



SHARPPS Newsletter

Surveillance for Healthcare-Associated and Resistant Pathogens Patient Safety (SHARPPS) Program

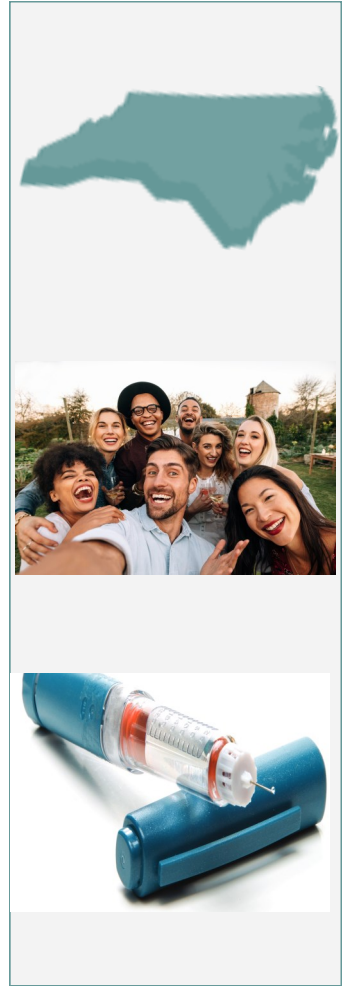
ANTIBIOTIC RESISTANCE

Antibiotic resistance is a growing public health concern. CDC estimates that over two million illnesses and 23,000 deaths occur each year due to antibiotic resistance. Multi-Drug Resistant Organisms (MDROs) are organisms that have become resistant to one or more classes of antimicrobial agents normally used to treat them.¹ Organisms can become resistant in a variety of ways as described below in Table 1. MDROs can cause infections in any body site. A person can also be colonized with a MDRO, meaning they have no clinical illness but can still spread the organism to others.

Bacteria continue to find ways to resist antibiotics, which is why aggressive action is needed to prevent new resistance from developing and to prevent current resistance from spreading. This newsletter will focus on one MDRO, Carbapenem-Resistant Enterobacteriaceae, including the mechanisms of its resistance and its threat to public health.

Table 1: Mechanisms of resistance to antibiotics¹⁰

Resistance Mechanisms	Description
Restrict access of the antibiotic	By limiting the number or changing the size of the openings in the cell wall, resistant bacteria can keep antibiotic drugs from entering the cell
Get rid of the antibiotic	Resistant bacteria can use pumps in their cell walls to remove antibiotic drugs that enter the cell
Destroy the antibiotic	Some resistant bacteria use enzymes to break down the antibiotic drug and make it ineffective
Change the antibiotic	Other resistant bacteria use enzymes to alter the antibiotic drug so that it loses its effectiveness
Bypass the effects of the antibiotic	Some antibiotic drugs are designed to disrupt important processes critical to a bacteria's survival, such as the processing of nutrients. Some resistant bacteria have altered these processes to get around these drug disruptions.
Change the targets for the antibiotic	Many antibiotic drugs are designed to single out and destroy specific parts of a bacterium. Resistant bacteria can change the look of their targets so that the antibiotic does not recognize and destroy them



INSIDE THIS ISSUE

- ◇ Antibiotic Resistance 1
- ◇ What are Carbapenem-Resistant Enterobacteriaceae 2
- ◇ How are CRE resistant 2
- ◇ Why are CRE important to public health 2
- ◇ CRE in North Carolina 3
- ◇ Investigation Tools 3
- ◇ Management Of CRE in NC 4
- ◇ SHARPPS Program updates 4

WHAT ARE CARBAPENEM-RESISTANT ENTEROBACTERIACEAE?

Enterobacteriaceae are bacteria found naturally in human gastrointestinal tracts but are capable of causing infection.² Enterobacteriaceae can also be transferred person to person through unwashed hands, contaminated surfaces, and environmental reservoirs.² *Escherichia coli*, *Klebsiella pneumoniae*, and *Enterobacter* species are the most common Enterobacteriaceae known to cause infections.²

Carbapenem-Resistant Enterobacteriaceae (CRE) are resistant to a class of antibiotics called carbapenems (including imipenem, ertapenem, meropenem, and doripenem), a class of last resort antibiotics.² Understanding the mechanisms of resistance and epidemiology of these bacteria is crucial to preventing the spread of this MDRO.

WHAT MAKES CARBAPENEM-RESISTANT ENTEROBACTERIACEAE RESISTANT?

