

Carbapenem-Resistant *Enterobacteriaceae* Investigation Guidelines

1. DISEASE REPORTING

A. Purpose of Reporting and Surveillance

- To identify cases and associated outbreaks
- To prevent further transmission through containment and prompt infection control
- To better characterize the risk factors and epidemiology of this organism

B. Laboratory and Physician Reporting Requirements

- [Nebraska Administrative Title 173 – Control of Communicable Disease](#) stipulates that laboratories and healthcare providers report immediately (within 24 hours) of identifying a suspected or confirmed CRE

C. Local Health department (LHD) Reporting and Follow-up Responsibilities

- Report all suspected or confirmed CRE to the Nebraska Department of Health and Human Services (NE DHHS) within 24 hours of initial physician/lab report by: i) faxing lab report, ii) faxing the standard case report form, or iii) reporting through National Electronic Disease Surveillance System (NEDSS) Electronic Laboratory Reporting (ELR)
- Ensure that labs forward qualifying isolates (See Appendix for requisition form) to the NPHL for additional testing

D. State Health department Responsibilities

- NE DHHS will notify LHDs of carbapenemase-producing organisms and collaborate on any necessary follow-up including containment recommendations and surveillance testing as needed

2. THE DISEASE AND ITS EPIDEMIOLOGY

A. Etiologic agent

- CRE are Enterobacteriaceae that are resistant to any carbapenem antimicrobial (i.e., minimum inhibitory concentrations of ≥ 4 mcg/ml for doripenem, imipenem, meropenem or ≥ 2 mcg/ml for ertapenem) OR have been documented to produce carbapenemase
- Important cause of invasive infections and are often associated with high mortality rates (up to 50%)¹
- CRE have been found in most of the United States and are primarily associated with exposure to the healthcare system, however they have the potential to spread in the community¹
- Enterobacteriaceae are a family of gram-negative bacteria that include but are not limited to:^{1,2,3}

Genus	Species	Genus	Species
<i>Citrobacter</i>	<i>freundii, koseri, amalonaticus</i>	<i>Plesiomonas</i>	<i>shigelloides</i>
<i>Edwardsiella</i>	<i>tarda</i>	<i>Proteus</i>	<i>mirabilis, vulgaris</i>
<i>Enterobacter</i>	<i>cloacae, aerogenes, sakasakii</i>	<i>Providencia</i>	<i>stuartii, rettgeri</i>
<i>Escherichia</i>	<i>coli, albertii</i>	<i>Salmonella</i>	<i>enterica</i>
<i>Hafnia</i>	<i>alvei</i>	<i>Serratia</i>	<i>marcescens</i>
<i>Klebsiella</i>	<i>pneumoniae, oxytoca, granulomatis</i>	<i>Shigella</i> (belongs within the <i>E coli</i> species)	<i>dysenterii, flexneri, sonnei, boydii</i>
<i>Morganella</i>	<i>morganii</i>	<i>Yersinia</i>	<i>pestis, enterocolitica, pseudotuberculosis</i>
<i>Pantoea</i> (formerly <i>Enterobacter</i>)	<i>agglomerans</i>		

B. Description of illness

- Clinical presentation may vary according to what system of the body is affected
- May include bloodstream infections, pneumonia, wound infections, intra-abdominal abscesses, and urinary tract infections
- Patients can be infected or colonized (bacteria is present but not causing symptoms/disease)
- Colonized patients can subsequently develop infections
- Infected and colonized patients can both spread the organism to others

C. Treatment

- Treatment options for CRE are extremely limited and may lead to adverse reactions
- Infectious disease consultation is recommended for treatment decisions

D. Reservoirs

- *Enterobacteriaceae* can be carried in the intestines of many mammals and birds
- The reservoir for CRE infections in the United States is colonized and infected individuals, especially patients with frequent contact with the healthcare system
- *Enterobacteriaceae* can survive on inanimate objects and surfaces

E. Modes of Transmission

- CRE are transmitted person-to-person through direct contact with infected bodily tissues or fluids
- In healthcare settings, CRE are spread mainly through the hands of healthcare workers and direct contact with contaminated environmental services, such as bed rails and computer keyboards

F. Incubation period

- The incubation period is not well defined, particularly due to the ability of CRE to colonize an individual for an extended interval of time

