whom the strains were isolated were 80%. Given these data, the isolates evaluated by Endtz et al.\(^1\) would appear to be somewhat atypical, and we await, with interest, the results of the investigations of the mechanisms of resistance to meropenem seen in these strains.

References


A survey of susceptibility to erythromycin amongst *Streptococcus pyogenes* isolates in Italy

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Sir,

Although isolates of *Streptococcus pyogenes* have, to date, been uniformly susceptible to penicillin, it has long been recognized that these bacteria can develop resistance to the macrolide group of antibiotics. Resistance to erythromycin was first described in 1959\(^1\) and this was followed by similar reports from Japan,\(^2\) the USA\(^3\) and, more recently, Finland.\(^4\) The incidence of erythromycin resistance amongst isolates of *S. pyogenes* has shown wide geographical variation; in Italy, it remained below 10% until 1987.\(^5\) Increases in the incidence of resistance have always been linked to corresponding increases in the numbers of prescriptions for erythromycin and other macrolides. In Japan, for example, these drugs are used extensively; indeed, they are considered the antibiotics of choice as treatment of patients with streptococcal pharyngitis. Although the incidence of pharyngitis has not risen, in recent years, there have been increasing numbers of reports of life-threatening infections caused by *S. pyogenes*, including necrotizing fasciitis, septicemia and streptococcal toxic shock syndrome. Stimulated by concerns arising from these severe infections and increasing problems of resistance, we have monitored the susceptibilities of isolates of this bacterium to penicillin and erythromycin since 1985. We report here the in-vitro susceptibilities to these antibiotics of 3814 strains of *S. pyogenes* isolated from pharyngeal swabs collected between 1990 and 1995.

During the study period, 42,672 pharyngeal swabs obtained from in-patients and out-patients of the Departments of Medicine and Paediatrics, ICP Hospital of Milan, were cultured for *S. pyogenes*. Specimens were inoculated on to Columbia blood agar plates and incubated in an anaerobic atmosphere at 37°C for 24 h. After enzymatic extraction, the isolates were grouped by latex agglutination (Streptex–Wellcome, Rome, Italy). Susceptibilities to penicillin and erythromycin were determined by a disc diffusion method (Kirby–Bauer).

Strains of *S. pyogenes* were isolated from between 8.2% and 11.5% of pharyngeal swabs during the 6-year period; all of the isolates were susceptible to penicillin. Between 1990 and 1993, the incidence of erythromycin-resistant strains remained below 10% (8.2–8.8%). An increase to 16.2% (118 of 728 strains) was first noted in 1994, followed by a further sharp increase in 1995 to 30.7% (213 of 693 strains). Data for 1994 and 1995 are shown in detail in the Figure, which reveals seasonal variations in the isolation of *S. pyogenes*, i.e. peaks in the winter months and troughs in the summer. The Figure also shows an inexorable increase in the percentage of erythromycin-resistant strains isolated from October 1994 onwards. Moreover, the increase in resistance rates exhibits a characteristic pattern—a sharp increase, followed by a period of relative constancy, followed by a further sharp increase and a plateau.

The results of this study show an upward trend in the isolation rate for erythromycin-resistant strains of *S. pyogenes*, reaching an alarming peak of 30.7% in 1995; these observations are consistent with those of Seppala *et al.* in Finland,\(^6\) who reported an increase in resistance to erythromycin from 4% in 1988 to 24% in 1990. The sharp increase in the isolation rate observed by us is probably related to the introduction on to the market, and subsequent widespread use, of novel macrolides. The progressive, step-wise pattern might be explained by the constant selective pressures exerted by the macrolides. These agents differ from other antimicrobials in terms of the selective resistance to them that is exhibited by Gram-positive cocci. On the one hand, if resistance to erythromycin is constitutive, a bacterium will be resistant to all macrolides, lincosamides and streptogramin B-type antibiotics. On the other hand, if resistance is inducible, the bacterium will be resistant to 14- and 15-membered macrolides, but will remain susceptible to 16-membered macrolides;\(^6\) in our experience, 39 of 40 strains of *S. pyo genes* resistant to erythromycin (MIC\(_{90}\) of 8 mg/L) were
Correspondence

susceptible to miocamycin, a 16-membered macrolide (MIC$_{90}$ of 0.25 mg/L). The very considerable increase in the rate of isolating erythromycin-resistant strains of 

$S$. pyogenes requires an urgent response, ideally in the form of a major modification in the prescribing of macrolides. This should be accompanied by a continuing surveillance of the susceptibilities of these bacteria to the relevant antibiotics, particularly the macrolides. Susceptibility testing of 

$S$. pyogenes is essential, not only in the interests of individual patients, but also to facilitate identification of significant local changes in antibiotic resistance patterns.

References


The effect of reserpine, an inhibitor of multidrug efflux pumps, on the in-vitro susceptibilities of fluoroquinolone-resistant strains of 

$Streptococcus pneumoniae$ to norfloxacin

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Sir,

Fluoroquinolone resistance in 

$Streptococcus pneumoniae$ has recently been shown to be mediated by mutations in

Figure. $S$. pyogenes strains isolated monthly during 1994 and 1995 from pharyngeal swabs. ■ number of strains; ● number resistant to erythromycin; ▲ percentage resistant to erythromycin.