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Nationwide German Multicenter Study on Prevalence of Antibiotic Resistance in Staphylococcal Bloodstream Isolates and Comparative In Vitro Activities of Quinupristin-Dalfopristin

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Antibiotic-resistant gram-positive bacteria have become an increasing problem in the last two decades. In order to evaluate the prevalence of antibiotic resistance in staphylococcal bloodstream isolates in Germany, 2,042 staphylococci collected in 21 tertiary-care hospitals were investigated during a 3-year period (March 1996 to March 1999). Altogether, 1,448 *S. aureus* isolates and 594 coagulase-negative staphylococci (CoNS) that comprised 13 different species were included. Furthermore, the antistaphylococcal activities of quinupristin-dalfopristin were compared with those of eight other compounds by the broth microdilution method. The rates of oxacillin resistance in *Staphylococcus aureus*, *S. epidermidis*, *S. haemolyticus*, and other CoNS were 13.5, 69, 90, and 34%, respectively. In oxacillin-resistant strains high rates of resistance (up to 100%) to erythromycin, clindamycin, ciprofloxacin, and gentamicin were also observed. However, no strain appeared to be resistant to vancomycin or quinupristin-dalfopristin. The streptogramin combination exhibited excellent in vitro activity against all staphylococcal species tested, regardless of the patterns of resistance to other drug classes. In terms of MICs at which 90% of the isolates are inhibited, quinupristin-dalfopristin was 2 times more active against *S. aureus* isolates, 4 to 16 times more active against *S. haemolyticus*, and 8 to 32 times more active against *S. epidermidis* than vancomycin or teicoplanin.

Despite advances in antimicrobial therapy, the incidence of severe infections caused by multiple-drug-resistant bacteria has been increasing over the past 20 years. Whereas resistant gram-negative bacteria were a major problem in the 1970s, the past decade has seen an increase in the number of problems associated with multidrug-resistant gram-positive bacteria, including methicillin-resistant *Staphylococcus aureus* (MRSA), methicillin-resistant coagulase-negative staphylococci (MR-CoNS), penicillin-resistant *Streptococcus pneumoniae*, and vancomycin-resistant enterococci (1, 12).

The prevalence of MRSA and MR-CoNS as major causes of morbidity and mortality in the hospital setting has increased during the last decade (3, 9, 19). Because glycopeptides are often the only drugs still active against methicillin-resistant staphylococci, the emergence of staphylococcal strains exhibiting reduced sensitivity to vancomycin is of particular concern (4, 18).

Therefore, new antibiotics are urgently needed not only to treat infections caused by multidrug-resistant gram-positive cocci but also to reduce the increasing selection pressure by glycopeptides on gram-positive pathogens in hospitals.

Various new compounds have demonstrated significant in vitro activities against staphylococci including MRSA and MR-CoNS (1, 10). One of these compounds is the injectable strep-

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TABLE 1. In vitro activities of quinupristin-dalfopristin and seven other antibiotics against *S. aureus* strains (n = 1,448) isolated from patients with bloodstream infections in Germany[a]

Antibiotic	No. of strains for which MIC (mg/liter) is:											MIC_{90} (mg/liter)	Susceptibility[b]	
	≤0.06	0.125	0.25	0.5	1	2	4	8	16	32	≥64		% S	% R
Penicillin G	347	37	51	32	50	52	100	155	624	—	—	16	26.5	73.5
Oxacillin	195	240	373	320	125	44	19	14	118	—	—	4	86.5	13.5
Erythromycin	—	—	473	478	207	42	16	5	7	8	212	≥64	80.0	16.0
Clindamycin	—	—	1,317	13	3	4	0	0	0	2	109	0.25	92.0	7.7
Ciprofloxacin	44	150	382	513	158	42	12	27	120	—	—	8	86.0	11.0
Gentamicin	—	—	186	421	436	193	57	19	136	—	—	8	72.0	10.7
Teicoplanin	—	—	288	702	345	107	6	0	0	0	0	1	100	0
Vancomycin	—	—	81	585	705	74	3	0	0	0	0	1	100	0
Q-D	—	—	1,035	361	43	9	0	0	0	0	0	0.5	99.4	0

[a] Q-D, quinupristin-dalfopristin; S, susceptible; R, resistant; —, concentration not tested.

