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Emergence and Dissemination of a Highly Vancomycin-Resistant *vanA* Strain of *Enterococcus faecium* at a Large Teaching Hospital

DAVID A. PEGUES,[1,2,3]† CLARE F. PEGUES,[2]† PATRICIA L. HIBBERD,[1,3] DALE S. FORD,[2] and DAVID C. HOOPER[1,2,3]*

Infectious Disease Unit[1] and Infection Control Unit,[2] Massachusetts General Hospital and Harvard Medical School,[3] Boston, Massachusetts 02114-2696

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We prospectively identified patients at the Massachusetts General Hospital from whom vancomycin-resistant enterococci (VRE) were isolated from a clinical specimen from 1 January 1991 through 31 December 1995. VRE strains were available from 139 (82%) of the 169 patients with clinical cases. Of these, 39 (28%) were identical or closely related by pulsed-field gel electrophoresis (i.e., VRE type A strain), including 38 (43%) of 89 VRE strains in 1995. By multivariate analysis, acquisition of the VRE type A strain was associated with receipt of clindamycin (odds ratio [OR] = 10.5), 15 or more days of hospitalization before the first isolation of VRE (OR = 2.9), and residence on one of the general medical floors (OR = 7.8). The VRE type A strain was a *vanA* strain of *Enterococcus faecium* and was highly resistant to all antimicrobial agents tested except chloramphenicol. These findings document the rapid dissemination of a highly resistant strain of *E. faecium* among patients and among other extant VRE strains at the Massachusetts General Hospital in 1995.

In the United States, enterococci are a leading cause of nosocomial infections, and vancomycin resistance is increasingly a problem among enterococcal isolates (2, 9, 14). Most vancomycin-resistant enterococci (VRE) have the VanA phenotype, characterized by high-level resistance to vancomycin and teicoplanin (5). Outbreaks of VRE infection associated with a clonal strain of *Enterococcus faecium* or *Enterococcus faecalis* strains of the VanA phenotype have been reported among patients on special care units (1, 10, 16, 23). However, risk factors promoting the hospital-wide dissemination of a clone of *vanA* VRE have not been characterized previously.

In January 1993, we initiated prospective laboratory-based surveillance for VRE among patients at Massachusetts General Hospital (MGH), an 800-bed teaching hospital and tertiary care referral center in Boston, Mass. We now report on the epidemiologic and microbiologic characterization of the first 169 patients identified with clinical VRE infection at our hospital. Analysis of surveillance data and pulsed-field gel electrophoresis (PFGE) of DNA from VRE strains facilitated the identification and characterization of a highly resistant clone of *E. faecium vanA* that rapidly disseminated throughout the hospital in 1995. The observation that a single strain type was able to emerge among multiple other extant resistant strains to become the dominant VRE strain in the hospital is novel and suggests that this strain may have characteristics that differ from those of other equally resistant VRE strains that allow it to persist and spread in the hospital environment.

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* Corresponding author. Mailing address: Infectious Disease Unit, Massachusetts General Hospital, 55 Fruit St., Boston, MA 02114-2696. Phone: (617) 726-3812. Fax: (617) 726-7416. E-mail: hooperd@a1.mgh.harvard.edu.

† Present address: Division of Infectious Diseases, Center for the Health Sciences, University of California at Los Angeles, Los Angeles, CA 90095-1688.

MATERIALS AND METHODS

Surveillance definitions and case finding. A case patient was defined as any patient at MGH from whom a vancomycin-resistant enterococcal strain was isolated from a clinical specimen from 1 January 1991 through 31 December 1995. Thirty-four patients from whom VRE were isolated only from rectal swab surveillance cultures performed in 1995 were excluded from this study. Infection control practitioners identified patients infected with VRE by daily review of the computer listing of positive cultures generated by the Microbiology Laboratory. Demographic and clinical data were collected for all patients from whom VRE were isolated.

Clinical VRE isolates were classified as being associated with active infection or colonization by using standard definitions of the Centers for Disease Control and Prevention (13) and were classified as (i) community acquired if the sample that was cultured was obtained before or within the first 24 h of admission to MGH, (ii) nosocomially acquired if the sample for culture was obtained more than 24 h after admission and at least one culture of a sample from the same body site was negative for VRE before the index sample was culture positive (i.e., the first culture from which VRE was isolated), and (iii) indeterminate if the sample for culture was obtained more than 24 h after admission and there was not at least one culture of a sample from the same body site that was negative for VRE before the index sample was culture positive.

