Editorial

Diarrhea: A Neglected Nosocomial Hazard?

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"Common things occur commonly," is one of those platitudes that attending physicians like to cast as a reproving pearl before resident physicians who seem to be listening for the hoofbeats of a zebra. Just how common nosocomial gastrointestinal infections are has been a moot point in the infection control literature for the past several years, with prospective studies[1,2] finding incidence rates of infectious diarrhea several hundred times higher than those reported by the National Nosocomial Infections Study.3

Such differences may relate somewhat to differences in patient populations and infection control practices in different hospitals, but they also may relate to evolution in surveillance definitions or methods. At the University of Virginia Hospital in Charlottesville, Vii ginia, infectious diarrhea appeared to be a rare event in 1985, as only one case was documented by our surveillance that year. But after the clinical microbiology laboratory was asked to contact us with every positive ***Clostridium difficile*** result, alerting the nurses to possible nosocomial infection, we began to document 150 to 200 nosocomial cases per year.

Common things occur commonly, even when they are not being noticed. Hospital diarrhea almost always was assumed to be noninfectious in the past, because in many instances, it was noninfectious, and because when routine bacterial stool cultures were performed for ***Salmonella*** and ***Shigella, they*** almost always were negative. Now we know that we were not testing for the most frequent infectious agents in the hospital: C *difficile* and viruses, such as rotavirus (especially on pediatric wards).[4,5] As the number of test requests for such pathogens has risen, so has the perceived incidence of infectious diarrhea.

If we accept the evidence that infectious diarrhea is a more common hospital complication than once believed, concern arises as to its importance. Is it merely an unpleasant nuisance or something worse? The study by Zaidi et al did not confirm the findings of others-that it results in prolongation of hospital stay—perhaps because of matching controls by hospital duration to ten days beyond the time of diarrhea in the case. They did, however, find an even more alarming association with excess mortality.[6] The companion paper by Thibault et al showed a trend toward longer hospital stay, but had low statistical power to detect a statistically significant difference.[7] Diarrhea also has been suggested recently as a potential risk factor for other nosocomial infections, especially in the urinary tract,8 which Zaidi et al suggest may partially explain the 13% attributable mortality observed in their study.

The results of these two studies largely confirm the findings of others but also contain some important new information. Zaidi et al report that 5.5% of their patients in Mexico City, Mexico, had nosocomial diarrhea, which is similar to the rate in recent studies from the United States,[1,2] with risk factors similar to those found in other studies, but with an important difference in the frequency distribution of etiologic agents. *Candida* species, recently noted as a cause of diarrhea in several studies,[9,10] was the most frequent potential pathogen identified, followed by ***Entamoeba histolytica.*** ***C difficile*** was detected by culture and cytotoxin assay as frequently in controls as in patients with diarrhea, raising concern about the specificity and positive predictive value of these tests in this study. The authors' discussion about why immunosuppression and enemas might lead to reactivation of amebiasis is intriguing, as is the possibility of nosocomial transmission, which occurred in a chiropractic clinic in Colorado.[11] Seven-

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teen of 115 cases (15%) had amebic trophozoites. The proportions of cases and controls passing amebic cysts was not stated. If cases and controls had been found to have similar proportions with either trophozoites or cysts, this would have supported the suggestion that these cases more likely represented reactivation rather than nosocomial transmission. Two recent studies in the United States found that routine stool examinations for ova and parasites were unnecessary because they invariably were negative,[4,5] but this may not be true in developing countries.

The study by Thibault et al found risk factors for C *difficile* infection that mirrored those in other studies, except that metronidazole, a mainstay of therapy for this disease, was suggested to be a risk factor when given as perioperative prophylaxis. We would assume this observed association most likely to be due to confounding from other prophylactic antibiotics. The authors suggest that even if the metronidazole was not truly a risk factor, it did not appear to prevent postoperative C *difficile* when given as part of multidrug prophylaxis. This observed lack of protection could have a number of possible explanations, such as the following: Type II error (since there were only 26 cases and multiple independent variables to fit into the multivariate equation); a systematic difference or bias between the patients who received metronidazole and those who did not (i.e., the metronidazole recipients may have been more predisposed to *C difficile* for other reasons in this unrandomized study, and these were not adjusted for in the multivariate analysis); or a brief course of metronidazole simply may not significantly reverse the increased risk created by multiple other risk factors, such as surgery and other perioperative antibiotics, especially if these drugs continue longer than the metronidazole. Johnson et al found in a randomized trial that metronidazole and amikacin therapy of intra-abdominal infections was followed by significantly less C *difficile* diarrhea than similar regimens containing clindamycin (0% versus 31%, $p<.02$), but when the metronidazole regimen was followed by other antibiotic therapy, this protection was lost.[12]

Some suggest that extending the routine barrier approach of universal precautions to include all body fluids and moist substances, including feces, might result in lower risk for nosocomial transmission of agents such as C *difficile*.[13,14] The results of two studies lend support to this concept.[1,13] McFarland et al found that ungloved hands frequently became contaminated with C *difficile* during patient contact and that handwashing with soap and water did not reliably remove the organisms.[1] Johnson et al found an 80% relative reduction of the incidence of C *difficile* diarrhea after an intensive educational intervention recommending that gloves be worn to prevent contact with all moist body substances, including feces.[13]

The role of contamination of the patient's environment in transmission of C ***dificile*** to other patients remains unclear, although two investigators have reported a temporal association between increased efforts to disinfect the hospital rooms of cases and reduction of disease.[15,16] Confirmation of these initial results in a blinded randomized trial is necessary to document the efficacy of this approach.

The two articles in this issue give further evidence of the frequency, etiology, and importance of nosocomial diarrhea in hospitals in Mexico and Canada. More study is needed to identify effective means of prevention.

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