Antibiotic Resistance in Greece
Surveillance and Response

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National School of Public Health
&
Central Public Health Laboratory
KEELPNO
A. Surveillance
Surveillance of Antibiotic Resistance in Greece

   – Resistance rates

2. The Early Warning System.
   – To trace the spread of resistance.
The Greek System for the Surveillance of Antimicrobial Resistance

• In Operation Since 1996

• Involves about 40 Hospitals all over Greece
  – Voluntary Basis

• Coordination Dept of Microbiology, National School of Public Health in Collaboration with KEELPNO (Greek ECDC)

• Based on the collection and analysis of Routine data
  – Uses the WHONET software.

• Collaborates with EARSS
The Greek System for the Surveillance of Antimicrobial Resistance

• Calculates resistance rates (proportions)

• Collects ALL Routine Data

  – Analysis improves quality of Data
The Greek System for the Surveillance of Antimicrobial Resistance

- Mainly Automatic Download

- **All** lab records

- No added workload to the lab

- **PASKO**
- **VITEK**
- **SENSITITRE**
- **MICROSCAN**
- **WIDER**
- **SCANNERS**
  - OSIRIS
  - SIRSCAN
The Greek System for the Surveillance of Antimicrobial Resistance

**Deliverables** (every 6 months)

1. Publishes statistics (In the internet)

2. Produces a feedback for each hospital
The Greek System for the Surveillance of Antimicrobial Resistance (WHONET) is a national network for continuous monitoring of bacterial antibiotic resistance in the Greek hospitals.

Its function is based on the assumption that the routine results of the antibiotic sensitivity tests performed daily in each hospital clinical laboratory should be considered as a major resource for antibiotic resistance surveillance.

Moreover, since the quality and comparability of these data are in principle uncertain, our approach is to work in parallel, on both accessing the data and assessing its quality.

This is accomplished through the establishment of a quality control procedure and the adaptation of an electronic code and data format in all hospitals through the use of the WHONET software. The WHONET software was originally developed by WHO Collaborating Centre for Surveillance of Antibiotic Resistance in Boston, USA, and further developed in the Division of Emerging and Other Communicable Diseases Surveillance and Control, WHO (WHO/EMC), Geneva, Switzerland. WHONET is distributed free of charge by WHO/EMC and facilitates the management of antibiotic susceptibility test results from routine clinical isolates. A full description of the software and its potential has been published elsewhere [1-3].

The analysis of the information facilitates:

1. The understanding of the trends of resistance.
2. The detection of epidemics.
3. The differentiation of endemic from epidemic infections.
4. The development of a national antibiotic policy.
5. The hierarchy of priorities for further studying the genetic and molecular mechanisms responsible for the emergence of resistance.

Moreover, since the acquisition of the data is performed automatically, no additional workload at the laboratory level is generally required, and thus the system can function on a routine basis.

Antibiotic susceptibility is performed either by the disc diffusion method on Mueller-Hinton agar or by various automatic systems. The current recommendations of the National Committee for Clinical Laboratory Standards (NCCLS) are followed.

All hospitals receive the QC strains provided by the WHO/CDC Quality Control and Proficiency Testing Pilot Program.
CUMULATIVE RESULTS

July - December 2010
January - June 2010
July - December 2009
January - June 2009
July - December 2008
January - June 2008
July - December 2007
January - June 2007
July - December 2006
January - June 2006
July - December 2005
January - June 2005
July - December 2004
January - June 2004
**CUMULATIVE RESULTS**

Cumulative results from isolates from all hospitals of the network are presented. Only the first isolate per patient and species is being processed. (*List of Abbreviations and Acronyms Used in the Tables*)

### July - December 2010

**PERCENT (%) RESISTANCE TO SELECTED ANTIBIOTICS BY HOSPITAL**

- **Acinetobacter baumannii**
  - Amikacin ([all clinical specimens](#))
  - Cefazidime ([all clinical specimens](#))
  - Ciprofloxacin ([all clinical specimens](#))
  - Ampicillin/Sulbactam ([all clinical specimens](#))
  - Ceftazime ([all clinical specimens](#))
  - Imipenem ([all clinical specimens](#))
  - Piperacillin/Tazobactam ([all clinical specimens](#))
  - Multiresistance ([all clinical specimens](#))
  - Blood isolates ([results from all hospitals](#))

- **Pseudomonas aeruginosa**
  - Amikacin ([all clinical specimens](#))
  - Cefazidime ([all clinical specimens](#))
  - Ciprofloxacin ([all clinical specimens](#))
  - Imipenem ([all clinical specimens](#))
  - Piperacillin/Tazobactam ([all clinical specimens](#))
  - Multiresistance ([all clinical specimens](#))
### Klebsiella pneumoniae

