Carbapenemase Producing Enterobacteriaceae: Screening

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Aims

• Is CPE a problem?

• Does screening have the potential to help?

• What did we do? What do we do now?

• What approaches are there to screening?
Is CPE a problem?

- What do they cause?
- What is the epidemiology?
What are CPE?

Enzyme = -ase

- **KPC** Klebsiella pneumoniae carbapenemase
- **OXA** oxacillin-hydrolyzing

**Metallobetalactamase**
- **VIM** Verona integron-encoded metallo beta-lactamase
- **NDM** – New Delhi Metallobetalactamase
- **IMP** – active on Imipenem

- Successful Clones
  - KPC Klebsiella pneumoniae ST 258
What does it cause?

• Same infections as always

but...
Mortality rates associated with different antimicrobial drug regimen categories in patients with different presenting features

Mario Tumbarello et al. J. Antimicrob. Chemother. 2015;70:2133-2143
Characteristics and clinical outcomes of cases of prosthetic joint infection caused by carabapenem-resistant *Klebsiella pneumoniae*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Case 1</th>
<th>Case 2</th>
<th>Case 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), sex</td>
<td>58, male</td>
<td>72, male</td>
<td>70, female</td>
</tr>
<tr>
<td>Comorbidities</td>
<td>Osteoarthritis, diabetes</td>
<td>Osteoarthritis, coronary artery disease, congestive heart failure</td>
<td>RA on immunosuppression with methotrexate and hydroxychloroquine</td>
</tr>
<tr>
<td>Onset of first PJI (months from index surgery)</td>
<td>60</td>
<td>36</td>
<td>1</td>
</tr>
<tr>
<td>Primary organism PJI</td>
<td>MSSA</td>
<td>VSE, VRE, <em>Proteus mirabilis</em></td>
<td><em>Corynebacterium sp</em> and VSE</td>
</tr>
<tr>
<td>Onset of CRKP PJI (months from first PJI)</td>
<td>2</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Number of procedures (n)</td>
<td>10</td>
<td>12</td>
<td>57</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>Oxacillin; piperacillin–tazobactam; daptomycin and oral doxycycline; tigecycline and fluconazole; colistin, amikacin, and tigecycline</td>
<td>Ciprofloxacin, linezolid, and rifampin; daptomycin and ciprofloxacin; vancomycin and tigecycline → doxycycline; oxacillin, oxacillin and tigecycline → doxycycline</td>
<td>Vancomycin; tigecycline; colistin; tigecycline; tigecycline; tigecycline and vancomycin → oral ciprofloxacin and clindamycin; tigecycline; colistin; tigecycline, and amikacin; ciprofloxacin</td>
</tr>
<tr>
<td>WBC × 10⁹/l (median (IQR))</td>
<td>9.07 (0.63, 12.49)</td>
<td>8.45 (7.73, 9.75)</td>
<td>8.92 (7.40, 11.68)</td>
</tr>
<tr>
<td>Hospital LOS (days)</td>
<td>51</td>
<td>101</td>
<td>225</td>
</tr>
<tr>
<td>Hospitalization costs ($)</td>
<td>N/A</td>
<td>N/A</td>
<td>850 000</td>
</tr>
<tr>
<td>Functional status</td>
<td>Above-the-knee amputation</td>
<td>Full</td>
<td>Disarticulated</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Died</td>
<td>Died</td>
<td>Alive with major disability</td>
</tr>
</tbody>
</table>
Case 1

Despite:
- left above-the-knee amputation
- maximum medical support
- Combined IV colistin, amikacin, and tigecycline,
- patient died on postoperative day 3

Case 3

‘… required five subsequent wound debridements

Culture of tissue …. grew CRKP, ….resistant to amikacin and colistin’

Consider extra measures for high risk areas

Spreading and Worsening?

