WASHOE COUNTY HEALTH DISTRICT
ENHANCING QUALITY OF LIFE

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EPI-NEWS

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ANTIBIOTIC RESISTANCE THREATS

- The 1st Year Surveillance Findings of Carbapenem Resistant Organisms (CROs) in Washoe County

Introduction

On October 21, 2011 and March 31, 2017, the Washoe County Health District (WCHD) issued two issues of Epi-News addressing one of the top antibiotic resistance threats, i.e., carbapenem resistant Enterobacteriaceae (CRE). In those two issues, local surveillance data on CRE were published. In 2017, WCHD expanded surveillance from MDRB-CR (Multi-Drug Resistant Bacilli-Carbapenem Resistant) to CRO (Carbapenem Resistant Organisms). This included making CRO a reportable condition in Washoe County for hospital laboratories. This expansion also included investigating cases with carbapenemase-producing organisms (CPO), identifying contacts, and preventing further spread of CPO.

A primary mechanism of carbapenem resistance in Gram-negative bacteria is acquired carbapenemases, enzymes that hydrolyze these antibiotics to make them ineffective. There are five major carbapenemases which pose the largest public health risks. They are: Klebsiella pneumoniae carbapenemase (KPC), New Deli Metallo-β–lactamase (NDM), OXA-48 like enzymes, Verona Integron-encoded Metallo-β-lactamase (VIM), and Imipenem Metallo-β-lactamase (IMP). This means resistance genes that code for carbapenemases can be exchanged between different Gram-negative bacteria via genetic packets called plasmids. Resistance can then be spread between different bacteria among patients.

This issue will publish major findings from the first year of enhanced CRO surveillance. The surveillance is completed by a collaborative community-wide working group consisting of WCHD, hospitals, and laboratories.

Methods

Surveillance is primarily laboratory-based. However, a case having a CPO infection or colonization triggers an individual epidemiological investigation. A case of CRO is defined as an infection or colonization with a CRO organism of one individual per year regardless of their resident status. Infection or colonization with a second species of CRO organism or isolation of the same CRO organism in a new site in the same individual is counted as a separate case. Cases of CRO are first identified at local hospital laboratories through antibiotic susceptibility testing (AST). Specimens shown to be resistant to carbapenem drugs are then forwarded to the Nevada State Public Health Laboratory (NSPHL) for further testing. NSPHL performs its own AST, along with the modified carbapenem inactivation method (mCIM) to identify if the organism produces carbapenemase. If it does, this means the organism is positive for CPO. A PCR will then be performed to determine which carbapenemase is produced. The positive laboratory result will be reported by NSPHL to WCHD and to the hospital that submitted the specimen. WCHD and the hospital then work together to implement control measures if indicated.

Highlights of Findings

Morbidity of CROs and CPOs

In 2017, there were a total of 137 CRO cases and 6 CPO cases reported. Of 137 CRO cases, 36 (26%) had CRE; 82 (60%) had carbapenem resistant *Pseudomonas aeruginosa* (CRPA), and 19 (14%) had carbapenem resistant *Acinetobacter* (CRA) and other CROs. Of 36 CRE cases, five (14%) were CPO cases. Of 82 CRPA cases, one (1.2%) was a CPO case. The six CPO cases by organism and type of carbapenemase included the following:

- *Escherichia coli* – NDM (2),
- *Klebsiella pneumonia* - KPC (2),
- *Escherichia coli* - OXA-48-Like (1),
- *Pseudomonas aeruginosa* - VIM (1).

The two NDM cases reported in 2017 were epidemiologically linked, but were not epidemiologically linked to the NDM case reported in 2016. Over 50 contacts associated with these six CPO cases were identified and tested. Based on this testing it did not appear that further transmission occurred.

Demographics & Descriptive Characteristics

Of 137 CRO cases, the median age was 66 years (range: 2-99 years). The youngest patient, at 2 years old, was a pre-mature child and had many underlying conditions with an extensive history of antibiotic use during the previous year. Sixty-two percent (62%) of cases were male and 77% were White, non-Hispanic. Thirty percent (30%) were not Washoe County residents but they were patients of hospitals in Washoe County. The specimen sources included: urine (38%), respiratory (31%), wound (17%), rectal (5%), invasive sites (3%), surgical

sites (1%), and other (5%). Patient settings included: inpatient (45%), outpatient (27%), long-term acute care (21%), skilled nursing facility (5%), and intensive care unit (2%).