G. Period of communicability

- CRE can potentially be transmitted as long as the organisms are present in a person's bodily tissues or fluids
- It is unknown how long CRE can live on inanimate surfaces

CLINICAL AND CASE DEFINITION

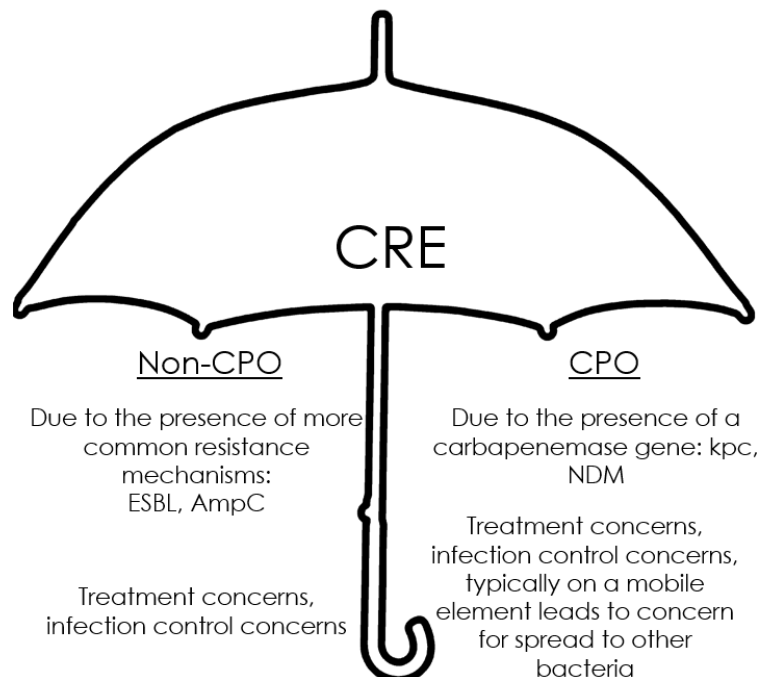
A. CRE are defined as *Enterobacteriaceae* that are:

Resistant to any carbapenem (minimum inhibitory concentrations of ≥ 4 mcg/ml for meropenem, imipenem, and doripenem or ≥ 2 mcg/ml for ertapenem)

OR

Produce a carbapenemase (e.g., KPC, NDM, VIM, IMP, OXA-48) as demonstrated by a recognized test (e.g., polymerase chain reaction, metallo- β -lactamase test, modified Hodge test, Carba NP)

B. A CP-CRE or CPO is a particularly concerning type of CRE that is resistant to the carbapenem class of antibiotics due to the production of a carbapenemase enzyme. This enzyme is made from a piece of genetic material called a plasmid that can be transferred to other types of bacteria and therefore represents a unique public health threat.



C. The detection of any single carbapenemase-producing organism in Nebraska will be considered an outbreak that requires investigation. In facilities not able to perform testing for carbapenemases, any CRE detected will be considered an outbreak that requires an investigation.

3. LABORATORY SERVICES

A. Isolates that meet the following criteria should be forwarded to NPHL using the requisition form (see Appendix) for additional testing:

Submission of all isolates of Enterobacteriaceae and/or *Pseudomonas aeruginosa* that are non-susceptible (intermediate or resistant) to any of the carbapenems

- Enterobacteriaceae: Ertapenem MIC ≥ 1 $\mu\text{g/ml}$ and/or meropenem or imipenem MIC ≥ 2 $\mu\text{g/ml}$, or non-susceptible by disc diffusion method.
- *Pseudomonas aeruginosa*: Meropenem or imipenem MIC ≥ 4 $\mu\text{g/ml}$, or non-susceptible by disc diffusion method
- Submission of all isolates of in-house or reference laboratory confirmed carbapenemase-producing Enterobacteriaceae (CPE) or *Pseudomonas aeruginosa* (CP-PA)

Rejection criteria: DO NOT submit the following isolates

- *Enterobacter cloacae* and *E. (Klebsiella). aerogenes* isolates non-susceptible only to ertapenem but susceptible to imipenem and meropenem
- *Proteus* species, *Providencia* species, and *Morganella morganii* non-susceptible only to imipenem but susceptible to meropenem and ertapenem
- *Pseudomonas aeruginosa* isolates that are mucoid or from cystic fibrosis patients

Isolate submissions must be submitted on the CRE/CPE Supplemental Form found on the NPHL website under forms.