[b] The following breakpoints were used for definition of susceptibility (resistance): penicillin, ≤0.125 mg/liter (≤0.25 mg/liter) (DIN); oxacillin, ≤1 mg/liter (≥2 mg/liter) (DIN); erythromycin, ≤1 mg/liter (≥8 mg/liter) (DIN); clindamycin, ≤1 mg/liter (≥8 mg/liter) (DIN); ciprofloxacin, ≤1 mg/liter (≥4 mg/liter) (DIN); gentamicin, ≤1 mg/liter (≥8 mg/liter) (DIN); teicoplanin, ≤1 mg/liter (≥16 mg/liter) (tentative breakpoint); vancomycin, ≤4 mg/liter (≥16 mg/liter) (DIN); quinupristin-dalfopristin, ≤1 mg/liter (≥4 mg/liter) (tentative breakpoint).

togramin quinupristin-dalfopristin, which comprises quinupristin (a type B streptogramin) and dalfopristin (a type A streptogramin) in a ratio of 30:70. It has a focused spectrum of in vitro activity against gram-positive cocci, including multidrug-resistant isolates of staphylococci, streptococci, and *Enterococcus faecium* (2). Moreover, it has demonstrated clinical efficacy for the treatment of various moderate and severe infections (11, 13; J. Y. Fagon, Abstr. 20th Int. Congr. Chemother. abstr. 843, 1997).

The aims of our project, entitled Multicenter Study on Antibiotic Resistance in Staphylococci and Other Gram-Positive Cocci, were twofold: (i) to evaluate the prevalence of antibiotic resistance in gram-positive bacteria isolated from patients with sepsis and (ii) to compare the in vitro activity of quinupristin-dalfopristin with those of eight other antibiotics. Isolates were included only if they were considered causative organisms. In this report results for *S. aureus*, as well as for CoNS, with particular regard to *Staphylococcus epidermidis* and *Staphylococcus haemolyticus*, are presented.

MATERIALS AND METHODS

Twenty-one microbiological laboratories that serve university hospitals in all regions in Germany participated in the study. Each site was requested to include 200 consecutive staphylococcal blood culture isolates. Isolates were included only if they were isolated from monomicrobic bloodstream infections. The causative role of CoNS had to be confirmed by isolation of the same strain in two separate blood cultures. Only one isolate per patient was included.

Staphylococci were identified on the basis of production of colony pigment and coagulase (Pasteurex-Staph-Plus; Sanofi Diagnostics Pasteur GmbH, Freiburg, Germany). CoNS were further identified with a commercial identification system (ID 32 Staph; bioMerieux, Nürtingen, Germany).

To evaluate the prevalence of resistance, the following antimicrobial agents were tested: penicillin, oxacillin, erythromycin, clindamycin, ciprofloxacin, gentamicin, teicoplanin, vancomycin, and quinupristin-dalfopristin.

All participating laboratories used the same method of susceptibility testing. MICs were determined by the broth microdilution method with Iso-Sensitest medium (Unipath, Wesel, Germany) according to the German DIN (Deutsches Institut für Normung) 58940 guidelines applied in previous multicenter studies in central Europe (8, 14). Strains were incubated at 35 to 37°C for 18 to 24 h. The MICs of oxacillin with 2% (wt/vol) NaCl were read after 48 h. Susceptibility to oxacillin was also determined by performing the screening test with agar plates that contained 6 mg of oxacillin per liter. In order to achieve a high degree of comparability between laboratories, microdilution plates with lyophilized antibiotics and all other material used for identification and susceptibility testing were identical in all participating laboratories. In the German DIN 58940 guidelines there is a breakpoint for the definition of resistance to vancomycin but not for that to teicoplanin. As the current National Committee for Clinical Laboratory Standards guideline breakpoints for the definition of resistance to these two glycopeptides are identical, in our study we also used identical breakpoints (MICs, ≥16 mg/liter) for the definition of resistance to teicoplanin and vancomycin. Although the susceptibility breakpoints for quinupristin-dalfopristin have not yet been established in Germany, organisms were deemed to be resistant when the MIC was ≥4 mg/liter.

