Candida auris:
Epidemiology, surveillance, and prevention

Patricia M. Barrett, MSD
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Disclosures

- I have nothing to disclose.
Acknowledgement

- Many of today’s slides come from presentations previously given in New Jersey.
- Some content was adapted from presentations given by Dr. Sharon Tsay and CDC Mycotic Diseases Branch.
Learning Objectives

1. Review the emergence, identification, resistance, and transmission of *Candida auris*

2. Identify key prevention and control activities for *Candida auris*
Agenda

▪ Rethinking ‘Candida’
  ▪ Emergence
  ▪ Identification
  ▪ Resistance
  ▪ Transmission

▪ Prevention

▪ Response

▪ New Jersey experiences

▪ Takeaways
Let’s talk *Candida.*
Candida

- Catch-all for asexual yeast
- Includes hundreds of unrelated species
- More added each year
Candidemia

- Bloodstream infections (BSIs) caused by *Candida* spp.
- *Candida* is the most common organism causing healthcare-associated BSIs
- Incidence ~10-14 per 100,000
- Mortality 30-50%

*Candida albicans*
Candida species distribution in bloodstream isolates
Emerging Infections Program Surveillance, US 2008-2016 (n = ~7,000 isolates)

Data provided courtesy of CDC Mycotic Diseases Branch
Who gets candidemia?

- Broad-spectrum antibiotic use
- Immunocompromised
- Central lines
- Prolonged ICU stay
- Surgical patients (abdominal surgery)

Clark et al., 2004
Source of infection

- **Conventional wisdom**: autoinfection with host flora
- Transmission in hospital environments not thought to be common
- Outbreaks rare, but reported with *Candida parapsilosis*
Conventional wisdom does not apply to *Candida auris*.
Cryptococcus neoformans
Rhodotorula glutinis
Candida rugosa
Candida krusei
Candida lusitaniae
**Candida auris**
Candida haemulonii
Candida duobushaemulonii
Candida pseudohaemulonii
Saccharomyces cerevisiae
Candida glabrata
Candida bracarensis
Candida nivariensis
Candida catenulata
Candida pelliculosa
Candida albicans
Candida dubliniensis
Candida tropicalis
Candida metapsilosis
Candida parapsilosis
Candida orthopsilosis
Candida famata
Candida fermentati
Candida guilliermondii

Closely related to other **Candida** species known for antifungal resistance
Global emergence of *C. auris*

- **First isolate identified**: *Auris* as “ear”
- **Oldest isolate identified (1996)**
- **Global emergence**
- **Year of first identification**
  - 2009: Japan
  - 2010: South Korea
  - 2011: India
  - 2012: South Africa, Kenya, Kuwait
  - 2013: Pakistan, Venezuela, Israel, Germany, U.K.
  - 2014: Colombia, Spain, U.S.A.
  - 2016: Global emergence

Chowdhary et al., 2017
Healthy skepticism

- Was *C. auris* with us all along?
- Maybe newer diagnostic methods responsible for supposed emergence?
  - MALDI-TOF
  - DNA sequencing
- Most systems misidentify as *Candida haemulonii* or other species
International collaboration to assess emergence
Emergence is not just improved detection

- EIP Candidemia Surveillance Program
  - No *C. auris* found

- SENTRY and ARTEMIS programs (private collections from 4 continents)
  - >30,000 Candida isolates from 1996-2015
  - No *C. auris* before 2009

Data provided courtesy of CDC Mycotic Diseases Branch
Whole genome sequencing of isolates show four clades

- Very different across regions (>40K-400K SNPs)
- Nearly identical within regions (<70 SNPs)

Simultaneous development?

Data provided courtesy of CDC Mycotic Diseases Branch
Introduction to North America

Data and concept provided courtesy of CDC Mycotic Diseases Branch
Identifying *C. auris*
Challenges with identification

- Identification varies by laboratory method.
- *C. auris* can be misidentified as:
  - *Candida haemulonii*
  - *Candida duobushaemulonii*
  - *Candida catenulate*
  - *Candida famata*
  - *Candida guilliermondii*
  - *Candida lusitaniae*
  - *Candida parapsilosis*
  - *Candida sake*
  - *Rhodotorula glutinis*
  - *Candida* spp. after a validated method of *Candida* identification attempted

Mizusawa et al., 2017 and CDC Mycotic Disease Branch, 2018
## Misidentifications of *C. auris* (1)

