



Diagnosics for Antibiotic Resistance

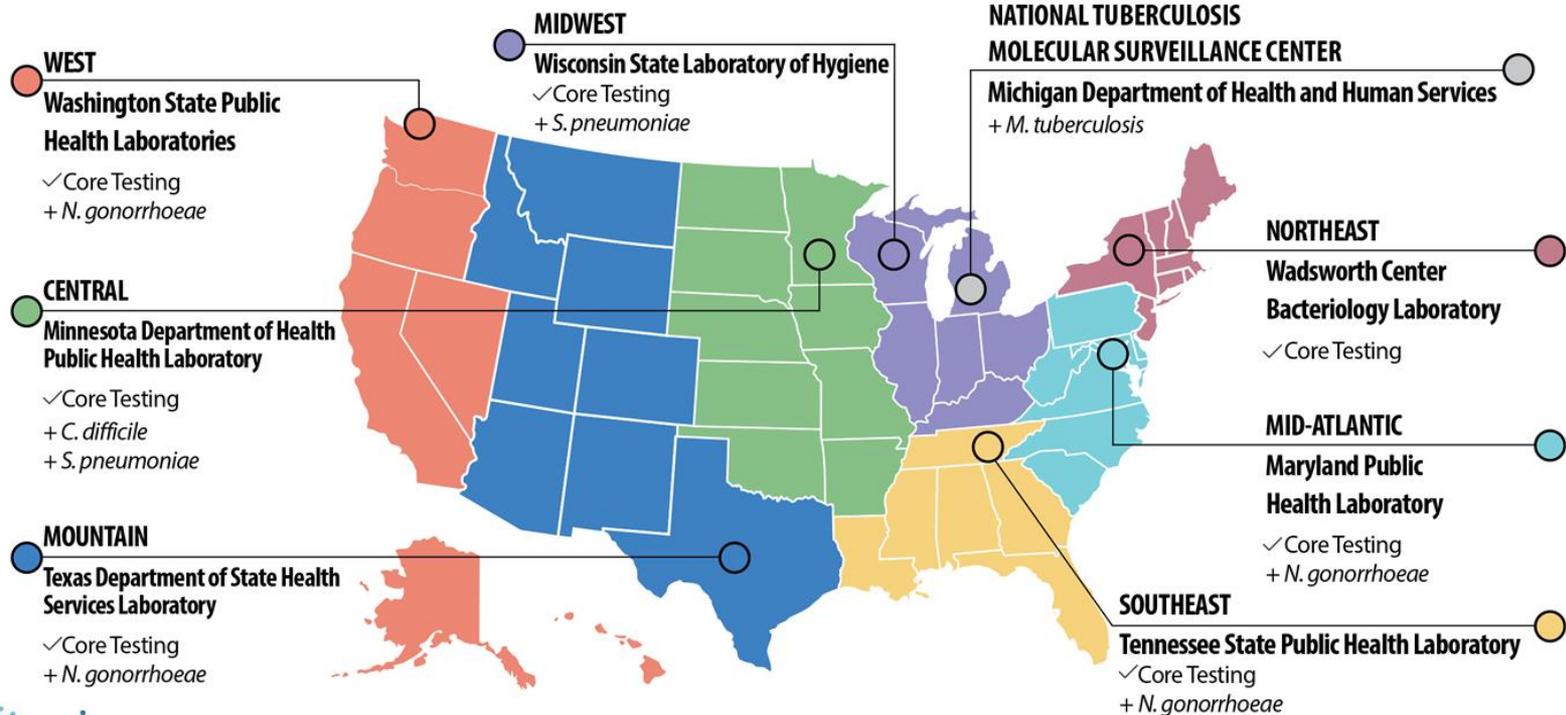
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Clinical Laboratory Improvement Advisory Committee

November 1, 2017

The Antibiotic Resistance Laboratory Network



Addressing Serious and Urgent AR Threats



Characterize resistance mechanisms of carbapenem-R gram-negative bacteria and test for colonization. WGS of *Salmonella* to detect resistance and outbreaks.



WGS of all *Mycobacterium tuberculosis* isolates to detect resistance and to identify transmission.



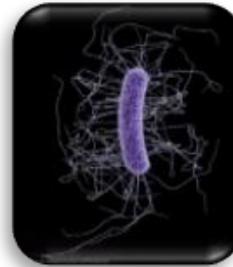
Reference susceptibility testing of *Neisseria gonorrhoeae* to guide treatment. WGS of isolates to identify resistance mechanisms.