The accuracy of susceptibility testing in participating laboratories was evaluated by MIC testing of control strains.

The following quality control strains were included: *S. aureus* ATCC 29213, *S. aureus* ATCC 25923, *S. aureus* 1309 (oxacillin resistant), and *Enterococcus faecalis* ATCC 29212. *S. aureus* 1309 was kindly provided by W. Witte, Robert Koch Institute (Wernigerode, Germany).

RESULTS

A total of 2,042 staphylococci, including 1,448 *S. aureus* isolates, were collected from March 1996 to March 1999. The CoNS comprised 456 *S. epidermidis* isolates, 50 *S. haemolyticus* isolates, and 88 other coagulase-negative staphylococcal isolates that belong to eight different species of novobiocin-susceptible CoNS (*S. hominis* [n = 39], *S. warneri* [n = 12], *S. capitis* [n = 16], *S. chromogenes* [n = 7], *S. simulans* [n = 3], *S. lugdunenis* [n = 2], *S. caprae* [n = 2], and *S. schleiferi* [n = 1], and to three different species of novobiocin-resistant CoNS (*S. sciuri* [n = 3], *S. xylosus* [n = 2], and *S. saprophyticus* [n = 1]).

A large number of strains were isolated from patients with nosocomial infections (n = 1,395 isolates from patients with onset of infection >72 h after admission). Fifty-seven percent of the patients had been hospitalized for at least 7 days (21% for at least 21 days) at the time that the blood for culture was taken. Among this group of patients infections were due to *S. aureus* (n = 740; 67.4%), *S. haemolyticus* (n = 43; 3.9%), and *S. epidermidis* (n = 315; 28.7%).

Three hundred thirteen staphylococcal infections were seen in neutropenic patients from hemato-oncological or transplantation units (white blood cell counts, $<1{,}000/mm^3$); and *S. aureus* (48.9%), *S. epidermidis* (40.9%), and *S. haemolyticus* (6.0%) were the most important pathogens.

By the broth microdilution method, the rate of oxacillin resistance (MICs ≥2 mg/liter) recorded among the *S. aureus* isolates was 13.5% (Table 1). In contrast, the corresponding oxacillin screening test revealed a resistance rate of 9.4%. The rate of methicillin resistance among *S. aureus* isolates varied considerably between centers, ranging from 1.7 to 41%. A geographic trend within geographic regions of Germany could not be identified. A subgroup of 118 of 195 (60%) MRSA isolates, i.e., 8% of all *S. aureus* strains, demonstrated a high level of resistance to oxacillin (MICs ≥16 mg/liter) (Table 1).

Among the isolates of *S. epidermidis* and *S. haemolyticus*, the prevalence of resistance to oxacillin, erythromycin, clindamy-

TABLE 2. In vitro activities of quinupristin-dalfopristin and seven other antibiotics against *S. epidermidis* strains (n = 456) isolated from patients with bloodstream infections in Germany[a]

