LETTERS TO THE EDITOR

Site of Acquisition of *Clostridium difficile* Colonization: Hospital or Nursing Home?

To the Editor—I would like to comment on the paper by Ponnado et al[1] published in the September 2017 issue of *Infection Control and Hospital Epidemiology*. The authors describe a study evaluating *Clostridium difficile* (CD) acquisition and infection after admission to a single long-term-care facility (LTCF). The authors hypothesized that patients admitted to the study facility who develop CD infection (CDI) are colonized with CD after admission to the facility rather than at the time of admission. This hypothesis contrasts with a hypothesis I published in 2008 stating that CD colonization usually occurs during hospitalization and is present on admission to an LTCF in those who develop CDI within 4 weeks of admission to the facility.[2] This hypothesis[2] was based on observations during care of patients in post-acute care and long-term care in community skilled-nursing facilities.

The study by Ponnado et al[1] was conducted in a Veterans Affairs LTCF during a 5-month period in 2009. Perianal swabs were cultured for CD on new admissions (N = 110) and weekly thereafter for 6 weeks. Study enrollees were monitored for CDI during the 6-week follow-up. Ribotyping was done on the initial CD-positive isolate and on isolates from those with CDI. Of 110 enrollees, 12 (11%) had CD colonization on admission to the facility. Of 98 enrollees with negative perianal swabs on admission, 82 (83%) had follow-up cultures and 22 (27%) developed CD colonization during the follow-up period. Only 4 cases of incident CDI were detected in the 6-week follow-up: 1 in the admission colonized group and 3 in the group with follow-up colonization. These findings were not consistent with my hypothesis.[2]

I would like to call attention to several considerations regarding the report by Ponnada et al.[1] First, this study was done 9 years ago —why did it take so long to be submitted for publication? Can we assume that it is still relevant? Second, a report from the same LTCF in the study by Ponnada et al[1] that covered the period from 2006 to 2008 found that, of 40 newly admitted people who developed CDI after admission, 85% did so within 30 days.[3] In the discussion section of that paper, the authors state that CD may have been acquired in the hospital (as I hypothesized) but that definitively pinpointing the site of acquisition of CD required serial stool cultures and typing. This finding may have been the motivation for the study by Ponnado et al,[1] but the authors did not provide more detail about this study in their paper. Third, in the 34 asymptomatic CD carriers (12 on admission and 22 after admission) detected in the study, 15 different ribotypes were identified. Unfortunately, the authors did not comment on this in their discussion. The source or sources of a relatively large number of colonizing ribotypes of CD in a small group of residents raises concerns about infection control procedures at the facility. For example, disinfection procedures may have been ineffective in the facility environment that was contaminated with spores of multiple ribotypes, and these spores were transmitted to residents after admission. Fourth, it would have been useful for the authors to provide information about the incidence of CDI in long-term residents who were not hospitalized; another aspect of my hypothesis[2] was that the incidence is low in this group compared to newly admitted people. I documented this finding in a study conducted in 4 community LTCFs.[4] Lastly, care should be taken when extrapolating the results of a study from a single facility to all LTCFs, and the authors briefly mention this in their discussion. This principle is exemplified by Brown et al[5] in a study that evaluated the variability of CDI rates in all LTCFs across all healthcare regions of the VA from 2006 to 2012. They found that CDI incidence varied widely by region (from 0.6 to 31 cases per 10,000 resident days). They also identified resident-level and region-level risk factors for CDI. Ponnado et al[1] refer to the study by Brown et al,[5] but they do not mention the wide range of CDI incidence in Veterans Affairs healthcare regions. The findings of Brown et al[5] demonstrate the variability of CDI incidence within a single large healthcare system, and the findings from a single facility in the system may not be relevant in general.

I agree with Ponnado et al[1] that antibiotic use in the hospital may alter colonic flora, making CD colonization more likely in the hospital or LTCF. I also agree that efforts to improve prescribing in both settings are required to reduce CDI occurrence regardless of the site of acquisition. Large-scale studies in community LTCFs to determine the site of acquisition of CD need to be conducted, but they will be costly and time-consuming. However, documenting the site of acquisition of CD has important implications for CDI surveillance and for public reporting of CDI incidence in hospitals and nursing homes.

