CRE Detect and Protect Crash Course
Illinois Infection Prevention and CRE Workshop
July 2015

Robynn Cheng Leidig, MPH
Public Health Prevention Service Fellow
Division of Patient Safety and Quality
Illinois Department of Public Health
Disclosures

• I have nothing to disclose
I want to cover:

• What is CRE and XDRO?
• The roles we each play
• What happens after a CRE case is reported?
What is CRE?

**Carbapenem**
- Class of broad-spectrum antibiotics

**Resistant**
- Bacteria with mutations that make antibiotics ineffective

**Enterobacteriaceae**
- Family of bacteria that includes *Escherichia coli*, *Klebsiella sp.*, and *Enterobacter*
CRE is

• KPC
• NDM
• OXA
• VIM
• IMP

CRE is **not**...

• VRE
• Pseudomonas
• Acinetobacter
• ESBLs
Why is CRE such a big deal?

- Deadly infection
- Few treatment options (if any)
- Spreading quickly

http://www.cdc.gov/drugresistance/threat-report-2013/
What is the XDRO registry?

**XDRO** = eXtensively Drug Resistant Organisms

**XDRO registry** = where CRE is reported in Illinois*

**Began:** November 1, 2013

**Required to report:**
- Acute care hospitals
- Long-term acute care hospitals
- Long-term care facilities
- Laboratories

* Illinois healthcare facilities and laboratories are required to report CRE to the XDRO registry per 77 Ill. Adm. Code 690, Control of Communicable Diseases Code.
But wait, let’s take a step back...

We all have a role to play:

State Health Department (IDPH)

Local Health Departments

Health Care Facilities

Laboratories

Other?
Illinois Department of Public Health
IDPH Office of Health Care Regulation

License, inspect or certify those that must comply with state and federal regulations.

May include:

- Ambulatory surgical treatment centers (ASTCs)
- Certified nurse aides
- Health maintenance organizations (HMOs)
- Home health agencies
- Hospices
- Hospitals
- Laboratories
- Nursing homes
- Physical therapists in independent practice
- Poison control resource centers
- Pregnancy termination centers
- Rural health clinics
- Sperm and tissue bank
IDPH Division of Patient Safety and Quality

- Promotes health care transparency
- Collects and reports health care provider data
- Develops and implements programs for improving the quality and value of health care
CRE “Detect and Protect” Campaign

- 30 stakeholder CRE Taskforce
- 6 webinars: 605 people
- 2 packets: 470 facilities
- 2 websites
- 1 Press release
- 3 regional workshops
IDPH Division of Infectious Disease

• Protect people from infectious diseases through disease surveillance, analysis, immunization, and education

• Mandated reporting of certain infectious diseases to Illinois’ National Electronic Disease Surveillance System (I-NEDSS)
IDPH and Local Health Departments

• Local Health Departments are typically the first point of contact

• Health care facilities are organized by Local Health Department jurisdictions

Local → State → Federal
If I work at a Local Health Dept...

- Refer facilities to report CRE to the XDRO registry
- Notify IDPH about unusual CRE (e.g. NDM), or potential CRE clusters
- Investigate clusters in collaboration with IDPH
- Facilitate communication when patients are transferred
- Refer facilities to CDC CRE Toolkit guidelines
- Maintain vigilance for clusters of CRE via INEDSS B.O.
- Refer CRE questions to IDPH CRE Team
If I work at a Health Care Facility…

• Communicate with the lab about CRE testing
• Report CRE cases to the XDRO registry
• Use the XDRO registry to query for admitted patients/residents
• Use the XDRO registry (or some other method) to keep track of CRE patients/residents
• Contact your local health department about unusual CRE or potential CRE clusters
• Implement appropriate infection control measures according to the CDC CRE Toolkit*

*http://www.cdc.gov/hai/organisms/cre/cre-toolkit/
If I work at a Laboratory...

- Communicate with your facilities about what type of CRE testing you do
- Report CRE cases to the XDRO registry
- Submit your first five CRE isolates to IDPH labs for validation testing (by 7/31/15)
- Submit any unusual CRE (e.g. NDM) to IDPH labs to send to CDC for confirmatory testing*

*Coordinate with your Local Health Department
What happens after CRE cases are reported to the XDRO registry?
CRE identified

Providers
Laboratories

Report

XDRO registry

Use XDRO data for surveillance

Query

Patient admit (Unknown CRE status)

Isolation Precautions (Y/N)
Once CRE cases are in the XDRO registry...

• Health Departments review the cases
  – Look for anything unusual (e.g. NDM, clusters)
  – Follow-up as necessary

• IDPH does **not** publicly report CRE cases by facility

• For now, CRE cases are in the XDRO registry indefinitely
What happens if there is an unusual CRE or potential cluster?

1. IDPH will contact the local health department with jurisdiction over the involved facility.

2. Local health department (or IDPH) will follow up with the healthcare facility to gather more information.

3. Local health department (or IDPH) may follow up with the laboratory that identified the CRE.

4. IDPH will notify CDC (as necessary).
More information for a CRE case

- Foreign travel
- Foreign healthcare exposure
- Invasive procedures
- Past medical history
- Dates and locations of previous healthcare facility exposure
- Surveillance cultures
- Adherence to CDC CRE Toolkit recommendations
Closing up a CRE case

• Make sure facilities know what to do to prevent spread of CRE

• Summary report to local health departments, IDPH, and CDC, as necessary
Who do I call for questions about CRE?

If you’re a **Health Care Facility** or **Laboratory**, start with your Local Health Department.

If you’re a **Local Health Department**, contact IDPH CRE Team:
- Mary Alice Lavin, Hektoen (MaryAlice.Lavin@illinois.gov)
- Jodi Morgan (Jodi.Morgan@illinois.gov)
- Angela Tang, Hektoen (Angela.Tang@illinois.gov)
- Robynn Cheng Leidig (Robynn.Leidig@illinois.gov)

When in doubt, call IDPH Division of Infectious Diseases at 217-785-7165 or email dph.xdroregistry@illinois.gov

Websites:  [www.xdro.org](http://www.xdro.org);  [www.idph.state.il.us/patientsafety/cre/](http://www.idph.state.il.us/patientsafety/cre/)
Recognizing Carbapenem-Resistant *Enterobacteriaceae*: Crash Course for Non-Microbiologists

Nicholas M. Moore, MS, MLS(ASCP)CM
Department of Medical Laboratory Science
Rush University Medical Center
Disclosures

• Research support through the CDC Chicago Prevention Intervention Epicenter (C-PIE), RA Weinstein, PI and MK Hayden, Co-I

• Industry sponsored grants/contracts (Cepheid)

• Unpaid research (AdvanDx)
Objectives

By the end of this presentation, the learner will be able to:

1. Define Carbapenem-Resistant Enterobacteriaceae (CRE)
2. Discuss laboratory techniques used to identify CRE
3. Distinguish between different mechanisms of carbapenem resistance
Carbapenem-Resistant Enterobacteriaceae

• CRE are serious public health threat
  – *Klebsiella pneumoniae* carbapenemase (KPC) is the most common worldwide

http://www.cdc.gov/drugresistance/biggest_threats.html
Carbapenems

- Imipenem
- Meropenem
- Ertapenem
- Doripenem
Carbapenemases

- Carbapenem-hydrolyzing beta-lactamases that confer carbapenem resistance
- The carbapenemases have been organized based on amino acid homology into the Ambler molecular classification schema
  - Class A, C, and D share a serine residue in the active site
  - Class B enzymes require the presence of zinc for activity
## Carbapenemases

<table>
<thead>
<tr>
<th>Ambler Class</th>
<th>Carbapenemase</th>
<th>Location of gene</th>
<th>Dissemination potential</th>
<th>Activity</th>
<th>Predominant Species</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>KPC</td>
<td>Plasmid</td>
<td>High</td>
<td>All β-lactams</td>
<td><em>K. pneumoniae</em></td>
</tr>
<tr>
<td>B</td>
<td>NDM-1</td>
<td>Plasmid</td>
<td>High</td>
<td>All β-lactams except aztreonam</td>
<td><em>K. pneumoniae, E. coli</em></td>
</tr>
<tr>
<td>D</td>
<td>OXA-48</td>
<td>Plasmid</td>
<td>High</td>
<td>Carbapenems, except 3rd gen cephalosporins</td>
<td><em>K. pneumoniae, E. coli, E. cloacae</em></td>
</tr>
</tbody>
</table>

**Plasmid**

**Chromosome**
Mandated Reporting in Illinois

- IDPH amended the Control of Communicable Diseases Code (77 Ill. Adm. Code 690) Rules to require reporting of CRE
- Began November 1, 2013
- XDRO Registry for CRE
Enterobacteriaceae

- *Enterobacteriaceae* are a large family of enteric Gram-negative bacilli
  - *Escherichia coli*
  - *Klebsiella pneumoniae*
  - *Citrobacter* spp.
  - *Enterobacter* spp.

- Other genera: *Proteus, Providencia, Serratia*
Defining CRE for the XDRO Registry

1. Molecular test (e.g. PCR) specific for a carbapenemase gene (e.g. bla_{KPC}, bla_{NDM})

2. Phenotypic test (e.g. modified Hodge test) specific for carbapenemase production

3. E. coli or Klebsiella spp. only: non-susceptible to ONE of the carbapenems (doripenem, meropenem, or imipenem) AND resistant to ALL third generation cephalosporins tested (ceftriaxone, cefotaxime, and ceftazidime)
What is PCR?

