Letters to the Editor

Enterobacter Plasmids: Molecular Epidemiology

To the Editor:

In the article by Jarvis[1] from the Third International Conference on the Prevention of Infection, there are several excellent molecular epidemiologic presentations. The last one, however, is supposed to represent an *EcoRI* digestion of a set of *Enterobacter cloacae* plasmids. It looks in the figure as though the plasmids in fact either were not cut or had no *EcoRI* sites. The former is more likely, and I suspect that the figure is supposed to represent only the redundant plasmid that was seen in the isolates from patients, technician, and the environment. Most *E cloacae* plasmids of the size portrayed in the figure would be expected to have one or more *EcoRI* sites, thus suggesting that the figure represents only undigested plasma DNA.

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REFERENCE

1. Jarvis WR. Usefulness of molecular epidemiology for outbreak investigations. *Infect Control Hosp Epidemiol 1994:15:500503.*

The author *replies.*

I thank Dr. John for bringing to my attention the error in my manuscript. He is correct that Figure 6 included in my article "Usefulness of Molecular Epidemiology for Outbreak Investigations" is of the plasmid analysis of the *Enterobacter cloacae* isolates obtained from the patient's blood cultures, the laboratory technician handwashings, and the laboratory environment. As mentioned in the article, we performed both plasmid analysis and restriction endonuclease analysis of the plasmids using *EcoRI.* Inadvertently, the figure of the plasmid analysis was included rather than the figure of the restriction endonuclease analysis. Shown here is the figure that should have been included (Figure 1). Note that the lane placement of the isolates in the two gels is identical in the two figures.

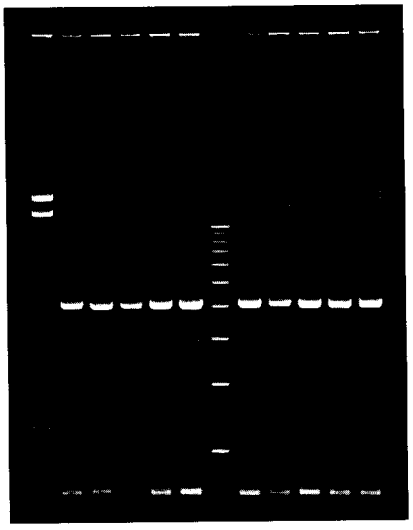


FIGURE 1. Restriction endonuclease analysis of *Enterobacter cloacae* isolates.

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CDAD Rates

To the Editor:

We applaud Olson et al for their recent comprehensive report on the epidemiology of *Clostridium difficile*-associated diarrhea (CDAD) at their medical center over a 10-year period.[1] However, several points of their article deserve further clarification and discussion.

First, although the rate of CDAD per hospital admissions was calculated for the entire 10-year period of surveillance, no such rate was furnished for each year of the study. Therefore, any trends in CDAD during the study period would be difficult to interpret. Did the number of yearly admissions and patient hospital days remain constant during the study period?

Second, it was reported that 93% of CDAD cases were acquired nosocomially. What was the definition of nosocomial CDAD in this study? Because CDAD may not become clinically manifest until after discontinuation of antibiotic therapy,[2] was there a mechanism by which development of CDAD in discharged patients receiving antibiotics was monitored? If so, did this mechanism remain constant during the study period?

Third, the authors report that implementation of body substance isolation was associated with a decrease in CDAD during the first 2 years of its implementation, and the subsequent increase in the rate of new CDAD cases in 1990 and 1991 at their medical center might have been related to the introduction of more virulent strains of *C difficile.* An alternative explanation to this apparent increase in cases of CDAD may be overuse of gloves and delay in their removal following their soilage, resulting in an increase in contamination of patients and their environment. Recent reports of *Acinetobacter,* methicillin-resistant *Staphylococcus aureus,* and CDAD outbreaks in the setting of universal precautions[3,4] seem to support this view.

