Public Health
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BACKGROUND

Carbapenemase-Producing Organisms (CPOs) refers to species belonging to the enterobacterales order of bacteria, *Acinetobacter baumannii complex*, and *Pseudomonas aeruginosa* that have acquired genes making them resistant to a broad spectrum of antibiotics including those known as carbapenem antibiotics. These genes are often contained on mobile genetic elements that can spread resistance quickly to other bacteria. The ability of bacteria to produce carbapenemase enzymes limits treatment options. Infections with CPOs are difficult to treat and are associated with high morbidity and mortality rates. Early detection and aggressive implementation of infection prevention and control strategies are necessary to prevent further spread of CPOs. These strategies require an understanding of the prevalence of CPOs in Iowa.

LABORATORY TESTING

Clinical laboratories play a critical role in preventing the transmission of carbapenemase-producing organisms. Distinguishing CPOs from gram-negative organisms that are carbapenem resistant due to non-carbapenemase-mediated mechanisms is important, as CPOs disseminate between patients more readily than non-CPO and warrant implementation of more intensive infection prevention and control measures that would be employed in the absence of carbapenemase production.

Laboratories have a number of culture-based (phenotypic) and culture-independent (molecular) tests available for carbapenemase gene detection.

1.0 Testing to detect CPOs

- Antimicrobial susceptibility testing (AST) alone will not reliably distinguish carbapenemase producers from non-carbapenemase producers but does help identify isolates that should be tested further for carbapenemase production.
- Clinical laboratories should follow CLSI guidance (M100) regarding which antimicrobials should be tested for each organism. M100Ed32 | Performance Standards for Antimicrobial Susceptibility Testing, 32nd Edition (clsi.org)
- Carbapenem-resistant organisms (CRO) are defined by CLSI breakpoints for ertapenem, doripenem, imipenem and meropenem.
    - *Morganella* spp., *Proteus* spp., and *Providencia* spp. have intrinsic elevated minimum inhibitory concentrations (MIC) to imipenem. MIC results for meropenem, doripenem, and/or ertapenem should be used instead of imipenem.

1.1. Laboratories with the capacity to detect carbapenemase production phenotypically or to detect carbapenemase genes should report to public health authorities any of the following laboratory results for any specimen:

- Positive phenotypic test result for carbapenemase production, with or without identification of a specific carbapenemase gene (KPC; NDM; OXA; VIM; and IMP), OR
- Positive molecular test result detecting a carbapenemase gene (KPC; NDM; OXA; VIM; and IMP), OR
- Detection of a carbapenemase gene (KPC; NDM; OXA; VIM; and IMP) by sequencing, OR
- Specimen positive for a carbapenemase gene (KPC; NDM; OXA; VIM; and IMP) without bacterial species identification, (e.g., Xpert Carba-R rectal swabs, other CIDT).

2.0 Clinical labs should submit the following to the State Hygienic Laboratory (SHL):

- Carbapenem-resistant Enterobacterales (CRE)
- All CRE isolates should be tested for carbapenemase production. For *Escherichia coli, Klebsiella oxytoca, Klebsiella pneumoniae, and Enterobacter spp. r*esistance to one or more of the following: imipenem (≥4 µg/mL), meropenem (≥4 µg/mL), doripenem (≥4 µg/mL), or ertapenem (≥2 µg/mL). Any Enterobacterale that is resistant to one or more carbapenem (besides imipenem for PPM) should be sent to SHL.
    - The following should be submitted to SHL regardless of source and regardless of purpose (routine or surveillance) of the culture:
        - Any CRE isolate from a patient with a high suspicion of being a carbapenemase-producer
        - Any CRE isolate submitted from a patient with a history of infection or colonization with *C. auris*
- Carbapenem-resistant *Pseudomonas aeruginosa* (CRPA)
    - Carbapenem-Resistant *Pseudomonas aeruginosa* (CRPA) non-mucoid isolates:
        - Resistance to one or more of the following: imipenem (≥8 µg/mL), meropenem (≥8 µg/mL), or doripenem (≥8 µg/mL)
    - Prioritize the following CRPA isolates for carbapenemase testing:
        - Non-susceptible (i.e., intermediate, or resistant MIC ≥16µg/ml) to cefepime and/or ceftazidime

        - Any CRPA isolate submitted from a patient with a high suspicion of being a carbapenemase producer (e.g., epidemiologically linked isolate)
        - Any CRPA isolate that is non-susceptible to all antibiotics tested
        - Any CRPA isolate submitted from a patient with a history of infection or colonization with *C. auris*
- Carbapenem-resistant *Acinetobacter baumannii* (CRAB)
    - Carbapenem-Resistant *Acinetobacter spp*.:
        - Resistance to one or more of the following: imipenem (≥8 µg/mL), meropenem (≥8 µg/mL), or doripenem (≥8 µg/mL)
    - All CRAB isolates should be tested for carbapenemase gene targets. Phenotypic testing is not routinely performed on CRAB isolates and often gene targets are identified through molecular methods or WGS.
        - Any CRAB isolate submitted from a patient with a high suspicion of being a carbapenemase producer (e.g., epidemiologically linked isolate)
        - Any CRAB isolate submitted from a patient with a history of infection or colonization with *C. auris*

3.0 Public Health Laboratory role is to provide confirmatory organism identification, carbapenemase gene detection, and surveillance antimicrobial susceptibility testing, and whole genome sequencing to determine the specific type of carbapenemase gene target.

What to Report

Providers will report using a designated case report form that must be submitted either by direct electronic transmission, phone, or fax. The report must include, at a minimum, the following information:

- The patient's name.
- The patient's address.
- The patient's date of birth.
- The sex of the patient.
- The race and ethnicity of the patient.
- The patient's telephone number.
- The name and address of the laboratory.
- The date the test was found to be positive and the collection date.
- The name and address of the health care provider who performed the test.
- If the patient is female, whether the patient is pregnant.
- The name of the reportable disease.

How to report

The preferred method of reporting is through the Iowa Disease Surveillance System (IDSS). Reports can also be submitted via telephone (800-362-2736), facsimile (515-281-5698), or mail (Iowa Department of Health and Human Services, Lucas State Office building, 321 East 12th St, Des Moines, IA 50319-0075).

Pursuant to 641-1.7 (135, 139A) Investigation of reportable disease, upon receipt of the report, Iowa HHS epidemiologists or the local public health department may request additional information needed for the investigation.