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Differing Activities of Quinolones against Ciprofloxacin-Susceptible and Ciprofloxacin-Resistant, Methicillin-Resistant *Staphylococcus aureus*

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The in vitro activities of nine quinolones (seven fluoroquinolones, nalidixic acid, and acrosoxacin) against methicillin-resistant *Staphylococcus aureus* (MRSA) were compared with those of the glycopeptides teicoplanin and vancomycin. MICs against 160 strains of ciprofloxacin-susceptible (MIC, <2.0 μg/ml) MRSA and 40 strains of ciprofloxacin-resistant (MIC, ≥2.0 μg/ml) MRSA were determined. The following MICs for 50% of the strains tested (in micrograms per milliliter) were obtained for ciprofloxacin-susceptible and -resistant strains, respectively: tosufloxacin, 0.06 and 2.0; ofloxacin, 0.25 and 16; ciprofloxacin, 0.5 and 16; pefloxacin, 0.5 and 32; acrosoxacin, 1.0 and >256; enoxacin, 1.0 and 64; fleroxacin, 1.0 and 32; norfloxacin, 2.0 and 64; nalidixic acid, 64 and 512; teicoplanin, 1.0 and 1.0; vancomycin, 2.0 and 2.0. In mutation rate studies using a range of antibiotic concentrations to reflect those achievable in vivo, resistant mutants grew only on plates containing nalidixic acid (rate of mutation to resistance, 10^{-7} to 10^{-8}) and on plates containing low concentrations of ciprofloxacin, enoxacin, and norfloxacin (rate of mutation to resistance, 10^{-8} to 10^{-9}). In time-kill studies, 99.9% killing was found within 8 h for all of the quinolones tested (norfloxacin and nalidixic acid were not tested). Teicoplanin and vancomycin were less rapidly bactericidal. For the clinical isolates of ciprofloxacin-resistant MRSA, different levels and patterns of quinolone resistance were found. Generally, cross-resistance among the fluoroquinolones was complete; however, incomplete cross-resistance did occur with the nonfluorinated quinolone acrosoxacin.

Methicillin-resistant *Staphylococcus aureus* (MRSA) was first reported by Jevons in 1961 (14a). Throughout the 1960s and 1970s, these organisms were responsible for sporadic, although sometimes serious, outbreaks of hospital infections (4, 14). In the United States, few outbreaks of hospital infections due to MRSA were reported before 1980; however, since then, MRSA has caused increasing problems in hospitals in the United States (30) and worldwide (31).

Resistance of MRSA to methicillin is mediated primarily by production of a unique penicillin-binding protein (PBP 2′); thus, these organisms are regarded as resistant to all β-lactam agents (11). Furthermore, many MRSA strains are resistant to a variety of other antibiotics, including gentamicin, tobramycin, erythromycin, clindamycin, tetracycline, and streptomycin (19). The choices for treatment of infections due to MRSA are few, and in the absence of susceptibility testing data or in serious infections, vancomycin is regarded as the antibiotic of choice for treatment (12).

Nalidixic acid, the first quinolone agent to be developed, was active only against enterobacteria and possessed pharmacokinetics which restricted its use to treatment of urinary tract infections. In the 1980s, a new generation of quinolones, the fluoroquinolones, was introduced. These had broad-spectrum bactericidal activity, achieved satisfactory levels in serum and tissue, and because of their unique mode of action, were not affected by mechanisms of resistance to other antimicrobial agents (27). The properties of these agents have recently been reviewed by Wolfson and Hooper (35). Because of the differences in potency and pharmacokinetics (5, 13) among quinolones, the class-testing approach is not appropriate. Therefore, we tested a wide range of the compounds presently available: acrosoxacin, ciprofloxacin, enoxacin, fleroxacin, nalidixic acid, norfloxacin, ofloxacin, pefloxacin, and tosufloxacin.

Compared with vancomycin, fluoroquinolones are relatively nontoxic and offer clinicians a choice between oral and parenteral administration for systemic infections. Another new glycopeptide antibiotic, teicoplanin, has recently entered clinical use. This antibiotic can be administered parenterally, and it is believed to be less toxic than vancomycin (34).

