Carbapenemase-Producing Carbapenem-Resistant Enterobacteriaceae (CP-CRE): Updated Laboratory Reporting Requirements and Recommendations for Healthcare Facilities

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California Antimicrobial Resistance Lab-Epi Alliance Webinar

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Objectives

1. Provide background information on CRE and CP-CRE
2. Review the new CP-CRE reporting requirements
3. Describe facility-based surveillance, investigation, and infection control actions
4. Present facility thresholds for initiating an investigation and notifying public health
Background
Carbapenem-resistant Enterobacteriaceae (CRE)

- Gram-negative bacteria
- Enterobacteriaceae family
  - *E.g.*, *Klebsiella pneumoniae*, *E. coli*, *Enterobacter cloacae*
- Normally inhabit the gut
- Resistant to carbapenem antibiotics
  - *Doripenem, ertapenem, imipenem, and meropenem*
Carbapenemase-producing CRE (CP-CRE)

**Carbapenemases** are beta-lactamase enzymes

- Inactivate carbapenems, other beta-lactam antibiotics (e.g., penicillins, cephalosporins)
- On mobile genetic elements (plasmids), enabling transfer across bacterial species
- Examples include:
  - *Klebsiella pneumoniae* carbapenemase (KPC), most common in U.S. but also found in other genera/species
  - NDM, IMP, VIM, OXA-48-like
Detecting CP-CRE

2 types of carbapenemase testing

• Phenotypic
  • Detects presence of carbapenemase (yes/no)

• Molecular
  • Identifies specific carbapenemase (e.g., KPC, NDM)
CRE Identification Algorithm

1. Enterobacteriaceae Identified
2. Antimicrobial Susceptibility Testing
3. Carbapenem-Resistant Enterobacteriaceae (CRE)
4. Carbapenemase Testing (Phenotypic/Molecular)
   - Non-Carbapenemase-producing (non-CP) CRE
   - Carbapenemase-producing (CP) CRE
     E.g., KPC-producing Klebsiella pneumoniae
Dispelling Some Common Misconceptions

• Not all CRE are carbapenemase-producing
  • Distinguishing CP-CRE from non-CP-CRE informs clinical, infection prevention and public health actions
• CRE are carbapenem-resistant, not carbapenemase-resistant
• KPC = *Klebsiella pneumoniae* carbapenemase
  • Originally discovered in *K. pneumoniae*, but can be found in *E. coli*, *Enterobacter* spp. and other organisms
• KPC is not synonymous with CRE
Reporting Requirements
CP-CRE Reporting Requirements

- Title 17, Section 2505, Subsection (e)(2) laboratory reportable conditions list, effective October 1, 2019
- CDC case definition (https://wwwn.cdc.gov/nndss/conditions/carbapenemase-producing-carbapenem-resistant-enterobacteriaceae/)
- No clinical criteria, no submission requirements
- Local reporting requirements do not change
CP-CRE Reporting Requirements

1. Laboratories that perform carbapenemase testing, or use a public health or reference laboratory to obtain carbapenemase testing, will report the following:

Any *Enterobacter* spp., *E. coli*, or *Klebsiella* spp. where the isolate is:

- Positive for carbapenemase production by a **phenotypic** method

- **OR**

- Positive for a known carbapenemase resistance mechanism (KPC, NDM, IMP, VIM, OXA-48, novel carbapenemase) by a recognized **molecular** test
Carbapenemase Testing Methods

<table>
<thead>
<tr>
<th>Phenotypic tests for carbapenemase production</th>
<th>Molecular tests for resistance mechanism</th>
</tr>
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<tbody>
<tr>
<td>Carba NP</td>
<td>BioFire</td>
</tr>
<tr>
<td>Carbapenem inactivation method (CIM)</td>
<td>Polymerase chain reaction (PCR)</td>
</tr>
<tr>
<td>Metallo-β-lactamase test (e.g., E-test)</td>
<td>Verigene</td>
</tr>
<tr>
<td>Modified carbapenem inactivation method (mCIM)</td>
<td>Whole-genome sequencing (WGS)</td>
</tr>
<tr>
<td>Modified Hodge test (MHT)*</td>
<td>Xpert Carba-R</td>
</tr>
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</table>

*A positive MHT can be used to confirm CP-CRE for *Klebsiella* spp and *E. coli* but not *Enterobacter* spp. An isolate that tests positive on MHT but negative by PCR for KPC, NDM, OXA-48, VIM and IMP should have additional characterization performed with another phenotypic test for carbapenemase such as mCIM.*
Carbapenemase Testing Capacity among Hospital Labs in California (N=386)

Source: NHSN 2018 Annual Hospital Survey
CP-CRE Reporting Requirements

2. Laboratories that do not perform or obtain carbapenemase testing, will report the following:

Enterobacter spp., *E. coli*, or *Klebsiella* spp. from any site, resistant to at least one carbapenem.

