

Carbapenem-resistant Enterobacterales (CRE)

BASIC EPIDEMIOLOGY

Infectious Agent

Carbapenem-resistant Enterobacterales (CRE; previously known as Enterobacteriaceae) or Carbapenemase producing Enterobacterales, are gram-negative bacilli resistant to at least one of the carbapenem antibiotics (ertapenem, meropenem, doripenem, or imipenem) or produce a carbapenemase (an enzyme that can make them resistant to carbapenem antibiotics).

Common causes of CRE infections in healthcare settings include *Klebsiella* species, and *Escherichia coli*. Although *Enterobacter* species can be resistant to carbapenem antibiotics, *Enterobacter* species are not included in this CRE definition. *Klebsiella aerogenes*, previously known as *Enterobacter aerogenes*, does meet the case definition.

Carbapenem resistance by *Enterobacterales* can occur by many mechanisms, including the production of a metallo-beta-lactamase or a carbapenemase (such as *Klebsiella pneumoniae* carbapenemase, KPC) which can be transmitted from one *Enterobacterales* to another. Metallo-beta-lactamases such as New Delhi metallo-beta-lactamase (NDM), are more common outside the United States. CRE can also have additional resistance mechanisms such as Verona Integron-Mediated Metallo-B-lactamase (VIM) and OXA-48, which enable organisms to be non-susceptible to many other classes of commonly used antibiotics.

Transmission

CRE can colonize or infect any body site, causing infections including pneumonia, bloodstream infections, urinary tract infections, wound infections, and meningitis. CRE infections happen in the community and in the healthcare settings. A positive CRE culture may signify an infection or colonization. Colonization means the organism is present but not causing any symptoms or disease. Colonized CRE strains can escalate into active infections if they gain access to normally sterile body sites such as blood, urine, or joints.

Transmission occur, via direct person-to-person contact, or secondary contact with contaminated environmental surfaces, medical devices, or equipment. Additionally, healthcare workers' hands may transit CRE due to frequently touching objects in patient environments. Transmission is prevented through hand hygiene compliance, environmental cleaning, and adherence to transmission-based precautions.

Incubation Period

There is no set incubation period for CRE exposure-to-illness onset.

Communicability

The period of communicability is unknown, and may last as long as the organism is present in the individual's system. Studies found that 39% of individuals are still colonized with CRE 1 year after the initial CRE test.

Clinical Illness

Patients exposed to CRE in healthcare settings, such as hospitals or nursing homes, are at the highest risk for CRE infections. Patients with ventilators, urinary catheters, intravenous catheters, and/or long courses of certain antibiotics are particularly susceptible to CRE infections. CRE can cause infections in almost any part of the body. Infection types include bloodstream infections, ventilator-associated pneumonia, and intra-abdominal abscesses. Symptoms associated with CRE infections vary based on the site that is infected (e.g., cough if in the lungs, urinary symptoms if in the bladder). Symptoms can also be generalized such as fever or chills.

DEFINITIONS

Clinical Case Definition

When found in a clinical culture, CRE can represent an infection or colonization. There is no set clinical case definition for a CRE as it can cause many types of symptoms.

Laboratory Confirmation

A *Klebsiella* species or *E. coli* from any body site that is laboratory confirmed:

- *Klebsiella* species or *E. coli* resistant to any carbapenem, including meropenem, imipenem, doripenem, or ertapenem, **OR**
- Production of a carbapenemase (i.e. KPC, NDM, VIM, IMP, OXA-48) demonstrated by a recognized test (i.e. polymerase chain reaction, metallo- β -lactamase test (e.g., E-test) positive, modified Hodge test, Carba NP), **OR**
- Modified Carbapenem Inactivation Method (mCIM) positive or indeterminate, **OR**
- Carbapenem Inactivation Method (CIM) positive, **OR**
- Modified Hodge Test (MHT) positive

Case Classification

Confirmed: Carbapenem-resistant *Enterobacterales* (CRE):

- *Klebsiella* species, or *E. coli* from any body site that is laboratory confirmed.

Note: It is not possible to determine which organism the carbapenemase gene belongs to if a culture-independent diagnostic test (CIDT) reports multiple pathogens detected AND a carbapenemase gene detected is received. In this case, the recommendation is to collect a culture from the same site.

SURVEILLANCE AND CASE INVESTIGATION

Case Investigation

Local and regional health departments will promptly address all reports of CRE. The investigation steps below describe the public health activities to complete when a CRE case is reported. Investigations and control measures are required for infection or colonization with any type of CRE.

