CRE
Carbapenem-resistant
Enterobacteriaceae

September 25, 2014
Welcome & Objectives

Participants will:
1. Be educated in the CRE priority for state-wide focus
2. Learn how collaboration within the Indianapolis Patient Safety Coalition has led to the development of a CRE protocol in control and prevention across the continuum of care
3. Be provided with tools to conduct an organizational assessment
4. Be provided with resources to support organizational CRE protocol development by December 31, 2014
Measure Title: CDC CRE Toolkit

Description: The Facility has implemented the Core Measures described in the CDC CRE Toolkit to control transmission of Carbapenem-resistant Enterobacteriaceae (CRE).

*Evaluation Criteria: The Facility must have:*

- Systems in place to identify patients with a history of CRE colonization or infection at admission and place them on Contact Precautions if not known to be free of colonization.
- Laboratory protocols in place for the rapid notification of clinical and infection prevention staff whenever CRE are identified from clinical specimens to ensure timely implementation of control measures.
- A process in place for patients colonized or infected with CRE to be cared for by dedicated staff and to be housed in single patient rooms, and when single rooms are not available, cohorted together in specific areas. Preference for single rooms should be given to patients at highest risk for transmission such as patients with incontinence, medical devices, or wounds with uncontrolled drainage.
- A CRE screening process to identify unrecognized CRE colonization among epidemiologically linked contacts of known CRE colonized or infected patients, and/or point prevalence surveys for units containing unrecognized CRE patients are conducted.
## Program Agenda & Speaker Introductions

<table>
<thead>
<tr>
<th>Time (Eastern)</th>
<th>Presenter(s)</th>
<th>Topic Content</th>
</tr>
</thead>
<tbody>
<tr>
<td>1:00 – 1:05 pm</td>
<td>Welcome IHA Staff</td>
<td>Introduction speakers with review of program objectives</td>
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<tr>
<td>1:05 – 1:30 pm</td>
<td>Dr. Daniel Livorsi</td>
<td>Overview of CRE and CDC Priority; Control and Prevention</td>
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<tr>
<td>1:30 – 1:50 pm</td>
<td>Laurie Fish, RN CIC</td>
<td>Review of CRE Core Measures and CRE Protocol developed by Indianapolis Patient Safety Coalition</td>
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<tr>
<td>1:50 - 1:55 pm</td>
<td>Dr. Livorsi Laurie Fish, RN CIC</td>
<td>Question and Answers</td>
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<tr>
<td>1:55 - 2:00 pm</td>
<td>Summary IHA Staff</td>
<td>Review of objectives, available resources and announcement of future supportive programming to address next steps</td>
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</tbody>
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The Growing Threat of Carbapenem-resistant *Enterobacteriaceae* (CRE)

Daniel Livorsi, MD, MSc
dlivorsi@iu.edu
Recent WHO and CDC reports highlight the threat of increasing antibiotic resistance
Discovery of new classes of antibiotics has stalled

Note: Penicillins were the first beta-lactams. Other frequently used agents of the beta-lactam class include cephalosporins and carbapenems, developed in the 1960s and 1980s, respectively (European Medicines Agency & European Centre for Disease Prevention and Control 2009).

Source: Figure based on the findings of Levy 2002; Nordberg et al. 2004; Singh & Greenstein 2000 – constructed and provided courtesy of EMEA.
An elderly woman with multiple sclerosis complicated by paraplegia and a neurogenic bladder (chronic indwelling urethral catheter) was transferred to the hospital from her nursing home because of fevers and presumed sepsis.

- She was found to have bilateral ulcers over her ischium and sacrum that were contaminated with stool.

- Her blood culture grew multi-drug resistant E.coli, and her urine culture grew....
Klebsiella pneumoniae grew in a urine culture

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Susceptibility</th>
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<tbody>
<tr>
<td>Ampicillin-sulbactam</td>
<td>Resistant</td>
</tr>
<tr>
<td>Pip/tazobactam</td>
<td>Resistant</td>
</tr>
<tr>
<td>Cefazolin</td>
<td>Resistant</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>Resistant</td>
</tr>
<tr>
<td>Cefepime</td>
<td>Resistant</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>Resistant</td>
</tr>
<tr>
<td>Amikacin/Tobramycin</td>
<td>Resistant</td>
</tr>
<tr>
<td>Imipenem</td>
<td>Resistant</td>
</tr>
<tr>
<td>Meropenem</td>
<td>Resistant</td>
</tr>
<tr>
<td>Levofloxacain</td>
<td>Resistant</td>
</tr>
<tr>
<td>Trimeth-sulfa</td>
<td>Resistant</td>
</tr>
</tbody>
</table>
Carbapenem-resistant Enterobacteriaceae: the sobering facts