VRE infection control procedures. Since January 1993, any patient from whom VRE was isolated from a clinical specimen or surveillance rectal swab was placed on contact precautions (3). Since September 1994, the use of oral vancomycin was restricted for the primary treatment of *Clostridium difficile*-associated diarrhea. The use of intravenous vancomycin, however, was not restricted. Beginning in 1995, rectal swab culture surveys were conducted on an inpatient unit whenever three or more patients from that unit had been identified to be infected or colonized with VRE within the prior 30 days.

Microbiologic analysis. In the MGH Microbiology Laboratory, enterococci were identified by pyrazinamidase and esculin tests (VisiSpot; J & S Medical Associates, Natick, Mass.) and with the Vitek GPI Card (bioMerieux Vitek, Inc., Hazelwood, Mo.). Brucella agar supplemented with 5% horse blood (BBL, Cockeysville, Md.) was used to isolate enterococci. Standard disk diffusion antimicrobial susceptibility tests were performed on all clinical enterococcal isolates except those from respiratory and vaginal secretions (19). The MIC of vancomycin was determined for isolates with vancomycin zones of inhibition of 8 to 16 mm by the E-test (AB Biodisk, Solna, Sweden). For purposes of surveillance, enterococcal isolates with vancomycin zones of inhibition of $\leq$16 mm in diameter were considered to be VRE and were included in this study.

All clinical VRE isolates were further characterized by one of us (D.A.P.). Identification of enterococci was performed by using the test scheme defined by Facklam and Collins (12) with the modification of Ruoff and colleagues (20). The MICs of vancomycin, ampicillin, and teicoplanin were determined by the methods of the National Committee for Clinical Laboratory Standards, except that brain heart infusion agar (Difco Laboratories, Detroit, Mich.) was used instead of Mueller-Hinton agar to aid in identifying the growth of the enterococci (19, 21). High-level gentamicin (>500 μg/ml) and streptomycin (>2,000 μg/ml) resistance were determined by use of the brain heart infusion agar screening

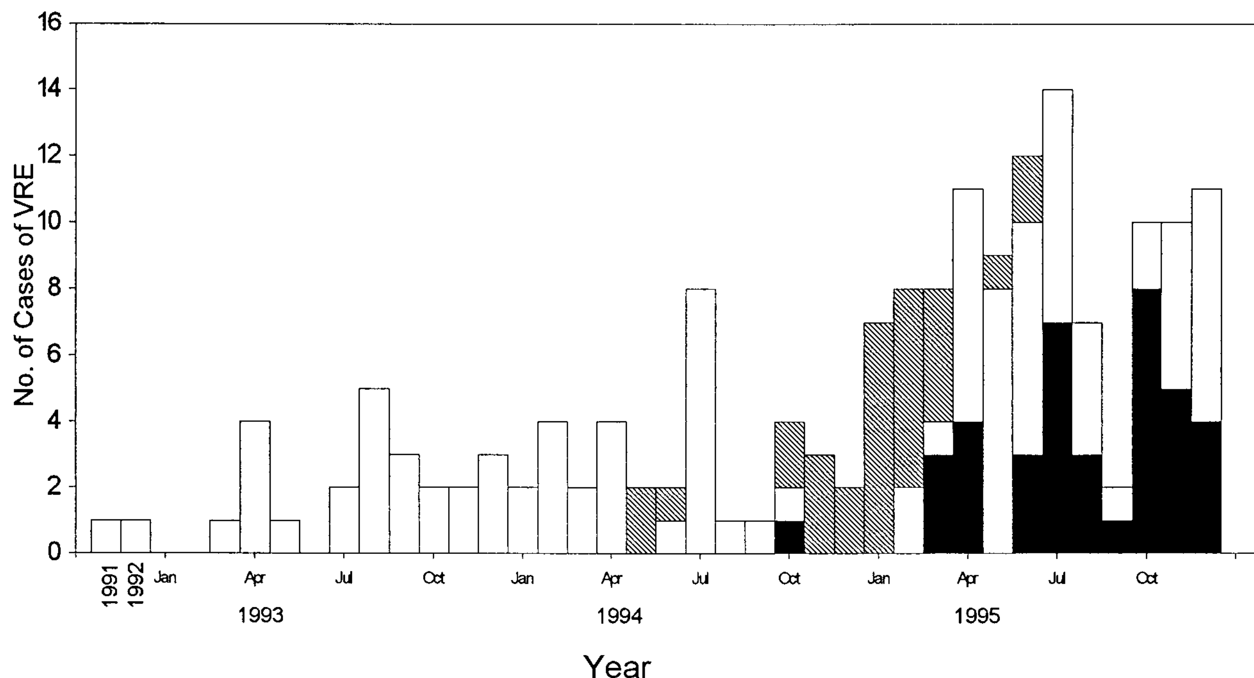

FIG. 1. Clinical cases of VRE infection or colonization determined by PFGE at MGH from 1991 to 1995. The solid bars indicate patients with cases of infection associated with VRE PFGE type A, the open bars indicate patients with cases of infection associated with VRE of other PFGE types, and the cross-hatched bars indicate patients from whom no isolate was available for typing.

