Letters to the Editor

Infections Linked to Anesthetic

To the Editor:

A recent article[1] describing investigations conducted by the Centers for Disease Control and Prevention (CDC) following postoperative infections at various hospitals was reported briefly in *Infection Control and Hospital Epidemiology*.[2] In the report by Bennett et al,[1] some findings, mainly epidemiological correlations, indicate that extrinsic contamination of propofol was responsible for infectious symptoms following surgery. However, definite proof could not be provided in any patient due to problems with some of the data. In no single case-patient has it been demonstrated conclusively that an anesthetist or any other healthcare worker transferred microorganisms recovered later from patients into a vial or an ampule of propofol and from these containers to the patient (for discussion, see references 3, 4).

It is interesting to note a major discrepancy between the first CDC report of 1990[5] and the updated report issued in 1995.[1] The first report included five patients in a California hospital who developed surgical wound infections after clean surgical procedures. A throat culture from the anesthetist involved grew *Staphylococcus aureus*, and the phage type was identical to that found in the patients' wounds.[5] In the second report, these patients are presumably among the 16 cases of postoperative infection in Hospital 1. However, no throat culture from an implicated anesthetist is mentioned now, but rather a scalp lesion.[1]

Furthermore, the first report states that the outbreak period for these five patients was 8 days.[5] In the second report, however, there is no outbreak period of 8 days that fits exactly to five patients. If we assume these hospitals to be identical, several more cases, including two fatalities, must have occurred *after* the first CDC investigation. If, on the other hand, the hospitals are not identical, the five patients mentioned in the first report are not included in the second one.[1]

Perhaps there is an easy explanation for these discrepancies. In any case, the authors must be congratulated for their repeated efforts to warn anesthesia personnel about the potential danger to the patients by breakdowns in aseptic technique when handling propofol.

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The author replies.

Thank you for your letter. You are correct that there is a simple explanation for the discrepancies that you note in the reports of infectious complications associated with the use of propofol published in the *Morbidity and Mortality Weekly Report (MMWR)* and the *New England Journal of Medicine (N Engl J Med)*.[1,2] The California hospital investigation included in the *MMWR* was conducted by the County Health Department in California and not directly by my staff at the Centers for Disease Control and Prevention. Therefore, although this investigation was included in the *MMWR,* it was not included in the *N Engl J Med* paper. The *N Engl J Med* paper only included investigations that my staff conducted on-site. Although we assisted several state or local health departments in their conduct of additional investigations, these were not included in the *N Engl J Med* paper. The hospital numbers in the *MMWR* bear no relationship with the numbers of the hospitals in the *N Engl J Med* paper. I hope this clarifies any confusion.

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Clostridium difficile and Sucralfate

To the Editor:

We were delighted to see that our initial study provoked additional inquiry in this area, and we offer the following comments. In our study of 147 critically ill patients, we identified a statistically significant negative association (adjusted odds ratio=0.15, $P<.001$) between sucralfate exposure and a positive *Clostridium difficile* toxin assay.[1] Watanakunakorn et al[2] found no such association in their retrospective study. What might explain these results? The answers may lie in methodological differences and study setting.

In the latter report, controls were selected by a non-random method; exposure assessment was not defined clearly, and it is uncertain whether data abstractors were masked to case-control status of the patient. What was the definition of sucralfate exposure? What was the duration of exposure, and were patients receiving the agent on the day the toxin assay was done? These factors are important in the design and interpretation of case-control studies.[3,4] Furthermore, cases were older, were more likely to be from nursing homes, and were hospi-

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talized longer prior to a cytotoxin assay. If these factors also were associated with increased sucralfate exposure, it may have obscured the negative association. More importantly, the settings for the two studies were different. We specifically chose critical-care units to identify risk factors other than antimicrobials. Sucralfate use was very common in this population, as estimated by the 70% exposure rate among our controls.

Statistically significant associations may be spurious and do not necessarily imply a cause-and-effect relationship. Biologic plausibility, although hypothetical, provides some support for a true causal effect. In a follow-up study, we presented data suggesting an in-vitro decrease in *C difficile* cytotoxin titer in the presence of sucralfate.[5] Finally, we noted that our findings may not be applicable to all critical-care or other types of patients. Pending further study, we would suggest similar reservations for the current article.

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The author replies.

We appreciate the comments of Drs. Jensen and Bross. In our study, the data extractors were not masked to case-control status of the patient. We find this not an important issue, because there was no subjective interpretation involved. The patient was either on sucralfate or not on sucralfate, as documented on the medication sheet. The definition of sucralfate exposure was the ingestion of sucralfate by the patient on the day the stool specimen was obtained for *Clostridium difficile* cytotoxin assay. If, indeed, ingestion of sucralfate is associated with the nondetection of *C difficile* cytotoxin in stool specimens, this should apply to all patients who ingest sucralfate, regardless of age, type of residence before admission, the location or length of stay in the hospital, and not just certain patients in certain critical-care units at certain hospitals.

The follow-up study by Jensen and Bross presented at a meeting in 1992 has not yet been published in a peer-reviewed journal.

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