Comparison of Hospital A and B Carbapenemase Rates

What Is The Epidemiology?
Rapid evolution and spread of carbapenemases among Enterobacteriaceae in Europe
Canton Clin Microbiol Infect 2012; 18: 413–431

FIG. 3. Evolution of the carbapenemase-producing Enterobacteriaceae (CPE) isolates in Belgium (92 isolates referred to the National Reference Centre, Belgium, January 2007–December 2011) (data have been updated from reference 150).
B Geographic distribution of CPE by resistance mechanism using the same epidemiological scale

**VIM**
- Non-visible countries
- Luxembourg
- Malta
- Cyprus

**KPC**
- Non-visible countries
- Luxembourg
- Malta
- Cyprus

**OXA-48**
- Non-visible countries
- Luxembourg
- Malta
- Cyprus

**NDM**
- Non-visible countries
- Luxembourg
- Malta
- Cyprus

A. Klebsiella pneumoniae carbapenemase (KPC)

B. Oxacillinase-48 (OXA-48)

C. New Delhi metallo-beta-lactamase (NDM)

D. Verona integron-encoded metallo-beta-lactamase (VIM)

Epidemiological stages, 2011-2015
Who to screen? All hospital transfers: UK and Abroad

FIG. 4. Numbers of UK laboratories referring at least one carbapenemase-producing Enterobacteriaceae (CPE) isolate to the Antibiotic
• National C.diff figures
Getting ahead of the curve??

CID 2011;52:848–855

Israel
Israel approach

Each hospital provides a daily census of:

• CRE carriers, including sample site
  – ADMISSION SCREENS
• Location of likely acquisition

Confirm
(1) labelled for contact isolation
(2) gowns/gloves required
(3) physical separation from non-carriers
(4) dedicated nursing staff

CID 2011;52:848–855
Our experience

• What did we do?

• What do we do now?

• What approaches are there to screening?
My Perspective: 700 yr old strategy

Effective separation = no transmission

Separate
• Isolate known positive cases
• ‘Quarantine’ suspect cases

Clean
• Hands/equipment/environment
Why screen?

1) Early isolation and IPC measures
   – Prevent further spread
   
   Can’t effectively separate if you don’t know who has it!

2) Early targeted treatment/prophylaxis
   – Reduce mortality/morbidity
First case May 2011

- Sputum with *Klebsiella pneumoniae*
  - Looks meropenem resistant

  - who to screen?
Who to screen?

- Bay contacts?
- All current ward contacts?
- Other?

Previous ward contacts?
Previous bay contacts?
Number of VIMS
May 2011 to Sept 2013

- 8/12 clinical
- 4/14 clinical
- 1 yr no HAQ cases
Then 6 months of no cases
Number of new cases of CPE (OXA-48)

Presumed Community acquired
Presumed Hospital acquired
But also

- Transfers/admissions carrying:
  - IMP
  - KPC
  - NDM

- With no subsequent transmission
  - Early identification through screening allowed implementation of IPC measures
Back to First Case: Results

- Index patient
  - Rectal screen negative x 2
  - Bay contacts negative
  - Ward contacts negative

- Interpretation??
Should I stop/start screening?

Patient is in side room
4 weeks of full ward screening is complete
No new positives
STOP screening?

Patient isolated on admission,
START screen contacts?
Should I stop screening as soon as last patient discharged?

What we did:
• 4 wks of ward screening AFTER last carrier discharged
• C.F. French guidelines
2013 *Acute trust toolkit* (PHE)

Advises

- 4 weeks of contact screening after identifying a case

- screening of patients in the same setting is NOT normally required if the case was identified on admission and isolated immediately

Our approach identified 13 (25%) additional cases compared with the PHE toolkit
Should discharged contacts be screened?

- Yes
- No
- Ridiculous!
Netherlands

Patients in the high-risk group were
• screened on readmission when hospitalised
• if not hospitalised through post-discharge screening
• received information and material for sampling to returned by mail (POO in the POST…!)

Successful control of a hospital-wide outbreak of OXA-48 producing Enterobacteriaceae in the Netherlands, 2009 to 2011
Eurosurveillance, Volume 19, Issue 9, 06 March 2014
Does anyone have it right?
Isolation in a single room and contact precautions
Increase numbers of healthcare workers
Dedicated staff or specific organization of care

No transfer of patients in another ward or hospital (eXDR carrier and contact patients)
Identification of contact patients present in the unit and those already transferred
Isolation of contact patients who were already transferred
Weekly screening of contact patients, repeated at least three times

If the first rectal screening of contact patients is negative (no secondary cases)

If the eXDR patient was hospitalized in a single room at the admission with contact precautions but without dedicated team
- Perform a weekly rectal screening of all contact patients as long as the eXDR carrier is present in the ward
- Perform at least one rectal screening of contact patients after the carrier discharge
- If a negative contact patient is transferred in another ward: isolate the patient in a single room and prescribe at least one rectal screening

One or more eXDR secondary cases (see Figure 4: outbreak control)

