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Role of the environment in the transmission of *Clostridium difficile* in health care facilitiesDavid J. Weber MD, MPH<sup>a,b,\*</sup>, Deverick J. Anderson MD, MPH<sup>c</sup>, Daniel J. Sexton MD<sup>c</sup>, William A. Rutala PhD, MPH<sup>a,b</sup><sup>a</sup> Department of Medicine, University of North Carolina at Chapel Hill, Chapel Hill, NC<sup>b</sup> Department of Hospital Epidemiology, UNC Health Care, Chapel Hill, NC<sup>c</sup> Division of Infectious Disease, Duke University, Durham, NC

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Disinfection  
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Room contamination

Recent data demonstrate that the contaminated hospital surface environment plays a key role in the transmission of *Clostridium difficile*. Enhanced environmental cleaning of rooms housing *Clostridium difficile*-infected patients is warranted, and, if additional studies demonstrate a benefit of “no-touch” methods (eg, ultraviolet irradiation, hydrogen peroxide systems), their routine use should be considered.

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*Clostridium difficile*, a gram-positive, anaerobic bacteria, was first isolated from stool in 1935. It is now recognized as the major cause of antibiotic-associated colitis.<sup>1</sup> Over the past decade, an increasing incidence has been recognized both for *C difficile* infection (CDI) and severe or fatal CDI.<sup>2-6</sup> USA Today reported that *C difficile* caused 346,800 hospitalizations and more than 30,000 deaths in the United States in 2010, which represented a greater than 4-fold increase in hospitalizations from 1993.<sup>7</sup> A recent study conducted among 30 community hospitals in the southeastern United States reported that health care-associated CDI was 21% more common than methicillin-resistant *Staphylococcus aureus* infection.<sup>8</sup> Associated with the increase in CDI has been the spread of a new *C difficile* strain throughout the United States that is characterized as restriction endonuclease analysis group B1, North American pulsed-field gel electrophoresis type 1 (NAP 1), also described as ribotype 027 and toxinotype III. This strain is also characterized by increased production of toxins A and B, production of a binary toxin, and fluoroquinolone resistance and particularly impacts patients >65 years of age with health care exposure such as nursing home resident.

The major mechanism of transmission of health care-associated pathogens among patients has been thought to be patient-to-patient transmission via the hands of health care providers.<sup>9</sup> Over the past decade, there has been a growing appreciation that environmental contamination of the surfaces and equipment in

patient's rooms makes an important contribution to hospital-acquired infection with methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant *Enterococcus* species, norovirus, *Acinetobacter* species, and *C difficile*.<sup>10-12</sup> This paper will review the scientific evidence demonstrating that the contaminated environment plays an important role in the transmission of *C difficile*. We will also review currently recommended methods to reduce the risk of environmental-mediated transmission of *C difficile* and discuss potential future technologies under development to disinfect hospital room surfaces and equipment. This paper will expand and update recent publications on this same topic.<sup>13,14</sup>

#### EVIDENCE THAT THE CONTAMINATED ENVIRONMENT PLAYS A ROLE IN TRANSMISSION OF *C DIFFICILE*

A number of microbiologic features of *C difficile* promote environmental survival and transmission of this pathogen (Table 1). These include prolonged environmental survival of spores, low inoculating dose (based on animal studies), frequent environmental contamination, continued environmental contamination despite treatment of symptomatic patients, 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 (Table 2).

#### Environmental survival

Vegetative *C difficile* bacilli survive for only a short time on hospital surfaces. Whereas vegetative bacilli survive for only 15 minutes on surfaces exposed to room air, they remain viable for

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**Table 1**

Microbiologic features of *Clostridium difficile* that favor a role for environmental transmission

- Stable in the environment for prolonged periods of time (spore forming bacillus)
- Low inoculating dose (based on animal studies)
- Relative resistance to germicides (antiseptics and disinfectants)
- Fecal-oral transmission

