

Carbapenem-resistant Enterobacteriaceae (CRE) Investigations – Part Two

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Objectives

1. Summarize what we learned about CRE and CP-CRE
2. Discuss the public health response to a case report
3. Review the available resources in the CRE Toolkit

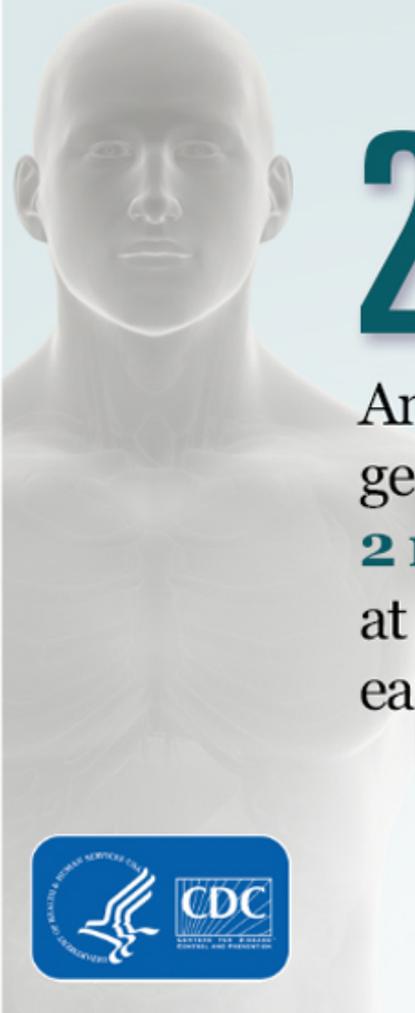
Antibiotic-Resistant Organisms

- Bacteria resistant to commonly used antibiotics
 - ▣ Use a different antibiotic
 - ▣ More costly
 - ▣ More side effects
 - ▣ Prolonged illness
 - ▣ Increased risk of death
 - ▣ **No available antibiotic treatment**

Emerging threat

- Antibiotic resistance (AR) is an emerging health threat
 - Antimicrobial-resistance for fungus also a threat
- Undermining ability to treat bacterial infections and to keep vulnerable patients safe

▶ Lost Lives



2 Million

Antibiotic-resistant
germs cause more than
2 million illnesses and
at least **23,000 deaths**
each year in the US.



Vital^{CDC}signs™

www.cdc.gov/vitalsigns/stop-spread



DETECT

CRE vs. CP-CRE

CRE



Enterobacteriaceae
that cannot be treated
with carbapenems

CP-CRE



CRE that have the
second type of
resistance mechanism,
the one that contains a
carbapenemase

CRE Example

- Patient admitted to **Hospital A** from **LTCF A** with shortness of breath and lethargy on 2/1
- Patient has bowel and bladder incontinence
- Urine specimen collected on 2/1
- Patient discharged back to LTCF A on 2/3
- On 2/6, the **hospital micro lab** reveals possible CRE
- Lab reports to **Public Health** and confirms isolate will be forwarded to **BOL** for mechanism testing
- Patient is placed on contact precautions
- **Patient and family** are notified of CRE status