Case Investigation Checklist

- The jurisdiction of the healthcare facility with a positive CRE confirmation will conduct the investigation (e.g., patient tested positive for CRE *E. coli* and is in hospital in

jurisdiction A, but the patient resides in jurisdiction B, jurisdiction A would conduct the investigation).

- Immediately ensure contact precautions are implemented for anyone with a reported CRE.
- Confirm the laboratory results meet the case definition.
 - If unclear, call a DSHS Healthcare Safety Unit (HSU) HAI or AR Epidemiologist for assistance.
- Ensure additional control measures are in place for cases and/or facilities (see “specific control measures” section below).
- Review the medical records and speak to an Infection Preventionist (IP) at the affected healthcare facility to verify demographics, symptoms, and course of illness.
- If the patient was discharged from the reporting healthcare facility and the receiving healthcare facility is known, the investigator ensures that the receiving healthcare facility is informed of the CRE cases and that control measures are in place.
- Refer to the CRE Investigation form (<http://www.dshs.texas.gov/idcu/investigation/>) for additional questions to address.
 - Use the CRE Investigation NCP-CRE Investigation and use CPO Investigation for CP-CRE.
- All cases of CRE require the investigation form to be completed.
- A paper copy of the Investigation form and laboratory report is NOT required to be sent to DSHS HSU unless specifically asked.
- Enter all confirmed case investigations and submit a notification in NEDSS within 30 days of the initial report.
 - The jurisdiction that conducted the investigation enters the case in TXNEDSS.
- The jurisdiction is entered as the jurisdiction who conducted the investigation and not the jurisdiction of residency.
- If the jurisdiction needs to be changed to the patient’s residential jurisdiction, the Investigator should add a comment prior to submitting notification, upon case approval.
- Once the case is reviewed and approved, the approver will update the jurisdiction of residency for aggregate reporting purposes.
 - NOTE: If a case involves multiple jurisdictions, it is the responsibility of the investigator to notify other jurisdictions of the case.
- Any labs collected and reported within six months of the initial investigation lab collection date should be associated to the same investigation.
- Following six months of the initial confirmed lab result date, a new investigation must be initiated, with every additional six-month period requiring a new investigation.

PREVENTION AND CONTROL MEASURES

Control measures for Cases

Ideally, the facility is performing control measures for the case. The investigator is communicating directly with the facility, most likely with the IP or the responsible representative overseeing infection prevention. The investigator ensures the below control measures are addressed with the reporting healthcare facility. Specific control measures might not be necessary for all case investigations.

Specific Control Measures

- Facilities are responsible for ensuring that healthcare personnel perform hand hygiene—use alcohol-based hand rub or wash hands with soap and water before and after contact with patients and their environment.
- Ensure the patient is on contact precautions.

- Recommend single patient rooms, if available.
 - If single rooms are not feasible, recommend only cohorting patients with the same organism (ex: a patient with CRE-Escherichia coli [CRE-E. coli] and another patient with CRE-E. coli)
- Don (put on) gown and gloves either before or upon immediate entry into the patient's room. (Note: Some facilities might require more personal protective equipment [PPE]).
- Doff (remove) gown, gloves and any other PPE immediately upon exiting the patient's room.
- No recommendation currently exists for discontinuing contact precautions for CRE. A facility should consult with an infectious disease physician, the IP, or the provider that initiated the precautions. The facility may also call a DSHS HAI Epidemiologist for assistance.
- Reduce risk factors associated with MDRO transmission
 - Recommend evaluating the need for invasive devices on a daily basis and discontinuing when no longer necessary.
- Recommend staff cohorting when feasible. This means that certain staff are dedicated specifically to the care of patients with the same organism, and the staff member does not care for any patients without the organism.
- Ensure the facility is using disposable noncritical patient-care equipment (e.g., blood pressure cuffs) or implement patient-dedicated use of such equipment. If common use of equipment for multiple patients is unavoidable, clean and disinfect such equipment with an EPA registered hospital grade disinfectant before use on another patient. Ensure manufacturer's recommendations are followed for contact time of the disinfectant. Note: Contact time is the time it takes for the disinfectant to kill the organism, e.g., two minutes).
- Verify appropriate EPA disinfectants are being utilized to clean all surfaces and contact times are being followed.
 - Encourage more frequent cleaning of "high touch surfaces" throughout the unit and/or facility.
- Verify the facility laboratory is immediately alerting clinical staff and the infection preventionist when CRE is identified.
- Ensure physicians, hospital staff, patients, and visitors are educated on MDROs

Treatment

Each case will have a unique treatment option. It is recommended that the reporting facility collaborate with a clinical pharmacist, an infectious disease physician, and/or an antibiotic stewardship resource for an individualized treatment plan.

