Identification of a cluster of antibiotic resistant VIM-CRPA cases in Connecticut

CSTE Stories FROM THE Field

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The Connecticut Department of Public Health identified an antibiotic resistant blaVIM gene in an isolate of carbapenem resistant *Pseudomonas aeruginosa* from a healthcare facility, which informed infection prevention activities and the identification over-the-counter medications contaminated with the organism.

The "What"

The Connecticut (CT) Department of Public Health (DPH) has used Epidemiology and Laboratory Capacity for the Prevention and Control of Emerging Infections Diseases (ELC) funding to form strategic partnerships with clinical providers and healthcare facilities to raise awareness of antimicrobial resistance, and to rapidly identify and characterize resistant organisms through resistance mechanism testing and whole genome sequencing (WGS) at the state public health laboratory (SPHL). At the CT SPHL, carbapenem resistant isolates are tested to identify specific genes that confer resistance to carbapenem antibiotics, and to assist clinicians in identifying treatment options for these difficult-to-treat infections.

In June of 2022, the CT SPHL identified a Verona Integron-encoded Metallo-beta-lactamase (VIM) carbapenemase enzyme in an isolate of *Pseudomonas aeruginosa* that had never been seen previously in Connecticut, which was resistant to nearly all antibiotics. Following the CDC Antimicrobial Resistance (AR) Containment Strategy, the CT Healthcare-Associated Infections and Antimicrobial Resistance (HAI-AR) Program initiated an investigation and response. A team of infection preventionists visited the healthcare facility where the infected patient lived to perform an Infection Control Assessment Response (ICAR) to identify potential gaps in practice that might result in spread of the organism to other vulnerable patients.

Working closely with the ELC-funded Antimicrobial Resistance Laboratory Network (ARLN) Regional Laboratory at Wadsworth, CT HAI-AR screened close contacts at the facility to determine whether additional patients might also be affected. Colonization testing efforts identified a cluster of VIM-producing CRPA cases in the healthcare facility. CT SPHL and Wadsworth performed WGS on clinical and colonization isolates from the outbreak, analyzed the sequences to identify key resistance markers, and uploaded sequencing results to the National Center for Biotechnology Information (NCBI). Bioinformatics experts were able to identify that the cluster of VIM-CRPA cases in CT were of a very rare strain type, producing two rare carbapenemase genes (VIM-80 and GES-9). These genes had not previously been identified in the United States. Using sequence comparison with other ARLN isolates uploaded to NCBI by other jurisdictions, laboratory staff identified highly-related sequences in other jurisdictions.

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Once a multi-state outbreak was identified, CDC gathered information from local AR teams to identify potential common sources of exposure. A joint team from CT and CDC conducted a case-control study at an affected CT healthcare facility leading to the identification of a potentially contaminated artificial tears product. Testing of these suspect artificial tears products from multiple jurisdictions including CT identified the rare organism in product samples. With this information, CDC teams worked with partners at the Food and Drug Administration (FDA) to further expand the product investigation and initiate regulatory actions to remove contaminated product from the market and prevent the import of additional potentially contaminated products. Following the announcement of product recalls, CT HAI-AR worked closely with healthcare partners to ensure broad dissemination of recall information.

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The "So What"

This investigation identified several widely-distributed over the counter medications contaminated with a highly-resistant organism that resulted in severe eye infections, loss of vision, and death. In CT alone, HAI-AR has identified 27 impacted patients from 5 healthcare facilities. Because of the inter-connected nature of the healthcare system, delayed identification of colonized individuals can result in rapid dissemination of emerging resistant pathogens. The CT ICAR team has worked very closely with affected facilities to ensure that they have the tools necessary to contain the spread of this pathogen while ensuring quality and compassionate care for affected patients.

CT HAI-AR partnered with affected facilities on infection prevention strategies. Serial colonization screening to monitor implementation has been extensive with nearly 800 colonization screens performed to date at Wadsworth. Screening capacity is an essential tool for the evaluation of containment efficacy and ensures the ongoing safety of the healthcare environment. Work continues to identify additional cases who may have been infected or colonized following use of these contaminated products. Although it's anticipated that this work will be ongoing, CT's most heavily impacted facilities have not identified new cases since removal of the implicated product.

The "Now What"

The introduction of VIM CRPA to CT through a contaminated product places the state at high risk for emergence of this resistance mechanism and establishment of endemicity of the organism. Early identification and removal of the contaminated source, paired with extensive early containment efforts led to the prevention of further spread. In response to the identification of VIM, the CT HAI-AR Program and SPHL worked with the CT Multidisciplinary Antimicrobial Resistance/Antimicrobial Stewardship Technical Advisory Group to develop a CRPA laboratory testing strategy to be implemented when CT made CRPA laboratory reportable in January 2023. Careful consideration of feasibility, funding, and the overall prevalence of carbapenemase production in *Pseudomonas aeruginosa* (only 2-3% of CRPA carry a carbapenemase gene) led the team to develop a broad laboratory surveillance structure using Carba5 testing at CT SPHL to monitor CRPA in CT over time. There will be ongoing evaluation of the impact of this program periodically and CT DPH will adjust their strategy accordingly. Increasing awareness of the emerging threat has led some clinical laboratories to onboard local testing of CRPA isolates to offer even faster identification and response.

Use of WGS as a part of this investigation clearly demonstrates the importance of routine and rapid analysis of sequencing data and uploading of local data to national databases. This capacity would not be possible without continued funding through ELC. CT DPH will work to lead the conversations around the role of WGS in investigations of AR pathogens and clusters both locally and nationally in order to respond to emerging threat.

Key contributors to this project include Meghan Maloney, Connecticut Department of Public Health; Staff at the Dr. Katherine A. Kelley State Public Health Laboratory.

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