➤ KPC-producing CRE

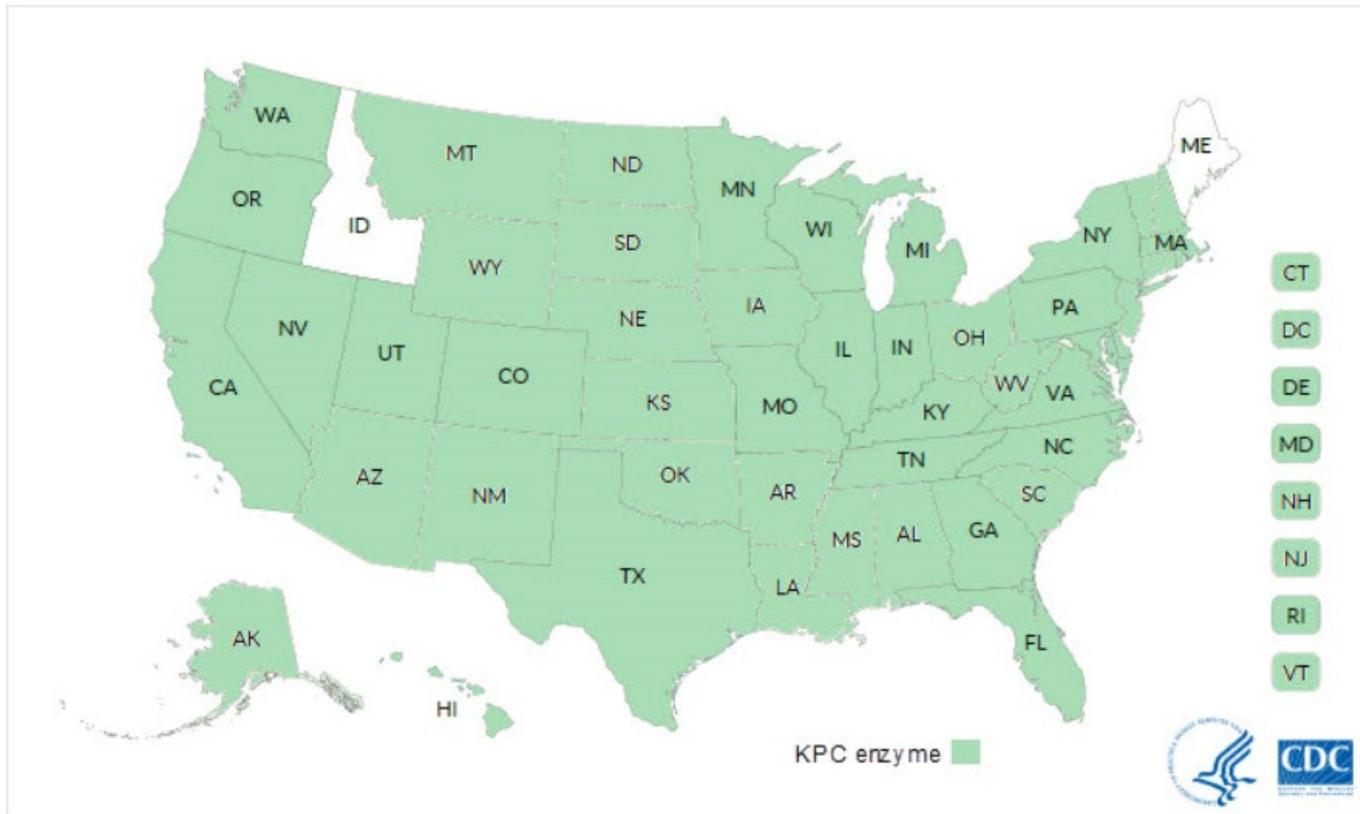
Klebsiella pneumoniae
Carbapenemase (KPC)



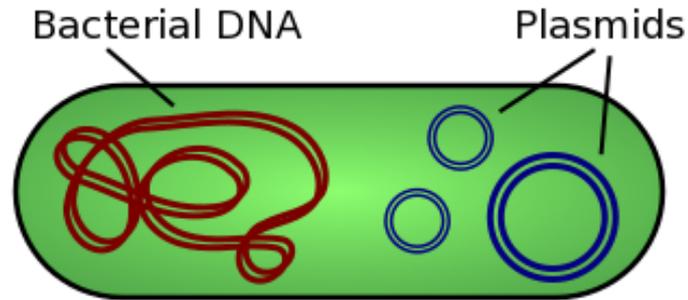
First identified in *Klebsiella pneumoniae* bacteria, but has crossed over and can now be in other *Enterobacteriaceae*, such as *E. coli*.

▶ KPC-producing CRE

Patients with KPC-producing *Carbapenem-resistant Enterobacteriaceae* (CRE) reported to the Centers for Disease Control and Prevention (CDC) as of January 2017, by state



Other Plasmid Varieties



- Plasmids can carry genes to make carbapenemases
 - ▣ **Carbapenemase** is an enzyme that chews up Carbapenems
 - ▣ **KPC- *Klebsiella pneumoniae* carbapenemase**
 - ▣ NDM
 - ▣ VIM
 - ▣ OXA-48
 - ▣ IMP

