

Multi-drug Resistant Organism Guidance for Carbapenem-resistant *Enterobacteriaceae* (CRE) and Multi-drug resistant *Acinetobacter* (MDR-A)

Disease Reporting

Purpose of Reporting and Surveillance

- To prevent transmission of infections with carbapenem-resistant *Enterobacteriaceae* (CRE), specifically CR-*Escherichia coli* and CR-*Klebsiella* species as well as multi-drug resistant *Acinetobacter* (MDR-A) in and among health care facilities and between health care facilities and the community.
- To improve the detection, monitoring and epidemiological characterization of CRE/MDR-A in Texas.
- To develop, implement and evaluate strategies to prevent the emergence, transmission and persistence of CRE and MDR-A.
- To conduct and support epidemiological studies to identify outbreaks and potential sources of ongoing transmission in various populations.

Requested Reporting

- Health care providers, facilities and/or laboratories: as of April 20, 2014 CRE & MDR-A are notifiable conditions. Report to local health jurisdiction **immediately**.

Local Health Jurisdiction Investigation Responsibilities

- Local health departments may choose to request assistance with the investigation and reporting of CRE/MDR-A from a regional or central office Health Care Safety Epidemiologist.
- Because of the potential for transmission of CRE to vulnerable patients in health care settings, public health action is required to institute control measures, and identify and screen close contacts of cases that could transmit in health care settings, if indicated; ensure that the facility infection preventionist (IP) has been notified and appropriate infection control measures are in place.
- For all confirmed and probable cases, complete case investigation in NBS.

Basic Epidemiology

Infectious Agent

Carbapenem-resistant *Enterobacteriaceae* (CRE):

Carbapenemase producing *Enterobacteriaceae* or Carbapenem-resistant *Enterobacteriaceae*, specifically *Klebsiella* species and *E. coli*, are gram-negative bacilli that have the ability to break down the carbapenem antibiotic rendering it 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 but, in rare cases, have been identified in American patients with exposure to health care in other

countries where these strains are endemic. CRE can also have additional resistance mechanisms that enable them to be nonsusceptible to many other classes of commonly used antibiotics. Texas has received one report of an individual with recent international travel that was identified with the NDM resistance mechanism.

Multi-drug Resistant *Acinetobacter* (MDR-A):

Acinetobacter are strictly aerobic gram negative coccobacilli of the Moraxellaceae family and have more than 25 species within the genus (Rosenbaum et. al.). They have an intrinsic resistance factor that enables them to hydrolyze carbapenem, causing resistance to carbapenems and penicillins (Rosenbaum et. al.). Multi-drug resistant *Acinetobacter* strains can also circumvent antibiotics by producing porins, modifying penicillin-binding proteins and producing aminoglycoside modifying enzymes, among other ways (Rosenbaum et. al.).

Transmission

Enterobacteriaceae are a family of bacteria that can be found in people's gastrointestinal tract that can cause infections both in community and health care settings. When found in a clinical culture, CRE can represent an infection or colonization (present but not causing any symptoms or disease). Colonizing CRE strains can escalate into full blown infections if they gain access to body sites that are usually sterile, like the bloodstream, bone or joints.

Acinetobacter species are ubiquitous in nature and have been found in soil, water, animals and humans. In humans, it has been isolated from the skin, throat and rectum, and has been reported to be a colonizer of the respiratory tract in health care settings (Rosenbaum et. al.).

Transmission for both organisms can occur via direct person-to-person contact or secondary contact with contaminated environmental surfaces, medical devices, or equipment. Additionally, the hands of health care workers who frequently touch these objects in patient environments often become vectors of transmission if hand hygiene compliance and/or transmission-based precautions are not adhered to.

Incubation Period

Symptoms associated with CRE and MDR-A infections generally 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. There is no set incubation period for exposure-to-illness onset.

Communicability

The period of communicability is unknown and may be as long as the organism is present in the individual. Studies have shown that 39% of individuals may remain colonized with CRE at 1 year from initial test date (Zimmerman et. al.).

Acinetobacter is capable of surviving on inanimate surfaces for extended periods of time: from a few weeks to a month or more (Rosenbaum et. al.). When outbreaks occur, often due to incomplete surface cleaning of the environment and medical instrument, and *Acinetobacter* becomes endemic to a health care setting, implementing successful and sustainable elimination can prove to be extremely challenging (Rosenbaum et. al.).