- Polymerase chain reaction
- Laboratory method developed to rapidly generate copies of nucleic acids (DNA or RNA)
- Bacterial colony provides the template (DNA)
- Series of primers and probes specific for carbapenemase gene will bind to and recognize complementary sequence in bacterial DNA, if present
- Rapid cycles of denaturing, annealing, and extending will generate exponential copies of region of interest
- Fluorescent threshold → positive result
PCR

Pros
• Quick turn-around time
• Specific for carbapenemase
• Definitive
• Can multiplex targets into single assay (e.g. KPC/NDM)
• Does not require viable organisms

Cons
• Expensive
• High-complexity testing
• Organisms not available for additional testing, epidemiologic studies
Phenotypic Test: Modified Hodge

- Uses a pan-susceptible *E. coli* (indicator) to create a lawn of confluent growth on a Mueller Hinton agar plate
- Carbapenem disk applied to center of plate (meropenem or ertapenem)
- Suspicious isolates struck from center of disk to edge of plate
- Examine after 18-24 hour incubation for a growth of *E. coli* around the isolate streak
Modified Hodge Test

1:10 dilution of 0.5 McFarland of ATCC 25922 *E. coli*

ATCC BAA-1705
*K. pneumoniae*
MHT positive

ATCC BAA-1706
*K. pneumoniae*
MHT negative
Modified Hodge Test

Pros
• Inexpensive
• Easy to perform
• Organisms available for additional testing

Cons
• Requires additional overnight incubation
• Not specific
• Lacks sensitivity for MBLs (e.g. NDM)
MβL Etest® Phenotypic Screening

- Presence of MβL indicated by a reduction of the MP MIC by ≥ 3 doubling dilutions in the presence of EDTA
- Phenotypic method requires confirmation
Chromogenic Media

- CHROMagar™ KPC – research use only
- Brilliance™ CRE agar – not for sale in US
- chromID® CARBA agar
- HardyCHROM™ CRE agar

- Inexpensive and convenient
- No definitive ID
- Does not provide mechanism
- Studies with various sensitivity, specificity
Suspect KPC from a Micro Report

- **Enterobacteriaceae**
- Non-susceptible to all β-lactam antibiotics
  - Penicillins
  - Cephalosporins
  - Cephamycins
  - Monobactams
  - Carbapenems

\[ \text{bla}_{\text{KPC}} \text{ PCR = POSITIVE} \]
Suspect NDM from a Micro Report

- **Enterobacteriaceae**
- Non-susceptible to all β-lactam antibiotics
  - except aztreonam

$bla_{NDM-1}$ PCR = POSITIVE
**Suspect OXA-48 from a Micro Report**

- **Enterobacteriaceae**
- Non-susceptible to β-lactam antibiotics
- Remains susceptible to 4th generation cephalosporin

\[
\text{\textit{bla}_{OXA-48}} \text{ PCR} = \text{POSITIVE}
\]
Summary

• XDRO Registry is tracking Carbapenem-resistant Enterobacteriaceae (CRE)

• Report isolates based off molecular, phenotypic or susceptibility test results
  – Reporting using only AST data is valid only if isolate is *E. coli* or *Klebsiella* spp.

• Some patterns in susceptibility profiles may suggest a particular mechanism, but must to be confirmed
Questions
Acknowledgements

Don Blom
Manon Haverkate
Mary Hayden
David Hines
Sarah Kemble
Michael Lin
Karen Lolans
Rosie Lyles
Kavya Poluru
Kavitha Prabaker
Koh Okomoto
Yoona Rhee
Monica Sikka
Caroline Thurlow
Shayna Weiner
Robert Weinstein
Contact Information

• Questions? Comments? Troubleshooting?

Nicholas Moore
Nicholas_Moore@rush.edu
312-942-4629
Carbapenem-Resistant Enterobacteriaceae (CRE) in Illinois: A Situational Update

Allison Arwady, MD, MPH

Southern Illinois Infection Prevention and CRE Workshop

July 23, 2015
Conflict of Interest and Disclaimer

No conflicts of interest to report.

The findings and conclusions in this report are those of the author and do not necessarily represent the official position of the Illinois Department of Public Health.
Carbapenem-Resistant Enterobacteriaceae (CRE)

- **Enterobacteriaceae: Large family of bacteria**
  - *Escherichia coli*, *Klebsiella sp.*, *Enterobacter sp.*…

- **Carbapenem Resistance**
  - CRE can have an enzyme (-ase) that breaks down carbapenem antibiotics and makes them ineffective
    - *Klebsiella pneumoniae* carbapenemase (KPC)
    - New Delhi Metallo-beta-lactamase (NDM)

- **Patients who develop invasive infections with CRE have few antibiotic options and a high mortality rate**
Recommendations: Keep It Simple

- **Examples: E. coli** and urinary tract infections
- **Communication between labs and care facilities**
- **Original susceptibility reports**

---

**Blood Culture (Peripheral) Abnormal**:

**Procedure**: Blood Culture (Peripheral)
**Source**: Blood
**Collected**: [redacted]

------------------- FINAL REPORT -------------------

**Final Identification**: Klebsiella Pneumoniae

This isolate demonstrates carbapenemase production. Carbapenems, cephalosporins, and penicillins are unlikely to be effective in treatment of serious infections. Contact precautions required.

---------- SUSCEPTIBILITY TESTING ----------

<table>
<thead>
<tr>
<th>Drug</th>
<th>MIC (μg/ml)</th>
<th>Interpretaion</th>
<th>MIC (μg/ml)</th>
<th>Interpretaion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trimeth/Sulfadiazine</td>
<td>&gt;2/38</td>
<td>Resistant</td>
<td>------------</td>
<td>--------------</td>
</tr>
<tr>
<td>Cefazolin</td>
<td>&gt;16</td>
<td>Resistant</td>
<td>1.00</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Tigecycline</td>
<td></td>
<td></td>
<td>1.00</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>&gt;4</td>
<td>Resistant</td>
<td>1.00</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>16</td>
<td>Intermediate</td>
<td>1.00</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Piperacetamide</td>
<td>&gt;64</td>
<td>Resistant</td>
<td>1.00</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Ticarcillin/K Clavulanate</td>
<td>&gt;64</td>
<td>Resistant</td>
<td>1.00</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>&gt;32</td>
<td>Resistant</td>
<td>1.00</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>&lt;=4</td>
<td>Susceptible</td>
<td>1.00</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Tobramycin</td>
<td>&gt;8</td>
<td>Resistant</td>
<td>1.00</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Amikacin</td>
<td>16</td>
<td>Susceptible</td>
<td>1.00</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Imipenem</td>
<td>8</td>
<td>Resistant</td>
<td>1.00</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Meropenem</td>
<td>&gt;8</td>
<td>Resistant</td>
<td>1.00</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Cefepine</td>
<td>16</td>
<td>Resistant</td>
<td>1.00</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Colistin</td>
<td></td>
<td></td>
<td>1.38</td>
<td>Susceptible</td>
</tr>
<tr>
<td>A. Ertapenem</td>
<td>&gt;4</td>
<td>Resistant</td>
<td>1.00</td>
<td>Susceptible</td>
</tr>
</tbody>
</table>
Antibiotic Use: Key Driver of Resistance

In 2010 alone

– 73 billion units of antibiotics used in humans
  • 10 antibiotic units for every man, woman, and child on earth; 36% increase from 2000
  • India and China were largest consumers by country
    – However, half of per-capita use compared to US (22 units/person)

– 63,151 tons of antibiotics used in livestock

• Van Boeckel et al. The Lancet 2014
• Van Boeckel et al. PNAS 2015

Slides: Trick, Lin (CDC Prevention Epicenter)
# The ABCs of CRE

<table>
<thead>
<tr>
<th>Class</th>
<th>Enzyme</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>KPC</td>
</tr>
<tr>
<td>B (metallo-(\beta)-lactamases)</td>
<td>NDM-1, VIM, IMP</td>
</tr>
<tr>
<td>D</td>
<td>OXA</td>
</tr>
</tbody>
</table>
KPC – Quick Facts

• “Klebsiella pneumoniae carbapenemase”
• Origin: USA
• First identified: 1996
• Associated bacteria:
  – Klebsiella pneumoniae >>> E. coli > Enterobacter
• Primarily found in debilitated hospitalized patients (not community)
NDM – Quick Facts

- “New Delhi metallo-β-lactamase”
- Origin: South Asian continent
- First identified: 2008
- Species: *Klebsiella pneumoniae* = *E. coli*, others (*Enterobacter*, *Citrobacter*, *Proteus*, *Salmonella*, *Providentia*, *Acinetobacter*, *Pseudomonas*)
- Found in both in hospitalized pts and in the community
NDM Global Distribution

- High prevalence of NDM producers (endemicity)
- Outbreaks and interregional spread of NDM producers
- Sporadic description of NDM producers

OXA-48 Quick Facts

• OXA = “Oxacillinase”
• Origin: Turkey
• First identified: 2001
• Claim to fame: is a weak carbapenemase, and does not have cephalosporin resistance.
• Species: *Klebsiella pneumoniae* >>> *E. coli*, others
OXA-48 Global

An Illinois Outbreak of NDM: First Steps

- Suspected NDM-producing CRE isolates identified by clinical laboratory in Illinois (first in March 2013)
  - Screened for metallo-\(\beta\)-lactamase (MBL) production by using carbapenem disks with and without inhibitors (Rosco Diagnostica)
  - MBL-positive isolates submitted to CDC for confirmation using polymerase chain reaction

- August 2013 on-site investigation at Hospital A
  - At that time, 9 confirmed NDM-producing *E. coli* cases
Background: New Delhi Metallo-β-Lactamase-Producing CRE (NDM)

- First reported in U.S. in 2009, in international travelers

- Gene encoding NDM-1: $\text{bla}_{\text{NDM-1}}$
  - On plasmids, transferable between species and genera (can replicate independently from chromosomal DNA)

- Between 2009 and 2012, 27 NDM isolates nationwide had been confirmed by CDC
## Initial Case Description (n=9)

<table>
<thead>
<tr>
<th></th>
<th>Mean (Range) or n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>70 (45-88)</td>
</tr>
<tr>
<td>History of international travel</td>
<td>0/9 (0%)</td>
</tr>
<tr>
<td>History of admission to hospital A</td>
<td>8/9 (89%)</td>
</tr>
<tr>
<td>History of admission to long-term care facility</td>
<td>4/9 (44%)</td>
</tr>
<tr>
<td><strong>History of Endoscopic Retrograde Cholangiopancreatography (ERCP)</strong></td>
<td>6/9 (67%)</td>
</tr>
</tbody>
</table>
Background: Endoscopic retrograde cholangiopancreatography (ERCP)

Endoscope is inserted through the mouth into the duodenum.
To access the ducts:

- Needs to make sharp angle
- Requires additional mechanical lever (elevator)
Background: Duodenoscopes

- Previous outbreaks of CRE epidemiologically linked to gastrointestinal procedures, and to duodenoscopes
  - Inadequate cleaning of elevator mechanism/channel
  - Manual cleaning required
Methods: On-site Investigation

- **Case definition**
  - NDM-producing *E. coli* isolate
  - Recovered from a patient in northeastern Illinois
  - With >85% similarity by pulsed field gel electrophoresis (PFGE) to the outbreak strain
  - Confirmed by CDC in 2013

- **Epidemiologic investigation**
  - Characterized known cases
  - Hospital and local health departments screened patient roommates, including at other facilities
  - Reviewed duodenoscope cleaning and reprocessing procedures, took environmental samples
Methods: Case Control Study

- Identify exposures that may contribute to NDM transmission

- Controls randomly selected from among 131 patients with negative surveillance cultures
  - Hospital A rehabilitation unit
Initial Patients’ (n=9) Facility Admissions

- Dates of admission to Hospital A
- Dates of admission to other area care facilities
- Date of NDM positive culture
Field Investigation

- C7
- C8
- S0

Scope A
- C1
- C2
- C3
- C4
- C5
- C6

Scope B

Legend:
- Blue: Case from hospital
- Green: Case, not from hospital
## Results: Case Control Study