Antibiotic	No. of strains for which MIC (mg/liter) is:											MIC_{90} (mg/liter)	Susceptibility[b]	
	≤0.06	0.125	0.25	0.5	1	2	4	8	16	32	≥64		% S	% R
Penicillin G	36	10	15	24	43	59	68	90	111	—	—	16	10.1	89.9
Oxacillin	69	27	20	5	19	20	37	41	218	—	—	≥16	30.7	69.3
Erythromycin	—	—	91	50	26	4	1	0	4	6	274	≥64	36.6	62.3
Clindamycin	—	—	265	6	3	1	0	1	0	5	175	≥64	59.9	39.7
Ciprofloxacin	3	26	68	72	17	9	24	52	185	—	—	≥16	40.8	57.2
Gentamicin	—	—	170	8	4	5	6	23	240	—	—	≥16	39.9	57.7
Teicoplanin	—	—	22	22	66	133	142	65	6	0	0	8	84.4	1.3
Vancomycin	—	—	1	37	224	187	7	0	0	0	0	2	100	0
Q-D	—	—	434	12	6	4	0	0	0	0	0	0.25	99.1	0

[a] Q-D, quinupristin-dalfopristin; S, susceptible; R, resistant; —, concentration not tested.
[b] The following breakpoints were used for definition of susceptibility (resistance): penicillin, ≤0.125 mg/liter (≥0.25 mg/liter) (DIN); oxacillin, ≤1 mg/liter (≥2 mg/liter) (DIN); erythromycin, ≤1 mg/liter (≥8 mg/liter) (DIN); clindamycin, ≤1 mg/liter (≥8 mg/liter) (DIN); ciprofloxacin, ≤1 mg/liter (≥4 mg/liter) (DIN); gentamicin, ≤1 mg/liter (≥8 mg/liter) (DIN); teicoplanin, ≤1 mg/liter (≥16 mg/liter) (tentative breakpoint); vancomycin, ≤4 mg/liter (≥16 mg/liter) (DIN); quinupristin-dalfopristin, ≤1 mg/liter (≥4 mg/liter) (tentative breakpoint).

cin, ciprofloxacin, and gentamicin ranged from 40 to 96% (Tables 2 and 3).

Among the *S. epidermidis* isolates, 316 strains (69%) were resistant to oxacillin by the broth microdilution method (MICs, ≥2 mg/liter) and 267 (59%) were resistant to oxacillin by the screening test. Two hundred eighteen strains exhibited a high level of resistance to oxacillin (MICs, ≥16 mg/liter). Sixty-five and six *S. epidermidis* strains were intermediate (MICs, 8 mg/liter) and resistant (MICs, ≥16 mg/liter) to teicoplanin, respectively. However, no vancomycin-intermediate or -resistant *S. epidermidis* strains were detected (Table 2).

Among the *S. haemolyticus* isolates, 45 of 50 strains (90%) were resistant to oxacillin by both the screening test and the broth microdilution method (Table 3).

Regarding the other species that belong to novobiocin-susceptible and novobiocin-resistant CoNS, only 32 of 88 strains (34%) were resistant to oxacillin. In comparison with *S. epidermidis* and *S. haemolyticus*, the rarely isolated CoNS were also more susceptible to the other compounds tested, with the prevalence of resistance to erythromycin, clindamycin, ciprofloxacin, and gentamicin ranging from 23 to 43%. Five of these strains were intermediate to teicoplanin and one strain was resistant to teicoplanin. No strains resistant to vancomycin or quinupristin-dalfopristin were detected.

Sixteen strains (nine *S. aureus* strains, four *S. epidermidis* strains, and one strain each of *S. haemolyticus*, *S. warneri*, and *S. schleiferi*) were classified as quinupristin-dalfopristin intermediate (MICs, 2 mg/liter), but no resistant strains were detected. In terms of the MICs at which 90% of isolates are inhibited (MIC_{90}s), quinupristin-dalfopristin was 2 times more active against *S. aureus* isolates, 4 to 16 times more active against *S. haemolyticus* isolates, and 8 to 32 times more active against *S. epidermidis* isolates than vancomycin or teicoplanin.