% resistance to imipenem per hospital

All clinical specimens

(July - December 2010)

| Hospital | Medical Ward | % IS | % NS | % R | % M | Surgical Ward | % IS | % NS | % R | % M | ICU | % IS | % NS | % R | % M |
|----------|--------------|------|------|-----|-----|--------------|------|------|-----|-----|-----|------|------|-----|-----|-----|
| GR001    | 9.4%         | 45   | 35.6| 35.6| 0.0 | 10.1%        | 19   | 26.3| 21.1| 1.3 |     | 17.3%| 36   | 72.3| 63.9| 8.3 |
| GR004    | 10.6%        | 5    | 11.0| 11.0| 0.0 | 10.2%        | 11   | 0.0 | 0.0  | 0.0 |     | 20.0%| 0    |     |     |     |
| GR005    | 9.4%         | 53   | 19.8| 22.5| 0.0 | 7.2%         | 23   | 30.4| 26.1| 4.3 |     | 12.2%| 23   | 67.2| 64.2| 15.1|
| GR007    | 11.3%        | 12   | 50.8| 37.0| 3.2 | 6.0%         | 3    | 0.0 | 0.0  | 0.0 |     | 10.0%| 23   | 69.6| 56.5| 13.0|
| GR008    | 5.0%         | 0    | 0.0 | 0.0  | 0.0 | 7.1%         | 5    | 0.0 | 0.0  | 0.0 |     | 5.0% | 6    | 0.0 | 0.0 | 0.0 |
| GR010    | 7.7%         | 85   | 2.6| 7.5 | 4.7 | 0.0         | 0.0  | 0.0 | 0.0  | 0.0 |     | 9.0% | 7    | 85.4| 85.4| 8.5 |
| GR011    | 9.1%         | 216  | 20.1| 20.1| 0.0 | 11.9%        | 20   | 38.5| 38.5| 0.0 |     | 16.4%| 16   | 84.6| 84.6| 0.0 |
| GR013    | 11.9%        | 206  | 20.1| 20.1| 0.0 | 11.0%        | 20   | 38.5| 38.5| 0.0 |     | 16.4%| 16   | 84.6| 84.6| 0.0 |
| GR014    | 9.0%         | 53   | 19.8| 22.5| 0.0 | 7.2%         | 23   | 30.4| 26.1| 4.3 |     | 12.2%| 23   | 67.2| 64.2| 15.1|
| GR015    | 10.8%        | 40   | 22.5| 17.5| 0.0 | 7.1%         | 20   | 40.0| 25.0| 0.0 |     | 18.3%| 19   | 58.8| 68.8| 0.0 |
| GR016    | 8.3%         | 57   | 49.8| 29.8| 8.8 | 0.0         | 0.0  | 0.0 | 0.0  | 0.0 |     | 12.4%| 13   | 76.4| 37.7| 30.2|
| GR017    | 5.0%         | 13   | 0.0 | 0.0  | 0.0 | 7.1%         | 25   | 44.0| 24.0| 20.0|     | 16.5%| 22   | 81.8| 45.5| 50.4|
| GR018    | 12.5%        | 121  | 29.8| 18.2| 11.6| 7.0%         | 31   | 41.9| 22.8| 19.4|     | 15.3%| 26   | 88.6| 80.6| 7.7 |
| GR019    | 10.3%        | 20   | 33.0| 30.0| 2.0 | 14.3%        | 2    | 0.0 | 0.0  | 0.0 |     | 8.9% | 23   | 56.7| 38.1| 17.4|
| GR020    | 9.9%         | 53   | 19.8| 22.5| 0.0 | 7.2%         | 23   | 30.4| 26.1| 4.3 |     | 12.2%| 23   | 67.2| 64.2| 15.1|
| GR021    | 13.2%        | 107  | 23.7| 23.4| 9.3 | 0.0         | 0.0  | 0.0 | 0.0  | 0.0 |     | 15.3%| 48   | 73.5| 61.2| 12.2|
| GR022    | 3.4%         | 12   | 0.0 | 0.0  | 0.0 | 7.1%         | 6    | 0.0 | 0.0  | 0.0 |     | 8.1% | 11   | 72.7| 36.4| 36.4|
| GR023    | 11.7%        | 19   | 52.6| 52.6| 0.0 | 1.0%         | 1    | 0.0 | 0.0  | 0.0 |     | 20.0%| 1    |     |     |     |
| GR024    | 11.7%        | 19   | 52.6| 52.6| 0.0 | 1.0%         | 1    | 0.0 | 0.0  | 0.0 |     | 20.0%| 1    |     |     |     |