<table>
<thead>
<tr>
<th>Identification Method</th>
<th>% NJ Labs</th>
<th>Organism <em>C. auris</em> can be misidentified as</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitek 2 YST</td>
<td>57%</td>
<td><em>Candida haemulonii</em></td>
</tr>
<tr>
<td>Proper ID possible with v.8.01</td>
<td></td>
<td><em>Candida duobushaemulonii</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>API 20C</td>
<td>32%</td>
<td><em>Rhodotorula glutinis</em> (characteristic red color not present)</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>Candida sake</em></td>
</tr>
<tr>
<td>BD Phoenix yeast identification system</td>
<td>4%</td>
<td><em>Candida haemulonii</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>Candida catenulata</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Microscan</td>
<td>8%</td>
<td><em>Candida famata</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>Candida guilliermondii</em> (no hyphae/pseudohyphae present on cornmeal agar)</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>Candida lusitaniae</em> (no hyphae/pseudohyphae present on cornmeal agar)</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>Candida parapsilosis</em> (no hyphae/pseudohyphae present on cornmeal agar)</td>
</tr>
</tbody>
</table>
### Misidentifications of *C. auris* (2)

<table>
<thead>
<tr>
<th>Identification Method</th>
<th>% NJ Labs</th>
<th>Databases needed to identify <em>C. auris</em></th>
</tr>
</thead>
<tbody>
<tr>
<td>MALDI-TOF</td>
<td>25%</td>
<td></td>
</tr>
<tr>
<td>Bruker Biotyper</td>
<td>--</td>
<td>Research use only database</td>
</tr>
<tr>
<td>VITEK MS</td>
<td>--</td>
<td>Saramis Ver 4.14 database and Saccharomycetaceae update</td>
</tr>
<tr>
<td>Molecular methods</td>
<td>--</td>
<td>Sequencing the D1-D2 region of the 28s rDNA or the Internal Transcribed Region (ITS) of rDNA</td>
</tr>
</tbody>
</table>
Candida auris identification requires speciation of Candida isolates

~30% of clinical cases in the U.S. have been from non-bloodstream isolates (urine, bile, wounds, etc.)
  - Isolates from non-sterile sites may not be worked up to species level

68% of surveyed clinical labs in New Jersey speciated isolates onsite
Challenges to detecting colonization
Establishing methods to culture and isolate *C. auris*

- Enrichment broth procedure
- Combination of high salt media (10% w/v) and high temperature (40°C) incubation
- Simple procedure readily adopted by advanced and resource limited laboratories

Welsh et al., 2017
Enrichment broth

Cloudy (left) = positive

CHROMagar

Candida auris appears pink

Welsh et al., 2017
Establishing methods to culture and isolate *C. auris*

Welsh et al., 2017
Culture independent diagnostic

- Culture dependent diagnostics take ~14 days
- CDC assisting the development of rapid diagnostics
  - Cepheid
  - T2
- PCR developments underway:
  - Rutgers contract with CDC to develop a rapid PCR assay
  - NYSDOH Wadsworth Laboratories
Antifungal resistance of *C. auris*
Antifungal susceptibility testing

- Susceptibility breakpoints for *C. auris* have not been established, but CDC developed the following as a general guide:

<table>
<thead>
<tr>
<th>Class/Drug</th>
<th>Tentative MIC Breakpoints (µg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluconazole</td>
<td>≥32</td>
</tr>
<tr>
<td>Amphotericin B</td>
<td>≥2</td>
</tr>
<tr>
<td>Anidulafungin</td>
<td>≥4</td>
</tr>
</tbody>
</table>

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<thead>
<tr>
<th>Class/Drug</th>
<th>Tentative MIC Breakpoints (µg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caspofungin</td>
<td>≥2</td>
</tr>
<tr>
<td>Micafungin</td>
<td>≥4</td>
</tr>
</tbody>
</table>

*Reference updated CDC guidance for more information and comments on interpretation.*
Drug resistance of *C. auris*

- **Polyenes**
  - 35% resistant to amphotericin B

- **Azoles**
  - 93% resistant to fluconazole
  - 54% resistant to voriconazole

- **Echinocandins**
  - 7% resistant to echinocandins

**41% multi-drug resistant**
**4% resistant to all three major antifungal classes**

Percentages based on susceptibility testing interpretations of 68 isolates tested by CDC, courtesy of CDC Mycotic Diseases Branch
Drug resistance of *C. glabrata*

