Multicenter Approach to Control Multidrug-Resistant Organisms

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Why Multicenter?

• Institutions in the same region share patients and organisms
• MDRO – can be transferred between institution
• Failure of one center may lead to reintroduction via patient transfer to centers that have succeeded in containment
• If interventions are not coordinated two adjacent hospitals may choose different target organisms and likely both will fail due to colonized patient transfer
Inter-hospital transfer

- Inter-hospital transfer of patients was recognized as an important mode by which resistant organism spread
  - Late 1970’s interstate spread of an single phage type MRSA strain traced to transfer of patient from affected hospital to another
• Analyzing the US outbreaks in the 70’s
  – When an index patient was traced - it was a patient transferred from an affected hospital or nursing home

• Large teaching hospital more often affected by transfer

• Smaller hospitals may be affected by transfer but establishment is less likely
Citywide Clonal Outbreak of Multiresistant Acinetobacter baumannii and Pseudomonas aeruginosa in Brooklyn, NY

The Preantibiotic Era Has Returned

David Landman, MD; John M. Quale, MD; David Mayorga, MD; Adedeyo Adedeji, MD; Kalyani Vangala, MD; Jayshree Ravishankar, MD; Carlos Flores, MD; Steven Brooks, PhD

Several imipenem R PA clones affecting multiple hospitals

Table 4. Automated Ribotyping Results for 136 Imipenem-Resistant Isolates of Pseudomonas aeruginosa

<table>
<thead>
<tr>
<th>Ribotype No.</th>
<th>No. (%) of Isolates</th>
<th>No. of Hospitals</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>26 (19)</td>
<td>12</td>
</tr>
<tr>
<td>2</td>
<td>20 (15)</td>
<td>10</td>
</tr>
<tr>
<td>3</td>
<td>17 (12)</td>
<td>5</td>
</tr>
<tr>
<td>4</td>
<td>6 (4)</td>
<td>4</td>
</tr>
<tr>
<td>5</td>
<td>5 (4)</td>
<td>3</td>
</tr>
<tr>
<td>6</td>
<td>5 (4)</td>
<td>3</td>
</tr>
<tr>
<td>7</td>
<td>4 (3)</td>
<td>2</td>
</tr>
<tr>
<td>8</td>
<td>4 (3)</td>
<td>3</td>
</tr>
<tr>
<td>9</td>
<td>3 (2)</td>
<td>3</td>
</tr>
<tr>
<td>10</td>
<td>3 (2)</td>
<td>2</td>
</tr>
<tr>
<td>11</td>
<td>2 (1)</td>
<td>2</td>
</tr>
<tr>
<td>12</td>
<td>2 (1)</td>
<td>1</td>
</tr>
<tr>
<td>13</td>
<td>2 (1)</td>
<td>1</td>
</tr>
<tr>
<td>14</td>
<td>2 (1)</td>
<td>1</td>
</tr>
<tr>
<td>15-47</td>
<td>38 (24)</td>
<td>1 Each</td>
</tr>
</tbody>
</table>

3 Acinetobacter clones affecting Multiple hospitals

Arch Intern Med 2002
Within 15 months 53 hospitals:
275 clonally related VEB producing
A. baumannii
Inter-hospital spread associated with patients transfer
Regional intervention:
Recommendation for surveillance
Contact precaution and ABX use
Reporting to health authorities
Information exchange between hospitals
Limiting patient transfer
Quantifying Interhospital Patient Sharing as a Mechanism for Infectious Disease Spread

- Orange County 2005 data (32 hospitals)
- 320,000 admissions
- 29% at least two admissions
  - median interval 53d
  - 75% more than 1 hospital
  - 94% indirect (not same day)
- 6 hospitals to readmitted pts to >50% of the hospitals
- 28 hospitals shared at least one patient

Huang S. ICHE 2010
Analyzing C. difficile patients transfer

- Within 12 weeks
- 25% readmitted
- 41% of readmissions to another hospital
- 30% direct (same day) transfer
Rapid spread various institutions

Network graph illustrate the central role of LTAC (red)

CID 2011
• Mid 90’s 63 cases of VRE reported to the CDC from Siouxland region (Iowa, S. Dakota, Nebraska)
  – 135,000 population
  – 4 acute care facilities
  – 28 LTCFs
<table>
<thead>
<tr>
<th>Intervention</th>
<th>Acute care</th>
<th>LTCF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screening on admission</td>
<td>High risk population</td>
<td>High risk population</td>
</tr>
<tr>
<td>Room assignment</td>
<td>Private or with other carriers</td>
<td>Private or with other carriers Allow exceptions</td>
</tr>
<tr>
<td>education</td>
<td>Flagging carriers</td>
<td>Flagging carriers</td>
</tr>
<tr>
<td>communication</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Persistent colonization and the spread of antibiotic resistance in nosocomial pathogens: Resistance is a regional problem

