

Carbapenem-resistant Enterobacteriaceae (CRE) Infection: Healthcare Provider Frequently Asked Questions

What are Carbapenem-resistant Enterobacteriaceae (CRE)?

Carbapenem-resistant *Enterobacteriaceae* (CRE) are a family of bacteria that often colonize the human gastrointestinal (GI) tract and have potential to cause infections. CRE are a serious threat to public health. Some *Enterobacteriaceae* have become resistant to all or most antibiotics. CRE have become increasingly common in the United States and have caused outbreaks in healthcare facilities across the healthcare spectrum.

CRE are defined as being resistant to at least one of four carbapenem antibiotics and/or produce a carbapenemase (the enzyme that inactivates carbapenems and can be spread to other bacteria).

How do *Enterobacteriaceae* become resistant to carbapenems?

Before the emergence of certain carbapenemases most CRE were likely resistant to carbapenems through a combination of mechanisms such as a beta-lactamase combined with a porin mutation that limited the ability of carbapenems to get into the bacteria.

In 2001, a *K. pneumoniae* isolate possessing a novel carbapenemase (i.e., KPC) was recognized in the United States. The genes that code for KPC are highly mobile and can be transmitted from one bacterium to another. Since 2001, KPC-producing bacteria have spread across the United States. Compared with other states, KPC CRE are less prevalent in NH.

In addition to KPC, other carbapenemases exist that can lead to carbapenem resistance, including: 1) New Delhi metallo-beta-lactamase (NDM), 2) Verona integron-encoded metallo-beta-lactamase (VIM), and 3) imipenemase metallo-beta-lactamase (IMP).

Of note, some *Enterobacteriaceae* are intrinsically nonsusceptible to imipenem, such as *Morganella morganii*, *Proteus* species, and *Providencia* species. As a result these organism need to be resistant to another carbapenem to be considered at CRE.

What is the difference between CRE and carbapenemase-producing (CP)-CRE?

CRE are defined by their phenotype (i.e., based on the antibiotic susceptibility pattern) and include bacteria with multiple mechanisms of resistance. These mechanisms include:

- CP-CRE have carbapenemases that inactivate carbapenems and related antibiotics. These include enzymes like KPC, NDM, VIM, and IMP.
- Non-CP-CRE have other mechanisms of resistance; most commonly the production of beta-lactamases (e.g., AmpC) in combination with alterations in the bacteria's cell membrane (e.g., porin mutations).

CP-CRE are epidemiologically important and targeted for prevention due to the ability to spread rapidly and association with high mortality rates (up to 50% for blood stream infections).

U.S. phenotypic CRE definitions have attempted to target CP-CRE for both surveillance and prevention; however, no phenotypic CRE definition is perfect and some non-CP-CRE can also meet these definitions.

Why is CP-CRE considered epidemiologically important?

CRE are important for a number of reasons.

1. These organisms are often resistant to multiple classes of antimicrobials, substantially limiting treatment options.

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2. Infections caused by these organisms are associated with high mortality rates, up to 50% in some studies.
3. Many CRE possess carbapenemases which can be transmitted from one *Enterobacteriaceae* to another, potentially facilitating transmission of resistance.
4. *Enterobacteriaceae* are a common cause of infections in both community and healthcare settings. Carbapenem resistance among these organisms could therefore have far-reaching impact. For these reasons, the Centers for Disease Control and Prevention (CDC) and the New Hampshire Division of Public Health Services (DPHS) have developed recommendations designed to decrease transmission of CRE.
 - a. [CDC Recommendations](#) [1]
 - b. [NH CRE Response Checklist](#)
 - c. [NH Recommendations for the Prevention and Control of Multidrug-Resistant Organisms \(MDROs\)](#) [2]

Which patients are at increased risk for CRE acquisition?

The main risk factors for CRE acquisition in the U.S. include exposure to healthcare and antimicrobials. Healthcare-related risk factors include poor functional status and exposures to an intensive care unit, mechanical ventilation, and multiple inpatient admissions across different types of facilities. Several antimicrobials have been associated with CRE acquisition, including: carbapenems, cephalosporins, fluoroquinolones, and vancomycin.

What infections do CRE cause?

CRE can cause infections in almost any part body, including: bloodstream infections, ventilator-associated pneumonia, and intra-abdominal abscesses. Based on information from a CDC pilot surveillance system, most CRE infections involve the urinary tract, often in people who have a urinary catheter or have urinary retention.