50% Mortality rate for CRE bloodstream infections

2 The number of systemic antibiotics that would have been active against this patient’s K. pneumoniae strain.

Both are given IV and are of limited efficacy.
Enterobacteriaceae

- Large family of bacteria
- Normal inhabitants of human intestinal tract
- Causes a range of clinical infections that are normally treatable
- CRE are Enterobacteriaceae resistant to multiple antibiotics, including a group of last-resort antibiotics called carbapenems
CDC’s current definition for CRE: carbapenem-resistant *Enterobacteriaceae*

**Enterobacteriaceae**  
*E.coli, Klebsiella spp. Enterobacter, etc.*

<table>
<thead>
<tr>
<th>Non-susceptible to $\geq 1$ carbapenem:</th>
<th>Resistant to all 3rd generation cephalosporins that were tested:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doripenem</td>
<td>Ceftriaxone</td>
</tr>
<tr>
<td>Meropenem</td>
<td>Cefotaxime</td>
</tr>
<tr>
<td>Imipenem</td>
<td>Ceftazidime</td>
</tr>
</tbody>
</table>

**This definition will likely be changing.**
Different forms of CRE

Enzymes that break down antibiotics

- **KPC**: *Klebsiella pneumoniae* carbapenemase
- **NDM**: New Dehli metallo-beta-lactamase
- **VIM**: Verona Integron metallo-beta-lactamase

Combination of anti-antibiotic mechanisms
Transmission of KPC Plasmids between Bacteria
How is CRE transmitted

CRE-positive patient:
Asymptomatic carrier or active infection

CRE-negative patient
32 CRE cases linked to a contaminated endoscope used for ERCP

No lapses were observed in endoscope reprocessing
CRE is becoming more prevalent across the United States

<table>
<thead>
<tr>
<th>Type of organism</th>
<th>% of healthcare-associated infections resistant to carbapenems</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NNIS 2001</td>
</tr>
<tr>
<td>Klebsiella spp.</td>
<td>1.6%</td>
</tr>
<tr>
<td>E.coli</td>
<td>1.0%</td>
</tr>
<tr>
<td>Enterobacter spp.</td>
<td>1.4%</td>
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</table>

MMWR 3/8/2013
Epidemiology of CRE in 2009

Carbapenemase-producing CRE in the United States

CDC, unpublished data

Nov, 2006
Epidemiology of CRE in 2013

This map was last updated on December 31, 2013
Global dissemination of CRE

CDC Antibiotic Report 2013
CRE is an immediate threat to public health
Why should we focus on CRE?

- CRE infections are extremely difficult to treat, and there are few effective antibiotics in the pipeline.

- The incidence of CRE is increasing, but it has yet to firmly establish itself in our region.

- CDC ranks CRE as an immediate threat to public health that requires urgent and aggressive action.
“To prevent the emergence and further spread of CRE, a coordinated regional control effort among healthcare facilities is recommended.”
Network graph of CRE outbreak in Chicago: LTACs, SNFs, and hospitals

Long-term care facilities are a reservoir of CRE

% of patients colonized with CRE based on rectal screen

- Acute care hospital ICUs: 3%
- Long-term acute care hospitals: 30%

Israel: Monthly incidence of CRE detected by clinical cultures per 100,000 patient-days
Jan 2005-March 2008

Compliance with Infection Control Guidelines at 13 post-acute care hospitals in Israel

A Regional Approach to the Prevention and Control of CRE in Indianapolis

Indianapolis Coalition for Patient Safety
MDRO Work Group
Part 1: Prevention and Control within a facility
  - Defines core and supplemental measures for control within healthcare facilities

Part 2: Regional Control through public health
  - Coordination across facilities
  - CRE added as reportable event
Core Measures for CRE Prevention at all Acute and Long-term Care Facilities

1. Hand Hygiene
2. Contact Precautions, including pre-emptive precautions
3. Healthcare personnel education
4. Minimize use of invasive devices
5. Patient and staff cohorting
6. Laboratory notification
7. CRE screening
8. Promote antimicrobial stewardship
# Contact Precautions in Long-term care Settings

