California Antimicrobial Resistance Laboratory Network

Presented by Webinar
November 15, 2016
Objectives

• Present the CDC’s national Antibiotic Resistance Laboratory Network (ARLN)
• Describe the CDC ARLN’s “detect, respond, prevent, and innovate” strategy
• Define the role of the Washington State Public Health Laboratory in the ARLN
• Introduce the California AR Laboratory Network
• Discuss how the California AR Laboratory Network will interface with the national ARLN
California Antimicrobial Resistance Laboratory Network – Kickoff Session

Guests

**Centers for Disease Control**
Jean Patel, PhD, D(ABMM)
Deputy Director, Office of Antimicrobial Resistance, National Center for Emerging Zoonotic and Infectious Diseases

Allison C Brown, PhD, MPH
Lead, AR Capabilities and Special Studies Team
Clinical and Environmental Microbiology Branch
Division of Healthcare Quality Promotion

**Washington State**
Sopheay Hun, MBA, MLS(ASCP)
Antimicrobial Resistance Regional Laboratory (ARLN) Supervisor
Washington State Department of Health
Public Health Laboratories
Activities Focused on DHQP Pathogens
Main Activities

Core Testing for CRE/CRPA

Colonization Testing

Enhanced Surveillance
Objectives

- Increase testing capacities
  - 55 sites nationwide
  - 7 regional labs (overlap PulseNet regions)
- Improve infection control
  - Detect of CRE-infected/colonized patients
  - Isolate contacts to decrease transmission
- Characterize resistance mechanisms
  - Detect novel and emerging mechanisms
  - Understand distribution (facility, local, state, region)
- Estimate burden
  - Characterize colonizations, illnesses, transmission
Establishing a Network of Participating Facilities

Goal
Establish network of clinical laboratories that provides isolates from all types of healthcare facilities

- At minimum, collect from laboratories serving short- and long-term acute care hospitals
- Ideally, include those serving long-term care facilities and other critical care settings
Isolate Collection

CRE

• Target species: *Escherichia coli, Klebsiella oxytoca, Klebsiella pneumoniae*, and *Enterobacter* spp

• Resistant to imipenem, meropenem, doripenem, or ertapenem by standard AST methods

CRPA

• All *Pseudomonas aeruginosa*

• Resistant to imipenem, meropenem, or doripenem by standard AST methods
Methods

Species identification
Confirmatory AST
Phenotypic screening for carbapenemase production
Molecular detection of mechanism
Species Identification

Confirm species of Enterobacteriaceae and *Pseudomonas*

- MALDI-TOF mass spectrometry
- Automated instruments (VITEK 2, MicroScan, Phoenix, etc.)
Antimicrobial Susceptibility Testing

1. Confirm phenotypic detection of carbapenem resistance
2. Further characterize isolates (epidemiologically important resistance; possible mechanisms)
3. Method used should complement rather than duplicate those of submitting clinical laboratory

Drugs used to confirm and further characterize carbapenem-resistant Enterobacteriaceae (CRE) and carbapenem-resistant *P. aeruginosa* (CRPA)

<table>
<thead>
<tr>
<th>Drug class</th>
<th>CRE</th>
<th>CRPA</th>
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<tbody>
<tr>
<td><strong>Carbapenems</strong></td>
<td>2 carbapenems (ertapenem and either imipenem, doripenem or meropenem)</td>
<td>2 carbapenems (selected from imipenem, doripenem and meropenem)</td>
</tr>
<tr>
<td><strong>Cephems</strong></td>
<td>Ceftazidime, ceftriaxone, and ceftepime</td>
<td>ceftazidime and ceftepime</td>
</tr>
<tr>
<td><strong>B-lactam/B-lactamase inhibitor combinations</strong></td>
<td>NA</td>
<td>piperacillin-tazobactam</td>
</tr>
<tr>
<td><strong>Monobactams</strong></td>
<td>aztreonam</td>
<td>aztreonam</td>
</tr>
<tr>
<td><strong>Polymyxins</strong></td>
<td>colistin</td>
<td>colistin</td>
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</table>
Detection of Carbapenemase Production

- Determine whether an isolate produces a carbapenemase (+/-)
- Will not identify which one
- Carbapenem Inactivation Method (CIM) or CarbaNP assay
Molecular Detection of Resistance Genes

Required and optional targets for CRE and CRPA

<table>
<thead>
<tr>
<th>PCR</th>
<th>CRE</th>
<th>CRPA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Required</td>
<td>$\text{bla}<em>{\text{KPC}}, \text{bla}</em>{\text{NDM}}, \text{OXA-48-like genes}$</td>
<td>$\text{bla}<em>{\text{KPC}}, \text{bla}</em>{\text{NDM}}, \text{bla}_{\text{VIM}}$</td>
</tr>
<tr>
<td>Optional</td>
<td>$\text{bla}<em>{\text{IMP}}, \text{bla}</em>{\text{VIM}}, \text{mcr-1}$</td>
<td>$\text{bla}_{\text{IMP}}, \text{mcr-1}$</td>
</tr>
</tbody>
</table>
Storage and Sending Isolates