method (19). *E. faecium* or *E. faecalis* isolates were defined as having the VanA phenotype if the vancomycin MIC was ≥64 μg/ml and the teicoplanin MIC was ≥2 μg/ml. These two species were defined as having the VanB phenotype if the vancomycin MIC was ≥8 μg/ml and the teicoplanin MIC was <2 μg/ml. For VanC strains vancomycin MICs were 8 to 16 μg/ml and teicoplanin MICs were <2 μg/ml.

PFGE was performed with a CHEF-DRII apparatus (Bio-Rad, Hercules, Calif.) after digestion of chromosomal DNA with *Sma*I (7). Strains that differed by three or fewer bands by visual inspection were considered to be derived from the same strain (22). Electrophoretic studies were repeated by digestion of chromosomal DNA of the predominant strain identified by initial analysis (i.e., VRE type A) with *Apa*I. The vancomycin resistance genotype of VRE type A was determined by PCR with *vanA*- and *vanB*-specific primers selected from published gene sequences (8, 11, 15).

Data analysis. Surveillance data were collected and analyzed by using EpiInfo software (version 6.01) (6). Proportions were compared by using the chi-square test or Fisher's exact test, as appropriate. Continuous variables were compared by the Wilcoxon rank sum test. To determine risk factors for acquisition of VRE type A compared with acquisition of VRE of other PFGE strain types, we restricted the analysis to the cohort of patients infected or colonized with clinical VRE isolates during 1995 from whom VRE strains were available for analysis. We then calculated the isolation rate ratios and 95% confidence intervals for the isolation of VRE strain type A according to selected demographic and clinical characteristics. Stepwise logistic regression analysis was performed by using SPSS/PC+ software (version 4.0; SPSS Inc., Chicago, Ill.) and BMDP software (release 7.0; BMDP Statistical Software, Los Angeles, Calif.), and the goodness-of-fit chi-square value for the model was determined. All *P* values are two-tailed.

RESULTS

Surveillance data. From 1 January 1991 through 31 December 1995, VRE were isolated from one or more clinical specimens from 169 patients at MGH (Fig. 1). The proportion of enterococci that were resistant to vancomycin increased from 0.06% in 1991 to 9.0% in 1995 ($P < 0.001$). The rate of clinical VRE per 1,000 patient-days increased significantly, from 0.084 in 1993 to 0.15 in 1994 to 0.46 in 1995 ($P < 0.001$).

Of the 169 patients who had clinical cases, 97 (57%) were female, and the patients ranged in age from 4 to 96 years (median age, 64 years). Acquisition of VRE was classified as nosocomial for 97 (57%) patients, indeterminate for 40 (24%) patients, and community acquired for 32 (19%) patients. All but six (4%) patients were hospitalized at MGH on the date that VRE was first cultured. Patients with VRE isolates were identified from 34 of the 43 patient care units, including 7 (79%) of 9 intensive care units and 27 (79%) of the 34 non-intensive care units. VRE were most frequently isolated from urine and wound specimens (55 and 14%, respectively); 43 (25%) VRE isolates were from sterile body sites, including blood (14 [8%]), bile (12 [7%]), and abscess fluid (10 [6%]). One-half of the clinical VRE isolates ($n = 85$) were associated with infections. Most patients (147 [87%]) had received one or more antimicrobial agents within the previous 30 days, most commonly intravenous vancomycin (84 [50%]).

Microbiological data. VRE strains from 139 (82%) of 169 patients with clinical cases were available for further analysis (Table 1). Most of the strains were *E. faecium*, which comprised 28% (7 of 25), 48% (12 of 25), and 89% (79 of 89) of the VRE strains from the periods 1991 to 1993, 1994, and 1995, respectively ($P < 0.001$). Of the 98 strains identified as *E. faecium*, two had low levels of resistance to vancomycin and were susceptible to ampicillin (MICs, ≤8 μg of vancomycin per ml and ≤1 μg of ampicillin per ml), suggesting the possibility that they were motility-negative *Enterococcus gallinarum*. These two strains were isolated in 1993 and 1994.

