Preventing Transmission of *Clostridium difficile*: Is the Answer Blowing in the Wind?

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(See the article by Best et al, on pages 1450–1457.)

During the past decade, the emergence of an epidemic *Clostridium difficile* strain, known as North American pulsed-field gel electrophoresis type 1 (NAP1) or polymerase chain reaction ribotype 027, has been associated with large outbreaks of *C. difficile* infection (CDI) in North America and Europe [1–4]. These outbreaks have posed enormous challenges for infection control programs in hospitals and long-term care facilities. Successful control of outbreaks has often required years of effort and sequential implementation of multiple control measures, including antibiotic restriction [3, 4]. For example, Valiquette et al [4] found that multiple efforts directed at reducing transmission failed to control an outbreak, but an antimicrobial stewardship program that reduced use of high-risk antibiotics was effective.

As shown in Figure 1, patients with symptomatic CDI are the major source of transmission. These patients shed large numbers of spores in stool, resulting in contamination of their skin, clothing, bedding, and nearby environmental surfaces and creating what has aptly been termed a *fecal veneer* [5, 11]. The hands of health care workers serve as an important vector for transmission of spores from these sites to susceptible patients [5, 11]. Patients may also acquire spores through direct contact with contaminated surfaces or equipment [5, 11]. Shedding of spores decreases significantly during treatment as diarrhea resolves and concentrations of spores in stool are reduced (Figure 1B) [6]. Therefore, the basic practices recommended by the Society for Healthcare Epidemiology and the Infectious Diseases Society of America for prevention of CDI focus on reducing the risk of transmission from symptomatic patients [8]. These recommendations include the placement of patients with CDI under contact precautions until diarrhea resolves and disinfection of CDI rooms and portable equipment after discharge of patients, preferably with a sporicidal agent (such as sodium hypochlorite) if CDI rates are high [8].

What should medical facilities do if CDI rates remain high despite the implementation of basic control measures? These facilities must first ask themselves, how good is our compliance with the basic practices recommended for the prevention of CDI? Unfortunately, compliance with contact precautions and the effectiveness of environmental cleaning are suboptimal in many facilities [8, 12–14]. Before concluding that basic measures are ineffective, facilities should develop strategies to assess compliance with these measures and provide feedback to improve performance [8, 13, 14]. In several studies, such interventions have resulted in significant improvements in environmental disinfection [13, 14]. Although not recommended in the current guidelines, automated technologies provide an alternative strategy to improve environmental disinfection in CDI rooms [15].

The difficulty in controlling CDI has also led many infection control practitioners to question whether the current control strategies may be missing important sources of transmission. Some of these potential sources are shown in Figure 1. Because there is currently limited evidence that interventions addressing these sources are beneficial, they are considered special measures that can be added if basic measures are unsuccessful [8]. In evaluating these potential sources, it is necessary to consider the plausibility that they greatly contribute to transmission and the practicality of interventions needed to address them. For example, it is plausible that patients with CDI who are not given a diagnosis and isolated in a timely fashion may contribute to transmission.
Interventions to expedite diagnostic testing and/or preemptively place patients with suspected CDI under contact precautions are therefore recommended as a special measure if rates remain high despite basic measures [8]. Paradoxically, use of diagnostic tests with increased sensitivity could be beneficial as a control measure, because patients whose infections remain undetected by less sensitive testing methods (eg, enzyme immunoassay for toxin) often shed considerable numbers of spores (author’s unpublished data). Asymptomatic carriers might contribute to transmission in some settings [5–7], but it is not practical for most facilities to screen for carriage. Interventions to enhance facility-wide environmental cleaning or to increase use of hypochlorite on wards with a high incidence of CDI, however, are practical strategies that might reduce the burden of spores in non-CDI rooms. Finally, my colleagues and I found that contamination of surfaces outside patient rooms (eg, computer keyboards) was common in our facility [10]. However, we have not been able to demonstrate acquisition of spores on hands after contact with such surfaces, whereas hand acquisition was easily demonstrated after contact with surfaces in CDI rooms (author’s unpublished data). These findings suggest that the concentration of spores on surfaces outside CDI rooms may be much lower than that on surfaces in CDI rooms.

