Infection-Control Measures Reduce Transmission of Vancomycin-Resistant Enterococci in an Endemic Setting

Marisa A. Montecalvo, MD; William R. Jarvis, MD; Jane Uman, MPH; David K. Shay, MD, MPH; Coleen Petrullo, RN; Karen Rodney, BS; Cheryl Gedris, MS; Harold W. Horowitz, MD; and Gary P. Wormser, MD

Background: Vancomycin-resistant enterococci (VRE) are nosocomial pathogens in many U. S. hospitals.

Objective: To determine whether enhanced infection-control strategies reduce transmission of VRE in an endemic setting.

Design: Prospective cohort study.

Setting: Adult oncology inpatient unit.

Patients: 259 patients evaluated during use of enhanced infection-control strategies and 184 patients evaluated during use of standard infection-control practices.

Interventions: Patient surveillance cultures were taken, patients were assigned to geographic cohorts, nurses were assigned to patient cohorts, gowns and gloves were worn on room entry, compliance with infection-control procedures was monitored, patients were educated about VRE transmission, patients taking antimicrobial agents were evaluated by an infectious disease specialist, and environmental surveillance was performed.

Measurements: VRE infection rates, VRE colonization rates, and changes in antimicrobial use.

Results: During use of enhanced infection-control strategies, incidence of VRE bloodstream infections decreased significantly (0.45 patients per 1000 patient-days compared with 2.1 patients per 1000 patient-days; relative rate ratio, 0.22 [95% CI, 0.05 to 0.92]; $P = 0.04$), as did VRE colonization (10.3 patients per 1000 patient-days compared with 20.7 patients per 1000 patient-days; relative rate ratio, 0.5 [CI, 0.33 to 0.75]; $P < 0.001$). Use of all antimicrobial agents except clindamycin and amikacin was significantly reduced.

Conclusion: Enhanced infection-control strategies reduced VRE transmission in an oncology unit in which VRE were endemic.

Ann Intern Med. 1999;131:269-272.

For author affiliations and current author addresses, see end of text.

Shortly after the emergence of vancomycin resistance in enterococci, vancomycin-resistant enterococci (VRE) spread throughout the United States (1). In some hospitals, VRE became established as endemic nosocomial pathogens (2). The Centers for Disease Control and Prevention issued comprehensive recommendations for preventing VRE transmission (3). These recommendations, in combination with a program for reducing antimicrobial use, are referred to as enhanced infection-control strategies. They were instituted in an adult oncology unit in which VRE were endemic (4). We report the results of a prospective study that compared the effectiveness of enhanced infection-control strategies with the effectiveness of standard VRE infection-control practices.

Methods

Our study was conducted at an 11-room, 22-bed adult oncology unit in a 650-bed tertiary care hospital. Standard infection-control practices and enhanced infection-control strategies are given in **Table 1**. Standard practices were in effect from November 1993 until July 1994, and enhanced strategies were in effect from July 1994 until July 1995. Perianal surveillance cultures were obtained by using previously reported methods (4). Our study was approved by the institutional review boards of New York Medical College, Westchester Medical Center, and the Centers for Disease Control and Prevention.

Data Collection

Patients "at risk" for VRE were patients with VRE-negative perianal cultures. "New VRE-positive" patients were patients who had a first VRE-positive culture while they were hospitalized in the oncology unit. Bloodstream infection with VRE was defined by using standard criteria (5). Demographic characteristics and clinical patient data were collected prospectively from patient charts. Antimicrobial use was abstracted from computerized pharmacy records. Observational monitoring of health care worker compliance with handwashing and gown and glove use was conducted regularly.

Microbiological Methods

Perianal swabs and environmental cultures were inoculated into M-enterococcus broth (Difco Laboratories, Detroit, Michigan) or Enterococcosel broth (Becton Dickinson Microbiology Systems, Sparks, Maryland), both of which were supplemented with 6 μg of vancomycin. Vancomycin-resistant enterococci were identified from broths (6), isolates were characterized to the species level (7), minimum inhibitory concentrations for vancomycin were determined (8), and selected isolates were compared for

Table 1. Standard Infection-Control Practices Compared with Enhanced Infection-Control Strategies for Patients in an Adult Oncology Unit*

