

Carbapenem-Resistant Enterobacteriaceae

Summary

Carbapenem-resistant Enterobacterales (CRE) include organisms under the Enterobacteriaceae family that are resistant to carbapenems. Antibiotics within the carbapenem class include imipenem, meropenem, ertapenem and doripenem. Enterobacteriaceae commonly found to exhibit significant clinical resistance to carbapenems include *E. coli*, *Klebsiella* and *Enterobacter* species. These bacteria are found in normal human intestines (gut). Sometimes these bacteria can spread outside the gut and cause serious infections, such as urinary tract infections, bloodstream infections, wound infections, and pneumonia. Enterobacteriaceae can cause infections in people in both healthcare and community settings.

CRE are frequently resistant to multiple antibiotic groups, making treatment of CRE infections challenging. Carbapenem resistance may be chromosomal in nature or acquired through plasmids. Different mechanisms of resistance exist; of these the production of carbapenemases, typically acquired via plasmids is of great concern due its proclivity to spread, hence the focus on infection prevention. Early detection and aggressive implementation of infection control and prevention strategies are necessary to prevent further spread of CRE.

Agent

The Enterobacteriaceae are a large family of over 70 genera of gram-negative bacilli that include *Escherichia coli*, *Klebsiella* species, and *Enterobacter* species (see table below). These organisms are normally found in the gastrointestinal tract of humans and other animals and can cause infections that range from mild to severe. These organisms are a common cause of community-acquired and healthcare-associated infections. Antibiotic resistance has become more widespread among this class of bacteria over the past several decades, and of particular concern is the increase of resistance to a class of antibiotics known as carbapenems, a powerful last resort antibiotic.

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

Transmission

Reservoir:

CRE is found in the gastrointestinal tract of humans and animals. Colonized patients and the healthcare environment can also serve as significant reservoirs of CRE bacteria.

Mode of Transmission:

- Person to person through contact with infected or colonized people, particularly through secretions, wounds or stool
- Contact with contaminated equipment
- Through the hands of healthcare personnel
- Self-inoculation of gut bacteria

Period of communicability:

- Once infected or colonized, colonization is considered indefinite and patient should be placed on contact precautions at time of admission.

Clinical Disease

Illness:

CRE can cause pneumonia, bloodstream infections, urinary tract infections, intra-abdominal infections, and surgical site infections, among others. Patients can be colonized with CRE (positive clinical culture without symptoms of infection); however, they can serve as vectors to other patients or sources for health care facility outbreaks. Patients most at risk for CRE infection are those with chronic medical conditions, frequent or prolonged stays in health care settings, invasive medical devices (e.g., ventilators or intravenous catheters), or a history of taking certain antibiotics for long periods of time.

Laboratory Diagnosis

A confirmed case of CRE is a patient whose clinical or surveillance specimen culture yields a bacterium of the *Enterobacteriaceae* family that test resistant to any carbapenem including doripenem, ertapenem, imipenem, or meropenem using the current M100-S26 CLSI breakpoints. All confirmed isolates should be forwarded to the State Public Health Laboratory (SLD) for further characterization.

Current MIC Breakpoints (µg/mL)¹			
MIC Interpretation²			
Carbapenems	Susceptible	Intermediate	Resistant
Doripenem	≤1	2	≥4
Ertapenem	≤0.5	1	≥2
Imipenem	≤1	2	≥4
Meropenem	≤1	2	≥4

¹MIC = minimum inhibitory concentration ²CLSI. *Performance Standards for Antimicrobial Susceptibility Testing Twenty-Sixth Informational Supplement* ³CLSI document M100-S26, Wayne, PA: Clinical and Laboratory Standards Institute: Jan 2016.

OR

Positive for a carbapenemase by a nucleic acid amplification test; (e.g., PCR-positive for KPC, NDM, IMP, VIM, or OXA-48)

OR

Are positive for carbapenemase production by a phenotypic test.

Note: *Proteus* spp., *Providencia* spp. and *Morganella* spp. are excluded from this definition if only imipenem resistance is detected because these species have intrinsic resistance to imipenem. For example, isolates that test ertapenem susceptible but imipenem resistant would not meet the definition.

Treatment

Treatment is case specific and based on clinical signs and symptoms as well as pertinent laboratory or radiologic findings. Containment is the priority for public health.

Surveillance

Case Definition:

Confirmed: meets laboratory criteria (below)

Probable: not applicable

Suspect: not applicable

When to Report:

- Laboratory isolation of any Enterobacteriaceae genera with resistance to imipenem, meropenem, doripenem, or ertapenem *from any site*.
- Whenever an Enterobacteriaceae genera organism is tested for resistance mechanism.
- Any diagnosis of Carbapenem-resistant Enterobacteriaceae (CRE) or carbapenamase producing CRE (CP-CRE) infection or colonization.

What to Report:

- The Enterobacteriaceae genera that is resistant to carbapenems.
- The results of all susceptibility testing done on the specimen, including MIC and interpretations
- All results (positive and negative) resistance mechanism tests (Modified Hodge Test, CarbaNP, KPC, NDM, VIM, IMP, OXA-48, etc).