- State labs will store all CRE and CRPA isolates with confirmed carbapenem resistance (one isolate per patient) for a **minimum of 2 years**
- When a novel and/or unusual mechanism is suspected, selected isolates will be submitted to designated AR regional lab **within 1 working day**
- CDC may request some isolates; requested isolates should be submitted to CDC **within 1 working day**
Required Reporting

• **Within 1 working day of results**: Report any novel and/or unusual AMR in CRE or CRPA to CDC; send isolate to regional laboratory
  
  o Unusual AMR includes isolates with discordant results (phenotypic vs molecular) or unknown mechanisms of resistance

• **Within 2 working days of results**: Report results back to submitting clinical laboratories
  
  o Use secure communications
  
  o Include disclaimer that results can only be used to support infection prevention measures
  
  o Should not be a substitute for diagnostic procedures
  
  o Should not be used to guide clinical decisions

• **Monthly**: Submit a report of all CRE and CRPA testing results to CDC
CRE Colonization Testing
Colonization Testing: Rationale

- If patient isolate is carbapenem-resistant, facilities should consider screening for transmission
- Patients contacts might vary from setting to setting
- Minimum would include roommates of index patient for the duration of stay
- Longer stays may require broader group, point prevalence study(s) that includes unit or ward
- Colonization testing requires approval by state HAI coordinator and regional lab
- Appropriate uses should be approved unless capacity of regional lab has been/would be exceeded
## Colonization Testing Scenarios

<table>
<thead>
<tr>
<th>Appropriate Use (One-Time Testing)</th>
<th>Non-Priority or Inappropriate Use (Ongoing Testing)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screening roommates of new cases</td>
<td>Regional lab has exceeded capacity</td>
</tr>
<tr>
<td>Screening contacts of contaminated device</td>
<td>Routine inpatient screening</td>
</tr>
<tr>
<td>Point prevalence study (PPS) for new resistance or first identification of CRE</td>
<td>Admission screening</td>
</tr>
<tr>
<td>PPS when transmission suspected</td>
<td>Testing not linked to a facility or network prevention program</td>
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Colonization Testing Turnaround

1 day turnaround time

Simultaneous reporting to submitting facility and jurisdictional health department within 1 day of results

Initiate infection control/contact precautions

Provide or request assistance; initiate investigation
Enhanced Surveillance Activity
K7 Activity 2

- Reference testing to better understand an emerging or changing AR threat
- Conducted by regional labs among network of collaborating clinical laboratories within jurisdictional states
- Flexible; may cover variety of different organisms
- Can assess utility and effectiveness of this system
FY17: CR-Acinetobacter and mcr-1 genes in *E. coli* and *Klebsiella spp.*
West Regional Lab
West Regional Lab

- Facility

ARLN West Region
Washington State Department of Health
Public Health Laboratories
1610 NE 150th Street
Shoreline, WA 98155
Phone (206) 418 – 5400
Fax (206) 418 – 5485
West Regional Lab

- ARLN West Region Leadership Team

William A. Glover II, Ph.D., D(ABMM), MT(ASCP)
Director of Science & Technology
CLIA Director

Sopheay Hun, MBA, MLS(ASCP)
ARLN Supervisor

Brian Hiatt
Office Director for Microbiology

Marisa D’Angeli, MD, MPH
Public Health & Epidemiologist

Left to Right: Dr. William Glover, Maryann Watkins, Sopheay Hun
November 2016
Overview

- Update
- Testing
- Shipping
- Reporting
- Communication
Update

- New ARLN lab construction started Nov. 1st
- Procurement process for capital equipment acquisitions
- Increase ARLN lab personnel capacity
- Working on IT infrastructure with APHL technical assistance support
- ARLN West Region lab team received training at CDC Nov. 1-4, 2016
West Regional Lab

- CRE Surveillance Testing

  - Direct Molecular detection for most carbapenemase: KPC, NDM, VIM, OXA-48, IMP-1 group
  - Only FDA-approved NAAT system at present for direct rectal swab
  - Double swab allows use of 2nd swab for repeat PCR
  - Stable for 5 days
  - Quick visual reference job aids will be provided for proper collection
West Regional Lab

- Additional AR testing and emerging resistance detection

- Training Assistance and Support for your State CRE program
West Regional Lab

• Shipping

• CDC paid for ARLN FedEx shipping account has been created for West region
• Quick reference instruction guide and login access for creating shipping labels for sending samples
• Shipping services are limited to FedEx Priority Overnight
West Regional Lab

- Reporting

- Electronic Test Ordering and Resulting (ETOR) web-based portal in development for online reporting