**Polyenes**
- <1% resistant to amphotericin B

**Azoles**
- 11% resistant to fluconazole

**Echinocandins**
- Up to 12% resistant to echinocandins

Data from EIP surveillance testing provided courtesy of CDC Mycotic Diseases Branch
Resistance mechanisms

- A significant portion of the *C. auris* genome encodes
  - ATP-binding cassette (ABC)
  - Major facilitator superfamily (MFS) transporter families
  - Drug transporters
- ABC-type efflux activity by Rhodamine 6G transport was significantly greater among *C. auris* than *C. glabrata* isolates
- ERG-11 hotspot mutations
  - Different mutations in different clades

Chowdhary et al., 2017
Transmission of *C. auris*
C. auris transmission: what we know

- Environmental surfaces, equipment
  - Piedrahita et al. (2017), *Infection Control & Hospital Epidemiology*
  - New York State and CDC investigation

- Patients and healthcare workers
  - Selenchez et al. (2016), *Antimicrobial Resistance and Infection Control*

- Donor-derived
  - Azar et al. (2017), *Clinical Infectious Diseases*
More research is needed to better understand \textit{C. auris} transmission.

Currently, the majority of public health response and recommendations assume transmission is similar to CRE.

Various studies are ongoing.

Image source: Won et al., 2011
C. auris in the environment
Environmental contamination
Survival and persistence

Remains viable by culture for at least **two weeks**

Remains viable by esterase activity for at least **four weeks**

Welsh et al., 2017
Survival and persistence

Piedrahita et al., 2017
Cleaning and disinfection

Cadnum et al., 2017
Ultraviolet light

Cadnum et al., 2018
Patient + healthcare worker transmission
Findings from a European hospital

- Minimal contact with a case is needed for *C. auris* acquisition
  - Root cause analysis found acquisition required $\geq 4$ hour contact period with a known case or contaminated environment

- Transient carriage of *C. auris* by a healthcare worker
  - 1 of 285 HCWs had a positive nares swab
  - The positive staff had extensive care with a colonized patient

Schelenz et al., 2016
**C. auris colonization**

- Little is known about *C. auris* colonization.
- Axilla and groin appear to be the highest-yield sites to identify *C. auris* colonization, per CDC.
- CDC continues to offer re-screening of *C. auris* colonization, however few patients have met basic requirements to be considered ‘decolonized’
C. auris colonization example

**Candida auris colonization**

- **June 2017**
  - Axilla/groin swab
  - *Candida auris* identified

- **September 2017**
  - Axilla/groin swab
  - *C. auris* identified

- **October 2017**
  - Axilla/groin swab
  - No *C. auris* growth

- **November 2017**
  - Axilla/groin swab
  - *C. auris* identified

- **December 2017**
  - Blood and urine culture
  - *C. auris* identified

- **January 2018**
  - Axilla/groin swab
  - *C. auris* identified

**Infection**

*Candida auris* shed into environment
Decolonization regimens?

Abdolrasouli et al., 2017
Unknowns of *C. auris* colonization

- **Length of colonization**
  - Possibly indefinite
- **Colonization dynamics**
  - Skin recolonization from gut or oral cavity?
- **True risk of *C. auris* infection after colonization**
- **No public health recommendations for *C. auris* decolonization**
Donor-derived transmission

- Illinois organ donor had premortem respiratory culture that grew *C. haemulonii* (misidentification)
- Lung from this donor went to a Massachusetts patient
  - Pre and post-transplant cultures grew *C. auris*
- These isolates were closely related to IL isolates by whole genome sequencing (WGS)

Azar et al., 2017
Transmission in New Jersey

- No ‘smoking gun’
  - Multiple overlaps in units, staff, equipment, specialty care, etc.
- Patient movement within a healthcare transfer network
  - High-acuity units, facilities
- Little information derived from WGS
  - Per CDC, NJ isolates are ~99.9% related
Preventing *C. auris*
Antimicrobial stewardship

- Many *C. auris* patients received broad-spectrum antimicrobials in the weeks before first culture yielding *C. auris*.
- >50% of patients in a NJ long-term acute care hospital (LTACH) with an ongoing *C. auris* outbreak received antifungals
- Antimicrobial therapies may *create* an opportunity for *C. auris* acquisition or infection
Who receives antifungals?

