

## Percentages and Distributions of Teicoplanin- and Vancomycin-Resistant Strains among Coagulase-Negative Staphylococci

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The activities of teicoplanin and vancomycin against 362 coagulase-negative staphylococci were determined by an agar dilution method. At the 4- and 32- $\mu\text{g/ml}$  breakpoint levels of the National Committee for Clinical Laboratory Standards, 23.2% of the strains were intermediate and 1.7% were resistant to teicoplanin, in contrast to <0.3% intermediate to vancomycin. Resistant strains belonged to the species *Staphylococcus epidermidis* (74%) and *S. haemolyticus* (19%).

Teicoplanin is a valuable drug for the treatment of infections caused by methicillin-resistant staphylococci, which represent 35 to 50% of all staphylococci isolated in our hospital. Teicoplanin is more active than vancomycin against streptococci and enterococci and equally active against *Staphylococcus aureus* but less active against coagulase-negative staphylococci. Few teicoplanin-resistant coagulase-negative staphylococci have been reported (1, 2, 4-7, 9). Exact identification of coagulase-negative staphylococci to the species level is important, since most resistant strains belong to the species *Staphylococcus haemolyticus*. The aim of this study was to delineate the prevalence of teicoplanin-resistant coagulase-negative staphylococci in a general hospital.

A total of 362 consecutive coagulase-negative staphylococci were isolated from clinical specimens from November 1988 through April 1989.

Detection of coagulase (rabbit plasma; Bio-Mérieux, Marcy L'Etoile, France) and DNase production (DNase agar; Diagnostics Pasteur, Marne La Coquette, France) was routinely performed for all staphylococcal isolates. Coagulase-negative staphylococci were further identified by using the ATB 32 Staph (API, La Balme les Grottes, France).

MICs were determined on Mueller-Hinton agar (Diagnostics Pasteur) with an inoculum of  $10^3$  to  $10^4$  CFU per spot (Steers replicator) incubated for 18 h at 37°C in air. MIC susceptibility breakpoints were according to the 1988 National Committee for Clinical Laboratory Standards recommendations for vancomycin (8): susceptible,  $\leq 4$   $\mu\text{g/ml}$ ; intermediate, 8 to 16  $\mu\text{g/ml}$ ; resistant,  $\geq 32$   $\mu\text{g/ml}$ . *S. aureus* ATCC 25923 was used as the control.

The distribution of MICs for the 362 coagulase-negative staphylococci is presented in Table 1, and the species distribution of the teicoplanin-resistant coagulase-negative staphylococci is presented in Table 2.

The effect of medium and inoculum on the MIC (and zone sizes) of teicoplanin and vancomycin against staphylococci has been emphasized (3). Previous studies (F. W. Goldstein, M. D. Kitzis, A. Coutrot, and J. F. Acar, 4th Eur. Congr. Clin. Microbiol., Nice, France, abstr. no. 1167, 1989) have demonstrated that regression line analysis of MICs versus inhibitory zone sizes exhibited a very poor correlation ( $r = 0.59$ ) for teicoplanin. However, as indicated by our results with repeatedly testing control strain ATCC 25923 (data not

TABLE 1. Distribution of MICs for 362 coagulase-negative staphylococci

| Agent       | No. of organisms inhibited at the following concn ( $\mu\text{g/ml}$ ): |     |     |     |    |    |    |
|-------------|---|-----|-----|-----|----|----|----|
|             | <0.5  | 1   | 2   | 4   | 8  | 16 | 32 |
| Teicoplanin | 30  | 38  | 77  | 127 | 58 | 26 | 6  |
| Vancomycin  | 3   | 113 | 229 | 16  | 1  | 0  | 0  |

shown), reproducible results can be obtained in the clinical laboratory if Mueller-Hinton agar is used.

Unlike with vancomycin, the distribution of teicoplanin MICs was wide, ranging from 0.5 to 32  $\mu\text{g/ml}$ . At the 4- and 32- $\mu\text{g/ml}$  breakpoint levels, respectively, 23.2% of the strains were intermediate and 1.7% of the strains were resistant to teicoplanin, while only one strain was intermediate to vancomycin.

In contrast to previous reports, *S. epidermidis* represented 74% of teicoplanin-resistant strains.

This study demonstrated that susceptibility of coagulase-negative staphylococci to teicoplanin cannot be inferred from results of tests of vancomycin susceptibility and should be routinely determined, at least for patients treated with teicoplanin.

Vancomycin and teicoplanin are widely used in our hospital because of the prevalence of methicillin-resistant *S. aureus*. However, most of the teicoplanin-resistant strains were isolated from patients not previously treated with vancomycin or teicoplanin.

Further studies are necessary to determine (i) the role of vancomycin and teicoplanin in the increase in teicoplanin-

TABLE 2. Species distribution of teicoplanin-resistant coagulase-negative staphylococci

| Organism                      | No. of organisms inhibited at the following teicoplanin concn ( $\mu\text{g/ml}$ ): |    |    |
|-------------------------------|---|----|----|
|                               | 8   | 16 | 32 |
| <i>S. epidermidis</i>         | 45  | 13 | 5  |
| <i>S. haemolyticus</i>        | 7   | 9  | 1  |
| Other CNS <sup>a</sup>        | 5   | 2  |    |
| <i>S. aureus</i> <sup>b</sup> | 1   | 2  |    |

<sup>a</sup> CNS, Coagulase-negative staphylococci.

<sup>b</sup> Coagulase-negative staphylococci identified as *S. aureus* by API.

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resistant coagulase-negative staphylococci, (ii) the clinical significance of strains with intermediate susceptibility to teicoplanin, and (iii) the breakpoints for teicoplanin.

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