Clinical Illness

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.

Health care-associated *Acinetobacter* respiratory tract infections, including ventilator associated pneumonia, catheter related urinary tract infections, bloodstream infections, and wound infections have all been well documented in medical literature. There have also been reports of *Acinetobacter* meningitis, endocarditis, osteomyelitis, corneal perforation and infection associated with peritoneal dialysis (Rosenbaum et. al.).

Severity

The case fatality rate of CRE can be as high as 50%, as reported for bloodstream infections (National Center for Emerging and Zoonotic Infectious Diseases). MDR *Acinetobacter* patients, per one study, showed higher in-hospital mortality rates up to 26% infected patients were more likely to have both longer hospital and ICU lengths of stay than uninfected patients (Sunenshine, et. al.).

Case Definitions & Laboratory Services

Clinical Case Definition

When found in clinical culture, CRE and MDR-A can represent an infection or colonization. There is no set clinical case definition as both can cause many types of symptoms.

Laboratory Confirmation Tests

1. Carbapenem-resistant *Enterobacteriaceae* (CRE):
 - a. **Confirmed CRE:** *Klebsiella* species or *E. coli* from any body site/source that possess/contain a gene sequence specific for carbapenemase.
 - i. A positive PCR test.
 - b. **Probable CRE:** *Klebsiella* species or *E. coli* from any body site/source that is:
 - i. Positive for carbapenemase production by a phenotypic test (e.g., Modified Hodge Test)
 - OR**
 - ii. Nonsusceptible (i.e. intermediate or resistant) to at least one of the following carbapenems: doripenem, meropenem, or imipenem. Minimal Inhibitory concentration (MIC) listed below as guidance.

Antibiotic	MIC (µg/mL)		
	Susceptible	Intermediate	Resistant
Doripenem	≤1	2	≥4
Imipenem	≤1	2	≥4
Meropenem	≤1	2	≥4

2. Multi-drug resistant *Acinetobacter*
 - a. **Confirmed MDR-A:** *Acinetobacter* species that are:
 - i. Nonsusceptible (i.e., intermediate or resistant) to at least 1 antibiotic in at least 3 antimicrobial classes of the following 6 antimicrobial classes:

Beta-Lactam	Aminoglycosides	Carbapenems	Fluoroquinolones	Cephalosporins	Sulbactam
Piperacillin Piperacillin/	Amikacin Gentamicin	Imipenem Meropenem	Ciprofloxacin Levofloxacin	Cefepime Ceftazidime	Ampicillin/ sulbactam

tazobactam	Tobramycin	Doripenem			
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Case Classification

- Confirmed CRE: *Klebsiella* species or *E. coli* from any body site/source that meets the confirmed laboratory criteria for CRE.
- Probable CRE: *Klebsiella* species or *E. coli* from any body site/source that meet the probable CRE laboratory criteria for CRE.
- Confirmed MDRA: *Acinetobacter* species from any body site/source that meets the confirmed laboratory criteria for MDRA.

Case Categories

- Confirmed and probable cases should be separated into case categories as follows (National Healthcare Safety Network) and this will be determined by the central office staff:
 - Health care-associated case: Any specimen collected >3 days after admission to the facility (i.e., on or after day 4)
 - Community-acquired case: Any specimen collected as an outpatient or an inpatient ≤3 days after admission to the facility (i.e., days 1, 2, or 3 of admission)
- Cluster or Outbreak Definition
 - Texas will be collecting baseline data during the calendar years 2014-2015. At this time there are no defined criteria for an outbreak. If your health department believes they are working an outbreak, it is recommended to speak with the MDRO Epidemiologist in Central Office.