Enterobacteriaceae can become resistant to antibiotics through a variety of mechanisms as described in the table above.⁴ One way CRE can become resistant to carbapenems is the presence of plasmids, mobile elements that can be easily transmitted between bacteria, that can encode enzymes called Carbapenemases.⁵ CRE that are able to produce carbapenemase enzymes are known as Carbapenemase Producing CRE or CP-CRE. There are five major types of carbapenemases: *Klebsiella pneumoniae* carbapenemase (KPC), New Delhi metallo- β -lactamase (NDM), Verona integron-encoded metallo- β -lactamase (VIM), IMP, and Oxacillinase (OXA).²

WHY IS CRE IMPORTANT TO PUBLIC HEALTH?

In 2013, the CDC placed CRE infections on the ‘Urgent Threats’ list.⁶ Pathogens on this list are considered “high-consequence antibiotic-resistant threats because of significant risks identified across several criteria. These threats may not be currently widespread but have the potential to become so and require urgent public health attention to identify infections and to limit transmission.”⁶ CRE cause approximately 9,000 infections each year resulting in 600 deaths.^{3,6} If an infection with a CRE reaches the bloodstream the likelihood of death can reach 50%.³ Many CRE are resistant to other classes of antibiotics as well making them very difficult to treat.²

Carbapenemase mediated resistance is highly transmissible because of the presence of plasmids, which are not only easily transmitted between bacteria but are also stable in the environment. Environmental reservoirs of CRE can develop in the healthcare environment placing patients at risk. A study in China established the resilience of a plasmid encoding the IMP carbapenemase in contaminated sinks in an Intensive Care Unit.⁸ This plasmid was also found to be present in other environmental bacteria that form biofilms.⁸ Biofilms are difficult to eliminate due to their structure and ability to resist antibiotics.⁹ Though this study couldn’t prove that the patients became infected from these sinks, it established the importance of environmental reservoirs as a possible mode of transmission. Another study in Virginia assessed the implementation of toilet hopper covers to reduce KPC organism acquisition.¹¹ Use of the covers reduced the acquisition of KPC organisms by 50%.¹¹ Studies such as these have demonstrated that plasmids are able to persist in the healthcare environment where they can be acquired by patients.

The transmissibility, environmental persistence, and virulence of CP-CRE is a dangerous combination. Understanding the dynamics of CP-CRE is necessary to prevent the spread of this dangerous bacteria and is a priority public health concern.

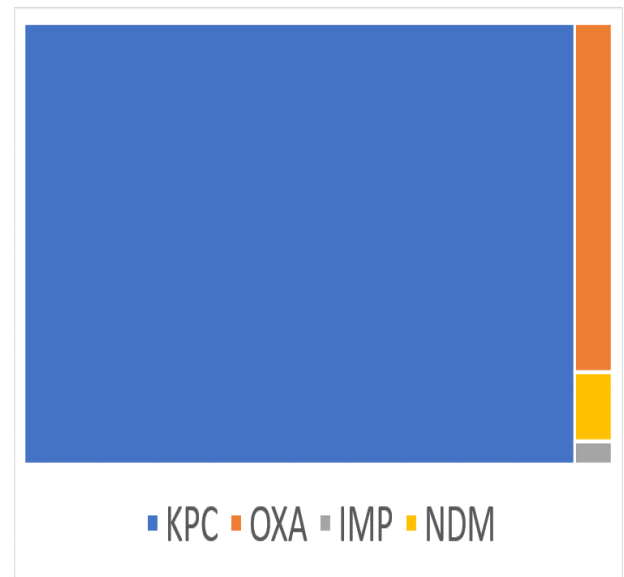
CRE IN NORTH CAROLINA

In 2001 the first KPC CRE was discovered in North Carolina.¹² The SHARPPS Program conducted CRE sentinel surveillance during March 2015 – September 2016. Since that time, we continue to partner with sentinel laboratories for routine submission of CRE isolates to the State Laboratory of Public Health for molecular characterization. Over 50% of CRE identified through formal sentinel surveillance and ongoing laboratory surveillance are CP-CRE. The most common carbapenemase in NC is KPC. As of December 2017, North Carolina had identified KPC, NDM, and IMP carbapenemases.⁷ In January 2018 North Carolina reported its first OXA (OXA-48) carbapenemase producing CRE. As of July 2018 there have been 297 cases of CP-CRE in North Carolina, the majority of which are KPC CP-CRE, as shown in the figure below.