- All labs report AST results
- Labs performing or obtaining multiple tests wait until final results available before reporting
- CDPH Microbial Diseases Lab (MDL) can do phenotypic and molecular testing
Other Reporting Requirements

• Unusual infectious disease occurrence
  • Other carbapenemase-producing organisms
    • *Pseudomonas aeruginosa*
    • *Acinetobacter baumannii*
    • Other Enterobacteriaceae (e.g., *Citrobacter freundii*)
  • No organism identified (e.g., rectal swab)

• Outbreaks
CRE Epidemiology
CRE among isolates reported to NHSN* (2015-2018)

*National Healthcare Safety Network SSI, CAUTI, and CLABSI Klebsiella and Enterobacter spp. and E. coli isolates in hospitals
## Regional CRE Prevalence Definitions

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<td>High or endemic</td>
<td>CRE are routinely identified; e.g., hospitals have &gt;1 case a month</td>
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<td>Lower prevalence</td>
<td>CRE identified with regularity; e.g., hospitals have 3-12 cases a year</td>
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<td>Very low prevalence</td>
<td>CRE rarely identified; e.g., hospitals have 1 or 2 cases a year</td>
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- Highest prevalence facilities: Long-term acute care hospitals (LTACH), ventilator-equipped skilled nursing facilities (vSNF)

Sources: [CORHA Proposed Definitions](https://corha.org/resources-and-products/)

CRE: An Urgent Threat

Carbapenem-resistant Enterobacteriaceae (CRE) are a major concern for patients in healthcare facilities. Some bacteria in this family are resistant to nearly all antibiotics, leaving more toxic or less effective treatment options.

Source: CDC Biggest Threats and Data (https://www.cdc.gov/drugresistance/biggest-threats.html)
CP-CRE Epidemiology

• Highly-transmissible in healthcare settings
• Colonized and infected patients can serve as sources of transmission

• Risk factors:
  • International healthcare exposure
  • Antimicrobial treatment
  • Presence of indwelling devices (e.g., urinary catheters, endotracheal tubes)
  • Mechanical ventilation
• Difficult-to-treat infections → high mortality rates

The Case for Carbapenemase Testing

- CP-CRE warrant measures to assess and prevent further transmission in healthcare settings

- Carbapenemase testing to distinguish CP-CRE from non-CP CRE informs
  - Better understanding of hospital CRE epidemiology
  - Immediate infection control interventions
  - Epidemiologic investigation
  - Public health response actions
  - Clinical treatment options
Scenario: Hospitalized Patient Identified with CRE

- Single room, contact precautions
  - CRE isolate submitted for carbapenemase testing
    - Carbapenemase-negative
      - No additional measures unless transmission suspected
        - Continue routine surveillance
    - Carbapenemase-positive (e.g., KPC, NDM)
      - Cohort patients with CP-CRE on same unit/ward
      - Dedicated staffing
      - Colonization testing of epi-linked patient contacts
        - Patient contact(s) CRE -
          - Continue routine surveillance
        - Patient contact(s) CRE +
          - Public health investigation
CP-CRE is a public health priority
Facility Actions
Facility Actions: Routine Surveillance

- Detect CRE and notify clinical and IP staff
- Perform or obtain carbapenemase testing
- Establish baseline
Facility Actions: Active Surveillance

• Screen for CP-CRE, pre-emptive Contact precautions
  • Admitted from LTACH or facility with transmission
  • Epi-linked to new case
  • History of international healthcare exposure in last year
Thresholds for Facility Action and Reporting and Public Health Investigation

Source: [CORHA Proposed Definitions](https://corha.org/resources-and-products/)
## Thresholds*: Higher or Endemic

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<td>Same organism within 4 weeks:</td>
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<tr>
<td></td>
<td></td>
<td>• 2 KPC-CRE</td>
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<td></td>
<td></td>
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<td>• 2 CP-CRE (unknown mechanism)</td>
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Facility Actions: Initial Communications

