June 2023

Carbapenem-Resistant Enterobacterales

Surveillance Protocol

Background [2]

Carbapenem-resistant Enterobacterales (CRE) are gram-negative bacteria that are resistant to the broad-spectrum, "last resort" carbapenem class of antibiotics. CRE includes bacteria from the Enterobacterales order, such as *E. coli* and *Klebsiella pneumoniae.* A taxonomy change was adopted to use Enterobacterales as the new scientific order. *Enterobacteriaceae* are now a family with Enterobacterales. Patients with CRE infections have significantly worse outcomes than patients with susceptible infections. Certain CRE are resistant because they produce carbapenemase enzymes that make carbapenems ineffective, which are referred to as Carbapenemase-producing Organisms (CPO). Carbapenemase genes can be transferred between different kinds of bacteria and lead to the spread of antibiotic resistance.

Public Health Significance [2]

The appearance and distribution of CRE and CPO represent a serious threat to public health. CPO, most commonly producing *Klebsiella pneumoniae* carbapenemase (KPC), have spread widely throughout the United States since first being reported in 2001. In recent years, several new mechanisms of resistance have been identified; examples of these include New Delhi metallo-beta-lactamase (NDM), Verona integron-encoded metallo-beta-lactamase (VIM), and Imipenemase metallo-beta-lactamase (IMP). These metallo-beta-lactamases have been identified rarely in the United States and are most commonly in patients with exposure to healthcare in endemic countries.

In August 2013, mandatory CRE laboratory reporting began to provide better information on the incidence and distribution of CRE in the state (see current West Virginia CRE Surveillance Report at oeps.wv.gov/cre/pages/default.aspx). Decreasing the impact of these organisms requires a coordinated effort involving a variety of stakeholders including healthcare facilities and providers, public health, and industry.

Provider Responsibilities

1. Ensure that your laboratory is immediately reporting carbapenem-resistant test results to you and that your office staff notifies you of CRE results immediately.
2. When you are notified by your laboratory that your patient has CRE:
    a. Follow Centers for Disease Control and Prevention (CDC) recommendations: https://www.cdc.gov/hai/organisms/cre/cre-clinicians.html
    b. Notify the Infection Preventionist at the facility where the patient is hospitalized; and/or
    c. Ensure that the Infection Preventionist and other providers are notified before a patient is admitted or transferred so that they can also follow CDC guidelines.

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3. Immediately notify the local health department (LHD) of CRE outbreaks in your facility.

Laboratory Responsibilities

1. Report CRE immediately to healthcare facilities. Clearly highlight carbapenem resistance on the report so resistance is readily apparent to healthcare providers.
2. Report all positive CRE tests to the LHD within one week of the result. Report the result by electronic messaging when feasible.
3. Follow current guidelines from the CDC/Clinical and Laboratory Standards Institute (CLSI) for testing for carbapenem resistance.
4. Immediately report CRE outbreaks to your LHD.
5. Follow the guidance provided by the West Virginia Department of Health and Human Resources (DHHR), Bureau for Public Health's (BPH) Office of Laboratory Services (OLS) for sending CRE specimens to OLS for further characterization.

LHD Responsibilities

Complete the CRO Case Report Form by contacting the provider and/or facility listed on the lab report, as well as the patient and/or their family, as needed.

1. Enter lab results and complete information from the CRE Case Report Form into the West Virginia Electronic Disease Surveillance System (WVEDSS) in a timely manner.
2. Encourage labs to report electronically when feasible.
3. When a case of CRE is identified in a Long-term Care Facility (LTF) in your county, assess the facility's knowledge about CRE using the "Initial Assessment for Long-term Care Facility (LTCF) Reported Case of Carbapenem-Resistant Organisms (CRO) including Carbapenem- Resistant Enterobacterales (CRE)". www.oeps.wv.gov/cre/documents/lhd/Initial_Assessment_for_LTCF_Reported_CRE.pdf

    a. Provide education and resources to the facility based on the assessment results, including the "CRO including CRE Infection Prevention and Control Guidance ", available at www.oeps.wv.gov/cre/documents/hcp/CRE_Infection_Prevention_and_Control_Guidnace.pdf

