

WEST VIRGINIA CARBAPENEM-RESISTANT ENTEROBACTERIACAE (CRE) SURVEILLANCE REPORT

January 1, 2015—December 31, 2015

INTRODUCTION

Enterobacteriaceae are a family of bacteria that commonly colonize the human digestive tract. These organisms are capable of causing a wide range of infections, including urinary tract infections, blood infections and sepsis, respiratory infections, and wound infections. Carbapenem-resistant *Enterobacteriaceae* (CRE) are organisms in this family that have developed resistance to a last line antibiotic class, the carbapenems. Infections with these organisms are often extremely difficult to treat and are associated with a high mortality rate, up to 50% in some studies.¹ Carbapenem resistance is spreading, making surveillance of CRE an important aspect of prevention and control efforts.

Since August 2013, laboratories testing specimens from West Virginia residents have been required to report cases of CRE to the local health department of the patient's county of residence within one week of detection (see 64CSR7 <http://apps.sos.wv.gov/adlaw/csr/readfile.aspx?DocId=25071&Format=PDF>). The following surveillance report summarizes data from CRE cases between January 1, 2015 and December 31, 2015.

METHODS

For 2015 surveillance purposes, a case of CRE was defined as an *Enterobacteriaceae* that is nonsusceptible to one of the following carbapenems: doripenem, meropenem, or imipenem and resistant to all of the following third-generation cephalosporins that were tested: ceftriaxone, cefotaxime, and ceftazidime. Two types of cultures are described, clinical and surveillance. Clinical cultures were taken in an effort to diagnose active infection, and surveillance cultures were rectal cultures taken to establish whether or not a patient was colonized with CRE.

Case counts are based on date of report. Each individual case is only counted one time, regardless of how many lab results are received for each individual. The exception to this is if a single individual is reported as being infected or colonized with more than one CRE organism.

The data were analyzed two ways: at the organism level (see Organism data) and at the patient level (see Demographics). Data were analyzed at the state and regional level. Variables with 0-4 cases are indicated with a value of "<5" in order to protect patient confidentiality. When variables have missing data, the number of cases included in the analysis is noted beside the variable name. Missing data were removed for additional analyses.

As per the West Virginia Division of Infectious Disease Epidemiology CRE Notification Protocol,² local health departments are expected to conduct an initial assessment of long term care facilities whose residents test positive for CRE. The assessment is typically conducted over the phone using the "CRE in Long Term Care Facilities Initial Assessment" questionnaire.³ The intent of the interview is to assess the number of residents in the facility who either have active infections or are colonized, infection control measures in place, and whether they are using or have access to the Centers for Disease Control and Prevention (CDC) CRE Toolkit. From this assessment, local health departments and/or regional epidemiologists can gauge the knowledge of the facility's staff, and decide whether to proceed with additional interviews or site visits.

¹ CDC, 2012 CRE Toolkit - Guidance for Control of Carbapenem-resistant *Enterobacteriaceae* (CRE)

² DIDE, 2016 CRE Notification Protocol <http://www.dhhr.wv.gov/oeps/disease/AtoZ/documents/cre/cre-protocol.pdf>

³ DIDE, 2016 CRE LTCF Initial Assessment <http://www.dhhr.wv.gov/oeps/disease/AtoZ/Pages/CRE.aspx>

The data were analyzed for potential associations using Fisher exact tests, and Monte Carlo simulations where appropriate. All analyses were conducted in SAS Version 9.3 and Microsoft Excel.

RESULTS

Organisms

From January-December 2015, one individual was diagnosed with two or more different CRE organisms. One hundred organisms were reported from 99 patients. The most frequently identified organism was *Klebsiella pneumoniae*, with 43 (43.0%) isolates. *Enterobacter cloacae* followed with 27 (27.0%) isolates (Figure 1). The focus of the remainder of this report will be on *K. pneumoniae*, *Enterobacter* species, and *E. coli*. The single *Klebsiella* spp. is reclassified into the “Other” category as it was not identified to the species level and cannot be grouped with any specific species.