**Note:** The data table represents the percentage of Klebsiella pneumoniae isolates resistant to imipenem across different hospitals and wards, with columns for Hospital, Medical Ward, Surgical Ward, and ICU, and rows for % IS, % NS, % R, and % M.
<table>
<thead>
<tr>
<th>Drug</th>
<th>Medical Wards</th>
<th>Surgical Wards</th>
<th>ICU</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Isolates Tested</td>
<td>%NS</td>
<td>%R</td>
</tr>
<tr>
<td>Ticarcillin/Clavulanic acid</td>
<td>238</td>
<td>58.8</td>
<td>55.0</td>
</tr>
<tr>
<td>Piperacillin/Tazobactam</td>
<td>381</td>
<td>52.8</td>
<td>50.1</td>
</tr>
<tr>
<td>Amoxicillin/Clavulanic acid</td>
<td>361</td>
<td>53.5</td>
<td>47.9</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>367</td>
<td>43.6</td>
<td>37.6</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>226</td>
<td>55.3</td>
<td>49.1</td>
</tr>
<tr>
<td>Cefazidime</td>
<td>386</td>
<td>51.6</td>
<td>46.9</td>
</tr>
<tr>
<td>Aztreonam</td>
<td>297</td>
<td>53.5</td>
<td>51.9</td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>326</td>
<td>39.9</td>
<td>37.8</td>
</tr>
<tr>
<td>Imipenem</td>
<td>382</td>
<td>38.7</td>
<td>28.3</td>
</tr>
<tr>
<td>Meropenem</td>
<td>345</td>
<td>37.1</td>
<td>34.2</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>338</td>
<td>16.8</td>
<td>14.7</td>
</tr>
</tbody>
</table>
High proportion of hospitals and isolates are represented.

<table>
<thead>
<tr>
<th>Country</th>
<th>K. pneumoniae</th>
<th>P. aeruginosa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Austria</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>Bulgaria</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Cyprus</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Czech Republic</td>
<td>1</td>
<td>30</td>
</tr>
<tr>
<td>Estonia</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Finland</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>France</td>
<td>33</td>
<td>20</td>
</tr>
<tr>
<td>Greece</td>
<td>25</td>
<td>24</td>
</tr>
<tr>
<td>Hungary</td>
<td>15</td>
<td>16</td>
</tr>
<tr>
<td>Iceland</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Ireland</td>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td>Malta</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Netherlands</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Norway</td>
<td>7</td>
<td>9</td>
</tr>
<tr>
<td>Slovenia</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>Spain</td>
<td>10</td>
<td>9</td>
</tr>
<tr>
<td>Sweden</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>4</td>
<td>9</td>
</tr>
<tr>
<td>Total</td>
<td>140</td>
<td>168</td>
</tr>
</tbody>
</table>

* In some countries, data from several laboratories may be reported to EARS-Net from one central laboratory.
The Early Warning System

• Each hospital lab must report immediately certain “new” or “important resistant phenotypes.
  – To the Hospital Infection Control Committee
  – To KEELPNO

• The isolate must also be available for further testing.
  – Confirmation of the mechanism
  – Typing
Early Warning System

- **2005**: 97 isolates from 22 Hospitals
- **2006**: 110 isolates from 19 Hospitals
- **2007**: 58 Isolates from 14 Hospitals.
- **2008**: 511 Isolates from 41 Hospitals
- **2009**: 602 Isolates from 45 Hospitals
- **2010**: 1250 Isolates from 58 Hospitals

- Carbapenem resistant gram negatives
- CA MRSA
- Multiresistant *Acinetobacter*
University Hospital

• Epidemic of VIM + ESBL producing *Klebsiella*
  
  – Proven clonal

  – Infection Control Measures established

  – Epidemic controlled
Hospital of Athens

- Epidemic of VIM + ESBL producing *Klebsiella*
  - *Not all strains clonal*
  - Infection Control Measures established
  - Epidemic controlled
Surveillance in Greece

The Good News
No C.dif 027 in Greece!
Blood cultures
Trends 2000 -2010
21 Hospitals

Many rates are decreasing
Many rates are decreasing.
Many rates are decreasing
Many rates are decreasing

E faecalis

% gentamicin high-level resistance
Blood cultures
Trends 2000 - 2010
21 Hospitals

E. faecium

23 Nov 2011
Many rates are decreasing

E. faecium

The bar chart shows the percentage of vancomycin resistance across different countries. The symbols * and ** indicate significant increasing and decreasing trends, respectively. The asterisks indicate significant trends in the overall data that were not supported by data from laboratories consistently reporting for all four years. Data for Ireland showed a significant increasing trend only for data from laboratories which reported continuously for the last four years.
Blood cultures
Trends 2000 -2010
21 Hospitals

Many rates are decreasing
Blood cultures
Trends 2000 - 2010
21 Hospitals

P. aeruginosa

Axis Title

0% 5% 10% 15% 20% 25%


whonet Greece
The Greek System for Surveillance of Antimicrobial Resistance
Many rates are decreasing

\[ P\ aeruginosa \]
Trends

The bad News
Blood cultures
Trends 2000 -2010
21 Hospitals

A. baumannii
Blood cultures
Trends 2000 -2010
21 Hospitals

K. pneumoniae

Axis Title

whards
icu

0% 5% 10% 15% 20% 25% 30%


WHONET Greece
The Greek System for Surveillance of Antimicrobial Resistance
Carbapenem resistance
2009

Percentage resistance
- < 1%
- 1 to < 5%
- 5 to < 10%
- 10 to < 25%
- 25 to < 50%
- ≥ 50%
- No data reported or less than 10 isolates
- Not included

