Carbapenem-Resistant Enterobacteriaceae (CRE): Epidemiology and Prevention

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Division of Healthcare Quality Promotion
Centers for Disease Control and Prevention

No Disclosures
The findings and conclusions in this report are those of the author and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Objectives
- At the end of the presentation attendees should be able to:
  - Recognize the importance of preventing further carbapenem-resistant Enterobacteriaceae (CRE) dissemination
  - Describe the basic epidemiology of CRE in the United States
  - Understand interventions that can prevent CRE transmission in healthcare settings

Enterobacteriaceae
- Normal human gut flora & environmental organisms
- More than 70 species
  - Most common cause of HAI: E. coli, Klebsiella, and Enterobacter
  - These three make up about ¼ of HAI reported to NHSN
- Also important cause of community-associated infections
  - Some of the most common organisms encountered in clinical laboratories
- Resistance to β-lactams has been a concern for decades
  - Extended-spectrum β-lactamases (ESBLs)
- Carbapenems
  - Imipenem, meropenem, doripenem, ertapenem
- Carbapenem-resistance rare before 2000, involved combination of mechanisms
Carbapenemases – Enzymes that break down carbapenem and β-lactam antibiotics (generally)


CDC, unpublished data

Carbapenemase-producing CRE in the United States


CDC, unpublished data

KPC-producing CRE in the United States


CDC, unpublished data
### Main Carbapenemases

<table>
<thead>
<tr>
<th>Enzyme</th>
<th>Classification</th>
<th>Activity</th>
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</thead>
<tbody>
<tr>
<td>KPC</td>
<td>Class A</td>
<td>Hydrolyzes all β-lactam agents</td>
</tr>
<tr>
<td>NDM</td>
<td>Class B: metallo-β-lactamase (MBL)</td>
<td>Hydrolyzes all β-lactam agents except aztreonam</td>
</tr>
<tr>
<td>IMP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VIM</td>
<td>Class D</td>
<td>Hydrolyzes carbapenems but not active against 3rd generation cephalosporins</td>
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<tr>
<td>OXA</td>
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### Carbapenemase-producing CRE in the United States

**KPC, NDM, VIM, IMP, OXA**

### Change in CRE incidence, 2001-2011

<table>
<thead>
<tr>
<th>Organism</th>
<th>National Nosocomial Infection Surveillance System, Number (%) of isolates</th>
<th>National Healthcare Safety Network, Number (%) of isolates</th>
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<tr>
<td><strong>Klebsiella pneumoniae and oxytoca</strong></td>
<td>654</td>
<td>253 (38.7)</td>
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<td>E. coli</td>
<td>1,424</td>
<td>421 (29.6)</td>
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<td>553</td>
<td>288 (52.1)</td>
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<td>962 (36.6)</td>
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**Why are CRE Clinically and Epidemiologically Important?**

- Cause infections associated with high mortality rates
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- Cause infections associated with high mortality rates
- Resistance is highly transmissible
  - Between organisms – plasmids
  - Between patients
- Treatment options are limited
  - Pan-resistant strains identified
  - Could be decades before new agents are available to treat

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**Mortality**

![Mortality graph](image)

- Overall Mortality: OR 3.71 (1.97-7.01)
- Attributable Mortality: OR 4.5 (2.16-9.35)

*Patel et al. Infect Control Hosp Epidemiol 2008;29:1099-1106*
Why are CRE Clinically and Epidemiologically Important?

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- Resistance is highly transmissible
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  - Between patients
- Treatment options are limited
  - Pan-resistant strains identified
  - Could be decades before new agents are available to treat
- Potential for spread into the community
  - E. coli common cause of community infection

In most areas in the United States this organism appears to infrequently identified

Facilities Reporting at least 1 CRE (CAUTI or CLABSI) to NHSN, First Half 2012

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<td>Long-term acute care hospital</td>
<td>36</td>
<td>202</td>
<td>17.8</td>
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Prevention

http://www.cdc.gov/hai/organisms/cre/cre-toolkit/

Surveillance and Definitions

- Facilities/Regions should have an awareness of the prevalence of CRE in their Facility/Region
- No easy way right now to check for carbapenemases
  - MHT can miss NDM and be "false-positive" for Enterobacter
  - Molecular testing not available at most local labs
- Could concentrate on Klebsiella and E. coli that are NS to a carbapenem
  - Adding it to a third-generation cephalosporin to the definition might increase specificity for most carbapenemase-producers
  - Ceftazidime, cefotaxime, ceftazidime
Interventions

