

# Carbapenem-Resistant *Enterobacteriaceae* (CRE)

## Surveillance Protocol

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### **Background** <sup>(2)</sup>

Enterobacteriaceae are a family of bacteria that commonly colonize the human digestive tract. These organisms are capable of causing a wide range of infections, including urinary tract infections, blood infections and sepsis, respiratory infections, and wound infections. CRE are organisms in this family that have developed resistance to a last line antibiotic class, the carbapenems. Infections with these organisms are often extremely difficult to treat and are associated with a high mortality rate. Carbapenem resistance is spreading, making surveillance of CRE an important aspect of prevention and control efforts.

### **Public Health Significance** <sup>(2)</sup>

The appearance and distribution of carbapenem resistance among Enterobacteriaceae in the United States represents a serious threat to public health. These organisms are associated with high mortality rates, up to 40-50% in some studies, and have the potential to spread widely. CRE, most commonly producing *Klebsiella pneumoniae* carbapenemase (KPC), have spread widely throughout the United States since first being reported in 1996. 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. As of 2018, one case of NDM positive CRE has been identified in West Virginia along with several KPC positive specimens.

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 [oepe.wv.gov/cre/pages/default.aspx](https://oepe.wv.gov/cre/pages/default.aspx)). While most cases in West Virginia have historically been associated with healthcare visits, 52% of the cases in 2017 were neither long term care facility (LTCF) residents nor hospitalized at the time of specimen collection. This indicates a shift toward community transmission. Decreasing the impact of these organisms requires a coordinated effort involving a variety of stakeholders including healthcare facilities and providers, public health, and industry.

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### **Division of Infectious Disease Epidemiology (DIDE)**

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### Provider Responsibilities

1. Assure that your laboratory is immediately reporting carbapenem resistant test results to you and that your office staff notify 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: [www.cdc.gov/hai/organisms/cre/cre-toolkit/index.html](http://www.cdc.gov/hai/organisms/cre/cre-toolkit/index.html);
  - b. Notify the Infection Preventionist at the facility where the patient is hospitalized; and/or
  - c. Assure that the Infection Preventionist and other providers are notified before a patient is admitted or transferred so that they can also follow CDC guidelines.
3. Immediately notify 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 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 guidance provided by the West Virginia Office of Laboratory Services (OLS) for sending CRE specimens to OLS for further characterization.

### LHD Responsibilities

Complete the CRE Disease Reporting Form by contacting 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 Disease Reporting 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 LTCF in your county, assess the facility's knowledge about CRE using the "Initial Assessment for Long-Term Care Facilities Reporting Carbapenem Resistant Enterobacteriaceae (CRE)": [oepls.wv.gov/cre/documents/lhd/cre\\_ltcf\\_assessment.pdf](http://oepls.wv.gov/cre/documents/lhd/cre_ltcf_assessment.pdf)

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- a. Provide most recent version of CDC CRE toolkit ([www.cdc.gov/hai/organisms/cre/cre-toolkit/index.html](http://www.cdc.gov/hai/organisms/cre/cre-toolkit/index.html)), and additional education/resources to the facility based on the assessment results, including the DIDE information sheet for long term care facility healthcare workers: [oeps.wv.gov/cre/documents/hcp/cre\\_ltcf\\_faq.pdf](http://oeps.wv.gov/cre/documents/hcp/cre_ltcf_faq.pdf)  
Consult with DIDE for suggestions.
4. When a case of CRE is identified in an outpatient setting or the case's LTCF residential status is "No" or "Unknown":
  - 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 DIDE patient information sheet ([oeps.wv.gov/cre/documents/community/cre\\_patient\\_faq.pdf](http://oeps.wv.gov/cre/documents/community/cre_patient_faq.pdf)) and link to or provide copies of information from the CDC patient information page ([www.cdc.gov/hai/organisms/cre/cre-patients.html](http://www.cdc.gov/hai/organisms/cre/cre-patients.html))
  - b. If you are in a low incidence area, or you notice multiple cases with one or more healthcare providers is common for higher incidence areas, contact the provider to supply education/resources, including the DIDE provider information sheet ([oeps.wv.gov/cre/documents/hcp/cre\\_hcp\\_faq.pdf](http://oeps.wv.gov/cre/documents/hcp/cre_hcp_faq.pdf)) and the link to the CDC clinician FAQ information page ([www.cdc.gov/hai/organisms/cre/cre-clinicianFAQ.html](http://www.cdc.gov/hai/organisms/cre/cre-clinicianFAQ.html)). Report these situations to DIDE immediately.
  - c. For providers/facilities with multiple CRE cases, consult with DIDE for assistance in determining if there is an outbreak.

#### **State Health Department Responsibilities**

1. Maintain updated facility, patient and healthcare worker education materials on the DIDE website.
2. Maintain awareness of new developments in the 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 the shipping of CRE isolates to OLS and/or CDC for further characterization.

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### 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.

