**LETTERS**

_Citrobacter freundii, Enterobacter cloacae, and Morganella morganii_ and has shown resistance to nearly all classes of antibacterial agents, except polymyxins and tigecycline (2, 3). Kumarasamy et al. recently reported the identification of 37 isolates with NDM-1 in the United Kingdom. The isolates came from 29 patients, of whom at least 17 had traveled to India or Pakistan in the year preceding identification of NDM-1; 14 patients had been admitted to a hospital in those countries (2).

NDM-1 has also been isolated from 3 patients in the United States, all of whom had recently received medical care in India (7). In contrast, 1 of the 2 patients with _K. pneumoniae_ carrying NDM-1 reported here was transferred to our hospital from Kosovo in southeastern Europe and had an unremarkable travel history. Immediate action is needed to control the spread of NDM-1 and avoid a worldwide public health problem.

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**References**


**Letters**

Letters commenting on recent articles as well as letters reporting cases, outbreaks, or original research are welcome. Letters commenting on articles should contain no more than 300 words and 5 references; they are more likely to be published if submitted within 4 weeks of the original article’s publication. Letters reporting cases, outbreaks, or original research should contain no more than 800 words and 10 references. They may have 1 Figure or Table and should not be divided into sections. All letters should contain material not previously published and include a word count.

**Carbapenemases in Enterobacteria, Hong Kong, China, 2009**

To the Editor: Carbapenemases are often recommended for serious infections caused by extended-spectrum β-lactamase–producing enterobacteria. However, enzyme-mediated carbapenem resistance is increasingly reported worldwide. Carbapenemases are represented by 3 molecular classes of β-lactamase: A, B, and D (1). The best known class A carbapenemase is _Klebsiella pneumoniae_ carbapenemase (KPC); KPC-producing enterobacteria are responsible for many hospital outbreaks. Class B carbapenemases are metallo-β-lactamases (MBL), which have the widest substrate spectrum. Class D OXA-type carbapenemases are found mainly in nonfermenting bacteria, except for OXA-48, which has been found only in enterobacteria.

In Hong Kong Special Administrative Region, People’s Republic of China, the Public Health Laboratory Centre routinely provides microbiological diagnostic services for government outpatient clinics and confirms the identity of bacterial isolates referred by other clinical laboratories. In 2009, among 18 enterobacteria isolates determined to be not susceptible to carbapenem, only 4 isolates—_Citrobacter freundii, Enterobacter cloacae, Escherichia coli, and K. pneumoniae_—were confirmed to produce carbapenemase. The _E. coli_ isolate was from a government outpatient clinic; the others were from a regional hospital laboratory (Table).

For all 4 isolates, the modified Hodge test (2) demonstrated enzyme activity against ertapenem and meropenem. Previously described PCR and sequencing methods (1) identified the MBL IMP-4 in the _C. freundii_ and _K. pneumoniae_ isolates; the _C. freundii_ isolate also possessed extended-spec-
trum β-lactamase CTX-M-9. The *E. coli* isolate harbored the recently described MBL called New Delhi metallo-β-lactamase (NDM-1) (GenBank accession no. FN396876) from India (3). The *E. cloacae* isolate possessed a class A carbapenemase IMI-like (Nmc-type) gene, and DNA sequencing confirmed its 97.2% nt and 97.6% aa identity to IMI-1. This IMI allele was subsequently designated IMI-3 (GenBank accession no. GU015024). For all 4 enterobacteria isolates, PCR was negative for OXA-48.

MIC determination by Etest and VITEK 2 (bioMérieux, Marcy l’Etoile, France) showed that all 4 isolates were resistant to ampicillin, amoxicillin/clavulanate, piperacillin/tazobactam, cefotaxin, cefuroxime, cefotaxime, and ceftazidime, according to Clinical and Laboratory Standards Institute breakpoints (2). Because IMI-1 was inhibited by clavulanate and tazobactam, the corresponding resistance in the IMI-3 positive *E. cloacae* isolate might result from other mechanisms, possibly AmpC β-lactamase, although PCR results for common AmpC alleles were negative (4).

All 4 isolates showed resistance to all 3 carbapenems according to the Clinical and Laboratory Standards Institute MIC criteria updated in June 2010 (Table), except for the NDM-1 positive *E. coli* isolate, which had an intermediate MIC for meropenem of 2 μg/mL. The IMP-4 positive *C. freundii* and *K. pneumoniae* isolates also seemed to be more multidrug resistant; they were resistant to nalidixic acid, ciprofloxacin, nitrofurantoin, and co-trimoxazole and susceptible to only amikacin and gentamicin. Conversely, the 2 organisms harboring IMI-3 and NDM-1 were susceptible to all these agents except for the NDM-1–positive *E. coli*, which was resistant to amikacin and gentamicin.

IMP-4 in *Acinetobacter* spp. was first described in 2001 in a teaching hospital in Hong Kong (5). Since then, IMP-4 has been detected in several enterobacteria from mainland China and Australia. IMP-4 has spread throughout Hong Kong, crossing geographic and genus barriers; other new carbapenemases are also emerging. The association of IMP-4 with integrons and conjugative plasmids has been documented and possibly contributed to its propensity to spread. IMI-1 in *E. cloacae* was originally described in the United States in 1996. In 2005, IMI-2 (99% aa identity to IMI-1) in *Enterobacter asburiae* isolated from rivers in the United States was reported. (6), and in 2006, a blood culture *E. cloacae* was found to possess IMI-2 in Hangzhou, China (7).