Challenges with Identification

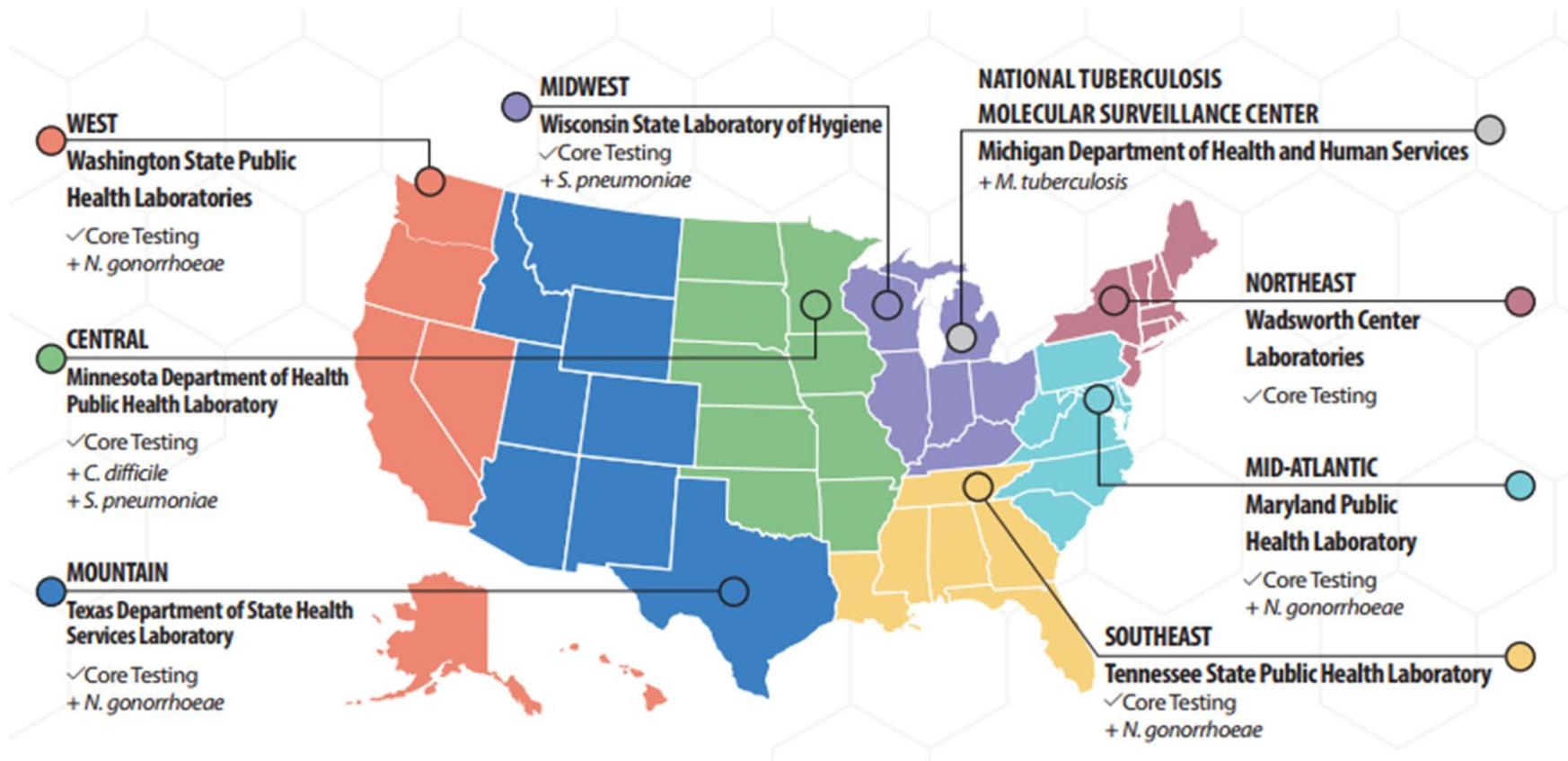
- Many labs do not have the capability to test
- Recommendation from CDC and DOH: treat all CRE like they are highly transmissible
- Important to be aware of regional resources to prevent the spread to other people or other organisms

What is the ARLN?



- ▣ Established in 2016 via CDC cooperative agreements
- ▣ Rapidly detects AR in healthcare, food, and the community
- ▣ Inform local responses to prevent spread of resistance and protect people

ARLN Map



Source: Antibiotic Resistance Lab Network
<https://www.cdc.gov/drugresistance/pdf/2016-arln-map-regions-and-tests---508.pdf>

Sick or colonized patient is tested/screened at facility

Enterobacteriaceae

Susceptibility testing:
Resistant to 1 or more
Carbapenems

Department of Health

Healthcare Provider



CONTAIN

Transmission

“Due to the movement of patients throughout the healthcare system, if CRE are a problem in one facility, then typically they are a problem in other facilities in the region as well.”

–CDC, 2015

<https://www.cdc.gov/hai/organisms/cre/cre-toolkit/index.html>

Facilities work together to protect patients.

Common Approach *(Not enough)*

- Patients can be transferred back and forth from facilities for treatment without all the communication and necessary infection control actions in place.

Independent Efforts *(Still not enough)*

- Some facilities work independently to enhance infection control but are not often alerted to antibiotic-resistant or *C. difficile* germs coming from other facilities or outbreaks in the area.
- Lack of shared information from other facilities means that necessary infection control actions are not always taken and germs are spread to other patients.

