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Carbapenem-resistant Enterobacterales (CRE)

Recommended Practices for Healthcare Outbreak Response

A. Background

Carbapenem-resistant *Enterobacterales* (CRE) are often resistant to many other antimicrobials, limiting therapeutic options. Invasive CRE infections are associated with a mortality rate of up to 50%.[1] They are primarily identified among patients with current or recent hospitalization, surgeries, or stays in long-term care facilities (LTCFs), and most transmission appears to occur in these settings.[2] CRE have spread throughout most parts of the United States and have the potential to spread more widely.[2] Coordination between public health departments and healthcare facilities is necessary to identify CRE-colonized and CRE-infected patients, and to 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]), which directly breaks down carbapenems and other β-lactam antibiotics. Carbapenemases are often encoded on a mobile genetic element that facilitates transfer of resistance among *Enterobacterales* 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.[2] In the U.S., the proportion of CRE that harbor carbapenemases, and the carbapenemases identified, vary geographically. Information about carbapenemases in CRE, by region, is available on CDC's Antibiotic Resistance & Patient Safety Portal.[3] The potential for rapid spread of CP-CRE has made these organisms a particularly important target for prevention and healthcare outbreak response.

B. Detection and Reporting of Potential Outbreaks

1. **Proposed Investigation/Reporting Thresholds and Outbreak Definition**

The thresholds and definitions suggested below are based on expert opinion and intended to reflect the local epidemiology of CRE. Case numbers include instances of 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 CP-CRE as part of the Nationally Notifiable Disease Surveillance System.[2] The intended use of the suggested thresholds for facilities to investigate and report to public health authorities 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 the CDC.[4,5] Healthcare facilities should consult public health agencies if they have questions.

	Long-Term Care Facilities (LTCF), Critical Access Hospitals, Dialysis Facilities, and Outpatient Facilities
Threshold for facility to start investigation	1 CRE (CP, non-CP, or unknown CP)
Threshold for reporting to public health	1 CRE (CP, non-CP, or unknown CP)
	Acute Care Hospitals, Long-Term Acute Care Hospitals, and High-Acuity LTCF[§]
	Very Low Prevalence – CRE are rarely identified; typically, facilities experience only one or a few cases per year
Threshold for facility to start investigation	1 CRE (CP, non-CP, or unknown CP)
Threshold for reporting to public health	1 CRE (CP, non-CP, or unknown CP)
	Low Prevalence – CRE are identified with some regularity; facilities might average one case per month
Threshold for facility to start investigation	1 CP-CRE (*Klebsiella pneumoniae* carbapenemase [KPC], New Delhi metallo-β-Lactamase [NDM], Verona integron-encoded metallo- β-lactamase [VIM], active-on-imipenem metallo-β-lactamase [IMP], or oxacillinase [OXA-48 type], or positive by phenotypic test) OR 2 CRE (non-CP or mechanism testing not performed) of the same organism in a 4-week period in patients on the same unit[**]
Threshold for reporting to public health	1 CP-CRE (KPC, NDM, VIM, IMP, OXA-48 type, or positive by phenotypic test) OR 2 CRE (non-CP or mechanism testing not performed) of the same organism in a 4-week period in patients who are epidemiologically linked[†] with confirmatory laboratory testing
	High Prevalence/Endemic – CRE are routinely identified; facilities might average several cases per month, trending to one or more cases per week in endemic sites
Threshold for facility to start investigation[††]	1 non-KPC CP-CRE (NDM, VIM, IMP, OXA-48 type) OR

	2 KPC-CRE, 2 CP-CRE (unknown mechanism), or 2 CRE (non-CP or mechanism testing not performed) of the same organism in a 4-week period in patients on the same unit**
Threshold for reporting to public health††	1 non-KPC CP-CRE (NDM, VIM, IMP, or OXA-48 type) OR 2 KPC-CRE, 2 CP-CRE (unknown mechanism) or 2 CRE (non-CP or mechanism testing not performed) of the same organism in a 4-week period in patients who are epidemiologically linked†
	All Healthcare Facilities
Outbreak definition*	≥ 2 CRE of the same organism (or mechanism, if mechanism testing is performed) in a 4-week period in patients who are epidemiologically linked† or determined to be genetically related by laboratory testing‡

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

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

‡ Laboratory testing methods commonly used for assessing genetic relatedness include pulsed-field gel electrophoresis (PFGE) and next generation sequencing (NGS).

§ 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.

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

†† 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 CRE among organisms other than K. pneumoniae, which could carry less common carbapenemases compared to carbapenem-resistant K. pneumoniae.

2. **Points for Consideration**

2.1. For some healthcare settings the suggested thresholds for starting an investigation and reporting to public health authorities are dependent on the prevalence of CRE, which varies from region to region and even from facility to facility within a region. Facilities should consult with public health for guidance about which prevalence category they should use; if the category is uncertain, one should consider beginning with the thresholds for low CRE prevalence and modifying this as more information becomes available.

2.2. CRE prevalence may vary among facilities in a region according 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.