When a CP-CRE is detected, the SHARPPS Program is alerted and a response is coordinated using the CDC's *Interim Guidance for a Public Health Response to Contain Novel or Targeted Multidrug-Resistant Organisms (MDROs)* (<https://www.cdc.gov/hai/outbreaks/docs/Health-Response-Contain-MDRO.pdf>). This document outlines the response to MDROs in a tiered fashion, and the response varies based on the mechanism of resistance. Responses aim to: identify if transmission is occurring; identify affected patients; and assure appropriate control measures are implemented. At a minimum, we recommend screening of roommates when a CP-CRE is identified. This recommendation may be expanded if 1) contact precautions were not implemented for the entire duration of admission or 2) based on the mechanism of resistance. DPH is available to coordinate this screening at no cost to facilities. We also recommend notification of transferring and receiving facilities of any CRE or other MDRO diagnosis, to ensure appropriate precautions across the continuum of care.

When screenings are recommended to facilities the Antibiotic Resistant Laboratory Network (ARLN) is used to aid with the surge capacity of swabs to be tested. ARLN was created as part of the Antibiotic Resistance Solutions Initiative at the CDC. This resource is available nationally with seven laboratories distributed throughout the United States. North Carolina utilizes the Maryland Laboratory for all CRE related screenings.

As CP CRE identification and response increases, NC SHARPPS continues to work with partners to educate facilities and local health departments on prevention and response.



INVESTIGATION TOOLS

CDC Guidance

Interim guidance for a Public Health Response to Contain Novel or Targeted Multidrug-Resistant Organisms (MDROs) (<https://www.cdc.gov/hai/outbreaks/docs/Health-Response-Contain-MDRO.pdf>). This document is intended for state and local health departments and healthcare facilities and serves as general guidance for resistance mechanisms.

MDRO Toolkit for Long Term Care Facilities

The NC SHARPPS Program first published a Multidrug-Resistant Organisms (MDROs) Toolkit for Long-Term Care Facilities in August 2017. This toolkit answers frequently asked questions about identifying, managing, and responding to MDROs in long-term care facilities. The toolkit can be found online on the North Carolina Division of Public Health Communicable Disease Manual at (https://epi.publichealth.nc.gov/cd/docs/MDROToolkit_r2.pdf).

SHARPPS Factsheet

COMING SOON The SHARPPS Program is developing a one-page fact sheet for both patients and physicians highlighting the important aspects of CRE and how to prevent it in healthcare settings.

MANAGEMENT OF CARBAPENEM-RESISTANT ENTEROBACTERIACEAE IN NORTH CAROLINA: ANTIBIOTIC STEWARDSHIP

CRE have developed in large part due to the overuse of antibiotics which creates pressure for the Enterobacteriaceae to adapt in order to survive. Because of this, antimicrobial stewardship is an important intervention, in addition to the containment strategies discussed above. Antimicrobial stewardship refers to coordinated programs in any healthcare setting that promote the appropriate use of antimicrobials, improve patient outcomes, reduce resistance, and decrease the spread of infections caused by MDROs within that setting. Stewardship programs help ensure that the correct drug, dose, duration of therapy and route of administration are used for every patient every time. Stewardship programs benefit from input of multiple partners and teams are encouraged to include physicians, pharmacists, nurses, infection preventionists, laboratory personnel, and IT specialists. The CDC has developed individual implementation guides for starting stewardship programs in different healthcare settings:

[Core elements of Stewardship – Acute Care Hospitals & National Quality Partners Playbook: Antibiotic Stewardship in Acute Care](#)

[Core elements of Stewardship – Long Term Care](#)

[Core elements of Stewardship – Small and Critical Access Hospitals](#)

[Core elements of Stewardship – Outpatient Care](#)

In addition to these resources [IDSA](#) and [SHEA](#) have developed stewardship implementation guides and CDC is releasing a [stewardship online training module](#) in four parts over 2018. Additionally, NC launched a statewide antimicrobial stewardship initiative in July 2018 called STewardship of Antimicrobial Resources (STAR) Partners. Please see more information in the announcement below.

*Interested in having SHARPPS present or exhibit at your upcoming event?
Contact us at nchai@dhhs.nc.gov.*

SHARPPS PROGRAM UPDATES

The SHARPPS program is excited to announce the launch of our statewide antimicrobial stewardship program: STAR Partners. This program encourages and motivates the implementation and growth of antimicrobial stewardship programs in acute care hospitals throughout the state with plans to expand to other healthcare settings in the future. The official launch date is 7/23/2018. More information can be found on the attached flyer and on the STAR Partner website: https://epi.publichealth.nc.gov/cd/antibiotics/star_partners.html

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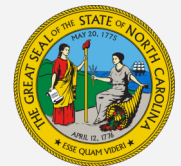
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