Table 1. CRE Isolates 2015 West Virginia

Organism (N = 100)	N (%)
<i>Klebsiella pneumoniae</i>	43 (43.0%)
<i>Enterobacter cloacae</i>	27 (27.0%)
<i>Escherichia coli</i>	10 (10.0%)
<i>Enterobacter aerogenes</i>	9 (9.0%)
<i>Citrobacter freundii</i>	5 (5.0%)
<i>Klebsiella oxytoca</i>	3 (3.0%)
<i>Klebsiella</i> spp.	1 (1.0%)
<i>Enterobacter gergoviae</i>	1 (1.0%)
<i>Cedecea</i> spp.	1 (1.0%)

Urine was the most common specimen to test positive for CRE, with 75 (75.0%) (Figure 2). Ninety-seven cultures (97.0%) were clinical, and three (3.0%) were surveillance. Two (2.0%) cases were epidemiologically linked to other CRE cases. Review of information entered into the West Virginia Electronic Disease Surveillance System (WVEDSS) and 2015 outbreak data did not reveal any evidence of outbreak related CRE cases in 2015. Data for cases that were not marked “No” for “Outbreak Related” were either missing, or entered incorrectly.

Table 2. CRE Isolates by Surveillance Region, West Virginia, 2015; N=100

CRE Isolates by Surveillance Region, West Virginia, 2015; N=100						
	Northwest (N=9)	Northeast (N=7)	East (N=11)	South (N=39)	West (N=12)	Central (N=22)
Organism Cultured						
<i>Klebsiella pneumoniae</i>	7 (78.0%)	3 (43.0%)	9 (82.0%)	20 (51.0%)	1 (8.0%)	3 (14.0%)
<i>Enterobacter cloacae</i>	1 (11.0%)	3 (43.0%)	0	11 (28.0%)	2 (17.0%)	10 (45.0%)
<i>Enterobacter aerogenes</i>	0	1 (14.0%)	1 (9.0%)	2 (5.0%)	3 (25.0%)	2 (9.0%)
<i>Escherichia coli</i>	0	0	1 (9.0%)	3 (8.0%)	2 (17.0%)	4 (18.0%)
Other	1 (11.0%)	0	0	3 (8.0%)	4 (33.0%)	3 (14.0%)
Type of Culture						
Clinical	9 (100.0%)	7 (100.0%)	8 (73.0%)	39 (100.0%)	12 (100.0%)	22 (100.0%)
Specimen Source						
Urine	6 (67.0%)	6 (86.0%)	8 (73.0%)	28 (72.0%)	9 (75.0%)	18 (82.0%)
Respiratory	<5	0	0	<5	<5	<5
Wound	<5	<5	0	6 (15.0%)	<5	<5
Blood	0	0	0	<5	<5	0
Rectal (Surveillance)	0	0	<5	0	0	0
Outbreak Related						
No	8 (89.0%)*	7 (100.0%)	10 (90.0%)*	36 (92.0%)*	12 (100.0%)	22 (100.0%)
Epi Linked to other CRE						
No	7 (78.0%)	6 (86.0%)*	9 (82.0%)*	36 (92.0%)*	12 (100.0%)	22 (100.0%)

* indicates Missing or Unknown data

Demographics

The mean age of cases in 2015 was 69.8 years, with a range of 7 to 100 years. Sixty-four (64.7%) were female. The majority of cases were white, with 83 (83.8%). Eighty-two (82.83%) were identified as not Hispanic or Latino, and for 16 (16.2%), information about ethnicity was missing.

The highest number of cases resided in Kanawha County with 17 (17.17%), followed by Mercer County residents with 11 (11.1%). When analyzed by surveillance region, the Southern region reported 38 (38.38%) cases, followed by the Central region with 22 (22.2%). Figure 3 shows the distribution of CRE cases by surveillance region.