Of the 139 VRE strains, 92 (66%) had a VanA phenotype, 28 (20%) had a VanB phenotype, and 19 (14%) had a VanC phenotype. The Van phenotypes for each species are indicated in Table 1. The proportion of VRE strains that had a VanA phenotype was significantly greater in 1995 compared with that in the period from 1991 to 1994 (74 of 89 [83%] versus 18 of 50 [36%], respectively; $P < 0.001$).

PFGE analysis of the 139 VRE strains revealed at least 74 distinct PFGE strain types, including 43 distinct PFGE strain types among the 98 *E. faecium* strains and 31 distinct PFGE strain types among 41 non-*E. faecium* VRE strains. Among the

TABLE 1. Identification and antimicrobial resistance of clinical VRE isolates, 1991 to 1995

Enterococcus species	No. (%) of isolates (n = 139)[a]	Antimicrobial agent	MIC (μg/ml)		Van Phenotype[b]	No. (%) of VRE isolates		
			Range	50%[c]		1991–1994	1995	Total
E. faecium	98 (71)	Vancomycin	8–2,048	1,024	VanA	14 (16)	73 (84)	87
		Ampicillin	0.5–128	64	VanB	5 (45)	6 (55)	11
		Teicoplanin	0.5–512	128				
E. faecalis	22 (16)	Vancomycin	8–2,048	64	VanA	4 (80)	1 (20)	5
		Ampicillin	0.5–64[d]	1	VanB	13 (76)	4 (24)	17
		Teicoplanin	0.5–512	0.5				
E. gallinarium	13 (9)	Vancomycin	8–16	16	VanC	11 (85)	2 (15)	13
		Ampicillin	0.5	0.5				
		Teicoplanin	0.5	0.5				
E. casseliflavus	6 (4)	Vancomycin	8–16	8	VanC	3 (50)	3 (50)	6
		Ampicillin	0.5	0.5				
		Teicoplanin	0.5	0.5				
All species					VanA	18 (24)	74 (76)	92
					VanB	18 (64)	10 (36)	28
					VanC	14 (74)	5 (26)	19

[a] VRE isolates were available from 139 (82%) of 169 patients from whom a clinical specimen grew VRE on culture.
[b] See Materials and Methods for definitions of Van phenotypes.
[c] 50%, MICs at which 50% of isolates are inhibited.
[d] For only a single isolate was the ampicillin MIC 64 μg/ml.

non-*E. faecium* isolates, there were 16 PFGE strain types among 22 *E. faecalis* isolates, 9 types among 13 *E. gallinarum* isolates, and 6 types among 6 *Enterococcus casseliflavus* isolates. No PFGE strain type was identified from more than 3 (7%) of 41 patients who had non-*E. faecium* VRE strains. In contrast, among the 98 *E. faecium* strains analyzed by PFGE, 39 (40%) were identical or closely related (VRE strain type A) (Fig. 2). No other *E. faecium* PFGE strain type was identified from more than four patients.

The *E. faecium* type A strain was highly resistant (MICs, 1,024 μg of vancomycin per ml, 256 μg of teicoplanin per ml, and 128 μg of ampicillin per ml) and expressed high-level resistance to both gentamicin and streptomycin. The strain exhibited in vitro susceptibility only to chloramphenicol. A 1-kb *vanA*-specific DNA fragment was amplified from the *E. faecium* type A strain by PCR. Of the remaining 41 non-type A *E. faecium* strains identified in 1995, 39 (95%) were also highly resistant to vancomycin (MIC, ≥256 μg/ml) and 35 (85%) were highly resistant to teicoplanin (MIC, ≥16 μg/ml).

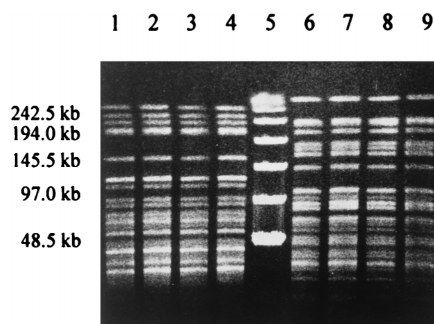

FIG. 2. PFGE banding pattern of chromosomal DNA from enterococcal strains from four patients infected with *E. faecium* type A. Strains were selected from the index patient from October 1994 (lanes 1 and 6) and one patient each from March (lanes 2 and 7), July (lanes 3 and 8), and November (lanes 4 and 9) 1995. DNA was digested with *Sma*I (lanes 1 to 4) or *Apa*I (lanes 6 to 9) and was subjected to electrophoresis with the CHEF-DRII system by using pulse intervals of 1 to 28 s at 180 V for 20 h. Lane 5, bacteriophage lambda ladder molecular size standards. Numbers to the left of the figure indicate DNA fragment sizes.

