Carbapenem-resistant Enterobacteriaceae (CRE): Surveillance and Response

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What are “Carbapenem-resistant Enterobacteriaceae” (CRE)?

- **Carbapenems** are a class of β -lactam antibiotic
  - Broad spectrum
  - Typically used as a “last resort” for infections that are resistant to other antibiotics
- **Enterobacteriaceae** are normal flora found primarily in our GI tract
  - *E. coli, Klebsiella spp., Enterobacter spp.,* etc
  - > 70 species of bacteria
  - Opportunistic infections
- Common organisms + highly resistant (superbug) = “Nightmare bacteria”
  - Few or no antibiotics are effective in some instances
  - Can cause invasive infections with high mortality
  - May have transmissible resistance mechanisms

Enterobacteriaceae genera

Averyella	**Hafnia**	**Pragia**	**Yersinia**
Budvicia	**Klebsiella**	**Proteus***	**Yokenella**
Buttiauxella	**Kluyvera**	**Providencia***	**Enteric Group 58**
Cedecea	**Leclercia**	**Rahnella**	**Enteric Group 59**
Citrobacter	**Leminorella**	**Salmonella**	**Enteric Group 60**
Cronobacter	**Moellerella**	**Serratia**	**Enteric Group 63**
Edwardsiella	**Morganella***	**Shigella**	**Enteric Group 64**
Enterobacter	**Pantoea**	**Tatumella**	**Enteric Group 68**
Escherichia	**Photorhabdus**	**Trabulsiella**	**Enteric Group 69**
Ewingella	**Plesiomonas**	**Xenorhabdus**	**Enteric Group 137**

*Elevated minimum inhibitory concentrations (MICs) to imipenem in ***Morganella*** spp., ***Proteus*** spp., and ***Providencia*** spp. are frequently due to mechanisms other than carbapenamases.

CP-CRE vs. CRE

Carbapenemase-producing CRE (CP-CRE)

- Resistance genes located on plasmids
  - Highly mobile genetic elements
- Transmissible - can transfer resistance horizontally to other bacteria
  - e.g., *E. coli* → *Klebsiella spp.*
- Distinction is epidemiologically important
  - Impact on clinical outcomes not definitively established
- Implications of CP-CRE
  - Infection control
  - Contact tracing
  - Surveillance cultures
    - Roommates
    - Equipment
    - Surfaces

http://www.micro-blog.info/wp-content/uploads/2015/01/theantibioticresistance.jpg

CP-CRE vs. CRE

- Tests for carbapenemase production are not widely available
  - PCR
  - Modified Hodge Test (MHT)
  - Carba-NP
- Instead, we use “phenotypic definition” based on the antibiotic susceptibility pattern
  - This definition has varied by state and over time
  - New CSTE guidance is helping standardize what we call “CRE”
- An organism that is resistant to carbapenems (CRE) may or may not be a carbapenemase producer (CP-CRE)

Goals of CRE Surveillance in New Mexico

- Conduct population-based surveillance
- Estimate CRE burden statewide
- Conduct descriptive epidemiological analysis
- Conduct molecular characterization of isolates
- Provide case-based recommendations to institutions
- Identify outbreaks & coordinate appropriate public health response

2016 New Mexico CRE Case Definition

- Resistant to any carbapenem
  - Ertapenem MIC ≥2
  - Meropenem MIC ≥4
  - Imipenem MIC ≥4*
  - Doripenem MIC ≥4

OR

- Production of a carbapenemase by a recognized test
  - Modified Hodge Test (MHT)
  - Metallo-β-lactamase test
  - Carba-NP
  - PCR

Klebsiella pneumoniae carbapenamase	KPC
New Delhi metallo-beta-lactamase	NDM
Imipenemase metallo-beta-lactamase	IMP
Verona integron-encoded metallo-beta-lactamase	VIM
Oxacillinase-48	OXA-48

***** For bacteria that have intrinsic imipenem non-susceptibility (i.e., *Morganella morganii*, *Proteus* spp., *Providencia* spp.), resistance to carbapenems other than imipenem is required. *Morganella morganii, Proteus* spp., *Providencia* spp. are excluded from this definition if only imipenem resistance is detected.

CRE Reporting

- CRE became reportable in New Mexico on June 15, 2016
- Routine reporting (within 24 hours)
- Laboratories and facilities, primarily
- Defined interventions based on classification (CP-CRE vs. non-CP-CRE)

Description	Organisms Included	Recommended Measures
Carbapenamase-producing CRE (CP-CRE)	Enterobacteriaceae-positive by PCR for KPC, NDM, IMP, VIM OXA-48, CarbaNP, MHT	Most aggressive infection control measures and public health investigation
CRE with acquired resistance NOT due to carbapenamse production (non-CP-CRE)	Enterobacteriaceae that meet definition, but are PCR, CarbaNP or MHT negative	Intensified infection control measures including contact precautions

