Carbapenem-resistant *Enterobacteriaceae* (CRE)

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BASIC EPIDEMIOLOGY

Infectious Agent

Carbapenemase producing *Enterobacteriaceae* or Carbapenem-resistant *Enterobacteriaceae* (CRE), specifically *Klebsiella* species and *E. coli*, are gram-negative bacilli that have the ability to break down the carbapenem class of antibiotics rendering them ineffective. Carbapenem resistance by *Enterobacteriaceae* 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 *Enterobacteriaceae* 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

Enterobacteriaceae are a family of bacteria that can be found in a person's gastrointestinal tract. These type of bacteria can cause infections both in the community and in the healthcare settings. A positive CRE culture can 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 can occur via direct person-to-person contact. Secondary contact with contaminated environmental surfaces, medical devices, or equipment can also lead to transmission. Additionally, the hands of healthcare workers who frequently touch objects in patient environments often become vectors of transmission. Transmission can be prevented through hand hygiene compliance, environmental cleaning, and adherence to transmission-based precautions.

Incubation Period

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

Communicability

The period of communicability is unknown. Communicability may be as long as the organism is present in the individual's system. Studies have shown that 39% of individuals may remain colonized with CRE at 1 year from initial test date.

Clinical Illness

Patients at highest risk for CRE infections are those exposed to healthcare settings such as hospitals or nursing homes. Patients with ventilators, urinary catheters, intravenous catheters, and patients taking long courses of certain antibiotics are at greater risk for developing 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 generally 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 anybody site that is laboratory confirmed.
    - *Klebsiella* species and *E. coli* that are **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, modified Hodge test, Carba NP).

Case Classification

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

- *Klebsiella* species or *E. coli* from anybody site that is laboratory confirmed.

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 be completed 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 where the healthcare facility is located and resulted in a positive confirmation of CRE 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 have been implemented for anyone with a reported CRE.
- ☐ Confirm that the laboratory results meet the case definition.
    - If it is unclear, call a DSHS HAI 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 healthcare facility to verify demographics, symptoms, and course of illness.
- ☐ If the patient has been 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 case and ensures control measures are in place.
- ☐ Refer to the CRE Investigation form for additional questions to address.
- ☐ The CRE Investigation Form is available on the DSHS Website: http://www.dshs.texas.gov/idcu/investigation/
- ☐ 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 EAIDU 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 TX NEDSS.

- The jurisdiction is entered as the jurisdiction who conducted the investigation and not the jurisdiction of residency.
- Investigator should add a comment prior to submitting notification if jurisdiction needs to be changed to the patient's residential jurisdiction, 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.
- Labs collected and reported within six months of initial lab collection should be associated with the initial investigation.
- Labs collected and reported after six months of an initial confirmed lab result require a new investigation every six months.

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 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 *Enterobacteriaceae* (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, specifically CRE-*E. coli* and CRE-*Klebsiella* species 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.

UPDATES

February 2021

- Updated verbiage from NBS to TX NEDSS.