Standard infection control
Inpatient surveillance: perianal cultures on admission and weekly
Handwashing before and after patient contact
Contact isolation for VRE-infected and VRE-colonized patients
Gown and glove use for *direct patient contact* with VRE-infected and VRE-colonized patients
Consultation with infectious diseases specialists for patients with persistent fever
Enhanced infection control
Inpatient surveillance: perianal cultures on admission and weekly
Handwashing before and after contact with the patient
Contact isolation for VRE-colonized and VRE-infected patients
Gown and glove use *on entry of rooms* of VRE-infected and VRE-colonized patients
Consultation with infectious disease specialists when infection is first suspected, with special emphasis on reducing all use of antimicrobial agents
Systematic recommendation by infectious disease specialists to discontinue empirical vancomycin use after 72 hours
Systematic recommendation by infectious disease specialists to use oral metronidazole rather than oral vancomycin for *Clostridium difficile* colitis
Spatial separation of patients into three cohorts: VRE positive, VRE negative, and VRE unknown
VRE-unknown patients housed on a separate unit until results of perianal culture become known
Surveillance perianal cultures taken for oncology inpatients housed off the oncology unit†
Gown and glove use on entry of rooms of VRE-unknown patients
Assignment of staff cohorts; nurses and nursing assistants assigned to VRE-positive patients or VRE-negative and VRE-unknown patients
Patient orientation about VRE with an explanatory brochure
Monitoring compliance by observational studies
Environmental cultures taken in VRE-positive patient rooms before and after patient discharge and room disinfection

* VRE = vancomcyin-resistant enterococci.
† Surveillance perianal cultures were performed on oncology patients housed in units other than the oncology unit to reduce the number of patients with unknown VRE status.

relatedness by pulsed-field gel electrophoresis (9, 10); all of these procedures were done by using previously reported methods.

Statistical Analysis

Patient characteristics were compared by using the chi-square test for categorical data and the Student *t*-test or Wilcoxon rank-sum test for continuous variables. Person-time rate comparisons were performed by using Pepi 2.0 software (Stone Mountain, Georgia). All *P* values are two-tailed.

Results

Incidence of Vancomycin-Resistant Enterococci

We obtained cultures for VRE from all 259 patients (100%) in 404 admissions to the unit during use of enhanced infection-control strategies and 167 of 184 patients (91%) in 210 admissions to the unit during use of standard infection-control practices. The number of patients at risk for acquiring VRE was 212 of 259 patients (82%) during use of enhanced infection-control strategies and 160 of 167 patients (96%) during use of standard infection-control practices.

Patients hospitalized during the use of enhanced infection-control strategies were older than patients hospitalized during the period when standard infection-control practices were used (mean age ± SD, 57.3 ± 15.4 years compared with 53.4 ± 18 years; $P = 0.03$). The two groups also differed with respect to oncologic diagnosis ($P = 0.06$). During use of enhanced infection-control strategies, more patients had gastrointestinal cancer (57 of 212 patients [26.9%] compared with 20 of 160 patients [12.5%]) and fewer patients had hematologic cancer (60 patients [28.3%] compared with 69 patients [43.1%]). However, the two groups were similar with respect to the percentages of patients with lung cancer (29 patients [13.7%] compared with 26 patients [16.3%]); breast, uterine, or prostate cancer (36 patients [17%] compared with 23 patients [14.4%]); and other diagnoses (aplastic anemia, melanoma, bladder cancer, renal cancer, or head and neck cancer) (30 patients [14.2%] compared with 22 patients [13.7%]). The two groups were also similar with respect to sex (118 men [55.7%] compared with 85 men [53.1%]; $P > 0.2$), patients requiring transfer to the intensive care unit during admission (18 patients [8.5%] compared with 8 patients [5.0%]; $P > 0.2$), and number of admissions in which patients received chemotherapy (242 admissions [59.9%] compared with 135 admissions [64.3%]; $P > 0.2$).

