Dissemination of the *Klebsiella pneumoniae* Carbapenemase in the Health Care Settings: Tracking the Trails of an Elusive Offender

Amos Adler\textsuperscript{a,b} and Yehuda Carmeli\textsuperscript{a,b}

Division of Epidemiology, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel,\textsuperscript{a} and National Center of Infection Control, Ministry of Health, Tel Aviv, Israel\textsuperscript{b}

**ABSTRACT** Transmission of antibiotic resistance genes may be mediated by a variety of molecular mechanisms, from mobility of small genetic elements to clonal spread. Since 1997, the carbapenem-hydrolyzing enzyme *Klebsiella pneumoniae* carbapenemase (KPC) has spread in the United States and across the world, mainly via a single *K. pneumoniae* clone, sequence type 258. By tracking the trail of dissemination of the \textit{bla}\textsubscript{KPC} gene inside their institution, Mathers et al. (\textit{mBio} 2:e00204–11, 2011) have shown evidence of the ability of this gene to spread by several modes, including plasmid transfer and clonal spread. The ever-evolving modes of transmission of resistance genes challenge our ability to detect, track, and eventually control the spread of what has become a major threat to hospitalized patients worldwide.
hence asymptomatic GIT carriers of CPE were likely missed. Identifying these patients might have allowed a better explanation of the transmission source in patients 6, 8, and 10 (see Fig. 4 and Fig. S3 in reference 15) and facilitated control measures. Also, it might have revealed the true extent of the epidemics (the “iceberg effect”) and allowed assessment of the dissemination and virulence potentials of the different CPE clones.

This study demonstrates the evolution of one of the most clinically important resistance mechanisms, the KPC carbapenemases, from a monoclonal mode of dissemination (16, 26) to a complex mode also involving the transfer of mobile genetic elements. In contrast, the carbapenemase OXA-48, initially characterized by the spread of a single plasmid (20), may also be involved in local outbreaks of a single strain (27, 28). Hence, thorough epidemiological investigation combined with comprehensive knowledge of the possible transmission modes will be invaluable for the understanding and successful control of future epidemics (29, 30).

REFERENCES

TABLE 1 Microbiological features and dissemination potential of four carbapenemases

<table>
<thead>
<tr>
<th>Carbapenemase</th>
<th>Class</th>
<th>Predominant species</th>
<th>Imipenem MIC</th>
<th>Location of gene</th>
<th>Dissemination potential/mode</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>SME-1/2/3</td>
<td>A</td>
<td>S. marcescens</td>
<td>High</td>
<td>Ch</td>
<td>Limited</td>
<td>1, 3, 15</td>
</tr>
<tr>
<td>KPC-2/3</td>
<td>A</td>
<td>K. pneumoniae</td>
<td>High</td>
<td>Pl</td>
<td>High/clonal (ST-258)</td>
<td>8–11</td>
</tr>
<tr>
<td>OXA-48</td>
<td>D</td>
<td>Variable</td>
<td>Low</td>
<td>Pl</td>
<td>High/plasmid</td>
<td>16, 17</td>
</tr>
<tr>
<td>NDM-1</td>
<td>B</td>
<td>Variable</td>
<td>Variable</td>
<td>Pl, Ch</td>
<td>High/combined</td>
<td>9, 20</td>
</tr>
</tbody>
</table>

a According to Ambler’s structural classification.

b Ch, chromosome; Pl, plasmid.