Infection Control/Antimicrobial Resistance (IC/AR) Webinar  
November 21, 2019  
1:30pm-2:30pm

Today’s Topic:
Containing Novel and Targeted Multidrug-Resistant Organisms (MDROs)

NJDOH, Public Health and Environmental Laboratories (PHEL)  
Alyssa MacMillan, PhD  
Public health surveillance testing for Carbapenemase Producing Carbapenem-Resistant Enterobacteriaceae (CP-CRE), Pseudomonas aeruginosa (CP-CRPA) and other novel and targeted MDROs (e.g., CRAB, C. auris)

NJDOH, Communicable Disease Service (CDS)  
Tara Fulton, MPH  
Update on Candida auris (C. auris) epidemiology, detection, and control strategies

Housekeeping
You will be on MUTE for the duration of this webinar
If you have a question please type into the “question” or “chat” box
This webinar is being recorded
Slides will be distributed after the webinar
If your question has not been answered at the end of the webinar, we will try to follow up with a written response
Next Webinar scheduled for winter 2020 - stay tuned!

Webinar Opportunity Tomorrow!
Edward Lifshitz, MD, FACP, Medical Director, Infectious & Zoonotic Disease Program, Communicable Disease Service of the New Jersey Department of Health will be speaking on an Antimicrobial Stewardship Webinar tomorrow!
Topic: Antimicrobial Stewardship: Protecting a Critical Resource
When: November 22, 2019, 11:00AM - 12:00PM
Register here: [link]
New Jersey and the Antibiotic Resistance Laboratory Network (ARLN):
Public health surveillance testing for Carbapenemase Producing-
Carbapenem-Resistant Enterobacteriaceae (CP-CRE), Pseudomonas aeruginosa (CP-CRPA) and other novel and targeted MDRs

ALYSSA MACMILLAN, PHD
PHLS MICROBIOLOGY PROGRAM MANAGER

CDC Reports: Antibiotic Resistance Threat in the United States 2019

• More than 2.8 million antibiotic-resistant infections in the US each year (35,000+ deaths)
• Since 2013, increase in number of cases but 18% decrease in deaths
• Categorized pathogens into threat categories

Urgent Threats
- Carbenem-resistant Acinetobacter
- Candida auris (C. auris)
- Clostridium difficile (C. difficile)
- Carbenem-resistant Enterobacteriaceae (CRE)
- Drug-resistant Neisseria gonorrhoeae (N. gonorrhoeae)

The Highlights:
What is carbapenem resistance?
How is it affecting New Jersey?
How do we detect and characterize it?
How are clinical and public health labs working together to control it?

Carbapenem Antibiotics
Broader spectrum of activity and greatest potency against gram-negative and gram-positive organisms
Inhibit cell wall formation
Relatively resistant to β-lactamas (bacterial defense mechanism)
First discovered in 1976, first available for treatment in 1985
Now include imipenem, meropenem, ertapenem, doripenem
*FDA approved
Considered "last resort": used for complicated or resistant infections
Acquiring Resistance

Mutation Based
1. Alter the protein target
2. Reduce permeability of outer membrane
3. Overexpress drug exporter proteins

Gene Acquisition
Plasmid (small genetic element) acquired from co-infecting organism
Enzyme-mediated resistance

Carbapenemase
β-lactamas with ability to hydrolyze penicillins, cephalosporins, monobactams, carbapenems

Big Five:
- KPC: Klebsiella pneumoniae carbapenemase
- NDM: New Delhi metallo-β-lactamase
- OXA-48: oxacillinase
- VIM: Verona integron-mediated metallo-β-lactamase
- IMP: imipenemase

CP-CRE: Carbapenemase-producing carbapenem resistant Enterobacteriaceae

Who is at risk?
Acute and long-term healthcare settings
Compromised immune system
- Cancer or transplantation
Ventilators, urinary catheters, central lines, chronic wounds
Long term antibiotic use
History of medical care abroad
30-70% mortality rate
2-3 times more likely to be fatal than infection with susceptible bacteria

New York/New Jersey: epicenter for KPC-CRE
Highest prevalence of CRE in the US
10% Klebsiella pneumoniae-bacteremia carbapenem resistant
Of all CP-CRE, 90%+ KPC-producing
NDM: sporadic
VIM/IMP/OXA-48: rare
Antimicrobial Resistance Laboratory Network

CDC-supported initiative established in 2016
Supports state and local health department surveillance

Beyond CRE:
• Clostridium difficile
• Streptococcus pneumoniae
• Neisseria gonorrhoeae
• Mycobacterium tuberculosis
• Candida auris
• MRSA