During use of enhanced infection-control strategies, significant reductions were seen in the rate of VRE bloodstream infection (0.45 patients per 1000 patient-days compared with 2.1 patients per 1000 patient-days; relative rate ratio, 0.22 [95% CI, 0.05 to 0.92]; $P = 0.04$) and the VRE colonization rate (10.3 patients per 1000 patient-days compared with 20.7 patients per 1000 patient-days; relative rate ratio, 0.5 [CI, 0.33 to 0.75]; $P < 0.001$] (**Table 2**). Among patients with an oncologic diagnosis of hematologic cancer, the VRE bloodstream infection rate (1.4 patients per 1000 patient-days compared with 3.2 patients per 1000 patient-days; relative rate ratio, 0.45 [CI, 0.10 to 1.96]; $P > 0.2$) and the VRE colonization rate (15.7 patients per 1000 patient-days compared with 24.4 patients per 1000 patient-days; relative rate ratio, 0.65 [CI, 0.37 to 1.13]; $P = 0.13$) were lower during use of enhanced infection-control strategies, but the differences were not statistically significant. Among patients with solid tumors, the VRE colonization rate was also lower during use of enhanced infection-control strategies (8.6 patients per 1000 patient-days compared with 13.2 patients per 1000 patient-days; relative rate ratio, 0.65 [CI, 0.34 to 1.24]; $P = 0.2$); no patient had VRE bloodstream infection.

Thirty-two of the 41 perianal isolates obtained during use of enhanced infection-control strategies were *Enterococcus faecium,* 5 isolates were *E. faecalis*, 3 isolates were *E. avium*, and 1 isolate was *E.*

gallinarum. The minimum inhibitory concentration of vancomycin for the 41 VRE isolates was at least 64 μg/mL (range, 64 to > 1024 μg/mL). Pulsed-field gel electrophoresis showed 23 distinct *E. faecium* isolates.

Environmental Surveillance

After discharge of VRE-positive patients and disinfection of the patients' rooms, the number of environmental surfaces with VRE was significantly lower than that detected while VRE-positive patients were still occupying their rooms (13 of 162 cultures [8%] compared with 45 of 167 cultures [26.9%]; $P < 0.001$). By using pulsed-field gel electrophoresis, we found that for all seven of the patient–environment pairs tested, vancomycin-resistant *E. faecium* isolates recovered from environmental surfaces were identical to the isolate recovered from the patient occupying the room.

Compliance with Enhanced Infection-Control Strategies

Most persons (111 of 121 [91.7%]) who entered the rooms of VRE-positive patients used gowns and gloves appropriately. Gowns and gloves were located immediately outside 48 of 66 rooms (72.7%). All persons using gowns and gloves washed their hands after glove removal.

Changes in Antimicrobial Use

Compared with use during the standard infection-control period, use of vancomycin, imipenem–cilastatin, ceftazidime, ciprofloxacin, aztreonam, and gentamicin during the enhanced infection-control period was significantly reduced (**Table 2**). Use of amikacin also decreased, although the difference was not statistically significant. Use of clindamycin increased significantly (**Table 2**).

Discussion

Infection-control experts anticipated that it would be difficult to interrupt transmission of VRE after the microorganism became established as an endemic nosocomial pathogen (3). Studies conducted in centers with endemic VRE found that contact isolation measures with surveillance cultures (11) and contact isolation measures with surveillance cultures and controlled vancomycin use (2) did not reduce VRE transmission.

Several factors may have contributed to the success of the enhanced infection-control strategies. Our study was conducted in a single unit, which allowed ongoing surveillance of a sample of patients that was infrequently transferred between hospital units. The enhanced infection-control strategies focused on comprehensive reduction of person-to-person VRE transmission by adding the following: assigning patients to geographic cohorts, assigning nurses to patient cohorts, providing extensive education to patients and staff members, using gowns and gloves on room entry, monitoring compliance, and obtaining environmental surveillance cultures to our standard infection-control practices of performing contact isolation and obtaining surveillance cultures. Although the presence of 23 distinct vancomycin-resistant *E. faecium* isolates in the unit made it difficult to demonstrate person-to-person transmission, the reduction in VRE colonization rates associated with enhanced infection-control strategies suggests that VRE was being spread by person-to-person contact.

Reduction in use of several classes of antimicrobial agents in addition to vancomycin was probably an important component in preventing VRE acquisition during use of enhanced infection-control strategies. Use of cephalosporin (12) and metronidazole (13) are risk factors for VRE colonization or infection, and reduction of cephalosporin use has been associated with possible reductions of VRE colonization rates (14).

