Candida auris: The Emergence of a Fungal Superbug

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NYSDOH AMR TASK FORCE SUMMIT
November 30, 2017

What the public thinks
What healthcare professionals think
Fungi can cause serious infections and be HAIs

- Candidemia
- Intra-abdominal candidiasis
- Invasive mold infections

Candidemia/ Invasive Candidiasis

- **Severe**: mortality 30-50%
- **Incidence**: 5-15/100,000
- **Conventional wisdom**: autoinfection with host flora, particularly from gut
- Outbreaks rare
Risk Factors for Invasive Candidiasis (“the other C. diff”)

- Broad-spectrum antibiotic use
- Immune compromise
- Prolonged ICU stay
- Abdominal surgery

Risk Factors for Invasive Candidiasis

- Broad-spectrum antibiotic use
- Immune compromise
- Prolonged ICU stay
- Abdominal surgery
- Central lines
Bloodstream *Candida* species distribution, EIP surveillance, U.S. 2008-2016 (n~7000 isolates)

- **C. albicans**, 39%
- **C. glabrata**, 28%
- **C. parapsilosis**, 16%
- **C. tropicalis**, 9%
- *Candida dubliniensis*, 2.6%
- *Candida krusei*, 2.0%
- *Candida lusitaniae*, 1.8%
- *Candida guilliermondii*, 0.5%
- *Candida orthopsilosis*, 0.3%
- *Candida metapsilosis*, 0.1%
- Other *Candida* species, 1.1%

**ANTIBIOTIC RESISTANCE THREATS in the United States, 2013**

**FLUCONAZOLE-RESISTANT CANDIDA**

- **Threat Level Serious**
- **3,400 Fluconazole-resistant *Candida* infections**
- **220 Deaths**
- **46,000 Candida infections per year**
Why We Care About an Obscure *Candida* Species

It always starts with an email...

February 2015

- Pakistani colleagues concerned about outbreak of *Saccharomyces cerevisiae* infections
  - 22 isolates over 2 months
  - 8 bloodstream, 3 burn wounds, 10 urine, 1 catheter tip
But it wasn’t *Saccharomyces*...

- A commercial test kit had been used for identification
- DNA sequencing revealed that the isolates were *Candida auris*

**Discovery of *C. auris*—2009**

*ORIGINAL ARTICLE*

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

Kazuo Satoh1,2, Koichi Makimura3,4, Yayo Hisumi5, Yayoi Nishiyama5, Katsuhisa Uchida5 and HDeyo Yamaguchi6

1Tokyo University Institute of Medical Mycology, 359 Otoku, Hachioji, Tokyo 192-0395, 2Japan Health Sciences Foundation, 13-4 Minato-ku, Chuo, Tokyo 103-0021 and 3Genome Research Center, Graduate School of Medicine and Faculty of Medicine, Tokyo University, Otoku 359, Hachioji, Tokyo 192-0395, Japan

*Auris* is Latin for ear
Cryptococcus neoformans
Rhodotorula glutinis
Candida rugosa
Candida krusei
Candida lusitaniae
Candida auris
Candida haemulonii
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

C. glabrata
C. albicans
Rapid emergence since 2009
Not ears anymore, mostly blood

CDC formed an international collaboration
Major Antifungal Resistance Seen

1. >90% Azoles
2. 7% Echinocandins
3. 35% Polyenes

- >40% multidrug resistant
- A few resistant to all three classes

By Comparison: *Candida glabrata*

1. 11% Azoles
2. Up to 12% Echinocandins
3. <1% Polyenes
Preliminary *C. auris* epidemiology

- Similar risk factors as for other *Candida* spp.
- Some patients on antifungal treatment when *C. auris* isolated
- Mortality ~60%
- Clustering in some hospitals

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
Not just improved detection

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

- SENTRY and ARTEMIS programs (private collections from 4 continents)
  - >30,000 *Candida* isolates from 1996-2015
  - 4 *C. auris* isolates before 2009

- Earliest known isolate of *C. auris* has been recorded in S. Korea in 1996

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How did *C. auris* emerge?

- Global spread of single epidemic strain? (e.g., through food or medical product)

- Many introductions from the environment or other sources?

- Whole-genome sequencing (WGS) provides remarkable but puzzling results
WGS of 47 isolates from 4 world regions

- **Very different across regions**
  (>40K-400K SNPs)

- **Nearly identical within regions**
  (<70 SNPs)

But this really got our attention...