Reporting

Report all infections, including non-healthcare-associated, within 24 hours to Epidemiology and Response Division (ERD) by fax at 505-827-0013 or by phone at 505-827-0006. Information needed includes the following: patient's name, age, date of birth, sex, race, ethnicity, home address, home phone number, occupation, specimen collection date, and health care provider.

Case Investigation

Use the CRE checklist to begin an investigation. Information should also be entered into NMEDSS per established procedures. Clinical laboratory should be contacted to ensure submission of isolates to SLD. Case should then be referred to Healthcare-associated Infections (HAI) epidemiologist for further management.

Carbapenem Resistant *Enterobacteriales* (CRE), Carbapenem Resistant *Pseudomonas aeruginosa* (CRPa), Carbapenem Resistant *Acinetobacter baumannii* (CRAB) and/or Carbapenemase Producing bacteria

INCLUSION CRITERIA

Isolate must meet one or more of the following criteria

1. Minimum Inhibitory Concentrations (MIC):

CRE

- ≥ 4 $\mu\text{g/ml}$ for meropenem, imipenem, or doripenem
- ≥ 2 $\mu\text{g/ml}$ for ertapenem

CRPa

- ≥ 8 $\mu\text{g/ml}$ for meropenem, imipenem, or doripenem **AND** ≥ 16 $\mu\text{g/ml}$ (nonsusceptible) for cefepime or ceftazidime

CRAB

- ≥ 8 $\mu\text{g/ml}$ for meropenem, imipenem, or doripenem, or if pan-nonsusceptible

Note: for bacteria that have intrinsic imipenem non-susceptibility (*Morganella*, *Proteus*, *Providencia spp*), resistance to carbapenems other than imipenem is required.

2. Disk Diffusion susceptibility testing methods:

CRE

- zone diameter breakpoint $\leq 19\text{mm}$ for meropenem, imipenem, or doripenem
- zone diameter breakpoint $\leq 18\text{mm}$ for ertapenem

CRPa

- zone diameter breakpoint $\leq 15\text{mm}$ for meropenem, imipenem, or doripenem **AND** $\leq 17\text{mm}$ for cefepime or ceftazidime

3. *Enterobacteriales* and other bacteria that exhibit evidence of carbapenemase production demonstrated by one of the following test:

- CarbaNP/CarbaR
- Polymerase Chain Reaction (PCR) for KPC, NDM, VIM, IMP, OXA-48
- modified carbapenem inactivation method (mCIM)
- other molecular methods

Note: Please do not submit duplicate isolates (same patient, specimen site, and organism) collected within 30 days.

NOTIFIABLE DISEASES in the State of New Mexico¹

Carbapenem Resistant *Enterobacteriales* (CRE), Carbapenem Resistant *Pseudomonas aeruginosa* (CRPa), Carbapenem Resistant *Acinetobacter baumannii* (CRAB) and/or Carbapenemase Producing bacteria

Report all infections, including non-healthcare-associated, **within 24 hours** to Epidemiology and Response Division (ERD) by fax at 505-827-0013 or by phone at 505-827-0006.

Carbapenem Resistant *Enterobacteriales Carbapenem Resistant *Pseudomonas aeruginosa** Carbapenem Resistant *Acinetobacter baumannii****

[*] Laboratory or clinical specimens are **required** to be sent to the Scientific Laboratory Division (SLD).

²NOTIFIABLE DISEASES OR CONDITIONS IN NEW MEXICO:

<https://nmhealth.org/publication/view/regulation/372/>

7.4.3.13 NEW MEXICO ADMINISTRATIVE CODE:

<http://www.nmcp.state.nm.us/nmac/parts/title07/07.004.0003.htm>

ALL REPORTS INCLUDING ELECTRONIC LABORATORY REPORTS OF NOTIFIABLE CONDITIONS MUST INCLUDE:

1. The disease or condition being reported;
2. Patient's name, date of birth/age, gender, race/ethnicity, address, patient's telephone numbers, and occupation;
3. Physician or licensed healthcare professional name and telephone number; and
4. Healthcare facility or laboratory name and telephone number, if applicable.

SUBMISSION

Please send isolates to SLD

1101 Camino de Salud NE Albuquerque, NM 87102

Collection: Send isolate on culture medium such as nutrient agar slants or MAC agar plates.

Special Requirements: Carbapenemase producing plasmids are not stable. Keep isolate **refrigerated** until shipment. Avoid multiple sub- cultures.

Handling: Refrigerate immediately upon growth of isolate.

Include: Copy of **susceptibility report** and Clinical Test Request form. <https://www.nmhealth.org/publication/view/form/6380/>

Analysis Requested: Under Bacteriology, please check "CRE Panel", select CRE, CRPa, or Other and write in organism genus and species.

Shipping: Send cold, on an ice pack. **Do not freeze.** Pack as a Category B Specimen in accordance with all Department of Transportation (DOT) and International Air Transport Association (IATA) guidelines. Send to the Scientific Laboratory Division (SLD).

Contact: GM Supervisor (505-383-9128), or GM Line Supervisor (505-383-9127).