This work compares the in vitro activities of the quinolones with those of teicoplanin and vancomycin with a view to the use of quinolones as alternatives to the glycopeptide antibiotics. For a comprehensive assessment, these compounds were tested against a collection of 200 strains of MRSA derived from 38 centers distributed throughout 26 countries.

MATERIALS AND METHODS

Strains. The *S. aureus* isolates used in this study were all catalase-positive, tube coagulase-positive, DNase-positive, gram-positive cocci. The strains were obtained from one center each in Australia, Austria, Belgium, Brazil, Chile, Denmark, the Federal Republic of Germany, Finland, the German Democratic Republic, Greece, Hong Kong, Italy, Japan, Kuwait, Poland, Portugal, Switzerland, Turkey, and the USSR; two centers each in France, Israel, the Republic of Ireland, South Africa, and Spain; three in England, and six in the United States.

For logistic reasons, only four selected methicillin-resistant strains (from different continents) were used in the

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time-kill and mutation rate studies. These were strains RM1, SA1, AUS10, and RL7, which were from centers in the United States, South Africa, Australia, and England, respectively. *S. aureus* NCTC 6571, a methicillin-susceptible, penicillin-susceptible strain (referred to here as strain SOX), was used as a control.

Antimicrobial agents. The antimicrobial agents used were supplied as follows: acrosoxacin and nalidixic acid, Sterling Winthrop Group Ltd., Guildford, England; ciprofloxacin, Bayer AG, Wuppertal, Federal Republic of Germany; enoxacin, Dainippon Pharmaceutical Co., Osaka, Japan; fleroxacin, Roche Products Ltd., Welwyn Garden City, England; norfloxacin, Merck Sharp & Dohme, Rahway, N.J.; ofloxacin, Hoechst UK Ltd., Hounslow, England; pefloxacin, May and Baker Ltd., Dagenham, England; tosufloxacin tosylate, Abbott Laboratories, Chicago, Ill.; teicoplanin, Merrell Dow Ltd., Egham, England; and vancomycin hydrochloride, Sigma Chemical Co., St. Louis, Mo.

Susceptibility testing. All of the isolates were tested for susceptibility to acrosoxacin, ciprofloxacin, enoxacin, fleroxacin, nalidixic acid, norfloxacin, ofloxacin, pefloxacin, tosufloxacin, teicoplanin, and vancomycin by an agar dilution technique. Doubling dilutions of the agents were incorporated into molten Iso-Sensitest agar (Oxoid, UK) kept at 50°C, and plates were immediately poured. The isolates were subcultured from blood agar plates into 3.0-ml volumes of peptone water broth, which were then incubated for 24 h at 37°C. These broth samples were inoculated onto antibiotic-containing plates by using a Multipoint Inoculator (Denley Instruments, Billingshurst, England) which delivered an initial bacterial inoculum of approximately 5.0×10^5 CFU. The inoculated plates were incubated for 24 h at 37°C before being read. The MIC of an agent was the lowest concentration at which visible growth of an isolate was not present.

Resistance to methicillin was determined by streaking isolates and appropriate controls onto nutrient agar (Oxoid, Basingstoke, England) and then placing paper strips containing 25 μg of methicillin (Mast Laboratories, Merseyside, England) at right angles to the inocula. These plates were then incubated for 40 h at 30°C, and strains were designated methicillin resistant if they grew within 3 mm or less of the edge of the strip.

Killing curves. For acrosoxacin, ciprofloxacin, enoxacin, fleroxacin, ofloxacin, pefloxacin, tosufloxacin, teicoplanin, and vancomycin, timed killing curves were determined with five selected strains. The strains were grown for 24 h at 37°C in 10 ml of Iso-Sensitest broth, and 0.5-ml samples were used to inoculate Erlenmeyer flasks (500 ml) containing various concentrations of the test substances in 100 ml of Iso-Sensitest broth. For all killing studies, an initial broth concentration of 5.0×10^5 to 1.0×10^7 CFU/ml was used. These flasks, along with control flasks to which no agent had been added, were placed in an orbital incubator (Gallenkamp, Loughborough, England) and shaken at 100 rpm for 24 h at 37°C. Quantitative bacterial counts at 0, 4, 8, and 24 h of exposure to the agents were performed by spreading 0.1 ml on Iso-Sensitest agar plates which were incubated for 24 h at 37°C before counting.

