Carbapenem-resistant Enterobacteriaceae

Recommendations for Healthcare Outbreak Response

A. Background

Carbapenem-resistant Enterobacteriaceae (CRE) are often resistant to many other antimicrobials, limiting therapeutic options; invasive CRE infections are associated with mortality of 40-50%. CRE are primarily identified among patients with healthcare exposure, and most transmission appears to occur in these settings. CRE have spread throughout most parts of the United States and have the potential to spread more widely. Coordination between public health and healthcare facilities is necessary to identify CRE colonized and infected patients and implement interventions to halt transmission within healthcare facilities and limit further spread across regions.

Some CRE possess a carbapenemase, e.g., Klebsiella pneumoniae carbapenemase (KPC), that directly breaks down carbapenems and is often contained on a mobile genetic element that facilitates transfer of resistance among Enterobacteriaceae and other gram-negative organisms. Much of the increase in CRE in the United States since 2000 has been due to the spread of carbapenemase-producing CRE (CP-CRE), particularly KPC-producing CP-CRE; other carbapenemases, e.g., New Delhi Metallo-beta lactamase (NDM) remain uncommon. The potential for rapid spread of CP-CRE has made these organisms a particularly important target for prevention.

B. Outbreak Detection and Reporting

1. Proposed Investigation/Reporting Thresholds and Outbreak Definition for *Carbapenem-resistant Enterobacteriaceae*

The suggested thresholds and definitions below were based on expert opinion and are intended to reflect the local epidemiology of carbapenem-resistant Enterobacteriaceae (CRE). Case numbers include both colonization and infection, identified in patients not previously known to have CRE. Note that state and local jurisdictions may have their own reporting requirements or outbreak definitions. For example, the information provided here does not replace reporting of carbapemenase-producing (CP)-CRE[1] as part of the Nationally Notifiable Disease Surveillance System. The intended use of the suggested thresholds for facilities to investigate and report to public health is to ensure that sentinel cases and possible outbreaks are detected early and controlled in an effective and timely manner. Guidance detailing the investigation of CRE is available from CDC.[2,3] Healthcare facilities should consult public health if they have questions.

2. For Long-Term Care Facilities (LTCF), Critical Access Hospitals, Dialysis Facilities, and Outpatient Facilities:

2.1. The threshold for starting investigation and reporting to public health is 1 CRE (CP, non-CP, or unknown CP[4])

2.2. Outbreaks[5] are defined as: ≥ 2 CRE of same organism (or mechanism, if mechanism testing performed) in a 4-week period in patients that are epidemiologically-linked[6] or determined to be genetically-related[7] by laboratory testing.

3. For Acute Care Hospitals, Long-Term Acute Care Hospitals and High-Acuity Long-Term Care Facilities[8]:

The suggested thresholds for starting investigation and reporting to public health are dependent on CRE prevalence, which varies from region to region and even from facility to facility within a region.[9] Facilities should consult with public health for guidance about which prevalence category they should use; if the category is uncertain, consider beginning with the thresholds for low CRE prevalence and modifying as more information becomes available.

3.1 Very Low – CRE are rarely identified; typically, facilities experience only one or a few cases per year

3.3.1. The threshold for starting investigation and reporting to public health is

i. 1 CRE (CP, non-CP, or unknown CP[4])

3.2 Low – CRE are identified with some regularity; facilities might average one case per month

3.3.1. The thresholds for starting investigation are

i. 1 CP-CRE (KPC, NDM, VIM, IMP, OXA-48 type, or positive by phenotypic test)

ii. 2 CRE (non-CP or mechanism testing not performed[4]) of same organism in a 4-week period in patients on the same unit[10]

3.2.2. The thresholds for reporting to public health are

i. 1 CP-CRE (KPC, NDM, VIM, IMP, OXA-48 type, or positive by phenotypic test)

ii. 2 CRE (non-CP or mechanism testing not performed[4]) of same organism in a 4-week period in patients that are epidemiologically-linked[6], with confirmatory laboratory testing

3.3 High/Endemic – CRE are routinely identified; facilities might average several cases per month, trending to one or more cases per week in endemic sites

3.3.1. The thresholds for starting investigation are

i. 1 non-KPC CP-CRE (NDM, VIM, IMP, OXA-48 type)[11]

ii. 2 KPC-CRE, 2 CP-CRE (unknown mechanism[4]), or 2 CRE (non-CP or mechanism testing not performed) of same organism in a 4-week period in patients on the same unit[10,12]

3.3.2. The thresholds for reporting to public health are

i. 1 non-KPC CP-CRE (NDM, VIM, IMP, OXA-48 type)[11]

ii. 2 KPC-CRE, 2 CP-CRE (unknown mechanism[4]), or 2 CRE (non-CP or mechanism testing not performed) of same organism in 4-week period patients that are epidemiologically-linked[6,12]

Outbreaks[5] are defined as: ≥ 2 CRE of same organism (or mechanism, if mechanism testing performed) in a 4-week period in patients that are epidemiologically-linked[6] or determined to be genetically-related[7] by laboratory testing.

