

Letters to the Editor

Glycopeptide Resistance in *Staphylococcus haemolyticus* During Treatment With Teicoplanin

To the Editor:

Teicoplanin and vancomycin are glycopeptide antibiotics active against most species of gram-positive bacteria. They are used especially for amoxicillin-resistant enterococcal and methicillin-resistant staphylococcal infections. In recent years, resistance to teicoplanin and vancomycin in coagulase-negative staphylococci (CNS) has been observed.^{1,2} We present a patient with repeated episodes of continuous ambulatory peritoneal dialysis (CAPD) peritonitis caused by *Staphylococcus haemolyticus*. Successive staphylococcal isolates displayed a stepwise increase in resistance to teicoplanin and vancomycin.

A 49-year-old man with end-stage renal disease treated with CAPD presented with symptoms of CAPD peritonitis. The patient was given empirical treatment with intraperitoneal cephalothin (250 mg/L). Clinical response was poor, with an increased white-cell count in the peritoneal fluid (100/mm³). Two different types of methicillin-resistant CNS were isolated from the CAPD fluid, and treatment was changed to intraperitoneal teicoplanin (40 mg/L); removal of the Tenckhoff cannula was strongly recommended. Although treated with teicoplanin, the patient continued to have cloudy peritoneal fluid. CNS were isolated on days 5, 26, 40, and 48. Eventually the cannula was removed.

According to our standard teicoplanin susceptibility test for staphylococci, a disk-diffusion method, all isolates were sensitive (zone diameter >16 mm). Antimicrobial sensitivity testing by the VITEK-GPS system (BioMérieux, 's-Hertogenbosch, The Netherlands) showed that all isolates were sensitive to vancomycin (minimum inhibitory concentration [MIC] ≤4 µg/mL), except the one isolated on day 48 (MIC=6 µg/mL). The MICs for teicoplanin and vancomycin of this isolate were retested using the E-test method (PDM Epsilon meter test, AB

FIGURE 1. Restriction enzyme analysis patterns of five *Staphylococcus haemolyticus* (A) and two *Staphylococcus epidermidis* (B) isolates using the staph-PSTI restriction enzyme.

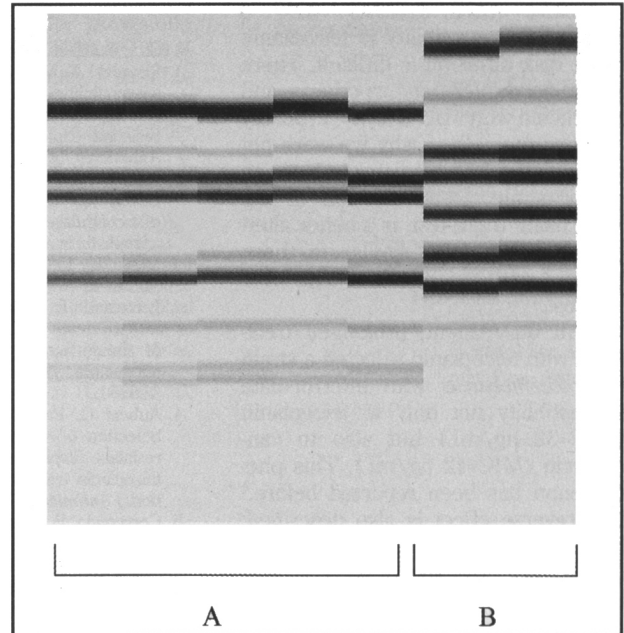
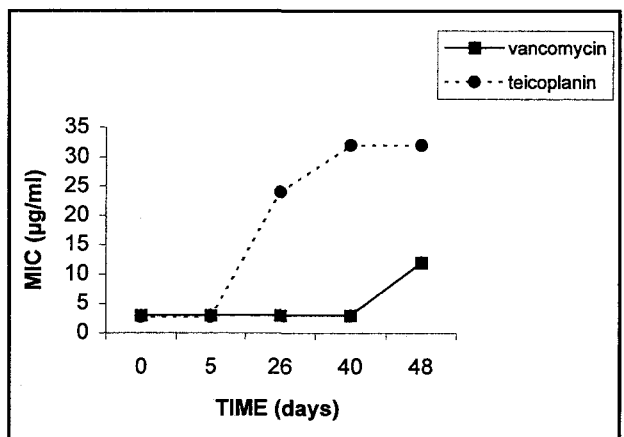


FIGURE 2. Susceptibility to vancomycin and teicoplanin expressed in minimum inhibitory concentrations of *Staphylococcus haemolyticus* strains for which cultures were obtained on days 0, 5, 26, 40, and 48.



Biodisk, Solna, Sweden). Intermediate sensitivity for teicoplanin (MIC=32 µg/mL) and for vancomycin (MIC=12 µg/mL) was now detected. This unexpected observation prompted us to determine the MICs for vancomycin and teicoplanin of all the isolated strains and to identify the CNS species. The patient was nursed in standard isolation.

Using biochemical tests, we identified two isolates as *Staphylococcus epidermidis* and five isolates as *S haemolyticus*. Restriction enzyme analysis (staph-PSTI restriction enzyme/Riboprinter; Qualicon, Warwick, Eng-

land) indicated that the *S haemolyticus* isolates were very closely related and likely to be of the same strain. The same was true for the *S epidermidis* isolates (Figure 1).

