Candida auris in New York State Healthcare Facilities: An Update for Laboratory Staff

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Division of Epidemiology
New York State Department of Health
Outline

• Background
• Emergence in New York State
• Infection control
• Identifying and reporting *C. auris*
• NYSDOH prevention and control activities
Background
Rapid Emergence Since 2009

<table>
<thead>
<tr>
<th>Year</th>
<th>Country</th>
</tr>
</thead>
<tbody>
<tr>
<td>2009</td>
<td>Japan</td>
</tr>
<tr>
<td>2010</td>
<td>South Korea</td>
</tr>
<tr>
<td>2011</td>
<td>India</td>
</tr>
<tr>
<td>2012</td>
<td>S. Africa</td>
</tr>
<tr>
<td>2013</td>
<td>Kuwait</td>
</tr>
<tr>
<td>2014</td>
<td>Pakistan</td>
</tr>
<tr>
<td>2015</td>
<td>Venezuela</td>
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<tr>
<td>2016</td>
<td>Israel</td>
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<tr>
<td></td>
<td>United Kingdom</td>
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</table>
C. auris around the World

- Lockhart 2016: 54 isolates from Pakistan, India, South Africa, Venezuela, and Japan
  - Susceptibility testing
    - 93% resistant to fluconazole, 54% to voriconazole, 35% to amphotericin B, 7% to echinocandins, 6% to flucytosine
    - 41% resistant to ≥2 classes, 2 isolates resistant to 3 classes
  - Whole genome sequencing
    - 4 clades: South Asia, South Africa, South America, East Asia
    - Minimal differences among isolates within a geographic cluster
    - Suggests simultaneous emergence rather than spread
  - Surveillance
Reasons for Concern

• Challenging to identify
  – MALDI-TOF or sequencing required to correctly identify \textit{C. auris}
• Often multi-drug resistant
  – Usually resistant to fluconazole
  – Variable susceptibility to other azoles, amphotericin B, and echinocandins
  – Some have been resistant to all 3 classes of antifungal medications
• Transmitted within healthcare facilities
  – Outbreaks in multiple countries
  – Persistent colonization
  – Survives for long periods in the hospital environment
Emergence in New York State
Case Counts as of August 25, 2017

- 78 clinical cases
- 72 screening cases
- 4 probable cases

- All infected persons had other serious medical conditions
Geographic Distribution

• All but 2 diagnosed in New York City facilities
  – Greatest numbers in Brooklyn, Queens
• One diagnosed in Monroe County (Rochester)
  – Recent admission to involved NYC hospital
• One diagnosed in Westchester County
  – No obvious link to NYC facilities
Epidemiologic Curve

Candida auris: Confirmed Clinical Cases in New York State
May 2013–August 2017
Reported as of August 25, 2017

Month First Positive C. auris Culture Collected
The Future
The Future

• India
  – Chowdhary 2013: *C. auris* represented 5% of candidemia in pediatric hospital, 30% of candidemia in tertiary general hospital
  – Chakrabarti 2015: *C. auris* isolated from 19/27 ICUs throughout India, 5.2% of ICU Candida isolates

• Kenya
  – Okinda, 2014: *C. auris* accounted for 38% of hospital-acquired candidemia
    • *Candida albicans* 27%
Facility Involvement

• From 90 days before 1st positive culture to the present
  – 34 NYS hospitals
  – 45 NYS nursing homes
  – 1 LTACH, 1 hospice
  – Additionally, 1 hospital outside the US, 1 LTACH in another state, numerous private medical offices, private homes
C. auris in the U.S.

<table>
<thead>
<tr>
<th>State</th>
<th>Clinical Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Connecticut</td>
<td>1</td>
</tr>
<tr>
<td>Florida</td>
<td>1</td>
</tr>
<tr>
<td>Indiana</td>
<td>1</td>
</tr>
<tr>
<td>Maryland</td>
<td>1</td>
</tr>
<tr>
<td>Oklahoma</td>
<td>1</td>
</tr>
<tr>
<td>Massachusetts</td>
<td>3</td>
</tr>
<tr>
<td>Illinois</td>
<td>4</td>
</tr>
<tr>
<td>New Jersey</td>
<td>23</td>
</tr>
<tr>
<td>New York</td>
<td>78</td>
</tr>
</tbody>
</table>

https://www.cdc.gov/fungal/diseases/candidiasis/candida-auris.html
Resistance

• All but one case resistant to fluconazole
  – Variable resistance to other azoles
• Most cases resistant to amphotericin B
• Only one case resistant to echinocandins
  – Recent development, NYC case
  – The resistant case’s isolates were initially susceptible to echinocandins but later developed resistance, a known treatment challenge
Identifying and Reporting *C. auris*
When to Suspect *C. auris*

- *C. haemulonii*
- “*Candida* spp.” after identification attempted, especially if infection not responding to treatment
- *Rhodotorula glutinis* or *Candida duobushaemulonii, sake, catenulata, famata, guilliermondii, lusitaniae, or parapsilosis* depending on type of laboratory identification system
- Increase in unidentified *Candida* spp. infections on a patient care unit, including in urine
• Mandated reporting under New York State Sanitary Code
• Candida auris not explicitly listed

However:
• “In addition to the diseases listed above, any unusual disease (defined as a newly apparent or emerging disease or syndrome that could possibly be caused by a transmissible infectious agent or microbial toxin) is reportable.”