Case Investigation and Treatment

Case Investigation

Local and regional health departments should immediately address all reports of CRE and MDR-A. Investigators should first review control measures with reporting facility, when applicable. An interview to get the required information can be performed at a later date, if needed; interviewee can be the case-patient, surrogate or an infection preventionist. Please use the Multi-drug Resistant Organism Investigation Form available on the DSHS Website: <http://www.dshs.state.tx.us/idcu/investigation/>

Case Investigation Checklist (also listed in Appendix A)

- Confirm that the laboratory results meet the confirmed or probable case definition
 - If it is unclear, call the DSHS MDRO Epidemiologist in the Central Office for assistance, 512-776-6356.
- Ensure control measures are in place for cases and/or facilities (see below)
- Review medical records or speak to an infection preventionist or physician to verify demographics, symptoms, underlying health conditions, and course of illness.
 - Refer to the MDRO Investigation form for list of questions to cover

- Document in NBS the previous 6 months of healthcare stays prior to the current admission or positive culture.
- Notify an MDRO Epidemiologist in the Austin central office by phone 512-776-6356, fax 512-776-7676, or email within 7 days of initial report.
- Enter all confirmed and probable case investigations and submit a notification in the NEDSS Base System (NBS) within 30 days of initial report.

Control Measures

Control measures for cases

Ideally the facility is performing control measures for the case and the Epi investigator is communicating directly with the facility, most likely with the person over infection prevention. Depending on the situation it may be the Epi investigator who is talking with the patient and will want to promote basic control measures, which include:

- Instruct patient that if they are prescribed antibiotics, they should take all that come in the package and to take them as listed on the instructions. If the patient does not understand the instructions, to talk with their pharmacist or physician. Additionally, remind them to not share or save antibiotics or to stop taking the antibiotics even if they feel better - to finish all the prescribed medication.
- Encourage patient to inform medical staff of their MDRO status, including future medical visits.
- Remind patient that during visits to a health care facility or office to wash or sanitize hands frequently and to ask others to do the same before having contact with patient or patient belongings.
- Encourage patient to stay involved in their care, such as asking if room has at least a daily thorough disinfection and that equipment is cleaned before and after it is used on patient;
 - If case is no longer in a health care setting, encourage routine disinfection of frequently touched places at their residence.

Control measures for facilities

- Facilities should ensure that health care personnel are vigilant on hand hygiene practices and that adequate hand hygiene stations are accessible, free from clutter/supplies and well stocked.
- Ensure the case is on contact precautions, aka contact isolation. Most infection preventionist are familiar with these basics:
 - Contact precautions entail: Performing hand hygiene before entry into room; donning gown and gloves either before or upon immediate entry into case's room; and removing gown and gloves and performing hand hygiene prior to exiting or upon immediate exit of case's room.
 - Disinfection of reusable equipment after use.
 - No recommendation currently exists for when to remove a case from contact precautions.
- Recommend optional screening for cohabitant of case (if one exists) for CRE, via rectal swab. See CDC Laboratory Protocol http://www.cdc.gov/hai/pdfs/labsettings/klebsiella_or_ecoli.pdf
- Recommend optional screening for cohabitant of case (if one exists) for MDR-A. Candidate body sites for screening cultures may include the nose, the throat, skin sites such as the axilla and/or groin, the rectum, open wounds and endotracheal aspirates.
- Recommend patient and/or staff cohorting, if feasible
- Recommend minimal use of invasive devices for patients on the unit where the case was cared for.
- If case has been discharged from reporting facility and the receiving facility has not been informed about the notifiable condition, the Epi may need to contact the receiving facility and inform. May need to go over control measures with receiving facility.

- If the case was transferred from another facility and the sending facility has not been informed about the notifiable condition, the Epi Investigator may need to contact the sending facility the patient was previously at and go over control measures with them.

Treatment

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

Exclusions

Students (K-12) and daycare age children with CRE or MDR-A 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.

Reporting and Data Entry Requirements

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

Cases of Carbapenem-resistant *Enterobacteriaceae* and Multi-drug resistant *Acinetobacter* should be reported **immediately** to the local or regional health department. If jurisdiction is unclear, call the DSHS MDRO Epidemiologist in the Central Office for assistance, 512-776-6356.

Local and Regional Reporting and Follow-up Responsibilities (Also listed in Appendix A)

Local and regional health departments should:

- Immediately investigate all reported cases
- Ensure control measures are in place and provide education to prevent further spread of disease
- Enter the case into NBS when first occurrence reported. Submit an NBS notification on all confirmed and probable cases of carbapenem-resistant *Enterobacteriaceae* and multi-drug resistant *Acinetobacter* to DSHS within 30 days.
 - Fax: 512-776-7616, or
 - Mailed to:
 - Emerging and Acute Infectious Disease Branch
 - Texas Department of State Health Services
 - Mail Code: 1960
 - PO Box 149347
 - Austin, TX 78714-9347

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

- Report suspected outbreaks within 24 hours of identification to the regional DSHS office or to the DSHS Central Office Infectious Disease Control Unit at 512-776-7676.
- 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.state.tx.us.

