

Letter to the Editor

Change in Prevalence and Antibiotic Resistance of *Enterococcus* Species Isolated from Blood Cultures over an 8-Year Period

The enterococci have emerged as a major cause of nosocomial bacteremia due in part to increasing resistance to antimicrobial therapy (1, 4, 7, 10, 11). To determine whether a shift in the prevalence of *Enterococcus* species was associated with an increase in antimicrobial resistance, we reviewed all enterococcal isolates from cultures of blood collected from January 1988 through December 1995. Isolates were identified by conventional biochemical assays and assessed for susceptibilities to ampicillin, vancomycin, and high levels of gentamicin and streptomycin by using an agar dilution procedure according to the recommendations of the National Committee for Clinical Laboratory Standards (NCCLS) (3, 5, 6). Resistance to ampicillin and to vancomycin was verified by the NCCLS broth macrodilution method. Beta-lactamase production was evaluated by the chromogenic cephalosporin (nitrocefin) disc method (BBL Microbiology, Cockeysville, Md.).

(This work was presented in part at the 95th General Meeting of the American Society for Microbiology, Washington, D.C., 21 to 25 May 1995.)

A total of 419 consecutive *Enterococcus* isolates from individual patients were studied. As shown in Table 1, the percentage of *Enterococcus faecalis* isolates per total number of enterococci isolated decreased significantly from 83.9% in 1988 and 1989 to 58.1% in 1994 and 1995 ($P = 0.001$). In the same time period, the percentage of *E. faecium* isolates increased significantly from 12.9% of total isolates to 36.3% ($P = 0.001$) while the number of other *Enterococcus* species remained stable.

The frequency of antibiotic resistance for both *E. faecium* and *E. faecalis* increased significantly during the time period studied ($P \leq 0.001$). For *E. faecalis*, the highest percent increase in resistance was to gentamicin (2.6 to 36.1%, $P < 0.001$), followed by streptomycin (7.7 to 20.8%, $P = 0.020$). Ampicillin resistance in this species was rare, and no vancomycin resistance was detected. In contrast, the greatest increase in resistance for *E. faecium* was to ampicillin (16.7 to 75.6%, $P = 0.001$), followed by gentamicin (0 to 28.9%, $P = 0.001$), vancomycin (0 to 23.2%, $P = 0.011$), and streptomycin

TABLE 1. Antimicrobial susceptibility of *Enterococcus* species isolated from blood cultures (1988 through 1995)^a

Species and time period	Total no. tested (%) ^b	No. (%) resistant to:				Multiple resistance ^c	Total resistance (%) ^d
		AM	GM	ST	VA		
<i>E. faecalis</i>							
1988–1989	78 (83.9) ^e	0	2 (2.6) ^e	6 (7.7) ^e	0	0 ^e	8 (10.3) ^e
1990–1991	64 (68.1)	0	5 (7.8)	5 (7.8)	0	1	9 (14.1)
1992–1993	73 (67.6)	1 (1.4)	22 (30.1)	11 (15.1)	0	5	29 (39.7)
1994–1995	72 (58.1) ^e	0	26 (36.1) ^e	15 (20.8) ^e	0	8 ^e	33 (45.8) ^{e,f}
<i>E. faecium</i>							
1988–1989	12 (12.9) ^g	2 (16.7) ^g	0 ^g	2 (16.7) ^g	0 ^g	2 ^g	2 (16.7) ^g
1990–1991	23 (24.5)	4 (17.4)	0	5 (21.7)	0	2	7 (30.4)
1992–1993	30 (27.8)	14 (46.7)	11 (36.7)	15 (50.0) ^g	7 (23.2)	13 ^h	18 (60.0)
1994–1995	45 (36.3) ^g	31 (75.6) ^g	13 (28.9) ^g	17 (37.8)	10 (22.2) ^g	24 ^{g,i}	33 (73.3) ^g
Other ^{j,k}							
1988–1989	3 (3.2)	0	0	0	0	0	0
1990–1991	7 (7.4)	0	0	0	0	0	0
1992–1993	5 (4.6)	1 (20.0) ^l	0	0	0	0	1 (20.0)
1994–1995	7 (5.6)	2 (28.6) ^l	0	0	0	0	2 (28.6)

^a Abbreviations: AM, ampicillin; GM, gentamicin; ST, streptomycin; VA, vancomycin. Statistical comparisons were made by either the chi-square or the Fisher exact test by using SAS software (version 6). A P value of >0.05 was considered not significant.