Outbreak strain. The type A VRE strain was first identified during October 1994 from a urine sample obtained from a 57-year-old female patient resident on a surgical unit 37 days following emergency transfer from another hospital; VRE had not been isolated from seven prior urine cultures. During 1995, VRE type A was isolated from 38 (43%) of the 89 patients with clinical VRE strains (Fig. 1). Patients infected with VRE type A were resident on 20 different patient care units, and no unit had more than five patients from whom VRE type A was identified. Of the 38 cases associated with VRE type A during 1995, 16 (47%) represented infections, including infections of urine (n = 9), blood (n = 3), abscess (n = 2), and other sites (n = 2). Acquisition was classified as nosocomial for 26 (68%) patients, indeterminate for 9 (24%) patients, and community acquired for 3 (8%) patients, each of whom was infected with VRE type A. The median durations of hospitalization before the samples referred for culture were obtained were 29 days (range, 5 to 168 days) and 4 days (range, 2 to 63 days) for those patients with nosocomial and indeterminate modes of acquisition, respectively. Each of the three patients with community-acquired VRE type A infection had been hospitalized at MGH within 30 days of the separate hospital admission when VRE was first isolated, with a median of 6 days of hospitalization (range, 1 to 8 days) between the last culture negative for VRE and the time that sample referred for culture was positive.

Risk factors for acquisition of VRE type A. By univariate analysis, the rate of acquisition of VRE type A was significantly greater among patients who had received intravenous clindamycin or vancomycin, had prior infection or colonization with methicillin-resistant *Staphylococcus aureus*, had a chest tube, and were hospitalized on one of the general medical floors (unit A) (Table 2). In addition, the rate of acquisition of VRE type A increased significantly with increasing duration of hospitalization before the date that VRE was first cultured (P = 0.041). The rate of acquisition of VRE type A also increased with an increase in the number of antimicrobial agents admin-

TABLE 2. Rate of isolation of VRE type A strains in 1995 among patients in MGH with VRE isolates, univariate analysis

Factor	Total no. of patients (n = 89)	No. of patients infected with type A strain (n = 38)	Rate (%)	Rate ratio (95% CI)	P value
Clindamycin treatment					
No	81	31	38.3	1.0	
Yes	8	7	87.5	2.2 (1.6–3.4)	0.019
Intravenous vancomycin treatment					
No	45	15	33.3	1.0	
Yes	44	23	52.3	1.6 (1.0–2.6)	0.071
Chest tube					
No	84	34	40.5	1.0	
Yes	5	4	80.0	2.0 (1.2–3.3)	0.16
Prior isolation of methicillin-resistant *S. aureus*					
No	73	28	38.4	1.0	
Yes	16	10	62.5	1.6 (1.0–2.6)	0.077
Patient was unit A on the day that VRE was first cultured (n = 86)[a]					
No	80	33	41.2	1.0	
Yes	6	5	83.3	2.0 (1.3–3.2)	0.057
Duration of hospitalization to date VRE first cultured (days)					
0–1	14	3	21.4	1.0	
2–14	25	8	32.0	1.5 (0.5–4.7)	
≥15	50	27	54.0	2.5 (0.9–7.1)	0.041[b]
No. of antimicrobial agents					
0	12	3	25.0	1.0	
1–3	42	15	35.7	1.4 (0.5–4.1)	
≥4	35	20	57.1	2.3 (0.8–6.4)	0.068[b]
Type of acquisition					
Community	15	3	20.0	1.0	
Indeterminate	21	9	42.9	2.1 (0.7–6.6)	0.15[c]
Nosocomial	53	26	49.1	2.4 (0.8–7.0)	0.044[c]

[a] Excludes outpatients (n = 3).
[b] Chi-square test for trend.
[c] Compared with community acquisition.

istered, but it did not reach the level of statistical significance (P = 0.068). Acquisition of VRE type A was also more likely to be classified as nosocomial or indeterminate compared with acquisition of other VRE types (35 of 38 [92%] versus 39 of 51 [76%], respectively; P = 0.015). The rate of acquisition of VRE type A did not differ significantly by patient sex or age, receipt of oral vancomycin or metronidazole, prior diagnosis of *C. difficile*-associated diarrhea, surgical procedure, or medical conditions. When outcome was examined, there was no significant difference between patients infected with VRE type A and patients infected with other VRE types according to the total duration of hospitalization (mean, 51.6 ± 38.1 versus 53.2 ± 51.0 days, respectively; P = 0.60) or in-hospital mortality (11 of 38 [29%] versus 9 of 51 [18%], respectively; P = 0.21).