We also have reviewed the yearly incidence of nosocomial CDAD

https://doi.org/10.1086/647056 Published online by Cambridge University Press

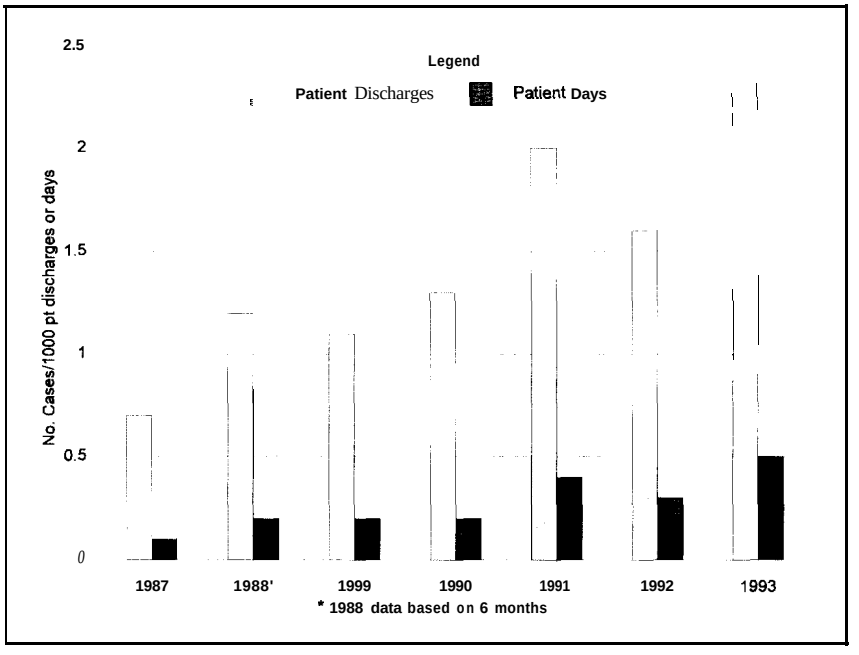


FIGURE 2. Yearly incidence of CDAD by patient discharges and patient days at St. John's Mercy Medical Center, 1987-1993.

(defined as diarrhea with positive stool for C *difficile* toxin developing in a patient >3 days following hospitalization) from 1987 through 1993 at our medical center, an 827-bed tertiary care community hospital (Figure 2). Despite implementation of universal precautions in 1988, there was a significant rise in the incidence of CDAD cases in that year when compared with the previous year (1.2 versus 0.7/1,000 discharges; chi-square, *P= 0.04).* Furthermore, despite implementation of universal precautions, an outbreak of CDAD occurred at our medical center in 1990,[4] and the yearly incidence of CDAD has remained elevated, with the rate in 1993 based on patient discharges being more than threefold higher than in 1987 (2.4 versus 0.7; $P<0.0001$). Similar increases in the incidence of CDAD based on patient days was observed during this period: 0.1 versus 0.5/1,000 patient-days for 1987 and 1993, respectively. Although it is likely that other factors such as use of multiple antibioticsplay an important role in causing CDAD,[5] our data suggest that, in practice, routine gloving by HCWs may not have an appreciable impact in reducing the overall incidence of nosocomial CDAD. In fact, it has the potential for having the opposite effect, possibly related to the delay in removal of soiled gloves and contamination of the environment.[4]

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2. Fekety R. Antibiotic-associated colitis. In: Mandell GL, Douglas RG, Bennett JE, eds. *Principles and Practices of Infectious Diseases.* New York, NY: Churchill Livingston; 1990:863-869.
3. Patterson JE, Vecchio J, Pantelick EL, et al. Association of contaminated gloves with transmission *of Acinetobacter calcoaceticus* var. *anitratus* in an intensive care unit. *Am J Med* 1991;91:479-483.
4. Meyer L, Jenne J, Manian E. *Clostridium difficile* outbreak associated with contaminated blood pressure cuffs and portable commodes. Presented at the 3rd Annual Meeting of The Society for Hospital Epidemiology of America: April 18-20, 1993; Chicago, Illinois.
5. Gerding DN, Olson MM, Peterson LR, et al. *Clostridium* difficile-associated diarrhea and colitis in adults. *Arch Intern Med* 1986;146:95-100.

The authors reply.

We thank Manian and Meyer for their interest in our work and offer the following reply to their questions and comments.

First, complete data for each year regarding discharges, patient hospital days, and annual rates of *Clostridium* difficile-associated disease (CDAD) are shown in the Table. The number of discharges was relatively constant, but days of care declined over the lo-year period. CDAD rates varied with the absolute number of cases each year, and upward and downward trends did not change when calculated as annual rates rather than absolute numbers of annual cases. Clearly, the more epidemiologically appropriate analysis is the rate of CDAD rather than the number of cases. We are grateful for the opportunity to add these data.

Second, we define nosocomial as "hospital related." As stated on page 374, patients who were admitted from outside hospitals with C. *difficile* diarrhea already present or who had never been hospitalized but were treated with antibiotics through our clinics were not included in the nosocomially acquired 93%. All the rest had been inpatients at the hospital and did not have diarrhea present on admission. All patients who were admitted to the hospital, did not have diarrhea at admission, and developed diarrhea in hospital were diagnosed as nosocomial CDAD if they met our CDAD definition. Follow-up of discharged patients was stated on page 372: "Patients were followed for 30 days . . . during the 1982 study, as were patients enrolled in an abdominal infection study. Other patients were followed while in the hospital and after returning to clinic or being admitted with symptoms of diarrhea and positive stool results or positive endoscopy." This is still being done.