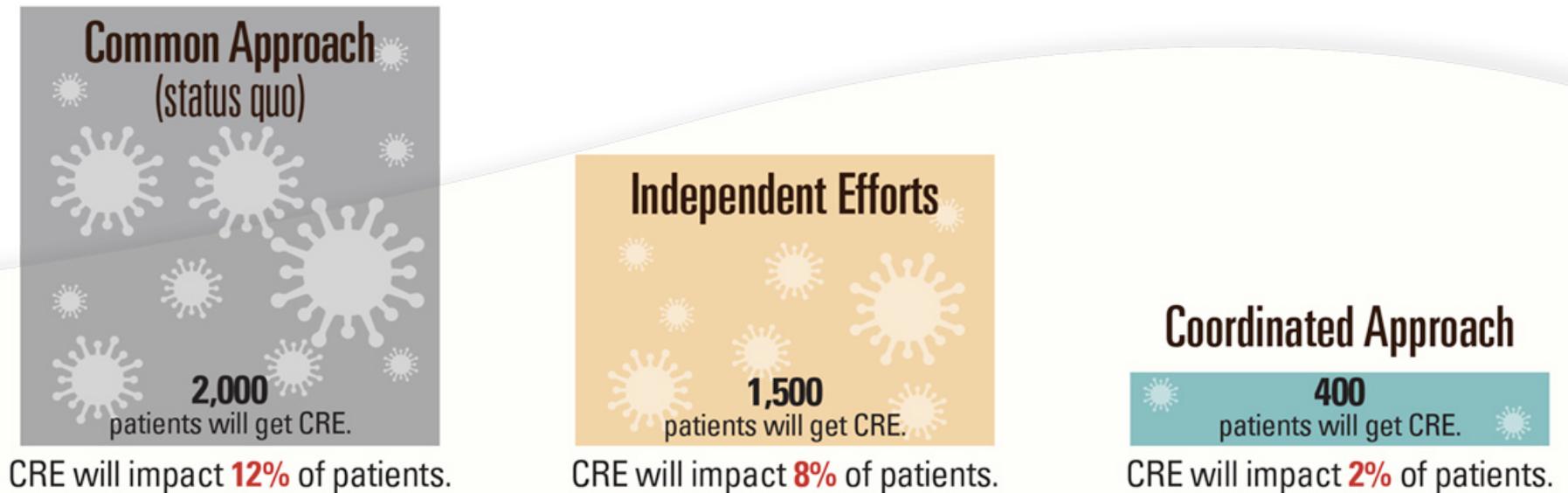
Coordinated Approach *(Needed)*

- Public health departments track and **alert** health care facilities to antibiotic-resistant or *C. difficile* germs coming from other facilities and outbreaks in the area.
- Facilities and public health authorities share information and implement shared infection control actions to stop spread of germs from facility to facility.



More patients get infections when facilities do not work together.

(Example: 5 years after CRE enters 10 facilities in an area sharing patients)



SOURCE: CDC Vital Signs, August 2015.

Transmission

- The key to prevention: Inter-facility communication
 - ▣ Verbal report including antibiotic-resistant organisms
 - ▣ Standardized transfer communication form
 - ▣ Oregon Inter-facility Infection Control Transfer Form (Oregon Toolkit)

Inter-facility Infection Control Transfer Form

SENDING FACILITY TO COMPLETE FORM and COMMUNICATE TO ACCEPTING FACILITY

Please attach copies of latest culture reports with susceptibilities, if available

Patient/Resident Last Name	First Name	Date of Birth
<i>Print or place Patient Label</i>		

Sending Facility Name	Sending Facility Unit	Sending Facility Phone #

Is the patient/resident currently on antibiotics? NO YES DX: _____

Does the patient/resident have pending cultures? NO YES

Is the patient/resident currently on precautions? NO YES

Type of Precautions (check all that apply) Contact Droplet Airborne Other: _____

Does patient currently have an infection, colonization OR a history of a multidrug-resistant organism (MDRO)?	Colonization or history <i>Check if YES</i>	Active infection on treatment <i>Check if YES</i>
MRSA (methicillin-resistant <i>Staphylococcus aureus</i>)	<input type="checkbox"/>	<input type="checkbox"/>
VRE (Vancomycin-resistant <i>Enterococcus</i>)	<input type="checkbox"/>	<input type="checkbox"/>
<i>C. diff</i> (<i>Clostridium difficile</i> , CDI)	<input type="checkbox"/>	<input type="checkbox"/>
<i>Acinetobacter</i> spp., multidrug-resistant	<input type="checkbox"/>	<input type="checkbox"/>
Gram-negative organism resistant to multiple antibiotics* (e.g., <i>E. coli</i> , <i>Klebsiella</i> , <i>Proteus</i> etc.)	<input type="checkbox"/>	<input type="checkbox"/>
CRE (carbapenem-resistant <i>Enterobacteriaceae</i>)	<input type="checkbox"/>	<input type="checkbox"/>
Other**:	<input type="checkbox"/>	<input type="checkbox"/>

*Culture report with multiple antibiotics marked resistant (R); send copy of report with susceptibilities.