The lowest number of bacteria for which our viable counting technique could reliably be used was 200 CFU/ml (i.e., 20 colonies on a neat plate); hence, a cutoff point of $\log_{10}$ 2.3 was used for the graphs shown (see Fig. 1). To assess the influence of antibiotic carryover on the viable counts observed, 0.1-ml samples of neat preinoculation broth and 10-fold dilutions of antibiotic-containing preinoculation broth were spread on Iso-Sensitest agar plates which were then inoculated with approximately 50 CFU by spreading 0.1 ml of an appropriate dilution of a 24-h-old broth culture of *S. aureus* NCTC 6571 (strain SOX). Viable counts were determined after 24 h of incubation at 37°C and compared with those on non-antibiotic-containing plates. No significant reduction in counts was seen on any of the antibiotic-containing plates as calculated with Student's *t* test ($P > 0.9$).

The following agents at the indicated concentrations (micrograms per milliliter) were used in the time-kill studies: acrosoxacin, 4.0; ciprofloxacin, 3.0; enoxacin, 10; fleroxacin, 5.0; ofloxacin, 8.0; pefloxacin, 8.0; tosufloxacin, 0.25; teicoplanin, 16; vancomycin, 16. These concentrations were chosen to reflect the attainable levels of these agents in serum.

Mutation rates. Cultures of the selected strains were grown in 10 ml of Iso-Sensitest broth at 37°C for 18 to 22 h. These were centrifuged and suspended in 2 ml of phosphate-buffered saline. Samples (0.1 ml) were spread on Iso-Sensitest agar plates containing various concentrations of antimicrobial agents. These plates were incubated for 48 h at 37°C and read at 24 and 48 h. Colonies which grew on these plates were picked off and reidentified as *S. aureus* by the criteria given previously, and development of resistance was confirmed by determination of MICs.

The following drugs at the indicated concentrations (micrograms per milliliter) were used: acrosoxacin, 10 and 50; ciprofloxacin, 5.0 and 25; enoxacin, 10 and 50; fleroxacin, 10 and 50; ofloxacin, 5.0 and 25; nalidixic acid, 256; norfloxacin, 10 and 50; pefloxacin, 5.0 and 25; tosufloxacin, 0.5 and 2.5; teicoplanin, 5.0 and 25; vancomycin, 10 and 50. These concentrations represented 10× and 25×, respectively, the MICs of the agents against MRSA.

RESULTS

Susceptibility results. For this study, 200 strains from 38 centers in 26 countries were preliminarily screened for susceptibility to ciprofloxacin. As a result, 160 isolates were found to be susceptible (MIC, <2 μg/ml) and 40 were found to be resistant (MIC, ≥2 μg/ml) to ciprofloxacin. Table 1 summarizes our findings on the susceptibilities of the 160 ciprofloxacin-susceptible isolates to a further eight different quinolones and the glycopeptides teicoplanin and vancomycin. The susceptibilities of the 40 ciprofloxacin-resistant strains to the other quinolones and the glycopeptides are also shown in Table 1. Teicoplanin and vancomycin were both equally active against the ciprofloxacin-susceptible and -resistant isolates. The quinolones tested possessed a range of activities against the ciprofloxacin-susceptible MRSA isolates tested; the most active quinolone was tosufloxacin (MIC for 50% of the strains tested, 0.06 μg/ml), and the least active quinolone was nalidixic acid (MIC for 50% of the strains tested, 64 μg/ml). Ofloxacin was the most active of the clinically available fluoroquinolones, followed closely by ciprofloxacin and pefloxacin; many strains were susceptible to concentrations of these agents of 1.0 μg/ml or lower.

Against the 40 strains of ciprofloxacin-resistant MRSA, tosufloxacin was the most active quinolone, followed by ciprofloxacin and ofloxacin. Different patterns and levels of quinolone resistance were seen among the strains of ciprofloxacin-resistant MRSA tested, and examples of these patterns and the origins of the strains possessing them are shown in Table 2. The pattern of elevations in MICs was unfixed among the quinolones, and the order of the potencies of the agents varied from strain to strain. Differences in

TABLE 1. Antibiotic susceptibilities of 160 ciprofloxacin-susceptible and 40 ciprofloxacin-resistant MRSA isolates