23 Nov 2011
Figure 5.25: *Klebsiella pneumoniae*: proportion of invasive isolates resistant to carbapenems in 2010

- < 1%
- 1% to < 5%
- 5% to < 10%
- 10% to < 25%
- 25% to < 50%
- ≥ 50%
- No data reported or less than 10 isolates
- Not included

Non-visible countries:
- Liechtenstein
- Luxembourg
- Malta
Figure 2.2: *Klebsiella pneumoniae*: Percentage of carbapenem-resistant invasive isolates reported to EARSS/EARS-Net by year, 2005-2010 (18 countries; 140 laboratories)

Only laboratories that continuously reported susceptibility results for carbapenems during the period 2005-2010 are included in the analysis.
A new way of reporting

## Table 2

<table>
<thead>
<tr>
<th>Epidemiological scale</th>
<th>Description</th>
<th>Stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>No cases reported</td>
<td>No cases reported</td>
<td>0</td>
</tr>
<tr>
<td>Sporadic occurrence</td>
<td>Single cases, epidemiologically unrelated</td>
<td>1</td>
</tr>
<tr>
<td>Single hospital outbreak</td>
<td>Outbreak defined as more than two epidemiologically related cases in a single institution</td>
<td>2a</td>
</tr>
<tr>
<td>Sporadic hospital outbreaks</td>
<td>Unrelated hospital outbreaks with independent, i.e. epidemiologically unrelated introduction or different strains, no autochthonous inter-Institutional transmission reported</td>
<td>2b</td>
</tr>
<tr>
<td>Regional spread</td>
<td>More than one epidemiologically related outbreak confined to hospitals that are part of a regional referral network, suggestive of regional autochthonous inter-institutional transmission</td>
<td>3</td>
</tr>
<tr>
<td>Inter-regional spread</td>
<td>Multiple epidemiologically related outbreaks occurring in different health districts, suggesting inter-regional autochthonous inter-institutional transmission</td>
<td>4</td>
</tr>
<tr>
<td>Endemic situation</td>
<td>Most hospitals in a country are repeatedly seeing cases admitted from autochthonous sources</td>
<td>5</td>
</tr>
</tbody>
</table>

**EUROROUNDUPS**

Carbapenem-non-susceptible Enterobacteriaceae in Europe: conclusions from a meeting of national experts

H Grundmann (Max-Grundmann@gmx.de), D.M. Livermore, C.G. Glover, R Cantón, G.M. Rossolini, J. Campos, A. Varela-Pérez, M. Galadówski, A. Tóth, Y. Pfeiffer, Y. Jacqous, Y. Carmeli, the CNS Working Group, EUAction of the European Commission, Directorate-General, Health and Consumers, Brussels, Belgium.
Carbapenem resistance

Carbapenemase*-producing Enterobacteriaceae (CPE) in Europe

- Not reported
- Sporadic occurrence
- Single hospital outbreak
- Independent hospital outbreaks
- Regional spread
- Inter-regional spread
- Endemic
- Other countries

*All carbapenemases (not only NDM-1).

Funding source: European Commission, DG Research, project number 223031 (TROCAR).
European nations in debt

Many European Union nations face large deficits and massive debt. Italy and Greece owe more than they earn. This map provides financial snapshots based on the latest available data from the European Commission.
Carbapenem\textsuperscript{R} \textit{Klebsiella} in Greece

TWO EPIDEMICS

\begin{itemize}
  \item VIM (2003 – 2007)
  \item KPC (2007 – PRESENT)
\end{itemize}

\textbf{Figure 2}

\textit{Trends in proportion of imipenem-resistant \textit{Klebsiella pneumoniae} isolates in hospitals in Greece, 2000-2006}

Data from the Greek System for the Surveillance of Antimicrobial Resistance (http://www.modnet.gov.gr/lonet)
• VIM Epidemic in *Klebsiella pneumoniae* in Greece

• Three outbreaks reported to us in ICU’s in autumn 2002 involving 17 patients

(Giakkoupi et al. 2003)

• Two more incidences in ICU’s in early 2003
VIM Epidemic in *Klebsiella pneumoniae* in Greece in the three ICUs

- VIM –1 .
- Class I Integron
- MICs from 1 - >32 mg/L
- Harbored by (different) conjugative plasmids
- Co existence with ESBLs (in some instances)
- Few bacterial clones – even in the same hospital

FIG. 2. (A) *PstI* restriction profiles of the *bla_{VIM-1}*-carrying plasmids extracted from *E. coli* transconjugants trc-1, trc-2 (plasmid type 1), trc-8, and trc-13 (plasmid type 2) are presented in lanes 1 to 4, respectively. (B) Hybridization of the preparations shown in panel A with a *bla_{VIM-1}* probe.

