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In Vitro Activity of Ro 13-9904, Cefuroxime, Cefoxitin, and Ampicillin Against *Neisseria gonorrhoeae*

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In vitro susceptibilities of 87 isolates of non-penicillinase-producing *Neisseria gonorrhoeae* and 8 isolates of penicillinase-producing *N. gonorrhoeae* to Ro 13-9904, cefuroxime, cefoxitin, and ampicillin were determined. Ro 13-9904 was the most effective of the four drugs, inhibiting growth of both non-penicillinase-producing and penicillinase-producing *N. gonorrhoeae*.

Ro 13-9904, (Z)-(6R, 7R)-7-[2-(2-amino-4-thiazolyl)-2-(methoxyimino) acetamido]-3-[(2,5-dihydro-6-hydroxy-2-methyl-5-oxo-as-triazin-3-yl) thiol] methyl-8-oxo-5-thia-1-azabicyclo (4.2.0) oct-2-ene-2-carboxylic acid disodium salt, a new parenteral cephalosporin, possesses considerable activity against various *Enterobacteraceae*, many strains of *Pseudomonas aeruginosa*, and gram-positive cocci, *Streptococcus faecalis* excepted. Moreover, Ro 13-9904 appears to be more resistant to various beta-lactamases compared with currently available cephalosporins. (*Investigational Drug Brochure*, Ro 13-9904, Hoffmann-La Roche, Nutley, N.J., 1980). This report is concerned with the relative activities of Ro 13-9904, cefuroxime, cefoxitin, and ampicillin against a total of 87 isolates of non-penicillinase-producing *Neisseria gonorrhoeae*; eight strains of penicillinase-producing isolates were included in the study.

All *N. gonorrhoeae* were genital isolates. They were identified by Gram stain, oxidase reaction, and sugar fermentation reactions. Penicillinase production was detected by a 1-min beta-lactamase test previously described (2). Susceptibility tests were performed with Mueller-Hinton agar (BBL Microbiology Systems, Cockeysville, Md.) enriched with IsoVitaleX (BBL Microbiology Systems). Serial twofold dilutions of Ro 13-9904 (Hoffmann-La Roche, Nutley, N.J.), cefuroxime (Glaxo Research, Fort Lauderdale, Fla.), cefoxitin (Merck, Sharp & Dohme, West Point, Pa.), and ampicillin (Bristol, Syracuse, N.Y.) were prepared and incorporated into the medium. The minimal inhibitory concentrations (MICs) were determined by agar dilution with a replicating apparatus (4), which delivered a mean inoculum of 5.9×10^4 colony-forming units. Plates were placed in candle jars and incubated at 37°C for 24 h. The MIC was defined as the lowest concentration of drug which yielded no visible growth. A control strain of *N. gonorrhoeae* with a known MIC was included in each determination for reproductibility.

Table 1 summarizes the MICs of the four antimicrobial agents for 50, 75, and 100% of non-penicillinase-producing *N. gonorrhea* strains. Against Ro 13-9904, 75% of the gonococcal isolates were inhibited at concentrations less than 0.006 μg/ml. All strains were inhibited at 0.0125

TABLE 1. *Susceptibilities of non-penicillinase-producing and penicillinase-producing N. gonorrhoeae*

Strains (no.)	Drugs	MIC (μg/ml)			
		Range	For % strains:		
			50	75	100
Non-penicillinase-producing (87)	Ro 13-9904	<0.006-0.0125	<0.006	<0.006	<0.0125
	Cefuroxime	<0.006-1.6	0.025	0.05	1.6
	Cefoxitin	0.0125-1.6	0.2	0.4	1.6
	Ampicillin	0.025-0.8	0.2	0.4	0.8
Penicillinase-producing (8)	Ro 13-9904	<0.006-0.012	0.006	0.012	0.012
	Cefuroxime	0.025-0.4	0.2	0.2	0.4
	Cefoxitin	0.05-1.6	0.4	1.6	1.6
	Ampicillin	100	100	100	100

μg/ml or less. Against cefuroxime, cefoxitin, or ampicillin, all strains of non-penicillinase-producing *N. gonorrhoeae* were susceptible at a concentration of 1.6 μg/ml or less.

Table 1 shows the MICs of the four antimicrobial agents against eight strains of penicillinase-producing *N. gonorrhoeae*. All strains were very susceptible to Ro 13-9904, with MICs of 0.012 μg/ml or less; three isolates were inhibited at less than 0.006 μg/ml. Against cefuroxime and cefoxitin, the MICs of all eight penicillinase-producing strains were ≤0.4 and 1.6 μg/ml, respectively. As expected, all isolates were highly resistant to ampicillin.

These in vitro data indicate that Ro 13-9904 is more active than ampicillin, cefuroxime, or cefoxitin against non-penicillinase-producing *N. gonorrhoeae*. In addition, the activity of Ro 13-9904 was superior to that of cefuroxime or cefoxitin against a limited number of penicillinase-producing strains. Cefoxitin has been shown to possess increased resistance to beta-lactamase activity and has been effective in treating urethritis caused by penicillinase-producing *N. gonorrhoeae* (1). These results suggest that Ro 13-9904 may have promise for treatment of infection with both non-penicillinase-producing and penicillinase-producing *N. gonorrhoeae*.

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