<http://nphl.org/forms.cfm>

- Personnel making submissions to NPHL must have proper training in packaging and shipping hazardous materials 6.2 from NPHL

Make arrangements for training through the State Training Coordinator, currently:

Karen Stiles, MT (ASCP) SM
kstiles@unmc.edu
Tel: 402-559-3590

4. CASE INVESTIGATION

A. Surveillance

- The NDHHS HAI program conducts daily surveillance for CRE via a database of electronically reported laboratory results that includes patient demographics,

- specimen source, ordering and reporting organizations, the organism identified and its associated antimicrobial susceptibility pattern
- These reports are accessed through the National Electronic Disease Surveillance System (NEDSS) system
 - They are monitored daily for results that are concerning for CREs, especially potential carbapenemase-producing organisms
 - The NPHL performs follow-up testing on isolates that are concerning for a carbapenemase-producing organism (criteria for testing on form in Appendix)
 - These results are shared with the ordering facility and the NDHHS HAI program for follow-up as needed

B. Epidemiologic information is collected for all submitted CRE reports as follows

- Patient demographics (name, date of birth, location)
- Local health department jurisdiction
- Ordering and reporting facility
- Inpatient/facility status

C. Additional information is collected for carbapenemase-producing organisms as follows

- Treatment course and duration as well as repeat testing
- History of prior contact with healthcare facilities
- Travel history
- Occupation

5. PREVENTING AND CONTROLLING FURTHER SPREAD

Efforts should be made to contain organisms that demonstrate resistance to the carbapenem class of antibiotics, regardless of the mechanism by which they are resistant. Facilities should take precautions to prevent the spread of a particular CRE from one patient to another. Additional steps might be needed for CREs that produce a carbapenemase due to the potential for spread of such a plasmid from one organism to others.

A. Infection Control Recommendations for facilities

- Confirm appropriate hand hygiene practices are being followed
- Confirm use of contact precautions (gowns and gloves available and used correctly)
- Private room if at all possible, cohorting if not possible
- Minimize device utilization where possible (indwelling lines, endotracheal tubes, urinary catheters, etc)
- Facility should examine need for special precautions if patient has a procedure with a reusable device
- Ensure appropriate antimicrobials are being used (stewardship)
- Cohort affected patients with minimal shared staff when possible
- Establish clear communication methods if inter-facility transfer is needed (Nebraska Interfacility Transfer Form can be used if there is not a current method in place)
- Ensure appropriate environmental cleaning is performed.
- Consider use of daily 2% chlorhexidine bathing for patients in high-risk settings/units

B. Personal protective equipment

- Contact precautions (gown and glove) in conjunction with appropriate hand-washing are sufficient to protect employees and other patients

C. Environmental Measures

- Refer to the Guideline for Disinfection and Sterilization in Healthcare Facilities (https://www.cdc.gov/hai/pdfs/Disinfection_Nov_2008.pdf) for specific guidance on sterilization and disinfection techniques

6. MANAGING SPECIAL SITUATIONS -Screening and Point Prevalence Surveys

Screening cultures will be considered as part of a containment strategy in the event that a carbapenemase-producing organism is identified from a patient that is currently admitted to a hospital, long-term care facility or similar institution. Screening via rectal swabs of relevant asymptomatic epidemiologic contacts of an identified case can provide important information on transmission and also allow for targeted containment efforts. The determination of who to screen will be made by the NDHHS HAI program and NPHL and based on assessing the most likely persons at risk (individuals who share rooms, bathrooms, provide assistance with toileting, changing undergarments etc).

Point prevalence surveys might be considered in this scenario and could be repeated depending on the number of identified cases and extent of spread. Additionally, active surveillance cultures and/or use of 2% chlorhexidine bathing for patients in high-risk settings might also be considered depending on the extent of the outbreak.