Forty-one (41.4%) cases were hospitalized, and six (6.1%) died. Three (50.0%) deaths occurred in the Southern surveillance region; however, no single county had more than one CRE related death. Of the 34 (34.3%) cases who resided in long term care facilities, assessments were performed for 32 (32.3%). An assessment was not performed for one case, and one result was missing.

Table 3. CRE Cases by Demographic Variable and Surveillance Region, West Virginia, 2015; N=99

CRE Cases by Demographic Variable and Surveillance Region, West Virginia, 2015; N=99						
	Northwest (N=9)	Northeast (N=7)	East (N=11)	South (N=38)	West (N=12)	Central (N=22)
Age, years (Avg. or N (%))	69.6	68.8	67.3	69.9	67.6	73.5
0-4	0	0	0	0	0	0
5-24	0	0	0	<5	<5	0
25-44	0	0	0	<5	0	<5
45-64	5 (56.0%)	<5	5 (45.5%)	12 (32.1%)	<5	5 (23.0%)
≥65	<5	5 (71.4%)	6 (54.5%)	24 (63.2%)	9 (75.0%)	16 (73.0%)
Sex						
Female	5 (56.0%)	7 (100.0%)	7 (64.0%)	25 (66.1%)	8 (67.1%)	12 (55.0%)
Race						
White	7 (78.0%)	6 (86.0%)*	9 (82.0%)*	31 (82.1%)*	12 (100.0%)	18 (82.0%)*
LTCF Resident						
Yes	<5	<5	<5	18 (47.4%)	0*	7 (32.0%)
Hospitalized						
Yes	<5	<5	<5	15 (39.5%)*	6 (50.0%)	8 (36.3%)*