Laboratory Procedures

Clinical laboratories are not required to submit isolates to the DSHS Laboratory. To obtain confirmatory, gene sequencing or phenotypic testing, clinical laboratories should 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 requires prior approval from a DSHS epidemiologist.

Additional Links & Useful Resources

CDC Website on CRE and the CRE 2012 toolkit:

<http://www.cdc.gov/HAI/organisms/cre/index.html>

CDC Website on Antibiotic Resistance Threats in the United States 2013:

<http://www.cdc.gov/drugresistance/threat-report-2013/pdf/ar-threats-2013-508.pdf>

Guide to the Elimination of Multidrug-resistant *Acinetobacter baumannii* Transmission in Healthcare Settings:

http://www.apic.org/resource/_eliminationguideform/b8b0b11f-1808-4615-890b-f652d116ba56/file/apic-ab-guide.pdf

Multidrug-resistant *Acinetobacter* infection mortality rate and length of hospitalization:

<http://wwwnc.cdc.gov/eid/article/13/1/06-0716.htm>

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Zimmerman F, Assous M, Bdolah-Abram T, Lachish T, Yinnon A, Wiener-Well Y. Duration of carriage of carbapenem-resistant Enterobacteriaceae following hospital discharge. *Am J Infect Control* 2013;41:190-4

Updates

Created 1/02/14

Revised 5/12/14

Appendix A. Case Investigation Checklist

- Confirm that the laboratory results meet the confirmed or probable case definition
 - If unclear, call the Central Office MDRO Epidemiologist for assistance, 512-776-6356.
- Ensure control measures are in place for cases and/or facilities (see below)
- Review medical records or speak to an infection preventionist or physician to verify demographics, symptoms, underlying health conditions, and course of illness.
 - Refer to the MDRO Investigation form for list of questions to cover
 - Document in NBS the previous 6 months of healthcare stays prior to the current admission or positive culture.
- Notify Central Office or the MDRO Epidemiologist within 7 days of initial report.
- Enter all confirmed and probable case investigations and submit a notification in the NEDSS Base System (NBS) within 30 days of initial report.

Control measures for cases

Should an investigator need to provide a case with information on basic control measures, these would include:

- Instruct patient that if they are prescribed antibiotics, they should take all that come in the package and to take them as listed on the instructions. If the patient does not understand the instructions, to talk with their pharmacist or physician. Additionally, remind them to not share or save antibiotics or to stop taking the antibiotics even if they feel better - to finish all the prescribed medication.
- Encourage patient to inform medical staff of their MDRO status, including future medical visits.
- Remind patient that during visits to a health care facility or office to wash or sanitize hands frequently and to ask others to do the same before having contact with patient or patient belongings.
- Encourage patient to stay involved in their care, such as asking if room has at least a daily thorough disinfection and that equipment is cleaned before and after it is used on patient; Or simply encourage routine disinfection of frequently touched places at their residence.

Control measures for facilities

- Facilities should ensure vigilant hand hygiene practices and access to hand hygiene stations.
- Ensure the case is on contact precautions/isolation. Contact precautions entail:
 - Performing hand hygiene before entry into room; donning gown and gloves either before or upon immediate entry into case's room; and removing gown and gloves and performing hand hygiene prior to exiting or upon immediate exit of case's room. Disinfection of reusable equipment after use.
 - No recommendation currently exists for when to remove a case from contact precautions.
- CRE: Recommend optional screening for cohabitant of case via rectal swab. See CDC Laboratory Protocol http://www.cdc.gov/hai/pdfs/labsettings/klebsiella_or_ecoli.pdf
- MDRA: Recommend optional screening for cohabitant of case. Candidate sites for screening cultures include the nose, throat, axilla, groin, rectum, open wounds and endotracheal aspirates.
- Recommend patient and/or staff cohorting, if feasible
- Recommend minimal use of invasive devices for patients on unit where the case was cared for.
- If case has been discharged from reporting facility and the transferring facility has not been informed about the notifiable condition, the Epi may need to contact transferring facility and inform or ask the reporting facility to communicate directly.