Diagnostics for Antibiotic Resistance

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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.

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

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

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

- Testing for antibiotic resistant Streptococcus pneumonia vaccine escape strains.

- 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.
Candida auris Outbreaks

Candida auris cases in the United States

Number of Cases Reported

- 1 - <20
- 20 - <39
- 39 - <58
- 58 - 77

Location | Number Reported | Dates of collection
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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 2013 - 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

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
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 or newer antimicrobial agents. Such testing can often be performed only by using labor-intensive, manual techniques, and lies outside the capacity of most clinical labs, necessitating reference laboratory testing and thereby a delay 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 utilized inkjet printer technology in the HP D300 digital dispensing system to dispense, directly from stock solutions to the microtiter plate, the 2-fold serial dilution series required for broth microdilution testing. This technology was compared to absorbance readings and data analysis to determine MICs. Performance was verified by testing members of the Clinical and Laboratory Standards Institute (CLSI) panel of bacteria and yeasts. The results were comparable to those obtained with a broth microdilution reference standard. In precision studies, essential and clinical isolates were used. The results showed that the D300-based measurements were in excellent agreement with the CLSI panel values, with a mean difference of 0.15 log₂ units. Furthermore, significantly fewer D300-based measurements were outside of the 2-fold change limits of the CLSI panel, 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 92%, 94%, and 3.4%, respectively. Based on these promising initial results, it is anticipated that the D300-based method will allow clinical laboratories to perform at-will broth microdilution testing of antimicrobials critical to clinical decision-making.
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
For more information on CDC AR Investments

https://wwwn.cdc.gov/arinvestments
Thank You

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For more information, contact CDC
1-800-CDC-INFO (232-4636)

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.