Additionally:
• “...a cluster or outbreak of cases of any communicable disease is a reportable event.”
• Don’t assume someone else is reporting
Reporting

• Notify facility infection preventionists and patient’s clinical team
• As described in previous NYSDOH health alert to laboratories, report to and coordinate with regional epidemiologist to forward suspicious isolates to Wadsworth Center
Infection Control
General

- Applies to both infected and colonized patients
- Standard and Contact Precautions
  - Generally, gown and gloves
- Hand hygiene
- Environmental cleaning and disinfection
Persistent Colonization

• Affected persons remain colonized for undefined but usually lengthy durations
• Remain under Standard and Contact Precautions indefinitely unless clearance documented
• Need at least 2 rounds of negative surveillance cultures (not on antifungals) at least 1 week apart before a person can be considered “cleared” – discuss with your NYSDOH regional epidemiologist
• No data and no recommendations for decolonization
Healthcare Personnel

• NYS - several healthcare personnel hands cultured – all negative
• Schelenz, 2016: UK hospital outbreak
  – Cultured 258 healthcare personnel
    • Hands, nose, axilla, groin, throat
  – Only 1 positive in nose
• *C. auris* is not generally considered a risk for healthcare personnel
NYSDOH Prevention and Control Activities
Goals

• Prevent transmission and further spread in affected facilities
• Define the extent of the problem
• Delay and blunt the impact of this organism in New York and the US
When We Find a Case

- NYSDOH regional epidemiologists contact facility
- Ensure appropriate infection control measures are in place
- Case investigation (e.g. medical record review, location tracking)
- Surveillance cultures of contacts (e.g. roommates)
- Point prevalence surveys of affected units
- Environmental cultures of surfaces
- Site visit
Acknowledgements

• NYSDOH
  – Eleanor Adams
  – Sudha Chaturvedi
  – Richard Erazo
  – Rafael Fernandez
  – Rosalie Giardina
  – Jane Greenko
  – Ronald Jean Denis
  – Sarah Kogut
  – Rutvik Patel
  – Monica Quinn
  – Karen Southwick

• CDC
  – Karlyn Beer
  – Tom Chiller
  – Nancy Chow
  – Janet Glowicz
  – Brendan Jackson
  – Alex Kallen
  – Ana Litvintseva
  – Shawn Lockhart
  – Abimbola Ogundimu
  – Eugenie Poirot
  – Sharon Tsay
  – Snigdha Vallabhaneni
  – Rory Welsh
References

Candida auris: An Emerging Threat

Laboratory testing

Ron Limberger Ph.D.
Wadsworth Center

Sudha Chaturvedi Ph.D.
Wadsworth Center
First Reported from Japan, 2009

*Candida auris* sp. nov., a novel ascomycetous yeast isolated from the external ear canal of an inpatient in a Japanese hospital

Kazuo Satoh\(^1,2\), Koichi Makimura\(^1,3\), Yayoi Hasumi\(^1\), Yayoi Nishiyama\(^1\), Katsuhisa Uchida\(^1\) and Hideyo Yamaguchi\(^1\)

\(^1\)Teikyo University Institute of Medical Mycology, 359 Otsuka, Hachioji, Tokyo 192-0395, \(^2\)Japan Health Sciences Foundation, 13-4 Nihonbashi-Kodenmacho, Chuo-ku, Tokyo 103-0001 and \(^3\)Genome Research Center, Graduate School of Medicine and Faculty of Medicine, Teikyo University, Otsuka 359, Hachioji, Tokyo 192-0395, Japan

- High temperature tolerance (45°C)
- High salt tolerance (10%)
- No specific features e.g. chlamydospore, hyphae, pseudohyphae, etc.
- Unique sugar assimilation profile
What methods can detect *C. auris*?

- Culture and identification of isolate
- PCR - currently only available at the Wadsworth Center
C. auris culture

- Can be grown on selective medium that contains 2% dulcitol & 10% salt at 40° C and CHROMagar Candida at 37° C.

Limitations

- Dulcitol is fairly selective but occasional growth of other yeasts seen (i.e. C. parapsilosis, C. guillermondii).

- CHROMagar Candida is selective in terms of color for some Candida spp. but cannot differentiate C. auris from C. parapsilosis and C. glabrata.
C. auris on CHROMagar Candida

C. auris
Culture (cont.)

• Wadsworth can share the CDC recipe for dulcitol medium.