**Other: lice, scabies, shingles, norovirus, influenza, tuberculosis, etc.

PREVENTION

CDC CRE Toolkit (snapshot)

Summary of Prevention Strategies For Acute and Long-Term Care Facilities

Please see text for details.

1. Hand Hygiene

- Promote hand hygiene
- Monitor hand hygiene adherence and provide feedback
- Ensure access to hand hygiene stations

2. Contact Precautions (CP)

- Educate and train healthcare personnel about CP including allowing time to practice donning and doffing
- Monitor CP adherence and provide feedback
- No recommendations for discontinuation of CP

Acute Care

5. Timely Notification from Laboratory When CRE are Identified

6. Communication of CRE Status for Infected and Colonized Patients at Discharge and Transfer

- Identify known CRE patients at re-admission

7. Promotion of Antimicrobial Stewardship

8. Environmental Cleaning

9. Patient and Staff Cohorting

- When available cohort CRE colonized or infected patients and the staff that care for them even if patients are housed in single rooms
- If the number of single patient rooms is limited, reserve these rooms for patients with highest risk for transmission (e.g., incontinence)

10. Screening Contacts of CRE Patients

- Screen patient with epidemiologic

Prevention Strategies

- Hand Hygiene
 - ▣ Promote HH
 - ▣ Monitor adherence – Audit and provide feedback
 - ▣ Ensure access to HH resources
- Contact Precautions
 - ▣ Educate on donning and doffing personal protective equipment (PPE)
 - ▣ Monitor adherence – Audit and provide feedback
 - ▣ Continue indefinitely
- Healthcare Personnel Education

Prevention Strategies

- Minimum Use of Invasive Devices
- Laboratory Notification
 - ▣ Notification should be timely
 - ▣ Have mechanism in place for reporting
- Inter-Facility Communication
 - ▣ Communicate status of infected or colonized patient at discharge, transfer, re-admission

Prevention Strategies

- Antimicrobial Stewardship
- Environmental Cleaning
 - ▣ Clean high-touch surfaces daily
 - ▣ Use EPA-registered disinfectant
- Patient and Staff Cohorting
 - ▣ When available, cohort CRE colonized or infected patients and cohort the staff that care for them
 - ▣ If limited amount of single rooms, reserve for patients with highest risk of transmission

Prevention Strategies

- Screening of Contacts of CRE Patients
 - Screen patients with epi links to unrecognized CRE colonized or infected patients
- Active Surveillance Testing
 - Consider screening high-risk patients at admission and periodically during their facility stay
- Chlorhexidine Bathing
 - Bathe patients with 2% chlorhexidine

▶ Hand Hygiene

Hand hygiene is a primary part of preventing MDRO transmission.

- Develop specific hand hygiene policy for your facility
- Frequent hand hygiene education
- Assure easy access to hand hygiene supplies
- Monitor hand hygiene adherence with monthly hand hygiene audits

Contact Precautions

- Persons colonized or infected with CRE should ***always*** be under **contact precautions** in the hospital



Contact Precautions

- Challenging in the long-term care setting
 - ▣ This is the resident's home
 - ▣ Negative impact on resident's well-being
 - ▣ Lack of private rooms
 - ▣ How long does it last?

Contact Precautions

- Modified contact precautions
 - ▣ Guided by the potential risk that residents will serve as a source for additional transmission
 - ▣ Consider when to use gown & gloves:
 - ▣ Wound dressing change
 - ▣ Toileting
 - ▣ Bathing
 - ▣ Manipulating devices (urinary catheter)

Contact Precautions

- Modified contact precautions
 - ▣ Consider contact precautions for residents who are:
 - ▣ Ventilator-dependent
 - ▣ Incontinent of stool that is difficult to contain
 - ▣ Draining secretions or draining wounds that cannot be controlled
 - ▣ For residents who do not have uncontrolled body fluids (vents, wounds, incontinence), activities outside the room allowed as usual

Environmental Cleaning

- For CRE colonized/infected residents:
 - ▣ Clean high-touch surfaces daily
 - ▣ Bed rails
 - ▣ Phone & call bell
 - ▣ Bathroom
 - ▣ Clean with EPA-registered hospital disinfectant
 - ▣ No need to use sporicidal agent (e.g. Clorox)

Prevention Strategies

- Identification
 - ▣ Laboratory notification
 - ▣ Communication at point of patient transfer
 - ▣ Screening contacts of known CRE carriers
- Preventing new resistant cases
 - ▣ Careful use of invasive medical devices
 - ▣ Antibiotic stewardship
- Preventing the spread
 - ▣ Hand hygiene
 - ▣ Contact precautions
 - ▣ Environmental cleaning

