Implementation of Public Health Surveillance of Carbapenemase-Producing Enterobacteriaceae in Victoria, Australia

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Communicable Disease Control Conference
27th June 2017

Background

• Carbapenemase producing enterobacteriaceae (CPE)
• Carbapenemases, enzymes that confer resistance to carbapenems
• Increased morbidity and mortality
• Outbreak potential

### Common Carbapenemases

<table>
<thead>
<tr>
<th>Class</th>
<th>Name</th>
<th>Abbreviation</th>
<th>Major sub-types</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td><em>Klebsiella pneumoniae</em> carbapenemase</td>
<td>KPC</td>
<td>KPC-2, KPC-3</td>
</tr>
<tr>
<td></td>
<td>New-delhi metallo-beta-lactamase</td>
<td>NDM</td>
<td>NDM-1, NDM-5, NDM-7</td>
</tr>
<tr>
<td>B</td>
<td>Imipenemase metallo-beta-lactamase</td>
<td>IMP</td>
<td>IMP-4</td>
</tr>
<tr>
<td></td>
<td>Verona imipenemase metallo-beta-lactamase</td>
<td>VIM</td>
<td>VIM-1, VIM-2</td>
</tr>
<tr>
<td></td>
<td>OXA-23-like carbapenemases</td>
<td>OXA-23-like</td>
<td>OXA-23</td>
</tr>
</tbody>
</table>

### Victorian KPC-2 Outbreak

Combined genomic and epidemiological investigation of a state-wide outbreak of KPC-producing Enterobacteriaceae

Session 4D: Element Room, 1:30pm, tomorrow.
Public Health Surveillance of CPE

- Identify transmission
- Implement standardised control measures
  - Oversight by a centralised incident management team (VCIMT)
- Communicate CPE risk to other facilities
- Inform response & empiric treatment (antibiograms)
Victorian CPE Surveillance and Response Unit

Suspected CPE isolate identified

- Isolate referred to MDU PHL
- DHHS and VICNISS notified

Confirmatory testing performed

- CPE Confirmed
- Not CPE (rejected)

Infection control actions initiated

Epidemiological data collected

- Genomic relatedness to other isolates assessed

Epidemiological and genomic data evaluated for local transmission

Local transmission suspected?

- Yes
  - Outbreak investigation
    - Transmission risk area may be designated by Vic CPE Incident management team

- No
  - No further action

Monitor trends

- If changes observed
  - Yes
    - Outbreak investigation
      - Transmission risk area may be designated by Vic CPE Incident management team
  - No

Victorian CPE Surveillance and Response Unit

- Suspected CPE isolate identified
- Epidemiological data collected
- Genomic relatedness to other isolates assessed
- Implementation of the Victorian Guideline on CPE

Gene(s) detected

- IMP
- KPC
- NDM
- NDM, OXA-48-like
- OXA-48-like
- Other OXA^*
- VIM
- SME

Implementation of the Victorian Guideline on CPE

Patients with CPE identified at MDU PHL, by month and carbapenemase gene type, 01 January 2012 – 31 December 2016
2016 Victorian CPE Cases

**Location at Specimen Collection**

<table>
<thead>
<tr>
<th>Location at Specimen Collection</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital – Admitted</td>
<td>67</td>
<td>(70%)</td>
</tr>
<tr>
<td>Hospital – Emergency/Outpatients</td>
<td>18</td>
<td>(19%)</td>
</tr>
<tr>
<td>Medical clinic (inc. GP)</td>
<td>10</td>
<td>(10%)</td>
</tr>
<tr>
<td>Aged care facility</td>
<td>1</td>
<td>(1%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>96</td>
<td></td>
</tr>
</tbody>
</table>

**Clinical Presentation**

<table>
<thead>
<tr>
<th>Clinical Presentation</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colonisation</td>
<td>57</td>
<td>(59%)</td>
</tr>
<tr>
<td>Infection</td>
<td>33</td>
<td>(34%)</td>
</tr>
<tr>
<td>Urinary tract</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>Bacteraemia</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>2</td>
<td>(6%)</td>
</tr>
</tbody>
</table>

**Risk Factors Differ by Carbapenemase**

**NDM**
- Majority (91%) overseas travellers, most hospitalised
- Some putative community acquisition in India

**Carbapenemase Genes**

NB: Genes included will exceed total number of isolates, due to 3 isolates with multiple gene types detected.