<table>
<thead>
<tr>
<th>Case-Control Analysis</th>
<th>Case Patients (n = 8)</th>
<th>Control Patients (n = 27)</th>
<th>Odds Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Procedures</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ERCP</td>
<td>6 (75.0)</td>
<td>1 (3.7)</td>
<td>78 (6.0-1008)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Other endoscopy</td>
<td>2 (25.0)</td>
<td>3 (11.1)</td>
<td>2.7 (0.4-19.7)</td>
<td>.34</td>
</tr>
<tr>
<td>Operating room</td>
<td>5 (62.5)</td>
<td>11 (40.7)</td>
<td>2.4 (0.5-12.3)</td>
<td>.29</td>
</tr>
<tr>
<td><strong>Radiology</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CT</td>
<td>7 (87.5)</td>
<td>20 (74.1)</td>
<td>2.5 (0.3-23.6)</td>
<td>.44</td>
</tr>
<tr>
<td>MRI(^{n,f})</td>
<td>1 (12.5)</td>
<td>0</td>
<td>6.0 (0.1-308.6)</td>
<td>.34</td>
</tr>
<tr>
<td>MRCP</td>
<td>5 (62.5)</td>
<td>1 (3.7)</td>
<td>43.3 (3.7-505.8)</td>
<td>.003</td>
</tr>
<tr>
<td><strong>Unit of stay</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interventional radiology</td>
<td>2 (25.0)</td>
<td>8 (29.6)</td>
<td>0.8 (0.1-4.8)</td>
<td>.80</td>
</tr>
<tr>
<td>Medical ICU</td>
<td>3 (37.5)</td>
<td>8 (29.6)</td>
<td>1.4 (0.3-7.4)</td>
<td>.67</td>
</tr>
<tr>
<td>Surgical ICU</td>
<td>3 (37.5)</td>
<td>10 (37.0)</td>
<td>1.0 (0.2-5.2)</td>
<td>.98</td>
</tr>
<tr>
<td>Oncology</td>
<td>2 (25.0)</td>
<td>3 (11.1)</td>
<td>2.7 (0.4-19.7)</td>
<td>.34</td>
</tr>
<tr>
<td>Neurology</td>
<td>2 (25.0)</td>
<td>7 (25.9)</td>
<td>0.95 (0.2-5.9)</td>
<td>.96</td>
</tr>
<tr>
<td>Surgical care</td>
<td>3 (37.5)</td>
<td>4 (14.8)</td>
<td>3.5 (0.6-20.5)</td>
<td>.17</td>
</tr>
<tr>
<td><strong>Other exposures</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antibiotics(^{f,g,h})</td>
<td>8 (100.0)</td>
<td>15 (55.6)</td>
<td>9.5 (1.0-304.4)</td>
<td>.05</td>
</tr>
<tr>
<td>Anesthesia</td>
<td>7 (87.5)</td>
<td>12 (44.4)</td>
<td>8.8 (0.9-81.2)</td>
<td>.06</td>
</tr>
</tbody>
</table>
Results: Duodenoscopy Reprocessing

- Observation of duodenoscope reprocessing
  - Pre-cleaning
  - Leak testing
  - Manual cleaning
  - High-level disinfection

- Duodenoscope and AER manufacturers also on-site

- No lapses identified
Results: NDM-producing \textit{E. coli} Recovered From Duodendoscope

- Duodensoscope A, used on 5 of the 6 original case-patients, was sent to CDC
  - Had undergone manual and high level disinfection using an AER
  - Had been out of service for two months

- NDM-producing \textit{E. coli} and KPC-producing \textit{K. pneumoniae} were recovered from the terminal section (the elevator channel) of the device

- Manufacturer did not identify structural defect in duodenoscope
Next steps: Expanded CRE Screening

- Hospital notified the 226 living patients who were exposed to any duodenoscope Jan.-Sept. 2013
  - Offered CRE (rectal swab) and blood-borne pathogen screening
  - 102 (45%) returned for screening
  - NDM-producing *E. coli* were recovered from 27 (26%)
  - All blood-borne pathogen testing was negative
Field Investigation

Scope A

Scope B

Additional Cases from Diagnostic Testing

Duodenoscopy Screening

94 notified
58 screened
23 cases

39 notified
16 screened
1 case

23 notified
15 screened
3 cases
Results: PFGE to Assess Relatedness

Dendrogram

PFGE Pattern

92%

Case isolates

Scope A isolate

Case isolates
Conclusion

- Largest known cluster of NDM-producing *E. coli* in the U.S.
  - In total, 39 case patients identified, 35 with duodenoscope exposure in one hospital
  - Appears duodenoscopes can be an efficient source of transmission

- No reprocessing breaches or scope defects identified
  - However, NDM-producing *E. coli* recovered from a reprocessed duodenoscope and shared more than 92% similarity to all case patient isolates by PFGE
  - Appears duodenoscopes can remain contaminated with pathogenic bacteria even after recommended reprocessing
Conclusions for Facilities

- Be aware of the potential for transmission of bacteria, including antimicrobial-resistant organisms, via this route
  - If CRE identified, consider possibility of ERCP-related transmission
  - Conduct regular reviews of duodenoscope reprocessing procedures to ensure optimal manual cleaning and disinfection

Original Investigation

New Delhi Metallo-β-Lactamase–Producing Carbapenem-Resistant *Escherichia coli* Associated With Exposure to Duodenoscopes
Priorities: Identify and Control Spread of Novel Carbapenemases

- Improve identification of novel carbapenemases by enhancing laboratory capacity
  - Few laboratories regularly perform CRE resistance mechanism testing
  - Many cannot differentiate organisms producing novel carbapenemases from those producing KPC

- Control spread of carbapenemases
  - CRE reporting and facility intercommunication has historically been poor, limiting effective infection control
    - CRE became reportable in Illinois in November, 2013
    - New eXtensively Drug Resistant Organism (XDRO) registry
    - Acute- and long-term care facilities can access registry directly, to implement appropriate infection control measures when patients are admitted
  - Antimicrobial stewardship
    - Recent antibiotic use was a risk factor for case status
Illinois: REALM project

CDC-sponsored

Twice-yearly point prevalence surveys

• CRE, since 2010

Slide: Trick, Lin (CDC Prevention Epicenter)
REALM project - KPC

Hospital ICUs: blue

LTACHs: red

Slide: Trick, Lin (CDC Prevention Epicenter)
Prevalence of KPC colonization among adult ICU patients

Survey

Percent

2010 2014

Slide: Trick, Lin (CDC Prevention Epicenter)
Prevalence of KPC colonization among ICU vs. LTACH patients

Survey

2010 2014

Percent

Adult ICUs
LTACHs

Slide: Trick, Lin (CDC Prevention Epicenter)
KPC Intervention for LTACHs

Hayden, Clin Infect Dis, 2014
REALM project 2015 update

Survey #12 is underway

– Now testing for all 5 major carbapenemases (KPC, NDM, OXA-48, VIM, IMP)

Thank you to REALM hospitals for continued participation

Slide: Trick, Lin (CDC Prevention Epicenter)
“Detect and Protect”

- **Detect**: Identify all patients with CRE
- **Protect**: Maintain CRE-colonized patients in isolation precautions throughout the healthcare system
Challenges

• Peripatetic Patients
  – Within 1 year of ICU discharge
    • Median 4 facility transitions

• Information lost between transfers
  – Patients may go home between facilities

Unroe, Annals Int Med, 2010; 153(3)
• Facilitates the Detect and Protect strategy

• Partnership
  – Illinois Department of Public Health
  – Chicago CDC Prevention Epicenter
  – Medical Research Analytics and Informatics Alliance (MRAIA)
XDRO Registry Overview

1. Mandatory CRE reporting

All Illinois facilities

Hospital A

Patient query

CRE status

2. CRE information exchange (inter-facility communication)

Participants: Illinois hospitals including LTACHs (142), nursing homes (784), laboratories
Illinois CRE definition: Enterobacteriaceae with one of the following test results

1. Molecular test (e.g., PCR) specific for carbapenemase
   OR
2. Phenotypic test (e.g., Modified Hodge) specific for carbapenemase production
   OR
3. For *E. coli* and *Klebsiella* species only: non-susceptible to ONE of the carbapenems (doripenem, meropenem, or imipenem) AND resistant to ALL third generation cephalosporins tested (ceftriaxone, cefotaxime, ceftazidime).

Report 1st CRE event per patient per encounter
Unique patients reported to XDRO registry

Data courtesy of IDPH
XDRO registry, year 1

**Reporting**
- Unique reports: 1,557 reports
- Unique patients: 1,095
- Reporting facilities: 175

**Querying**
- 30 unique facilities query the registry/month

<table>
<thead>
<tr>
<th>Facility Type</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute hospitals</td>
<td>115</td>
</tr>
<tr>
<td>LTACHs</td>
<td>5</td>
</tr>
<tr>
<td>SNFs</td>
<td>46</td>
</tr>
<tr>
<td>Reference labs</td>
<td>7</td>
</tr>
<tr>
<td>Outpatient clinics</td>
<td>2</td>
</tr>
</tbody>
</table>
### XDRO registry summary, 2014

**Characteristics of ALL submitted reports**

<table>
<thead>
<tr>
<th>Culture Type</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical</td>
<td>1254</td>
<td>80</td>
</tr>
<tr>
<td>Screening</td>
<td>301</td>
<td>20</td>
</tr>
</tbody>
</table>

**Organism**

<table>
<thead>
<tr>
<th>Organism</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Klebsiella spp.</td>
<td>1347</td>
<td>86</td>
</tr>
<tr>
<td>E. coli</td>
<td>103</td>
<td>7</td>
</tr>
<tr>
<td>Enterobacter spp.</td>
<td>77</td>
<td>5</td>
</tr>
</tbody>
</table>

Data and adapted slide from IDPH (A. Tang)
<table>
<thead>
<tr>
<th>Characteristics of ALL submitted reports</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type of testing performed</strong>*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1) Molecular test*</td>
<td>397</td>
<td>25</td>
</tr>
<tr>
<td>2) Phenotypic test*</td>
<td>751</td>
<td>48</td>
</tr>
<tr>
<td>3) Susceptibility test ONLY</td>
<td>449</td>
<td>29</td>
</tr>
<tr>
<td>Unknown</td>
<td>29</td>
<td>2</td>
</tr>
<tr>
<td><strong>Mechanism of resistance</strong> (applies only to reports with molecular test)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>KPC</td>
<td>363</td>
<td>91</td>
</tr>
<tr>
<td>NDM</td>
<td>11</td>
<td>3</td>
</tr>
<tr>
<td>Other/Unknown</td>
<td>23</td>
<td>6</td>
</tr>
</tbody>
</table>

*≥1 response accepted per isolate

Data from IDPH (A. Tang)
All XDRO reports by region

City of Chicago: 724
West Chicago: 586
Rockford: 36
Peoria: 70
Champaign: 14
Edwardsville: 53
Marion: 12
Missing/Unknown: 76

Data and adapted slide from IDPH (A. Tang)
XDRO data access for LHDs

- Local health departments can obtain access to XDRO data through I-NEDSS Business Objects
- Must fill out a user agreement form
- E-mail dph.xdrolegistry@illinois.gov for the form or questions about XDRO data access
XDRO Registry: Future Directions

1. Laboratory validation
2. Automated CRE alerts
3. Cluster detection
Laboratory Validation

First 5 consecutive CRE isolates from each lab should be sent to IDPH (Jan 1, 2015 - )
- Identification to species
- Antibiotic susceptibility testing
- $bla_{KPC/NDM}$ PCR
- Additional phenotypic and genotypic evaluation if necessary

Courtesy of M. Hayden
Validation Preliminary Results: 134 isolates (January-April, 2015)

- 115 (86%) carbapenemase-producing Enterobacteriaceae
  - 111 (97%) KPC PCR+
  - 2 (2%) NDM PCR+
  - 2 (2%) OXA-48-like

- 10 (8%) carbapenem-resistant Enterobacteriaceae
  - 9 Enterobacter spp, 1 E. coli

- 3 (2%) carbapenem-resistant Acinetobacter/Pseudomonas

- 6 (5%) carbapenem-susceptible E. coli

Courtesy of M. Hayden
Lab validation – moving forward

- Current protocol:
  - Labs should continue to send their first 5 consecutive CRE isolates of 2015 to IDPH until they meet their quota

- Proposed protocol for next year *(contingent on CDC support)*
  - Every lab sends 5 consecutive CRE isolates for 2016
  - For confusing CRE isolates, every lab can send an additional 5 CRE isolates
CRE automated alerts

In a REALM survey, 96% of hospitals indicated interest in receiving automated CRE alerts from the XDRO registry

Slide: Trick, Lin (CDC Prevention Epicenter)
Hospital A firewall

1.

