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Epidemiologic Evaluation of Antimicrobial Resistance in Community-Acquired Enterococci

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Fecal samples from 200 consecutive patients admitted to a community hospital yielded 107 enterococci. High-level gentamicin resistance occurred in 10 (14%) of the *Enterococcus faecalis* isolates. Ampicillin resistance occurred in two (3%) of the *E. faecalis* isolates and six (23%) of the *Enterococcus faecium* isolates. There were no vancomycin-resistant enterococci. Risk factors for enterococci with high-level aminoglycoside (gentamicin) or ampicillin resistance included prior hospitalization and previous antibiotic use.

Enterococci are widely distributed in nature. The natural habitat of these organisms is the intestinal tracts of humans and animals. Enterococci are important causes of hospital-acquired infection (19, 24). They are the second most common cause of nosocomial infections and the third most common cause of nosocomial bacteremia (24). Within recent years, a great deal has been learned about the epidemiology of and risk factors for nosocomial enterococcal infection, with person-to-person spread of antibiotic-resistant isolates well documented (23, 28, 29).

Enterococci are also important causes of community-acquired infection (15, 19). These enterococcal infections have been traditionally thought of as endogenous and arising from the patient's own flora. Microorganisms from endogenous sources subsequently cause infection by invasion of commensal flora which infect because of some alteration in host defenses. The sources and reservoirs that play a role in the resistance to antibiotics of enterococci that are community acquired are not known. In earlier studies in the United States and Europe, community acquisitions of gentamicin-resistant enterococci (21) and of glycopeptide-resistant enterococci (VRE) (2, 3, 14, 27), respectively, were documented, suggesting a reservoir in the community. Little is currently known concerning the epidemiology or prevalence of resistant enterococci in the community setting. We therefore evaluated the prevalence and risk factors for fecal carriage of antibiotic-resistant enterococci in patients admitted to the hospital.

William Beaumont Hospital is a 925-bed community teaching hospital. We prospectively studied 200 consecutive patients admitted to the hospital over a 3-month period in 1993. All hospitalized patients gave written informed consent and were hospitalized on three 60-bed medical floors. Demographic and risk factor information and stool samples were collected within 48 h of admission. Fecal samples were grown on Columbia CNA agar (BBL, Cockeysville, Md.) and brain heart infusion agar (Difco Co., Detroit, Mich.). From each culture, three separate colony types were evaluated. Identification to the species level was performed by biochemical reactions as described by Facklam and Collins (10). In vitro susceptibilities of strains to gentamicin, streptomycin, ampicillin, and vancomycin were determined by use of a published standardized microdilution technique (13, 22). β-Lactamase production was determined by nitrocefin disks (Becton Dickinson, Cockeysville, Md.). High-level aminoglycoside resistance was defined by an MIC of >2,000 μg/ml.

Patient groups that were compared in the statistical analysis included hospitalized patients with *Enterococcus faecalis* and *Enterococcus faecium* and control patients from whose stool samples enterococci were not isolated. Hospitalized patients with antimicrobial-susceptible enterococci and patients with ampicillin- or aminoglycoside-resistant enterococci were also compared. The statistical significance between groups was evaluated by using tests of homogeneity of odds and the two-tailed Fisher's exact test for bivariate analysis of dichotomous-outcome data. Continuous variables were compared with the Mann-Whitney U test. A multivariate logistic regression model was used to evaluate the independence of risk factors.

We monitored 200 patients with 200 admissions (94 men and 106 women). Of these patients, six had more than one enterococcal isolate. Hospitalized patients with *Enterococcus* spp. isolated ranged in age from 29 to 82 years (mean, 63 years); 100 (50%) of the patients were culture positive for *Enterococcus* spp. Of the enterococci cultured, 73 isolates (68%) were *E. faecalis*, 26 (24%) were *E. faecium*, 5 (4%) were *Enterococcus gallinarum*, and 3 (3%) were *Enterococcus hirae.*

Of the 73 *E. faecalis* isolates, 8 (11%) demonstrated high-level gentamicin plus high-level streptomycin resistance and 13 (18%) showed high-level streptomycin resistance in the absence of high-level gentamicin resistance. Of the 26 *E. faecium* isolates, none (0%) showed high-level gentamicin plus high-level streptomycin resistance and 4 (15%) demonstrated high-level streptomycin resistance in the absence of high-level gentamicin resistance. The MIC of vancomycin for all isolates was <8.0 μg/ml, with the exception of one *E. gallinarum* isolate, for which the MIC was 8.0 μg/ml. The other four *E. gallinarum* isolates required MICs of vancomycin of 4.0 μg/ml. Of the isolates with high-level streptomycin resistance, 21 were *E. faecalis* while 4 were *E. faecium*. No β-lactamase-positive isolates were identified.