Facility communicates patient’s CRE status:

- When transferring patient to another facility, including home healthcare
- During an outbreak
  - Screening, pre-emptive Contact precautions at receiving facility
- Within the facility by flagging the medical record
- To patients, their families and HCP
  - Provide education materials
- Adapt CDPH Infection Control Transfer Form
Infection Control Transfer Form (PDF)
(https://www.cdph.ca.gov/Programs/CHCQ/HAI/Pages/InterfacilityCommunication.aspx)
Public Health Response
Public Health Response: Initial Response and Recommendations

- Initial infection control recommendations
  - Room placement (single-bed room, like-with-like)
  - Transmission-based precautions
- Information gathering
  - Brief medical history
  - Current/previous/subsequent healthcare exposure, including admission/discharge dates and locations (e.g., units, wings)
  - Indwelling devices, invasive procedures, other risk factors
  - International travel, healthcare exposure in prior 12 months
- Retrospective and prospective lab surveillance
Public Health Response: Contact Investigation

- Colonization testing

*If already discharged, flag medical record so that patient can be screened if readmitted
Colonization Testing Resources

- Available at West Regional AR Lab in Washington free of charge
  - Rectal swab kits with instructions
  - Requisition form
  - Verbal assent script
- Request and coordinate through Local Health Department and HAI Program
Public Health Response: Infection Control

• Transmission-based precautions
  • Transmission-based precautions for duration of hospitalization
  • Enhanced standard precautions (PDF) (skilled nursing facilities) when transmission has been excluded (https://www.cdph.ca.gov/Programs/CHCQ/LCP/CDPH%20Document%20Library/Enhanced-Standard-Precautions.pdf)
  • Repeat cultures not necessary for “clearance” – patients remain colonized
  • Flag medical record for readmission
Public Health Response: Infection Control

- Dedicated equipment
- Patient and staff cohorting (if > 1 patient; does **not** imply 1:1 nursing ratio)
- Environmental cleaning, particularly of high-touch surfaces and shared equipment
- **Adherence monitoring**
  (http://www.cdph.ca.gov/programs/hai/Pages/AdherenceMonitoringTools.aspx)
- On-site infection control assessment as needed, depending on facility and extent of transmission
Public Health Response: Additional Follow-up

• Point prevalence survey (PPS)
  • Patients not previously identified with CP-CRE on same unit where transmission suspected
  • If 1+ patient identified with CP-CRE, conduct serial PPS at 2-week intervals until 2 consecutive negative PPS

• Follow-up on-site infection control assessment
  • Focus on gaps
  • Ensure implementation of recommendations

• Periodic phone check-in with facility
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Additional West Regional AR Lab Resources

- Colonization testing for CRE, carbapenem-resistant *P. aeruginosa* (CRPA) and *A. baumanii* (CRAB), and *C. auris* as part of investigation or containment response
- Expanded carbapenemase testing of CRAB (OXA-23, 24/40, 58)
- Expanded antimicrobial susceptibility testing
- Submission for targeted surveillance
  - CR-*Acinetobacter* spp.
  - CRPA
  - Non-*albicans* *Candida* spp. for antifungal susceptibility testing
Resources

• [CDPH CRE Website](https://www.cdph.ca.gov/Programs/CHCQ/HAI/Pages/CRE_InfectionPreventionStrategies.aspx)
• [CDPH FAQ for CP-CRE Reporting](https://www.cdph.ca.gov/Programs/CHCQ/HAI/CDPH%20Document%20Library/CP-CRE_ReportingFAQ_Approved_10.4.19_ADA.pdf)
• [CDPH California Antimicrobial Resistance Lab-Epi Alliance](https://www.cdph.ca.gov/Programs/CHCQ/HAI/Pages/CA_ARLN.aspx)
• [CDPH Adherence Monitoring Tools](https://www.cdph.ca.gov/Programs/CHCQ/HAI/Pages/MonitoringAdherenceToHCPracticesThatPreventInfection.aspx)
• [CDPH All Facilities Letter for Reporting Outbreaks and Unusual Infectious Disease Occurrences](https://www.cdph.ca.gov/Programs/CHCQ/LCP/CDPH%20Document%20Library/AFL-19-18.pdf)
Resources, cont’d

- **CDC CRE Website** (https://www.cdc.gov/hai/organisms/cre/index.html)
Questions?

For more information, contact the HAI Program at
HAIProgram@cdph.ca.gov