthcare personnel on wards without any known infected patients.[35]

Evidence of person-to-person transmission using molecular typing

Patient-to-patient transmission of *C. difficile* has been demonstrated by time-space clustering of incident cases using molecular typing.[27,28,30,58,59] Over time increasingly sophisticated methods of molecular typing have been used to demonstrate person-to-person transmission of *C. difficile*.

Other evidence of the role of environmental contamination

Being admitted to a room previously occupied by a patient with CDI has been demonstrated to be a risk factor for the development of CDI.[12,60,61] In a multivariate analysis of risk factors for acquisition of CDI, Shaughnessy reported that the hazard ratio for admission to a room whose previous occupant had CDI was 2.35 (strongest risk factor in the analysis).[12] Monsieur and colleagues described nine patients who developed *C. difficile* during their hospitalisation; four of these patients stayed in rooms where the previous patients had CDI and all acquired a type of *C. difficile* that was isolated from a previous patient.[61]

Improved room disinfection has led to decreased rates of CDI.[28,44,51,62,63].

Prevention of *Clostridium difficile* transmission due to the contaminated environment

Several guidelines are available from professional organisations that detail methods to prevent CDI in healthcare facilities.[64–67] In addition, several excellent reviews have summarised the methods to prevent CDI.[20,68,69] Key preventive measures include reducing the use of medications that are known to precipitate CDI, placing patients with CDI on Contact Precautions with use of gloves and gowns and appropriate hand hygiene, and improved room disinfection with sporicidal agents. New technologies for room disinfection are being investigated including 'no-touch' methods and self-disinfecting surfaces.

Hand hygiene

The *Guideline for Hand Hygiene in Health-Care Settings* states that 'none of the agents (including alcohols, chlorhexidine, hexachlorophene, iodophors, PCMX, and triclosan) used in antiseptic handwash or antiseptic hand-rub preparations are reliably sporicidal'.[70] Human challenge studies with *Bacillus atrophaeus* (surrogate for *C. difficile*), a spore-forming bacteria, revealed that a waterless rub containing 61% ethanol was ineffective in eliminating spores but that hand washing with soap and water, or water and 2% chlorhexidine gluconate eliminated 1.5–2.0-$\log_{10}$ spores with a 10, 30, or 60 s wash.[71] Human challenge studies with *C. difficile* have revealed that hand washing with soap and water (or water and an antiseptic) is significantly more effective at removing *C. difficile* spores from the hands of volunteers than alcohol-based hand rubs.[72,73] In general, alcohol-based hand rubs were equivalent to no intervention. Water and soap or water and chlorhexidine have similar efficacy on bare hands,[74] likely due to emulsification of spores and physical removal from the hands via vigorous washing. In addition, the use of disposable gloves has been shown to significantly reduce hand contamination of healthcare workers. Importantly, one study demonstrated that handshaking transferred a mean of 30% of the residual *C. difficile* spores to the hands of recipients.[73]

Despite the evidence that hand washing with soap and water (or an antiseptic soap) is superior to the use of waterless alcohol-based hand rubs for removing *C. difficile* in human challenge studies, current guidelines continue to recommend the widespread use of alcohol-based hand rubs to reduce the overall incidence of healthcare-associated infections. The Society for Healthcare Epidemiology of America/ The Infectious Disease Society of America (SHEA/IDSA) Guideline on *C. difficile* recommends that in a 'setting in which there is an outbreak or an increased CDI rate, instruct visitors and healthcare workers to wash hands with soap (or antimicrobial soap) and water after caring for or in contact with patients with CDI'.[65] However, the recommendations in Australia state that alcohol-based hand rubs may be used for hand hygiene when caring for patients with CDI provided the health care worker wore gloves.[75] They state if hands become soiled or gloves have not been used then hands must be washed with soap (or antimicrobial soap) and water. Further studies need to be done to define whether the routine use of soap and water when caring for CDI patients even when gloves are worn reduced the risk of CDI transmission.[75] Multiple studies have reported that increased use of alcohol-based hand rubs was not associated with an increase in CDI and was often associated with a reduction of healthcare-associated infections.[76–81]

Hospitalised patients with CDI should be placed on Contact Precautions: private room, use of gloves and gowns by both healthcare providers and visitors when entering the room, limiting patient movement throughout the hospital, preferential use of dedicated patient care equipment, and disinfection of all shared patient care equipment between patients. The current Centers for Disease Control and Healthcare Infection Control Practices Advisory Committee (CDC/HICPAC) *Guideline on Isolation Precautions* recommends that healthcare providers caring for patients with CDI use soap and water for hand hygiene rather than waterless antiseptic handrubs.[82]

Improved cleaning with sporicidal agents

Multiple studies have demonstrated that surfaces in hospital rooms are poorly cleaned during terminal cleaning. Although methods of assessing the adequate cleaning varied (i.e. visibly

clean, ATP, fluorescent marker, aerobic plate counts), several studies have demonstrated that less than 50% of many surfaces are cleaned.[83–86] Similar deficiencies have been reported for cleaning of portable medical equipment.[87] Despite terminal cleaning of hospital rooms, many surfaces remain contaminated with *C. difficile* spores.[51] This occurs because many rooms are inadequately cleaned by environmental service workers and *C. difficile* is not susceptible to most commonly used surface disinfectants (i.e. phenolics and quaternary ammonium compounds).