Patient admission list
(inpatient only)
1. Smith, John 1/5/1967
2. Doe, Jane 1/1/1989
3. Patient, Test 1/2/1977

2.

XDRO hashing software
1. 15234234235235
2. 23425252434325
3. 62624535363466

3.

XDRO registry
1. 55451934265235
2. 23425252434325
3. 62624535363466
4. 26236346345345
5. 24572457456554
6. 35683734564547
7. 34573453456456
8. 15234234235235

Query against registry (identifiers hashed using same algorithm)

4.

Positive match generates a generic email (no PHI)

Hospital A infection control dept
Infection preventionist logs into XDRO registry to retrieve alert and patient information

Trick, Lin (CDC Prevention Epicenter)
Piloting automated CRE alerts

• Pilot 1 (convenience sample)
  – 1 hospital (Stroger) active since Jan 2015
  – 2 hospitals in next month

• Pilot 2 (MedMined hospitals)
  – Plan for 2 hospitals to trial alerts
  – MedMined represents 60+ Illinois hospitals (~42% of hospital beds in state)
Detection of CRE Clusters in Illinois

Slide: Trick, Lin (CDC Prevention Epicenter)
National Intervention to Reduce CRE Incidence
Clinical Cultures at Acute Care Hospitals

<table>
<thead>
<tr>
<th>Variable</th>
<th>2008</th>
<th>2010</th>
<th>2011</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection control consultant</td>
<td>62</td>
<td>85</td>
<td>92</td>
<td>0.055</td>
</tr>
<tr>
<td>Hand hygiene(^22)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Presence of ABHR in each room</td>
<td>85</td>
<td>92</td>
<td>100</td>
<td>0.146</td>
</tr>
<tr>
<td>ABHR at site of care</td>
<td>15</td>
<td>54</td>
<td>85</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Presence of antiseptic soap</td>
<td>15</td>
<td>92</td>
<td>85</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Presence of sink in each room</td>
<td>23</td>
<td>31</td>
<td>46</td>
<td>0.164</td>
</tr>
<tr>
<td>Paper towel availability</td>
<td>69</td>
<td>85</td>
<td>100</td>
<td>0.032</td>
</tr>
<tr>
<td>Compliance audits</td>
<td>0</td>
<td>46</td>
<td>77</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Appropriate use of barrier precautions in context of standard precautions(^23)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gloves</td>
<td>31</td>
<td>69</td>
<td>92</td>
<td>0.001</td>
</tr>
<tr>
<td>Gowns</td>
<td>54</td>
<td>77</td>
<td>77</td>
<td>0.208</td>
</tr>
<tr>
<td>Masks</td>
<td>38</td>
<td>62</td>
<td>69</td>
<td>0.118</td>
</tr>
<tr>
<td>CRE prevention program</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placement of colonized patients in single rooms or cohorting</td>
<td>77</td>
<td>85</td>
<td>100</td>
<td>0.082</td>
</tr>
<tr>
<td>Use of gown and gloves in contact isolation</td>
<td>46</td>
<td>92</td>
<td>100</td>
<td>0.001</td>
</tr>
<tr>
<td>Designated medical equipment</td>
<td>92</td>
<td>100</td>
<td>100</td>
<td>0.221</td>
</tr>
<tr>
<td>Admission screening cultures</td>
<td>15</td>
<td>69</td>
<td>77</td>
<td>0.002</td>
</tr>
<tr>
<td>Contact screening</td>
<td>38</td>
<td>77</td>
<td>100</td>
<td>0.001</td>
</tr>
<tr>
<td>Discontinuation of isolation per standard protocol</td>
<td>15</td>
<td>46</td>
<td>100</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total infection control score (average, out of possible 16)</td>
<td>6.8</td>
<td>11.6</td>
<td>14.0</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Note.** Data are percentage of compliant hospitals (\(n = 13\)), unless otherwise indicated. ABHR, alcohol-based hand rub; CRE, carbapenem-resistant Enterobacteriaceae.
National Intervention to Reduce CRE Incidence: Clinical Cultures & Bacteremia at Acute Care Hospitals

- **CRE acquisitions by clinical culture / 100,000 patient-days**
- **Carbapenem-resistant**
  - *Klebsiella* spp. + *E. coli* bacteremia / 100,000 patient-days
Summary

CRE control can be successful

- Coordinated approach
- Improve detection and inter-facility communication (XDRO registry)
- Antibiotic stewardship
Thank you

<table>
<thead>
<tr>
<th>Illinois’ Infection Control Community</th>
<th>Chicago Dept of Public Health</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Illinois Dept of Public Health</strong></td>
<td></td>
</tr>
<tr>
<td>Craig Conover</td>
<td>Stephanie Black</td>
</tr>
<tr>
<td>Mary Driscoll</td>
<td>Sarah Kemble</td>
</tr>
<tr>
<td>Robynn Leidig</td>
<td>Massimo Pacilli</td>
</tr>
<tr>
<td>Michael Ray</td>
<td></td>
</tr>
<tr>
<td>Erica Runningdeer</td>
<td></td>
</tr>
<tr>
<td><strong>Hektoen Institute</strong></td>
<td><strong>Cook County Dept of Public Health</strong></td>
</tr>
<tr>
<td>Mary Alice Lavin</td>
<td>Mabel Frias</td>
</tr>
<tr>
<td>Angela Tang</td>
<td>Michael Vernon</td>
</tr>
<tr>
<td><strong>CDC</strong></td>
<td></td>
</tr>
<tr>
<td>Lauren Epstein</td>
<td>Wei (Vicky) Gao</td>
</tr>
<tr>
<td>Jennifer Hunter</td>
<td>Mary Hayden</td>
</tr>
<tr>
<td>John Jernigan</td>
<td>Michael Lin</td>
</tr>
<tr>
<td>Alex Kallen</td>
<td>William Trick</td>
</tr>
<tr>
<td></td>
<td>Robert Weinstein</td>
</tr>
</tbody>
</table>
ANTIBIOTIC STEWARDSHIP

And Carbapenem-Resistant Enterobacteriaceae (CRE) in the Acute Care Setting

HOLLY BROWER BSN, RN
INFECTION PREVENTION MANAGER
ST. JOSEPH MEMORIAL HOSPITAL
DISCLOSURE

- I have no relevant financial or nonfinancial relationships related to the Southern Illinois Infection Prevention CRE Workshop to disclose.
Have reduced illness and death since 1940’s

Once lethal infections are now treatable

30-50% of all Antibiotics prescribed in US hospitals are unnecessary or inappropriate

Have serious side effects

The infectious organisms the antibiotics were designed to kill have adapted to them and developed drug resistance
CDC estimates more than two million are infected with Antibiotic-Resistant Organisms.

Approximately 23,000 deaths each year.

Antibiotic Stewardship Programs began to appear in the late 1990’s.

2009 CDC launched “Get Smart for Healthcare” campaign.

http://www.cdc.gov/getsmart/healthcare/
NATIONAL SUMMARY DATA

Estimated minimum number of illnesses and deaths caused by antibiotic resistance*:

At least 2,049,442 illnesses, 23,000 deaths

*bacteria and fungus included in this report

Estimated minimum number of illnesses and death due to *Clostridium difficile* (*C. difficile*), a unique bacterial infection that, although not significantly resistant to the drugs used to treat it, is directly related to antibiotic use and resistance:

At least 250,000 illnesses, 14,000 deaths

WHERE DO INFECTIONS HAPPEN?
Antibiotic-resistant infections can happen anywhere. Data show that most happen in the general community; however, most deaths related to antibiotic resistance happen in healthcare settings, such as hospitals and nursing homes.

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention
EMPIRIC ANTIBIOTIC THERAPY

- When an antibiotic is prescribed based on “clinical judgment” or “best guess” related to patient’s symptoms
- Sensitivity returned and empiric is not always the best therapy
- Followed by Antimicrobial Stewardship Program
SIH AND ANTIBIOTIC STEWARDSHIP

- Began November 2014
- Deanna Olexia RPh, Antibiotic Stewardship Pharmacist for the System
  - Memorial Hospital of Carbondale
  - Herrin Hospital
  - St. Joseph Memorial Hospital
WHAT DOES AN ANTIBIOTIC STEWARDSHIP PHARMACIST DO AT SIH?

- Audit and give feedback to prescribers of Antimicrobial therapy at 48-72 hours
  - Match culture data to therapy.
  - Dose adjustments for renal insufficiency, site of infection, MIC, etc…
  - De-escalation of therapy (try to decrease number of patients on duplicate gram negative coverage or duplicate anaerobic coverage).
WHAT DOES AN ANTIBIOTIC STEWARDSHIP PHARMACIST DO CONT....

- Review Data from Computerized Surveillance system
  - Positive blood cultures
  - Drug-Bug mismatch
  - Identify patients on targeted antimicrobial agents for review (carbapenems, broad spectrum, MRSA agents etc.. for more than 48 hours)
WHAT DOES AN ANTIBIOTIC STEWARDSHIP PHARMACIST DO CONT....

- Developed an antimicrobial formulary
  - Restricted some agents to Infectious Disease physician only
  - Available to any physician for initial therapy (24-48 hrs)
  - Must be reviewed within 24 hours by a member of stewardship team for continuing therapy
WHAT DOES AN ANTIBIOTIC STEWARDSHIP PHARMACIST DO CONT....