Strains (*n*)	Agent	MIC (μg/ml)[a]		
		Range	50%	90%
Ciprofloxacin susceptible (160)	Acrosoxacin	0.5–4.0	1.0	4.0
	Ciprofloxacin	0.25–1.0	0.5	1.0
	Enoxacin	0.5–4.0	1.0	2.0
	Fleroxacin	1.0–4.0	1.0	2.0
	Nalidixic acid	16.0–256	64.0	128.0
	Norfloxacin	0.5–4.0	2.0	4.0
	Ofloxacin	0.12–1.0	0.25	1.0
	Pefloxacin	0.12–2.0	0.5	1.0
	Tosufloxacin	0.03–0.12	0.06	0.06
	Teicoplanin	0.5–2.0	1.0	2.0
	Vancomycin	1.0–4.0	2.0	2.0
Ciprofloxacin resistant (40)	Acrosoxacin	1.0–>256	>256	>256
	Ciprofloxacin	2.0–>128	16.0	64.0
	Enoxacin	8.0–>128	64.0	128
	Fleroxacin	2.0–>128	32.0	128
	Nalidixic acid	64.0–>512	512	>512
	Norfloxacin	8.0–>128	64.0	128
	Ofloxacin	1.0–32.0	16.0	32.0
	Pefloxacin	2.0–>128	32.0	>128
	Tosufloxacin	0.12–32.0	2.0	32.0
	Teicoplanin	0.5–2.0	1.0	2.0
	Vancomycin	1.0–4.0	2.0	2.0

[a] 50% and 90%, MIC for 50 and 90% of isolates tested, respectively.

activity between acrosoxacin and ciprofloxacin were particularly notable; some strains were similarly susceptible to both agents, whereas others were highly resistant to acrosoxacin only.

Rates of killing. The rates of killing produced by ciprofloxacin, enoxacin, ofloxacin, pefloxacin, teicoplanin, and vancomycin against the selected methicillin-resistant strains and the susceptible control strain are shown in Fig. 1. The concentrations of quinolones and glycopeptides used for the time-kill studies were chosen to reflect the maximum levels attainable in blood. With these agent concentrations, the quinolones—ciprofloxacin, enoxacin, ofloxacin, and pefloxacin—caused 99.9% killing after 8 h (Fig. 1A to D). Acrosoxacin, fleroxacin, and tosufloxacin also produced 99.9% killing after 8 h at the concentrations tested (data not shown). The glycopeptides teicoplanin and vancomycin (Fig. 1E and F) were less rapidly bactericidal; however, both agents produced 99.9% reduction of the original inocula of all five strains after 24 h.

Although ciprofloxacin and enoxacin were initially bactericidal against strain RL7, after 24 h of incubation, regrowth had occurred (Fig. 1A and D). Initially, the MIC of ciprofloxacin for strain RL7 was 1.0 μg/ml; however, the MIC of ciprofloxacin for the organisms regrowing in ciprofloxacin (3.0 μg/ml) broth and enoxacin (10 μg/ml) broth was 16.0 μg/ml. The susceptibilities of the regrowing strains to various quinolones are shown in Table 3. Although some regrowth was seen with the other strains, no visible turbidity appeared in the broths after 36 h of incubation and no increase in the ciprofloxacin MIC was found for the organisms isolated from these broths. The initial ciprofloxacin MICs for strains RM1, SA1, AUS10, and SOX were 0.5, 0.5, 0.5, and 0.25 μg/ml, respectively.

Mutation rates. The largest inoculum that could be used for the mutation rate studies was approximately 1.0×10^9 CFU, because denser inocula overgrew on some of the plates containing lower concentrations of the quinolones. Low rates of mutation to resistance were found for strain

TABLE 2. Patterns of quinolone resistance in ciprofloxacin-resistant[a] MRSA of clinical origin

Strain origin	MIC (μg/ml)[b]								
	Acr	Cip	Enx	Flx	NA	Nfx	Ofx	Pfx	Tsf
England	2	2	8	2	64	8	2	2	0.12
France, Italy, Federal Republic of Germany	2	4	8	4	512	32	2	4	0.25
United States, Chile	8	4	16	4	512	16	2	4	0.25
France	>256	4	16	32	512	32	2	8	0.5
Federal Republic of Germany, Israel	>256	16	64	16	>512	32	16	32	2.0
Finland	16	16	64	32	512	64	8	16	2.0
United States	4	16	32	16	512	32	2	4	0.5
France, United States	>256	32	128	64	>512	>128	16	64	8.0
Israel	>256	128	64	128	>512	>128	32	>128	32.0

[a] MIC, ≥2.0 μg/ml.

