

Carbapenem-resistant Enterobacteriaceae (CRE) Infection: Clinician FAQs

What are CRE?

CRE stands for “carbapenem-resistant Enterobacteriaceae.” Enterobacteriaceae are a family of bacteria that are often found in people’s gastrointestinal tract that can cause infections both in community and healthcare settings. Some Enterobacteriaceae have become resistant to all or almost all antibiotics. In general, CRE test nonsusceptible to at least one of the carbapenem antibiotics and/or produce an enzyme (carbapenemase) that can make them resistant to these antibiotics. These bacteria often have other resistance mechanisms that render them nonsusceptible to many other classes of commonly used antibiotics. These bacteria were uncommon in the United States before 1992. Since then they have become more common primarily due to the spread of Enterobacteriaceae that produce a carbapenemase called KPC (Klebsiella pneumoniae carbapenemase).

How do Enterobacteriaceae become resistant to carbapenems?

Unlike other multi-drug resistant organisms (MDRO) like MRSA for which a single mechanism leads to methicillin resistance, CRE can become nonsusceptible to carbapenems due to a number of mechanisms. Before the recent emergence of carbapenamases like KPC (*Klebsiella pneumoniae* carbapenemase), most CRE in the United States likely were resistant to carbapenems through a combination of mechanisms (e.g., 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 that possessed a novel carbapenemase called KPC was recognized in the United States. The genes that code for KPC are on a highly mobile genetic element that can be transmitted from one bacterium to another thereby spreading resistance. KPC-producing bacteria have spread widely across the United States. In addition to KPC, a number of other carbapenemases exist that can lead to carbapenem resistance; examples of these include New Delhi Metallo-beta-lactamase (NDM), Verona Integron-Encoded Metallo-beta-lactamase (VIM), and Imipenemase Metallo-beta-lactamase (IMP). These metallo-beta-lactamases are more common outside the United States but have been identified rarely in this country, most commonly in patients with exposure to healthcare in endemic countries. Of note, some Enterobacteriaceae are intrinsically nonsusceptible to the carbapenem imipenem, such as *Morganella morganii*, *Proteus* species, and *Providencia* species.

How common are metallo-beta-lactamase-producing CRE like NDM and VIM in The United States?

Although CDC does not conduct systematic surveillance for these organisms, NDM- and VIM-producing Enterobacteriaceae appear to be uncommon in the United States based on CDC’s passive surveillance for these organisms. Metallo-beta-lactamases have been primarily identified in patients who had exposure to healthcare in endemic countries.

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Why are CRE considered epidemiologically important?

CRE are important for a number of reasons. First, these organisms are often resistant to multiple classes of antimicrobials substantially limiting treatment options. Second, infections caused by these organisms are associated with high mortality rates, up to 50% in some studies. Third, many CRE possess carbapenemases which can be transmitted from one Enterobacteriaceae to another potentially facilitating transmission of resistance. Fourth, 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, CDC has developed [recommendations designed to decrease transmission of CRE.\(http://www.cdc.gov/hai/organisms/cre/cre-toolkit/index.html\)](http://www.cdc.gov/hai/organisms/cre/cre-toolkit/index.html)

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 on the body but it is not causing any symptoms or disease. Colonizing CRE strains can go on to 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 which vary based on the site that is infected (e.g., cough if in the lungs, urinary symptoms if in the bladder) but can also include general symptoms like fever or chills.

Which patients are at increased risk for CRE acquisition?

The main risk factors for CRE acquisition in the United States include exposure to healthcare and exposure to antimicrobials. Healthcare-related risk factors include poor functional status, exposure to an intensive care unit, and mechanical ventilation. Outbreaks of CRE have been associated with exposure to long-term care settings. Several antimicrobials have been associated with CRE acquisition including carbapenems, cephalosporins, fluoroquinolones, and vancomycin.

What can clinicians do to prevent CRE transmission?

Strategies to eliminate CRE transmission in healthcare settings focus primarily on recognizing cases, placing colonized or infected patients on Contact Precautions, and using medical devices and antimicrobials wisely. Specific detailed recommendations on preventing CRE transmission in healthcare settings can be found in the [CRE Toolkit](#). Utilize the South Dakota [Inter-facility transfer form](#) when transferring a patient from one healthcare facility to the next. Utilize the South Dakota CRE Workgroup's [screening criteria](#) based on the epidemiological profile of patients in South Dakota.

What infections do CRE cause?

CRE can cause infections in almost any part of the 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. It is important to note that CRE kill up to half of patients who get bloodstream infections from them.

Questions about CRE in South Dakota? Contact the South Dakota [Healthcare-associated Infections Program](#)
605-773-5348

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How are CRE transmitted?

In healthcare settings, CRE are usually transmitted from person to person often via the hands of healthcare personnel or via contaminated medical equipment. As Enterobacteriaceae can commonly be found in stool or wounds, contact with these might be particularly concerning. Ensuring the use of personal protective equipment during and good hand hygiene following exposure to the patient's immediate environment, especially when cleaning up stool or changing wound dressings, is very important. The role of transmission directly from the environment to patients is controversial and requires further investigation.

When can Contact Precautions be discontinued for patients colonized or infected with CRE?

There is currently not enough information for CDC to make a general recommendation on when isolation can be discontinued for patients colonized or infected with CRE. Of note, in investigations in which CDC has participated, it is clear that patients can be colonized for long periods of time (e.g., months). In addition, if considering discontinuing Contact Precautions based on the results of surveillance cultures, it is probably best not to base this decision on the results of a single negative culture as previous experience suggests that patients can be intermittently positive on serial surveillance culture.

Clinicians play a critical role in slowing the spread of CRE. Rapidly identifying patients colonized or infected with these organisms and placing them in Contact Precautions when appropriate, using antibiotics wisely, and minimizing device use are all important parts of preventing CRE transmission.

Steps Clinicians Should Take:

- Know if patients with CRE are hospitalized at your facility, and stay aware of CRE infection rates. Ask if a patient has received medical care somewhere else, including another country.
- Place patients currently or previously colonized or infected with CRE on Contact Precautions. Whenever possible, dedicate rooms, equipment, and staff to CRE patients.
- Wear a gown and gloves when caring for patients with CRE.
- Perform hand hygiene – use alcohol-based hand rub or wash hand with soap and water before and after contact with patient or their environment.
- Alert the receiving facility utilizing the [SD Inter-facility transfer form](#) when you transfer a CRE patient, and find out when a patient with CRE transfers into your facility.
- Make sure labs immediately alert clinical and infection prevention staff when CRE are identified.
- Prescribe and use antibiotics wisely.
- Discontinue devices like urinary catheters as soon as no longer necessary.