We report IMI-3 (aa identity 97.6% to IMI-2) in a urine isolate of *E. cloacae*, possibly a colonizer rather than the causative agent of the urinary tract infection because the urine specimen did not contain any leukocytes. The 2 IMP-4–positive enterobacteria isolates were also only transiently present; repeated cultures did not yield any carbapenem-resistant organisms despite the patients not having received any targeted therapy. Nonetheless, the presence of these transferable resistance determinants among patients with prolonged hospitalization is cause for concern. The NDM-1–positive *E. coli* isolate came from an outpatient of Indian ethnicity, who had hypertension, diabetes, and a urinary tract infection that responded to ciprofloxacin. This isolate was thought to have originated from the Indian subcontinent, where the patient had spent 3 weeks in March 2009; he had not been hospitalized in India. A similar case of travel-related NDM-1–positive *E. coli* isolated from urine has also been recently reported in Australia (8).

NDM-1 has the potential to be a worldwide public health problem (9). Our findings highlight the threat of carbapenemase-mediated resistance. Scrupulous surveillance must be maintained, and clinical microbiology laboratories should have adequate knowledge and capacity to identify these resistance determinants. To control the dissemination of these resistance determinants, coordinated infection control responses are needed at local, national, and international levels (10).

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Table. Antimicrobial susceptibility results and ESBL detected for 4 carbapenemase-harboring enterobacteria isolates, Hong Kong, 2009*

<table>
<thead>
<tr>
<th>Organism</th>
<th>Patient age, y/sex</th>
<th>Patient location</th>
<th>Specimen</th>
<th>MIC, μg/mL (CLSI breakpoint for resistance)</th>
<th>ESBL/ carbapenemase detected</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Citrobacter freundii</em></td>
<td>69/M</td>
<td>Hospital</td>
<td>Sputum</td>
<td>IMP (≥4) MEM (≥4) ERT (≥1) NA (≥32) CIP (≥4) NIT (≥128) AK (≥64) GN (≥16) SXT (≥80)</td>
<td>IMP-4, CTX-M-9</td>
</tr>
<tr>
<td><em>Klebsiella pneumoniae</em></td>
<td>60/M</td>
<td>Hospital</td>
<td>Bedsore</td>
<td>≥16 ≥16 ≥8 ≥32 ≥4 128 ≤2 ≤8 ≥320</td>
<td></td>
</tr>
<tr>
<td><em>Enterobacter cloacae</em></td>
<td>68/F</td>
<td>Hospital</td>
<td>Urine</td>
<td>≥16 ≥16 ≥8 ≤0.25 64 ≤2 ≤1 ≤0.25</td>
<td>≥20</td>
</tr>
<tr>
<td><em>Escherichia coli</em></td>
<td>64/M</td>
<td>Outpatient clinic</td>
<td>Urine</td>
<td>4 2 4 ≤2 ≤0.25 ≤16 ≥256 ≥16 ≥20</td>
<td>NDM-1</td>
</tr>
</tbody>
</table>

*ESBL, extended-spectrum β-lactamase; IMP, imipenem; MEM, meropenem; ERT, ertapenem; NA, nalidixic acid; CIP, ciprofloxacin; NIT, nitrofurantoin; AK, amikacin; GN, gentamicin; SXT, co-trimoxazole; NDM-1, New Delhi metallo-β-lactamase.

†CLSI, Clinical and Laboratory Standards Institute, updated June 2010.

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Change in Age Pattern of Persons with Dengue, Northeastern Brazil

To the Editor: Approximately 40% of the world’s population is at risk for dengue (1). Epidemiologic characteristics of dengue differ by region, and disease incidence varies by patient age. In Southeast Asia, incidence of dengue fever (DF) and dengue hemorrhagic fever (DHF) is highest among children (2,3); in the Western Hemisphere, incidence of these diseases is higher among adults.

In Brazil, which has ≈80% of dengue cases in the Western Hemisphere, adults are at risk for dengue virus (DENV) infection (3,4). However, in 2007, a total of 53% of persons in Brazil hospitalized with DHF were children <15 years of age; this proportion was highest (65.4%) in children in northeastern Brazil (5).

In Ceará, a state in northeastern Brazil, DENV-1 epidemics have occurred since 1987. DHF cases have been reported since 1994 when DENV-2 was identified. In 2003, a severe DENV-3 epidemic occurred, and DHF incidence was high among adults (6). However, since 2007, incidence of DENV infection has been highest among children (7). To better understand factors that could affect this change in risk by age group, we studied the temporal progression of age distribution of persons with dengue during 1998–2008 in Ceará.

We used data for Ceará from the National System of Notifiable Diseases (DF and DHF cases), the Hospital Admission Data System (dengue hospitalizations) (8), and the Central Public Health Laboratory (virus isolation). For each age group (<10, 10–19, 20–59, and ≥60 years), we calculated incidence of DF and hospitalization rate for DHF. We also calculated proportions of dengue serotypes per year (2001–2008). Medians for continuous variables were compared by using the Kruskal-Wallis test. Analyses were performed by using Epi Info version 6.0 software (Centers for Disease Control and Prevention, Atlanta, GA, USA).

From 1998 (10.8 cases/100,000 persons) through 2007 (236.7 cases/100,000 persons), DF incidence was lowest among persons <10 years of age. However, the incidence was highest (599.4 cases/100,000 persons) for this age group in 2008. In 2007, incidence among persons <10 years of age (236.7 cases/100,000 persons) was similar to that among persons 10–19, 20–59, and ≥60 years of age (305.6, 331.5, and 249.9 cases/100,000 persons, respectively).

Since 2007, the incidence of DHF among children was already higher (4,884 cases/100,000 persons) than among the other age groups (3,261, 3,387 and 2,789 cases/100,000 persons, respectively). In 2008, incidence of DHF among children was 8,992 cases/100,000 persons, which was 2× that among persons 10–19 and 20–59.