**Table 2**

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 HCP caring for patients with CDI
- Frequency of hand contamination of HCP 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

up to 6 hours on moist surfaces at room temperature.<sup>15,16</sup> On the other hand, bacterial spores are highly resistant to drying, heat, and chemical agents.<sup>17</sup> Kim et al reported that *C difficile* inoculated onto a floor persisted for 5 months.<sup>18</sup> Neither storage temperature (4°C, -20°F) nor multiple cycles of refrigeration/freezing and thawing have been found to affect the viability of *C difficile* vegetative cells or spores.<sup>19</sup>

#### Frequency and level of environmental contamination

In 1989 McFarland et al reported that 49% of rooms occupied by symptomatic patients with *C difficile* were contaminated and that 29% of rooms occupied by asymptomatic patients were contaminated.<sup>20</sup> Since that study, numerous other studies have demonstrated widespread and frequent contamination on hospital surfaces and equipment in the rooms of patients with CDI.<sup>18,21-26</sup> 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%<sup>18</sup>; Kaatz et al, 31.4%<sup>21</sup>; Samore et al, 58%<sup>22</sup>; Pulvirenti et al, 14.7%, 2.9%<sup>23</sup>; McCoubrey et al, 14%<sup>24</sup>; Martirosian et al, 12.2%<sup>25</sup>; and Dubberke et al, 27%.<sup>26</sup> Moreover, *C difficile* has been isolated from surfaces in rooms of patients not colonized or infected with *C difficile*, although with a lower frequency.<sup>18,26-28</sup> Other studies have also demonstrated a high frequency of environmental contamination but did not specify whether samples were collected from rooms of colonized or infected patients.<sup>29-37</sup> The frequency of environmental contamination has been associated with the time-course and treatment status of patients with CDI. Sethi et al demonstrated that the frequency of environmental contamination was highest prior to treatment, remained high at the time of resolution of diarrhea (37%), was lower at the end of treatment (14%), but again increased 1 to 4 weeks after treatment (50%).<sup>38</sup> Contamination of such rooms is likely a reflection of both the prolonged survival of *C difficile* spores and 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.<sup>39</sup> Because *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 colonized or infected patients.<sup>40,41</sup>

Most studies that evaluated the level of microbial contamination of the environment reported that surfaces were contaminated with <1- to 2-log<sub>10</sub> *C difficile*.<sup>18,21,22,27,42</sup> However, some studies have reported somewhat higher levels of contamination.<sup>43,44</sup> Two studies reported >2-log<sub>10</sub> *C difficile* on surfaces; one reported "1 to >200" colonies,<sup>43</sup> and a second study that sampled several sites with a sponge found up to 1,300 colonies.<sup>44</sup> Importantly, the frequency of acquisition of *C difficile* has been linked with the level of environmental contamination.<sup>22,37,45</sup> For example, Fawley et al 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 health care personnel (HCP).<sup>45</sup>

*C difficile* has also been isolated from medical devices such as ultrasound machines, electrocardiogram machine's blood, pulse oximeters, blood pressure cuffs,<sup>23,39,46</sup> and personal equipment such as stethoscopes and flashlights.<sup>27,47</sup> McFarland et al demonstrated in 1981 that a contaminated portable commode chair was responsible for secondary spread to 8 other patients on the ward within the span of 1 week.<sup>20</sup> A before-and-after study<sup>48</sup> and a cross-over study<sup>49</sup> 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 health care personnel

*Clostridium difficile* has commonly been isolated from the skin and hands of infected patients.<sup>28,38,50</sup> Sethi et al demonstrated that the frequency of skin contamination of patients with CDI was similar to the frequency of stool detection.<sup>38</sup>

*C difficile* has also been frequently isolated from the hands of health care personnel providing care to patients with CDI.<sup>8,22,28,29</sup> The frequency of positive hand cultures for health care personnel has been shown to be strongly correlated with the intensity of environmental contamination.<sup>22,28,37</sup> For example, hand contamination was 0% when environmental contamination was 0% to 25%, 8% when environmental contamination was 26% to 50%, and 36% when environmental contamination was greater than 50%.<sup>22</sup> Bobulsky et al 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.<sup>50</sup> In a recent study, Guerrero et al reported that acquisition of *C difficile* spores on gloved hands was as likely after contact with commonly touched environmental surfaces (eg, bed rails, bedside table) as after contact with commonly examined skin sites (ie, chest, arm, hand).<sup>51</sup> Importantly, *C difficile* has been isolated from the hands of health care personnel on wards without any known infected patients.<sup>28</sup>