Testing for antibiotic resistant *Streptococcus pneumoniae* vaccine escape strains.



Confirmation of *Candida auris*, colonization testing, antimicrobial susceptibility testing.



WGS of *Clostridium difficile* to characterize transmission dynamics.

New Lab Capacity to Detect AR Threats

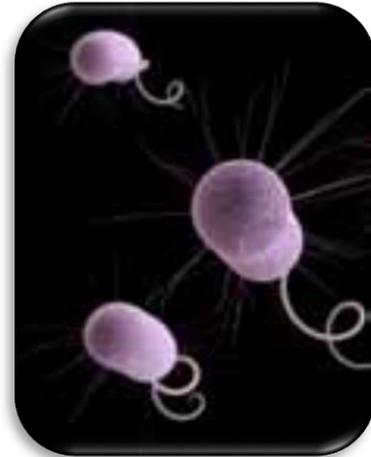


- Detecting new AR
- Delivering data to prevent infections
- Delivering data to treat infections

EXAMPLES...

VIM+ *Pseudomonas aeruginosa*

- Carbapenem-R *P. aeruginosa* are common, but few produce a carbapenemase
- Before ARLN, few VIM-producing PA cases were identified
- Since implementing the ARLN, we've:
 - Identified an outbreak at a FL long term acute care facility.
 - Leveraged ARLN capacity to support outbreaks in IL and FL.
 - Isolated cases in NV, TX, CA and OR. Two cases associated to healthcare abroad. No ongoing transmission identified.



Changing Susceptibility of *Neisseria gonorrhoeae*

- 2015 Treatment Recommendation: ceftriaxone + azithromycin
- Testing in ARLN increases the number of isolates tested and the turn-around time for results
- ARLN testing results are being closely monitored for increasing azithromycin resistance to determine if treatment recommendations need to be revised.



There are about **820,000** new gonorrhea infections each year in the U.S.



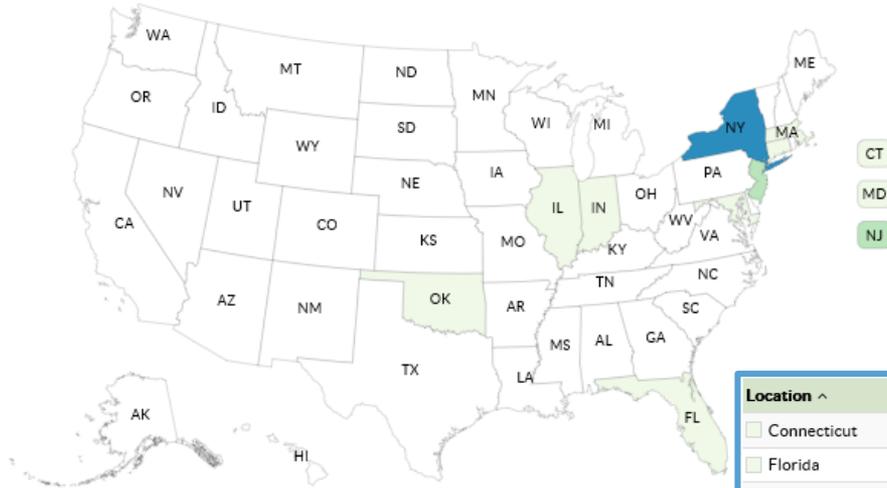
Gonorrhea is the **2nd** most commonly reported infectious disease



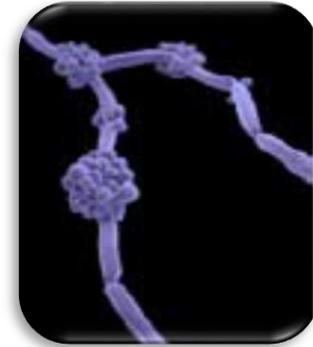
We are down to **1** recommended effective class of antibiotics to treat it

Candida auris Outbreaks

Candida auris cases in the United States



Number of Cases Reported



Location ^	Number Reported	Dates of collection
Connecticut	1	Jun 2017
Florida	1	Apr 2017
Illinois	4	May 2016 - Jan 2017
Indiana	1	Mar 2017
Maryland	1	Apr 2016
Massachusetts	3	Jan 2017, Jul 2017
New Jersey	23	Jun 2015 - Jul 2017
New York	77	May 2013, Apr 2016 - Jul 2017
Oklahoma	1	Apr 2017