Oxacillin-resistant staphylococci were also frequently resistant to other antimicrobial agents. High rates of resistance to erythromycin (63 to 87%), clindamycin (42 to 54%), ciprofloxacin (63 to 100%), and gentamicin (58 to 98%) were observed among *S. aureus*, *S. epidermidis*, and *S. haemolyticus* isolates (Table 4). In terms of MIC_{90}s, quinupristin-dalfopristin was 2 to 32 times more active against MRSA, methicillin-resistant *S. epidermidis*, and methicillin-resistant *S. haemolyticus* than vancomycin and teicoplanin.

One thousand three hundred twenty-seven strains (1,156 [87.1%] *S. aureus* strains, 165 [12.4%] *S. epidermidis* strains, 6 [<0.1%] *S. haemolyticus* strains) were susceptible to erythromycin and clindamycin. Two hundred forty-three strains (119 [48.9%] *S. aureus* strains, 104 [42.7%] *S. epidermidis* strains, 20 [8.2%] *S. haemolyticus* strains) were erythromycin resistant and clindamycin susceptible (probably in association with the inducible macrolide-lincosamide-streptogramin B phenotype),

TABLE 3. In vitro activities of quinupristin-dalfopristin and seven other antibiotics against *S. haemolyticus* strains (n = 50) isolated from patients with bloodstream infections in Germany[a]

Antibiotic	No. of strains for which MIC (mg/liter) is:											MIC_{90} (mg/liter)	Susceptibility[b]	
	≤0.06	0.125	0.25	0.5	1	2	4	8	16	32	≥64		% S	% R
Penicillin G	1	0	0	1	1	1	1	3	42	—	—	16	2.0	98.0
Oxacillin	4	0	0	0	1	0	1	1	43	—	—	≥16	10.0	90.0
Erythromycin	—	—	2	5	0	0	1	0	2	9	31	≥64	14.0	84.0
Clindamycin	—	—	27	0	0	2	1	1	0	0	19	≥64	54.0	40.0
Ciprofloxacin	0	0	0	2	0	0	0	1	47	—	—	≥16	4.0	96.0
Gentamicin	—	—	4	0	0	0	1	3	42	—	—	≥16	8.0	90.0
Teicoplanin	—	—	2	3	3	10	17	10	5	0	0	8	70.0	10.0
Vancomycin	—	—	0	5	24	16	5	0	0	0	0	2	100	0
Q-D	—	—	36	12	1	1	0	0	0	0	0	0.5	98.0	0

[a] Q-D, quinupristin-dalfopristin; S, susceptible; R, resistant; —, concentration not tested.
[b] The following breakpoints were used for definition of susceptibility (resistance): penicillin, ≤0.125 mg/liter (≥0.25 mg/liter) (DIN); oxacillin, ≤1 mg/liter (≥2 mg/liter) (DIN); erythromycin, ≤1 mg/liter (≥8 mg/liter) (DIN); clindamycin, ≤1 mg/liter (≥8 mg/liter) (DIN); ciprofloxacin, ≤1 mg/liter (≥4 mg/liter) (DIN); gentamicin, ≤1 mg/liter (≥8 mg/liter) (DIN); teicoplanin, ≤1 mg/liter (≥16 mg/liter) (tentative breakpoint); vancomycin, ≤4 mg/liter (≥16 mg/liter) (DIN); quinupristin-dalfopristin, ≤1 mg/liter (≥4 mg/liter) (tentative breakpoint).