<table>
<thead>
<tr>
<th>Residents at high risk for transmission</th>
<th>Residents at low risk of transmission</th>
</tr>
</thead>
<tbody>
<tr>
<td>Totally dependent for ADLs</td>
<td>Able to perform ADLs independently</td>
</tr>
<tr>
<td>Ventilator-dependent</td>
<td>Able to perform hand hygiene</td>
</tr>
<tr>
<td>Incontinent of stool</td>
<td>Continent of stool</td>
</tr>
<tr>
<td>Wounds with uncontrolled drainage</td>
<td>No draining wounds</td>
</tr>
</tbody>
</table>
“Laboratories should have protocols in place that facilitate the rapid notification of appropriate clinical and infection prevention staff whenever CRE are identified from clinical specimens...”
Laboratory Standardization in Indianapolis

Indianapolis Coalition for Patient Safety – Multi-Drug Resistant Organism Workgroup  7/23/14

Multicenter Standardized Approach for CRE Infection Prevention and Control Measures for Hospitals

CRE Definition per CDC

Enterobacteriaceae that...
    Are non-susceptible (i.e., intermediate or resistant) to ANY carbapenem (e.g., doripenem, ertapenem, imipenem, meropenem) AND resistant to ANY of the following 3rd generation cephalosporins tested:
    cefotaxime, ceftriaxone, or ceftazidime

1. Detection

   • Standardize CLSI version 2010 or more recent
Situational Awareness

• Each healthcare facility should be aware if they have had any patients with positive CRE cultures (even identified at other facilities)
• Evaluate the timing of the positive cultures related to admission to determine if hospital acquired
• Document key data on CRE positive patients
Core and Supplemental Measures

Obtain historical data on CRE incidence within facility

- No
  - Hospital transmission identified?
    - No: Implement Core Measures
    - Yes: Implement Core and Supplemental Measures

- Yes: Implement Core and Supplemental Measures
General Approach to CRE Control in Facilities with < 1 new case/month

New CRE-colonized or CRE-infected patient identified

- Notify appropriate personnel (i.e. clinical staff, IP staff)

- Place patient on Contact Precautions in single room
- Reinforce hand hygiene and use of Contact Precautions on affected unit
- Educate healthcare personnel about preventing CRE transmission

Ensure Contact precautions are maintained
General Approach to CRE Control in Facilities with < 1 new case/month

New CRE-colonized or CRE-infected patient identified who has not been on Contact Precautions

- Screen patient contacts for CRE
- Consider point-prevalence survey of affected units
- Consider pre-emptive Contact Precautions

- If screening cultures identifies additional CRE patients, consider additional screening
- Consider cohorting patients and staff
Laboratory Protocol for Detection of Carbapenem-Resistant or Carbapenemase-Producing, Klebsiella spp. and E. coli from Rectal Swabs

Purpose
To identify patients colonized with carbapenem-resistant or carbapenemase-producing Enterobacteriaceae in the intestinal tract. Patients who grow these organisms should be placed on Contact Precautions (5) to prevent transmission of the resistant bacteria. The procedure described below is a modification of the procedure described by Landman et al. (4). See the procedural notes for steps in the procedure which can be modified.

Background
Carbapenem-resistant Enterobacteriaceae (CRE) are usually resistant to all β-lactam agents as well as most other classes of antimicrobial agents. The treatment options for patients infected with CRE are very limited. Healthcare-associated outbreaks of CRE have been reported. Patients colonized with CRE are thought to be a source of transmission in the healthcare setting (1). Identifying patients who are colonized with CRE and placing these patients in isolation precautions may be an important step in preventing transmission (6).

Carbapenem resistance in Enterobacteriaceae occurs when an isolate acquires a carbapenemase or when an isolate produces an extended-spectrum cephalosporinase, such as an AmpC-type β-lactamase, in combination with porin loss. In the United States, the most common mechanism of carbapenem resistance is the Klebsiella pneumoniae carbapenemase (KPC).
The MDRO workgroup within the Indianapolis Coalition of Patient Safety (ICPS) has developed...