ARLN: Carbapenem Resistance

Testing Menu

<table>
<thead>
<tr>
<th>Task</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Species ID</td>
<td>VITEK 2 or Bruker MALDI ToF</td>
</tr>
<tr>
<td>Susceptibility Testing</td>
<td>Disk Diffusion</td>
</tr>
<tr>
<td>Carbapenemase Screening</td>
<td>Modified Carbapenem Inactivation Method (mCIM)</td>
</tr>
</tbody>
</table>
| Molecular Detection of AR Determinants | Real-time PCR
                                      |
                                      | KPC, NDM, CRO-48, IMP, VM          |

Drugs used to confirm and further characterize CRE and CRPA

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>CRE</th>
<th>CRPA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbapenems</td>
<td>ertapenem, imipenem, doripenem</td>
<td>imipenem, meropenem, doripenem</td>
</tr>
<tr>
<td>Cephems</td>
<td>ceftazidime, ceftriaxone, ceftazidime and cefepime</td>
<td>ceftazidime and cefepime</td>
</tr>
<tr>
<td>β-lactam/β-lactamase inhibitor combinations</td>
<td>piperacillin-tazobactam</td>
<td>piperacillin-tazobactam</td>
</tr>
</tbody>
</table>

Monobactams
piperacillin-tazobactam

Combination
| KPC, NDM, CRO-48, IMP, VM | aminoglycoside, aminoglycoside, aminoglycoside | aminoglycoside, aminoglycoside, aminoglycoside |
So now what?

Alert Values

Pan-resistance
Possible novel resistance
- Carbapenemase+ but PCR negative
- non-KPC CP-CRE
- CP-CRPA

Other AR Laboratory Services
provided by New York Department of Health

*Candida auris* isolate characterization
- Identification (MALDI-ToF)
- Antifungal susceptibility

*Candida auris* culture from patient swab (surveillance samples)
Carbapenemase-producing *Acinetobacter baumannii* characterization (including whole genome sequencing)
Expanded Antimicrobial Susceptibility Testing for Hard-to-Treat Infections (including aztreonam-avibactam)

Thanks!

NJ PHL ARLN Team
Maria Ohshin
Parul Patel
Hita Shah
Krupa Patel
Lisa Schlitt
Tom Kirn

NJ HA/AR Epidemiologists (past and present)
Patricia Barrett
Tara Fulton
Aaron Rosenbaum
Lab-Epi Liaison Alicia Sloughfy
Regional Laboratory Partners: NY DOH
Centers for Disease Control & Prevention ARLN Team
Funding
Submitting clinical lab partners
Multidrug Resistant *Candida auris*: Update on Current Epidemiology, Detection, and Control Strategies

TARA FULTON, MPH

HEALTHCARE ASSOCIATED INFECTIONS & ANTIMICROBIAL RESISTANCE EPIDEMIOLOGIST

Concerns About *Candida auris*

- Highly drug-resistant
- Patients can become colonized and develop invasive infections
- Spreads in healthcare settings

Global Emergence of *C. auris*

First isolate identified: 1996

- Global emergence: 2009
- First isolate identified: 2009

Japan

South Korea

India

South Africa

Kuwait

Kuwait

Pakistan

Venezuela

Israel

Germany

U.S.A.

Year of first identification

Calls For Health Emergency As Dangerous NJ Superbug: Super Yeast

CDC Says NJ Has Third-Most Hospitalizations with Drug-Resistant Fungus

A Mysterious Infection, Spanning the Globe in a Climate of Secrecy

The rise of *Candida auris* embodies a serious and growing public health threat: drug-resistant germs.
Countries Reporting Cases of *C. auris*  
September 30, 2019


Four Distinct Clades of *C. auris*  
Lockhart et al., 2017

South Asian clade  
East Asian clade  
African clade  
South American clade

[Chow et al., 2018](https://www.cdc.gov/fungal/candida-auris/tracking-auris.html)

U.S. Importation  
Followed by Local Transmission

Concerns About C. auris

Patients can become colonized and develop invasive infections.