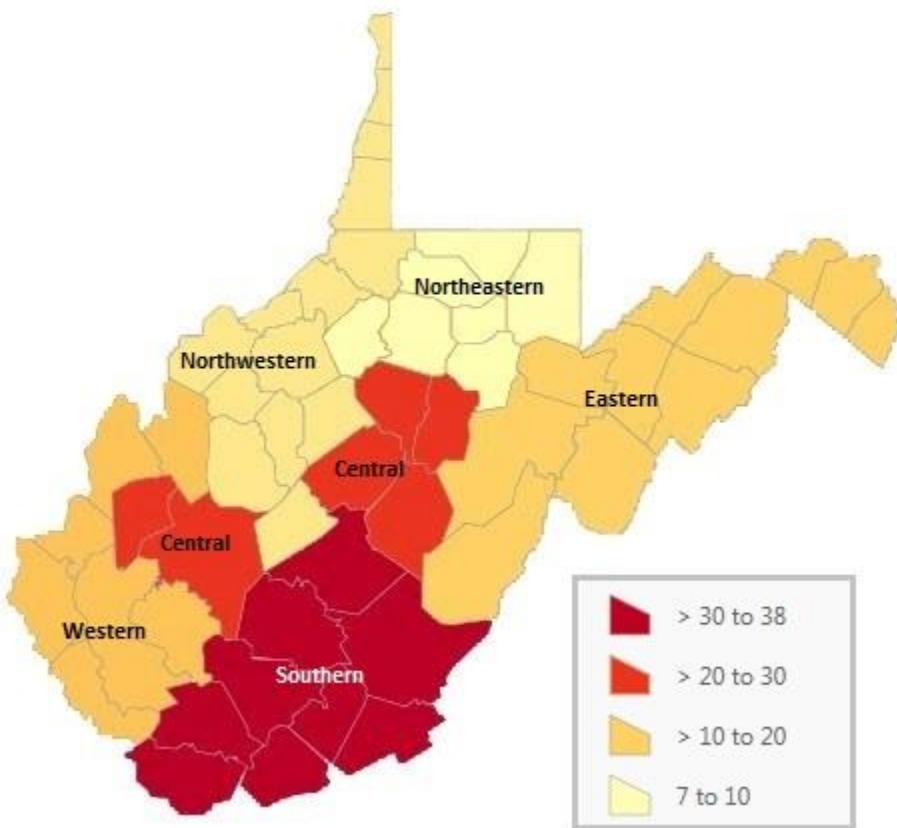
* indicates Missing or Unknown data

CRE incidence rates for the six surveillance regions were calculated per 100,000 population using 2010 Census data. Statewide, the rate of new CRE cases identified was 6.5 per 100,000 persons. The Southern region of the state saw the highest incidence with 12.1 new CRE cases per 100,000 persons (Table 4).

Table 4. CRE Incidence by Surveillance Region, West Virginia, 2015

2015 CRE Incidence by Surveillance Region, West Virginia, 2015			
	Population (2010 Census)	Cases (No. of Organisms)	Incidence (per 100,000 population)
Northwestern	309,445	9	2.9
Northeastern	296,912	7	2.4
Eastern	297,587	11	3.7
Southern	322,213	39	12.1
Western	313,985	12	3.8
Central	312,852	22	7.0
State Total	1,540,142	100	6.5

Figure 1. CRE Cases by Surveillance Region, West Virginia, 2015; N=99

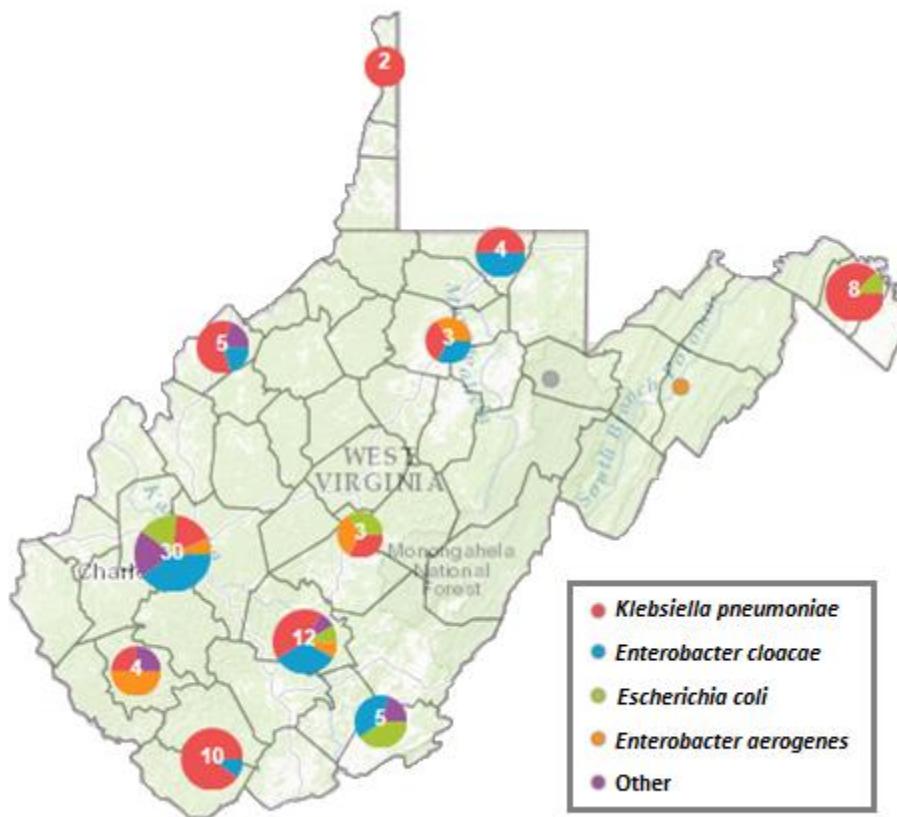


Additional Analyses

For questions concerning the patient outcomes (nursing home residency, hospitalization, death), the data were analyzed at the person level (n=99). There was an association between hospitalization and death ($p = 0.04$), but no association between long term care facility residence and either hospitalization ($p = 0.19$) or death ($p = 0.55$).