More Resistant Bacteria and Bacteria that are Resistant to More Drugs

Morbidity and Mortality Weekly Report

Notes from the Field

Pan-Resistant New Delhi Metallo-Beta-Lactamase-Producing *Klebsiella pneumoniae* — Washoe County, Nevada, 2016

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On August 25, 2016, the Washoe County Health District in Reno, Nevada, was notified of a patient at an acute care hospital with carbapenem-resistant Enterobacteriaceae (CRE) that was resistant to all available antimicrobial drugs. The specific CRE, *Klebsiella pneumoniae*, was isolated from a wound specimen collected on August 19, 2016. After CRE was identified, the patient was placed in a single room under contact precautions. The patient had a history of recent hospitalization outside the United States. Therefore, based on CDC guidance (1), the isolate was sent to CDC for testing to determine the mechanism of antimicrobial resistance, which confirmed the presence of New Delhi metallo-beta-lactamase (NDM).

The patient was a female Washoe County resident in her 70s who arrived in the United States in early August 2016 after an extended visit to India. She was admitted to the acute care hospital on August 18 with a primary diagnosis of systemic inflammatory response syndrome, likely resulting from an infected right hip seroma. The patient developed septic shock and died in early September. During the 2 years preceding this U.S. hospitalization, the patient had multiple hospitalizations in India related to a right femur fracture and subsequent osteomyelitis of the right femur and hip; the most

tion in India had been in June 2016. asceptibility testing in the United States indi-

A point prevalence survey, using rectal swab specimens and conducted among patients currently admitted to the same unit as the patient, did not identify additional CRE. Active surveillance for multidrug-resistant bacilli including CRE has been conducted in Washoe County since 2010 and is ongoing; no additional NDM CRE have been identified.

This report highlights three important issues in the control of CRE. First, although CRE are commonly sent to CDC as part of surveillance programs or for reference testing, isolates that are resistant to all antimicrobials are very uncommon. Among >250 CRE isolate reports collected as part of the Emerging Infections Program, approximately 80% remained susceptible to at least one aminoglycoside and nearly 90% were susceptible to tigecycline (2). Second, to slow the spread of bacteria with resistance mechanisms of greatest concern (e.g., gene encoding NDM or *mer-1*) or with pan-resistance to all drug classes, CDC recommends that when these bacteria are identified, facilities ensure that appropriate infection control contact precautions are instituted to prevent transmission and that health care contacts are evaluated for evidence of transmission (3). Third, the patient in this report had inpatient health care exposure in India before receiving care in the United States. Health care facilities should obtain a history of health care exposures outside their region upon admission and consider screening for CRE when patients report recent exposure outside the United States or in regions of the United States known to have a higher incidence of CRE (1).

¹Washoe County Health District, Nevada; ²University of Nevada, Reno; ³Nevada State Public Health Laboratory; ⁴Division of Healthcare Quality Promotion, National Center for Emerging and Zoonotic Infectious Diseases, CDC.

An Example:

- 70 yo female hospitalized for an infection in her hip
- The patient recently traveled to India and was hospitalized for treatment of a hip fracture
- Infecting isolate: NDM-producing *Klebsiella pneumoniae* that was pan-resistant
- The patient developed septic shock and died

Antimicrobial Susceptibility Testing of New Drugs

- Challenge - There are often gaps in between a new drug being approved for use and the availability of a FDA-approved antimicrobial susceptibility test on a commercial device.
- Why?
 - Device manufacturers have competing priorities for test development
 - There is limited room on a MIC panel for new drugs
 - Drug development times are getting shorter so test development times are getting shorter

At least, a disk diffusion testing should be available when the drug is approved

A Pilot Program

- Antimicrobial Susceptibility Testing of New Antibiotics
 - There is often a gap between the approval of a new drug and the availability of testing methods in hospital laboratories
 - This gap can result in under use and over use of a new antibiotic
 - Testing is most important for pan or nearly pan-resistant bacteria
 - We can leverage ARLN lab capacity to place reference broth microdilution testing capabilities in regional labs and use ARLN electronic test order and report capabilities for rapid reporting