Surface disinfectants such as 70% isopropanol,[25] phenols,[25] and quaternary ammonium compounds[25,88] are not sporicidal. Further, exposure to a cleaning agent or disinfectant has been shown to increase the sporulation rate of *C. difficile*.[89,90] In a comprehensive study of 32 disinfectants using a suspension test and only 1 and 60 min exposure times, only chlorine dioxide products achieved a >4-$\log_{10}$ reduction in *C. difficile* spores under both clean (0.3% albumin) and dirty (3% albumin) conditions.[91] Products based on hypochlorites, triamine or a hypochlorite-based mixture only achieved a >4-$\log_{10}$ reduction after 60 min in clean and dirty conditions. Sodium hypochlorite has been demonstrated to be effective in killing *C. difficile* spores.[89,92–94] However, the killing is both time- and concentration-dependent and up to 5–10 min may be required to achieve a greater than 3-$\log_{10}$ reduction, especially with concentrations of less than 1000–3000 ppm.[92,93,95] Perez *et al.* showed acidified bleach and regular bleach at 5000 ppm proved to be the most reliable to inactivate *C. difficile* spores by ≥99.9999% in 3–10 min.[92] Rutala and colleagues found that wiping with a 1 : 10 dilution of bleach (6000 ppm chlorine) eliminated ≥3.90-$\log_{10}$ *C. difficile* by a combination of inactivation and physical removal.[96] In a suspension test, an improved hydrogen peroxide product (0.5% hydrogen peroxide) demonstrated a ~2-$\log_{10}$ reduction of *C. difficile* spores compared with the >5-$\log_{10}$ decreased achieved with 5000 ppm sodium hypochlorite at 1 min.[95]

The use of 1 : 10 diluted household bleach (hypochlorite) solutions for surface disinfection have been demonstrated to reduce CDI rates when used either in outbreak settings or when hyperendemic rates of CDI have been documented.[28,63,97–100] For example, Mayfield and colleagues demonstrated that initiation of room disinfection with 1 : 10 hypochlorite led to a decrease in CDI from 8.6 to 3.3 cases per 1000 days ($P < 0.05$) in a bone marrow transplant unit.[97] Reverting back to a quaternary ammonium compound resulted in an increase in CDI to 8.1 cases per 1000 patient-days. Similarly, a before-and-after study using bleach wipes (0.55% active chlorine) for both daily and terminal cleaning, Orenstein and colleagues demonstrated a reduction of *C. difficile* on two wards for which *C. difficile* was hyperendemic (ward A dropped from 24.2 cases per 10 000 hospital-days to 3.5 cases while ward B dropped from 24.1 cases per 10 000 hospital-days to 3.7 cases).[63] While cleaning by environmental service workers has been shown to be effective in reducing *C. difficile* contamination in hospital rooms, surface disinfection with diluted bleach applied by research staff was even more effective.[49]

The CDC and HICPAC recommend consistent environmental cleaning and disinfection be used as one of the control measures for *C. difficile* and that 'hypochlorite solutions (5000 ppm) may be required if transmission continues.'[82] The 2008 IDSA/SHEA *Clostridium difficile* Guideline recommended that 'facilities should consider using a 1 : 10 dilution of sodium hypochlorite (household bleach) for environmental disinfection in outbreak settings and settings of hyperendemicity in conjunction with other infection prevention and control measures… the bleach solution should have a contact time of at least 10 minutes'.[64] The 2010 IDSA/SHEA *Clostridium difficile* Guideline recommends using a 'chlorine-containing cleaning agent or other sporicidal agent to address environmental contamination in areas with increased rates of CDI'.[65] The Association for Professionals in Infection Control and Epidemiology (APIC) also recommends a 1 : 10 dilution of hypochlorite for use when there is ongoing transmission, but they recommend a contact time of 1 min for nonporous surfaces.[67] Multiple surface disinfectants are now Environmental Protection Agency-registered as effective against *Clostridium difficile*; most contain sodium hypochlorite but several other germicides have also been registered (ethaneperoxoic acid/hydrogen peroxide, silver, terraacetylethylenediamine).[101] Current evidence suggests that the APIC recommendation for contact time (i.e. 1 min) is adequate to inactive *C. difficile* spores based on the relatively low numbers of *C. difficile* contaminating specific environmental surfaces. At University of North Carolina Health Care, we use a sporicidal solution (5000 ppm chlorine) in all CDI rooms for routine daily and terminal cleaning. This is done by one application of the sporicide covering all hand contact surfaces to allow sufficient wetness for >1 min contact time. All the guidelines emphasise the need to provide adequate cleaning of all surfaces in the room. Ideally, noncritical patient care items, such as blood pressure cuffs, stethoscopes, and thermometers should be dedicated to a single patient with CDI. When this is not possible, adequate cleaning and disinfection of shared items between patients should be ensured.

'No touch' methods for room decontamination

New 'no touch' methods have recently been introduced that provide room decontamination. The most promising of these methods uses either ultraviolet light[9,102,103] or hydrogen peroxide systems.[102,104,105] The advantages and limitations of ultraviolet (UV) and hydrogen peroxide devices have been reviewed.[9] As the different UV room decontamination devices and hydrogen peroxide systems differ in important aspects, each device should be validated in the scientific literature to reduce environmental contamination and ideally, as a method to prevent healthcare-associated infection.

Conclusions

C. difficile is an increasingly problematic infectious diarrhoea and healthcare-associated pathogen. Preventing these infections will require improved antibiotic stewardship, rapid identification and use of Contact Precautions for patients with CDI and enhanced environmental disinfection.

Conflict of interest

Dr Rutala provides consultation to Advanced Sterilisation Products and Clorox and Dr Weber provides consultative service to Clorox.

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