TABLE 4. In vitro activities of quinupristin-dalfopristin and seven other antibiotics against oxacillin-resistant strains of *S. aureus*, *S. epidermidis*, and *S. haemolyticus* isolated from patients with bloodstream infections[a]

Species	Antibiotic	No. of strains for which MIC (mg/liter) is:										MIC_{90} (mg/liter)	Susceptibility[b]	
		≤0.125	0.25	0.5	1	2	4	8	16	32	≥64		% S	% R
S. aureus	Erythromycin	—	25	29	11	4	4	1	2	4	115	≥64	33.3	62.6
(*n* = 195)	Clindamycin	—	89	0	1	3	0	0	0	2	100	≥64	46.2	52.3
	Ciprofloxacin	2	19	32	15	5	4	12	106	—	—	16	34.9	62.6
	Gentamicin	—	5	20	32	21	4	4	109	—	—	16	29.2	57.9
	Teicoplanin	—	20	46	70	55	4	0	0	0	—	2	100	0.0
	Vancomycin	—	5	44	121	23	2	0	0	0	—	2	100	0.0
	Q-D	—	81	82	26	6	0	0	0	0	—	1	97.0	0.0
S. epidermidis	Erythromycin	—	43	21	8	2	0	0	1	4	237	≥64	22.8	76.6
(*n* = 316)	Clindamycin	—	139	3	3	0	0	1	0	4	166	≥64	45.9	54.1
	Ciprofloxacin	6	22	42	13	3	23	47	160	—	—	16	26.3	72.8
	Gentamicin	—	63	3	2	2	3	20	223	—	—	16	21.2	76.9
	Teicoplanin	—	11	7	38	87	116	52	4	0	1	8	82.0	1.6
	Vancomycin	—	0	15	141	154	6	0	0	0	—	2	100	0.0
	Q-D	—	298	9	6	3	0	0	0	0	—	0.25	99.0	0.0
S. haemolyticus	Erythromycin	—	1	4	0	0	1	0	2	9	28	≥64	11.1	86.7
(*n* = 45)	Clindamycin	—	23	0	0	2	1	1	0	0	18	≥64	51.1	42.2
	Ciprofloxacin	0	0	0	0	0	0	1	44	—	—	16	0.0	100
	Gentamicin	—	0	0	0	0	1	3	41	—	—	≥16	0.0	97.8
	Teicoplanin	—	0	2	3	10	16	9	5	0	—	16	68.9	11.1
	Vancomycin	—	0	2	23	15	5	0	0	0	—	2	100	0.0
	Q-D	—	32	11	1	1	0	0	0	0	—	0.5	97.8	0.0

[a] Q-D, quinupristin-dalfopristin; S, susceptible; R, resistant; —, concentration not tested.

[b] The following breakpoints were used for definition of susceptibility (resistance); penicillin, ≤0.125 mg/liter (≥0.25 mg/liter) (DIN); oxacillin, ≤1 mg/liter (≥2 mg/liter) (DIN); erythromycin, ≤1 mg/liter (≥8 mg/liter) (DIN); clindamycin, ≤1 mg/liter (≥8 mg/liter) (DIN); ciprofloxacin, ≤1 mg/liter (≤4 mg/liter) (DIN); gentamicin, ≤1 mg/liter (≥8 mg/liter) (DIN); teicoplanin, ≤1 mg/liter (≥16 mg/liter) (tentative breakpoint); vancomycin, ≤4 mg/liter (≥16 mg/liter) (DIN); quinupristin-dalfopristin, ≤1 mg/liter (≥4 mg/liter) (tentative breakpoint).

and 309 strains (110 [35.6%] *S. aureus* strains, 180 [58.3%] *S. epidermidis* strains, 19 [6.2%] *S. haemolyticus* strains) were erythromycin as well as clindamycin resistant (probably in association with the constitutive macrolide-lincosamide-streptogramin B phenotype). For staphylococci that exhibited the constitutive macrolide-lincosamide-streptogramin B type of resistance, quinupristin-dalfopristin MICs were slightly elevated (for *S. aureus*, the MIC_{90} was 1.0 mg/liter, whereas it was 0.5 mg/liter for the other strains).