CRE & CP-CRE Investigation and Response

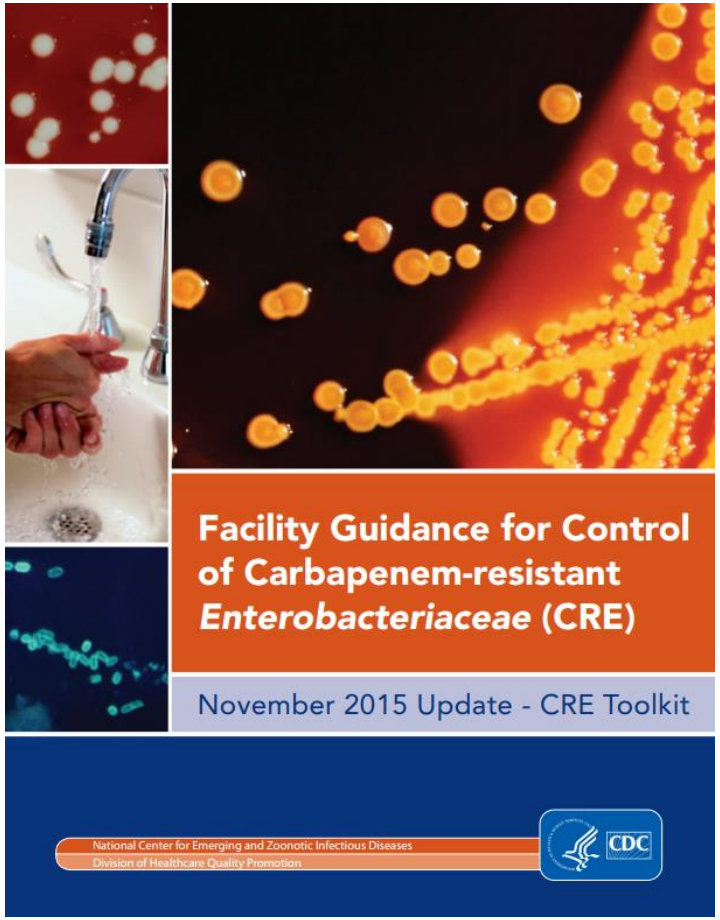
CRE

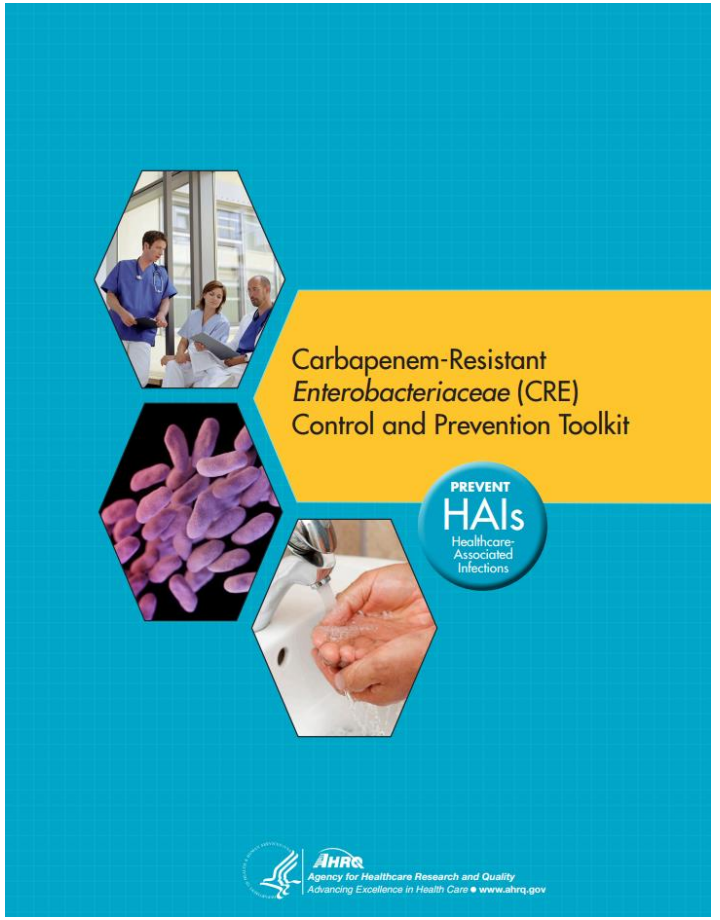
- Report to IDEB (call, fax or ELR)
- Report given to HAI epi
- Data entered in database
- Verify facility aware of result
- Provide recommended response and control measures to facility staff
- Submit isolate to SLD

CP-CRE

- Report to IDEB (call, fax or ELR)
- Report given to HAI epi
- Data entered in database
- Verify facility aware of result
- Assure response and control measures are implemented
  - Implement strict hand hygiene
  - Institute contact precautions
  - Place in private room or cohorting, if possible
  - Dedicate staff, if possible
  - Screen roommates
  - Perform daily chlorhexidine bathing
  - Discontinue devices
- Flag chart
- Inter-facility notification
- Submit isolate to SLD

CRE Response: Toolkits





CRE Outbreaks

- Only respond to outbreaks of CP-CRE for public health purposes
- 2 or more cases that a genotypically identical in a facility concurrently

Steps:

1. Conduct point prevalence
2. Conduct admission cultures of high risk patients
3. Cohort patients and staff, if possible
4. Consult with CDC
5. Daily conference calls
6. Consider facility IC assessment

Laboratory Submission

Planned Steps:

1. Clinical laboratory identifies CRE
2. Submit isolate to SLD, along with susceptibility report
3. SLD performs test for carbapenamase production, regardless of prior phenotype testing
4. SLD reports results back to submitter and IDEB
5. IDEB HAI Epidemiologists respond as appropriate

Challenges

- Awareness among providers
- Antimicrobial stewardship
- Implementing certain recommendations
- Developing laboratory capacity in clinical laboratories and at SLD
- Developing inter-facility & healthcare provider communication platforms
- Estimating the work load

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Questions?

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