The MICs were determined using the E-test. The MICs for teicoplanin and vancomycin for *S epidermidis* did not exceed the breakpoints of susceptibility, and after day 26 *S epidermidis* was not detected anymore. However a stepwise resistance for *S haemolyticus* to teicoplanin and, to a lesser extent, to vancomycin was found (Figure 2).

Although susceptibility testing of

CNS to glycopeptides using the standard agar dilution test still is recommended by the National Committee for Clinical Laboratory Standards, this test is rather time-consuming and therefore not used routinely in our laboratory. Detecting CNS isolates with a decreased susceptibility to teicoplanin using disk diffusion is difficult. There are no good interpretative criteria, and correlation with MIC is low.^{2,3} Probably this was the reason why we were not able to detect intermediate strains in an earlier stage. Determination of the MIC, using the E-test, is a better alternative, with results similar to those obtained with the standard agar dilution test.³

In our patient, prolonged treatment with teicoplanin selected a strain of *S. haemolyticus* with intermediate susceptibility not only to teicoplanin (MIC=32 µg/mL) but also to vancomycin (MIC=12 µg/mL). This phenomenon has been reported before.⁴ The reverse effect is also described; clinical reports and experimental data have shown selection of bacteria with increased teicoplanin MICs during vancomycin treatment.⁵ Although not exclusive for *S. haemolyticus*, the majority of glycopeptide resistance is found in these staphylococci.²

The mechanisms by which coagulase-negative staphylococci develop glycopeptide resistance are still poorly understood. Selection of subpopulations with increased resistance to glycopeptides during treatment demonstrates that heterogeneous phenotypes exist. Cultures of these phenotypes can be obtained from pre-antibiotic isolates and suggest an intrinsic factor in these species.^{1,2} There are several reports on production of cellular aggregates sequestering antibiotic molecules by CNS during glycopeptide treatment.¹

The poor clinical response to intraperitoneal teicoplanin therapy in our patient was caused by selection of a subpopulation of *S. haemolyticus* with reduced susceptibility to teicoplanin in the presence of a foreign body. Intermediate resistance to vancomycin was also found. The appearance of glycopeptide resistance among CNS is alarming, since these drugs are often the only reasonable therapy available for methicillin-resistant staphylococci or amoxicillin-resistant enterococci. To prevent the emergence of resistant strains, the removal of foreign-body devices should be strongly recom-

mended in case of infection. Furthermore it is advisable to monitor susceptibility to glycopeptides by MIC determination of isolated staphylococci before and during prolonged treatment.

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Alarming Baseline Rates of Nosocomial Infection and Surgical Prophylaxis Errors in a Small Teaching Hospital in Argentina

To the Editor:

Nosocomial infections are a worrisome problem worldwide, leading to increased morbidity and mortality in hospitalized patients and increasing the cost of health care.¹ Despite several efforts to design and establish a national nosocomial infection surveillance system in Argentina, currently, there is no systematic program; therefore, reliable data on nosocomial infection rates from hospitals are scarce.

We recently developed an infection control team in a 250-bed teaching hospital attending adult patients. A hos-

pitalwide survey was conducted to estimate baseline rates in order to design a specific infection control program.

On August 13, 1999, all hospitalized patients were examined for the presence of hospital-acquired infection following the guidelines of the Centers for Diseases Control and Prevention.² A total of 126 inpatients were eligible for evaluation, and 36 had nosocomial infection (overall point prevalence, 28.6%; 95% confidence interval [CI₉₅], 20.2%-36.9%). Mean ages (years ± standard deviation) were 53.7 ± 16 and 54.1 ± 18 for infected and uninfected patients, respectively (*P* > .05, Student's *t* test). The respective lengths of stay were 33.6 ± 36 and 11.2 ± 9.1 days (*P* < .0001). The prevalence of nosocomial infection among the different units is given in the Table. Although a high prevalence was observed in all of the units, the most worrisome infection frequencies were those found in the surgery, trauma, and intensive care units.

The 90 uninfected patients were followed until discharge (5 patients undergoing surgery, other than prosthetic implant, were followed for 30 days after discharge for detection of surgical-site infection); 14 patients became infected (cumulative incidence, 15.6%; CI₉₅, 7.5%-23.6%) for an incidence density of 8 per 1,000 patient-days. A simple linear regression analysis showed a close relation between the incidence of infections and the length of stay (*r*² = 0.91, *P* = .05).

Staphylococcus aureus and *Pseudomonas aeruginosa* were among the most prevalent organisms, 22.4% and 11.1%, respectively. Methicillin resistance was displayed by 46% of the *S. aureus* strains and imipenem resis-

TABLE
PREVALENCE OF NOSOCOMIAL INFECTION
AMONG DIFFERENT MEDICAL UNITS

Unit	No. of Infections/ No. of Inpatients (%)
Internal medicine	7/43 (16)
Surgery*	12/42 (29)
Trauma	8/15 (53)
Hematology-oncology	3/18 (17)
Intensive care	6/8 (75)
All	36/126 (29)

* Includes general surgery, urology, gynecology, and neurosurgery.