CRE TOOLKIT

CRE Toolkit

- CRE Fact Sheet
- FAQs for Carbapenemase-producing organisms
- Quick Guide
- Public health response to novel or targeted HAI organisms (tiers)
- Single case Tier 3 letter
- Guidance on the collection of peri-rectal specimens
- Containment Checklist

CRE Fact Sheet



CARBAPENEM-RESISTANT ENTEROBACTERIACEAE (CRE) FACT SHEET

BACKGROUND

Enterobacteriaceae are a family of bacteria that are normally found in the human intestines. *Klebsiella*, *Enterobacter* and *Escherichia coli* (*E. coli*) are three of the well-known types of Enterobacteriaceae. When these bacteria spread outside the intestines and get into other areas of the body, they can cause serious infections such as urinary tract (kidney or bladder) infections, bloodstream infections, wounds or surgical site infections, pneumonia and meningitis.

Carbapenem antibiotics (imipenem, meropenem, doripenem, and ertapenem) are broad spectrum antimicrobials that are usually reserved for severe, life-threatening infections. However, some types of Enterobacteriaceae have developed resistance to carbapenems. These bacteria are called carbapenem-resistant Enterobacteriaceae (CRE).

Some CRE possess an enzyme called a carbapenemase (carbapenemase-producing CRE or CP-CRE) that directly breaks down carbapenem antibiotics. CP-CRE are a special type of CRE.

WHO DOES THE ISSUE IMPACT?

Healthy people usually don't get CRE infections. In hospitals and other health care settings, certain patients are at higher risk of developing CRE infection. These include patients whose care requires medical devices such as ventilators (breathing machines), intravenous catheters, or urinary catheters, and patients who are taking antibiotics for a long time.

HOW IS IT TRANSMITTED?

CRE bacteria are mostly spread through direct person-to-person contact, particularly contact with wounds or stool. In healthcare settings, CRE can be spread by the hands of healthcare workers and through contact with contaminated objects such as medical equipment, bed rails, doorknobs, computer keyboards, cleaning supplies, and sink drains. The bacteria are not spread through the air.

WHAT ARE THE COMPLICATIONS?

CRE are often resistant to multiple classes of antibiotics substantially limiting treatment options. Infections caused by these organisms, particularly bloodstream infections, are associated with high rates of death, up to 50 percent.

HOW DO I KNOW IF I HAVE IT?

The only way to identify a CRE infection is to collect and test appropriate specimens in the laboratory. For



FAQs for CPOs



FREQUENTLY ASKED QUESTIONS (FAQS): CARBAPENEMASE-PRODUCING ORGANISMS (CPO) IN RESIDENTS OF LONG-TERM CARE FACILITIES

BACKGROUND

This frequently asked questions (FAQs) document is designed for residents, families of residents and staff of long-term care facilities. It is a supplement to the background information about CRE that is provided in the department Fact Sheet: Carbapenem-resistant Enterobacteriaceae.

Q. WHY IS IT IMPORTANT TO KNOW IF A RESIDENT HAS A CARBAPENEMASE-PRODUCING ORGANISM (CPO)?

A. Carbapenemase-producing organisms (CPOs) are bacteria that have an enzyme called a carbapenemase that directly breaks down strong antibiotics called carbapenems. This means that carbapenem antibiotics can't be used to treat these infections. An infection with a CPO may be difficult to treat.

Additionally, the presence of a carbapenemase means that this resistance is easily spread from person-to-person within a healthcare setting.

Q. WHAT KIND OF PRECAUTIONS SHOULD BE TAKEN WITH A PATIENT WHO HAS A CPO?

A. In long-term care facilities, it is recommended that residents with a CPO be placed in a private room, ideally with their own bathroom. Health care workers should follow specific infection control precautions. These might include wearing gowns and gloves when entering a room of these residents. This is called contact precautions. Health care workers should practice hand hygiene frequently, especially before and after patient contact and before and after using gloves.

Q. IF SOMEONE IS COLONIZED WITH A CPO, ARE THEY ABLE TO SPREAD IT TO OTHERS, EVEN IF THEY DON'T HAVE AN INFECTION?

A. For CPOs, the risk of spreading the organism from person-to-person or person-to-environment is the same whether a person has an infection or is colonized with the organism.

Q. IS THERE A TREATMENT THAT CAN BE GIVEN TO GET RID OF A CPO?



Quick Guide

QUICK GUIDE: CARBAPENEMASE-PRODUCING CARBAPENEM-RESISTANT ENTEROBACTERIACEAE (CP-CRE)

GENERAL INFORMATION AND COURSE OF DISEASE

Infectious Agent: Enterobacteriaceae are a family of bacteria that include *Klebsiella*, *Enterobacter*, and *Escherichia* species, among others. Carbapenems are a class of antibiotics that are powerful and often used as the last line of treatment. They include imipenem, doripenem, ertapenem, and meropenem. CRE stands for Carbapenem-resistant Enterobacteriaceae and refers to any organism in the Enterobacteriaceae family that also demonstrates laboratory evidence of resistance to one or more carbapenem antibiotic.