- Created pathways for pneumonia
- Created pathway for sepsis
- Help guide antimicrobial therapy
- Meet with Infection Prevention and Infectious Disease Physician monthly to go over findings
<table>
<thead>
<tr>
<th>Month</th>
<th>Total Intervention</th>
<th>Total Recommend</th>
<th>REC Accept</th>
<th>REC Unaccept</th>
<th>Automatic</th>
<th>Accept Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>January</td>
<td>126</td>
<td>90</td>
<td>82</td>
<td>8</td>
<td>36</td>
<td>91.1%</td>
</tr>
<tr>
<td>February</td>
<td>84</td>
<td>70</td>
<td>66</td>
<td>4</td>
<td>14</td>
<td>94.3%</td>
</tr>
<tr>
<td>March</td>
<td>113</td>
<td>88</td>
<td>83</td>
<td>5</td>
<td>25</td>
<td>94.3%</td>
</tr>
<tr>
<td>1st QTR</td>
<td>323</td>
<td>248</td>
<td>231</td>
<td>17</td>
<td>75</td>
<td>93.1%</td>
</tr>
</tbody>
</table>
ANTIBIOTIC STEWARDSHIP PROGRAMS IN THE HOSPITAL

- Optimize the treatment of infections
- Reduce adverse events
- Improve quality of patient care
- Improve patient safety
- Reduce treatment failures
- Increase frequency of correct prescribing therapy and prophylaxis
- Significantly reduce hospital rates of C-Diff and antibiotic resistance
- Save hospital money
CORE ELEMENTS OF HOSPITAL ANTIBIOTIC STEWARDSHIP PROGRAM

- Leadership commitment
- Accountability
- Drug expertise
- Action
- Tracking
- Reporting
- Education
LEADERSHIP

- CRITICAL TO SUCCESS OF PROGRAM
- CAN TAKE DIFFERENT FORMS:
  - Formal statements
  - Stewardship related duties in job descriptions
  - Ensure staff from relevant departments have time for stewardship duties
  - Support stewardship education
  - Ensure participation
ACCOUNTABILITY AND DRUG EXPERTISE

- STEWARDSHIP PROGRAM LEADER
  - Identify a single leader who will be responsible for program outcomes

- PHARMACY LEADER
  - Identify a single pharmacy leader who will co-lead the program
ACTIONS

- DEVELOP AND IMPLEMENT FACILITY SPECIFIC TREATMENT RECOMMENDATIONS
  - BASED ON NATIONAL GUIDELINES FOR ANTIBIOTIC USE IN:
    - Community acquired pneumonia
    - Urinary tract infection
    - Intra-abdominal infections
    - Skin and soft tissue infections
    - Surgical prophylaxis

- IMPLEMENT POLICIES THAT SUPPORT OPTIMAL ANTIBIOTIC USE
  - Document dose, duration, and indication
**TRACKING & REPORTING**

- **MONITOR ANTIBIOTIC PRESCRIBING**
  - Measure if policies and guidelines are being followed
  - Have interventions improved antibiotic use and patient outcomes?

- **ANTIBIOTIC USE MEASURES**
  - **DETERMINE IF PRESCRIBERS HAVE:**
    - Accurately applied diagnostic criteria for infections
    - Prescribed recommended antibiotics
    - Documented, indicated, and planned duration
    - Obtained cultures and relevant tests
    - Modified antibiotic findings to micro findings
EDUCATION

- ANTIBIOTIC STEWARDSHIP PROGRAM WILL PROVIDE REGULAR UPDATES:
  - Antibiotic prescribing
  - Antibiotic resistance
  - Infectious diseases
WHY IS THIS PROGRAM IMPORTANT?

- Promotes proper use of antibiotics
- Decrease C-diff
- Decrease drug resistant organisms
- Prevent NEW drug resistant organisms from forming
- Improves Patient Safety
Carbapenem-Resistant Enterobacteriaceae
An Emerging Threat
Between October 2014 and January 2015, two patients died from CRE at Ronald Reagan UCLA Medical Center after a duodenoscope procedure, 179 others were tested for the bacteria.

Between 2012 and 2014, 35 patients were infected with CRE and 11 died in a Seattle Hospital related to duodenoscope procedure.
SIH RESPONSE TO CRE OUTBREAK

- Be Proactive
- Infection Prevention began investigation
  - Contact Operating Room Managers
    - What duodenscopes are being used
  - Contact all staff processing scopes
    - Are manufacturer’s reprocessing recommendations present?
    - Are manufacturer’s reprocessing recommendations being followed?
    - Infection Prevention staff observe disinfection process at all three SIH Hospitals
WHAT DOES THE SCOPE LOOK LIKE?
SIH RESPONSE TO CRE OUTBREAK CONT....

- Olympus 180 duodenscope involved
  - What SIH facilities use this scope?
  - What is recommended to improve cleaning process?
    - New Brush for properly cleaning extra channel
  - Is all staff properly trained?
    - Staff travel to all three facilities
PROBLEM AREA

the "elevator"
Each facilities cleaning, drying, and reprocessing is evaluated

- Infection Prevention followed the process at each facility
- Findings discussed with Operating Room Managers
- Education planned and completed
**IS IT CLEAN?**

- Bacteria can not be sterilized or disinfected
- New product being used across the system
  - 3-in-1 Channel Check Residual Soil Test Strips
    - Hemoglobin
    - Protein
    - Carbohydrates
Duodenscope is cleaned per recommendations
Small bag attached to end of duodenscope
10 cc syringe with sterile water obtained
Sterile water injected through duodenscope
Sterile water ends in small bag
Small bag removed
Dip stick placed into small bag of sterile water
Wait 90 seconds
Checks for any residual hemoglobin, protein, and/or carbohydrate
Negative results allow duodenscope to move on to reprocessing stage
A positive result would indicate more cleaning needed
What role does Microbiology and Lab have with CRE?

- Calls the nurse caring for patient with any positive culture results
  - Blood
  - Sputum
  - Urine
  - Wound
MICRO, LAB, AND CRE CONT....

- Why is the positive culture called to the nurse?
  - No delay in diagnosis
    - Consult Infectious Disease Physician if needed
  - Treatment can begin sooner
    - Proper antibiotics
  - Move patient to private room without further delay
  - Use of proper PPE
  - Improve patient outcome
**WOUND CULTURE Final**

| Organism 1 | KLEBSIELLA PEUMONIAE |
| Organism 2 | PROTEUS MIRABILIS |

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Organism 1</th>
<th>Organism 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>TRIMETHOPRIM/SULFAMETHOXAZOLE</td>
<td>R $\geq$320</td>
<td>R $\geq$320</td>
</tr>
<tr>
<td>AMOXACILLIN/CLAVULANATE</td>
<td>R $\geq$32</td>
<td>S $\leq$2</td>
</tr>
<tr>
<td>AMPICILLIN</td>
<td>R $\geq$32</td>
<td>R $\geq$32</td>
</tr>
<tr>
<td>AMPICILLIN/SULBACTAM</td>
<td>R $\geq$32</td>
<td>S $\leq$2</td>
</tr>
<tr>
<td>CEFAZOLIN</td>
<td>R $\geq$64</td>
<td>S 8</td>
</tr>
<tr>
<td>CEFTRIAXONE</td>
<td>R $\geq$64</td>
<td>S $\leq$1</td>
</tr>
<tr>
<td>CEFTRIAZIDE</td>
<td>R $\geq$64</td>
<td>S $\leq$1</td>
</tr>
<tr>
<td>CEFEPIMIDE</td>
<td>R 16</td>
<td>S $\leq$1</td>
</tr>
<tr>
<td>CIPROFLOXACIN</td>
<td>R $\geq$4</td>
<td>R $\leq$4</td>
</tr>
<tr>
<td>LEVOFLOXACIN</td>
<td>R $\geq$8</td>
<td>R $\leq$8</td>
</tr>
<tr>
<td>GENTAMICIN</td>
<td>S $\leq$1</td>
<td>S $\leq$1</td>
</tr>
<tr>
<td>ERTAPENEM</td>
<td>R $\leq$0.5</td>
<td></td>
</tr>
<tr>
<td>EXTENDED SPECTRUM B LACTAMASE</td>
<td>-</td>
<td>NEG</td>
</tr>
<tr>
<td>TOBRAMYCIN</td>
<td>I 8</td>
<td>S $\leq$1</td>
</tr>
<tr>
<td>PIPERACILLIN/TAZOBACTAM</td>
<td>R $\geq$128</td>
<td>S $\leq$4</td>
</tr>
</tbody>
</table>

5/3/15-KLEBSIELLA PNEUMONIAE & PROTEUS MIRABILIS BOTH SENT TO ARUP FOR HO DG E TEST.

KLEBSIELLA PNEUMONIAE IS POSITIVE FOR HO DG E TEST.
PROTEUS MIRABILIS IS NEGATIVE FOR HO DG E TEST.
MODIFIED HODGE TEST

(MHT) detects carbapenemase production in isolates of Enterobacteriaceae. In the United States, the most common carbapenemase found in Enterobacteriaceae is the Klebsiella pneumoniae carbapenemase (KPC).

Carbapenemase production is detected when the test isolate produces the enzyme and allows growth of a carbapenem susceptible strain. The result is a characteristic cloverleaf-like indentation.
### SOME CARBAPENEM EXAMPLES

<table>
<thead>
<tr>
<th>Generic</th>
<th>Brand Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imipenem</td>
<td>Primaxin</td>
</tr>
<tr>
<td>Doripenem</td>
<td>Doribax</td>
</tr>
<tr>
<td>Meropenem</td>
<td>Merrem</td>
</tr>
<tr>
<td>Ertapenem</td>
<td>Invanz</td>
</tr>
</tbody>
</table>
HOW ARE WE WORKING TO DECREASE THE SPREAD OF CRE INFECTION?

- Infection Prevention makes daily rounds
  - Hand washing
  - Proper PPE
  - Dedicated equipment in room
  - Contact Precautions sign present
  - Documented Education
  - Private Room

- Infection Prevention reviews Data from Computerized Surveillance system

- Evaluate devices used
  - Central line
  - Foley Catheter
HOW DO WE TREAT CRE?

- Consult Infectious Disease Physician
  - Often resistant to many prescribed antibiotics
  - Decisions to treat made on a case by case assessment
  - Someone may be colonized but not infected and not need treatment
WHAT DO WE DO TO PREVENT THE SPREAD OF CRE?

- Early recognition
  - Nursing called with positive Drug Resistant Organism
- Placing colonized and infected patients on contact precautions
- Use proper PPE & Contact Precautions
- Using medical devices and antimicrobials wisely
  - Nurse driven protocols to review need for Catheters
  - Antibiotic Stewardship Program
  - Infectious Disease Physician to ensure proper antibiotics prescribed
- Education
  - Infection Prevention rounding
DO WE EVER DISCONTINUE CONTACT PRECAUTIONS FOR THE CRE PATIENT?

- There is not enough data for the CDC to make a recommendation.
- It is known that patients can be colonized for long periods of time.
- Do not base on a single negative culture, patients can be intermittently positive on serial surveillance cultures.
- We do not discontinue CRE contact precautions during hospital stay.
Questions?
CRE

Carbapenem Resistant Enterobacteriaceae

Jenny Pierce
Executive Nursing Director with RDK Management Services, Inc.