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Verification of an Automated, Digital Dispensing Platform for At-Will Broth Microdilution-Based Antimicrobial Susceptibility Testing

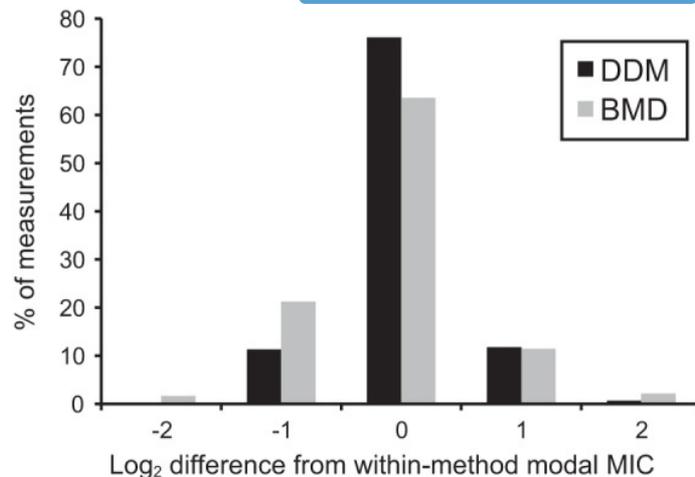
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With rapid emergence of multidrug-resistant bacteria, there is often a need to perform susceptibility testing using rapid or newer antimicrobial agents. Such testing can often be performed only by using labor-intensive, manual methods and lies outside the capacity of most clinical labs, necessitating reference laboratory testing and thereby increasing the time to diagnosis and the cost of susceptibility data. To address the compelling clinical need for microbiology laboratories to perform susceptibility testing, we explored a novel, automated, at-will broth microdilution-based susceptibility testing platform. Specifically, we explored the use of inkjet printer technology in the HP D300 digital dispensing system to dispense, directly from stock solution, the 2-fold serial dilution series required for broth microdilution testing. This technology was compared to standard broth microdilution testing using absorbance readings and data analysis to determine MICs. Performance was verified by testing members of the *Enterobacteriaceae* for susceptibility to ampicillin, cefazolin, ciprofloxacin, colistin, gentamicin, meropenem, and tetracycline. The results obtained with a broth microdilution reference standard. In precision studies, essential and categorical agreement rates were 96.8% and 98.3%, respectively. Furthermore, significantly fewer D300-based measurements were required to determine the modal MIC, suggesting enhanced reproducibility. In accuracy studies performed using a panel of 100 isolates, rates of essential and categorical agreement and very major, major, and minor errors were 94%, 98.3%, and 3.4%, respectively. Based on these promising initial results, it is anticipated that the D300-based method will allow clinical microbiology laboratories to perform at-will broth microdilution testing of antimicrobial susceptibility, thereby closing the critical testing gap.



FIG 1



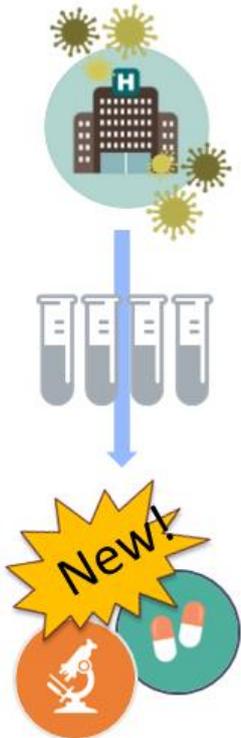
On Demand MIC Panels

- Easy method to place reference BMD capacity in ARLN labs
- Applications
 - Testing susceptibility of pan-R pathogens to new drugs
 - Collect AST data for breakpoint decisions
- Can leverage ARLN cloud based electronic test order and result for faster turn-around times



CDC & FDA Antibiotic Resistance Isolate Bank

New innovations can support earlier diagnoses and more effective treatment options that can slow antibiotic resistance.



CDC uses bacteria samples (isolates) from health departments, labs, and outbreak and surveillance activities.

CDC analyzes and sequences the bacteria's resistance and makes the data and sample available.

Researchers can use the bacteria and data to challenge, develop new diagnostic tests and antibiotics.

Laboratorians can validate lab tests to improve patient care.

BY THE NUMBERS

CDC curated 14 panels from its 450,000+ isolate collection

55,000 isolates shared since July 2015

571 unique customers

637 orders processed

Thank You

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For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

