Washington State Department of Health
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Changes to WADOH Surveillance for Carbapenem-resistant Enterobacteriaceae (CRE)

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Carbapenem-resistant Enterobacteriaceae (CRE) are highly antibiotic resistant bacteria that have been deemed an "urgent threat" because of their high morbidity and mortality, and their ability to spread readily in healthcare settings. CRE can be resistant to carbapenems by a variety of mechanisms; most concerning among these mechanisms are the carbapenemase producers, such as *Klebsiella pneumoniae* carbapenemase (KPC), New Delhi metallo-β-lactamase(NDM), Verona integron metallo-β-lactamase (VIM), imipenemase (IMP), and OXA-48-like carbapenemase (OXA-48), whose plasmids can transmit to other species and genera of bacteria.

In order to understand the frequency of these organisms in Washington, the Washington State Department of Health initiated systematic surveillance for carbapenem-resistant Enterobacteriaceae (CRE) in October of 2012 under Washington Administrative Code 246-101. The department recently completed review of one year of surveillance data on reported CRE cases. The summary was sent to labs in early January. Based on the information gathered through this surveillance system, the department updated the 2014 criteria for submission of CRE to the Public Health Laboratories.

As a review, beginning Oct. 23, 2012, the department requested submission of any Enterobacteriaceae resistant to all third-generation cephalosporins and non-susceptible to one or more carbapenem. Submitted isolates underwent confirmatory antimicrobial sensitivity testing at the Public Health Laboratories (PHL) using the latest Clinical Laboratories Standards Institute (CLSI) breakpoints. Through Dec. 31, 2013, after confirmatory testing was completed, the "confirmed" CRE case definition was:

- *E. coli*, *Klebsiella spp*. and *Enterobacter spp*. resistant to all third-generation cephalosporins tested and non-susceptible to one or more carbapenem; and
- Any other Enterobacteriaceae resistant to all third-generation cephalosporins tested and non-susceptible to two or more carbapenems.

Isolates meeting the above criteria were sent to our esearch laboratory partner for carbapenemase PCR testing. From Oct. 23, 2012 through Oct. 31, 2013, 103 suspected CRE isolates were tested at PHL, and 79 were confirmed as CRE by phenotypic testing. Of these 79 isolates, the genera represented included 40 *Enterobacter* (51 percent), 29 *Escherichia* (37 percent), 7 *Klebsiella* (9 percent), 2 *Citrobacter* (2 percent), and 1 *Proteus* (1 percent). In total, six isolates tested positive for carbapenemase by PCR, representing 1 KPC, 3 New Delhi metallo-β-lactamases (NDM), and 2 imipenemases (IMP); the other 73 isolates

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Practice Guidelines

The following practice guidelines have been developed by the Clinical Laboratory Advisory Council. They can be accessed at the LQA website.

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were carbapenem-resistant via a mechanism other than carbapenemase production, such as AmpC β-lactamase (AmpC) or extended-spectrum β-lactamase (ESBL) with porin loss.

In addition to carbapenemase-producing CRE, a patient with carbapenemase-producing *Acinetobacter* and *Pseudomonas* was reported in Washington. The source is thought to be international health care. These organisms were not part of the CRE surveillance but are reportable as rare diseases of public health significance (highly antibiotic-resistant organisms).

Updated criteria for CRE and carbapenemase surveillance and isolate submission to Washington State Public Health Laboratories (PHL) effective January 2014 is as follows:

1. Laboratory Submission: Laboratories should submit all *E. coli* and *Klebsiella spp*. resistant to all third-generation cephalosporins tested and non-susceptible to 1 or more carbapenem (exception: if the isolate is only non-susceptible to ertapenem, it must be resistant to ertapenem with MIC >=2mcg/ml or zone <=18mm). Submit antimicrobial susceptibility report with isolate.

2. Healthcare Provider and Infection Control Practitioner Reporting: Providers and infection preventionists should report to local health any CRE isolate, including genera other than *E. coli* and *Klebsiella spp*., which meets susceptibility profile in criterion 1 above and is obtained from a patient who was hospitalized outside of Washington or Oregon in the past six months. Request the laboratory to submit isolate with antimicrobial susceptibility report.

At PHL, submitted isolates confirmed to meet the above criteria by traditional antimicrobial sensitivity testing will be tested for presence of carbapenemase by polymerase chain reaction (PCR). *Proteus spp*., *Providencia spp*. and *Morganella spp*. that are non-susceptible ONLY to imipenem but susceptible to other carbapenems will be excluded from carbapenemase PCR and resistance will be attributed to "intrinsic" resistance. Any Enterobacteriaceae isolates that test positive for carbapenemase by PCR will be classified as carbapenemase-producing CRE (CP-CRE).

Results of antimicrobial sensitivity testing at PHL will be sent to the submitter. All positive carbapenemase PCR results will be communicated to the local public health jurisdiction and facility infection control. Negative PCR results will not be communicated to the submitter or to local health unless specifically requested.

We encourage laboratories to apply the latest CLSI breakpoints for determining carbapenem resistance as soon as feasible, and to develop and implement procedures for rapidly communicating MDRO status to clinicians and facility infection control, if not already doing so.

