

Carbapenem-resistant Enterobacteriaceae (CRE)

The carbapenem class of antibiotics is a group of powerful, broad-spectrum antibiotics effective against many Gram-negative infections. Carbapenems have been an important tool in the treatment of serious infections caused by multi-drug resistant Enterobacteriaceae. Resistance to carbapenems among Enterobacteriaceae is on the rise in the United States.

The term “Carbapenem-resistant Enterobacteriaceae” (CRE) refers to all strains which are non-susceptible (Intermediate or Resistant) to carbapenems. The molecular mechanisms which lead to this resistance can vary but generally include two main categories: chromosomally-mediated and plasmid-mediated. Chromosomally-mediated mechanisms include the production of β -lactamases (AmpC) in combination with alterations in the bacterial cell membrane (porin mutations or loss). Plasmid-mediated mechanisms include the production of carbapenemases, enzymes which break down carbapenems and related antibiotics, rendering them ineffective. The subset of CRE that carry genes which encode for carbapenemases are known as carbapenemase-producing CRE or CP-CRE.

All CRE, regardless of underlying mechanism, require careful consideration of treatment regimen and facilities should consider infection control strategies to minimize transmission. Many CRE also carry resistance mechanisms to other antibiotic classes heightening the need to manage these infections to prevent selection of additional resistance traits.

CP-CRE are currently believed to be primarily responsible for the increasing spread of CRE in the U.S. and around the globe, so this subset has been specifically targeted for aggressive prevention and containment.

Carbapenem antibiotics include



Doripenem
Ertapenem
Imipenem
Meropenem

Enterobacteriaceae include



E. coli
Klebsiella
Enterobacter
Serratia
Morganella
Proteus

Plasmid-mediated carbapenemases include



KPC
NDM
Oxa-48-like
Imp
VIM.



Antimicrobial stewardship plays a key role in the prevention of antibiotic resistance development and the containment of multi-drug resistant organisms (MDROs) including CP-CRE.



CP-CRE has been associated with travel to endemic regions, particularly among individuals receiving medical care in those regions. Endemic spread of CRE has also been observed in regions of the United States including the Northeast.

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In CT, CRE has been laboratory reportable since 2014, but laboratory testing to identify CP-CRE has been largely unavailable to date.

Beginning in 2017, clinical laboratories should submit all CRE isolates identified using the case definition to the CT Department of Public Health Laboratory (DPHL). DPHL will provide reference laboratory testing including expanded microbroth dilution and disk diffusion MIC testing, phenotypic testing for carbapenemase production using the Modified Carbapenemase Inactivation Method (modified CIM), and PCR-based detection of the 5 most common carbapenemases (KPC, NDM, Oxa-48, VIM, IMP). This testing panel will allow facilities and providers to identify patients with known and/or novel carbapenemases. DPHL will work closely with partners in our Antibiotic Resistance Laboratory Network (ARLN) regional laboratory and the Centers for Disease Control and Prevention (CDC) to identify and characterize novel resistance and catalog resistant isolates for use in drug discovery and development efforts as well as ongoing research on resistance mechanisms. Information on resistance mechanisms should be used to guide infection control and containment strategies.

More information on the work and mission of the ARLN can be found online at: <https://www.cdc.gov/drugresistance/solutions-initiative/ar-lab-networks.html>.



Up to 50% of bloodstream infections caused by CRE result in death



In 2012, 4% of U.S. hospitals and 18% of long-term acute care hospitals (LTACHs) had at least one CRE



In CT, from 2014-2016, 26/30 (87%) of CT hospitals reported at least one case of CRE



In CT, approximately one-third of CRE is diagnosed and treated in the outpatient setting



Among hospitalized patients in CT from 2014-2015, approximately 45% of CRE isolates are collected in the Emergency Department



Although only a small fraction of CRE has had mechanistic testing to date, CT has identified cases of KPC, NDM, and Oxa-48



In 2014, at least one CRE-positive patient was admitted for 360/365 days in hospitals across CT