David L. Smith, Jonathan Dushoff, Eli N. Perencevich, Anthony D. Harris, and Simon A. Levin

Fig. 1. A diagram of the general model. Individuals move among subpopulations, such as hospitals, LTCFs, and the community. The subpopulation is assumed to be well mixed with respect to the transmission of ARB. The population is also classified by group, based on some epidemiologically important difference. The size of the population at each location, \( N_j \), and the proportion of each group, \( q_{g,j} \), are constants by assumption. The admission rate is equal to the discharge rate, \( \alpha_{g,j} \), \( \rho_{g,j} \). The portion of discharged individuals from subpopulation \( j \) that move to \( k \) is \( \omega_{g,j,k} \). The portion of admitted individuals to subpopulation \( k \) that are from \( \alpha_{g,k,i} \).

Fig. 5. LTCFs (dashed-dotted trace) may be the most important type of institution in health-care networks because LTCF patients are frequently hospitalized and receive a similar level and type of care as hospitalized patients. Single-stay reproductive numbers for the hospital and community are identical to those in Figs. 3a and 4. In this simulation, the single-stay reproductive numbers in the LTCF and hospital are identical, but the closed-population reproductive rate for the LTCF is much lower than the hospital because of the longer LOS. Compared with earlier simulations, prevalence increases faster and reaches a higher equilibrium in hospitals (solid trace) and the community (dashed trace).
Nationwide emergence of carbapenem-resistant Kpn - Israel

Incidence: 60-100 cases per 1,000 hospital beds/year
Total number of cases: ~1000 (per 7 million population) mortality 44%
Genetic relatedness to US outbreak strains

Navon-Venezia S. AAC 2009
Dendrogram of the CDC's KPC-producing *K. pneumoniae* PFGE database (n = 248)

Predominance of a single clone - ST258

Kitchel et al, AAC, 2009
One hospital’s experience – moving from single room contact to cohorting and dedicated staff

Incidence of KPC-producing *Klebsiella* spp.

Implementation of guidelines

Schechner, unpublished
Targeted screening for CRE upon admission
Tale of one outbreak

- 2.4 patient A admitted (recent previous hospital elsewhere) to Tel Aviv Medical Center (multi-patient room)
- 2.5 urine culture taken
- 2.6 suspected carbapenem resistance – but requires further testing
  - pt isolated in single patient room
- 2.7 technical problem with confirmation
  - test needs to be repeated
- 2.8, 2.9 – weekend
- 2.10 carbapenem resistance confirmed
  - patient cohorted in a dedicated ward
  - Screen culture taken from 10 patients – all negative
Figure: The movement of KPC Kp through 30 patients in 4 different wards

Index case

Note:
- Internal medicine X
- Internal medicine Y
- Internal medicine Z
- Internal medicine W
- Positive KPC Kp clinical culture
- Positive KPC Kp surveillance culture
- Negative surveillance culture
- Dedicated KPC Kp ward

Schechner V. ICAAC 2008
Consequences of not acting immediately

- Admission of an unidentified carrier of KPC Klebsiella and 5 days delay until cohorting led to a difficult to control outbreak, involving 30 patients (6 clinical infections) in 4 wards\(^1\)

- Transfer overseas of a known carrier, but failure to isolate immediately, resulted in 9 additional clinical cases

1 Schechner V. ICAAC/IDSA 2008, paper 3806
2 Morris M. ICAAC/IDSA 2008, paper 1015
Summary of intervention results to date:

CRE nosocomial acquisitions, clinical culture, general hospitals, Jan 2005-Oct 2010

- March 12, 2007: National guidelines issued
- May 1, 2007: Task Force begins intervention
- June 5, 2008: Screening guidelines issued
Israeli Nationwide Intervention

- Task force
- To provide regional coordination and supervision
- National guidelines
- Strict isolation with dedicated staff
- Rapid identification of carriers by flagging, information transfer, and surveillance of high risk population
- Continuous root-cause analysis
Laboratory algorithm – common language and definitions

Growth of CRE → MHT

CPE: isolate and cohort

Non-CP-producing CRE: isolate w/o cohorting

CPE (not KPC): isolate and cohort

OR

KPC PCR

CPE: isolate and cohort

Non-CP-producing CRE: isolate w/o cohorting

Once a CPE carrier, always a CPE carrier, until proven otherwise
Assuring adherence to guidelines

These 2 non-compliant hospitals responsible for 30% of acquisitions this month

Complete containment

Hospital A Hospital B

CRE Incidence per 1000 Beds, October 2007 (average prevalence >= 4 CRE carriers)