#### 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.<sup>20,21,23,45,52,53</sup> 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 previous occupied by a patient with CDI has been demonstrated to be a risk factor for the development

of CDI.<sup>54-56</sup> In a multivariate analysis of risk factors for acquisition of CDI, Shaughnessy et al reported that the hazard ratio for admission to a room whose previous occupant had CDI was 2.35 (strongest risk factor in the analysis).<sup>56</sup> Monsieur et al described 9 patients who developed *C difficile* during their hospitalization; 4 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.<sup>55</sup> Improved room disinfection has led to decreased rates of CDI.<sup>21,37,44,57,58</sup>

## PREVENTION OF *C DIFFICILE* TRANSMISSION BECAUSE OF CONTAMINATED ENVIRONMENT

Several guidelines are available from professional organizations that detail methods to prevent CDI in health care facilities.<sup>59-62</sup> In addition, several excellent reviews have summarized the method to prevent CDI.<sup>6,63,64</sup> 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 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, iodophores, PCMX, and triclosan) used in antiseptic handwash or antiseptic hand-rub preparations are reliably sporicidal.”<sup>65</sup> 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 handwashing with soap and water or water and 2% chlorhexidine gluconate eliminated 1.5- to 2.0- $\log_{10}$  spores with a 10-, 30-, or 60-second wash.<sup>66</sup> Human challenge studies with *C difficile* have revealed that handwashing with soap and water (or water and an antiseptic) is significantly more effective at removing *C difficile* spores from the hands of volunteers than are alcohol-based hand rubs.<sup>67,68</sup> In general, alcohol-based hand rubs were equivalent to no intervention. Water and soap or water and chlorhexidine have similar efficacy on bare hands<sup>69</sup> likely because of emulsification of spores and physical removal from the hands via rinsing. Importantly, one study demonstrated that handshaking transferred a mean of 30% of the residual *C difficile* spores to the hands of recipients.<sup>68</sup>

Hospitalized patients with CDI should be placed on Contact Precautions: private room, use of gloves and gowns by both HCP 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. Despite the evidence that handwashing 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 health care-associated infections. 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 health care-associated infections.<sup>70-76</sup> The current Centers for Disease Control and Prevention (CDC)/Healthcare Infection Control Practices Advisory Committee Guideline on Isolation recommends that HCP caring for patients with CDI use soap and water for hand hygiene rather than waterless antiseptic hand rubs.<sup>77</sup> However, the most recent Infectious Diseases Society of America (IDSA)/Society for Healthcare Epidemiology of America (SHEA) Guideline

recommends the use of soap (or antimicrobial soap) and water after caring for or contacting patients with CDI only in a “setting in which there is an outbreak or an increased CDI rate.”<sup>60</sup>

### 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 (ie, visibly clean, ATPase, fluorescent dye, aerobic plate counts), several studies have demonstrated that less than 50% of many surfaces are cleaned.<sup>78-81</sup> Similar deficiencies have been reported for cleaning of portable medical equipment.<sup>82</sup> Despite terminal cleaning of hospital rooms, many surfaces remain contaminated with *C difficile* spores.<sup>44</sup> This occurs most likely because many rooms are inadequately cleaned by environmental service workers and because *C difficile* is not susceptible to most commonly used surface disinfectants (ie, phenolics and quaternary ammonium compounds).