Giakkoupi et al. 2003
Tsakris et al., 2000; Mavroidi et al., 2000; Pournaras et al., 2002; Pournaras et al., 2003; Miriagou et al., 2003; Giakkoupi et al., 2003a & 2003b; Scoulica et al., 2004; Galani et al., 2005; Ikonomidis et al., 2005; GenBank.
Ongoing epidemic of \textit{bla}_{VIM-1}-positive \textit{Klebsiella pneumoniae} in Athens, Greece: a prospective survey

M. Psychogiou\textsuperscript{1}, P. T. Tassios\textsuperscript{2}, A. Avlamis\textsuperscript{2}, I. Stefanou\textsuperscript{2}, C. Kosmidis\textsuperscript{2}, E. Platsouka\textsuperscript{2}, O. Panlara\textsuperscript{2}, A. Xanthaki\textsuperscript{2}, M. Toutouza\textsuperscript{2}, G. L. Daicos\textsuperscript{2} and L. S. Tzouvelekis\textsuperscript{2}

Conclusions: A multiclonal epidemic of \textit{bla}_{VIM-1}-carrying \textit{K. pneumoniae} is under way in the major hospitals in Greece. Microorganisms producing both \textit{VIM-1} and \textit{SHV-5} constitute the prevalent multi-drug-resistant population of \textit{K. pneumoniae} in this setting.
Short report

Identification of Klebsiella pneumoniae Carbapenemase (KPC) in Sweden

K Tegmark Wisell (karen.tegmark-wisell@smi.ki.se), S Häggman, L Gezelius, O Thompson, I Gustafsson, T Råpå, B Olsson-Liljequist

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2. Department of Infectious Disease, County Hospital of Halmstad, Sweden
3. Department of Clinical Microbiology and Infectious Disease Control, County Hospital of Halmstad, Sweden

A Klebsiella pneumoniae expressing carbapenemase type 2 (KPC-2) enzyme has been identified in Sweden. The patient, who had a history of chronic obstructive lung disease, developed a respiratory tract infection while on holiday in Greece. After initial intensive care treatment in Greece, the patient was transferred to Sweden. Upon recovery, the central venous catheter was withdrawn and a multidrug-resistant Klebsiella pneumoniae was isolated from the patient. KPC-producing Enterobacteriaceae have now been identified in at least four European countries, and we therefore encourage microbiological laboratories to be observant of abnormal carbapenem resistance phenotypes in order to detect KPC-producing isolates. Based on the New York experience, we stress the importance of early identification followed by intensified infection control measures to prevent the dissemination of Enterobacteriaceae with KPC enzyme.
Short report

Identification of Klebsiella Pneumoniae Carbapenemase (KPC) in Sweden

K Tegmark Wisell (kari.tegmark-wisell@smi.ki.se), S Håggman, L Gezelius, O Thompson, I Gustafsson, T Råpå, B Olsson-Liljequist

1. Swedish Institute for Infectious Disease Control, Stockholm, Sweden
2. Department of Infectious Disease, County Hospital of Halmstad, Sweden
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23 Nov 2011
Plasmid-Mediated Carbapenem-Hydrolyzing β-Lactamase KPC-2 in Klebsiella pneumoniae Isolate from Greece

The emergence and dissemination of Enterobacteriaceae isolates harboring carbapenemases in various geographic regions.
Plasmid-Mediated Carbapenem-Hydrolyzing β-Lactamase KPC-2 in Klebsiella pneumoniae Isolate from Greece

The emergence and dissemination of Enterobacteriaceae isolates harboring carbapenemases in various geographic regions.
Phenotypic Detection and differentiation of the main types of carbapenemases

<table>
<thead>
<tr>
<th>Hodge Test</th>
<th>EDTA TEST</th>
<th>Possible enzyme</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>+</td>
<td>Metalloenzyme ($\pi\chi$ VIM)</td>
</tr>
<tr>
<td>+</td>
<td>-</td>
<td>KPC type</td>
</tr>
<tr>
<td>-</td>
<td>-</td>
<td>Carbapenemase Negative*</td>
</tr>
</tbody>
</table>

* Possible due to AmpC production or reduced permeability etc

To be applied on strains displaying reduced susceptibility to carbapenems
Summary of epidemiological, antibiotic susceptibility and transferability data by pulsotype of the KPC producing *Klebsiella pneumoniae* in Greece 2008

**Table**

Summary of epidemiological data and information on antibiotic susceptibility and transferability of the KPC-2-producing *Klebsiella pneumoniae* isolates described in this study.