In a multivariate model including all 89 patients with clinical VRE, independent predictors of acquisition of VRE type A were receipt of clindamycin (odds ratio [OR] = 10.5; 95% confidence interval [95% CI] = 1.1 to 97.5; P = 0.012), 15 or more days of hospitalization before the first isolation of VRE (OR = 2.8; 95% CI = 1.1 to 7.5; P = 0.027), and residence on medical unit A (OR = 7.8; 95% CI = 0.8 to 79.8; P = 0.044). The model fit the data well (Hosmer-Lemeshow goodness-of-fit chi-square = 2.35; P = 0.80). When the analysis was restricted to cases of infection classified as nosocomial or indeterminate or as nosocomial only, receipt of clindamycin was the only independent predictor of acquisition of VRE type A.

DISCUSSION

MGH experienced a dramatic rise in the proportion of enterococci that were resistant to vancomycin beginning in 1993. Analysis of surveillance and microbiology data suggested that before 1995, VRE were introduced into MGH from multiple sources and that nosocomial transmission of VRE was not sustained. During the period from 1991 to 1994, there was a heterogeneity of VRE species and a diversity of the PFGE strain types that were identified, with no one PFGE strain type being identified from more than three patients. In contrast, during 1995, there were at least 38 cases of infection or colonization of a clinical site with a single clone of highly resistant *vanA E. faecium.*

The hospital-wide dissemination of a single clone of *vanA E. faecium* has not been reported previously, nor have risk factors for acquisition been characterized except for those involving outbreaks in special care units (1, 10, 16, 23). Although the

clonal dissemination of a single *E. faecium vanB* strain was identified at five hospitals in the San Antonio, Tex., area during 1993 and 1994, cross-transmission of *E. faecium vanA* was limited (17). In addition, a clone of *E. faecium* was isolated from nine patients at three hospitals in Michigan and Illinois from 1990 to 1992, but the resistance phenotype of the strain was not stated, nor were risk factors for interhospital transmission examined (4). VRE type A appears to differ from other VRE strains present at the time of its emergence in its ability to establish dominance in the hospital. We are investigating microbial factors that might promote the selection and dissemination of the type A VRE strain over other prevalent VRE strains.

Of note, VRE type A continued to be isolated from clinical specimens and rectal swabs obtained from patients at MGH during 1996 and was isolated from patients from at least one other Boston teaching hospital during 1996 (12a). At this other hospital in 1996, type A also emerged as a dominant VRE strain among other extant VRE strains, thus providing further evidence for the distinct biological properties of strain A. Although we cannot rule out the possibility that VRE type A was periodically reintroduced into the hospital from new source patients during 1995, ongoing nosocomial transmission seems the most likely source of acquisition of the outbreak strain. For most patients (68%), nosocomial acquisition was documented during prolonged hospitalizations. In addition, each of the three patients classified as having community-acquired VRE type A had recently been hospitalized at MGH and therefore could have acquired the strain during the previous admission. The classification of cases as community acquired was for surveillance purposes and does not exclude the possibility that patients may have acquired VRE during a previous hospital admission.

By univariate analysis, we found that receipt of clindamycin and vancomycin and prior isolation of methicillin-resistant *S. aureus* (a correlate of having received vancomycin) were each associated with an increased rate of isolation of VRE type A compared with VRE strains of other PFGE types. These findings suggest that antimicrobial pressure, particularly receipt of agents with activity against anaerobes and vancomycin, may have promoted the development of VRE infection among patients with stool colonization and the emergence of the VRE type A strain among other extant VRE strains at MGH during 1995. We did not determine the duration of antimicrobial therapy in this heavily treated cohort of patients. Several studies, however, have correlated the acquisition of VRE with the intensity and duration of antimicrobial therapy (10, 16).

Although the outbreak of VRE type A could not be attributed to a change in infection control policies or patient care practices, acquisition of VRE type A was associated with an increased duration of hospitalization, suggesting that exposures in the hospital setting promoted the emergence and dissemination of this strain. A common vehicle of transmission was unlikely to account for the outbreak. While one medical unit was associated with the acquisition of VRE type A, only 5 (13%) of the 38 patients infected with this strain were resident on this unit during 1995, and infected or colonized patients were associated with 20 different patient care units. We were, however, limited in our ability to characterize the epidemiology of the early outbreak period, especially the distribution of PFGE types by unit, because only eight (25%) VRE isolates were available from the 32 patients with cases of infection identified from October 1994 to March 1995.