### Disease Prevention Objectives

Reduce the incidence of CRE by:

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

### Surveillance Objectives

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

### Clinical Description <sup>(2, 7)</sup>

Patients can be infected or colonized with CRE. Colonization occurs when the organism lives and reproduces in a patient's body, but is not causing 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 Enterobacteriaceae, whether CRE or not, are found in the human digestive tract, and drug sensitive bacteria 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 <sup>(1, 2, 8)</sup>

Enterobacteriaceae are a family of rod-shaped gram-negative bacteria that are often found in the human gastrointestinal tract. Enterobacteriaceae can cause infections in both community and healthcare settings. Some Enterobacteriaceae have become resistant to all or almost all antibiotics through a variety of mechanisms. CRE have developed a high level of resistance to the carbapenem class of antibiotics. The increase of CRE seen in the United States is primarily due to the spread of Enterobacteriaceae that produce an enzyme called KPC, which breaks

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down carbapenems and makes them ineffective. Medically important Enterobacteriaceae include but are not limited to.

Genus	Species	Genus	Species
<i>Citrobacter</i>	<i>freundii, koseri, amalonaticus</i>	<i>Plesiomonas</i>	<i>shigelloides</i>
<i>Edwardsiella</i>	<i>tarda</i>	<i>Proteus</i>	<i>mirabilis, vulgaris</i>
<i>Enterobacter</i>	<i>cloacae, aerogenes, sakasakii,</i>	<i>Providencia</i>	<i>stuartii, rettgeri</i>
<i>Escherichia</i>	<i>coli, albertii</i>	<i>Salmonella</i>	<i>enterica</i>
<i>Hafnia</i>	<i>alvei</i>	<i>Serratia</i>	<i>marcescens</i>
<i>Klebsiella</i>	<i>pneumoniae, oxytoca, granulomatis</i>	<i>Shigella</i> (belongs within the <i>E coli</i> species)	<i>dysenterii, flexneri, sonnei, boydii</i>
<i>Morganella</i>	<i>morganii</i>		
<i>Pantoea</i> (formerly <i>Enterobacter</i> )	<i>agglomerans</i>	<i>Yersinia</i>	<i>pestis, enterocolitica, pseudotuberculosis</i>

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](https://oeps.wv.gov/cre/documents/lhd/cre_report_form.pdf)

### **Reservoir** <sup>(2)</sup>

Enterobacteriaceae can be carried in the intestines of many mammals and birds. The reservoir for CRE infections in the United States is colonized and infected individuals, especially patients with frequent contact with the healthcare system. *Enterobacteriaceae* can survive on inanimate objects such as bed rails, counter tops, and on medical equipment such as catheter tubing and flexible endoscopes.

### **Mode of Transmission** <sup>(2)</sup>

CRE is transmitted person-to-person through direct contact with infected bodily tissues or fluids. In healthcare settings, CRE are spread mainly through the hands of healthcare workers and direct contact with contaminated environmental services, such as bed rails and computer keyboards.

### **Incubation Period** <sup>(2)</sup>

The incubation period is not well defined, particularly due to the ability of CRE to colonize an individual for an extended period of time.

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### **Infectious Period** <sup>(2)</sup>

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. For more information, see DIDE's Healthcare-Associated Infections (HAI) Outbreak Protocol: [oepe.wv.gov/hai/documents/lhd/hai-protocol.pdf](https://oepe.wv.gov/hai/documents/lhd/hai-protocol.pdf)

### **Case Definition** <sup>(2, 3)</sup>

CRE are defined as Enterobacteriaceae that are:

- Resistant to any carbapenem (minimum inhibitory concentrations of  $\geq 4$  mcg/ml for meropenem, imipenem, and doripenem or  $\geq 2$  mcg/ml for ertapenem).
- OR**
- Production of a carbapenemase (e.g., KPC, NDM, VIM, IMP, OXA-48) demonstrated by a recognized test (e.g., polymerase chain reaction (PCR), metallo- $\beta$ -lactamase test, modified Hodge test, Carba NP, matrix assisted laser desorption/ionization time of flight (MALDI-TOF)).

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[oepe.wv.gov/cre/documents/lhd/cre\\_report\\_form.pdf](https://oepe.wv.gov/cre/documents/lhd/cre_report_form.pdf)

### **Preventive Interventions** <sup>(1, 2, 8)</sup>

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 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.

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Core facility-specific prevention measures include:

- Compliance with hand hygiene policies
- Contact precautions or modified contact precautions in LTCFs
- Education of healthcare personnel
- Minimizing device use
- Cohorting of staff and patients
- Collaboration with laboratories regarding testing and notification
- Antimicrobial stewardship
- Screening for CRE when indicated

### **Treatment** <sup>(4)</sup>

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

### **Surveillance Indicators**

- Proportion of investigations with complete demographic information.
- Proportion of investigations with complete antimicrobial sensitivity information.
- Proportion of investigations with complete information on LTCF residence.
- Portion of LTCFs that were provided education on CRE.

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#### References

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