Colonization Protocol for Contacts of a Patient with CP-CRE (or CPO) **Screening cultures will be performed as follows:**

1. Who to screen

- Members of HAI Team and the IP at the facility will identify appropriate epidemiologic contacts for screening:
 - Roommates
 - Patients on the same hallway (approximately 3 rooms down on either side) for 3 days of shared admission with index patient (this is a guideline that can be altered based on each particular case)
 - Patients that have had an invasive procedure such as an endoscopy would need to consider screening those who have been scoped with the same device after index patient.
- Pursue outpatient screening only for high risk patients (particularly roommates)
- See following protocols for those in LTC, AL, and Rehab
- <http://dhhs.ne.gov/HAI%20Documents/CREScreeninginAssistedLivingQuestionnaire.pdf>
- <http://dhhs.ne.gov/HAI%20Documents/CREScreeninginSkillednursingquestionnaire.pdf>

2 All colonization screening is sent to our Antibiotic Resistance Laboratory Network

(ARLN) lab in Minnesota. You will receive a specimen kit from the ARLN. Please refer to the information outlined below.

- A) You should receive the following in your CRO Colonization Test Sampling Kit:
- 1) Guidance for Carbapenem-resistant organism (CRO) Colonization Test Sampling and Specimen Handling Methods packet
 - 2) One SafTPak (STP-210) box (pre-assembled so that “Biological Substance, Category B” signage is facing outward)
 - 3) One SafTPak (STP-710) white Tyvek® bag
 - 4) One SafTPak (STP-711) clear bag
 - 5) One absorbant pad
 - 6) Ten Copan brand Transystem swabs
 - 7) MDH submission Form
- B) MDH submission Form can be found
<https://www.health.state.mn.us/diseases/idlab/forms.html#arforms>
Fill out a form for each patient/resident who has a colonization swab is collected.
- C) Information needed to fill out the form.
- a. Patient last name
 - b. Patient first name
 - c. Patient middle initial
 - d. Patient date of birth
 - e. Patient sex
 - f. Specimen collection date
 - g. Specimen source (type) is swab
 - h. Specimen source site is rectum
 - i. Original submitters Patient ID is your patient’s medical record number
- D) Specimens must be clearly labeled with the following:
- a. A minimum of 2 patient identifiers. Acceptable identifiers include:
 - i. Patient’s full name
 - ii. Date of birth
 - iii. Medical record number
 - iv. Sample ID number
 - b. Date of specimen collection
 - c. Site of collection
- E) Packaging information after swabs are collected.
- a. Place the swabs in their transport tubes in the clear Saf-T-Pak bag (STP-711) along with the absorbent pads provided in the kit . All swabs can be placed into a single bag provided they fit.
 - b. Fold tape closure over so that the white paper liner is visible and remove the liner to expose adhesive.
 - c. Gently lay tape over the bag opening and smooth with fingers to seal tightly.
 - d. Place clear Saf-T-Pak bag (STP-711) sealed with its contents into white Saf-T-Pak bag (STP-710).
 - e. Fold tape closure over so that the white paper liner is visible and remove the liner to expose adhesive.

- f. Gently lay tape over the bag opening and smooth with fingers to seal tightly.
- g. Place white Saf-T-Pak (STP-710) sealed with its contents into cardboard box (STP-210) folded so that “Biological Substance, Category B” is outwardly showing.
- h. Place filled-out paperwork inside box, close flap, seal with tape, and continue onto Fed-Ex shipping instructions.

F) Shipping Instructions

1. Go to [FedEx.com](https://www.fedex.com)
2. In the Login area, enter the following information:
 - a. User ID: MDHARLN
 - b. Password*: PHLidl2017
 - c. Click the purple “Login” button**
3. [Area 1] Enter the “From” shipping address by clicking on “Edit.”
4. [Area 2] Enter the “To” shipping information as:
 - a. Minnesota Department of Health
 - b. PHL, Infectious Disease
 - c. 601 Robert St N
 - d. Saint Paul, MN 55155
 - e. 651-201-5200
5. [Area 3] Complete the Package & Shipping Details:
 - a. Priority Overnight is the only shipping option.
 - b. Choose package type (i.e. Box).
 - c. Enter number of packages. If there is more than one package, indicate whether packages are identical or not.
 - d. Enter total weight.
 - e. Verify or change ship date.
 - f. Area 4] Verify account number “CDC_OID_NCEZID_ARLN-237” is the account in the “Billing Details” box.
 - g. Optional: Review available options between Areas 4 & 5.
 - h. [Area 5] Click the “Ship” button.
 - i. Check the box next to “Label” and then click on the “Print” button.
 - j. Print the shipping label and attach it to the package for pickup.