Disclosure Statement: None
What is CRE?

- A gram-negative bacteria that is nearly resistant to all antibiotics that are listed in the Carbapenem class
- It is considered the new drug resistant “super bug”
- The mortality rate is greater than two of the other known health care infections:
  - MRSA
  - C-Diff
- Statistics show that the death rate is between 40% and 50% of patients infected
Who is at risk?

- Patients in Long-Term Care health settings are the most vulnerable
- Patients in Acute Care settings
- Patients who have had excessive use of certain antibiotics
- Patients who have had certain medical procedures
How does it spread?

- Transmitted person to person
- A person must come in contact or be exposed to the bacteria in order to become infected
- Can be transmitted by direct contact with contaminated skin, feces, or wounds
- By patients who are colonized
- Contaminated medical devices such as:
  - Intravenous Catheters
  - Urinary Catheters
Symptoms

- NO specific symptoms
- Problems that can alert physicians:
  - Severe Pneumonia
  - Sepsis
  - Severe UTI
  - Resistance to Antibiotic Therapy
Diagnosis

- Blood Tests
  - Blood Cultures
  - Drug Sensitivity
Treatment

- A combination of antibiotics can be prescribed to inhibit the growth of the bacteria
- Contact Infectious Disease Expert
  - This bacteria is very difficult to treat and not many treatments have been successful
  - There are currently no new antibiotics in development that show any promise to kill the bacteria
Prevention

- Education
- Hand Hygiene
- Isolating Infected Patients
- Wearing Gowns & Gloves
- Limit Antibiotic Usage
- Limit Usage of Invasive Medical Devices
Conclusion

- Infection Control is **KEY**
- Updated Infection Control Log
- Good Communication
- Education & Knowledge
- Documentation
Contact Information

- Phone
  - (618) 841-6329
- Email
  - jenny@rdkmgmt.com
Laboratory Detection of Carbapenem Resistant Enterobacteriaceae

Thomas Kirn MD PhD
NorthShore University HealthSystem
Evanston, IL
Disclosures

• I have nothing relevant to this presentation to disclose
Objectives

• Participants will be able to:
  – Describe the general structure, mechanism of action and clinical utility of the β lactam class of antibiotics
  – Describe mechanisms of resistance to β lactam antibiotics in Enterobacteriaceae with emphasis on carbapenem resistance
  – Compare/contrast laboratory methods that may be employed to detect and/or characterize carbapenemase producing organisms
  – Critically evaluate (and improve if necessary) current procedures employed in their own laboratories for the detection of carbapenem resistant organisms
Nomenclature

• MDRO
  – Multi drug resistant organism

• CRE
  – Carbapenem resistant Enterobacteriaceae

• CP-CRE
  – Carbapenemase producing CRE
β-Lactams

http://faculty.ccccmd.edu/courses/bio141/lecguide/unit2/control/blactam.html
Mechanisms of Resistance to $\beta$ Lactam Antibiotics
β Lactamase Inhibitors

http://homepage.ntlworld.com/diamonddove/08_BILnhibitors/BILnhi30.gif
<table>
<thead>
<tr>
<th>Penicillins</th>
<th>Cephalosporins</th>
<th>Cephamycins</th>
<th>Monobactams</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin</td>
<td>1st Generation (narrow, G+) Cephalothin</td>
<td>(2nd Gen + Anaerobes)</td>
<td>Aztreonam</td>
</tr>
<tr>
<td>Methicillin</td>
<td>Cefazolin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ampicillin</td>
<td>2nd Generation (expanded, G-) Cefamandole</td>
<td>Cefoxitin</td>
<td></td>
</tr>
<tr>
<td>Ticaricillin</td>
<td>Cefuroxime</td>
<td>Cefotetan</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cefmetazole</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3rd Generation (broad, more G-)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cefotaxime</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ceftazidime</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ceftriaxone</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>4th Generation (extended, G-)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cefepime</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>5th Generation(G+ incl MRSA)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ceftaroline</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Evolution of Carbapenems

A.

- O'Brienic acid (1)
  - MM22381
- Clavulanic acid (2)
- Thienamycin (3)

B.

- Imipenem (4)
  - MK-0787
- Panipenem (5)

- Cilastatin (6)
- Betamipron (7)
- Meropenem (8)
  - SM1343
- Ertapenem (9)
  - MK-0826
  - L-749345
  - D900303
  - LS-18707
  - LS-187767
- Biapenem (10)
  - L627
  - L1C-10627
  - AR10010844
  - CL-186815
- Duripenem (11)
  - S-4611
  - D-23805
Carbapenems

- 4:5 fused ring lactam of penicillins with a double bond between C-2 and C-3 but with substitution of carbon for sulfur at C-1
- First stable carbapenem was imipenem
- Mechanism of action
  - Do not diffuse easily across OM
  - Must be transported by OMPs (porins)
  - Permanently acylate PBPs, inhibiting cell wall synthesis
- Activity
  - Broader spectrum than penicillins/cephalosporins and combinations
  - Imipenem/doripenem – better gram + coverage
  - Meropenem/ertapenem/doripenem – Better gram – coverage
  - Erta less active against *Pseudomonas aeruginosa*
  - Mero less active against *A. baumanii*
  - Dori exhibits lower MICs against Pa and Ab
  - Dori is the most stable in the face of beta-lactamases
<table>
<thead>
<tr>
<th>Penicillins</th>
<th>Cephalosporins</th>
<th>Cephamycins</th>
<th>Monobactams</th>
<th>Carbapenems</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin</td>
<td>1&lt;sup&gt;st&lt;/sup&gt; Generation (narrow, G+)</td>
<td>(2&lt;sup&gt;nd&lt;/sup&gt; Gen + Anaerobes)</td>
<td>Aztreonam</td>
<td>Imipenem</td>
</tr>
<tr>
<td>Methicillin</td>
<td>Cephalothin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ampicillin</td>
<td>Cefazolin</td>
<td></td>
<td></td>
<td>Meropenem</td>
</tr>
<tr>
<td>Ticaricillin</td>
<td>2&lt;sup&gt;nd&lt;/sup&gt; Generation (expanded, G-)</td>
<td>Cefoxitin</td>
<td></td>
<td>Ertapenem</td>
</tr>
<tr>
<td></td>
<td>Cefamandole</td>
<td>Cefotetan</td>
<td></td>
<td>Doripenem</td>
</tr>
<tr>
<td></td>
<td>Cefuroxime</td>
<td>Cefmetazole</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3&lt;sup&gt;rd&lt;/sup&gt; Generation (broad, more G-)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cefotaxime</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ceftazidime</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ceftriaxone</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>4&lt;sup&gt;th&lt;/sup&gt; Generation (extended, G-)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cefepime</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>5&lt;sup&gt;th&lt;/sup&gt; Generation (G+ incl MRSA)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ceftaroline</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Carbapenem resistance is a public health problem

- Increased length of stay
- Increased mortality
  - Limited treatment options for serious infections
- Few new drugs for resistant GNRs
- Mobile genetic elements transmit resistance
- Infection control practices are essential to limit spread of colonization and infection

http://www.cdc.gov/hai/organisms/cre/TrackingCRE.html
Mechanisms of Carbapenem Resistance

# Carbapenemase Classes

<table>
<thead>
<tr>
<th>$\beta$ lactamase Molecular Class</th>
<th>Enzymes</th>
<th>Common Bacteria</th>
<th>Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>KPC, SME, IMI, NMCA, GES</td>
<td><em>K. pneumoniae</em>, others</td>
<td>Chromosomal or Plasmid encoded, partially inhibited by clavulanate and boronic acid</td>
</tr>
<tr>
<td>B - MBLs</td>
<td>IMP, VIM, GIM, SPM, NDM-1</td>
<td><em>S. maltophilia</em>, <em>P. aeruginosa</em></td>
<td>Do not hydrolyze aztreonam, inhibited by EDTA</td>
</tr>
<tr>
<td>C</td>
<td>AmpC</td>
<td>Enterobacteriaceae</td>
<td>Some activity against carbapenems, resistance associated with porin mutations/efflux</td>
</tr>
<tr>
<td>D</td>
<td>OXA</td>
<td><em>A. baumanii</em> Enterobacteriaceae</td>
<td>Not inhibited by EDTA, boronic acid or clavulanate</td>
</tr>
</tbody>
</table>

KPC

- Most prevalent carbapenemase in USA
- At least 22 types of KPC identified
- Encoded by the bla\textsuperscript{KPC} gene which is present on a plasmid
- Plasmid often encodes resistance to other drug classes
- Enterobacteriaceae
- Inhibited by boronic acid compounds

http://www.cdc.gov/hai/organisms/cre/TrackingCRE.html
MBLs

- Require zinc for activity (inhibited by zinc chelators)
- NDM most common example in US
- Carried on a mobile genetic element with additional resistance genes
- Highly transmissible
- Environmental reservoirs in Indian subcontinent, Middle East and Balkan countries
- Enterobacteriaceae, *P. aeruginosa*, *Acinetobacter*

http://www.cdc.gov/hai/organisms/cre/TrackingCRE.html
OXA

- Nearly 500 types
- Most plasmid encoded
- Enterobacteriaceae
- A. baumanii
- Most challenging to detect using current phenotypic methods

http://www.cdc.gov/hai/organisms/cre/TrackingCRE.html
Other Mechanisms of Carbapenem Resistance

• Cephalosporinase combined with altered permeability
  – AmpC, CTX-M may have low-level carbapenemase activity
  – Porin loss limits entry of the carbapenem into the periplasm
  – When combined, these two traits can mediate resistance to carbapenems (organisms will test I or R \textit{in vitro})
  – \textit{Enterobacter} spp., other Enterobacteriaceae

• Intrinsic non-susceptibility
  – \textit{Proteus} spp., \textit{Morganella morganii}, \textit{Providenica} spp. VS imipenem for example
# β-lactam Antibiotics

<table>
<thead>
<tr>
<th>Penicillins</th>
<th>Cephalosporins</th>
<th>Cephamycins</th>
<th>Monobactams</th>
<th>Carbapenems</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin</td>
<td>Penicillin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methicillin</td>
<td>Methicillin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ampicillin</td>
<td>Ampicillin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ticaricillin</td>
<td>Ticaricillin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1&lt;sup&gt;st&lt;/sup&gt; Generation (narrow, G+)</td>
<td>Cefalothin</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cefazolin</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2&lt;sup&gt;nd&lt;/sup&gt; Generation (expanded, G-)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cefamandole</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cefuroxime</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3&lt;sup&gt;rd&lt;/sup&gt; Generation (broad, more G-)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cefotaxime</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ceftazidime</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ceftriaxone</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>4&lt;sup&gt;th&lt;/sup&gt; Generation (extended, G-)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cefepime</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>5&lt;sup&gt;th&lt;/sup&gt; Generation (G+ incl MRSA)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ceftaroline</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Penicillins</td>
<td>Cephalosporins</td>
<td>Cephamycins</td>
<td>Monobactams</td>
<td>Carbapenems</td>
</tr>
<tr>
<td>-------------</td>
<td>---------------------</td>
<td>--------------</td>
<td>-------------</td>
<td>---------------</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(2nd Gen +</td>
<td></td>
<td>Imipenem</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Anaerobes)</td>
<td></td>
<td>Meropenem</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cefoxitin</td>
<td></td>
<td>Ertapenem</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cefotetan</td>
<td></td>
<td>Doripenem</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cefmetazole</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ESBL