<table>
<thead>
<tr>
<th>Pulsotype</th>
<th>Number of isolates</th>
<th>Number of hospitals</th>
<th>Resistance to other drug classes*</th>
<th>blaKPC gene transferred via conjugation</th>
<th>Other drug classes transferred</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>166</td>
<td>18</td>
<td>an, net, tb, spt, sxt, c, cip</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>1</td>
<td>1</td>
<td></td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>2</td>
<td>1</td>
<td>an, net, tb, spt, sxt, cip</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>D</td>
<td>2</td>
<td>1</td>
<td>gm, an, net, tb, spt, sxt, cip</td>
<td>Yes</td>
<td>gm an net tb spt sxt c</td>
</tr>
<tr>
<td>E</td>
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<td>2</td>
<td>net, tb, spt, sxt, c, cip</td>
<td>Yes</td>
<td></td>
</tr>
</tbody>
</table>

Figure 1. Geographical map showing the locations of the participating hospitals as well as the number of isolates collected during the initial survey (numbers in italics) and the update described in this study (numbers in bold). Black rectangle, Athens–Piraeus; grey rectangles, mainland cities; white rectangles, islands.
An update of the evolving epidemic of bla<sub>KPC-2</sub>-carrying Klebsiella pneumoniae in Greece (2009–10)

Panagiotis Giakoumis<sup>1</sup>, Costas C. Papageorgiou<sup>1</sup>, Vivi Mirkou<sup>1</sup>, Olga Papa<sup>1</sup>, Michalis Palexis<sup>2</sup>, Kyriaki Triantafyllopoulou<sup>1</sup>, Leonidas S. Tsavureikis<sup>1</sup> and Alkiviadis C. Vatopoulos<sup>1</sup><sup>,##</sup>

Table 1. Regional distribution of 378 KPC-2-producing K. pneumoniae isolates and their classification by molecular typing

<table>
<thead>
<tr>
<th>Geographical distribution (no. of hospitals)</th>
<th>PFGE types (STs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Athens (26)</td>
<td>216 12 2 9 6 4 — 3 2 1 3 1</td>
</tr>
<tr>
<td>Other mainland cities (6)</td>
<td>43 8 — 1 — — — — 1 2</td>
</tr>
<tr>
<td>Crete and other islands (8)</td>
<td>63 — — — — — 1 — — — 1 2</td>
</tr>
<tr>
<td>Total no. of hospitals (40)</td>
<td>322 20 2 1 9 6 4 1 3 2 1 4 3</td>
</tr>
</tbody>
</table>

ND, not determined.

Figure 1. Geographical map showing the locations of the participating hospitals as well as the number of isolates collected during the initial survey (numbers in italics) and the update described in this study (numbers in bold). Black rectangle, Athens–Piraeus; grey rectangles, mainland cities; white rectangles, islands.
### Table 1. Characteristics of 256 K. pneumoniæ isolates.

<table>
<thead>
<tr>
<th>β-Lactamase content</th>
<th>Total No (%)</th>
<th>PFGE types (No of strains typed)</th>
<th>No of strains isolated in each hospital</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>I (Athens) II (Athens) III (Athens) IV (Athens) V (Athens) VI (Thess.) VII (Thess.) VIII (Crete)</td>
</tr>
<tr>
<td>CMY-4</td>
<td>3 (1.2)</td>
<td>E (1)</td>
<td>2</td>
</tr>
<tr>
<td>CMY-4 + SHV-12</td>
<td>1 (0.4)</td>
<td>A (1)</td>
<td>1</td>
</tr>
<tr>
<td>CMY-4 + CTX-M-15</td>
<td>4 (1.2)</td>
<td>E (2)</td>
<td>1</td>
</tr>
<tr>
<td>CMY-4 + CTX-M-15 + VEB-1</td>
<td>1 (0.4)</td>
<td>E (1)</td>
<td>1</td>
</tr>
<tr>
<td>VEB-1</td>
<td>1 (0.4)</td>
<td>Nd*</td>
<td>1</td>
</tr>
<tr>
<td>CTX-M-15</td>
<td>5 (2.0)</td>
<td>U (1)</td>
<td>1</td>
</tr>
<tr>
<td>SHV-12</td>
<td>11 (4.3)</td>
<td>A (2), E (1)</td>
<td>2</td>
</tr>
<tr>
<td>KFC-2</td>
<td>13 (5.1)</td>
<td>U (3), E (1)</td>
<td>3</td>
</tr>
<tr>
<td>KPC-2 + VEB-1</td>
<td>1 (0.4)</td>
<td>U (1)</td>
<td>1</td>
</tr>
<tr>
<td>KPC-2 + CMY-4</td>
<td>2 (0.8)</td>
<td>E (1)</td>
<td>2</td>
</tr>
<tr>
<td>KPC-2 + CMY-4 + SHV-12</td>
<td>1 (0.4)</td>
<td>A (1)</td>
<td>1</td>
</tr>
<tr>
<td>KPC-2 + CMY-4 + CTX-M-15</td>
<td>1 (0.4)</td>
<td>E (1)</td>
<td>1</td>
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<tr>
<td>KPC-2 + SHV-12</td>
<td>85 (33.2)</td>
<td>A (7), B (1)</td>
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<tr>
<td>KPC-2 + VIM-19 + CMY-4</td>
<td>1 (0.4)</td>
<td>E (1)</td>
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</tr>
<tr>
<td>KPC-2 + VIM-1 + SHV-12</td>
<td>2 (0.8)</td>
<td>U (1)</td>
<td>2</td>
</tr>
<tr>
<td>KPC-2 + VIM-1</td>
<td>4 (1.6)</td>
<td>B (2)</td>
<td>4</td>
</tr>
<tr>
<td>VIM-1</td>
<td>12 (4.7)</td>
<td>B (1)</td>
<td>9</td>
</tr>
<tr>
<td>VIM-27</td>
<td>1 (0.4)</td>
<td>B (1)</td>
<td>1</td>
</tr>
<tr>
<td>VIM-1 + SHV-12</td>
<td>3 (1.2)</td>
<td>B (1)</td>
<td>1</td>
</tr>
<tr>
<td>VIM-27 + SHV-5</td>
<td>1 (0.4)</td>
<td>B (1)</td>
<td>1</td>
</tr>
<tr>
<td>VIM-19 + CMY-4</td>
<td>2 (0.8)</td>
<td>E (1)</td>
<td>1</td>
</tr>
<tr>
<td>VIM-19 + CMY-4 + CTX-M-15</td>
<td>3 (1.2)</td>
<td>E (1)</td>
<td>1</td>
</tr>
<tr>
<td>no tested (susceptible isolates)</td>
<td>96 (38.3)</td>
<td>–</td>
<td>8</td>
</tr>
<tr>
<td>Totals (No of strains)</td>
<td>256</td>
<td>59</td>
<td>41</td>
</tr>
</tbody>
</table>