Surface disinfectants such as 70% isopropanol,<sup>17</sup> phenols,<sup>17</sup> and quaternary ammonium compounds<sup>17,83</sup> are not sporicidal. Furthermore, exposure to a cleaning agent or disinfectant has been shown to increase the sporulation rate of *C difficile*.<sup>84,85</sup> In a comprehensive study of 32 disinfectants using a suspension test and only 1- and 60-minute exposure times, only chlorine dioxide products achieved a  $>4\text{-log}_{10}$  reduction in *C difficile* spores under both clean (0.3% albumin) and dirty (3% albumen) conditions.<sup>86</sup> Products based on hypochlorites, triamine, or a hypochlorite-based mixture only achieved a  $>4\text{-log}_{10}$  reduction after 60 minutes in clean and dirty conditions. Sodium hypochlorite has been demonstrated to be effective in kill *C difficile* spores.<sup>84,87-90</sup> However, the killing is both time and concentration dependent and up to 5 to 10 minutes may be required to achieve a greater than 3- $\log_{10}$  reduction, especially with concentrations of less than 1,000 to 3,000 ppm.<sup>87,88,90</sup> Rutala et al found that wiping with a 1:10 dilution of bleach (6,000 ppm chlorine) eliminated  $>3.90\text{-log}_{10}$  *C difficile* by a combination of inactivation and physical removal.<sup>91</sup> In a suspension test, an improved hydrogen peroxide product (0.5% hydrogen peroxide) demonstrated a  $\sim 2\text{-log}_{10}$  reduction of *C difficile* spores compared with the  $>5\text{-log}_{10}$  decrease achieved with 5,000-ppm sodium hypochlorite at 1 minute.<sup>90</sup>

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.<sup>21,58,92-95</sup> For example, Mayfield et al demonstrated that initiation of room disinfection with 1:10 hypochlorite led to a decrease in CDI from 8.6 to 3.3 cases per 1,000 days ( $P < .05$ ) in a bone marrow transplant unit.<sup>92</sup> Reverting back to a quaternary ammonium compound resulted in an increase in CDI to 8.1 cases per 1,000 patient-days. In a before-and-after study using bleach wipes (0.55% active chlorine) for both daily and terminal cleaning, Orenstein et al demonstrated a reduction of *C difficile* on 2 wards for which *C difficile* was hyperendemic (ward A dropped from 24.2 cases per 10,000 hospital-days to 3.5 cases, and ward B dropped from 24.1 cases per 10,000 hospital-days to 3.7 cases).<sup>58</sup> Whereas 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.<sup>42</sup>

The CDC and Healthcare Infection Control Practices Advisory Committee recommend consistent environmental cleaning and disinfection be used as one of the control measures for *C difficile* and that “hypochlorite solutions (5,000 ppm) may be required if transmission continues.”<sup>77</sup> 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.”<sup>59</sup> 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.”<sup>60</sup> The Association for Professionals in Infection Control and Epidemiology also recommends a 1:10 dilution of hypochlorite for use when there is ongoing transmission, but they recommend a contact time of 1 minute for nonporous surfaces.<sup>62</sup> 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 (ethane-peroic acid/hydrogen peroxide, silver, tetraacetythylenediamine).<sup>96</sup> Current evidence suggests that the Association for Professionals in Infection Control and Epidemiology recommendation for contact time is adequate to inactivate *C difficile* spores based on the relatively low numbers of *C difficile* contaminating specific environmental surfaces. All the guidelines emphasize 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 disinfection