CTX-M, SHV, TEM
β-lactam Antibiotics

<table>
<thead>
<tr>
<th>Penicillins</th>
<th>Cephalosporins</th>
<th>Cephamycins</th>
<th>Monobactams</th>
<th>Carbapenems</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin</td>
<td>Methicillin</td>
<td>Ampicillin</td>
<td>Ticaricillin</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Imipenem</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Meropenem</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Ertapenem</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Doripenem</td>
</tr>
</tbody>
</table>

4th Generation (extended, G-)
Cefepime

AmpC
<table>
<thead>
<tr>
<th>Penicillins</th>
<th>Cephalosporins</th>
<th>Cephamycins</th>
<th>Monobactams</th>
<th>Carbapenems</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin</td>
<td>Methicillin</td>
<td>Ampicillin</td>
<td>Ticaricillin</td>
<td>Cephalothin</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1st Genera</td>
<td>1st Genera</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(narrow,</td>
<td>(narrow,</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>G+ )</td>
<td>G+ )</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Cefamandole</td>
<td>Cefuroxime</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2nd Genera</td>
<td>2nd Genera</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(expanded,</td>
<td>(expanded,</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>G- )</td>
<td>G- )</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Cefotaxime</td>
<td>Cefazidime</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3rd Genera</td>
<td>3rd Genera</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(broad,</td>
<td>(more</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>G- )</td>
<td>G- )</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Cefepime</td>
<td>Ceftazidime</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>4th Genera</td>
<td>4th Genera</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(extended,</td>
<td>(extended,</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>G- )</td>
<td>G- )</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Cefaroline</td>
<td>Aztreonam</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**MBL**
### β-lactam Antibiotics

<table>
<thead>
<tr>
<th>Penicillins</th>
<th>Cephalosporins</th>
<th>Cephamycins</th>
<th>Monobactams</th>
<th>Carbapenems</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin</td>
<td>Methicillin</td>
<td>Ampicillin</td>
<td>Ticaricillin</td>
<td></td>
</tr>
<tr>
<td>Cephalothin</td>
<td>Cefuroxime</td>
<td>Cefotaxime</td>
<td>Cepazidime</td>
<td></td>
</tr>
<tr>
<td>Cefamandole</td>
<td>Cefuroxime</td>
<td>Cefotaxime</td>
<td>Cepazidime</td>
<td></td>
</tr>
<tr>
<td>Cefoxitin</td>
<td>Cefoxitin</td>
<td>Cepazidime</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cefotetan</td>
<td>Cefoxitin</td>
<td>Cepazidime</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cefmetazole</td>
<td>Cefoxitin</td>
<td>Cepazidime</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **1st Generation (narrow, G+)**
- **2nd Generation (expanded, G-)**
- **3rd Generation (broad, more G-)**
- **4th Generation (extended, G-)**
- **5th Generation (G+ incl MRSA)**

**Carbapenems**
- Imipenem
- Meropenem
- Ertapenem
- Doripenem

**KPC**
CDC Definition of CRE

- As of January 2015:
  - **Resistant** to imipenem, meropenem, doripenem, or ertapenem OR documentation that the isolate possesses a carbapenemase

- The previous CDC CRE definition (nonsusceptible to imipenem, meropenem, or doripenem, AND resistant to all third generation cephalosporins tested) was designed to be more specific for CP-CRE; however, it has proven to be complicated, difficult to implement, and has been found to miss some CP-CRE

http://www.cdc.gov/hai/organisms/cre/definition.html
Distinguishing CP-CRE from other CRE

• Why?
  – Identify isolates resistant to all carbapenems and other β-lactams
  – May need to modify antibiogram (2010 and earlier CLSI carbapenem breakpoints)
  – Infection control
    • CP-CRE are the greatest public health/infection control threat
  – Contribute to national surveillance efforts
Distinguishing CP-CRE from other CRE

• How?
  – Methods that detect carbapenemases
  – Methods that characterize carbapenemases
  – Combinations
# CLSI Carbapenem Breakpoints

<table>
<thead>
<tr>
<th>Antimicrobial</th>
<th>CLSI M100-S19 (2009) MIC (µg/mL)</th>
<th>Updated CLSI M100-S23 (2013) MIC (µg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>S</td>
<td>I</td>
</tr>
<tr>
<td>Imipenem</td>
<td>≤ 4</td>
<td>8</td>
</tr>
<tr>
<td>Meropenem</td>
<td>≤ 4</td>
<td>8</td>
</tr>
<tr>
<td>Ertapenem</td>
<td>≤ 2</td>
<td>4</td>
</tr>
<tr>
<td>Doripenem</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Antimicrobial</th>
<th>CLSI M100-S19 (2009) disk zones (mm)</th>
<th>Updated CLSI M100-S23 (2013) disk zones (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>S</td>
<td>I</td>
</tr>
<tr>
<td>Imipenem</td>
<td>≥ 16</td>
<td>14-15</td>
</tr>
<tr>
<td>Meropenem</td>
<td>≥ 16</td>
<td>14-15</td>
</tr>
<tr>
<td>Ertapenem</td>
<td>≥ 19</td>
<td>16-18</td>
</tr>
<tr>
<td>Doripenem</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>
Detection of Carbapenemases - CLSI

Introduction to Tables 3B and 3C. Tests for Carbapenemases in Enterobacteriaceae, Pseudomonas aeruginosa, and Acinetobacter spp.

Institutional infection control procedures or epidemiological investigations may require identification of carbapenemase-producing Enterobacteriaceae, P. aeruginosa, and Acinetobacter spp. Such testing is not currently recommended for routine use.

Carbapenemase-producing isolates of Enterobacteriaceae usually test intermediate or resistant to one or more carbapenems using the current interpretive criteria as listed in Table 2A (NOTE: Ertapenem nonsusceptibility is the most sensitive indicator of carbapenemase production), and usually test resistant to one or more agents in cephalosporin subclass III (eg, cefoperazone, cefotaxime, cefazidime, ceftazidime, ceftriaxone, and cefotaxime). However, some isolates that produce carbapenemases such as SME or IMI often test susceptible to these cephalosporins.

Laboratories using Enterobacteriaceae minimal inhibitory concentration (MIC) interpretive criteria for carbapenems described in M100-S20 (January 2010) should perform the modified Hodge test (MHT), the Carba NP test, and/or a molecular assay as described below when isolates of Enterobacteriaceae are suspicious for carbapenemase production based on imipenem or meropenem MICs of 2–4 μg/mL or ertapenem MIC of 2 μg/mL. Refer to Tables 3B-1 or 3C-1 for specific steps to use with interpretive criteria for carbapenems listed in M100-S20 (January 2010).

<table>
<thead>
<tr>
<th>Tests Used for Epidemiological or Infection Control-Related Testing</th>
<th>MHT</th>
<th>Carba NP</th>
<th>Other (eg, molecular assays)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Organisms</td>
<td>Enterobacteriaceae that are nonsusceptible to one or more carbapenems</td>
<td>Enterobacteriaceae, P. aeruginosa, and Acinetobacter spp. that are nonsusceptible to one or more carbapenems</td>
<td>Enterobacteriaceae, P. aeruginosa, and Acinetobacter spp. that are nonsusceptible to one or more carbapenems to determine the presence of a carbapenemase, or to determine carbapenemase type in isolates positive by MHT or Carba NP</td>
</tr>
<tr>
<td>Strengths</td>
<td>Simple to perform</td>
<td>Rapid</td>
<td>Determines type of carbapenemase in addition to absence or presence of the enzyme</td>
</tr>
<tr>
<td>Limitations</td>
<td>False-positive results can occur in isolates that produce ESBL or AmpC enzymes coupled with porin loss. False-negative results are occasionally noted (eg, some isolates producing NDM carbapenemase). Only applies to Enterobacteriaceae.</td>
<td>Special reagents are required, some of which require in-house preparation (and have a short shelf life). Invalid results occur with some isolates. Certain carbapenemase types (eg, OXA-type, chromosomally encoded) are not consistently detected.</td>
<td>Special reagents and equipment required. Specific to targeted genes; false-negative result if specific carbapenemase gene present is not targeted</td>
</tr>
</tbody>
</table>

Abbreviations: ESBL, extended-spectrum β-lactamase; MHT, modified Hodge test; NDM, New Delhi metallo-β-lactamase.
## Detection of Carbapenemases - CLSI

**Table 3B-1. Modifications of Table 3B When Using Interpretive Criteria for Carbapenems Described in M100-S20 (January 2010)**

<table>
<thead>
<tr>
<th>Test</th>
<th>Confirmatory Test</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>When to Do This Test:</strong></td>
<td>Until laboratories can implement the current carbapenem MIC interpretive criteria, this test (or an alternative confirmatory test for carbapenemases) should be performed when isolates of <em>Enterobacteriaceae</em> are suspicious for carbapenemase production based on imipenem or meropenem MICs of 2–4 µg/mL or ertapenem MIC of 2 µg/mL.</td>
</tr>
<tr>
<td><strong>Reporting</strong></td>
<td>For isolates that are MHT positive and have an ertapenem MIC of 2–4 µg/mL, imipenem MIC of 2–8 µg/mL, or meropenem MIC of 2–8 µg/mL, report all carbapenems as resistant. If the MHT is negative, interpret the carbapenem MICs using CLSI interpretive criteria as listed in Table 2A in M100-S20 (January 2010). <strong>NOTE:</strong> Not all carbapenemase-producing isolates of <em>Enterobacteriaceae</em> are MHT positive and MHT-positive results may be encountered in isolates with carbapenem resistance mechanisms other than carbapenemase production.</td>
</tr>
</tbody>
</table>

Abbreviations: MHT, modified Hodge test; MIC, minimal inhibitory concentration.
Modified Hodge Test

- Not specific for carbapenemases
- AmpC with porin loss/efflux could be positive
- May miss NDM producing isolates
Carba NP

- Nordmann and Poirel
- Enterobacteriaceae, *P. aeruginosa* and *Acinetobacter*
- Imipenem is hydrolyzed, producing a color change

<table>
<thead>
<tr>
<th>Solution A</th>
<th>Solution B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Red</td>
<td>Orange</td>
</tr>
<tr>
<td>Red</td>
<td>Light Orange</td>
</tr>
<tr>
<td>Red</td>
<td>Dark Yellow</td>
</tr>
<tr>
<td>Red-orange</td>
<td>Yellow</td>
</tr>
<tr>
<td>Red-orange</td>
<td>Yellow</td>
</tr>
</tbody>
</table>

**Results for Patient and QC Tubes**

<table>
<thead>
<tr>
<th>Tube “a”: Solution A (serves as internal control)</th>
<th>Tube “b”: Solution B</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Red or red-orange</td>
<td>Red or red-orange</td>
<td>Negative, no carbapenemase detected</td>
</tr>
<tr>
<td>Red or red-orange</td>
<td>Light-orange, dark yellow, or yellow</td>
<td>Positive, carbapenemase producer</td>
</tr>
<tr>
<td>Red or red-orange</td>
<td>Orange</td>
<td>Invalid</td>
</tr>
<tr>
<td>Orange, light-orange, dark yellow, or yellow</td>
<td>Any color</td>
<td>Invalid</td>
</tr>
</tbody>
</table>
Carba NP

- Sometimes difficult to interpret results
- Reagents must be made fresh
- Not great for detection of OXA-48
Carbapenem Inactivation Method

Suspend full loop of bacteria in H₂O → Add 10 µg meropenem disk → Incubate for 2 hours 35°C → Place on Mueller Hinton agar inoculated with *E. coli* ATCC 25922

Incubate for at least 6 hours 35°C → Read presence or absence of inhibition zone

Fig 1. Schematic of the CIM.
Table 1. Isolates used for validation of the CIM.