- **Core**
  - Hand hygiene
  - Contact Precautions
  - HCP education
  - Minimizing device use
  - Patient and Staff cohorting
  - Laboratory notification
  - Antimicrobial stewardship
  - CRE Screening

- **Supplemental**
  - Active surveillance cultures
  - Chlorhexidine bathing

Contact Precautions

- CP for patients colonized or infected with CRE
- Systems in place to identify patients at readmission
- Adherence monitoring
- Duration of CP not clear
  - Carriage can be prolonged (months)
  - In one study, 13/55 (24%) >720 days from first CRE culture still positive
- Risk factors for persistent carriage
  - Abx use (Quinolones)
  - D/c to or from LTC
  - Short duration (< 3 mos) since positive CRE culture
  - Poor functional status
  - Presence of devices

Schechner V et al. ICHE 2011;32:497-503

Number of Cultures for CRE Clearance

- One negative (N=97) – 65 (67%) cleared
- Two negative (N=67) – 57 (85%) cleared
- Three negative (N=50) – 45 (90%) cleared

Patient and Staff Cohorting

- Place CRE patients in single rooms (when available)
- Consider cohorting (even when in single rooms) patients and staff that care for them if multiple cases
- If limited single rooms, preference should be given to patients at highest risk for transmission such as patients with incontinence, medical devices, or wounds with uncontrolled drainage

CRE Screening Rationale

- Studies suggest that only a minority of patients colonized with CRE will have positive clinical cultures
  - A study of surveillance cultures at a US hospital found that they identified a third of all positive CRKP patients.
  - Not having these patients in CP resulted in about 1400 days of unprotected exposure.

  Calfee et al. ICHE 2008;29:966-8

CRE Screening

- Stool, rectal, peri-rectal; addition of inguinal might increase sensitivity
- Link to laboratory protocol http://www.cdc.gov/ncidod/dhqp/pdf/ar/Klebsiella_or_E.coli.pdf
- Description of types
  - Screening of epidemiologically-linked patients
    - Point prevalence survey
  - Active surveillance cultures
    - Ongoing systematic screening of patients (usually at admission) who are not necessarily epidemiologically-linked to cases
    - High-risk patients or patients admitted to high-risk settings

  Thurlow C et al. ICHE 2013;34:56-61
Chlorhexidine Bathing

- Limited evidence for CRE
  - Used effectively in outbreak in LTACH as part of a package of interventions
  - Applied to all patients regardless of CRE colonization status
  - Has shown decrease transmission of MRSA and VRE
- Some studies suggest CHG bathing may not always be done “well”

Munoz-Price et al. ICHE 2010;31:341-7

Regional Approach to CRE Prevention

Figure 3. Patient flow among regional health care facilities. Outbreaks of infection with multi-drug resistant organisms have been found to follow the flow of colonized patients across institutions.


Thanks for your attention
Carbapenem-Resistant *Enterobacteriaceae* (CRE): State Surveillance for Prevention

Wendy Bamberg, MD
Medical Epidemiologist, Infectious Diseases
Healthcare-Associated Infections Program Manager
Colorado Department of Public Health and Environment

Financial Disclosures

• None

Objectives

• Describe how state-level CRE surveillance is useful to infection preventionists.
• Describe challenges that might occur with CRE prevention efforts and steps to overcome them
• Describe the importance of collaboration between health departments, infection preventionists and other partners to prevent CRE transmission
CRE: A Public Health Problem

- Difficult to treat
- High mortality rates (up to half of invasive infections)
- Identified in at least 42 states
- **Transmission is preventable** through appropriate infection control measures

The prevalence and incidence of CRE in Colorado are unknown.

CDC 2012 CRE Toolkit*

“Health departments should understand the prevalence or incidence of CRE in their jurisdiction by performing some form of regional surveillance for these organisms.”