There are several mechanisms by which these organisms can become resistant to carbapenems. One such mechanism is through the production of carbapenemases. Carbapenemases are enzymes that can break down carbapenem antibiotics. Certain bacteria have genetic material that produces the carbapenemase enzyme, making them resistant to carbapenem antibiotics. These carbapenemase-producing carbapenem-resistant Enterobacteriaceae (CP-CRE) have great public health significance because the genetic element on the plasmid allows resistance to spread very rapidly from organism to organism and easily from person-to-person. There are several known types of carbapenemases including *Klebsiella pneumoniae* carbapenemase (KPC), New Delhi metallo- β -lactamase-type 1 (NDM-1), Verona integron encoded metallo- β -lactamase (VIM), imipenemase metallo- β -lactamase (IMP), and oxacillinase-48 (OXA-48). Currently, KPC is the most widespread carbapenemase in the United States.

NOTE: *Acinetobacter* and *Pseudomonas* spp. are not in the Enterobacteriaceae family and therefore are not specifically addressed in this Quick Guide. However, they are frequent causes of healthcare-associated infections, and may also produce carbapenemases. Most of the public health response(s) to carbapenem-producing *Acinetobacter* or *Pseudomonas* spp. are the same as for CP-CRE.

Mode of Transmission: Transmission of CP-CRE can occur whether a person is infected or colonized with CP-CRE, therefore the containment strategy will be applied to both. CP-CRE are transmitted via direct contact with an affected person or by contact with body fluids, especially those from wound drainage or stool. Transmission can occur through contact with contaminated materials or equipment and spread by healthcare worker hands.

Tiered responses

Public health response to novel or targeted HAI organisms in PA: Current guidance for determination of response 'Tier'

Updated October 25, 2018

The guidelines below were developed by the Department of Health, Bureau of Epidemiology based on assessment of the current available data on multidrug-resistant organisms in Pennsylvania. They are subject to change and should not be used to guide response outside the commonwealth.

Please refer to the CDC guidance entitled, "Interim Guidance for a Public Health Response to Contain Novel or Targeted Multidrug-resistant Organisms (MDROs)" to determine the appropriate public health response to novel or targeted organisms, based on the Tier designation suggested below. This guidance is available at:

<https://www.cdc.gov/hai/outbreaks/docs/health-response-contain-mdro.pdf>

Bacterial species or organism type	Carbapenemase mechanism	Response Tier
Enterobacteriaceae, any	KPC	Tier 3
Enterobacteriaceae, any	NDM IMP OXA-48 VIM	Tier 2*
<i>Pseudomonas</i> spp.	Any	Tier 2*
<i>Acinetobacter</i> spp.	Any	Tier 2*
Bacterial species or organism type	Resistance mechanism	Response Tier
<i>Candida auris</i>	n/a	Tier 2 ^{ab}
Pan-drug resistant organism (PDRO), defined as non-susceptible to all available antibiotics. Determination <u>must</u> be made by public health laboratories.	Any	Tier 1*
VRSA	n/a	Tier 1*
Organism with an mcr-1 or mcr-2 gene	mcr-1, mcr-2, any novel mcr gene	Tier 1*
Novel mechanism of resistance	Any	Tier 1*

*Tier 1 and Tier 2 organisms should be reported *immediately* to the local health jurisdiction and the PA Department of Health Bureau of Epidemiology by calling 717-787-3350.

Single case – Tier 3 letter

Dear [Addressee],

The Pennsylvania Department of Health (department), Bureau of Epidemiology recently became aware of a report of carbapenemase-producing carbapenem-resistant Enterobacteriaceae (CP-CRE) in a resident of your nursing home facility (hereafter referred to as index resident).

Containment of resistant organisms such as CP-CRE is a national problem and requires that health care facilities and public health agencies work together to prevent transmission. CP-CRE is particularly important to track, monitor and prevent due to its highly resistant nature, high mortality rates among infected persons, and increased likelihood of transmitting genetic material that confers antibiotic resistance to previously sensitive organisms. It is imperative to understand that identification of CP-CRE among a single resident requires public health action.