Pan-resistance

- Two pan-resistant C. auris cases in 2019 (NY)
- Cases were unrelated
- Developed resistance on echinocandin treatment
  - already resistant to fluconazole and amphotericin B
- No transmission of resistance seen
- Pan-resistance reported from a few other countries

C. auris Drug Resistance in the U.S.

<table>
<thead>
<tr>
<th>Class</th>
<th>Drug Resistance</th>
<th>Percentage</th>
</tr>
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<tbody>
<tr>
<td>Azoles</td>
<td>87.6%</td>
<td></td>
</tr>
<tr>
<td>Polyenes</td>
<td>33.7%</td>
<td></td>
</tr>
<tr>
<td>Echinocandins</td>
<td>1.7%</td>
<td></td>
</tr>
</tbody>
</table>

33% multidrug-resistant

Data provided courtesy of CDC Mycotic Diseases Branch

Clinical Cases of C. auris by State
August 31, 2019

https://www.cdc.gov/fungal/candida‐auris/tracking‐c‐auris.html

Concerns About C. auris

Highly drug-resistant

Spread in healthcare settings
Concerns About C. auris

- Highly drug-resistant
- Patients can become colonized and develop invasive infections
- Spreads in healthcare settings

Risk Factors for C. auris

- Ventilator-dependent
- Invasive medical devices
- Extensive healthcare exposure
- Recently received antibiotics and antifungals
- Colonized with other MDROs

Risk Factor: Stays in Certain Types of Post-acute Care Facilities

<table>
<thead>
<tr>
<th>Ventilator Skilled Nursing Facility</th>
<th>Skilled Nursing Facility</th>
</tr>
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<tr>
<td>7.7% prevalence</td>
<td>0.7% prevalence</td>
</tr>
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</table>

Risk Factor: Healthcare Abroad

Adams et al., 2018
Invasive Infections Cause by *C. auris*

- **CIARI**
- **Bone**
- **Wound**
- **SSI**

Concerns About *C. auris*

- Highly drug-resistant
- Patients can become colonized and develop invasive infections

Modes of Transmission

- **Person to Person**
- **Contaminated Environment**
- **Shared Equipment**

*C. auris* Colonization

- Primarily on skin, but other body sites can become colonized
- Persistent, perhaps indefinitely
- No known decolonization strategies
- Risk factor for infections
- Risk factor for transmission
Persistence in the Environment

Mobile Equipment: Contributor to Transmission

Colonization Spreads Beyond Roommates

Identification
Challenges with Identifying C. auris

- FDA Approvals
- VITEK MS MALDI
- Bruker Biotyper MALDI
- GenMark ePlex BCDD-FP panel blood culture test
- VITEK 2.8.01 update
- rt-PCR
- Awareness of the organism
- Confirmation at reference and public health labs

Common Misidentifications

<table>
<thead>
<tr>
<th>Identification Method</th>
<th>Organism C. auris can be misidentified as</th>
</tr>
</thead>
<tbody>
<tr>
<td>VITEK 2 YST</td>
<td>Candida hoitzae</td>
</tr>
<tr>
<td>Bruker i-Detect with vers 8.01</td>
<td>Candida adhaemulonii</td>
</tr>
<tr>
<td>API 20C</td>
<td>Rhodotorula glutinis</td>
</tr>
<tr>
<td>BD Phoenix yeast identification system</td>
<td>Candida krusei</td>
</tr>
<tr>
<td>Microscan</td>
<td>Candida famata</td>
</tr>
<tr>
<td>Candida parapsilosis</td>
<td>Candida lusitaniae</td>
</tr>
<tr>
<td>RapidID Yeast Plus</td>
<td>Candida parapsilosis</td>
</tr>
<tr>
<td>GenMark ePlex BCDD-FP panel blood culture test</td>
<td>Candida lusitaniae</td>
</tr>
<tr>
<td>VITEK 2 8.01 update</td>
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</table>

Misidentification Improvements

- Awareness of the organism
- Confirmation at reference and public health labs

Candida speciation: Yeast not determined to species level in many labs, except by request
- Sterile site isolates may only be performed by request
- Species from non-sterile isolates often not identified

Initial culture site of C. auris clinical cases (U.S.)
**Recommendations for Laboratory Diagnosis**

Speciate all Candida isolates from normally sterile sites

Speciate Candida isolates from non-sterile sites when:

- When *C. auris* patients have been identified in the facility or unit
- When patient had overnight stay at healthcare facility in a country with *C. auris* transmission within 1 year
- Clinically indicated in the care of a patient
- When patient is not responding to therapy

Suspect *C. auris* when there is an increase in infections of unidentified *Candida* spp. in a patient care unit.