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Laxative Use in the Setting of Positive Testing for *Clostridium difficile* Infection

To the Editor—*Clostridium difficile* infection (CDI) is the most common healthcare-associated infection in the United States.[1] In 2011, almost half a million infections and ~29,000 deaths were estimated to be associated with *C. difficile*.[2] Timely testing and treatment is critical for improving outcomes and reducing transmission.[3] Given the high rate of asymptomatic *C. difficile* carriage, appropriate testing is also essential.[4] In healthcare settings, *C. difficile* colonization is reportedly 5 to 10 times more common than CDI and other noninfectious causes of diarrhea.[5,6]

Unformed stools due to laxative use are often submitted for CDI testing, although these specimens are not appropriate for CDI diagnosis. Recent laxative use has been reported in up to 44% of CDI tested specimens.[3,7,8] Interventions to reduce the testing of inappropriate specimens, including those due to laxative use, have led to a reduction of CDI rates and treatment.[9] We further examined the relationship between laxative use and patients who tested positive for CDI.

A retrospective study was conducted at a 537-bed teaching community hospital and included hospitalized patients who tested positive for CDI in 2014 and 2015. Testing for CDI comprised an enzyme immunoassay (EIA) for glutamate dehydrogenase (GDH) and an EIA for detection of toxin A/B (*C. diff* Quik Check Complete, Alere, Waltham, MA). If the GDH test was positive and the EIA for the toxin A/B was negative, a confirmatory polymerase chain reaction (PCR) assay (Xpert *C. difficile*, Cepheid, Sunnyvale, CA) was performed. *Clostridium difficile* infection was diagnosed using either GDH-positive and toxin-positive or PCR-positive laboratory results.

Patients who received laxatives up to 24 hours prior to positive CDI testing were identified. Laxatives included docusate sodium, senna, polyethylene glycol, bisacodyl, milk of magnesia, sodium polystyrene sulfonate, and lactulose. Sodium polystyrene and lactulose were considered laxatives if the indications for use were neither hyperkalemia nor hepatic encephalopathy, respectively. Physician and nursing notes were reviewed to determine whether diarrhea (≥3 unformed stools over 24 hours) resolved within 24 hours of positive CDI testing. The medication administration record was reviewed to determine whether laxatives were administered for greater than 24 hours after positive testing. Validation procedures were conducted for >10% of the study population to ensure reviewer consistency.

TABLE 1. Demographic and Clinical Characteristics of Hospitalized Patients with Laxative Use Within 24 Hours of Positive Testing for *Clostridium difficile*

Demographic and Clinical Characteristics, n = 29	No. (%)[a]
Age, mean y (range)	68 (26–95)
Gender	
Female	9 (31)
Male	20 (69)
Race	
Black	6 (21)
White	23 (79)
Toxin EIA+	11 (38)
Toxin EIA−/PCR+	18 (62)
Ordering hospital service	
Medicine	15 (52)
Surgery	6 (21)
Intensive care unit (medical and cardiac)	8 (28)
Proton pump inhibitor use	19 (66)
H2 receptor blocker use	15 (52)
Corticosteroid use	13 (45)

NOTE. EIA, enzyme immunoassay; PCR, polymerase chain reaction.
[a]Unless units are otherwise specified.

A total of 211 patients with CDI were included in the study. Overall, 82 patients (39%) had received laxatives within 7 days prior to positive CDI testing. Of these, 29 (14%) had received laxatives in the 24 hours prior to positive testing (Table 1). In the 24 hours prior to positive testing, 11 patients (38%) received 1 laxative; 12 patients (41%) received 2 laxatives; 4 patients (14%) received 3 laxatives; and 2 patients (7%) received 4 laxatives. The most commonly administered laxatives were docusate sodium (72%), polyethylene glycol (41%), senna (38%), and bisacodyl (17%). Furthermore, 15 patients (52%) continued to receive laxatives for >24 hours after positive CDI testing.

Of the 29 patients, 12 (41%) had resolution of diarrhea within 48 hours of positive CDI testing, including 9 (31%) who had resolution within 24 hours. Of the 9 patients who had resolution of diarrhea within 24 hours, 2 patients (22%; both toxin EIA−/PCR+) did not receive CDI treatment, and 7 patients (78%; 3 toxin EIA+, 4 toxin EIA−/PCR+) received CDI treatment.

Other studies have reported the association of laxative administration with testing for CDI.[3,7,8,9] We reviewed this association for those patients who tested positive for CDI. Surprisingly, 82 patients (39%) received laxatives within 1 week of CDI diagnosis; 29 (14%) received laxatives (usually ≥2) within 24 hours of positive testing. Despite positive results for CDI, 15 patients (52%) continued to receive laxatives for >24 hours after diagnosis.

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