2.3. When the CP mechanism is unknown, facilities should consider arranging testing via the public health laboratory in their jurisdiction as part of the Antibiotic Resistance Laboratory Network (AR Lab Network). Note that screening tests to identify asymptomatic carriers are also available at no cost through AR Lab Network.[2]

2.4. 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's Interim Guidance for a Public Health Response to Contain Novel or Targeted Multidrug-resistant Organisms (MDROs).[4]

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). Components of an investigation and response to *CRE* generally include those listed in the CDC's Interim Guidance for a Public Health Response to Contain Novel or Targeted Multidrug-resistant Organisms (MDRO)[4] and additional information outlined in the CDC's Facility Guidance for Control of Carbapenem-resistant Enterobacteriacea (CRE) toolkit.[5] Typically, these investigations will be guided by state/local public health departments, possibly with active consultation with the CDC. 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 authorities helps ensure a successful investigation. Public health personnel should support the facility by providing guidance and resources. The health department may be able to assist 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 the CP mechanism is unknown, submit CRE isolates to a public health laboratory for CP testing; some public health laboratories may request all or a subset of CRE isolates, including the 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 healthcare encounters, including stays at other healthcare 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 the California Department of Public Health.[6]

2. Contact Screening

2.1. Screen epidemiologically linked patient contacts (e.g., roommates) for CRE with rectal swabs.[5] 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 (MDROs).[4]

2.1.1. Access to screening is available through the AR Lab Network.

2.2. Consider a point prevalence survey (PPS) of the entire affected unit, particularly if more than one CRE patient is identified.

2.3. Consider screening patient contacts in facilities where the CRE patient had overnight healthcare exposure during the 30 days prior to identification of the CRE (or in the period since suspected acquisition, if longer than 30 days).

3. Patient Placement and Cohorting

3.1. Cohorting patients and the primary staff who care for them has been shown to decrease transmission for resistant organisms such as CRE.[5] This intervention is costly and labor intensive, but it 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. Consider restricting staff caring for cohorted patients from providing care to non-cohorted patients. Considering including primary nursing staff to dedicated cohorting duties; including physicians or other specialty providers may present challenges.

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 CRE-infected patients in acute care hospitals and long-term acute care hospitals.

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

4.3. 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.

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

4.5. Sinks, toilets and other plumbing or wastewater features can become contaminated with MDROs. CDC's Reduce Risk from Water[7] page contains resources that healthcare facilities can use to evaluate and address these risks.

4.6. 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.

4.7. See the CDC Enhanced Barrier Precautions[8] for recommended infection control measures in skilled nursing facilities.
4.8. Consider conducting a site visit to review infection control practices, especially if transmission is documented or in high-acuity post–acute care settings, or in any setting where significant gaps have been identified.

5. Environmental Cleaning and Disinfection

5.1. Perform daily cleaning that includes high-touch surfaces and areas close to the patient (e.g., bed rails and patient tray).
5.1.1. Surfaces around sinks should be cleaned and disinfected regularly; medical equipment should not be stored close to sinks.
5.2. Delegate cleaning and disinfection of all environmental surfaces and equipment to designated personnel. Many of these duties will be managed by environmental services (EVS) staff. Ensure that there are not specific surfaces or equipment that designated staff (EVS or otherwise) are skipping because of mistaken expectations that someone else is doing it (e.g., differing expectations between nurses and EVS as to who cleans the nurses' station).
5.2.1. Consider using standardized checklists to ensure that all surfaces and equipment are cleaned.
5.3. Although dedicated patient equipment should be used whenever possible, equipment and devices that are shared (e.g., ultrasound machines or physical therapy equipment) must be cleaned and disinfected between uses. Ensure that the manufacturer's instructions for use pertaining to cleaning and reprocessing of medical equipment are followed.
5.4. Ensure that a disinfectant product is used according to instructions for use and for the recommended contact time.
5.5. Implement protocols for reviewing practice and performing audits to ensure that staff performing environmental services duties can demonstrate competency in essential functions (e.g., appropriate use of PPE, preventing contamination of carts and other equipment).

6. Communication

6.1. When patients are transferred to other healthcare facilities, ensure that the receiving facilities obtain notification of the patient's CRE infection or colonization, and understand the necessary infection control precautions.
6.1.1. 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; they should not be based on the presence or absence of CRE infection or colonization.
6.2. CRE status should also be communicated to accepting providers when a patient is moved or transferred within a hospital (e.g., to another unit or to the radiology department).

6.3. For guidance on making notifications in the context of a suspected healthcare-associated infection (HAI) outbreak, such as to potentially exposed patients, see CORHA's Framework for Healthcare-Associated Infection Outbreak Notification.[9]

7. Monitoring and Follow-up

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

7.1.1. Conducting serial PPSs every 2 weeks until transmission is controlled, as evidenced by no new cases identified on two sequential PPSs. Ongoing PPSs 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. Continued review of exposures to help direct assessments and further investigation.

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

D. References

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Web Sites:
https://corha.org
URLs in this document valid as of: February 15, 2023

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