[b] Abbreviations: Acr, acrosoxacin; Cip, ciprofloxacin; Enx, enoxacin; Flx, fleroxacin; NA, nalidixic acid; Nfx, norfloxacin; Ofx, ofloxacin; Pfx, pefloxacin; Tsf, tosufloxacin.

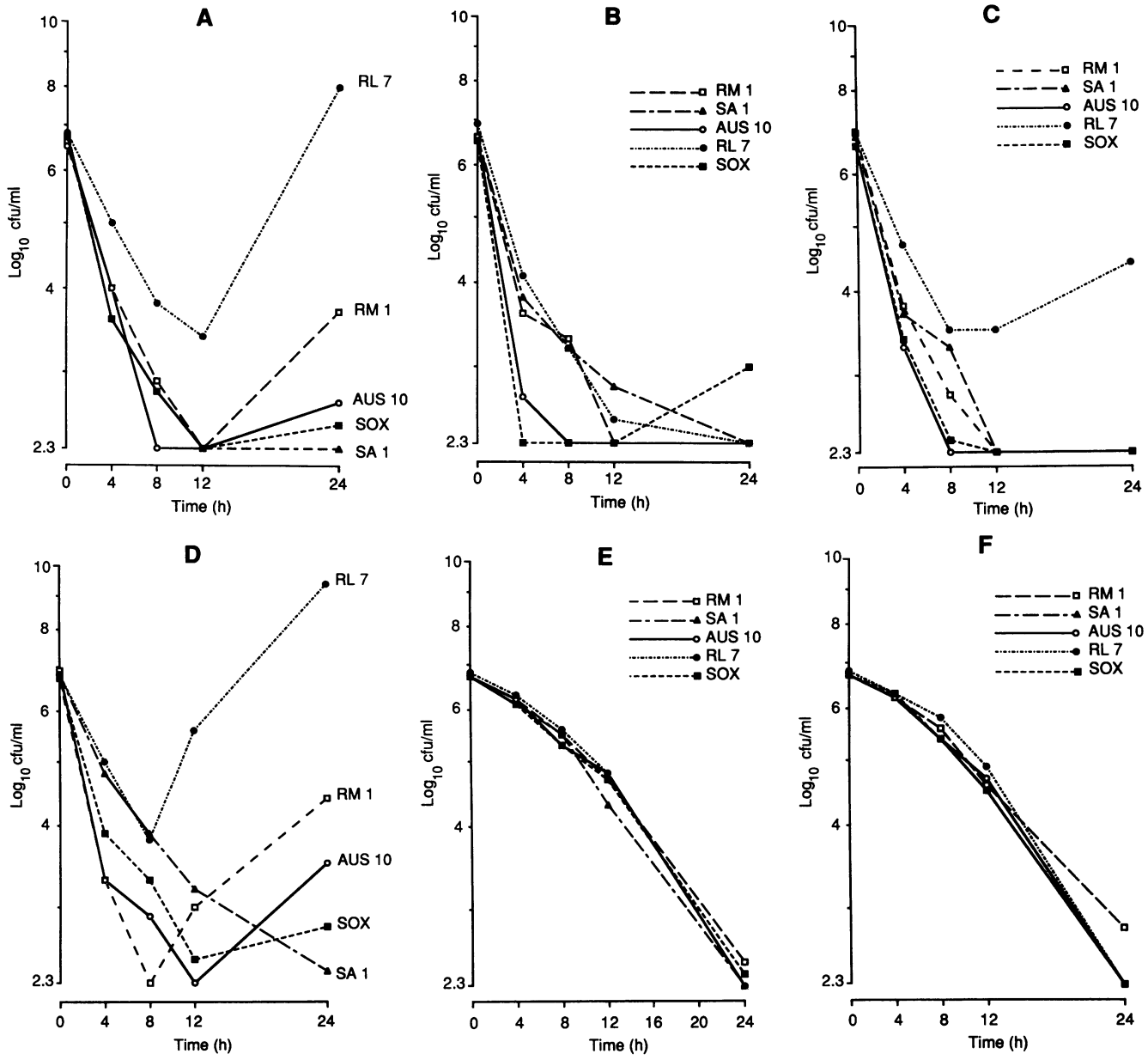

FIG. 1. Time-kill curves for ciprofloxacin at 3.0 μg/ml (A), ofloxacin at 8.0 μg/ml (B), pefloxacin at 8.0 μg/ml (C), enoxacin at 10 μg/ml (D), vancomycin at 16 μg/ml (E), and teicoplanin at 16 μg/ml (F) against representative MRSA strains from the United States (RM1), South Africa (SA1), Australia (AUS10), and England (RL7) and *S. aureus* NCTC 6571 (SOX), a methicillin- and penicillin-susceptible control strain.

RL7 in the presence of ciprofloxacin at 5.0 μg/ml (3.0×10^{-8}) and enoxacin at 10 μg/ml (5.0×10^{-8}) and for strains RM1 (3.0×10^{-9}) and SA1 (5.0×10^{-9}) in the presence of norfloxacin at 10 μg/ml. Rates of mutation to resistance of 10^{-7} to 10^{-8} were found for the strains in the presence of nalidixic acid at 250 μg/ml. MIC testing revealed that all of the mutants had decreased susceptibilities to the agents used to select for resistance, and the results for strain RL7 are shown in Table 3. The resistant mutants of strain RL7 which grew in the presence of either ciprofloxacin or enoxacin possessed cross-resistance to the other fluoroquinolones; however, the mutants which grew in the presence of nalidixic acid at 250 μg/ml failed to show cross-resistance to the fluoroquinolones.

DISCUSSION

Against the ciprofloxacin-susceptible MRSA strains, we found ciprofloxacin, ofloxacin, and pefloxacin to be equally highly active. Enoxacin, fleroxacin, and norfloxacin showed less activity, and nalidixic acid possessed little activity. Such findings for *S. aureus* are in general agreement with those reported by other workers (1, 22, 23, 29, 35). Tosufloxacin was the most active of the quinolones tested, which is in accordance with the findings of Barry and Jones (2); detailed reports of the clinical suitability of this compound are awaited.

Another interesting finding from susceptibility testing against ciprofloxacin-susceptible MRSA strains was the high

TABLE 3. Patterns of susceptibility to different quinolones for resistant mutants of strain RL7 obtained from killing rate and mutation rate studies