- Sickest of patients tend to receive antifungals
  - Immunocompromised
  - Indwelling devices
  - ICU patients receive more antifungals than general inpatient

- At-risk population is growing
  - Increasing number of transplants and immune-modulating therapies
  - More post-acute care facilities with ICU-like units (LTACHs, vSNF, etc.)
Challenges with fungal infections

- No single syndrome for fungal infections
- Delayed treatment may lead to increased mortality
  - Empiric treatment for invasive infections
- *Candida* colonization vs. infection
  - Is treatment needed from identification in non-sterile specimens?
- Infectious Disease consultation often needed
Challenges in antifungal stewardship

- Fungal ID by culture may be limited
  - Longer turnaround time for certain tests
  - Ancillary diagnostics do not allow for resistance testing
- Clinical data may be limited or unclear
- Staff are less familiar with concepts, compared to antibiotic stewardship
Existing guidelines

Clinical Practice Guideline for the Management of Candidiasis: 2016 Update by the Infectious Diseases Society of America
Activities do not significantly differ from antibiotic stewardship. Think *antimicrobial* stewardship program!
A majority of patients with *C. auris* infection or colonization have various types of invasive lines and tubes.

- E.g., central venous catheters, urinary catheters and tracheostomy tubes.

Strict adherence to insertion and maintenance practices of patient devices

Ensure continued assessment of need for devices and prompt removal when no longer needed

When *C. auris* patients are identified, review and assess these practices
For patients with *C. auris*, skin preparation should include alcohol-based agent unless contraindicated

- Schedule procedures for *C. auris* patients for the end of the day.
Responding to *C. auris*

“We have a patient with *Candida haemulonii*….. Now what?”
Ideal *C. auris* response

- Suspect and identify early
- Isolate quickly
- Report results
- Remove from the environment
- Communicate moving forward
Identify *C. auris* early

- Speciate all *Candida* isolates from normally sterile sites
- Suspect *C. auris* when there is an increase in infections of unidentified *Candida* spp. in a patient care unit
Identify *C. auris* early

- Speciate *Candida* isolates from non-sterile sites when:
  - Clinically indicated (e.g., patient is not responding to therapy)
  - When *C. auris* patients have been identified in the facility or unit
  - During outbreaks
  - When patient had overnight stay at healthcare facility in a country with *C. auris* transmission within 1 year
Countries with *C. auris* transmission
Isolate quickly

- Whenever *C. auris* is suspected, consider preemptive control measures until laboratory confirmation
- Standard and Contact Precautions
- Cohort *C. auris* patients to one area in a facility or unit
  - Minimize number of staff members caring for *C. auris* patients
- Placement in single rooms
  - *C. auris* patients can share rooms
  - If limited rooms, prioritize patients with highest level of care
PDPH *C. auris* isolation requirements

- Hospitals:
  - Contact precautions
  - Private room

- Long-term care:
  - Contact precautions or enhanced standard precautions
  - Private room if available

- Applies to current and future stays

- Dedicate reusable equipment to the patient, when possible
Reporting *C. auris* to PDPH

- *Candida auris* and *Candida haemulonii* from any body site is reportable to PDPH upon receipt of results
  - Applies to both providers and laboratorians
- See the Board of Health regulations: ‘*Regulations Governing the Control of Communicable and Non-communicable Diseases and Conditions*’
Environmental cleaning and disinfection

- Use Environmental Protection Agency (EPA)-registered hospital-grade disinfectant effective against Clostridium difficile spores
  - Ensure contact time, dilution, etc.
- Daily and terminal cleaning of:
  - C. auris patient room and any care areas (radiology, physical therapy, etc.)
  - Shared equipment of the unit
  - Common areas (handrails, nurse’s stations, etc.)
- Also required by PDPH
Communicate \textit{C. auris} transfer

- Prior to transfer, sending facility should notify the receiving facility of \textit{C. auris} infection or colonization
  - Required by PDPH
- Call ahead to receiving facility whenever possible
- Include \textit{C. auris} in intake or discharge documents
- NJ uses a \textit{C. auris} coversheet and UT form
Hemodialysis and infusion clinics
- Outpatient settings (physician offices, wound clinic, etc.)
- Home healthcare
- Home and family members
Summary

- *C. auris*...
  - Is challenging to identify
  - Is multidrug resistant
  - Can be transmitted in healthcare settings
  - Difficult to contain

- Early identification and meticulous infection control is needed to control its spread.

- Philadelphia facilities and providers need to be alert and informed in order to identify and prevent *C. auris* transmission.
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Questions?
Patricia M. Barrett, MSD
609-826-5964
patricia.barrett@doh.nj.gov
Antimicrobial Resistance Coordinator
Communicable Disease Service
New Jersey Department of Health

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References