Severity by Number of Antibiotic Classes

Of the reported CRO cases, 75% (103/137) were resistant to three classes of antibiotics and 58% (80/137) were resistant to four or more classes of antibiotics. Pan-resistance was defined as non-susceptible to all tested drugs at the clinical lab and 10% (14/137) were pan-resistant. The organisms identified as pan-resistant were *Acinetobacter* (11), *Pseudomonas fluorescens* (1) and *Pseudomonas aeruginosa* (2).

Antibiotic Susceptibility among CROs

Generally, when the bacteria are resistant to the carbapenem class, it is also resistant to multiple antibiotic classes. Based on the first year's surveillance findings, three quarters of CROs were resistant to three classes of antibiotics and more than half were resistant to four or more classes of antibiotics. The following table describes the antibiotic susceptibility among 36 cases of CRE and 82 cases of CRPA. CRA cases are not included in this table because the number of cases is smaller than 30. Therefore, the percentage may be misleading.

Table 1. Antibiotic Susceptibility (%) for CRE and CRPA, Washoe County, 2017

Antibiotic*	CRE (%S)	CRPA (%S)
Ampicillin	0	18
Piperacillin	14	79
Cefepime	38	48
Cefotaxime	16	0
Cefotetan	7	
Ceftazidime	26	49
Ceftriaxone	23	0
Cefuroxime	0	0
Cephalothin	0	
Ampicillin-sulbactam	0	0
Piperacilin-tazobactam	18	64
Ciprofloxacin	49	37
Levofloxacin	70	33
Amikacin	90	
Gentamicin	83	74
Tobramycin	69	90
T/S	61	0
Aztreonam	24	24
Tigecycline	72	
Nitrofurantoin	21	
Imipenem	71	3
Meropenem	59	15
Ertapenem	14	Intrinsic resistance

*If the number of tests is under 10 it is not included in this table.

A full surveillance report for 2017 can be obtained upon request by sending an email to epicenter@washoecounty.us.

Novel Treatment Strategies for CPOs

Based on Table 1, it is known that there are not very many antibiotics that are effective against CROs. Of six CPO cases identified in 2017, four were resistant to 4-9 antibiotics classes. Treatment of CPO remains very difficult. According to a recently published review article[1], combination chemotherapies seem to be effective against KPC-producing bacteria. Novel combinations (ceftazidime-avibactam paired with aztreonam) are also being explored.

Recommendations for Healthcare Providers

WCHD strongly recommends that healthcare providers (HCPs) in Washoe County take the following actions in terms of combating CROs:[2]

1. Stay aware of facility specific CRO rates (CRE, CRPA, CRA) and community-wide CRO rates by reading WCHD's annual antibiogram at www.tinyurl.com/WashoeAntibiogram.
2. Ask if a patient has received medical care somewhere else, including in another country within the past six months.
3. Place patients currently or previously colonized or infected with CPO on Contact Precautions. Whenever possible, dedicate rooms, equipment, and staff to CPO patients.
4. Wear a gown and gloves when caring for patients with CPO.
5. Perform hand hygiene – use alcohol-based hand rub or wash hands with soap and water before and after contact with the patient or their environment.
6. Alert the receiving facility when you transfer a CPO patient, and find out when a patient with CPO transfers into your facility.
7. Make sure labs immediately alert clinical and infection prevention staff when CPO are identified.
8. Prescribe and use antibiotics wisely.
9. Discontinue devices like urinary catheters as soon as no longer necessary.
10. Please always report CPO cases to WCHD at 775-328-2447 or fax to 775-328-3764.

Acknowledgement

We are grateful to all hospitals, infection control practitioners and laboratory staff for their reporting and collaboration to make this surveillance work possible.

[1] Robert A. Bonomo, et. al. Carbapenemase-Producing Organisms: A Global Scourge. Clinical Infectious Disease. 2017;XX(00):1-8.

[2] https://www.cdc.gov/hai/organisms/cre/cre-clinicians.html