4. When a case of CRE is identified in an outpatient setting or the case's LTCF residential status is "No" or "Unknown":

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a. Contact the patient and/or their family, as appropriate, to verify LTCF residential status and provide education/resources to the patient/family, including the "CRO including CRE Patient FAQ" and link to or provide copies of information from the CDC patient information page.
www.oeps.wv.gov/cre/documents/community/cre_patient_faq.pdf
www.cdc.gov/hai/organisms/cre/cre-patients.html
b. If you notice a rise in reported CRE above your county endemic level, or baseline, or you notice multiple cases with a healthcare provider(s), contact the provider(s) to supply education/resources, including the link to the CDC clinician FAQ information page. Report these situations to the West Virginia Department of Health and Human Resources immediately.
www.cdc.gov/hai/organisms/cre/cre-clinicians.html
c. For providers/facilities with multiple CRE cases, consult with the BPH Healthcare Associated Infections (HAI) program for assistance in determining if there is an outbreak. Email: OEPSMDRO@wv.gov Phone: (304) 558-5358 ex.2.

Bureau for Public Health Responsibilities

1. Provide updated educational resources and materials to the facility, patient, and healthcare personnel.
2. Maintain awareness of new developments in medical literature and through ongoing surveillance.
3. Provide technical expertise and consultation regarding reporting, investigation, or control of cases or outbreaks of CRE, including direct support of outbreak investigation if needed.
4. Summarize surveillance data for new cases of CRE on at least an annual basis.
5. Serve as liaison between clinical laboratories, LHD, and OLS for shipping CRE isolates to OLS and/or CDC for further characterization.

Disease Control Objectives

Prevent additional cases of CRE through:

- Investigation of CRE outbreaks and delivery of recommendations related to outbreak control/resolution.
- Education of patients and healthcare providers, including LTCFs and outpatient providers, as appropriate, about CRE prevention and control.

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CRE

Surveillance Protocol

Disease Prevention Objectives

Reduce the incidence of CRE by:

- Providing education and resources related to preventing the transmission of CRE.

Surveillance Objectives

- Determine the incidence and regional distribution of CRE in West Virginia.
- Detect outbreaks of CRE.
- Describe the demographic characteristics of persons with CRE in West Virginia.

Clinical Description [2]

Patients can be infected or colonized with CRE. Colonization occurs when the organism lives and reproduces in a patient's body but does not cause symptoms or disease. A colonized individual can still transmit the bacteria to others and can go on to develop an infection themselves. Several species of Enterobacterales, whether CPO or not, may acquire resistance mechanisms from either living or dead drug-resistant bacteria.

CRE can cause bloodstream infections, ventilator-associated pneumonia, wound infections, and intra-abdominal abscesses, but most CRE infections involve the urinary tract, often in people who have a urinary catheter or have urinary retention.

Etiologic Agent [1, 2, 4, 5]

Enterobacterales are a large order of rod-shaped, gram-negative bacteria that commonly cause infections in healthcare settings. Examples of bacteria in the Enterobacterales order include *Escherichia coli* (*E. coli*) and *Klebsiella pneumonia*. Some have become resistant to all or almost all antibiotics through a variety of mechanisms. They have developed a high level of resistance to the carbapenem class of antibiotics. The increase of this type of infection seen in the United States is primarily due to the spread of Enterobacterales which produces an enzyme called KPC, which breaks down carbapenems and makes them ineffective.

Reporting

For CRE surveillance purposes, any CRE species should be reported as noted on the WVEDSS CRE Report Form: oeps.wv.gov/cre/documents/lhd/cre_report_form.pdf

Reservoir [2]

The reservoir for CRE infections in the United States is colonized and infected individuals, especially patients who have frequent contact with the healthcare system. Enterobacterales

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can survive on inanimate objects such as bed rails, countertops, and on medical equipment such as catheter tubing and flexible endoscopes.

Mode of Transmission [2]
CRE is transmitted person-to-person through direct contact with infected bodily tissues or fluids. In healthcare settings, CRE is spread mainly through the hands of healthcare workers and by direct contact with contaminated environmental surfaces, such as bed rails and computer keyboards.

Incubation Period [2]
The incubation period is not well defined, particularly due to the ability of CRE to colonize an individual for an extended period.