Conditions for RL7 growth	MIC (μg/ml)[a]						
	Acr	Cip	Enx	NA	Nfx	Ofx	Pfx
Antibiotic-free broth	0.5	1.0	4.0	64	4.0	1.0	1.0
Overgrowth in broth containing (concn [μg/ml]):							
Ciprofloxacin (3.0)	2.0	16	64	>256	>64	4.0	32
Enoxacin (10.0)	2.0	16	64	>256	>64	4.0	32
Mutants in agar containing (concn [μg/ml]):							
Ciprofloxacin (5.0)	4.0	32	128	>256	>64	8.0	64
Enoxacin (10.0)	4.0	32	128	>256	>64	8.0	32
Nalidixic acid (256.0)	2.0	1.0	4.0	>256	4.0	1.0	1.0

[a] For abbreviations, see Table 2, footnote *b*.

activity of acrosoxacin, a nonfluorinated quinolone, against MRSA. In terms of chemical structure, acrosoxacin is 1-ethyl-1,4-dihydro-4-oxo-7-(4-pyridyl)-quinolone-3-carboxylic acid. Although acrosoxacin activities similar to those reported here have been found by other workers (8), this compound, suprisingly, finds use only in the treatment of acute gonorrhea. The MICs determined for teicoplanin and vancomycin are similar to those reported by many workers (21). Because the glycopeptides act on the cell wall, it is not unexpected that ciprofloxacin-susceptible and -resistant strains were equally susceptible to teicoplanin and vancomycin.

For ciprofloxacin-resistant MRSA strains from different geographical sources, and even for resistant strains from the same center, different levels and patterns of resistance to the quinolones tested were seen. Whether these differences are due to different evolutionary pathways or different mechanisms of resistance remains to be established. Very little data on how fluoroquinolone resistance arises in MRSA in clinical situations are available. Factors possibly responsible for development of different levels and patterns of resistance include the use of different quinolones and exposure to quinolones at different body sites at which greatly differing concentrations may be encountered. Kojima et al. (16) have shown that different patterns and levels of resistance may arise following exposure to different quinolones and that different strains may produce different types of resistance. Because of the difficulties encountered in examining the mechanisms of quinolone resistance in *S. aureus* (32), our understanding of these phenomenona in MRSA is still rudimentary.