If the eXDR patient was hospitalized in a single room at the admission with contact precautions and with a dedicated team

It is not necessary to continue systematic rectal screening of contact patients

Figure 3. Recommendations to control the spread of emerging extensively resistant (eXDR) bacteria when detected from a clinical sample during hospitalization.
Low risk

*Isolated at admission*

- Weekly rectal screening on all contacts with the carrier
- Screening all contacts before transfer to another ward or hospital
- Screening repeated at least once after they have been transferred
- At least one post-exposure rectal screen on all contacts who are still hospitalized after carrier discharged
- Screen readmitted contacts
Intermediate risk

*Detected after admission with no isolation*

- Line list
- Rectal screening on hospitalized contacts
- Letter to inform discharged patients and the need to declare that they have been in contact with a carrier
- No transfers of contacts (except emergency)
  - If happens, a single room and three-weekly rectal screening
- If 3 weeks screening of all contacts negative, the risk of cross-transmission becomes low
High risk of transmission
Several secondary cases have been identified (outbreak)

Recommendations:
• 3 rectal screens of all contact patients
• Do not transfer contact patients
• Vigilance for conversion in contacts exposed to antibiotic treatment
• Dedicate nurse and medical staff in three different cohorts
  – to separate clean/exposed/carrier
rapidly isolating index patients with barrier precautions was not always sufficient to avoid secondary cases and these occurred in six of 55 events

- Dedicated nursing staff is probably one of the most relevant measure to avoid cross transmission
Sensitivity of one swab?

2004 Lowbury Lecture: the Western Australian experience with vancomycin-resistant enterococci from disaster to ongoing control Pearman. JHI(2006) 63, 14-26

<table>
<thead>
<tr>
<th>Number of rectal swabs</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7 or more</th>
</tr>
</thead>
<tbody>
<tr>
<td>VREF carriers detected for first time</td>
<td>96</td>
<td>31</td>
<td>17</td>
<td>15</td>
<td>4</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>Cumulative number of carriers detected</td>
<td>96</td>
<td>127</td>
<td>144</td>
<td>159</td>
<td>163</td>
<td>165</td>
<td>172</td>
</tr>
<tr>
<td>Cumulative percentage of carriers detected (sensitivity)</td>
<td>56</td>
<td>74</td>
<td>84</td>
<td>92</td>
<td>95</td>
<td>96</td>
<td>100</td>
</tr>
</tbody>
</table>

Results
25 patients were identified (14 VIM-4, 11 OXA-48). The mean conversion time was 26 days. Range of 4 to 85 days. Comparing VIM-4 with OXA-48, the mean was 23 days vs 31 days. 72% of cases were identified by 4 weeks, 88% by 6 weeks, 100% by 13 weeks.
Are “dirty” rectal swabs better than “clean” rectal swabs for the detection of Carbapenemase Producing Enterobacteriaceae and Vancomycin Resistant Enterococci?

Total Rectal screens for CPE & VRE (N=3311).

- **50% Clean**
- **50% Dirty**

Percentage of total CPE positive (N=28)
- 61%
- 39%

Percentage of total VRE positive (N=95)
- 63%
- 37%
Is all this screening really worth it?

2013 fiscal year
- 102000 universal MRSA vs 7100 targeted CPE

33 new cases found
- ~1% of unique patient screens

Compare with VRE
Ostrowsky et al. screening and isolation
\[ \rightarrow \text{prevalence 2.2\% in 1997} \rightarrow 0.5\% \text{ in 1999.} \]

HICPAC: Management of Multidrug-Resistant Organisms In Healthcare Settings, 2006
PCR vs conventional

• PCR
  – Increased sensitivity
  – Can be delivered Near/Point of Care
    • Direct from rectal swab
    • Immediate IPC decisions
  – Rapid confirmation of clinical isolates
Summary

ACTIVE SURVEILLANCE TESTING
- Screen: all transfers *PCR*
- Screen: high risk areas admission (*PCR*), weekly

EPIDEMIOLOGICALLY TRIGGERED TESTING
- Screen: weekly if carrier is inpatient
- Screen: even if rapidly isolated
- Track back to find all linked patients
- Screen: 4 weeks after last carrier discharged (*3 weeks if PCR*)
- Screen: minimum 6 weeks from exposure
- Screen: discharged high risk contacts in community
- Screen all readmitted contacts *PCR*
- Screen all hospital readmissions once once a threshold of cases reached
- Screen all admissions??
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