Diversity of acquired β-lactamases amongst *Klebsiella pneumoniæ* in Greek hospitals

*International Journal of Antimicrobial Agents*

23 Nov 2011
### Table 1. Characteristics of 256 *K. pneumoniae* isolates.

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Diversity of acquired β-lactamases amongst *Klebsiella pneumoniae* in Greek hospitals

*International Journal of Antimicrobial Agents*

23 Nov 2011
B. Response

“Procrustes”
Principles of the Action Plan

• the estimation and follow-up of the incidence and temporal trends of MDR-GNB infections in hospitalized patients.

• the implementation of enhanced infection control measures in order to contain the spread of MDR-GNB within acute-care hospitals.
Principles of the Action Plan

- Establishment and operation at the Hellenic Center for Disease Control and Prevention (HCDCP), of a national surveillance system for MDR-GNB infections in hospitals in Greece.

- Systemic monitoring of the implementation of the appropriate infection control measures.

- Issue relevant legislations by the General Directorate – MoH ns.
Incidence VS resistance rates

- Describes burden of disease
- Is a more sensitive indicator of the results of the intervention
TARGET

• All cases of specific clinical infections caused by carbapenem-resistant *K. pneumoniae*, *Pseudomonas aeruginosa*, and *Acinetobacter baumanii* are **obligatory notifiable** to HCDCP, starting on November 1, 2010

23 Nov 2011
METHODS

– Weekly notification to the HCDCP of all newly-detected cases of carbapenem-resistant *K. pneumoniae*, *P. aeruginosa*, and *A. baumanii* clinical infections.

– Immediate notification to the HCDCP, in case of onset of a MDR-GNB outbreak.

– Systemic communication to the hospital CEO regarding the burden and trends of MDR-GNB infections, the implementation of infection control measures, and possible deficits and problems that emerged during the daily implementation of the Action Plan within the hospital.

– Organization of educative activities in order to increase compliance of HCWs with infection control measures.

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METHODS

Responsibility at the hospital level

• Hospital Task Force
  – Hospital CEO
  – Medical Director of the Committee for Nosocomial Infections
  – Director of the microbiology laboratory
  – Infection control nurse

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Hospital Task Force

• **Daily review of microbiology laboratory records** in order to promptly identify all cases of MDR-GNB clinical infection or colonization.

• **Daily communication with the physicians caring for known cases of MDR-GNB infections** in order to follow:
  – the patients outcome
  – the strict and systemic implementation of infection control measures in order to contain the spread of MDR-GNB within the health-care facility
  – the compliance of health-care personnel with hand hygiene
  – the coordination of active surveillance cultures for colonization

23 Nov 2011
Hospital Task Force

- Weekly notification to the HCDCP of all newly-detected cases of carbapenem-resistant *K. pneumoniae, P. aeruginosa,* and *A. baumanii* clinical infections.

- Immediate notification to the HCDCP, in case of onset of a MDR-GNB outbreak.

- Systemic communication to the hospital CEO regarding the burden and trends of MDR-GNB infections, the implementation of infection control measures, and possible deficits and problems that emerged during the daily implementation of the Action Plan within the hospital.