The VRE isolates recovered from environmental surfaces were identical to the VRE isolates recovered from patients, which suggests that the environ-

Table 2. Outcomes of Enhanced Infection-Control Strategies Compared with Outcomes of Standard Infection-Control Practices in an Adult Oncology Unit

Outcome	Standard Infection-Control Practices	Enhanced Infection-Control Strategies	Relative Rate Ratio (95% CI)	*P* Value
VRE bloodstream infection rate, *patients per 1000 patient-days*	2.1	0.45	0.22 (0.05–0.92)	0.04
VRE colonization rate, *patients per 1000 patient-days*	20.7	10.3	0.5 (0.33–0.75)	<0.001
Antimicrobial use, *g per 1000 person-days*				
Vancomycin	605	435	0.72 (0.69–0.76)	<0.001
Imipenem–cilastatin	333	293	0.88 (0.82–0.94)	<0.001
Ceftazidime	1220	1028	0.84 (0.81–0.87)	<0.001
Ciprofloxacin	48.5	39	0.81 (0.67–0.96)	0.02
Aztreonam	133	78.6	0.60 (0.53–0.67)	<0.001
Gentamicin	30.2	7.8	0.26 (0.19–0.35)	<0.001
Amikacin	96.4	87.8	0.91 (0.81–1.03)	0.13
Clindamycin	47.5	72.9	1.5 (1.31–1.78)	<0.001

ment may be a reservoir for VRE. Appropriate environmental decontamination (15) may have been an important part of these enhanced infection-control strategies. Although it is controversial to require persons entering the rooms of VRE-positive patients to wear gowns and gloves (16, 17), such attire may provide a barrier against VRE transmission and may increase overall compliance with infection-control measures (17).

Our study has several limitations. First, it was conducted in a single hospital. Second, because standard infection-control practices and enhanced infection-control strategies were conducted sequentially, the standard-practices period may have favorably influenced adherence with enhanced infection-control strategies. Third, we could not control for the changes in the oncologic diagnosis of the patient sample. The reduced rates of VRE bloodstream infection and VRE colonization among patients with hematologic cancer as well as among patients with solid tumors suggest that these improvements were not entirely a result of changes in the oncologic diagnosis of the patient sample. Fourth, the use of different time intervals for standard infection-control practices (8 months) and enhanced infection-control strategies (12 months) may have allowed seasonal effects to influence our results, although no seasonal distribution in VRE infections has been reported. Finally, because the enhanced infection-control strategies implemented 15 infection-control measures simultaneously, our study cannot indicate which components were most useful in reducing VRE transmission.

The effectiveness of enhanced infection-control strategies may have been underestimated. The reduction in VRE transmission was measured on the basis of comparison with the standard-practices period, during which fairly extensive infection-control measures were already in place. An even greater improvement might have been observed if no specific VRE infection-control measures had been performed in the comparison group. Further studies are needed to determine which components of enhanced infection-control strategies are most effective at reducing VRE transmission and whether these strategies can be implemented in other hospital settings.

From New York Medical College and Westchester Medical Center, Valhalla, New York; and the Centers for Disease Control and Prevention, Atlanta, Georgia.

Presented in part at the 37th Interscience Conference in Antimicrobial Agents and Chemotherapy, Toronto, Ontario, Canada, 1997; Abstract no. J84.

Acknowledgments: The authors thank Robert C. Moellering Jr. for his review of this manuscript. They also thank Tauseef Ahmed, Eric Feldman, Karen Seiter, Carmello Puccio, Hoo Chun, Robert Nadelman, John Nowakowski, Margaret Carraher, Catharine Spratt, Connie Engleking, Matthew Arduino, Paul Visintainer, Carol Diventi, and the nursing staff of the oncology unit for their contributions to this study and Barbara Moreland for secretarial assistance.

Grant Support: Contract no. 200-94-0860 from the Centers for Disease Control and Prevention.

Requests for Reprints: Marisa A. Montecalvo, MD, Division of Infectious Diseases, New York Medical College, Macy Pavilion 209SE, Valhalla, NY 10595.

Current Author Addresses: Dr. Montecalvo, Ms. Petrullo, and Drs. Horowitz and Wormser: Division of Infectious Diseases, New York Medical College, Macy Pavilion 209SE, Valhalla, NY 10595.
Dr. Jarvis: Centers for Disease Control and Prevention, 1600 Clifton Road NE, MS E-69, Atlanta, GA 30333.
Ms. Uman: 317 Broxton Road, Baltimore, MD 21212.
Dr. Shay: Centers for Disease Control and Prevention, 1600 Clifton Road, MS A-34, Atlanta, GA 30333.
Ms. Rodney and Ms. Gedris: Department of Microbiology, Westchester Medical Center, Valhalla, NY 10595.