Recommendations for detecting, preventing, and controlling the spread of VRE have recently been published and emphasize the use of barrier precautions and the prudent use of vancomycin (3). Since 1994, oral vancomycin has not been used at MGH for the primary treatment of antibiotic-associated colitis, and the annual pharmacy expenditure for oral vancomycin formulations (tablets and liquid) decreased 51%, from $31,932 in 1994 to $15,914 in 1995. In contrast, intravenous vancomycin use has not been restricted and the annual pharmacy expenditure for injectable vancomycin increased 51%, from $214,897 in 1991 to $324,881 in 1995. To date, the effectiveness of the restriction on vancomycin use on reducing the rate of VRE colonization and infection has not been demonstrated. Despite substantial reductions in both oral and intravenous vancomycin use, Morris et al. (18) found no decrease in the prevalence of vancomycin resistance among enterococci at a large hospital with a consistent level of 20% colonization with VRE strains. Further careful epidemiologic studies are needed to determine the impact of restriction of antimicrobial use in limiting the spread of VRE, especially in hospitals where VRE is now endemic. This study emphasizes the importance of the systematic collection of surveillance data and strain typing in characterizing the epidemiology of the evolving VRE epidemic. The study further suggests that VRE strains differ in their biological properties that allow them to persist and spread within the hospital. Elucidating the bacterial virulence factors that contribute to the organism's survival in the hospital environment and transmissibility have been little studied and may prove to be as important as epidemiologic factors in understanding the acquisition and pathogenesis of nosocomial VRE infections.

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REFERENCES

1. **Boyce, J. M., L. A. Mermel, M. J. Zervos, L. B. Rice, G. Potter-Bynoe, C. Giorgio, and A. A. Medeiros.** 1995. Controlling vancomycin-resistant enterococci. Infect. Control Hosp. Epidemiol. **16:**634–637.
2. **Centers for Disease Control and Prevention.** 1993. Nosocomial enterococci resistant to vancomycin—United States, 1989–1993. Morbid. Mortal. Weekly Rep. **42:**597–599.
3. **Centers for Disease Control and Prevention.** 1995. Recommendation for preventing the spread of vancomycin resistance: recommendations of the Hospital Infection Control Practices Advisory Committee (HICPAC). Morbid. Mortal. Weekly Rep. **44:**1–12.
4. **Chow, J. W., A. Kuritza, D. M. Shlaes, M. Green, D. F. Sahm, and M. J. Zervos.** 1993. Clonal spread of vancomycin-resistant *Enterococcus faecium* between patients in three hospitals in two states. J. Clin. Microbiol. **31:**1609–1611.
5. **Clark, N. C., R. C. Cooksey, B. C. Hill, J. M. Swenson, and F. C. Tenover.** 1993. Characterization of glycopeptide-resistant enterococci from U.S. hospitals. Antimicrob. Agents Chemother. **37:**2311–2317.
6. **Dean, A. G., J. A. Dean, J. A. Burton, and R. C. Dicker.** 1994. EpiInfo, version 6: a wordprocessing, database, and statistics program for epidemiology for public health on IBM-compatible microcomputers. Centers for Disease Control and Prevention, Atlanta, Ga.
7. **Donabedian, S. M., J. W. Chow, J. M. Boyce, R. E. McCabe, S. M. Markowitz, P. E. Coudron, A. Kuritza, C. L. Pierson, and M. J. Zervos.** 1992. Molecular typing of ampicillin-resistant, non-β-lactamase-producing *Enterococcus faecium* isolates from diverse geographic areas. J. Clin. Microbiol. **30:**2757–2761.
8. **Dutka-Malen, S., C. Molinas, M. Arthur, and P. Courvalin.** 1990. The VanA glycopeptide resistance protein is related to D-alanyl-D-alanine ligase cell wall biosynthesis enzymes. Mol. Gen. Genet. **224:**364–372.
9. **Edmond, M. B., R. N. Jones, M. A. Pfaller, S. E. Wallace, R. P. Wenzel, and SCOPE Consortium Hospitals.** 1996. Multicenter surveillance for nosocomial enterococcal bacteremia: a comparison of vancomycin-sensitive vs. vancomycin-resistant cases. Infect. Control Hosp. Epidemiol. **17**(Suppl. 2)**:**18. (Abstract 14).
10. **Edmond, M. B., J. F. Ober, D. L. Weinbaum, M. A. Pfaller, T. Hwang, M. D.**

Sanford, and R. P. Wenzel. 1995. Vancomycin-resistant *Enterococcus faecium* bacteremia: risk factors for infection. Clin. Infect. Dis. **20:**1126–1133.

