

## NOTES

# Methicillin-Resistant Strains of *Staphylococcus aureus* Resistant to Quinolones

SAM SCHAEFLER

*Bureau of Laboratories, New York City Department of Health, and Public Health Research Institute  
of the City of New York, Inc., New York, New York 10016*

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**Since January 1988, *Staphylococcus aureus* strains with a high level of quinolone resistance have been isolated at 17 hospitals and 15 nursing homes in New York City. The majority of these strains were methicillin resistant. The bacteriophage types and susceptibility to other antibiotics were similar to those of quinolone-susceptible strains isolated at the same hospitals.**

Clinical isolates of *Staphylococcus aureus* are susceptible to quinolones such as ciprofloxacin and ofloxacin (1, 6). Quinolones are among the relatively small number of drugs used in the therapy of infections caused by methicillin-resistant strains. Mutants with a low level of ciprofloxacin resistance (MIC, 2 to 4 µg/ml) have been reported during the treatment of staphylococcal infections (2, 3). However, no published data on the spread of quinolone-resistant strains in the hospital environment are available to date.

My laboratory routinely screens for the presence of antibiotic-resistant *S. aureus* strains among isolates received for bacteriophage typing from hospitals in New York City (4, 5). Strains received between May 1987 and July 1988 were screened for susceptibility to the quinolones fleroxacin (Hoffmann-La Roche Inc., Nutley, N.J.) and ciprofloxacin (Miles Laboratories, Inc., West Haven, Conn.).

Trypticase (BBL Microbiology Systems, Cockeysville, Md.) soy broth cultures of *S. aureus* which served as inoculum for phage typing (5) were tested on agar plates containing 1.5, 3, or 5 µg of fleroxacin or ciprofloxacin per ml. The plates were incubated for 18 h at 37°C. Of the 2,193 strains received between May 1987 and mid-January 1988, positive growth responses were detected only on plates containing 1.5 or 3 µg of drug per ml, but not on plates containing 5 µg/ml. The susceptibility of strains showing detectable growth on quinolone plates was then tested by MIC determinations (7). Overnight cultures of single-colony isolates were diluted to give an inoculum of approximately 10<sup>4</sup> CFU and tested on Mueller-Hinton agar plates containing fleroxacin and ciprofloxacin at concentrations ranging from 0.03 to 16 µg/ml. The results obtained with these two drugs were similar. For one strain the MIC was 4 µg/ml, and for 19 strains it was 2 µg/ml, values which correspond to a low level of clinical resistance (3). For susceptible control strains, MICs of both drugs were 0.25 to 0.5 µg/ml.

Strains which grew on plates with 5 µg of drug per ml were first detected during the second half of January 1988 and were found to be highly resistant to quinolones. Strains showing detectable growth on plates with 5 µg of drug per ml were retested from single-colony isolates on plates with 1.5, 3, 5, 7.5, 10 µg of fleroxacin or ciprofloxacin per ml. MICs

were determined with a concentration range of 0.05 to 100 µg/ml. The susceptibility of the quinolone-resistant strains to other antibiotic agents was tested by the disk diffusion method (7).

Of the 2,833 isolates received between January and July 1988, 149 were quinolone resistant. The MICs of the two drugs ranged from 12.5 to 100 µg/ml, with MICs for most isolates ranging from 12.5 to 25 µg/ml. Agar diffusion susceptibility tests with 5-µg ciprofloxacin disks gave results consistent with those obtained by plate dilution, with most strains showing no detectable inhibition zone. With the exception of nine strains, the quinolone-resistant strains were resistant to methicillin (Table 1).

Quinolone-resistant strains were isolated at 17 hospitals and 15 nursing homes in four boroughs of New York City. These strains were recovered from blood, wounds, bronchial washings, urine, and sputum. The results of phage typing with the international set of typing phages and an additional set of experimental phages (4, 5) are summarized in Table 1. Among the strains isolated in hospitals, 56 belonged to international phage group III and 45 were experimental phage type 88. Strains of experimental phage type 88 were frequently found among methicillin-resistant *S. aureus* strains isolated in New York City (4).

Characteristic features of the emerging quinolone-resistant *S. aureus* strains isolated in New York City are their high level of resistance and their almost simultaneous appearance in a relatively large number of hospitals and nursing homes in different parts of the city. The data obtained so far seem to suggest an independent selection of quinolone-resistant strains in different institutions, as indicated by the distribution of strains of experimental phage type 88. Initially, strains of experimental phage type 88 were rifampin resistant (4). However, during the last few years, strains of type 88, present in some hospitals, became susceptible to rifampin. Of the 45 quinolone-resistant strains of experimental phage type 88 isolated in New York City, 35 were rifampin resistant (four hospitals) and 10 were rifampin susceptible (three hospitals). The rifampin susceptibility of the quinolone-resistant strains was similar to that of the endemic quinolone-susceptible strains of experimental

TABLE 1. Distribution of quinolone-resistant strains

Source of isolates	No. of strains					
	Total <sup>a</sup>	Methicillin resistant	Group III	Susceptible to experimental phage:		
				Type 88	Other than type 88	Non-typeable
Hospitals	123	122	56	45	11	11
Nursing homes	26	18	19	1	1	1

<sup>a</sup> Isolates obtained from different patients.

phage type 88 present in these institutions. In several instances, strains of phage group III originating in the same hospital were very similar in their susceptibility to individual typing phages and to antibiotics, while there were marked dissimilarities between strains isolated at different hospitals.

A comparison of strains isolated at hospitals with those isolated at nursing homes (Table 1) showed a higher ratio of methicillin-susceptible strains among strains isolated at nursing homes. While strains of experimental phage type 88 isolated at hospitals are usually resistant to most antistaphylococcal antibiotics (4), the quinolone-resistant strain isolated at a nursing home was resistant only to penicillin. Given the frequent transfer of patients between nursing homes and hospitals, a further study of the relationship between the two groups could be of interest.

Phage typing was performed by W. Perry and T. Baradet. Antibiotic susceptibility testing was performed by C. Rampersad and E. Mayr.

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