References

1. Nosocomial enterococci resistant to vancomycin—United States, 1989–1993. MMWR Morb Mortal Wkly Rep. 1993;42:597-9.
2. **Morris JG Jr, Shay DK, Hebden JN, McCarter RJ Jr, Perdue BE, Jarvis W, et al.** Enterococci resistant to multiple antimicrobial agents, including vancomycin. Establishment of endemicity in a university medical center. Ann Intern Med. 1995;123:250-9.
3. Recommendations for preventing the spread of vancomycin resistance. Recommendations of the Hospital Infection Control Practices Advisory Committee (HIPAC). MMWR Morb Mortal Wkly Rep. 1995;44(RR-12):1-13.
4. **Montecalvo MA, Horowitz H, Gedris C, Carbonaro C, Tenover FC, Issah A, et al.** Outbreak of vancomycin-, ampicillin-, and aminoglycoside-resistant *Enterococcus faecium* bacteremia in an adult oncology unit. Antimicrob Agents Chemother. 1994;38:1363-7.
5. **Garner JS, Jarvis WR, Emori TG, Horan TC, Hughes JM.** CDC definitions for nosocomial infections, 1988. Am J Infect Control. 1988;16:128-40.
6. **Van Horn KG, Gedris CA, Rodney KM.** Selective isolation of vancomycin-resistant enterococci. J Clin Microbiol. 1996;34:924-7.
7. **Facklam RR, Washington, JA II.** Streptococci and related catalase-negative gram-positive cocci. In: Balows A, Hausler WJ Jr, Herrmann KL, Isenberg HD, Shadomy HJ, eds. Manual of Clinical Microbiology. 5th ed. Washington, DC: American Soc Microbiology; 1991:238-57.
8. **Sahm DF, Washington JA II.** Antibacterial susceptibility tests: dilution methods. In: Balows A, Hausler WJ Jr, Herrmann KL, Isenberg HD, Shadomy HJ, eds. Manual of Clinical Microbiology. 5th ed. Washington, DC: American Soc Microbiology; 1991:1105-16.
9. **Murray BE, Singh KV, Heath JD, Sharma BR, Weinstock GM.** Comparison of genomic DNAs of different enterococcal isolates using restriction endonucleases with infrequent recognition sites. J Clin Microbiol. 1990;28:2059-63.
10. **Tenover FC, Arbeit RD, Goering RV, Mickelsen PA, Murray BE, Persing DH, et al.** Interpreting chromosomal DNA restriction patterns produced by pulsed-field gel electrophoresis: criteria for bacterial strain typing. J Clin Microbiol. 1995;33:2233-9.
11. **Wells CL, Juni BA, Cameron SB, Mason KR, Dunn DL, Ferrieri P, et al.** Stool carriage, clinical isolation, and mortality during an outbreak of vancomycin-resistant enterococci in hospitalized medical and/or surgical patients. Clin Infect Dis. 1995;21:45-50.
12. **Tornieporth NG, Roberts RB, John J, Hafner A, Riley LW.** Risk factors associated with vancomycin-resistant *Enterococcus faecium* infection or colonization in 145 matched case patients and control patients. Clin Infect Dis. 1996;23:767-72.
13. **Edmond MB, Ober JF, Weinbaum DL, Pfaller MA, Hwang T, Sanford MD, et al.** Vancomycin-resistant *Enterococcus faecium* bacteremia: risk factors for infection. Clin Infect Dis. 1995;20:1126-33.
14. **Quale J, Landman D, Saurina G, Atwood E, DiTore V, Patel K.** Manipulation of a hospital antimicrobial formulary to control an outbreak of vancomycin-resistant enterococci. Clin Infect Dis. 1996;23:1020-5.
15. **Anderson RL, Carr JH, Bond WW, Favero MS.** Susceptibility of vancomycin-resistant enterococci to environmental disinfectants. Infect Control Hosp Epidemiol. 1997;18:195-9.
16. **Boyce JM, Opal SM, Chow JW, Zervos MJ, Potter-Bynoe G, Sherman CB, et al.** Outbreak of multidrug-resistant *Enterococcus faecium* with transferable *vanB* class vancomycin resistance. J Clin Microbiol. 1994;32:1148-53.
17. **Slaughter S, Hayden MK, Nathan C, Hu TC, Rice T, Van Voorhis J, et al.** A comparison of the effect of universal use of gloves and gowns with that of glove use alone on acquisition of vancomycin-resistant enterococci in a medical intensive care unit. Ann Intern Med. 1996;125:448-56.