<table>
<thead>
<tr>
<th>Species</th>
<th>Carbapenemase gene</th>
<th>CIM</th>
<th>CarbaNP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Klebsiella pneumonia</td>
<td>KPC-2</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Klebsiella pneumonia</td>
<td>NDM-1</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Klebsiella pneumonia</td>
<td>OXA-48</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Klebsiella pneumonia</td>
<td>OXA-48</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Klebsiella pneumonia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Klebsiella pneumonia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Escherichia coli</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Escherichia coli</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Escherichia coli</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Escherichia coli</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Escherichia coli</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Escherichia coli ATCC25922</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enterobacter cloacae</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enterobacter cloacae</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Salmonella Barilly</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Salmonella Heidelberg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>VIM-2</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>VIM-2</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>IMP-1</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>GIM-1</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>SPM-1</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>AIM-1</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>BIC-1</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>DNI-1</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Acinetobacter baumannii</td>
<td>OXA-23</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Acinetobacter baumannii</td>
<td>OXA-40</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Acinetobacter baumannii</td>
<td>OXA-58</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Acinetobacter baumannii</td>
<td>OXA-143</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Acinetobacter baumannii</td>
<td>SIM-1</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>
EPI-CRE

Carbapenem-Resistant Enterobacteriaceae (CRE)

It’s Easy to See...

CRE Negative - Red

CRE Positive - Yellow (with violet precipitate)

Specifications

Time to Results:
- **Positive** – as soon as the sample changes from red to yellow.
- **Negative** – after 24 hours if no color change from red occurs.

Storage:
- From 2 to 30 °C under dry conditions, EPI-CRE® is stable for 1 year from date of manufacture.

Sensitivity & Specificity:
- EPI-CRE® detects only living bacteria. It is 100% specific.

Regulatory:
- CE/IVD approved.

Distributed by:

Pilots Point
Pilots Point LLC
Building 174
242 S. Washington Blvd
Sarasota, FL 34236
info@pilotspoint.net
www.pilotspoint.net

Patents: U.S. and/or international patents issued, pending, or applied for.
EPI-CRE, Pilots Point, and the Pilots Point logo are trademarks or registered trademarks of Pilots Point LLC.
EPI-CRE® is intended to be used as an epidemiological surveillance tool. It is not an antibiotic susceptibility test.
MALDI

Characterization of Carbapenemases
MBL Disk Test/MBL Etest

- EDTA, dipicolinic acid, mercaptopropionioic acid all may be used as inhibitors of MBLs
- EDTA may permeabilize cells

Figure 2. Clear cut MBL negative: MP/MPi IC <0.125/<0.032

Figure 3. Clear cut MBL positive: MP/MPi IC >8/0.15 = >42

Figure 4. Phantom zone between MP/MPi is indicative of MBL
Boronic Acid Methods

Carba NP Test II

A

No carbapenemase
Impiperon + Zn²⁺
Impiperon + Zn²⁺ + Tazobactam
Impiperon + EDTA

No antibiotic
Ambler class A carbapenemase
Ambler class B carbapenemase
Ambler class D carbapenemase
Not interpretable

B

No antibiotic
Impiperon + Zn²⁺
Impiperon + Zn²⁺ + Tazobactam
Impiperon + EDTA

K. pneumoniae A28006 (KPC-2)
E. coli L1-1 (KPC-2)
E. coli JAT (IMP-1)
P. aeruginosa 12870 (IMP-1)

E. coli MAD (VIM-1)
P. aeruginosa KA-209 (VIM-2)
E. coli 271 (NDM-1)
P. aeruginosa 73-5674 (GIM-1)
P. retgeri RAP (OXA-181)
K. pneumoniae B1C (OXA-48)
Limitations of Inhibition Assays

- Interpretation can be subjective
- Requires overnight incubation in most cases
- Limitations in detecting OXAs
- Multiple methods may need to be used in combination to detect more than one enzyme (AmpC plus KPC for example)
NAATs

• Single PCR reactions vs multiplex panels
• Target driven:
  – KPC, NDM, VIM, IMP, OXA, etc...
• FDA cleared assays for signal positive BC panels exist (Biofire, Verigene)
• BD MAX CRE assay (KPC, NDM, OXA48)
• Check Points (KPC, VIM, NDM, OXA48, OXA181)
• Others, LDTs
• Time consuming, technically complex, validation
CRE Surveillance Cultures

- Active surveillance allows for detection of patients colonized with CRE in the intestinal tract.
- Patients who are found to be colonized or infected with CRE should be placed on Contact Precautions in order to prevent transmission of the resistant bacteria.
- Additionally, it allows additional opportunities for recovery of organisms.
- Who to screen?
  - Everyone, critically ill
- When to screen?
  - Admission, at defined intervals
- How to screen
  - Broth enrichment followed by selective culture
  - Direct KB disk test
  - Chromogenic Agar
  - NAATs
  - Combinations
MDRO Surveillance at NorthShore

• Screen all ICU admissions
• Weekly sampling from patients in the ICU (rotating among 4 hospitals)
• Respiratory (sputum/throat), axillae, rectum
• Pooled specimens inoculated to VACC agar
• Pooled specimen PCR (CTX-M, KPC, NDM)
• Quarterly point prevalence screening
IDPH Guidance/Recommendations

• For *E. coli* and *Klebsiella* spp. non-susceptible to any carbapenem and resistant to all 3rd generation cephalosporins, test for carbapenemases. Testing should include a method for detection of metallo-beta-lactamase (MBL). Examples of acceptable testing methods are shown below.
  
  – Modified Hodge Test (MHT)
  – MBL Etest*
  – MBL Screen test*
  – Tablet/disc diffusion detection of KPC/MBL resistance mechanisms* 
  – Boronic Acid Inhibition Test for KPC and AmpC
  – Broth microdilution-BMD MBL screen6,7*
  – CarbaNP test to detect carbapenemases* 
  – MALDI-TOF detection of carbapenemases* 

*These tests have the potential to detect MBL production

1. Perform Modified Hodge Test (MHT) for carbapenemase detection AND
2. Perform MBL Etest3. 
3. If MBL Etest positive, regardless of MHT results, report results as follows:

• **Carbapenem resistant Enterobacteriaceae (CRE) detected by EDTA Inhibition Test –probable MBLtype. Implement infection control measures according to facility policy.”**
• **Isolates that are MBL positive should be forwarded to IDPH lab for confirmation and further characterization. Prior to sending specimens, laboratories should contact local health department for approval. The authorization number provided by the LHD must be printed on the laboratory test requisition form in order for the specimen to be tested.**

If MHT positive, but MBL Etest negative report results as follows:

• **Carbapenem resistant Enterobacteriaceae (CRE) detected by Modified Hodge Test –probable KPC type. Implement infection control measures according to facility policy.”**
**CRE surveillance criteria**

Enterobacteriaceae (e.g., *E. coli*, *Klebsiella* spp, *Enterobacter* spp, *Proteus* spp, *Citrobacter* spp, *Serratia* spp, *Morganella* spp, or *Providentia* spp) with one of the following laboratory test results:

1. Molecular test (e.g., polymerase chain reaction [PCR]) specific for carbapenemase;
2. Phenotypic test (e.g., Modified Hodge) specific for carbapenemase production;
3. Susceptibility test (for *E. coli* and *Klebsiella* spp only): non-susceptible (intermediate or resistant) to ONE of the following carbapenems (doripenem, meropenem, or imipenem) AND resistant to ALL of the following third generation cephalosporins tested (ceftiraxone, cefotaxime, and ceftazidime). **Note: ignore ertapenem for this definition.**

Report 1<sup>st</sup> CRE event per patient per encounter
Submission of Isolates to IDPH (1)
Submission of Isolates to IDPH (2)

For all possible CRE, labs should attempt to identify mechanism of resistance:
Is the isolate a carbapenemase producer?

**Option A: Genotypic testing** (e.g. PCR)
- Positive PCR
- Negative PCR

**Option B: Phenotypic testing**
- For example: Modified Hodge Test (MHT) AND meropenem MBL Test
- Both tests Negative
- Either test Positive
- No other testing done

**Option C: Lab unable to identify mechanism of resistance**
(No further testing or ONLY Modified Hodge Test done)

- Discuss result and epidemiologic risk factors with referring facility.
- Submit isolate to IDPH if patient has risk factors for non-KPC carbapenemase (e.g. international travel in last 6 months, exposure to non-KPC strains, or newly recognized cluster).

For carbapenemase-producing CRE (e.g. KPC, NDM, VIM, IMP, OXA)
- Submit isolate to IDPH if carbapenemase is NOT KPC.

For likely not carbapenemase-producing CRE
- Do not routinely submit isolate to IDPH.

For likely carbapenemase-producing CRE
- Negative MBL Test and Positive MHT
- Likely KPC-producing CRE
- Do not submit isolate to IDPH unless KPC has not previously been identified in your laboratory.

For positive MBL Test (MHT positive OR negative)
- Likely MBL-producing CRE (e.g. NDM, VIM)
- Submit isolate to IDPH.

*Other phenotypic tests are available and may be used; this two-step process is most common.*
What about new drugs?

<table>
<thead>
<tr>
<th></th>
<th>Gram +</th>
<th>Gram −</th>
<th>AmpC</th>
<th>ESBL</th>
<th>KPC</th>
<th>Metallo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ceftolozane/Tazobactam</td>
<td>−</td>
<td>++</td>
<td>+/−</td>
<td>++</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>Ceftazidime/Avibactam</td>
<td>+/−</td>
<td>+++</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>−</td>
</tr>
</tbody>
</table>
Summary

• CRE are an important cause of serious infections and of infection control/epidemiologic importance

• Detecting and/or characterizing CP-CRE is important for epidemiologic purposes and may have therapeutic decision making utility

• A perfect method for CP-CRE detection/characterization does not yet exist