Exclusions

Students (K-12) and daycare age children with CRE or CP-CRE wound infection need to be excluded from attendance until drainage from wounds or skin and soft tissue infections is contained and maintained in a clean dry bandage; restrict from situations that could result in the infected area becoming exposed, wet, soiled, or otherwise compromised. No other exclusions apply.

MANAGING SPECIAL SITUATIONS

Outbreaks

If an outbreak is suspected, immediately notify a DSHS HAI Epidemiologist. The DSHS HAI Epidemiologist will notify their leadership.

Outbreak Definition

At this time there are no defined criteria for an outbreak.

REPORTING AND DATA ENTRY REQUIREMENTS

Provider, School and Child-care Facilities, and General Public Reporting Requirements

Cases of Carbapenem-resistant *Enterobacterales* (CRE) should be reported within 1 working day to the local or regional health department. If the jurisdiction is unclear, call a DSHS HAI Epidemiologist or the Healthcare Safety Unit at 512-776-7676 for assistance.

Local and Regional Reporting and Follow-up Responsibilities

- Promptly investigate all reported CRE labs.
- Ensure control measures are in place, this should occur promptly prior to transfer to another unit, healthcare facility, or discharge home.
- Provide facility education to prevent further spread of disease (see specific control measures section located in this document).
- If an electronic laboratory report (ELR) notification is in TX NEDSS, follow-up promptly to obtain lab susceptibility report.
- Enter the confirmed case into TX NEDSS when the first occurrence is reported and create the TX NEDSS notification to DSHS on all cases of CRE. Complete additional case information and enter the remaining information within 30 days of initial report.
 - Please refer to the NBS Data Entry Guide for specific details on how to properly complete an TX NEDSS investigation, how to data enter a laboratory report and submit a notification.
- Local health departments may request assistance with the investigation of CRE by contacting both the DSHS Regional Lead Epidemiologist and the DSHS HAI Epidemiologists for the respective public health region (PHR).
- Because of the potential for transmission of CRE to vulnerable patients in healthcare settings, public health action is imperative in controlling further transmission by instituting control measures, identifying and screening close contacts of cases that could transmit in healthcare settings, if indicated, and ensuring that the facility IP has been notified and that appropriate infection control measures are in place.

When a cluster or an outbreak is investigated, local and regional health departments should:

- Report suspected outbreaks within 24 hours of identification to a DSHS HAI Epidemiologist.
- All investigation forms and other supporting documents will be shared with the DSHS HAI Epidemiologist per region specific process.
 - Fax documents securely to designated region.
 - Upload documents into Texas Public Health Information Network (Phin).
 - Upload in NBS under supplemental documentation.

If labeling a case as part of an outbreak, the outbreak must be named in NBS. Outbreak names must be requested through the NEDSS (NBS) office. The staff can be reached by phone (512) 458-7111 ext. 7729 or email NEDSS@dshs.texas.gov.

DISEASE REPORTING

Purpose of Reporting and Surveillance

- To prevent transmission of infections with CRE, in healthcare facilities and the community, by decreasing the likelihood of transmission through the investigation process.
- To improve the detection, monitoring, epidemiological characterization, antibiotic resistance mechanisms, and identification of CRE trends in Texas.
- To develop, implement and evaluate strategies to prevent the emergence, transmission and persistence of CRE.
- To conduct and support epidemiological studies to identify outbreaks and potential sources of ongoing transmission in various populations.

Reporting

- Report CRE *E. coli* and CRE-Klebsiella species to your local health jurisdiction **within 1 working day**.

LABORATORY PROCEDURES

Clinical laboratories are not required to submit isolates to the DSHS Laboratory at this time. To obtain confirmatory, gene sequencing or phenotypic testing, clinical laboratories can contact a reference laboratory for those services. The reference lab will give guidance on specimen collection, submission form and shipping.

Any specimen sent to the DSHS Laboratory for possible outbreak situations or molecular testing requires prior approval from a DSHS HAI epidemiologist.

REVISION HISTORY

- February 2021
 - Updated verbiage from NBS to TX NEDSS.
- December 2021
 - Added CP-CRE with the case definition and laboratory identification criteria.
- January 2023
 - Exclude CP-CRE from CRE
 - Edited disease transmission section
 - Added note on CIDT under case classification