![CDC CRE Toolkit Image](http://www.cdc.gov/hai/organisms/cre/cre-toolkit/index.html)

Engaged Partners

- Formed a working group to determine the best next steps for detecting and preventing the transmission of CRE
  - Physicians, infection control experts, pharmacists, laboratorians, public health officials, and the hospital association
  - Recommended systematically tracking CRE in Colorado
  - Very interested in seeing accurate data on CRE in Colorado and regionally
- Engaged laboratories, health-care facilities, and providers in the process of making CRE a reportable condition in Colorado
- The process itself increased awareness of the public health importance of CRE
CRE Outbreak

- August 2012, Hospital A reported 2 cases of carbapenem-resistant Klebsiella pneumoniae to the health department
- Hospital A had been part of CRE working group
- 6 additional cases were found
- Cases were positive for the New Delhi metallo-beta-lactamase (NDM) enzyme
- First NDM in Colorado; largest NDM outbreak in the U.S. at that time

Objectives of Performing CRE Surveillance

- Colorado early in the emergence of CRE – opportunity for prevention
- Provide facility-specific education
  - Each new case – opportunity to provide education and guidance to the facility in real time
  - Laboratories – provide education about CRE
- Provide statewide and regional data
- Ability to track rates over time
- Ability to detect outbreaks
- Ability to detect new community onset cases

Colorado CRE Definition

CRE became reportable November 30, 2012

- Escherichia coli, Klebsiella species, and Enterobacter species that are intermediate or resistant to at least one carbapenem (including imipenem, meropenem, doripenem, or ertapenem) AND resistant to all third-generation cephalosporins tested (ceftriaxone, cefotaxime, and ceftazidime)
- OR
- Escherichia coli, Klebsiella species, and Enterobacter species that test positive for carbapenemase production (by any method, including the Modified Hodge Test, disk diffusion, or PCR)
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Utility of State Surveillance for Infection Preventionists

- Provides information about what is happening in your state and your region
  - Incidence and prevalence
  - Patient populations
  - Types of facilities where CRE is concentrated
  - If facility-specific information reported, specific facilities that might be a risk

- Detect outbreaks earlier, including multi-facility outbreaks.

CDC 2012 CRE Toolkit*

6. Screening
Screen patients with epidemiologic links to unrecognized CRE colonized or infected patients and/or conduct point prevalence surveys of units containing unrecognized CRE patients

Purpose
To identify unrecognized CRE colonization

Specimen type
Stool, rectal, or peri-rectal cultures
(sometimes wounds or urine in select cases)

Facility types
Both acute and long-term care settings

Who should be screened?
Epidemiologically linked contacts of known CRE colonized or infected patients:
- When previously unrecognized CRE is detected.
- Point prevalence surveys: Can be useful when unreported CRE is detected in a review of clinical cultures.
- High risk patients at admission: Patients who received medical care outside the US. Patients transferred from facilities known to have CRE.

CRE Screening Test

- Ertapenem or Meropenem disc
- Rectal, peri-rectal or stool specimen
- Broth
- Incubate overnight
- Agar plate (MacConkey)
- Incubate overnight
- Confirm CRE by antimicrobial susceptibility or carbapenemase test

CRE Screening Challenges

- Takes laboratories several weeks to get up and running. Advisable to get this done in advance.
- Can miss some patients who are colonized with CRE (sensitivity not 100%)
- Positive screen needs confirmation with routine microbiologic methods (specificity not 100%)
- CDC laboratory protocol* for screening is validated only for *E. coli* and *Klebsiella* sp.

*http://www.cdc.gov/HAI/pdfs/labSettings/Klebsiella_or_Ecoli.pdf
Example of Screening Success
CRE Outbreak

• 3 patients with CRE with infections had been located on 4 units
• Point prevalence surveys were undertaken on these 4 units
• An additional 5 patients with CRE colonization were detected through screening
• 10 other patients were found to have CRE that were not part of the outbreak

Example of Infection Control Challenges

• Rehabilitation facility identified a patient with CRE in urine
• Facility has a unique patient population: traumatic brain injuries
• Rehabilitation involved daily living situations
• Initial precautions involved use of gloves/gowns for contact only with colonized areas (urine, stool)
• Screening of 21 epidemiologically linked patients yielded no additional patients with CRE