Quarterly Update on Carbapenem-Resistant Enterobacteriaceae and Other Carbapenemase-Producing Organisms for Washington State

ISOLATES REPORTED TO THE DEPARTMENT OF HEALTH AND TESTED AT THE PUBLIC HEALTH LABORATORIES, BY DATE OF COLLECTION, OCTOBER - DECEMBER 2018

Washington State Department of Health has performed surveillance and testing for CRE since October 2012. This update summarizes reports of carbapenem-resistant Enterobacteriaceae (CRE) isolates and other carbapenemase-producing organisms (CPO) collected from October through December, 2018. We include all CRE and CPO isolates diagnosed in-state and isolates from Washington residents diagnosed out-of-state and reported to the department. Isolates were included if they were the first unique genus/species/carbapenemase profile reported from an individual patient since surveillance began in 2012. If an isolate produced more than one carbapenemase, it was counted once for each novel carbapenemase.

The CRE case definition since May 2015, is:
*E. coli*, *Klebsiella* spp., and *Enterobacter* spp. resistant to any carbapenem, according to Clinical Laboratory Standards Institute (CLSI) breakpoints: minimum inhibitory concentrations of ≥4 mcg/ml for meropenem, imipenem, and doripenem or ≥ 2 mcg/ml for ertapenem.


Testing performed at PHL includes confirmation of identification and antibiotic sensitivity (AST), a phenotypic test to detect carbapenemase activity using the Modified Carbapenem Inactivation Method (mCIM), and PCR for the five most common carbapenemase genes.

The Washington State Public Health Laboratories (PHL) test CRE isolates for the following carbapenemase genes:
- *Klebsiella pneumoniae* carbapenemase (KPC)
- New Delhi metallo-β-lactamase (NDM)
- Oxacillin-hydrolyzing β-lactamase-48 (OXA-48)
- Verona integron-encoded metallo-β-lactamase (VIM)
- Imipenem-hydrolyzing β-lactamase (IMP)

The Modified Carbapenem Inactivation Method (mCIM) is a phenotypic test used at the Public Health Laboratory to confirm production of carbapenemase. If PCR at WAPHL is negative for the five most common carbapenemase genes (KPC, NDM, VIM, IMP or OXA-48) but mCIM positive, we suspect an unknown variant or a novel carbapenemase, and these isolates are submitted to Centers for Disease Control and Prevention for further testing.

In addition to CRE, PHL solicits and tests other Gram-negative organisms using the same methods. CR-*Pseudomonas* isolates are submitted by 22 sentinel laboratories in Washington. The department requests that CR-*Acinetobacter* isolates be submitted by all laboratories in the state. Other CR-genera within the family Enterobacteriaceae may be submitted and tested by special request. Carbapenem-resistance in other genera of bacteria is determined by CLSI breakpoints.
The bar graph shows CRE and carbapenemase-producing Enterobacteriaceae isolates collected in 2018, compared to those submitted and tested in 2017 (Figure 1).

**Figure 1. Carbapenem-Resistant Enterobacteriaceae Isolates, Washington, 2017 and 2018**

Quarter 4 2018

**CRE surveillance:**

- Sixty-eight (68) CRE isolates were reported statewide in the fourth quarter of 2018. The contrasting color/pattern at the top of each bar represents the number of CRE isolates that were confirmed by PCR testing to carry a carbapenemase gene (Figure 1).
- Of 68 CRE isolates, 61 (90%) were big-three genera isolates that are required to be reported: 26 (38%) *Enterobacter* spp., 19 (28%) *E. coli*, and 16 (24%) *Klebsiella* spp. Other Enterobacteriaceae genera were submitted and tested: 3 (4%) *Morganella* spp., 3 (4%) *Serratia* spp., and 1 (2%) *Citrobacter* spp. (Figure 2).
- Of 68 CRE isolates, 15 (22%) isolates from 12 individual patients tested positive for carbapenemase: 5 KPC, 4 OXA-48 like, 4 NDM, 1 VIM and 1 unidentified carbapenemase (mCIM+). (Figure 2)
- Nine of 16 (56%) of *Klebsiella* isolates were carbapenemase-positive, as were 4 of 19 (21%) *E.coli* isolates. One *Citrobacter* isolate and one *Serratia* isolate was also positive for carbapenemase production, however a proportion is not given for these genera due to small number of isolates tested. (Figure 2)
- There were two unique cases of a single isolate positive for two or more carbapenemase genes in quarter 4: one *E. coli* isolate that harbored two carbapenemase genes (OXA-48 and NDM), and one *Klebsiella pneumoniae* isolate positive for three carbapenemase genes (OXA-48, NDM, and VIM).
- The likely source of acquisition for 6 of the 12 patients with CP-CRE was healthcare in Washington. The other 6 CP-CRE cases likely acquired the carbapenemase during international travel or healthcare. (Table 1)
- We offer a breakdown of cases by county to inform local health, facilities, and providers of recent carbapenemase activity in their region. The quarter 4 map of cases by county of residence (non-WA residents) is shown in Figure 3.

**CRPA/CRA surveillance:**

- Seventy-one (71) CR-*Pseudomonas* and six (6) CR-*Acinetobacter* isolates were submitted for carbapenemase testing in the fourth quarter of 2018. (Figure 2)
- Six (6) of 71 (9%) *Pseudomonas* isolates were positive for carbapenemase: 4 VIM and 2 unidentified carbapenemase (mCIM+).
- None of the *Acinetobacter* isolates were positive for carbapenemase production in quarter 4.
Table 1. Carbapenemases Identified and Likely Source, Washington State, Quarter 4, 2018

<table>
<thead>
<tr>
<th>Carbapenemase</th>
<th>Number of cases</th>
<th>Likely Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>KPC</td>
<td>5</td>
<td>Healthcare in Washington (5) and Europe (1)</td>
</tr>
<tr>
<td>NDM</td>
<td>1</td>
<td>Healthcare in Washington</td>
</tr>
<tr>
<td>NDM</td>
<td>1</td>
<td>International Healthcare in Asia</td>
</tr>
<tr>
<td>OXA-48</td>
<td>1</td>
<td>Healthcare in Washington</td>
</tr>
<tr>
<td>OXA-48</td>
<td>1</td>
<td>International Healthcare in Africa</td>
</tr>
<tr>
<td>VIM</td>
<td>3</td>
<td>International Healthcare in North America (2) or Asia (1)</td>
</tr>
<tr>
<td>VIM</td>
<td>1</td>
<td>Healthcare in Washington</td>
</tr>
<tr>
<td>OXA-48 and NDM</td>
<td>1</td>
<td>International Healthcare in Asia</td>
</tr>
<tr>
<td>OXA-48, NDM and VIM</td>
<td>1</td>
<td>International Healthcare in Asia</td>
</tr>
<tr>
<td>mCIM+ (unknown)</td>
<td>3</td>
<td>Unknown</td>
</tr>
</tbody>
</table>
The Public Health Laboratories accepts and tests other carbapenem-resistant Gram-negative organisms, such as other genera in the family Enterobacteriaceae, upon request, or if specialized screening tests (e.g., Metallo-B-lactamase test, modified Hodge test (MHT) (for E. coli and Klebsiella species only), CarbaNP, Carbapenem Inactivation Method (CIM) or modified CIM (mCIM) indicate suspicion for carbapenemase production.

Please contact Kelly Kauber at 206-418-5500 or kelly.kauber@doh.wa.gov for any questions or comments about this report, or for information on becoming a sentinel lab.