- StarLIMS auto-fax results immediately to submitters and LHJ/public health upon completion of testing
West Regional Lab

- **Communication**
  - Regular state check-in conference calls
  - Monthly ARLN West regional webinars
  - Distribution email for ARLN West Region for questions, feedback and/or comments: [ARLN@doh.wa.gov](mailto:ARLN@doh.wa.gov)
  - Any questions contact: Sopheay Hun [Sopheay.Hun@doh.wa.gov](mailto:Sopheay.Hun@doh.wa.gov)
California Antimicrobial Resistance Laboratory Network
California AR Lab Network Goals

1. **Enhance situational awareness** of healthcare-associated AR pathogens by facilitating information and data sharing

2. **Connect healthcare facilities and laboratories to additional laboratory testing resources** to enhance patient care and infection control activities

3. **Strengthen collaboration** among clinical and public health laboratorians, infection control practitioners, and public health epidemiologists
# Laboratory Testing Resources – Initial Framework

<table>
<thead>
<tr>
<th>Healthcare Providers and Laboratories</th>
<th>Local Public Health Laboratories</th>
<th>CDPH Microbial Diseases Laboratory</th>
<th>CDC ARLN (Washington State)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Work with local &amp; state health department to understand when and where to submit isolates or specimens</td>
<td>CRE confirmation and characterization testing (e.g. CRE mechanism testing)*</td>
<td>CRE colonization testing of rectal swab specimens</td>
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</tr>
<tr>
<td>Report outbreaks/clusters to local public health &amp; L&amp;C District Office</td>
<td>Genetic relatedness testing (e.g., whole genome sequencing)*</td>
<td>Characterization of novel/unusual resistance (e.g., mcr-1 and other mcr variants, unusual <em>Candida</em> spp.)</td>
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*Some testing may be available at local public health laboratories*
Los Angeles County Department of Public Health (LACDPH) Surveillance Project

- Enhanced lab surveillance to detect β-lactamases and carbapenem resistance mechanisms
  - Includes Maldi-TOF and modified Nanosphere BC-GN assay
  - Enrollment is open to labs currently not participating in enhanced surveillance
- Outbreaks should be reported to LACDPH Acute Communicable Disease Control
  - Isolates from healthcare facilities should be sent to LACDPH PHL
- For any enhanced surveillance enrollment or lab testing questions please contact Nicole Green, PhD, D(ABMM) at nicgreen@ph.lacounty.gov
California AR Lab Network – Data Sharing

- Aggregated reports
- Cumulative antibiograms
- Quarterly reports
  - Carbapenem Resistant Enterobacteriaceae
  - Multidrug Resistant (MDR) *Pseudomonas aeruginosa* and *Acinetobacter baumanii*
  - For labs that perform carbapenemase testing: numbers of carbapenemase-producing isolates, by specific carbapenemase (where possible)
- Any other unusual or novel resistance phenotype or mechanism
Submission of Aggregated Data

• Annual Cumulative Antibiograms
• Include questions about development and design
  o Population-specific? Diagnosis specific?
  o How are repeat isolates represented?
  o How are <30 isolates per category handled?
  o If selective/cascade reporting, are suppressed results included?
  o Does your laboratory use the most updated CLSI breakpoints?
Submission of Aggregated Data

- Proposed quarterly data collection templates for specific AR pathogens
- Excel-based, multiple submission options (fax, email)

<table>
<thead>
<tr>
<th>Organism</th>
<th>Total Isolates Tested</th>
<th>No. Isolates Resistant to at Least one Carbapenem*</th>
<th>No. Isolates Documented to Possess Carbapenemase**</th>
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<tbody>
<tr>
<td>Klebsiella pneumoniae</td>
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<tr>
<td>Klebsiella oxytoca</td>
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<td>E. coli</td>
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<td>Enterobacter aerogenes</td>
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<tr>
<td>Enterobacter cloacae</td>
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<tr>
<td>Other Enterobacter species</td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Total Isolates Tested</td>
<td>No. Isolates Multidrug Resistant (MDR)†</td>
<td>No. Isolates Documented to Possess Carbapenemase**</td>
</tr>
<tr>
<td>Acinetobacter baumanii</td>
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<tr>
<td>Pseudomonas aeruginosa</td>
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- *Using updated CLSI Breakpoints
- **If carbapenemase testing is performed; labs will be asked to indicate number of isolates identified with each carbapenemase(s), by organism
- †Multidrug resistance defined by Magiorakos et al. 2011
Timeline

• December 2016
  o Participants submit 2015 cumulative antibiogram
  o Provide feedback on proposed data sharing template

• January-February 2017
  o Participants submit Q4 2016 aggregated data

• March 2017
  o Next quarterly conference call
  o Present preliminary reports of aggregated AR data
Questions?

For more information, please contact the HAI Program at HAIProgram@cdph.ca.gov

Thank you