Risk factors and demographic characteristics for hospitalized patients and controls are summarized in Table 1. The mean age of patients with *E. faecalis* was 64 years (range, 20 to 80 years), the mean age of patients with *E. faecium* was 65 years (range, 20 to 80 years), and the mean age of controls was 61 years (range, 20 to 80 years). Prior hospitalization was most common in patients with *E. faecalis*. There were no significant

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TABLE 1. Risk factors for species of *Enterococcus* isolated from inpatients

Characteristic	No. (%) of patients with:			P^a
	E. faecalis	*E. faecium*	No enterococci (controls)[b]	
Total patients	73	26	100	
Male/female	33/40	12/14	49/51	NS
Prior hospitalization	27 (37)	4 (15)	25 (25)	NS
Prior surgery	7 (10)	2 (8)	12 (12)	NS
Prior antibiotics	30 (41)	6 (23)	32 (32)	NS
Underlying diseases	70 (96)	26 (100)	98 (98)	NS
Fast food >3×/week	4 (5)	2 (8)	8 (8)	NS
Dental procedure	16 (22)	7 (27)	16 (16)	NS
Prior nursing home	2 (3)	0 (0)	5 (5)	NS
Travel	30 (41)	11 (42)	30 (30)	NS

[a] NS, values not significantly different in multivariate analysis.
[b] Enterococci were not cultured from these patients.

differences in the risk factor variables specific for *Enterococcus* spp. studied.

A comparison of risk factors for patients with ampicillin-resistant enterococci, high-level-gentamicin-resistant enterococci, and ampicillin-susceptible plus gentamicin-susceptible enterococci is shown in Table 2. Prior hospitalization was significantly more common in patients with high-level-gentamicin-resistant and ampicillin-resistant enterococci than in controls ($P < 0.001$). Previous antibiotic use was significantly more common in patients with ampicillin-resistant enterococci than in controls ($P = 0.03$). None of the variables analyzed was significant in the multivariate analysis.

In the past decade, there has been a rapid rise in the number of serious nosocomial infections caused by enterococci resistant to multiple antibiotics. Enterococci with high-level gentamicin resistance were first identified in the 1980s, with intra- and interhospital spread seen in nursing homes and hospitals (23, 28, 29). Subsequently, ampicillin-resistant enterococci, including β-lactamase-producing and non-β-lactamase-producing strains, were isolated (4, 9, 12, 20). Most recently, glycopeptide-resistant strains among hospitals in separate states have become a major concern (5–7, 11, 18, 26).

TABLE 2. Risk factors for antimicrobial resistance in hospitalized patients from whom enterococci were isolated

Characteristic	No. (%) of patients with:			P^f
	Ampicillin-resistant enterococci	HLGR[a] enterococci	Aminoglycoside- and ampicillin-susceptible enterococci[b]	
Total patients	9[c]	10[d]	68[e]	
Male/female	3/6	4/6	33/35	NS
Prior hospitalization	8 (89)	9 (90)	15 (22)	<0.001
Prior surgery	1 (11)	2 (20)	5 (7)	NS
Prior antibiotics	6 (67)	3 (30)	24 (36)	0.03
Underlying diseases	7 (78)	10 (100)	60 (89)	NS
Fast food >3×/week	0 (0)	0 (0)	3 (4)	NS
Dental procedure	1 (11)	2 (20)	21 (31)	NS
Prior nursing home	0 (0)	1 (10)	1 (2)	NS
Travel	2 (22)	2 (20)	29 (42)	NS

[a] HLGR, high-level-gentamicin-resistant.
[b] Gentamicin and streptomycin MIC, <2,000 μg/ml; ampicillin MIC, <16 μg/ml.
[c] Includes six *E. faecium*, two *E. faecalis*, and one *E. gallinarum* isolates.
[d] All *E. faecalis* isolates.
[e] Includes 48 *E. faecalis* isolates and 20 *E. faecium* isolates.
[f] All variables were not significant (NS) in multivariate analysis.

To help determine the basis for the spread of antibiotic resistance in enterococci, we analyzed the prevalence of resistance in fecal samples, risk factors, and epidemiology in patients admitted to a large community teaching hospital in southeastern Michigan. For patients admitted to the hospital, we found that 50% of them had enterococci isolated from stool, with 68% of the isolates being *E. faecalis* and 24% of them being *E. faecium*. These findings show a lower level of fecal colonization with enterococci than that demonstrated by other surveys (15). Enterococci present in stool in small numbers or some strains exhibiting resistance may have been below the limits of detection by our methods. Since media specifically selective for VRE isolation were not used, some of these strains may have been missed. In the United States, VRE appear to have spread in hospitals. Community acquisition of strains has not been reported (8). Importantly, vancomycin-resistant enterococci were not cultured from the population we studied. In Europe, however, vancomycin-resistant strains have been isolated from asymptomatic outpatients and from animals, food, and sewage, showing various community reservoirs (1–3, 16, 17, 25); these findings indicate important differences in the epidemiology of VRE in Europe and the United States. These differences may be related to the use of avoparcin in animal feed in Europe and the overuse of vancomycin in hospitalized patients in the United States.

In this study, previous antibiotic administration and hospitalization within the past 3 months were significant variables associated with colonization by enterococci with ampicillin or high-level gentamicin resistance. The small numbers of patients with resistant organisms limited the statistical analysis. In patients without recent hospitalization, resistant strains were rare, suggesting nosocomial acquisition of strains during prior admissions. Increasing awareness of these resistant organisms as colonizing strains may lead to a change in control measures at sites where patients are known to be frequently readmitted, such as oncology or renal units; at such sites, periodic surveillance cultures and screening for resistance may be warranted.

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