Another interesting finding following susceptibility testing of ciprofloxacin-resistant MRSA was incomplete cross-resistance between the fluoroquinolones and acrosoxacin in a few strains. Such reversed, incomplete cross-resistance has been previously reported only for a strain of *Flavobacterium multivorans* (32a) and may indicate a novel resistance mechanism. Generally, cross-resistance among the fluoroquinolones and other quinolones was complete, and these findings agree with those of other workers (17).

The fluoroquinolones tested in our time-kill studies were bactericidal, and it is well known that members of this class of agents are characteristically bactericidal (23, 29). Teicoplanin and vancomycin are also bactericidal (20), although killing seems to be slower than that seen with the fluoroquinolones. In our time-kill studies, strain RL7 overgrew in the presence of ciprofloxacin and enoxacin, and organisms with reduced susceptibilities were isolated from these broths. Foster et al. (9) compared the in vitro activities of quinolone antibiotics and vancomycin against gentamicin-resistant MRSA by time-kill studies and reported overgrowth of *S. aureus* in the presence of broth containing ciprofloxacin. Unlike those researchers, we found no regrowth with vancomycin in our time-kill studies.

In the mutation rate studies, strain RL7 had a relatively high rate of mutation to ciprofloxacin and enoxacin resistance. This may explain the overgrowth of this strain in the ciprofloxacin and enoxacin time-kill studies, especially as the development of quinolone resistance has been reported to be due to single-step mutations (15). A notable property of the fluoroquinolones is the reported low rate of bacterial mutation to resistance (6). This contrasts with nalidixic acid, the use of which was restricted by the emergence of nalidixic acid-resistant mutants (24). In vitro selection of resistance to vancomycin is very difficult with staphylococci (10), and no clinical isolates of *S. aureus* resistant to this agent have been reported. Watanakunakorn (33) has found it easier to induce resistance to teicoplanin; however, we obtained no isolates resistant to teicoplanin, and for both agents we failed to isolate resistant mutants in the time-kill or mutation rate studies.

Disturbing levels of quinolone resistance in MRSA have been reported (18), and a number of workers have reported outbreaks of infection due to ciprofloxacin-resistant MRSA (25, 26). Although the fluoroquinolones are rapidly bactericidal, mutation to resistance can occur, resulting in overgrowth in vitro. To prevent further emergence of staphylococcal fluoroquinolone resistance, we strongly recommend that fluoroquinolones be used only in combination with unrelated agents to minimize selection of resistant mutants. Encouraging clinical results have been obtained with ciprofloxacin and rifampin in combination (7). Furthermore, there is evidence that all quinolones are not equal in antistaphylococcal activity and potential to select resistant strains (28). Fluoroquinolones under development, such as tosufloxacin and AT-4140 (16), may prove to be much more potent against *S. aureus* than those currently available. Until our understanding of how fluoroquinolone resistance develops and spreads is more complete, it would be appropriate to use fluoroquinolones with restraint.

To conclude, we believe that fluoroquinolones are potentially useful agents for treatment of staphylococcal infections, especially as new, even more active agents, such as tosufloxacin, are in the process of development. It is most

important that a proper understanding of the way in which fluoroquinolone-resistant staphylococci emerge and spread be reached; otherwise, the therapeutic value of these agents will be diminished. The glycopeptide antibiotics teicoplanin and vancomycin are less potent against MRSA than ciprofloxacin, but no resistance in MRSA has been reported. The cost, toxicity, and universal lack of staphylococcal resistance to vancomycin indicate that this agent should be held in reserve for treatment of serious staphylococcal infections. Teicoplanin has been used successfully to treat MRSA infections so long as adequate levels are maintained. Earlier reports of a lack of efficacy of teicoplanin in treating MRSA infections were due to inadequate dosing (3). Teicoplanin and certain fluoroquinolones may prove most useful as alternative agents for treatment of infections due to MRSA, although vancomycin is still the agent of choice for blind treatment of serious infections.

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