4. Points for Consideration

4.1. CRE-related acronyms are defined as follows: CP=carbapenemase-producing; non-CP = non carbapenemase-producing; KPC=Klebsiella pneumoniae carbapenemase; NDM = New Delhi Metallo-β-Lactamase; OXA-48-type = oxacillinase; VIM = Verona-Integron encoded carbapenemase; IMP = active-on-Imipenem Metallo-β-lactamase

4.2. CDC. Interim Guidance for a Public Health Response to Contain Novel or Targeted Multidrug-resistant Organisms (MDROs). Available at: https://www.cdc.gov/hai/containment/guidelines.html

4.3. CDC. Facility Guidance for Control of Carbapenem-resistant Enterobacteriaceae (CRE). Available at: https://www.cdc.gov/hai/organisms/cre/index.html

4.4. When CP mechanism is unknown, facilities should consider arranging testing via the public health laboratory in their state as part of the Antibiotic Resistance Laboratory Network (ARLN). Note that screening tests to identify asymptomatic carriers are also available at no cost through ARLN.

4.5. Facilities in high prevalence or endemic areas whose baseline exceeds this level should work with public health to consider adjusting these parameters.

4.6. Examples of epidemiologic links include (but are not limited to) patients who: resided on same unit (or within same facility if facility is small), were transferred from or seen at the same outside facility, were assigned to same primary or consultative service, had facility staff in common, or had same procedure.

4.7. Laboratory testing methods commonly used for assessing genetic relatedness include pulsed field gel electrophoresis (PFGE) and whole genome sequencing (WGS).

4.8. The term High Acuity Long Term Care Facilities is used here to refer to Nursing Homes and Skilled Nursing Facilities that provide care to residents who require mechanical ventilation or complex wound care.

4.9. CRE prevalence may vary among facilities in a region due to facility bed size, patient population, whether admission screening or active surveillance is conducted, and other factors, such as transfer patterns. Facilities whose prevalence differs from the regional average might be advised to use a different threshold. Of note, some facilities might fall into one prevalence group for CP-CRE and a different prevalence group for CRE.

4.10. Patients do not need to have overlapping stays to meet the threshold for investigation. In addition to admission on a common unit, consider additional factors that might indicate a common exposure, such as invasive procedures, as triggers for additional investigation.

4.11. Non-KPC CRE remain rare throughout the U.S. Identification of any non-KPC CP-CRE (or KPC CRE in non-endemic areas) should result in a public health investigation as described in the CDC Interim Guidance for a Public Health Response to Contain Novel or Targeted Multidrug-resistant Organisms.

4.12. In high prevalence or endemic areas, the threshold of 2 CRE was selected for greatest sensitivity. For some facilities (e.g., in KPC endemic settings), this threshold might be too sensitive and burdensome. In this case, facilities should know their baseline CRE prevalence and collaborate with public health to determine appropriate thresholds that represent a rise above baseline and carefully balance sensitivity with specificity. Facilities in these regions might have a lower threshold for investigating and reporting non-K. pneumoniae CRE, which could carry less common carbapenemases, compared to carbapenem-resistant K. pneumoniae.

C. Investigation and Control

The following sections outline important actions and considerations in conducting a CRE investigation in an Acute or Long-Term Care Facility (please see the primary references for additional details). Some of these actions can be conducted by the facility, while others may require assistance from the health department. Collaboration between the facility and public health helps ensure a successful investigation. Public health should support the facility by providing guidance and resources. The health department may be able to provide assistance with infection control assessment, medical record review, laboratory testing, data analysis, and other activities as appropriate for the investigation. This will depend on the circumstances of the potential outbreak as well as the resources of the facility and the health department. The need for an on-site visit to the facility should be determined based on the number of the cases, patient population, severity of illness, and level of assistance required.

1. **Initial Investigation/Case Review**
   - 1.1. When CP mechanism is unknown, submit CRE isolates to public health laboratory for CP testing; some public health laboratories may request all or a subset of CRE isolates, including known CP-CRE.
   - 1.2. Perform additional case finding by reviewing microbiology records and establishing prospective laboratory surveillance.
   - 1.3. Perform case review(s) to identify recent health care encounters, including stays at other health care facilities during the 6-12 months prior to CRE identification.
   - 1.4. Construct a line list that includes information such as admission date, admission source, location(s) in the facility, movement of the patient within the facility, procedures (e.g., duodenoscopy), date of positive test, and specimen source. See the example of a line list from CDPH.
2. **Contact Screening**
   - 2.1. Screen epidemiologically-linked patient contacts (e.g., roommates) for CRE with rectal swabs[1]. Decisions about which contacts to screen depend on characteristics of the organism, the setting, and in some cases the patient; refer to CDC's Interim Guidance for a Public Health Response to Contain Novel or targeted Multidrug-Resistant Organisms[2].
   - 2.2. Consider a point prevalence survey (PPS) of the entire affected unit particularly if more than one CRE patient is identified.