**Challenges with Detecting Colonization**

- Asymptomatic
- Limited testing availability through CDC, ARLN
  - Specialized enrichment broth
  - PCR
- Turnaround time
  - Specialized enrichment broth ~ 12 days
  - PCR ~ 3 days

**Identification and Containment Support**

- *C. auris* confirmatory testing (isolate submission)
- Surveillance testing of high risk contacts and when transmission is suspected
- Support includes shipping costs and screening supplies

**Direct plating methods misses ~25% of the positive *C. auris* patients screened compared to enrichment broth procedure**
Infection Prevention Strategies

Facility Level Prevention Strategies: Back to the Basics

Hand Hygiene
Personal Protective Equipment
Environmental Cleaning & Disinfection

Hand Hygiene when dealing with *C. auris*

Alcohol-based hand rub (ABHR) is preferred over soap and water except when hands are visibly soiled because it:

- Is more effective at killing germs on hands than soap
- Requires less time
- Is more accessible than handwashing sinks
- Produces reduced bacterial counts on hands
- Improves skin condition with less irritation and dryness than soap and water

Personal Protective Equipment: Transmission Based Precautions

Transmission Based Precautions - Second tier of basic infection control and are to be used in addition to Standard Precautions for patients/residents who may be infected or colonized with certain infectious agents for which additional precautions are needed to prevent infection transmission.
Personal Protective Equipment: Enhanced Barrier Precautions

- Specific to MDROs in nursing homes - not intended for use in acute care or long-term acute care hospitals
- Falls between Standard and Contact Precautions
- CMS acknowledges least restrictive isolation
- CDC recommendation
- Does not replace existing guidance regarding use of Contact Precautions for other pathogens (e.g., C. difficile, norovirus) in nursing homes

Personal Protective Equipment (PPE): Acute and Long-Term Acute Care Hospitals

Patients that are colonized or infected with C. auris in acute care or long-term acute care hospitals should be placed on Contact Precautions in a single room, with dedicated equipment and minimal staff entering the room.

Personal Protective Equipment (PPE): Nursing Homes

Patients that are colonized or infected with C. auris in nursing homes should be placed on Enhanced Barrier Precautions

- Gown and gloves during high-contact resident care activities that provide opportunities for transfer of MDROs to staff hands and clothing
- Can leave their rooms as long as secretions, excretions, and bodily fluids are contained and the resident can perform hand hygiene when appropriate, e.g., prior to leaving their room

C. auris Transmission Based Precautions

Transmission Based Precautions

- Acute Care
- Contact
- Nursing Homes

Enhanced-barrier Precautions

- Contact
- Acute diarrhea, draining wounds, secretions or excretions that are unable to be covered or contained
Environmental Cleaning & Disinfection: Products

Product must have an EPA claim for:
- **C. auris**
  - Medline Micro-Kill Bleach Germicidal Bleach Wipes EPA # 37549-1
  - Oxivir® 1 Ready-to-use EPA #70627-74
  - Oxivir® 1 wipes EPA # 70627-77
  - If not, C. difficile (see EPA List K)
- Consider use of these products throughout facility if multiple cases of **C. auris**

Cleaning and Disinfection of Shared Medical Equipment

Multidisciplinary approach (e.g., EVS, patient/resident care staff)

All equipment should be cleaned/disinfected after contact with or use on resident/patient (e.g. stethoscopes, X-ray machines, respiratory therapy equipment)

Recommendations for Facilities Caring for **C. auris** Patients

- **Dedicate staff and medical equipment for **C. auris** patients**, if possible (e.g., temperature probe, pulse ox, etc.)
- **For all staff and visitors, round strategically to prevent spread of **C. auris**
  - Standard Precautions → General iso rooms → **C. auris** iso rooms
  - Prioritize auditing and additional rounding in units with **C. auris** patients
  - Hand hygiene, PPS use, environmental cleaning, etc.

Recommendations for Facilities Caring for **C. auris** Patients

- Speciate **Candida** isolates from all patients to ensure **C. auris** possible transmission is identified quickly
Recommendations for Facilities Caring for *C. auris* Patients

Communicate the patient’s *C. auris* status to any receiving facilities

When *C. auris* Transmission is Suspected

Intensify Infection Control efforts throughout the units where transmission is suspected

Identify overlaps in location, equipment and care types for patients with *C. auris* (possible sources of transmission)

Conduct point prevalence screening for *C. auris* colonization in areas deemed ‘high risk’

- Findings from screening will inform next steps

Consultative onsite visit from HAI/AR team to identify areas for improvement

Clinical Cases of Candida auris, as of October 31, 2019

- Confirmed clinical case count: 145

  Confirmed clinical cases are those with isolates that have been confirmed as *C. auris* in the laboratory.

Reporting

- When *C. auris* is confirmed or suspected contact CDS!
  - 609-826-5964
  - Tara.Fulton@doh.nj.gov; HAIAR@doh.nj.gov

- Ensure *C. auris* specific infection prevention and control measures are in place

- Conduct surveillance in collaboration with CDS
Questions?

THANK YOU!

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