New antimicrobial deliveries per 1000 beds

0 5 10 15 20 25

October November

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### Interventions Undertaken to Curtail the Epidemic Spread of Carbapenem-Resistant *Klebsiella pneumoniae* (CRKP)

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Description</th>
<th>Date begun</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention 1</td>
<td>Single-room isolation and contact precautions</td>
<td>March 2006</td>
</tr>
<tr>
<td>Intervention 2</td>
<td>Cohorting of patients and nursing staff, screening of patients in the same room as newly identified carriers of CRKP (“snow ball” active surveillance), and local protocol for continued cohorting of returning patients</td>
<td>March 2007</td>
</tr>
<tr>
<td>Intervention 3</td>
<td>Weekly active surveillance in the intensive care unit</td>
<td>August 2008</td>
</tr>
<tr>
<td>Intervention 4</td>
<td>Active surveillance of patients on admission to the emergency department</td>
<td>March 2009</td>
</tr>
</tbody>
</table>

#### Incidence

<table>
<thead>
<tr>
<th>Intervention (period)</th>
<th>No. of cases per 1,000 hospital beds</th>
<th>Median</th>
<th>Slope</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention 1 (Mar 2006–Mar 2007)</td>
<td>8.4</td>
<td>6.45</td>
<td>1.9</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Intervention 2 (Apr 2007–Aug 2008)</td>
<td>13.4</td>
<td>11.6</td>
<td>-0.7</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Intervention 3 (Sep 2008–Mar 2009)</td>
<td>8.3</td>
<td>7.7</td>
<td>-0.8</td>
<td>.76</td>
</tr>
<tr>
<td>Intervention 4 (Apr 2009–Aug 2010)</td>
<td>4.3</td>
<td>3.8</td>
<td>-0.008</td>
<td>.27</td>
</tr>
</tbody>
</table>

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A: Graph showing the number of cases per 1,000 hospital beds by month and year.

B: Graph showing the number of cases per 1,000 hospital beds by quarter and year.
Borer A. ICHE 2011
Active surveillance of high risk population and high risk areas, combined with contact isolation led to dramatic decrease in clinical cases

>700 surveillance cultures/month

4% positivity on admission

**FIGURE 1.** Scatterplots showing the change in the number of clinical cases of infection with carbapenem-resistant *Klebsiella pneumoniae* per 10,000 patient-days, before and after the intervention, implemented in month 17. Solid lines represent the linear regression fits across all cases.
Interventions in 13 large LTCF (2913 beds)

<table>
<thead>
<tr>
<th>Strategies for prevention of CRKP</th>
<th>2008</th>
<th>2010</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection control score</td>
<td>6.7</td>
<td>10.9</td>
<td>0.02</td>
</tr>
<tr>
<td>cohorting patients</td>
<td>10</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>dedicated medical equipment</td>
<td>12</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>single-use gown</td>
<td>6</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>admissions screening</td>
<td>2</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>contact screening</td>
<td>5</td>
<td>10</td>
<td></td>
</tr>
</tbody>
</table>
Incidence of carbapenem resistant *K. pneumoniae* acquisitions

<table>
<thead>
<tr>
<th></th>
<th>Period I</th>
<th>Period II</th>
<th>Prevented fraction</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence of clinical acquisitions</td>
<td>5.2</td>
<td>2.4</td>
<td>53.7%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Incidence of screening acquisitions</td>
<td>6.5</td>
<td>7.4</td>
<td></td>
<td>0.12</td>
</tr>
<tr>
<td>% identified by screening cultures</td>
<td>36.2%</td>
<td>69.9%</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total incidence</td>
<td>11.8</td>
<td>9.9</td>
<td>16.1%</td>
<td>0.01</td>
</tr>
</tbody>
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Cross section prevalence studies

<table>
<thead>
<tr>
<th>Type of ward</th>
<th>2008 (n=1004)</th>
<th>2010 (n=1027)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skilled nursing care</td>
<td>25.9%</td>
<td>15.6%</td>
</tr>
<tr>
<td>chronic mechanical ventilation</td>
<td>11.9%</td>
<td>10.9%</td>
</tr>
<tr>
<td>sub acute</td>
<td>9.6%</td>
<td>7.7%</td>
</tr>
<tr>
<td>Rehabilitation</td>
<td>2.5%</td>
<td>1.1%</td>
</tr>
<tr>
<td>TOTAL</td>
<td>12.0%</td>
<td>8.3%</td>
</tr>
</tbody>
</table>
Multicenter regional approach

- Is important to control MDRO
- Require inclusion of all healthcare facilities
- LTCF may serve as important reservoir and amplify MDRO
- Control in LTCFs is particularly challenging