

Carbapenam-Resistant Enterobacteriaceae

Summary

Carbapenam-resistant Enterobacteriaceae (CRE) include organisms under the Enterobacteriaceae family that are resistant to carbapenems. Antibiotics within the carbapenam 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. Carbapenam 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 Interpretation ²			
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 Carbapenemase producing
CRE (CP-CRE) infection or colonization.

What to Report:

- The Enterobacteriaceae genera that is resistant to Carbapenemase.
- 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: 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.

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 *Enterobacteriaceae* 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.

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

BACTERIOLOGY	
<input type="checkbox"/>	B. anthracis
<input type="checkbox"/>	B. cereus/S. aureus
<input type="checkbox"/>	Culture, OMI
<input type="checkbox"/>	Culture, OMI anaerobic
<input type="checkbox"/>	Campylobacter species: _____
<input type="checkbox"/>	E. coli O157:H7
<input type="checkbox"/>	G. culture
<input type="checkbox"/>	H. influenzae typing
<input type="checkbox"/>	L. monocytogene
<input type="checkbox"/>	Plague FA and culture
<input type="checkbox"/>	Salmonella, serotype: _____
<input type="checkbox"/>	Shigella, serotype: _____
<input type="checkbox"/>	Shiga Toxin test/isolation
<input type="checkbox"/>	Strep, Group B, isolation
<input type="checkbox"/>	Tularemia culture
<input type="checkbox"/>	Vibrio
<input type="checkbox"/>	Yersinia enterocolitica: _____
<input checked="" type="checkbox"/>	Other: <u>CRE Klebsiella pneumoniae</u>

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. Launder 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

If patient is infected or has been colonized with either a **carbapenem-resistant Enterobacteriaceae (CRE)**, **carbapenemase-producing CRE (CP-CRE)**, or a **carbapenemase-producing Pseudomonas aeruginosa (CP-PA)**.

Depending on the bacteria, the following actions items need to be **implemented immediately**.

Acute Care Hospitals				
Patient Recommendations				
Infection Prevention Measures	CRE		CP-CRE/CP-PA	
	Infected	Colonized	Infected	Colonized
Standard Precautions	Yes	Yes	Yes	Yes
Contact Precautions	Yes	Yes	Yes	Yes
Designated or Disposable Equipment	Yes	Yes	Yes	Yes
Private Rooms	Yes, if available ¹	Yes, if available ¹	Yes	Yes
Door Signage	Yes	Yes	Yes	Yes
Chlorhexidine (CHG) Bathing	Yes	Yes	Yes	Yes
Visitor Recommendations				
Frequently perform hand hygiene, emphasizing after leaving resident's room	Yes	Yes	Yes	Yes
Wear gown/gloves if contact with body fluids is anticipated	Yes	Yes	Yes	Yes
Wear gown/gloves if no contact with body fluids is anticipated	No	No	No	No

Long Term Care Facilities				
Patient Recommendations				
Infection Prevention Measures	CRE		CP-CRE/CP-PA	
	Infected	Colonized	Infected	Colonized
Standard Precautions	Yes	Yes	Yes	Yes
Contact Precautions	Yes	No, unless at higher risk ²	Yes	Yes
Designated or Disposable Equipment	Yes	No, unless at higher risk ²	Yes	Yes
Private Rooms	Yes, if available ¹	No, unless at higher risk ²	Yes	Yes

Restricted to room	No, unless at higher risk ²	No, unless at higher risk ²	Yes	No, unless at higher risk ²
Door Signage	Yes	No, unless at higher risk ²	Yes	Yes
Chlorhexidine (CHG) Bathing	Yes	No, unless at higher risk ²	Yes	Yes
Enhanced Environmental Cleaning ³	Yes	No	Yes	Yes
Visitor Recommendations				
Frequently perform hand hygiene, emphasizing after leaving resident's room	Yes	Yes	Yes	Yes
Wear gown/gloves if contact with body fluids is anticipated	Yes	Yes	Yes	Yes
Wear gown/gloves if no contact with body fluids is anticipated	No	No	No	No

1. Private room is highly recommended but is left to the discretion of the infectious disease consult and/or the infection preventionist. Please refer to the microbiology laboratory results for susceptibility pattern.
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. MMWR 2003/52(RR10);1-42)

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