

Carbapenem-Resistant *Enterobacteriaceae* (CRE) Notification Protocol



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 right away.
2. When you are notified by your laboratory that your patient has CRE:
 - a. Follow CDC recommendations: <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 of CRE outbreaks in your facility.

Laboratory Responsibilities

1. Report CRE immediately to healthcare facilities. Clearly highlight carbapenem resistance on report so resistance is readily apparent to healthcare providers.
2. Report all positive CRE tests to the local health department within 1 week of result. Report the result by electronic messaging when feasible.
3. Follow current guidelines from the CDC/CLSI for testing for carbapenem resistance.
4. Immediately report CRE outbreaks to your local health department.

Local Health Department Responsibilities

1. Complete 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.
2. Enter lab results and complete information from the CRE Disease Reporting Form into WVEDSS in a timely manner.
3. Encourage labs to report electronically when feasible.
4. When a case of CRE is identified in a long-term care facility (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)" located here:
<http://www.dhhr.wv.gov/oeps/disease/atoz/documents/cre/crqp-ltcf.doc>
 - a. Provide CDC 2012 CRE toolkit (<http://www.cdc.gov/hai/organisms/cre/cre-toolkit/index.html>) and additional education/resources to the facility based the assessment, including the DIDE information sheet for long term care facility healthcare workers (http://www.dhhr.wv.gov/oeps/disease/AtoZ/documents/cre/cre_faq.pdf). Consult with DIDE for suggestions.

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5. When a case of CRE has a specimen collected 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 (<http://www.dhhr.wv.gov/oeps/disease/AtoZ/Documents/CRE%20Patient%20Information%20Sheet.pdf>) and link to or copies of information from the CDC patient information page (<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 in common for higher incidence areas, contact the provider to provide education/resources, including the DIDE provider information sheet (<http://www.dhhr.wv.gov/oeps/disease/AtoZ/Pages/CRE.aspx>) and the link to the CDC clinician FAQ information page (<http://www.cdc.gov/hai/organisms/cre/cre-clinicianFAQ.html>). 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 elbow-to-elbow support of outbreak investigation if needed.
4. Summarize surveillance data for new cases of CRE on at least an annual basis.

Disease Control Objectives

Prevent additional cases of CRE through:

- Investigation of CRE outbreaks and delivering 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

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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

Public Health Significance

The appearance and distribution of carbapenem resistance among *Enterobacteriaceae* in the United States represent a serious threat to public health. These organisms are associated with high mortality rates, up to 40-50% in some studies¹, and have the potential to spread widely. CRE, most commonly producing *Klebsiella pneumoniae* carbapenemase (KPC), appear to have been uncommon in the United States before 1992, but have spread widely throughout the United States since first being reported in 2001¹. 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 are more common outside the United States but have been identified rarely in this country, most commonly in patients with exposure to healthcare in endemic countries. Of note, some *Enterobacteriaceae* are intrinsically nonsusceptible to the carbapenem imipenem, such as *Morganella morganii*, *Proteus* species, and *Providencia* species.

Outbreaks of CRE, including Carbapenem-Resistant *Klebsiella pneumoniae* (CRKP), were reported in WV for the first time in 2011, with 9 CRE outbreaks reported during 2011, 3 during 2012, 3 during 2013, 1 in 2014 and 0 in 2015. The number of outbreaks has decreased due to a change in the outbreak definition; WVBPH no longer considers a single case of CRE in a facility to constitute an outbreak. However, the WV Bureau for Public Health still receives several requests for guidance in preventing the spread of CRE each year when a single case is identified in a non-endemic facility. The purpose of mandating CRE laboratory reporting in August 2013 was to provide better information on the incidence and distribution of CRE in the state (See 2014 WV CRE Surveillance Report at <http://www.dhhr.wv.gov/oeps/disease/AtoZ/documents/cre/2014-cre-report.pdf>). While most cases in West Virginia have been associated with healthcare visits, 22% of the cases in 2014 were neither LTCF residents nor hospitalized at the time of specimen collection, indicating the potential for 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 industry¹.