In this issue of Clinical Infectious Diseases, Best and colleagues [16] provide evidence for airborne dispersal of spores from patients with CDI and suggest that this could be another important transmission source that is not adequately addressed by current control measures. The researchers collected air samples near the beds of patients with CDI and also cul-

**Figure 1.** Overview of potential sources of *Clostridium difficile* transmission (A) and shedding of spores by patients with *Clostridium difficile* infection (CDI) (B). Approximately one-third of patients who acquire *C. difficile* colonization develop CDI, whereas the remaining two-thirds become asymptomatic carriers [5–7]. Patients with CDI shed spores through fecal contamination. Susceptible patients acquire spores from the contaminated hands of health care workers or from contaminated environmental surfaces. Basic measures to prevent transmission include (1) contact precautions while diarrhea is present and (2) environmental disinfection of CDI rooms after discharge of patients [8]. Other potential sources of transmission and potential interventions include the following: (3) CDI not being diagnosed and patients not being isolated in a timely fashion (intervention: preemptive isolation of patients with suspected CDI); (4) CDI not being diagnosed because of insensitive testing methods, such as enzyme immunoassay for toxin [9] (intervention: use of testing methods with increased sensitivity); (5) environmental surfaces in CDI rooms and the skin of patients with CDI (interventions: daily disinfection of surfaces in isolation rooms and daily bathing to reduce the burden of spores on skin); (6) persistent shedding of spores after resolution of diarrhea [6] (intervention: continuation of contact precautions to time of discharge); (7) asymptomatic carriers [5–7] (intervention: improve environmental disinfection in non-CDI rooms); (8) contaminated surfaces outside patient rooms [10] (intervention: improve environmental disinfection); and (9) overuse of antibiotics contributing to high numbers of susceptible patients (intervention: antimicrobial stewardship).
tered environmental sites. In an initial cohort of 50 patients with CDI, only 6 (12%) had positive culture results for air from 1 h of sampling. However, 7 (70%) of 10 patients with CDI had 1 or more positive air samples when the duration of sampling was extended to several hours. Roberts et al [17] also recently provided evidence of airborne dispersal of *C. difficile* spores. The study of Best and colleagues expands on those findings by using molecular typing to show that airborne isolates are often identical to concurrent environmental and stool isolates and by demonstrating that airborne dispersal may correlate with increased activity in the room and with bed making.

It is plausible the *C. difficile* spores may be dispersed in air. As has been noted previously, the skin, clothing, and bedding of patients with CDI are often contaminated with spores [5, 6, 11]. Skin scales are continually shed (as many as 1 × 10^4–1 × 10^5 skin particles in 24 h), providing a source for airborne dispersal of spores from patients with CDI, particularly during periods of activity [18]. Similarly, bed making generates airborne dispersal of microorganisms, including *Staphylococcus aureus* [19]. Upper respiratory tract infections increase airborne dispersal of *S. aureus* in nasal carriers, creating “cloud adults” [20]. It is possible that diarrhea might similarly enhance airborne dispersal of spores.

The studies of Best et al [16] and Roberts et al [17] provide evidence of airborne dispersal of spores, but further studies will be needed to determine whether this is an important route of transmission. For several reasons, it is possible that this is an interesting observation with limited clinical relevance, akin to culturing spores from neckties or name badges. First, the number of spores recovered from air by Best et al [16] was very low. It is possible that this is related in part to technical issues, such as the use of plates that were not prerduced. Roberts et al [17] collected particulate matter from air into a solution that was then plated onto prerduced medium and recovered much higher numbers of spores from air. Second, most of the contaminated sites were frequently touched surfaces, suggesting that the source of contamination may have been the hands of health care workers. Third, even if spores are disseminated in air, it may not change our current practices. High-touch surfaces in CDI rooms will be targeted for disinfection regardless of the mechanism of contamination. Airborne dispersal to infrequently touched surfaces may be irrelevant, given that the surfaces are infrequently touched. As has been mentioned previously, preemptive isolation of patients with suspected CDI, as recommended by Best and colleagues, is a reasonable supplemental control strategy even in the absence of concern regarding airborne transmission.

Although the clinical relevance of airborne dispersal of spores is unclear, it is disconcerting to contemplate a “fecal cloud” in addition to a “fecal veneer” in health care settings. Research is needed to assess whether airborne dispersal may contribute to widespread dissemination of spores outside CDI rooms. The infectious inculom of *C. difficile* is very low (at least in hamsters), so airborne dispersal of small numbers of spores could present a risk to antibiotic-treated patients. It is also possible to imagine scenarios in which airborne dispersal might be important in CDI rooms. For example, housekeeping activities (such as handling of bedding) might inadvertently lead to airborne dispersal of spores that subsequently settle on cleaned surfaces.

In summary, the study of Best and colleagues raises important questions about airborne transmission of *C. difficile* that deserve further study. In the meantime, should we place airborne isolation signs next to our CDI contact precautions signs and entertain calls from companies wanting to sell us air-purification products? Not yet. For most workers in the infection control trenches, the essential questions are more mundane. With apologies to Bob Dylan:

How many times must a doctor be told
Wash your hands and wear gloves, please?
Yes, and how many times will another stand by
Pretending he just doesn’t see?
And how many times must we remind
Those things that we touch must be cleaned?
The answer, my friend, is blowin’ in the wind

The answer is blowin’ in the wind.

Acknowledgments

Financial support. Department of Veterans Affairs.

Potential conflicts of interest. C.D.D. has received recent research funding from Optimer, Ortho-McNeil, ViroPharma, and GOJO.

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