New “no touch” methods have recently been introduced that provide room disinfection. The most promising of these methods uses either ultraviolet (UV) light<sup>97,98</sup> or gaseous hydrogen peroxide.<sup>97,99,100</sup> There are currently at least 3 devices available for room disinfection that use UV-C light: (1) a device (Tru-D Smart UVC; TRU-D, Memphis, TN) that emits UV-C (254 nm) and uses a computer and sensors to monitor the amount of energy delivered, (2) a second device (IRIS; Medline Industries, Inc, Mundelein, IL) that also uses UV-C irradiation, and (3) a device (Xenex Health care Services; San Antonio, TX) that uses pulsed-xenon UV radiation (200–320 nm) and a UV sensor for dose assurance. In study using Formica sheets contaminated with *C difficile* spores, one UV-C device was shown to eliminate > 4-log<sub>10</sub> spores in direct line of sight and 2.43-log<sub>10</sub> spores using indirect UV reflection within 50 minutes.<sup>101</sup> Other investigators using the same device and similar study designs have demonstrated similar findings. Boyce et al reported log<sub>10</sub> reductions in *C difficile* spores of 1.7 for the toilet to 2.9 for the floor under the bed with a mean exposure time of 67.8 minutes (range, 34.2–100.1 minutes).<sup>102</sup> Nerandzic et al reported a reduction of *C difficile* spores at a reflected dose of 22,000 μWs/cm<sup>2</sup> (spore-killing dose) for ~45 minutes by >2- to 3-log<sub>10</sub>.<sup>103</sup>

Several different devices for the generation of hydrogen peroxide have been evaluated<sup>100</sup> including those produced by Glosair (formerly Sterinis), which produces a dry mist (5% hydrogen peroxide, <50-ppm silver cations, <50-ppm ortho-phosphoric acid); Steris, which produces vaporized hydrogen peroxide (35% hydrogen peroxide); and Bioquell, which produces hydrogen peroxide vapor (35% hydrogen peroxide).<sup>100</sup> Both the Bioquell and Steris systems are highly sporicidal (>6-log<sub>10</sub> reduction), whereas the Glosair system results in a ~4-log<sub>10</sub> reduction.<sup>88</sup> In a hyperendemic setting, Boyce et al demonstrated that terminal disinfection with a device that produces hydrogen peroxide reduced the incidence of CDI on high-incidence wards and significantly reduced the incidence of the epidemic strain hospital wide.<sup>44</sup>

Few comparative trials of the different “no touch” methods have been published. A comparison of the Bioquell hydrogen peroxide system with the Tru-D UV-C system demonstrated that hydrogen

peroxide achieved a 6-log<sub>10</sub> reduction in *C difficile* spores inoculated onto carriers and placed in a patient room, whereas the UV-C system achieved an average log<sub>10</sub> reduction of 2.2.<sup>104</sup> The mean times to complete the hydrogen peroxide decontamination process was 153 minutes (range, 140–177 minutes), whereas UV-C decontamination required a mean length of time of 73 minutes (range, 39–100 minutes) during the study.

To date, only a single study discussed above of a “no touch” method of room decontamination used health care-associated infections as an outcome.<sup>44</sup> Thus, the effectiveness of these devices to reduce health care-associated infections have not been demonstrated. Furthermore, no cost benefit studies of these devices have been published. Major limitations of all current devices include the fact that they are only able to be used for terminal disinfection because patients and staff must be removed from the room; they are costly; and their use is associated with substantial “down time” for the room decreasing room turnover. The advantages and limitations of UV light and hydrogen peroxide devices have been reviewed.<sup>101</sup> Because the different UV room disinfection devices and hydrogen peroxide methods differ in important aspects, each device should be validated as a method to prevent health care-associated infection prior to being accepted for routine use.

#### Self-disinfecting surfaces

The potential use of self-disinfecting surfaces has been reviewed.<sup>105</sup> To date, only copper coating of room surfaces has been assessed for its effectiveness in reducing *C difficile*. Copper has been shown to kill greater than 6-log<sub>10</sub> of vegetative *C difficile* cells within 30 minutes.<sup>106</sup> However, the same authors demonstrated no reduction in viability of dormant *C difficile* spores within 3 hours. Greater than 3-log<sub>10</sub> of *C difficile* spores have been shown to be completely inactivated by copper surfaces in 24 to 48 hours.<sup>107</sup> Copper-coated surfaces have not been demonstrated to reduce *C difficile* in trials using coated surfaces in patient rooms. The application of copper to prevent and control infection has been reviewed.<sup>108</sup>

#### CONCLUSION

The incidence of health care-associated infections continues to increase. Preventing these infections will require improved antibiotic stewardship, rapid identification, and use of contact precautions for patients with CDI and enhanced environmental disinfection.

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