**Carbapenemase Gene Group**

- South and Central Asia
- South East Asia
- Middle East
- China
- Greece
- Other
- No
- Unknown
Risk Factors Differ by Carbapenemase

<table>
<thead>
<tr>
<th>Carbapenemase Gene Group</th>
<th>Number of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>South and Central Asia</td>
<td>30</td>
</tr>
<tr>
<td>South East Asia</td>
<td>25</td>
</tr>
<tr>
<td>Middle East</td>
<td>20</td>
</tr>
<tr>
<td>China</td>
<td>15</td>
</tr>
<tr>
<td>Greece</td>
<td>10</td>
</tr>
<tr>
<td>Other</td>
<td>5</td>
</tr>
<tr>
<td>No</td>
<td>2</td>
</tr>
<tr>
<td>Unknown</td>
<td>1</td>
</tr>
</tbody>
</table>

**NDM**
- Majority (91%) overseas travellers, most hospitalised
- Some putative community acquisition in India

**OXA-48-like**
- Found in travellers (76%) and non-travellers (24%), suggesting some unrecognised local transmission

**KPC**
- Small number of cases with overseas hospitalisation (Greece)
- Most within well defined local *K. pneumoniae* outbreaks
### Risk Factors Differ by Carbapenemase

<table>
<thead>
<tr>
<th>Carbapenemase</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NDM</strong></td>
<td>Majority (91%) overseas travellers, most hospitalised Some putative community acquisition in India</td>
</tr>
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<td><strong>OXA-48-like</strong></td>
<td>Found in travellers (76%) and non-travellers (24%), suggesting some unrecognised local transmission</td>
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<tr>
<td><strong>KPC</strong></td>
<td>Small number of cases with overseas hospitalisation (Greece) Most within well defined local <em>K. pneumoniae</em> outbreaks</td>
</tr>
<tr>
<td><strong>IMP</strong></td>
<td>Rarely associated with travel Widely distributed across species Local transmission observed in multiple species</td>
</tr>
</tbody>
</table>

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### Local Transmission of CPE

<table>
<thead>
<tr>
<th>Gene</th>
<th>Species</th>
<th>2016 cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>KPC-2</td>
<td><em>K. pneumoniae</em></td>
<td>6</td>
</tr>
<tr>
<td>KPC-2</td>
<td><em>C. farmeri</em></td>
<td>2</td>
</tr>
<tr>
<td>IMP-4</td>
<td><em>K. pneumoniae</em></td>
<td>3</td>
</tr>
<tr>
<td>IMP-4</td>
<td><em>K. oxytoca</em></td>
<td>2</td>
</tr>
<tr>
<td>IMP-4</td>
<td><em>C. freundii</em></td>
<td>4</td>
</tr>
</tbody>
</table>

??Unidentified transmission networks
Why?

• Long colonisation periods
  • Cases temporally/geographically dispersed at CPE identification

• Same carbapenemase gene, bacterial species +/- multi locus sequence type

• Epidemiological and genomic investigation

Person, place and time \downarrow Consistent with transmission

Hypothesis for time and place of transmission (direct or indirect)

Centralised combined epidemiological and genomic investigation needed:
- Long time frames
- Frequent and complex patient movements
- Transmission at multiple facilities
- Multiple possible exposures.


