Mechanisms of Macrolide Resistance in Clinical Pneumococcal Isolates in France

FREDERIC FITOSSI,1 CATHERINE DOIT,1 PIERRE GESLIN,2 NAIMA BRAHMI,1 AND EDOUARD BINGEN1,4

Service de Microbiologie, Hôpital Robert Debré, 75019 Paris, 1 and Centre National de Référence des Pneumocoques, Centre Hospitalier de Créteil, 94010 Créteil, 2 France

Received 18 September 2000/Returned for modification 24 October 2000/Accepted 20 November 2000

The genetic basis of macrolide resistance was investigated in a collection of 48 genotypically unrelated clinical isolates of Streptococcus pneumoniae obtained between 1987 and 1997 in France. All strains were resistant to erythromycin, clindamycin, and streptogramin B, exhibiting a macrolide-lincosamide-streptogramin B resistance phenotype, and harbored the erm(B) gene. None of the strains carried the mef(A) or erm(A) subclass erm(TR) gene.

Antibiotic resistance in Streptococcus pneumoniae, especially to β-lactam antibiotics, has been a matter of growing concern in the last two decades. Resistance in this species has also been noted with tetracyclines, chloramphenicol, cotrimoxazole, and macrolides. In the United States, 19 to 34% of pneumococcal isolates are currently resistant to macrolides (8; M. R. Jacobs, D. Felminghan, P. C. Appelbaum, and The Alexander Project Group, Abstr. 39th Intersci. Conf. Antimicrob. Agents Chemother., abstr. 1044, p. 151, 1999). In Western Europe, the low prevalence of macrolide resistance in Germany, Austria, Portugal, The Netherlands, and Switzerland (1.5 to 4.6%) contrasts with the high rates observed in Spain, Italy, and Belgium (53, 24, and 31%, respectively) (1, 17; D. Felminghan and R. N. Gruneberg, Abstr. 40th Intersci. Conf. Antimicrob. Agents Chemother., abstr. 1790, p. 108, 2000). In France, the prevalence of pneumococcal resistance to erythromycin was 53% in 1997 (10). Four mechanisms of macrolide resistance have been described in S. pneumoniae. The first is a target modification involving a ribosomal methylase, associated with the erm(B) gene (15, 25). A macrolide-specific efflux mechanism encoded by the mef(A) gene was described in 1996 (21, 23). The erm(B) gene is associated with high-level resistance to macrolides, lincosamides, and streptogramin B (MLS_b phenotype), while the mef(A) gene is associated with low-level resistance to 14- and 15-membered-ring macrolides (M phenotype). More recently, erythromycin resistance in clinical isolates of S. pneumoniae harboring the erm(A) subclass erm(TR) gene has been described (3; G. A. Syrogianiopoulos, I. N. Grivea, A. Tait-Kamradt, G. D. Katopodis, N. G. Beratis, J. Sutcliffe, P. C. Appelbaum, and T. A. Davies, Abstr. 40th Intersci. Conf. Antimicrob. Agents Chemother., abstr. 139, p. 65, 2000). Finally, macrolide-resistant pneumococcal strains with mutations in the 23S rRNA and ribosomal protein L4 or L22 have been selected by macrolide passage in vitro (22; A. Canu, B. Malbruny, M. Coquemont, T. A. Davies, P. C. Appelbaum, and R. Leclercq, Abstr. 40th Intersci. Conf. Antimicrob. Agents

1 Corresponding author. Mailing address: Service de Microbiologie, Hôpital R. Debré, 48 Bd Séruirier, 75019 Paris, France. Phone: 33 (1) 40 03 23 40. Fax: 33 (1) 40 03 24 50. E-mail: edouard.bingen@rdh.ap-hop-paris.fr.

DOI: 10.1128/AAC.45.2.636–638.2001

0066-4804/01/$04.00+0 DOI: 10.1128/AAC.45.2.636-638.2001
Copyright © 2001, American Society for Microbiology. All Rights Reserved.
TABLE 1. MICs of macrolides and related agents and of penicillin G for 48 erythromycin-resistant 
S. pneumoniae isolates

<table>
<thead>
<tr>
<th>Antimicrobial agent</th>
<th>MIC (µg/ml)</th>
<th>50%</th>
<th>90%</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythromycin</td>
<td>&gt;128</td>
<td>&gt;128</td>
<td>&gt;128</td>
<td></td>
</tr>
<tr>
<td>Azithromycin</td>
<td>&gt;128</td>
<td>&gt;128</td>
<td>&gt;128</td>
<td></td>
</tr>
<tr>
<td>Josamycin</td>
<td>&gt;128</td>
<td>&gt;128</td>
<td>&gt;128</td>
<td></td>
</tr>
<tr>
<td>Clindamycin</td>
<td>&gt;128</td>
<td>&gt;128</td>
<td>&gt;128</td>
<td>64–&gt;128</td>
</tr>
<tr>
<td>Streptogramin B</td>
<td>128</td>
<td>&gt;128</td>
<td>2–&gt;128</td>
<td></td>
</tr>
<tr>
<td>Penicillin G</td>
<td>0.5</td>
<td>4</td>
<td>0.016–8</td>
<td></td>
</tr>
</tbody>
</table>

<sup>*</sup> 50 and 90%, MICs at which the growth of 50 and 90% of isolates, respectively, was inhibited.

We thank Joyce Sutcliffe for providing S. pyogenes reference strains 02C 1061, 02C 1064, and 02C 1110 and R. Leclercq for helpful discussions.

REFERENCES