- A common plan for intra-facility CRE control
- A shared Marion County database to track CRE
Indianapolis Coalition of Patient Safety Abbreviated CRE protocol

**Known CRE carrier is admitted to the hospital or transferred between hospital units**
- Admitting unit and Infection Control notified
- Isolation of CRE case and education of staff
  - Isolate patient immediately
  - Real-time education of staff
  - Monitor compliance with precautions

**New presumptive/confirmed case of CRE colonization or infection**
- Microbiology lab contacts Infection Control
- Epidemiologic investigation
  - If hospital transmission is suspected, screen epidemiologic contacts.
  - Notify transferring/receiving facility, if applicable.
  - Report to Marion County HD.
ICPS CRE Protocol

Protocol for Preventing Patient-to-Patient Transmission of Carbapenem-resistant Enterobacteriaceae (CRE)

**Known CRE carrier is admitted to the hospital or transferred between hospital units**

Admitting unit, physician team, and Infection Control notified

**Isolation of CRE case and Education of Staff**
- Place patient in contact isolation immediately
- Patient will be placed in private room or cohorted with other CRE patient
- Strict adherence to isolation precautions is reinforced.
  - The importance of strict adherence to precautions is enforced.
- Hospital Epidemiologist notified of CRE status (recommended)
- CRE education cards for providers and patients (standard language)

Infection Control conducts rounds to assess for compliance with precautions and hand hygiene.

**New presumptive/confirmed case of infection/colonization with CRE**

Microbiology contacts Infection Control

**Epidemiologic Investigation**
Infection Control investigates the case of CRE and assesses for transmission, as appropriate.
- If hospital transmission of CRE is suspected, perform surveillance cultures.
- Screening should be performed on roommates and other patients cared for by the same providers. (rectal / perirectal / stool screening preferred)
- Suspect cases may be preemptively isolated until CRE carriage is ruled-out.
- Notify originating Director of Nursing at outside facility (ECF/NH), or LTAC if not hospital acquired unless hospital epidemiologist agrees.
- Marion County facilities voluntarily report to MCPHD.
Voluntary reporting of CRE cases to the Marion County Health Department

New CRE case identified

MCHD database:
- Microbiology data
- Admission date
- Recent stays at other facilities

<table>
<thead>
<tr>
<th>Characteristics of 234 CRE cases</th>
<th>%  (n)</th>
</tr>
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<tbody>
<tr>
<td><em>Klebsiella pneumoniae</em></td>
<td>59% (138)</td>
</tr>
<tr>
<td><em>Escherichia coli</em></td>
<td>27% (64)</td>
</tr>
<tr>
<td>Resided at a long-term or extended care facility within the past 3 months</td>
<td>52% (120)</td>
</tr>
<tr>
<td>Cases associated with specific ECFs/LTACs</td>
<td></td>
</tr>
<tr>
<td>Facility A</td>
<td>20% (47)</td>
</tr>
<tr>
<td>Facility B</td>
<td>16% (37)</td>
</tr>
<tr>
<td>Facility C</td>
<td>7% (16)</td>
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</table>
What’s Next?

ICPS Expanding Scope to Long-term Care

• Development of educational materials geared toward long-term care frontline workers
  – Aim to address and guide implementation of the basic infection control practices contained in the core measures
• Outreach will be completed by hospital infection prevention or designee at the time of notification of a CRE positive patients
• Development of tools and resources for facilities with ongoing transmission
CRE Control:
A gap analysis for your facility
Summary of Gap Analysis: Part 1

1. Talk to your microbiology lab
   - Are they looking for CRE? Do they use the latest CLSI standards?
   - If they suspect CRE, do they call you right away?
   - Would they know how to screen rectal swabs for CRE, if needed?

2. Review your isolation protocols
   - How do you ensure patients are promptly isolated?
   - Do you monitor compliance with hand hygiene and CP?
   - Do you have a method for real-time education of staff?
3. Antibiotic Stewardship
   - Have you reviewed the CDC’s checklist?
   - If there are deficits, who do you need to engage at your hospital?

4. Regional collaboration
   - Do you know the prevalence of CRE within your region?
   - Is your local health department engaged?
   - Are the LTACs at the table?
Thanks also to Dr. Livorsi for sharing his slides on CRE and the CRE Tool Kit and Jim Fuller, President of ICPS.
Questions For Panelists
What Are Your Organization’s Next Steps?

1. Conduct an organizational assessment regarding CRE
2. Develop CRE protocol by December 31, 2014

Resources:
CDC Guidance for Control of CRE: 2012 CRE toolkit
AHRQ CRE Control & Prevention Toolkit
CDC Checklist for Core Elements of Hospital Antibiotic Stewardship
Evaluation & Follow-up

• Webinar funded by CMS through the Partnership for Patients
• CMS reviews results and wants 80% of participants to evaluate educational sessions
• Please complete the simple three question evaluation by Oct. 9, 2014:
• Link to evaluation and webinar recording will be distributed to participants within one week
Thank you!