Third, we do not know the precise reason for the increase in the CDAD rate in 1991, but we do have data published in abstract form that document the presence in 1991 of a new *C. difficile* type W3, which was never found in 1990.[1] All *C. difficile* isolates available (95%) from the 4 years were typed by restriction endonuclease analysis (REA) using HindIII restriction enzyme. Type W3 (later designated K1) accounted for 20% of *C. difficile* cases in 1991, and was the single most common C *difficile* isolate. In contrast, none of these isolates were found prior

https://doi.org/10.1086/647056 Published online by Cambridge University Press

TABLE
ANNUAL RATES OF *CLOSTRIDIUM DIFFICILE*-ASSOCIATED DIARRHEA

	Cases	Discharges	Rate per 1,000 Discharges	Patient Days	Rate per 1,000 Patient Days
1982	149	15,018	9.9	211,185	0.71
1983	122	15,771	7.7	203,290	0.60
1984	81	16,509	4.9	202,530	0.40
1985	116	16,274	7.1	195,264	0.59
1986	86	15,666	5.5	187,384	0.46
1987	83	15,809	5.3	179,013	0.46
1988	59	16,412	3.6	179,695	0.33
1989	50	15,753	3.2	166,478	0.30
1990	62	15,736	3.9	164,972	0.38
1991	100	15,704	6.4	162,379	0.62

to 1991, and no single REA type accounted for more than 10% of CDAD cases in 1990. In 1988 and 1989, REA types Y1 and L1 accounted for 13% and 18% of CDAD cases, respectively.

Delay in changing gloves also may account for this increase in CDAD cases, but we have no data to support this hypothesis, nor are any presented by Manian and Meyer. However, we do have data to indicate that a change in the *C. difficile* organisms occurred in 1991. Our data suggest a decreased or low CDAD rate in 1988, 1989, and 1990 (the first years of body substance isolation and presumed increased glove use) and an increased rate in 1991 (double the rate of 1989). To support inappropriate use of gloves as a causative factor in our institution, we would have to postulate a breakdown in usage practice in 1991 that did not occur from 1988 through 1990, an hypothesis that is possible but difficult to prove.

We also have typed *C. difficile* strains from the peak CDAD incidence months of 1982 to 1987 and have shown that during the high incidence years of 1982, 1983, and 1985 (Table), two closely related REA types, B1 and B2, accounted for 64% of all CDAD cases.[2] Types B1 and B2 were never found after mid-1986 These data lead us to postulate that changes in epidemic or endemic *C. difficile* organisms may account for the variability in CDAD rates from year to year, although we cannot rule out changes in infection control practices as also possibly playing a role in these changing CDAD rates.

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1. Clabots CR, Bettin KM, Olson MM, et al. An increased rate of *Clostridium difficile*-associated diarrhea caused by appearance of a new *C. difficile* strain. Presented at the 32nd Interscience Conference on Antimicrobial Agents and Chemotherapy; October 11-14, 1992; Anaheim, California. Abstract 481.
2. Clabots CR, Pearson AC, Bettin K, et al. Typing of *Clostridium difficile* strains responsible for epidemics in a hospital with a high endemic incidence of *C. difficile-associated* diarrhea. Presented at the 31st Interscience Conference on Antimicrobial Agents and Chemotherapy; September 29-October 2, 1991; Chicago, Illinois. .Abstract 1520.

Defining Catheter-Related Infections

To the Editor:

I want to congratulate Dr. Raad et al (1994;15:231-238) for their important article on the prevention of central venous catheter-related infections by using maximal sterile barrier precautions during insertion.

However, there does appear to be a contradiction in the article. On page 235, they report that 25% of the catheter-related septicemias in the MSB arm occurred during the first 2 months of follow-up, but in the table on page 236, the only septicemia occurring in that arm of the study appears to have occurred 98 days after insertion.

They use reasonable definitions of significant colonization of catheters and catheter-related septicemias. However, it would have been more appropriate in the abstract of the article to refer to numbers of patients with catheter colonization or catheter-related septicemia rather than referring to both groups together as catheter-related infections. Their definition of catheter-related infections can only be inferred from the article.

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The author replies.

We appreciate the comments and correction by Dr. Nafziger. The issue raised here is very important and relates to the definitions of catheter-related infections. In the past, significant colonization ($\geq$ 15 colony-forming units per catheter segment) was referred to as local catheter infection.[1,2] In this article, we tried to differentiate catheter-related septicemia (infection) from significant colonization. Because significant colonization was considered a prelude for septicemia, we often used the term "catheter-

https://doi.org/10.1086/647056 Published online by Cambridge University Press