DISCUSSION

The worldwide emergence of multidrug-resistant gram-positive cocci such as MRSA, penicillin-resistant *S. pneumoniae*, and vancomycin-resistant enterococci as well as the corresponding increase in the number of enterococcal, streptococcal, and particularly staphylococcal infections in certain patient populations has limited clinicians' ability to use currently available antibiotics for therapy. Thus, new antimicrobial agents like quinupristin-dalfopristin are urgently needed (1, 10). Staphylococci and enterococci account for approximately one-third of all bloodstream infections and as much as 50% of all nosocomial bloodstream infections (6).

Prospective antibiotic resistance surveillance studies conducted by the Resistance Study Group of the Paul Ehrlich Society for Chemotherapy investigated the prevalence of antibiotic resistance in staphylococci in Germany, Switzerland, and Austria and revealed that the frequency of resistance to oxacillin among *S. aureus* isolates remained low and largely unchanged until 1990 (below 3%) in this Central European area. However, between 1990 and 1995 a significant increase in the rate of resistance to oxacillin (and other antimicrobial agents) was observed. By the broth microdilution method the rates of oxacillin resistance in 1995 among *S. aureus*, *S. epidermidis*, and *S. haemolyticus* strains were found to be 12.9, 60.2, and 82.7%, respectively (7, 8, 22).

The oxacillin resistance rates found for *S. aureus*, *S. epidermidis*, and *S. haemolyticus* strains by the broth microdilution method in our study (13.5, 69, and 90%, respectively) were, despite a slight increase, comparable to those in the study conducted in 1995 by the Paul Ehrlich Society (7, 8). Thus, a further significant increase in the rate of oxacillin resistance as was observed in the early 1990s was not registered. However, one may speculate that these rates would have been even higher if we had also included isolates from body sites other than blood, as was done in former studies (8, 21).

The 13.5% rate of methicillin resistance among *S. aureus* strains is low compared to the rate in the United States or some southern European countries, where the proportion has already exceeded 30%, but it is significantly higher than the rates found in Canada, Switzerland, The Netherlands, and Scandinavia (15, 21; C. L. C. Wielders, F. J. Schmitz, J. Verhoef, A. C. Fluit, and The European SENTRY Participants, Abstr. 39th Intersci. Conf. Antimicrob. Agents Chemother. abstr. 1236, p. 162, 1999).

Glycopeptides are the main antimicrobial agents available for the treatment of serious infections with MRSA. Teicoplanin and vancomycin have similar activities against methicillin-susceptible isolates of *S. aureus*, although the MIC of teicoplanin for some strains can rise up to 16 mg/liter (17). For the characterized vancomycin-resistant and vancomycin-heterogeneously-resistant *S. aureus* strains (vancomycin MICs, 8 mg/liter) recently isolated in Japan, the United States, and France, teicoplanin MICs ranged from 8 to 32 mg/liter (4, 5, 16, 20).

In the present study, both glycopeptides were similarly active against *S. aureus*, as determined from the MIC_{90}s. None of the

1,448 *S. aureus* strains tested was resistant or intermediate to either glycopeptide. The highest MIC obtained by the microdilution method was 4 mg/liter for nine isolates (six isolates for which the teicoplanin MIC was 4 mg/liter and three isolates for which the vancomycin MIC was 4 mg/liter).

However, the antimicrobial susceptibilities of CoNS to the glycopeptides were generally in agreement with those reported by other investigators (8, 17), showing that teicoplanin is less active than vancomycin, although we tested a larger number of methicillin-resistant isolates, including 14 staphylococcal species and all isolates from patients with septic episodes.

In this study, quinupristin-dalfopristin exhibited excellent in vitro activity against staphylococci including MRSA and MR-CoNS, as has been shown in part in other investigations reviewed by Bouanchaud (2). In addition, quinupristin-dalfopristin demonstrated significant inhibition of staphylococci resistant to macrolides and lincosamides.

New drugs like quinupristin-dalfopristin are needed not only for the treatment of severe infections due to multidrug-resistant gram-positive pathogens but also to provide an ecological benefit by reducing the selective pressure due to overuse of glycopeptides in the hospital setting.

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