• After isolation, the suspect \textit{C. auris} colonies must be further tested.
Culture confirmation

➢ Current diagnostic methods used in the majority of clinical labs are inadequate for *C. auris* ID
**Candida auris** can be misidentified as

<table>
<thead>
<tr>
<th><strong>Candida haemulonii</strong></th>
<th>VITEK2 YST</th>
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<tbody>
<tr>
<td><strong>Rhodotorula glutinis</strong> (absence of red pigment)</td>
<td>API 20C</td>
</tr>
<tr>
<td><strong>Candida sake</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Candida haemulonii</strong></td>
<td>BD Phoenix yeast identification system</td>
</tr>
<tr>
<td><strong>Candida catenulata</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Candida famata</strong></td>
<td>Microscan</td>
</tr>
<tr>
<td><strong>Candida guillermondii</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Candida lusitaniae</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Candida parapsilosis</strong></td>
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</tbody>
</table>

These and all *C. auris* isolates should be sent to the Wadsworth Center Mycology Laboratory for confirmation. Also, any yeast that cannot be identified to the species level, should be sent for ID.
Culture confirmation of *Candida auris*

MALDI & Sequencing

(1) MALDI-TOF-MS BRUKER

(2) VITEK 2 YST with Ver 8.01 software (BIOMERIEUX)

(3) Sequencing-Ribosomal gene
How do I validate MALDI-TOF for *C. auris*?

- If already CLEP-approved for using MALDI-TOF for yeast then just validate in-house. No need to submit validation to CLEP.

- If **not** CLEP-approved for using MALDI-TOF for yeast, then follow guidelines at [https://www.wadsworth.org/regulatory/clep/clinical-labs/obtain-permit/test-approval/submission-checklists](https://www.wadsworth.org/regulatory/clep/clinical-labs/obtain-permit/test-approval/submission-checklists) and submit to CLEP.
How do I validate ITS sequencing for *C. auris*?

If already CLEP approved for yeast identification by sequencing then just validate in-house. No need to submit to CLEP.

If not CLEP approved for yeast identification by sequencing then follow guidelines at https://www.wadsworth.org/regulatory/clep/clinical-labs/obtain-permit/test-approval/submission-checklists and submit to CLEP.
How do I validate the Wadsworth *C. auris* PCR in my laboratory?

- Request the *C. auris* PCR protocol from Wadsworth Mycology Laboratory
- Perform a streamlined in-house validation
Streamlined Validation

• Perform a limit of detection using 10-fold dilutions in matrix

• Perform a blinded accuracy study of 20 positive samples and 10 negatives for each matrix

• Submit above data and the SOP to CLEP
More on validation

NOTE: as of 8/30/2017 the Wadsworth PCR has only been approved for skin and nares swabs

If you intend to perform the testing using other matrices, a validation must be submitted to CLEP for the modification of this test
Yeast DNA extraction

The Wadsworth *C. auris* PCR has a fairly cumbersome DNA extraction process. We are working to improve this part of the assay and open to collaboration.
Susceptibility testing

Can be done using microbroth dilution and E-test methods as per the guidelines of Clinical Laboratory Standard Institute (CLSI).

No need to submit validation data to CLEP.
Reporting

• As described in a previous NYSDOH health alert to laboratories, report to and coordinate with regional epidemiologist to forward suspicious isolates to Wadsworth Center
Sending specimens to Wadsworth

- Fill out ID requisition form (available on wadsworth.org)
- Pack and ship appropriately for infectious agents (category B). Ship at room temperature.
- For commercial carrier, send to Mycology Laboratory, Wadsworth Center, Axelrod Institute, 120 New Scotland Ave, Albany, NY 12208
- If using USPS, send to the above at PO Box 22002, Albany, NY 12201
Laboratory Workflow

**Surveillance samples (sponges & swabs)**

- **Non selective agar medium (SAB+)**
  - Growth
    - MALDI
      - *Candida auris* & *Candida spp.*
  - No Growth
- **Selective agar (salt+dulcitol)**
  - Growth
    - MALDI
      - *Candida auris*
  - No Growth
- **Selective broth (salt + dulcitol)**
  - Cloudy
    - SAB+
      - No Growth
        - Growth
          - MALDI
            - *Candida auris*
  - Negative culture

**Real-time PCR assay**
- TAT = 4 h

- **Sequencing of the ribosomal gene (ITS & D1/D2)**
  - (Phylogenetic Analyses)
- **Antifungal susceptibility testing**
Lab Contact information

For Mycology test details: sudha.chaturvedi@health.ny.gov
For CLEP guidance: clep@health.ny.gov
Unsure or general questions: ronald.limberger@health.ny.gov

Web resource for validation guidance:
https://www.wadsworth.org/regulatory/clep/clinical-labs/obtain-permit/test-approval/submission-checklists
Epi Contact Info

NYSDOH Regional and Central Office Contact Information:
Western Regional Office (716) 847-4503
Central New York Regional Office (315) 477-8166
Metropolitan Area Regional Office (914) 654-7149
Capital District Regional Office (518) 474-1142
Central Office (518) 474-1142
General questions or comments can be sent to icp@health.ny.gov