The Public Health Benefit of CRE Colonization Testing

Allison C Brown, PhD MPH
Team Lead, AR Capacities and Special Studies
Division of Healthcare Quality Promotion
CDC
Carbapenem Resistance

- **Serious threat to public health**
  - Infections are difficult/impossible to treat
  - Up to 50% mortality from carbapenem-resistant *Enterobacteriaceae* (CRE)

- **Patients can spread CRE as they move throughout the healthcare system**

- **Carbapenemase-producing CRE (CP-CRE) spread rapidly via plasmids**

- **“Big 5” carbapenemases in the United States**
  - KPC
  - NDM
  - OXA-48-like
  - VIM
  - IMP
Geographical distribution of KPC-CRE *

*As of January 6, 2017
Geographical distribution of NDM-CRE*

*As of January 6, 2017
Geographical distribution of OXA-48-CRE*

*As of January 6, 2017
Geographical distribution of VIM-CRE*

*As of January 6, 2017
Geographical distribution of IMP-CRE*

*As of January 6, 2017
State/Local CRE and CRPA testing

Network of participating clinical laboratories

CRE/CRPA isolates → PHD

State/Local testing

- Species identification
- Confirmatory AST
- Phenotypic screening for carbapenemase production
- Molecular detection of mechanism
**Tiered testing**

Network of participating clinical laboratories

- CRE/CRPA isolates

**State/Local testing**
- Species identification
- Confirmatory AST
- Phenotypic screening for carbapenemase production
- Molecular detection of mechanism

**Regional lab testing**
- Isolates with suspected novel resistance*

**CDC testing**
- Confirmatory testing for full directory
- Targeted surveillance for CR-Acinobacter and mcr genes in ESBLs
- Colonization screening

*Positive for carbapenemase production but PCR-negative
Reporting results

• Testing results reported back to submitting clinical laboratories within 2 working days of completion
  • Results support infection prevention measures

• Alert notifications sent to HAI program and CDC within 1 day
  • Pan-resistant*, non-KPC carbapenemase in Enterobacteriaceae, unknown/novel** mechanism, mcr-positive, or CP-Acinetobacter or –Pseudomonas
  • Alerts sent to CDC shared with epi and lab outbreak response groups; provide additional testing and epi support if needed

• Monthly summary of all CRE and CRPA testing results reported sent to HAI coordinator and CDC
  • All CRE testing results, including any non-target Enterobacteriaceae species tested

• Lab and epi coordination essential
  • Results may be impetus for outbreak investigation, facility assessment, colonization screening

*Resistant to all drugs tested by clinical and public health labs; **Positive for carbapenemase production but PCR-negative
State testing through April

- 24 states ≥1 monthly report
- 861 CRE tested
  - 289 carbapenemase producers
  - 3 mcr-1 positive isolates
- 168 CRPA tested
  - 1 carbapenemase producer

![Diagram showing CRE and CRPA testing results](image)
CP-CRE organisms reported through April

- Klebsiella: 62%
- Enterobacter: 18%
- E coli: 10%
- Citrobacter: 2%
- Serratia: 1%
- Providencia: 1%
- Proteus: 0%
- Unknown: 6%
Carbapenemase genes detected through April

<table>
<thead>
<tr>
<th>Carbapenemase Gene</th>
<th>Number of Isolates</th>
</tr>
</thead>
<tbody>
<tr>
<td>KPC</td>
<td>238</td>
</tr>
<tr>
<td>NDM</td>
<td>29</td>
</tr>
<tr>
<td>OXA</td>
<td>16</td>
</tr>
<tr>
<td>VIM</td>
<td>3</td>
</tr>
<tr>
<td>IMP</td>
<td>3</td>
</tr>
<tr>
<td>IMP</td>
<td>1</td>
</tr>
<tr>
<td>CRPA</td>
<td></td>
</tr>
</tbody>
</table>
Emerging epidemiologic trends

Non-KPC carbapenemases reported in *Enterobacteriaceae* other than *Klebsiella*, *Enterobacter*, and *E. coli*

---

<table>
<thead>
<tr>
<th>Year of Specimen Collection</th>
<th>Number of Isolates</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011</td>
<td>1</td>
</tr>
<tr>
<td>2013</td>
<td>1</td>
</tr>
<tr>
<td>2014</td>
<td>2</td>
</tr>
<tr>
<td>2015</td>
<td>6</td>
</tr>
<tr>
<td>2016</td>
<td>4</td>
</tr>
<tr>
<td>2017</td>
<td>5</td>
</tr>
</tbody>
</table>

**Organism**

- *Proteus mirabilis*: 5
- *Providencia rettgeri*: 5
- *Morganella morganii*: 4
- *Citrobacter freundii*: 3
- *Serratia marcescens*: 3
- *Providencia stuartii*: 1

**Total**: 21

*Graph includes data on specimens collected through Q1 of 2017*

*Graph excludes 2 non-KPC CP-CRE with unknown year of collection*
Emerging epidemiologic trends

Increased detection of IMP, VIM, and OXA-48

*Graph includes data on specimens collected through Q1 of 2017*
MDRO response is dependent on epidemiology