^b Percentage calculated from the number of *E. faecalis*, *E. faecium*, or other species of *Enterococcus* per total number detected during each time period.

^c Number of isolates showing resistance to two or more of the antimicrobials tested.

^d Percentage of total isolates tested.

^e For *E. faecalis* isolates from 1988–1989 versus those from 1994–1995, P values were as follows (the chi-square test was used unless specified): total number tested, $P = 0.001$; gentamicin, $P < 0.001$; streptomycin, $P = 0.020$; multiple resistance, $P = 0.002$ (Fisher exact test); total resistance, $P < 0.001$.

^f For total resistance of *E. faecalis* versus *E. faecium* in 1994–1995, $P = 0.004$ (chi-square test).

^g For *E. faecium* isolates from 1988–1989 versus those from 1994–1995, P values were as follows (the chi-square test was used unless specified): total number tested, $P = 0.001$; ampicillin, $P = 0.001$; gentamicin, $P = 0.001$ (Fisher exact test); streptomycin (1988–1989 versus 1992–1993), $P = 0.048$ (Fisher exact test); vancomycin, $P = 0.011$ (Fisher exact test); multiple resistance, $P = 0.023$; total resistance, $P = 0.001$.

^h Nine isolates showed resistance to three (two isolates) or four (seven isolates) of the antimicrobials tested.

ⁱ Ten isolates showed resistance to three (six isolates) or four (four isolates) of the antimicrobials tested.

^j Other *Enterococcus* species included *E. gallinarum* (six isolates), *E. casseliflavus* (five isolates), *E. raffinosus* (five isolates), *E. durans* (three isolates), *E. hirae* (two isolates), and *E. avium* (one isolate).

^k The vancomycin MIC for 5 (all *E. gallinarum*) of the 11 motile enterococci with intrinsic low-level vancomycin resistance was 8 μ g per ml (intermediate), with MICs for the other six ranging from 2 to 4 μ g per ml (sensitive).

^l Species identified as *E. raffinosus*; the ampicillin MIC for all was 16 μ g per ml.

(16.7 to 50%, $P = 0.048$). This higher incidence of resistance in *E. faecium* has been reported previously (1, 4, 8, 9).

Multiple antibiotic resistance increased significantly from 1988 and 1989 to 1994 and 1995 for both *E. faecalis* ($P = 0.002$) and *E. faecium* ($P = 0.023$). In the majority of cases, multiple antibiotic resistance was observed with *E. faecium*, with 10 of the 24 isolates from 1994 and 1995 showing resistance to at least three of the antimicrobial agents tested. No *E. faecalis* isolate showed resistance to more than two antimicrobial agents tested. Multiple-antibiotic-resistant enterococci have been shown by us and others to be associated with nosocomial outbreaks (1, 2, 4).

Antibiotic resistance in the *Enterococcus* species other than *E. faecalis* and *E. faecium* was rare. Additionally, no beta-lactamase-producing enterococci were detected.

Our observations confirmed that enterococci isolated from blood cultures showed an alarming rate of increased resistance to the standard antimicrobial agents used for therapy. In contrast to current reports, we found that *E. faecium* rather than *E. faecalis* contributed most to this increased antibiotic resistance while the prevalence and resistance in other *Enterococcus* species remained low.

We thank Marge Boyden for secretarial assistance with this project.

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