CRE are associated with high mortality for patients who get bloodstream infections (~50%).

How are CRE infections transmitted?

CRE are usually transmitted from person to person often via the hands of healthcare personnel or via contaminated medical equipment. As *Enterobacteriaceae* are found in stool and may contaminate wounds, contact with these might be particularly concerning. Ensuring proper infection prevention practices such as the use of personal protective equipment (PPE) during care and hand hygiene prior to, during, and before patient care (especially when cleaning up stool or changing wound dressings). The role of transmission directly from the environment to patients is controversial and requires further research.

What is the difference between CRE colonization and infection?

When found in clinical culture, CRE can represent an infection or colonization. Colonization means that the organism can be found in or on the body but it is not causing any symptoms or disease. Colonizing CRE strains can cause infections if they gain access to body sites that are usually sterile like the bladder, the lungs, or the bloodstream.

Infections are usually associated with symptoms. Those symptoms can vary based on the location or site of infection (e.g., cough if in the lungs, urinary symptoms if in the bladder), but can also include general symptoms like fever or chills.

How do I treat a patient with a CRE infection?

The best way to ensure your patient is receiving the best possible treatment for a CRE infection is to consult with an infectious disease specialist. For proper expanded precautions, contact your infection prevention department. You can also contact the Healthcare-Associated Infections (HAI) Program, Bureau of Infectious Disease Control, NH DPHS at (603)271-4496.

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What can clinicians do to prevent CRE transmission?

Strategies to eliminate CRE transmission in healthcare settings focus primarily on: 1) recognizing and reporting cases of CRE to public health, 2) placing colonized or infected patients on [contact precautions](#) [3], 3) ensuring proper disinfection and sterilization of medical devices, and 4) using antimicrobials wisely. Specific detailed recommendations on preventing CRE transmission in healthcare settings can be found in the [2015 CDC Facility Guidance for CRE](#) [1]. Below are some steps that can be taken as soon as a patient's CRE status is identified. Also see the [NH CRE Response Checklist](#).

- Report CRE/CP-CRE cases to the NH DPHS (He P301.02) Phone: 603-271-4496.
Fax: 603-271-0545
- Add CRE/CP-CRE to the patient's problem list
- Flag the patient in the medical record as having CRE and requiring contact precautions
- Implement contact precautions for each visit and contact NH DPHS if unsure what precautions should be used.
- Communicate the patient's CRE status with transferring and receiving facilities (see [NH Infection Control Interfacility Transfer Form](#))

When can contact precautions be discontinued for patients colonized or infected with CRE?

Contact precautions should be maintained for the duration of an inpatient stay when a patient's CP-CRE or CRE status is first identified. For subsequent hospitalizations, patients with a previous CRE (not CP-CRE) infection do not require contact precautions if the patient has no transmission risk factors (e.g., stool incontinence, unable to practice hand hygiene) and can follow medical directions independently.

For patients with a previously identified CP-CRE infection or colonization contact precautions should be

implemented during any future admissions and in place until the following criteria can be demonstrated.

- >6 months have passed since the last positive culture
- The patient must not be taking any antibiotics at the time of the screening
- The patient does not have an active infection
- No transmission risk factors to others (e.g. stool incontinence, unable to practice hand hygiene) [2]
- 2 sequential negative rectal screening swabs must be obtained at least one week apart

These guidelines for contact precautions and the discontinuation of contact precautions are catered towards acute care hospital settings. The needs of other healthcare facility settings may differ slightly. Please contact NH DPHS at 603-271-4496 regarding specific guidance, questions, or clarification.

What steps do I need to take to protect myself from CRE?

It is rare for healthy people to have CRE infections. However, there is a potential to become colonized with CRE or spread the organism to other patients if proper precautions are not followed. If the patient is known to have CRE, [contact precautions](#) [3] are the best method to ensure containment. In addition, it is necessary to ensure [standard precautions](#) [4] (e.g., PPE and hand hygiene) as you may not know a patient's CRE status when providing care.

Additional Information: For additional information, please go to the [CDC's Clinicians page for CRE](#) [5].

If you have additional questions or are seeking more information, please contact the Healthcare-Associated Infections (HAI) Program, Bureau of Infectious Disease Control, NH DPHS at (603)271-4496 or haiprogram@dhhs.nh.gov.

References:

This frequently asked questions document for clinicians have been adapted from the CDCs Carbapenem-resistant Enterobacteriaceae (CRE) Infection: Clinician FAQs [6].

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