Infectious Period [2]
CRE can potentially be transmitted as long as the organisms are present in a person's bodily tissues or fluids. It is unknown how long CRE can live on inanimate surfaces. These bacteria are capable of transmitting resistance mechanisms in the absence of living organisms.

Outbreak Recognition
Outbreak recognition involves ongoing and systematic CRE surveillance using a standardized case definition in each facility. CRE surveillance will allow one to determine when an increase in cases above the baseline occurs and should trigger an investigation into the reason for the increase.

Case Definition [2, 3]
CRE are defined as Enterobacterales that are:

- Resistant to any carbapenem (minimum inhibitory concentrations of ≥4 mcg/ml for meropenem, imipenem, and doripenem or ≥ 2 mcg/ml for ertapenem).

OR

- Positive phenotypic test (e.g., Carba NP, Carbapenem inactivation method (CIM), Modified Hodge test, Metallo-βlactamase test) result for carbapenemase production, with or without identification of a specific carbapenemase gene (e.g., blaKPC, blaNDM, blaVIM, blaIMP, blaOXA-48, but other carbapenemase genes include but are not limited to blaSIM, blaGIM, blaSPM, other OXA genes, etc.)

OR

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- Positive molecular test (e.g., BD Max Check-Points CPO, FilmArray (BioFire), Nucleic acid amplification test (NAAT) (e.g., PCR), Whole-genome sequencing (WGS) result detecting a carbapenemase gene.

OR

- Detection of a carbapenemase gene by NGS

OR

- Specimen positive for a carbapenemase gene without bacterial species identification, (e.g., Xpert Carba-R rectal swabs, other CIDT)

Criteria to Distinguish a New Case from an Existing Case [6]

- Different organisms/species/carbapenemases are counted as separate events from other organisms/species/carbapenemases.
- There is at least a 12-month interval from the previous notification event for clinical cases.
- A person with a clinical case should not be counted as a screening/surveillance case thereafter (e.g., a patient with a known infection who later has colonization of the GI tract is not counted as more than one case).
- A person with a screening case can be later categorized as a clinical case (e.g., a patient with a positive peri-rectal screening swab who later develops bloodstream infection would be counted in both categories).

Preventive Interventions [1, 2]

Prevention of CRE transmission requires a coordinated effort involving a variety of stakeholders including healthcare providers, acute and long-term care facilities, and state and local public health departments. It requires an understanding of the local and regional prevalence of these organisms, rapid identification of colonized and infected patients in healthcare settings, and implementation of facility-specific and regional interventions to prevent transmission.

Facility-specific prevention measures include:

- Onsite infection control assessments
  - Contact the HAI program to schedule an Infection Control Assessment and Response (ICAR). Email: OEPSICAR@wv.gov
- Educate all healthcare personnel (HCP) and environmental services (EVS) personnel about CRE.

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- Reinforce and follow hand hygiene practices.
- Use Transmission-Based Precautions
    - Contact precautions including gown and gloves.
    - Enhanced Barrier Precautions for nursing home residents.
- Monitor adherence to infection control practices and provide feedback.
- Ensure adequate supplies are available.
- Ensure appropriate signage is on the patient's door to alert HCP, EVS, and visitors of recommended precautions.
- Collaborate with laboratories regarding testing and notification.
- Implement antimicrobial stewardship.
- Consider screening for CRE upon admission and colonization screening.

Treatment [4]

Treatment options for CREs are extremely limited and may lead to adverse outcomes. Infectious disease consultation is recommended for treatment decisions.

Surveillance Indicators

The purpose of CRE surveillance indicators in West Virginia is to ensure the sufficient performance of surveillance and case investigation and to identify areas of improvement. The West Virginia Department of Health and Human Resources, Bureau for Public Health, Office of Epidemiology and Prevention Services currently monitors the following indicators through WVEDSS on a regular basis and reports annually.

- The proportion of investigations with complete demographic information.
- The proportion of investigations with complete antimicrobial sensitivity information.
- The proportion of confirmed lab results of carbapenemase-producing organisms (CPO).
- The proportion of investigations with complete information on LTCF residence.
- The proportion of LTCFs that were provided education.

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