Control Measures

Hand washing is the most important measure for preventing transmission of CRE. Wash hands before preparing or eating food, before and after changing wound dressings, after coughing or sneezing, after blowing your nose, and after using the bathroom. Use household hand soap and warm water and rub hands for at least 20 seconds before rinsing. If an individual requires continued care at home, caregivers should wear gloves when handling body fluids (urine, wound drainage, etc.), when providing care, or when in contact with surfaces contaminated with body fluids. They should wash hands immediately after removing gloves.

Disposable items soiled by body fluids (dressings, diapers, used gloves, etc.) should be placed in the trash immediately. Good cleaning with soap and water followed by a household disinfectant such as bleach is adequate to disinfect surfaces contaminated with CRE. Laundry used clothing, sheets and linens using standard laundry detergent and make sure items are completely dry before using. Used dishes and utensils can be handled and washed as usual.

See Appendix A for Facility Control Measures

Please refer to CDCs toolkit at: <https://www.cdc.gov/hai/pdfs/cre/CRE-guidance-508.pdf> for additional facility recommendations.

Management of CRE in Child Care Centers

Refer to recommendations above.

References

Centers for Disease Control and Prevention. Vital Signs Aug 4, 2015. Making Health Care Safer: Stop Spread of Antibiotic Resistance. www.cdc.gov/vitalsigns/stop-spread/index.html.

Centers for Disease Control and Prevention. 2012 CRE Toolkit: Guidance for Control of Carbapenem-resistant Enterobacteriaceae (CRE). Available at: www.cdc.gov/hai/organisms/cre/cre-toolkit/index.html.

Clinical and Laboratory Standards Institute (CLSI). Performance standards for antimicrobial susceptibility testing. Twenty-fifth informational supplement. CLSI Document M100-S25. Wayne, PA, 2015.

Appendix A

Infection Prevention Action Needed

This patient is infected or has been colonized with either a **carbapenem-resistant Enterobacterales (CRE)** or a **carbapenemase-producing Organism (CPO)**, which can include: KPC, VIM, NDM, OXA-48, IMP.

Or with *Candida auris* (C. auris).

The following actions items need to be **implemented immediately**.

Acute Care Hospitals			
Patient Recommendations			
Infection Prevention Measures	CRE	CPO	<i>C. auris</i>
Standard Precautions	Yes	Yes	Yes
Contact Precautions	Yes	Yes	Yes
Designated or Disposable Equipment	Yes	Yes	Yes
Private Rooms	Yes	Yes	Yes
Door Signage	Yes	Yes	Yes
One to One Nursing Care	No	May be considered ¹	May be considered ¹
Enhanced Environmental Cleaning	Yes	Yes	Yes
Visitor Recommendations			
Frequently perform hand hygiene, emphasizing after leaving resident's room	Yes	Yes	Yes
Wear gown/gloves if contact with body fluids is anticipated	Yes	Yes	Yes
Wear gown/gloves if no contact with body fluids is anticipated	No	No	No

Long Term Care Facilities			
Patient Recommendations			
Infection Prevention Measures	CRE	CPO	<i>C. auris</i>
Standard Precautions	Yes	Yes	Yes
Contact Precautions	Yes	Yes	Yes
Enhanced Barrier Precautions	May be considered ¹	May be considered ¹	May be considered ¹
Designated/Disposable Equipment	No	No	Yes
Private Rooms	No	Yes	Yes
Door Signage	Yes	Yes	Yes
Enhanced Environmental Cleaning ^{3,4}	Yes	Yes	Yes
Visitor Recommendations			
Frequently perform hand hygiene, emphasizing after leaving resident's room	Yes	Yes	Yes
Wear gown/gloves if contact with body fluids is anticipated	Yes	Yes	Yes
Wear gown/gloves if no contact with body fluids is anticipated	No	No	No

1. Dependent upon patient acuity and internal facility policies. Consult with infection prevention and/or NMDOH at 505-827-0006.
2. Contact precautions should be maintained and, if feasible, provided a private room for residents who are at higher risk for transmission (i.e. ventilator-dependent patients, wounds with difficult to control drainage, incontinence of urine or stool, or those who engage in behavior that spreads infection).
3. Ensure that environmental cleaning procedures adhere to Hospital Infection Control Practices Advisory Committee (HICPAC) recommendations. (CDC. *The Guidelines for Environmental Infection Control in Health-Care Facilities*. www.cdc.gov/infectioncontrol/pdf/guidelines/environmental-guidelines-P.pdf)
4. For a current list of EPA-approved products effective against *C. auris*, please visit www.epa.gov/pesticide-registration/list-p-antimicrobial-products-registered-epa-claims-against-candida-auris
5. Long term care facilities may choose between Contact Precautions and Enhanced Barrier Precautions when caring for a resident with a CRE or CPO, for guidance regarding Enhanced Barrier Precautions, please visit www.cdc.gov/hicpac/pdf/EnhancedBarrierPrecautions-H.pdf
6. For additional information on containment of MDRO's, please visit www.cdc.gov/hai/containment/guidelines.html

See Carbapenam-resistant Enterobacteriaceae (CRE) Fact Sheets
([English](#)) ([Spanish](#)).