- **Tier 1**
  - Novel resistance mechanisms (never or very rarely identified previously) in U.S.
  - No current treatment options exist (pan-R) and have potential to spread more widely
  - Organisms and resistance mechanisms for which our experience is extremely limited and a more extensive evaluation might better define the risk for transmission

- **Tier 2**
  - MDROs found primarily in healthcare settings but not believed to be found regularly in the region

- **Tier 3**
  - MDROs already established in the U.S. and in the region but not thought to be endemic
MDRO response is dependent on epidemiology

- **Tier 1**
  - Novel resistance mechanisms (never or very rarely identified previously) in U.S.
  - No current treatment options exist (pan-R) and have potential to spread more widely
  - Organisms and resistance mechanisms for which our experience is extremely limited and a more extensive evaluation might better define the risk for transmission

- **Tier 2**
  - MDROs found primarily in healthcare settings but not believed to be found regularly in the region

- **Tier 3**
  - MDROs already established in the U.S. and in the region but not thought to be endemic
Containment of MDROs

• Conduct investigation of patient’s healthcare exposures

• Conduct investigation of patient contacts and epidemiologically-linked patients to identify those infected or colonized

• Implement improved infection control measures
Colonization screening following MDRO detection

- Lab lookback
- Healthcare roommate screening
- Prospective surveillance
- Broader healthcare contact screening
- Household contact screening
- Environmental sampling
- Healthcare personnel screening

Tier 1
Tier 2
Tier 3

Yes
Sometimes
No
Colonization screening in ARLN

- Swabs from CP-CRE+ patient contacts
- Rapid PCR-based detection from swab (Cepheid)

Swabs positioned regionally for rapid deployment to facilities where screening taking place.
Colonization screening in ARLN

Initiate infection control practices and contact precautions

Swabs from CP-CRE+ patient contacts

≤1 day turnaround

Regional lab

Report within 1 working day of results

Provide or request assistance; Initiate investigation

Report within 1 working day of results

Report within 1 working day of results

Initiate infection control practices and contact precautions

Swabs from CP-CRE+ patient contacts

≤1 day turnaround

Regional lab

Provide or request assistance; Initiate investigation

Report within 1 working day of results

Initiate infection control practices and contact precautions

Swabs from CP-CRE+ patient contacts

≤1 day turnaround

Regional lab

Provide or request assistance; Initiate investigation

Report within 1 working day of results

Initiate infection control practices and contact precautions

Swabs from CP-CRE+ patient contacts

≤1 day turnaround

Regional lab

Provide or request assistance; Initiate investigation

Report within 1 working day of results

Initiate infection control practices and contact precautions

Swabs from CP-CRE+ patient contacts

≤1 day turnaround

Regional lab

Provide or request assistance; Initiate investigation

Report within 1 working day of results
Screening for KPC-producing *K. pneumoniae*

- First colonization screenings conducted through ARLN in December
  - In late 2016, a skilled nursing facility (SNF) had reported 13 CR-*K. pneumoniae* cases since 2015
    - 7/8 CP-CRE upon testing at local clinical laboratory
    - 5 patients still at facility
  - State conducted site visit; noted multiple areas of concern for infection control.
  - Screened roommates of cases during 2015-2016 and any patients with history of CRE since 2015
    - KPC-producing *K. pneumoniae* identified in 1 roommate and 4 CRE patients
  - Facility-wide point prevalence survey (PPS) conducted
    - ARLN regional lab identified 13 positives from 77 patients swabbed (17% CP-CRE)
Screening for IMP-producing *Proteus mirabilis*

- **IMP-*Proteus mirabilis*** detected in patient of SNF on 3/9
  - Roommate screened 4/26; positive
  - **PPS 1**: conducted on same wing of SNF on 5/8; 3 new positives detected among 9 patients screened
  - **PPS 2**: 1 new positive among 21 patients screened on 5/22 in same wing
- **Infection control recommendations now being implemented**
- **Investigations are ongoing**
Models simulated spread of CRE among patients

- acute care hospitals, long-term acute care hospitals, nursing homes

3 intervention scenarios

- **Common approach**: infection control activity currently in common use
- **Independent efforts**: augmented efforts implemented independently
- **Coordinated approach**: augmented efforts coordinated across a health care network
Projected prevalence of CRE, based on models

Projected *regional* prevalence of CRE over 5-yr period under 3 intervention scenarios
*10 facility model, Veterans Health Administration*

Projected *countywide* prevalence of CRE over 15-year period under 3 intervention scenarios
*102 facility model, Orange County, California*

Coordinated prevention approaches assisted by public health agencies have the potential to more completely address emergence and dissemination of MDROS and in comparison to independent facility based efforts.
Benefits of colonization testing

- Help detect additional cases/colonizations
- Help facilities identify infection control problems
- Help facilitate infection control when CP-CRE-positive patient is transferred or readmitted
  - States asked to maintain database of colonization screening results
ARLN testing and screening: detect, contain, and prevent

- Detection is the key to containing, controlling, and preventing the spread of resistance
- State and regional lab testing and colonization screening for CP-CRE are essential for public health response
- Coordinated approach to infection control will be our most effective means of preventing additional AR infections
Thank you

Contact:
Allison Brown acbrown1@cdc.gov
ARLN ARLN@cdc.gov

For more information, contact CDC
1-800-CDC-INFO (232-4636)

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.