The data were analyzed at the organism level (n = 100) for questions regarding the region in which the organism was isolated, and outcomes associated with each organism. The type of organism appeared to be associated with the surveillance region ($p = 0.005$). Forty-five percent of *Klebsiella pneumoniae* and 41 percent of *Enterobacter cloacae* isolates were found in the Southern surveillance region. Thirty-seven percent of *Enterobacter cloacae* isolates were found in the Central region (Figure 3). Type of organism did appear to be associated with residence in a long term care facility ($p = 0.006$). Of 34 resident CRE cases, 24 (71%) presented with *K. pneumoniae*.

Figure 2. CRE Isolates by County, West Virginia, 2015; N=11. Number indicates total cases.



DISCUSSION

The spread of carbapenem resistance among Enterobacteriaceae is considered an urgent public health threat by the United States Centers for Disease Control and Prevention (CDC). The data presented in this report paint a concerning picture of CRE's foothold on West Virginia. A large portion of the burden rests on the southern region of the state; however, health facilities throughout the state should implement the CDC CRE prevention and control plan as no health facility is likely to remain unaffected.

These data should be interpreted with some caution. West Virginia conducts passive surveillance of CRE and relies on laboratory or facility reporting of cases. Although CRE is a reportable condition for laboratories in West Virginia, some cases may go unreported. Determining the true cause for hospitalization is not possible during the analysis of these data as the information gathered pertains only to patient status at the time of specimen collection. True cause of death is similarly unclear.

There are some limitations to determining an accurate CRE incidence, chief among them assessing the population actually at risk. While some CRE infections may be acquired in the community, the majority have historically been associated with exposure to health care facilities and prolonged use of broad spectrum antibiotics. Hospital populations are not stable, making it difficult to ascertain who is most at risk. Though somewhat more stable, nursing home populations change over the course of a year as well. The number of people residing in nursing homes is also relatively small, despite a generally older

population in West Virginia. According to the Kaiser Family Foundation,⁴ the population residing in West Virginia certified nursing facilities was 8,852 in 2014—a mere 0.5% of the estimated total state population in 2014. As the rates for this report were calculated using the West Virginia population as a whole, the results should be interpreted with some caution, and may be much higher than stated here. Additional studies would need to be conducted to accurately discern who in West Virginia is at highest risk of infection with a CRE organism.

West Virginia does not currently track which laboratories perform resistance mechanism testing, such as modified Hodge testing, to detect carbapenemase production among CRE isolates. This type of testing is not necessary to direct clinical care of patients, but it is useful in planning aggressive infection prevention efforts in areas with a high prevalence of carbapenemase producing CRE organisms (CP-CRE). Carbapenemases, enzymes that inactivate carbapenem antibiotics, are typically located on mobile bits of genetic material called plasmids. These plasmids are easily exchanged between different bacteria, thus facilitating rapid spread of carbapenem resistance. The CDC recommends more stringent infection prevention practices in areas where CP-CRE are prevalent as these organisms are suspected to be responsible for much of the spread throughout the country.⁵

Despite the limitations, these data have implications for important infection prevention activities. Health care facilities in all regions of the state should adhere to recommendations for standard and contact precautions for patients who are either infected or colonized with a CRE organism. A robust infection prevention program includes antibiotic stewardship implemented facility wide. These programs should include appropriate use guidelines for first line treatments of common conditions that are supported by evidence based practices. Educating providers, patients, and the general public on the dangers of overusing antibiotics remains an important investment of time and effort on the part of state and local health departments.

⁴ Kaiser Family Foundation, 2016 Total Number of Residents in Certified Nursing Facilities. <http://kff.org/>

⁵ CDC, Healthcare-associated Infections (HAIs)-FAQs about Choosing and Implementing a CRE Definition