- Organization of educative activities in order to increase compliance of HCWs with infection control measures.
The role of the HCDCP

• **Surveillance**
  - Statistical analysis, interpretation, and follow-up of the burden and trends of infections due to MDR-GNB in acute-care hospitals in Greece.
  - The incidence of MDR *K. pneumoniae*, *P. aeruginosa*, and *A. baumanii* clinical infections will be estimated per 1000 hospital days, based on data provided by hospitals.
  - Monthly feedback to hospitals about the burden and trends of infections due to MDR-GNB

• **Interventions**
  - Communication with the Task Force of the hospital and the Director of the department
  - When necessary, a HCDCP-based team intervenes in order to contain a nosocomial outbreak.
  - Monthly communication to the General Directorate/ MoH of surveillance results and implemented measures.
  - Issue and dissemination to all acute-care hospitals of guidelines about the management of patients with MDR-GNB infections,
  - Organization of campaigns for the promotion of hand hygiene within health-care facilities and follow-up of HCW compliance.
  - Organization of routine visits at hospitals
  - Organization of training activities for the hospital Task Force teams.
  - Communication to the general public about MDR nosocomial infections.

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• Search and destroy strategy at the hospital level

• Close inspection of the hospitals

- Commitment at central level
- Commitment at peripheral level
- Commitment at hospital level
Figure 2. Algorithm of procedures following the detection of a carbapenem-resistant pathogen

1. Active surveillance cultures (colonization) from patients at risk for colonization with carbapenem-resistant pathogens (patients admitted in intensive care units, patients with a history of colonization/infection, hospitalization in an ICU, or carbapenem administration the last 6 months, hospitalization in the same room with a MDR-GNB carrier, or admission in a health-care facility in India or Pakistan the last 6 months (for NDM carriage).

2. Implementation of infection control measures as for infected patients, until culture results are available.

1. Stringent infection control measures
   - contact precautions, personal protective equipment, hand hygiene
   - isolation or cohorting of infected patients
   - care by dedicated personnel, if feasible
2. Active surveillance of patients hospitalized in the same ward (see right column)
3. Notification to the HCDCP of infected cases
4. Restrict patient transportation and visitors
5. Disinfection of inanimate objects
6. Environmental microbiologic investigation: in case of a cluster of cases

Daily review of cultures at the microbiology laboratory

Identification of a carbapenem-resistant pathogen
   Immediate notification: 1. Task Force, 2. Infection Control Committee, and 3. Department of the infected patient

No identification of a carbapenem-resistant pathogen
   Continue daily review of cultures
Παραδείγματα φαινοτυπικού ελέγχου στο εργαστήριο για παραγωγή MBL (C), KPC (B) ή MBL/KPC (A)

Tsakris et al. 2010
Of 128 acute-care hospitals

- 99 hospitals participated in the surveillance system notifying a total of 2,060 cases
- 16 hospitals did not send reports at all
- 13 hospitals were included in the surveillance system at a later stage

1,926 validated cases from 64 hospitals
2,044 Isolates in 1,926 Notified Cases

- Acinetobacter: 734 (35.9%)
- Pseudomonas: 428 (20.9%)
- Klebsiella: 882 (43.2%)

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Outcome of Notified Cases by Department*

ICU
- Exit: 21.6%
- Still in hospital: 34.9%
- Death: 43.6%

Internal medicine
- Exit: 15.9%
- Still in hospital: 30.2%
- Death: 53.9%

Surgical
- Exit: 31.9%
- Still in hospital: 19.5%
- Death: 48.7%

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H Maltezou
HCDCP
Mechanisms of Resistance in *Klebsiella* Isolates

**KPC**
- 471 (84.4%)

**VIM**
- 53 (9.5%)

**VIM + KPC**
- 34 (6.1%)
Mean incidence of infections due to MDR-GNB pathogens in patients hospitalized in hospitals by number of beds

<table>
<thead>
<tr>
<th>Number of Beds</th>
<th>Mean Incidence /1000 Hospital Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 200 beds</td>
<td>0.356</td>
</tr>
<tr>
<td>201 – 500 beds</td>
<td>0.491</td>
</tr>
<tr>
<td>&gt; 500 beds</td>
<td>0.506**  p-value=0.03</td>
</tr>
</tbody>
</table>

Mean incidence /1000 hospital days

23 Nov 2011
Stepwise regression analysis to identify hospital characteristics associated with an increased prevalence of MDR-GNB infections

<table>
<thead>
<tr>
<th></th>
<th>Mean incidence /1000 hospital days</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICU in the hospital</td>
<td>0.73</td>
</tr>
<tr>
<td>no ICU in the hospital</td>
<td>0.21</td>
</tr>
</tbody>
</table>

p-value < 0.001
Response

The very early very good news!

23 Nov 2011
Incidence of CPKP BSIs in Hematology Clinic

No. of Cases / 1000 pt-days

Dec-Feb 2009
Mar-May 2010
Jun-Aug

0
0.3
0.6
0.9
1.2
1.5

Intervention

Daikos G
Unpublished

23 Nov 2011
Response

• A public health problem to be confronted must be recognized.
  – By those involved
  – By the society in large
  – By all leaderships

• Commitment

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With out commitment "Procrustes" will be..
Without commitment will be “sisyphus”
miracles do happen
Antibiotic resistance in Greece

• Commitment should be the driving force

• Time (persistence and patience) is needed