Because CP-CRE are thought to be more easily transmitted and have greater potential for exponential growth in healthcare settings than non-carbapenemase producing CRE, we believe that the focus of future public health CRE surveillance should be on detecting CP-CRE and preventing their spread. This change does not diminish the importance of appropriate infection control based on commercial laboratory results, but emphasizes public health resources on the highest priority organisms. Planned changes in surveillance will decrease the workload attendant on this surveillance system while continuing to allow identification of most CP-CRE. The department believes that concerted efforts by multiple levels of healthcare and public health will be most effective in preventing the spread of these organisms.

We sincerely thank laboratories for their diligence in reporting and submitting CRE isolates to public health. A summary of all reported CRE surveillance data through Dec. 31, 2013 will be available upon completion of pending reports through the end of 2013. The Healthcare Associated Infections Program is available for consultation on any aspect of MDRO surveillance and infection prevention. Please call Marisa D'Angeli at 206-418-5595 with questions or comments.

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Department of Health
Laboratory Quality Assurance
Public Health Laboratories

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Table 1: Characteristics of CRE cases, Washington, 10/23/12 - 10/31/13

All Confirmed CRE[1] cases	
Characteristics	**N =71[2]**
	n (%)
Sex	
Female	42 (59)
Age (years)	
0-17	5 (7)
18-64	30 (42)
≥ 65	36 (51)
Place of Residence	
Western Washington	52 (73)
Eastern Washington	16 (23)
Outside Washington	3 (4)
Place of Diagnosis	
Western Washington	45 (62[3])
Eastern Washington	12 (17)
Oregon	15 (21)
Died due to CRE infection	
Yes	4 (6)
Specimen Site	
Urinary tract	46 (65)
Surgical site	10 (14)
Wound	4 (6)
Sputum	3 (4)
Bloodstream/Sepsis	4 (6)
Chronic Conditions[4]	
Diabetes Mellitus	19 (27)
Heart Disease	11 (15)
Lung Disease	11 (15)
Cancer	9 (13)
Immune Suppression	9 (13)
Renal Disease	9 (13)
Urinary Tract Abnormality	8 (11)
Risk Factors in 6 Months Prior to Diagnosis[4]	
Hospitalization	41 (58)
ICU admission (among 41 hospitalized)	11 (27)
Surgery	23 (32)
Long Term Care Facility admission	20 (28)

[1] Includes one isolate that did not meet surveillance cases definition, but was KPC postive by PCR

[2] N refers to number of case patients, not nmber os isolates submitted.

[3] Bases on N of 72 because 1 patient with two CRD isolates was diagnosed in both Western and Eastern Washington

[4] Patient may have more than one

Surveillance for CRE, cont'd from page 3

Table 2: Characteristics of CP-CRE cases, Washington, 10/23/12 - 10/31/13

Carbapenemase-Producing CRE Cases					
Characteristics					
Clinical Features					
	Case 1	Case 2	Case 3	Case 4	Case 5
Age category (years)	≥65	≥65	≥65	0-17	18-64
Site of infection	Wound	Urine	Urine	Urine	Urine
Died due to CRE infection	No	No	No	No	No
Chronic condition (s)	Diabetes, Heart	Diarrhea	None noted	Shunt	Diabetes, Heart, Lung
Risk Factors in Past 6 Months					
Hospital admission	Yes	No	Yes	Yes	Yes
ICU admission (if hospitalized)	Yes	NA	No	No	No
Surgery	Yes	No	Yes	Yes	No
Long Term Care Facility admission	Yes	No	Yes	No	No
International travel	No	Yes	Yes	Yes	Yes
International hospitalization	No	No	Yes	Yes	Yes
Organism					
Species	*K. pneumo*	*E. coli*	*K. pneumo*	*K. pneumo, E. aerogenes*	*E. coli*
Antimicrobial Resistance[1]					
Ceftazidime	I	R	R	R	R
Ceftriaxone	S	R	R	R	R
Ertapenem	R	R	R	R	R
Imipenem	R	R	R	R	R
Meropenem	I	R	R	R	R
Carbapenemase Testing					
Modified Hodge Test	P	P	N	P	N
Polymerase Chain Reaction	KPC	NDM	NDM	IMP[2]	NDM

[1] Accordintg to lateset CLSI breakpoints (S: Sensitive; I: Intermediate; R: Resistant

[2] IMP was detected i nboth orgamisims

Approved PT Providers

Amer. Acad. of Family Physicians (800) 274-7911

Amer. Assoc. of Bioanalysts (800) 234-5315

American Proficiency Institute (800) 333-0958

ASIM Medical Lab Evaluation (800) 338-2746

California Thoracic Society (714) 730-1944

College of American Pathologists/EXCEL
(800) 323-4040

WSLH (800) 462-5261

For answers to your PT questions, go to the LQA website or call Leonard Kargacin at (253) 395-6747.

Calendar of Events

Training Classes:

2014 ASCLS-WA Spring Meeting
April 24-26 Spokane

2014 Northwest Medical Laboratory Symposium
October 1-4 Portland, OR

21st Annual Clinical Laboratory Conference
November 10 Tukwila

Contact information for the events listed above can be found on page 2. The Calendar of Events is a list of upcoming conferences, deadlines, and other dates of interest to the clinical laboratory community. If you have events that you would like to have included, please mail them to ELABORATIONS at the address on page 2. Information must be received at least one month before the scheduled event. The editor reserves the right to make final decisions on inclusion.

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