- *C. auris* outbreak in a UK hospital
- 9 *C. auris* bloodstream infections
- >40 people colonized on skin
- Cultured from many hospital surfaces
- Clear patient-to-patient transmission
Hard to control
- Contact precautions
- Screening for colonization
- Chlorhexidine bathing
- Cleaning room with bleach 3x/day
- Terminal cleaning with higher concentration bleach
- Eventually closed unit

Intensive care unit closed after new deadly superbug emerges in the UK

CDC Clinical alert to healthcare facilities – June 2016

Global Emergence of Invasive Infections Caused by the Multidrug-Resistant Yeast *Candida auris*

**Summary:** The Centers for Disease Control and Prevention (CDC) has received reports from international healthcare facilities that *Candida auris*, an emerging multidrug-resistant (MDR) yeast, is causing invasive healthcare-associated infections with high mortality. Some strains of *C. auris* have elevated minimum inhibitory concentrations (MICs) to the three major classes of antifungals, severely limiting treatment options. *C. auris* requires specialized methods for identification and could be misidentified as another yeast when relying on traditional biochemical methods. CDC is aware of one isolate of *C. auris* that was detected in the United States in 2013 as part of ongoing surveillance. Evidence outside the United States suggests that *C. auris* has high potential to cause outbreaks in healthcare facilities. Given the occurrence of *C. auris* in nine countries on four continents since 2009, CDC is alerting U.S. healthcare facilities to be on the lookout for *C. auris* isolates.
Was *C. auris* in the US?

- Definitely, unfortunately, YES

CDC identifies first US cases of drug-resistant fungal infection

Noteworthy press coverage

*A Deadly, Drug-Resistant Yeast Infection Is Spreading Around the World, It's Fine Guys*

Me? I'm calm. I'm so calm!
**C. auris** cases reported by state — United States, 2013–August 2016

**C. auris** cases reported by state — United States, 2013–December 2016
Epidemiologic Characteristics of US Cases

- Median age: 70 (1 neonate)
- Multiple underlying medical conditions and indwelling devices
  - Tracheostomy tube, central venous catheter, gastrostomy tube
- Extensive healthcare exposure
- ~30% 30-day mortality

Evidence for Transmission of C. auris

- Clusters at both hospitals and long-term care facilities
- Several patients received care at same hospital
- Several patients at same long-term acute care hospital
Patients are colonized with *C. auris*

- Skin >> gut
- Long-term colonization (months → indefinitely)
- Colonization poses risk for:
  - Invasive infection
  - Transmission to others

Close contacts of patients become colonized

N=8

N=9

N=12

N=12

(central line tip) (blood)
Patients on the same ward often colonized

<table>
<thead>
<tr>
<th>LTACH, N=65</th>
<th>vSNF, N=66</th>
<th>Acute care hospital, N=26</th>
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C. auris can Persist in the Hospital Environment
Survival on Surfaces

- In lab, persists for >4 weeks on plastic surfaces
- Quaternary ammonium compounds inadequate for disinfection

Isolates from the same facility are very closely related by WGS

Venezuela isolates

- B11245 Venezuela
- B11247 Venezuela
- B11244 Venezuela
- B11892
- B11894
- B11893
- B11895
- B11897
- B11896
- B11778 Colombia Barranquilla
- B11846 Colombia Cartagena
- B11851 Colombia Bogota

Colombia isolates

- B11842 USA IL001
- 300014782 IL LTACH2
- B12046 IL LTACH1
- B11889 IL environmental
- B11891 IL environmental
- B11843 USA IL002
- 3015360055 USA IL001

<5 SNPs
Transmission Through Organ Transplantation

- *C. auris* cultured from lungs shortly after transplant in Massachusetts
- No clear evidence of invasive *Candida* infection
- Donor lungs found to have had *C. auris* pre-transplant
- Donor from Illinois
- Isolate nearly identical to other Illinois isolates
U.S. Cases with Recent Hospitalizations in Other Countries

- India
- Pakistan
- South Africa
- Venezuela
Multiple introductions of *C. auris* followed by local transmission

A paradigm shift for *Candida* infections

- Antifungal resistance is the norm
- Thrives on skin
- Contaminates patient rooms
- CAN SPREAD IN HEALTHCARE SETTINGS
Controlling the spread of *C. auris*

CDC issued guidance on management of *C. auris*

Recommendations for Infection Control for *Candida auris*:

- Placing the patient with *C. auris* in a single-patient room and using Standard and Contact Precautions.
- Emphasizing adherence to hand hygiene.
- Cleaning and disinfecting the patient care environment (daily and terminal cleaning) with recommended products.
- Screening contacts of the patients to identify *C. auris* colonization. Because patients colonized with *C. auris* can be a source of *C. auris* transmission, these patients should be managed using the same infection control measures as for patients with *C. auris* infection.
Challenges with identification

*C. auris* can be **misidentified** as:
- *Candida haemulonii*
- *Candida famata*
- *Candida sake*
- *Candida catenulate*
- *Candida guilliermondii*
- *Candida lusitaniae*

- *Rhodotorula glutinis,*
- *Candida* spp. after a validated method of *Candida* identification attempted.

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Challenges with identification

- 40% of clinical cases in the U.S. have been from non-bloodstream isolates (e.g., urine, bile, wounds)

- Species from non-sterile isolates often not identified
Challenges with identifying colonized individuals

- Skin mycobiome is complex
- Culture based methods are slow
- Lots of patients need to be screened

Treatment

- Echinocandins are first line
- Resistance can be problematic
  - Some isolates resistant to echinocandins
  - At least one case with documented development of echinocandin resistance on treatment
- Monitor patients closely
Infection control is key for stopping transmission of *C. auris*

Comprehensive regional approach is also needed

- Alerts/updates/education for laboratories and clinicians
- Surveillance and reporting
- Notifying facilities when transfer of patients occurs
- Admission screening
- Point prevalence surveys to identify colonized individuals at high-risk facilities
- Infection control assessments
- Integration into other HAI prevention activities
Map of US \textit{C. auris} cases - September 2017

\textit{C. auris} cases reported by state — United States, 2013–September 2017
CDC issued clinical update – September 2017

- Updates June 2016
- Latest findings
- Recommendations
  - Determine species for all *Candida* isolates from blood and sterile sites
  - Determine species for non-invasive site *Candida* isolates in certain situations
  - Screen close contacts
  - Monitor for treatment failure
  - Clean with EPA-registered product against *C. difficile*

CDC is assisting State and Local Health Departments

- Candida auris email box: Candidaauris@cdc.gov
- Candida auris website
- Resources (fact sheets, guidance)
- Identification of suspect isolates
- PPS swabs
- Environmental cultures
- Webinars to nearly 1500 participants
ARLN Labs – *Candida* part of CORE

- **WEST**
  - Washington State Public Health Laboratories
    - Core Testing
    - *N. gonorrhoeae*

- **MIDWEST**
  - Wisconsin State Laboratory of Hygiene
    - Core Testing
    - *S. pneumoniae*

- **CENTRAL**
  - Minnesota Department of Health Public Health Laboratory
    - Core Testing
    - *C. difficile*
    - *S. pneumoniae*

- **MOUNTAIN**
  - Texas Department of State Health Services Laboratory
    - Core Testing
    - *N. gonorrhoeae*

- **NORTH EAST**
  - Wadsworth Center Bacteriology Laboratory
    - Core Testing

- **MID-ATLANTIC**
  - Maryland Public Health Laboratory
    - Core Testing
    - *N. gonorrhoeae*

- **SOUTHEAST**
  - Tennessee State Public Health Laboratory
    - Core Testing
    - *N. gonorrhoeae*

ARLN Success Story

- Florida DOH issued *C. auris* alert
- Lab recognized suspect isolate
- Isolate sent to TN ARLN
- Case identified
- No further transmission found
Global *C. auris* situation

- Now common in some international hospitals
  - Up to 40% of *Candidas* in 1 Indian and 1 Kenyan hospital
  - 10% of *Candidas* in private South African hospitals
- UK continues to have introductions; seem to have controlled initial spread
- No further isolates in Japan; relatively few in South Korea
- Major unknowns in most of Africa and parts of Latin America

*C. auris* cases reported by state — United States, 2013–December 2016

![Bar chart showing *C. auris* cases reported by state in the United States from 2013 to December 2016.](chart)
The US *C. auris* Situation Report

- **Likely several introductions** into United States

- **Has gained a foothold** in some healthcare facilities and regions

- Still in a **window of opportunity** to contain this superbug
For more information, contact CDC
1-800-CDC-INFO (232-4636)

Contact us at:
candidaauris@cdc.gov

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.