Correspondence

Whether carbapenemase-producing strains of *Acinetobacter* spp. are unique to the QMUH Burns Unit or are more widespread throughout the UK is not currently known, although data from abroad suggest that they are becoming more prevalent. What is not in doubt is that diagnostic laboratories should be aware of the difficulties in identifying them. With regard to our isolates, the disc diffusion method detected reduced susceptibility to meropenem, but not to imipenem. The efficacy of carbapenems as treatment of patients with infections caused by these bacteria is also unclear. Although the MICs of both agents, and particularly those of imipenem, are below the susceptibility breakpoint, we have adopted a cautious approach to the use of these drugs and would welcome data regarding clinical response rates in other patient populations. For the treatment of patients infected with such organisms, the therapeutic options at QMUH include sulbactam/ampicillin and polymyxin, these being the only antibiotics to which the isolates are consistently susceptible.

References


Worldwide emergence of carbapenem-resistant *Acinetobacter* spp.

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Sir,

*Acinetobacter* spp., especially *Acinetobacter baumannii*, are common opportunistic pathogens in immunocompromised patients. Historically, they were susceptible to many penicillins, cephalosporins, aminoglycosides and quinolones but, more recently, resistance to multiple antibiotics has been recognized increasingly. Imipenem and meropenem have retained in-vitro activities that are superior to those of other antimicrobials and, in many centres, they are the drugs of choice for patients with infections caused by *Acinetobacter* spp. Carbapenem-resistant strains have been identified, but infrequently. One such strain, isolated in Scotland in 1985, produced ARI-1, a plasmid-mediated carbapenemase, while others, isolated in a New York medical centre, owed their resistance to target inaccessibility, rather than to drug inactivation by *ß*-lactamases.

During the past 2 years, we have actively sought carbapenem-resistant *Acinetobacter* spp. worldwide and have received representative strains from Argentina, Belgium, Hong Kong, Kuwait, Singapore and Spain (Table). MICs for these isolates were determined by the agar dilution method with IsoSensitest agar and inocula of 10^4 cfu per spot. Many of the isolates exhibited low-level resistance, with the MICs of imipenem and meropenem ranging from 2 to 8 mg/L, compared with MICs of 0.12–0.25 mg/L for historical isolates and relative to a MIC breakpoint of 4 mg/L. Other strains were more resistant, with carbapenem MICs of 16–128 mg/L (Table). Amongst all these isolates, cross-resistance to penicillins, cephalosporins, aminoglycosides and quinolones was virtually complete.

*ß*-Lactamase extracts of the referred strains, which were prepared by sonicating cells harvested from nutrient agar cultures in 0.1 M phosphate buffer pH 7.0, were subjected to isoelectric focusing. In addition, their activities against imipenem and meropenem, at concentrations of 20 mg/L, were evaluated by a biological assay. Each antibiotic and an extract were incubated together for 1 h before being transferred to wells cut into a bioassay plate containing...
Mueller–Hinton agar, the surface of which was inoculated with *Escherichia coli* NCTC 10418 as the indicator organism. The extracts of all of the strains, with the exception of one from Hong Kong, hydrolysed one or both carbapenems (Table), whereas extracts of the carbapenem-susceptible control strains (MICs ≤ 0.25 mg/L) did not do so. The isoelectric points (pIs) of the β-lactamases were highly variable, with most extracts yielding multiple bands and with no single band common to all. In several cases, we isolated individual β-lactamases by ion-exchange chromatography and identified those with carbapenemase activities. The biochemical characteristics of these enzymes, which also varied from isolate to isolate, will be described in a separate report. All of those that have been purified to date (indicated by a in the Table) were inhibited by tazobactam, but not by EDTA, thereby indicating that, unlike most carbapenemases, they are not zinc-dependent.4,5

This account of the worldwide emergence of carbapenem resistance amongst *A cinetobacter* spp. reinforces the concerns expressed by Weinbren *et al*.5 who described the persistence of such bacteria over a 1 year period in a UK burns unit. Others, from Argentina and South Africa, have also described carbapenem-resistant isolates.7,8 Many of these strains were susceptible only to sulbactam,3,6 which is not available as a single agent, and to polymyxin, the in-vivo efficacy of which remains unconfirmed.

**Acknowledgements**

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**Table.** Properties of referred and control *A cinetobacter* spp. isolates

<table>
<thead>
<tr>
<th>Source</th>
<th>No. of isolates</th>
<th>MICs (mg/L)</th>
<th>Hydrolysis by cell-free extracts of:</th>
<th>pIs of β-lactamases</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>imipenem</td>
<td>meropenem</td>
<td>imipenem</td>
</tr>
<tr>
<td>Argentina</td>
<td>2</td>
<td>4</td>
<td>2</td>
<td>+</td>
</tr>
<tr>
<td>Belgium</td>
<td>3</td>
<td>64–128</td>
<td>&gt;128</td>
<td>+</td>
</tr>
<tr>
<td>Spain</td>
<td>15</td>
<td>64</td>
<td>128</td>
<td>+</td>
</tr>
<tr>
<td>Hong Kong</td>
<td>1</td>
<td>64</td>
<td>128</td>
<td>+</td>
</tr>
<tr>
<td>Kuwait</td>
<td>1</td>
<td>4</td>
<td>16</td>
<td>–</td>
</tr>
<tr>
<td>Singapore</td>
<td>3</td>
<td>8–16</td>
<td>128</td>
<td>+</td>
</tr>
<tr>
<td>Control&lt;sup&gt;b&lt;/sup&gt;</td>
<td>40</td>
<td>0.12</td>
<td>0.25</td>
<td>–</td>
</tr>
</tbody>
</table>

<sup>a</sup>Enzyme purified and shown to have carbapenemase activity.
<sup>b</sup>Mode data for isolates collected at the Royal London Hospital during 1982–4.

+, hydrolysed; –, not hydrolysed.

**References**