*Password is: 3 uppercase letters, 3 lowercase letters, and then 4 numbers.

**You may receive an error if you press Enter instead of clicking on the “Login” button. If you still have issues logging in, try clearing your browser’s cookies and/or turning pop-ups on.

G) Results

- a. Results called to HAI Director, HAI IP, and/or HAI Epidemiologist.
- b. Results will be faxed to a secure fax number that has been provided by facility collecting colonization screens.

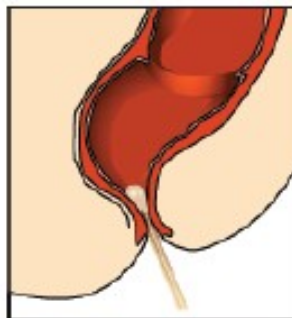
Other Information to consider

- Perform screening for at-risk contacts every other week while case is admitted in facility
- Consider performing follow-up point prevalence surveys or active surveillance cultures upon admission to a unit if transmission is identified
- Strongly suggest the use of daily 2% chlorhexidine bathing for patients in high-risk settings/units

Establish method for communication CRE status upon transfer of patients to other facilities (e.g. Interfacility transfer form at <http://dhhs.ne.gov/HAI%20Documents/Interfacility%20Infection%20Control%20Transfer%20Form.pdf>)

Sample Collection and Preparation

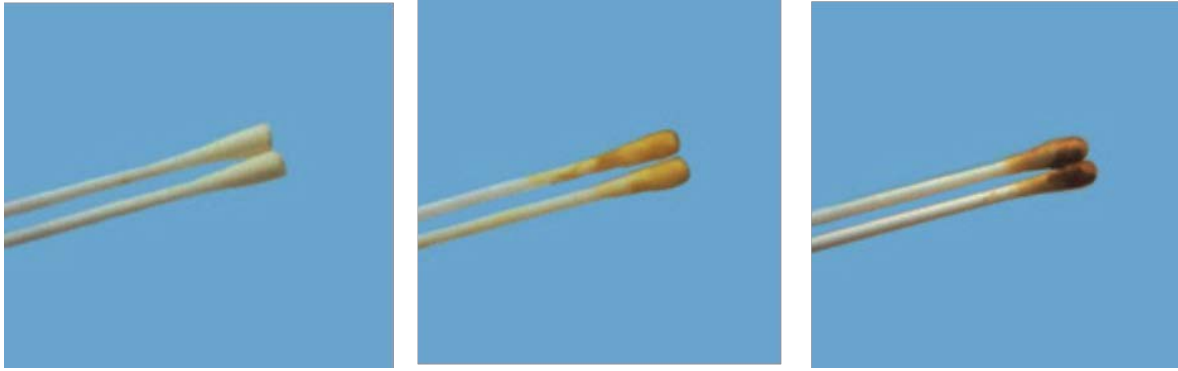
1. Before beginning, perform hand hygiene and don appropriate personal protective equipment (PPE) as indicated by the patient's clinical care team.
2. Open the outer packaging of the swabs.
3. Carefully remove the tube from the plastic packaging and label the tube (see label instructions below)
 - a. While labeling, leave the dual swab enclosed in the plastic packaging to prevent contamination
4. Pull the dual swab from the plastic packaging, being careful not to touch the cotton tips.
5. The dual swab may be moistened with sterile saline or transport medium only
6. Carefully insert both swab tips approximately 1 cm beyond the anal sphincter and gently rotate against the walls of the rectum 3 times. See figure for proper swab depth.



- a. Diapered infants: The cotton swab may be used to swab the stool present in the soiled diaper.
- b. Patients with an ostomy: Use the cotton applicator to obtain specimen from the stoma site.

7. Confirm swab is not overloaded or underloaded. See figures below for reference.

Acceptable Specimens



Unacceptable Specimens



8. Insert dual swab into tube and firmly close cap. Seal with Parafilm if available.
9. Swabs in transport tube can be stored at 15-28C (room temperature) for up to five days. However, it is optimal to transport to as soon as possible.

Contact information

Office of Epidemiology

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