2017 so far

*Includes carbapenem degrading only, such as OXA-23-like, OXA-24/40-like and OXA-51-like genes
Conclusions

• Local acquisition mainly limited to IMP-4 and KPC-2
• Considerable importation of CPE
• Centralised combined epi and genomic surveillance critical to:
  • Identifying local transmission networks
  • Implementing targeted control measures
Acknowledgements

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Susan Ballard

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Marion Easton
Annaleise van Diemen
Suzana Talevska
VCIMT members

VICNISS
Judy Brett
Ann Bull

IMP-4 Complexity
Local transmission networks

<table>
<thead>
<tr>
<th>Gene</th>
<th>Species</th>
<th>2016 cases</th>
<th>Facilities of suspected transmission</th>
<th>All cases identified at facility where transmission is suspected</th>
</tr>
</thead>
<tbody>
<tr>
<td>KPC-2</td>
<td><em>K. pneumoniae</em></td>
<td>6</td>
<td>3</td>
<td>x</td>
</tr>
<tr>
<td>KPC-2</td>
<td><em>C. farmeri</em></td>
<td>2</td>
<td>1</td>
<td>x</td>
</tr>
<tr>
<td>IMP-4</td>
<td><em>K. pneumoniae</em></td>
<td>3</td>
<td>1</td>
<td>x</td>
</tr>
<tr>
<td>IMP-4</td>
<td><em>K. pneumoniae</em></td>
<td>2</td>
<td>1</td>
<td>v</td>
</tr>
<tr>
<td>IMP-4</td>
<td><em>K. oxytoca</em></td>
<td>4</td>
<td>1</td>
<td>v</td>
</tr>
</tbody>
</table>

Patient Demographics

<table>
<thead>
<tr>
<th>Sex, n (%)</th>
<th>All</th>
<th>Carbenemase gene detected</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>213/382 (56%)</td>
<td>43/96 (45%)</td>
<td>170/286 (59%)</td>
<td></td>
</tr>
<tr>
<td>Age, median (range)</td>
<td>72 (0 – 99)</td>
<td>66 (3 – 90)</td>
<td>74 (0 – 99)^</td>
<td></td>
</tr>
</tbody>
</table>

^Age unknown for two rejected cases
Travel

### Overseas travel

<table>
<thead>
<tr>
<th>Yes</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>49</td>
<td>(51%)</td>
</tr>
<tr>
<td>No</td>
<td>45</td>
<td>(47%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>2</td>
<td>(2%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>96</strong></td>
<td></td>
</tr>
</tbody>
</table>

**Country of travel**

- **South & Central Asia** (India, Sri Lanka, Bangladesh, Pakistan, Afghanistan) - 24
- **South East Asia** (Vietnam, Cambodia, Thailand, Philippines, Malaysia) - 11
- **Greece** - 4
- **Middle East** (Turkey, Lebanon) - 4
- **China** - 2
- **Other** - 4

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Parallel Outbreak investigations

Genomics --- Epidemiology

- Consistent with transmission
- Commonality in person, place and time.
- Hypothesis for time and place of transmission (direct or indirect - enviro, staff, colonisation)
- Transmission risk area
<table>
<thead>
<tr>
<th>Travel group</th>
<th>Gene</th>
<th>Organism</th>
<th>Travel location(s)</th>
<th>(12 months prior to identification)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overseas</td>
<td>KPC-2</td>
<td>K. pneumoniae</td>
<td>India and south Asia</td>
<td>Greece</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Europe</td>
<td>OXA-181</td>
<td>E. coli</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asia</td>
<td>NDM-5</td>
<td>E. coli</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Includes carbapenem degarding only, such as OXA-23-like, OXA-24/48-like and OXA-51-like genes

*October 2012, MDU PHL conducted a one month snapshot of CRE in Victoria.
Current and Future Research

- Understanding local IMP-4 diversity and transmission networks
- Prevalence and role of environmental contamination
- Duration and role of long term colonisation
- Screening sensitivity, antibiotic exposure
Carbapenemase status, by species

High % carbapenemase producers
Low % carbapenemase producers