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Education on CRE prevention is particularly important in the effort to decrease the impact of these organisms, particularly for LTCF staff. In the US, LTCFs have been implicated in regional spread of KPC-producing bacteria²⁻⁵. Seventy-five percent of carbapenem-resistant *K. pneumoniae* isolates within a northeastern-Ohio healthcare system came from patients admitted to the system from LTCFs². A *Klebsiella pneumoniae* carbapenemase (KPC)-producing *Enterobacteriaceae* outbreak investigation in adjacent counties in Indiana and Illinois showed 24/40 (60%) of cases were linked to a single long-term acute care hospital, while 75% (12/16) of the remaining cases were linked to 3 nursing homes³. In West Virginia, an outbreak of carbapenem-resistant *Klebsiella pneumoniae* (CRKP) was reported by a local hospital that noticed an increase of CRKP infections in patients associated with a nearby long term care facility⁴. Of the 19 patients identified in this investigation, 16 (84%) were from LTCFs, 14 of which were from a single local LTCF⁴. Finally, a multihospital case-control study in Chicago found that patients admitted to one of the four hospitals from skilled nursing facilities with ventilator care or from long-term acute care hospitals were 7 times more likely to be colonized with KPC-producing *Enterobacteriaceae* than patients admitted from the community⁵.

However, there is perhaps no better example of the need for a regional approach to CRE control and prevention than the centrally coordinated intervention that succeeded in containing a nationwide CRE outbreak in Israel⁶. The initial intervention, which included strict adherence to contact isolation and patient and staff cohorting for every patient with CRE hospitalized in acute-care facilities, halted the steep increase in incidence and led to a continuous downward trend⁶. One year later, incidence had reached an all-time low, but an assessment of the reasons for continued nosocomial transmission led to two new plans of action: 1) intervention in long-term care facilities, and 2) guidance for active CRE surveillance in acute-care hospitals⁶.

Surveillance of CRE in the state of West Virginia, and subsequent education of LTCFs with CRE patients will greatly assist in the effort to prevent and control the spread of CRE in the state.

Clinical Description

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 transmit the infection to others and can go on to develop an infection themselves.

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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 retention⁷.

Etiologic Agent

Enterobacteriaceae are a family of rod-shaped gram-negative bacteria that are often found in people’s 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. Carbapenem-resistant *Enterobacteriaceae* 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 (*Klebsiella pneumoniae* carbapenemase)⁷, which breaks down carbapenems and makes them ineffective. Medically important *Enterobacteriaceae* include⁸:

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, the WV Bureau for Public Health is interested in carbapenem-resistant *Klebsiella pneumoniae*, *E. coli* and *Enterobacter cloacae*. However, other species of CRE should be reported as “Other” on the WVEDSS CRE Report Form located here:

<http://www.dhhr.wv.gov/oeps/disease/atoz/documents/cre/cre-form.pdf>

Reservoir

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.

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Mode of Transmission

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

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

Infectious Period

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.

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. See DIDE's HAI Outbreak Protocol (<http://www.dhhr.wv.gov/oeps/disease/hai/documents/hai-protocol.pdf>) for more information on outbreak recognition and investigation.

Case Definition

CRE are defined as *Enterobacteriaceae* 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

- Production of a carbapenemase (e.g., KPC, NDM, VIM, IMP, OXA-48) demonstrated by a recognized test (e.g., polymerase chain reaction, metallo- β -lactamase test, modified Hodge test, Carba NP)

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Report Form located here:

<http://www.dhhr.wv.gov/oeps/disease/atoz/documents/cre/cre-form.pdf>

Preventive Interventions

Prevention of CRE transmission requires a coordinated effort involving a variety of stakeholders including acute and long-term care facilities and providers 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 health care settings, and implementation of facility-specific and regional interventions to prevent transmission.

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.

Please see CDC's 2012 CRE Toolkit¹ for more detailed recommendations.

Treatment

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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