11. **Evers, S., D. F. Sahm, and P. Courvalin.** 1993. The *vanB* gene of vancomycin-resistant *Enterococcus faecalis* V583 is structurally related to genes encoding D-Ala:D-Ala ligases and glycopeptide-resistance proteins VanA and VanC. Gene **124:**143–144.
12. **Faklam, R. R., and M. D. Collins.** 1989. Identification of *Enterococcus* species isolated from human infections by a conventional test scheme. J. Clin. Microbiol. **27:**731–734.

12a. **Fridkin, S., and D. C. Hooper.** Unpublished data.

13. **Garner, J. S., W. R. Jarvis, T. G. Emori, T. G. Horan, and J. M. Hughes.** 1988. CDC definitions for nosocomial infections, 1988. Am. J. Infect. Control **16:**128–140.
14. **Gaynes, R., J. Edwards, and the National Nosocomial Infection Surveillance System.** 1996. Nosocomial vancomycin resistant enterococci (VRE) in the United States, 1989–1995: the first 1000 isolates. Infect. Control Hosp. Epidemiol. **17**(Suppl. 2)**:**18. (Abstract 13).
15. **Gold, H. S., S. Unal, E. Cercenado, C. Thauvin-Eliopoulos, G. M. Eliopoulos, C. B. Wennersten, and R. C. Moellering, Jr.** 1993. A gene conferring resistance to vancomycin but not teicoplanin in isolates of *Enterococcus faecalis* and *Enterococcus faecium* demonstrates homology with *vanB*, *vanA*, and *vanC* genes of enterococci. Antimicrob. Agents Chemother. **37:**1604–1609.
16. **Livornese, L. L., Jr., S. Dias, C. Samel, B. Romanowski, S. Taylor, P. May, P. Pitsakis, G. Woods, D. Kaye, M. E. Levison, et al.** 1992. Hospital-acquired infection with vancomycin-resistant *Enterococcus faecium* transmitted by electronic thermometers. Ann. Intern. Med. **117:**112–116.
17. **Moreno, F., P. Grota, C. Crisp, K. Magnon, G. P. Melcher, J. H. Jorgensen, and J. E. Patterson.** 1995. Clinical and molecular epidemiology of vancomycin-resistant *Enterococcus faecium* during its emergence in a city in southern Texas. Clin. Infect. Dis. **21:**1234–1237.
18. **Morris, J. G., Jr., D. K. Shay, J. N. Hebden, R. J. McCarter, Jr., B. E. Perdue, W. Jarvis, J. A. Johnson, T. C. Dowling, L. B. Polish, and R. S. Schwalbe.** 1995. Enterococci resistant to multiple antimicrobial agents, including vancomycin. Establishment of endemicity in a university medical center. Ann. Intern. Med. **123:**250–259.
19. **National Committee for Clinical Laboratory Standards.** 1993. Performance standards for antimicrobial disk susceptibility tests for bacteria that grow aerobically, 3rd ed. Approved standard. Abstract. National Committee for Clinical Laboratory Standards, Villanova, Pa.
20. **Ruoff, K. L., L. de la Maza, M. Murtagh, J. D. Spargo, and M. J. Ferraro.** 1990. Species identities of enterococci isolated from clinical specimens. J. Clin. Microbiol. **28:**435–437.
21. **Shlaes, D. M., A. Bouvet, C. Devine, J. H. Shlaes, S. Al-Obeid, and R. Williamson.** 1989. Inducible, transferable resistance to vancomycin in *Enterococcus faecalis* A256. Antimicrob. Agents Chemother. **33:**198–203.
22. **Tenover, F. C., R. D. Arbeit, R. V. Goering, P. A. Mickelsen, B. E. Murray, D. H. Persing, and B. Swaminathan.** 1995. Interpreting chromosomal DNA restriction patterns produced by pulsed-field gel electrophoresis: criteria for bacterial strain typing. J. Clin. Microbiol. **33:**2233–2239.
23. **Wells, C. L., B. A. Juni, S. B. Cameron, K. R. Mason, D. L. Dunn, P. Ferrieri, and F. S. Rhame.** 1995. Stool carriage, clinical isolation, and mortality during an outbreak of vancomycin-resistant enterococci in hospitalized medical and/or surgical patients. Clin. Infect. Dis. **21:**45–50.