Consider screening patient contacts in facilities where the CRE patient had overnight healthcare exposures during the X time frame prior to identification of CRE.

3. Patient Placement and Cohorting

3.1. Cohorting patients and the primary staff that care for them has been shown to decrease transmission for resistant organisms like CRE. This intervention is costly and labor intensive but could be considered when transmission continues despite initial infection control efforts.

3.2. If cohorting is implemented, cohort patients in the same area of the facility even if in single rooms. The staff caring for cohorted patients should be dedicated to those patients; in general, cohorted staff should include primary nursing staff and does not typically include physicians and other specialty providers.

3.3. If necessary, multiple patients with CRE can be placed in the same multi-occupancy room based on resistance mechanism.

4. Infection Control Measures

4.1. Implement Standard and Contact Precautions for CRE colonized or infected patients in acute care hospitals and long-term acute care hospitals.

4.1.1. In multi-occupancy rooms, ensure healthcare workers change gloves and gowns and perform hand hygiene between patients.

4.2. Emphasize rigorous adherence to hand hygiene; alcohol-based hand rub is acceptable unless hands are visibly soiled, in which case soap and water are indicated.

4.3. Dedicate patient care equipment such as blood pressure cuffs, thermometers, blood glucose meters, and stethoscopes; use single use disposable items when possible.

4.4. Audit infection control practices on affected unit(s), including hand hygiene, Contact precautions (e.g., donning and doffing of gowns and gloves), and environmental cleaning and disinfection. Provide feedback, education, and additional audits to raise compliance, as needed.

4.5. See CDC Enhanced Barrier Precautions for recommended infection control measures in skilled nursing facilities.

4.6. Consider conducting a site visit to review infection control practices especially if transmission is documented or in high-acuity post-acute care settings

5. Environmental Cleaning and Disinfection

5.1. Perform daily cleaning that includes high touch surfaces and areas in close proximity to the patient (e.g., bed rails, patient tray

5.1.1. Surfaces around sinks should be cleaned and disinfected regularly; medical equipment should not be stored in close proximity to sinks.

5.2. Delegate cleaning and disinfection of all environmental surfaces and equipment to designated personnel and consider using standardized checklists to ensure all surfaces and equipment are cleaned.

1.1. 5.3. Although dedicated patient equipment should be used whenever possible, equipment and devices that are shared (e.g., ultrasounds, physical therapy equipment) must be cleaned and disinfected between uses Ensure manufacturer's instructions for use pertaining to cleaning and reprocessing of medical equipment are followed.

1.2. Ensure disinfectant product is used according to instructions for use and for the recommended contact time.

6. Communication

6.1. When patients are transferred to other healthcare facilities, ensure receiving facilities receive notification of the patient's CRE infection or colonization, and understand the necessary infection control precautions. Decisions to transfer a patient from one level of care to another should be based on clinical criteria and the ability of the accepting facility to provide care, and not on the presence or absence of CRE infection or colonization.

6.2. CRE status should also be communicated to accepting providers when moved or transferred within a hospital (e.g., to another unit or to radiology)

7. Monitoring and Follow-up

7.1. If additional CRE cases are identified at a healthcare facility, additional considerations include:

7.1.1. Conducting serial PPS might every 2 weeks until transmission is controlled, as evidenced by no new cases identified on 2 sequential PPS. Ongoing PPS might be coupled with admission screening to distinguish importation from transmission within the facility.

7.1.2. Repeated onsite infection control assessment(s) to reinforce adherence to infection control measures.

7.1.3. Additional case finding around newly identified cases.

7.1.4. Regional notification and surveillance in coordination with local/state public health department(s).

Content with no reference specified is based on CORHA subject matter expert opinion.

D. References

1. CDC. Facility Guidance for Control of Carbapenem- resistant Enterobacteriaceae (CRE)- CRE Toolkit. https://www.cdc.gov/hai/organisms/cre/cre-toolkit/index.html.

2. CDC. Interim Guidance for a Public Health Response to Contain Novel or Targeted Multidrug- resistant Organisms (MDROs). https://www.cdc.gov/hai/outbreaks/mdro/index.html.

E. Further Resources

1. CDPH. MDRO CDI LineList Template. MDRO%20CDI%20Linelist%20Template%2020190312.xlsx

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