Carbapenem-Resistant Enterobacteriaceae (CRE) Disease Reporting and Surveillance Case Definition

What to report:

Identification of CRE from a clinical specimen associated with either infection or colonization, including all susceptibility results and all phenotypic or molecular test results.

For the purpose of reporting, CRE are defined as:
(1) *Enterobacter* spp, *E.coli* or *Klebsiella* spp positive for a known carbapenemase resistance mechanism or positive on a phenotypic test for carbapenemase production; or
(2) *Enterobacter* spp, *E.coli* or *Klebsiella* spp resistant to any carbapenem in the absence of carbapenemase resistance mechanism testing or phenotypic testing for carbapenemase production.

Isolate Submission:

Further characterization of CRE isolates is available at no cost to the submitter through the state laboratory of public health. Isolate submission is requested for the following:

- *Enterobacter* spp., *E. coli* or *Klebsiella* spp. resistant to any carbapenem in the absence of carbapenemase resistance mechanism testing
- *Enterobacter* spp., *E. coli* or *Klebsiella* spp. resistant to any carbapenem and positive for carbapenemase production via phenotypic test
- *Enterobacter* spp., *E. coli* or *Klebsiella* spp. with discordant phenotypic and molecular results for carbapenemase production

Identification of CRE producing a carbapenemase other than Klebsiella pneumoniae carbapenemase (KPC) may also be requested for isolate submission. If your facility identifies Carbapenemase Producing Carbapenem-Resistant Enterobacteriaceae (CP-CRE) among Enterobacteriaceae spp. other than Enterobacter spp., E. coli or Klebsiella spp., consider sending these isolates for testing as well.

CRE Case Definition:

Enterobacter spp, E. Coli, or Klebsiella spp. resistant to any carbapenem* (minimum inhibitory concentrations of ≥4 mcg/ml for meropenem, imipenem, and doripenem or ≥ 2 mcg/ml for ertapenem)

*Carbapenem interpretive criteria are based on the current Clinical and Laboratory Standards Institute guidelines.

CP-CRE 2018 CDC Case Definition:

E. coli, Klebsiella spp., or Enterobacter spp. where the isolate is:

- Positive for carbapenemase production by a phenotypic method

  -OR-

- Positive for a known carbapenemase resistance mechanism by a CDC recognized test (see methods below)

Methods for detecting Carbapenemase production:

Phenotypic methods for carbapenemase production:

- Carba NP positive
- Metallo-β-lactamase testing (e.g., E-test) positive
- Modified Carbapenem Inactivation Method (mCIM) positive or indeterminate
- Carbapenem Inactivation Method (CIM) positive
- Modified Hodge Test (MHT) positive

Molecular methods for resistance mechanism:

- PCR positive (for Klebsiella pneumoniae Carbapenemase [KPC], New Delhi metallo-β-lactamase [NDM], oxacillinase-48 [OXA-48], Verona integron-encoded metallo-β-lactamase [VIM], or imipenemase [IMP])
- Xpert Carba-R positive (for KPC, NDM, OXA-48, VIM, IMP)
- PCR or Xpert Carba-R positive for novel carbapenemase

Criteria to Distinguish a New CP-CRE Case from an Existing CP-CRE Case:

- Different organisms/species/carbapenemases are counted as separate events from other organisms/species/carbapenemases.
- There is at least a 12-month interval from previous notification event for clinical cases.
- A person with a clinical case should not be counted as a screening/surveillance case thereafter (e.g., patient with known infection who later has colonization of GI tract is not counted as more than one case).
- A person with a screening case can be later categorized as a clinical case (e.g., patient with positive peri-rectal screening swab who later develops blood stream infection would be counted in both categories).

CP-CRE Case Classification Comments:

1. Cases involving isolates that are phenotypically positive for carbapenemase production (e.g., mCIM), but negative for KPC, NDM, OXA-48, VIM, and IMP should be counted as confirmed CP-CRE. Isolates should be submitted to the regional laboratories of the Antibiotic Resistant Laboratory Network (ARLN) for further characterization (potential novel carbapenemase).
2. A positive Modified Hodge Test (MHT) can be used to confirm CP-CRE for Klebsiella spp and E. coli but not Enterobacter spp. An isolate that tests positive on MHT but negative PCR for KPC, NDM, OXA-48, VIM and IMP should have additional characterization performed with another phenotypic test for carbapenemase such as mCIM.
3. If an isolate is indeterminate on mCIM and negative by PCR for KPC, NDM, OXA-48, VIM and IMP, isolate should be tested using CarbaNP (at state public health laboratory or regional ARLN)

Purpose of reporting:

Reporting and surveillance aim to:

1. Prevent transmission of infections with carbapenem-resistant Enterobacteriaceae (CRE) between patients, within or among health care facilities, or between health care facilities and the community.
2. Identify and respond to outbreaks
3. Better characterize the epidemiology of these infections

Early detection and aggressive implementation of infection prevention and control strategies are necessary to prevent further spread of CRE, especially novel CP-CRE. These strategies require an understanding of the prevalence or incidence of CRE. Public Health authorities must be notified promptly when cases of CRE are detected to contain CRE.

References:

1. https://wwwn.cdc.gov/nndss/conditions/carbapenemase-producing-carbapenem-resistant-enterobacteriaceae/case-definition/2018/