The Centers for Disease Control and Prevention (CDC) has published a containment strategy specifically designed to reduce the transmission of CP-CRE in the United States (2017). The department supports this strategy for the safety of Pennsylvania patients and residents. The containment strategy guides public health and facility interventions by categorizing CP-CRE into three different Tiers. The specific gene of interest, or carbapenemase producer, that was recently identified in a resident of your facility is known as *Klebsiella pneumoniae* carbapenemase (KPC) and is considered a Tier 3 organism in Pennsylvania.

The purpose of this letter is to provide you with recommended actions your facility should take in response to the identification of a resident with a Tier 3 organism. The department recommendations emphasize the importance of infection control practices and other prevention activities to reduce the spread of CP-CRE in nursing homes. **Please see the attached facility-level recommendation checklist.** The purpose of the checklist is to assist facilities in the implementation of communication strategies, detection protocols, targeted screening practices and prevention activities.

Both colonized and infected persons can spread CP-CRE, and colonization can persist for many years. Therefore, it is important to maintain infection prevention and control measures, including contact precautions, for the duration of a resident's stay. There is no evidence that treatment will eradicate CP-CRE colonization, and persons who are colonized should not receive treatment.

We appreciate your commitment to infection control and prevention and your dedication to the well-being of your residents and staff. If you have any questions regarding this information, please do not hesitate to contact [insert appropriate district staff names and contact info].

Guidelines for specimens

Guidelines for the Collection of Peri-Rectal Colonization Specimens for Carbapenemase Testing

Note: Colonization screening requires pre-approval and coordination with the Pennsylvania Department of Health (DOH) or the local health department.

Procedure:

1. Obtain pre-approval and guidance from DOH or the local health department. An outbreak investigation number will be provided for the colonization screening process.
2. Obtain specimen collection kits with instructions from the Bureau of Laboratories.
3. Explain the procedure to patients/residents and/or their caregivers. Although written consent is not necessary, patient or caregiver assent is needed. The screening process is a vital step in protecting the health of Pennsylvania residents and patients and should be strongly encouraged. Materials to assist with communicating to patients and their families are available at http://www.cdc.gov/hai/outbreaks/docs/Screening-FAQs-verbal-consent-example_updated-09_2017.docx
4. On the day of specimen collection, DOH or the local health department will enter data into Antibiotic Resistance Laboratory Network (ARLN) Lab-Web Portal: <https://lwp-web.aimsplatform.com/md/#/login>. It is preferred that data not be entered ahead of time to reduce errors and incomplete orders. Guidance for entering test orders for specimens can be found at the MD DOH website: <https://health.maryland.gov/laboratories/Pages/ARLNHome.aspx>
5. The following information is needed to ARLN Lab-Web Portal:
 - a. Patient Name
 - b. Date of Birth
 - c. Ordering Physician from Facility (usually the Medical Director)
 - d. Full name and Address of the Facility
6. Collect specimens using the Cepheid dual-swab collection devices provided by the Bureau of Laboratories. Following the instructions below:

Containment Checklist

Containment Checklist for Public Health

For use by public health staff during the investigation of suspected or confirmed carbapenemase-producing organisms (CPO), including carbapenem-resistant Enterobacteriaceae (CRE) or carbapenemase-producing carbapenem-resistant Enterobacteriaceae (CP-CRE).

Epi Details – Clinical and Travel History

- Obtain details about the patient's clinical needs
 - Is the patient bed bound?
 - Does the patient require respiratory care?
 - Does the patient require wound care?
 - Does the patient require any indwelling devices?
 - Any bowel or bladder incontinence? Any catheter? If yes, what type?
 - How dependent is the patient on healthcare personnel for bathing, toileting, etc.?
- Determine the recent healthcare exposures and travel history of the patient (within 6 months)
 - Is the patient currently hospitalized? Was the patient transferred from a nursing home? It is critical to gather any healthcare exposures 30 days prior to the positive culture to the time of identification.
 - Has the patient travelled or received medical care abroad in the last 6 months? If yes, obtain dates and description.
- Verify if patient had a roommate during any recent inpatient healthcare
 - It is critical to gather roommate information in the 30 days prior to the positive culture until the time of identification to assist in screening decisions.
 - If the suspected or confirmed CPO case had a roommate, screening of the roommate may be required. Obtain the dates (start date to end date) of when the roommate was present.
 - In some cases, patients have been found to have had more than one roommate. In that case, information on all roommates, the dates they were roomed together, and the current whereabouts of the roommates will be helpful to determine if screening should occur and if it will be feasible.
 - Work with the Healthcare-associated Infection Prevention/Antimicrobial Stewardship (HAIP/AS) team to determine if screening is appropriate and to coordinate screening through a public health laboratory that can conduct mechanism testing.

Communication

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DOH/CDC

THANK YOU!

Healthcare-associated Infection
Prevention/Antimicrobial
Stewardship (HAIP/AS) team

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717-787-3350