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## PEARLS OF LABORATORY MEDICINE

*Candida auris*

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# Candidiasis

- *Candida* is a genus of yeast
- *Candida* is part of the normal human microbiota
  - Mouth, throat, gastrointestinal tract, and vagina
  - Usually does not cause infections in immunocompetent individuals
- Candidiasis in the:
  - Mouth or throat → Thrush or oropharyngeal candidiasis
  - Vagina → Yeast infection
  - Bloodstream and internal organs → Invasive candidiasis (Overlapping syndromes of deep-seated candidiasis and candidemia)



# Invasive candidiasis

- Approximately 25,000 cases each year nationwide
- Up to 95% of all Candidemia are caused by 5 species
  - *C. albicans*, *C. glabrata*, *C. parapsilosis*, *C. tropicalis*, and *C. krusei*

Pfaller MA, Diekema DJ. Epidemiology of invasive candidiasis: a persistent public health problem. *Clin Microbiol Rev* 2007; 20:133-163.



# Mortality of Invasive candidiasis

- CDC's surveillance data indicates that in-hospital all-cause (crude) mortality among people with invasive candidiasis is approximately 25%
- *C. auris* has been an increasing cause of invasive *Candida* infections globally

Pfaller MA, Diekema DJ. Epidemiology of invasive candidiasis: a persistent public health problem. *Clin Microbiol Rev* 2007; 20:133-163.



# Global Emergence of *C. auris*

- First reported in 2009 from the ear discharge of a patient in Japan
- First blood stream infection in 2011 from South Korea
- (As of May 2020) Isolated from several body sites in multiple countries on five continents

Forsberg K, Woodworth K, Walters M, Berkow EL, et al. *Candida auris*: The recent emergence of a multidrug-resistant fungal pathogen. *Medical Mycology* 2019; 57:1–12.

Centers for Disease Control and Prevention. *Candida auris*. <https://www.cdc.gov/fungal/candida-auris/index.html>12. Accessed July 30, 2020.



## *C. auris* Cases in U.S.

- Sudden increase starting in 2015
- Mostly in large metropolitan areas
- (As of May 2020) Total of 1,167 cases in 20 States

Forsberg K, Woodworth K, Walters M, Berkow EL, et al. *Candida auris*: The recent emergence of a multidrug-resistant fungal pathogen. *Medical Mycology* 2019; 57:1–12.

Centers for Disease Control and Prevention. *Candida auris*. <https://www.cdc.gov/fungal/candida-auris/index.html>12. Accessed July 30, 2020.



# Clinical Symptoms

- Similar to other *Candida* species
  - Types of infections include blood, central venous catheter tip, central nervous system, upper and lower respiratory tracts, urogenital system, abdominal, skin, wounds, soft tissue, and bone
- Infects critically ill patients
- Mortality estimated to be 30–60 %

Jeffery-Smith A, Taori SK, Schelenz S, Jeffery K, et al. *Candida auris*: A review of the literature. *Clin Microbiol Rev* 2017; 31:e00029-17.

# Colonization and Transmission

- *Candida* species are generally not considered transmissible in healthcare settings
- *C. auris* appears distinct among yeast in that it readily spreads in healthcare settings

Forsberg K, Woodworth K, Walters M, Berkow EL, et al. *Candida auris*: The recent emergence of a multidrug-resistant fungal pathogen. *Medical Mycology* 2019; 57:1–12.





# Colonization and Transmission

- Patients and healthcare workers can be colonized on their skin
  - Particularly the axilla and groin and can persist for many months
- Transmission between patients via healthcare contacts
  - In the U.S., 12% of close healthcare contacts of *C. auris* patients were colonized

Forsberg K, Woodworth K, Walters M, Berkow EL, et al. *Candida auris*: The recent emergence of a multidrug-resistant fungal pathogen. *Medical Mycology* 2019; 57:1–12.



# Colonization and Transmission

- Environmental spread
  - People infected or colonized with *C. auris* shed the organism
  - Persists on various surfaces for at least 7 days
  - Requires thorough decontamination of patient areas

Forsberg K, Woodworth K, Walters M, Berkow EL, et al. *Candida auris*: The recent emergence of a multidrug-resistant fungal pathogen. *Medical Mycology* 2019; 57:1–12.



# Culture and morphology

- Sabouraud dextrose agar – Light colored colonies
- Chromogenic agar Candida medium – Pink to beige colonies



Diagnostic method (manufacturer)	Misidentification
Biochemical	
API 20CAUX	<i>Rhodotorula glutinis</i> , <i>C. sake</i> , Unidentified
API Candida	<i>C. famata</i>
Phoenix (BD Diagnostics)	<i>C. haemulonii</i> , <i>C. catenulate</i>
Vitek	<i>C. haemulonii</i> , <i>C. lusitaniae</i> , <i>C. famata</i>
MicroScan (Beckman Coulter)	<i>C. famata</i> , <i>C. lusitaniae</i> , <i>C. guilliermondii</i> , <i>C. parapsilosis</i> , <i>C. albicans</i> , <i>C. tropicalis</i>
MALDI-TOF MS	
Vitek MS (bioMerieux)	<i>C. albicans</i> , <i>C. haemulonii</i> , Not identified
MALDI Biotyper (Bruker Daltonics)	<i>Neisseria meningitides</i> serogroup A, <i>Pseudomonas rhizosphaerae</i>

Jeffery-Smith A, Taori SK, Schelenz S, Jeffery K, et al. *Candida auris*: A review of the literature. *Clin Microbiol Rev* 2017; 31:e00029-17.



# Antibiotic Resistance Threats in U.S

- Urgent Threats
  - Carbapenem-resistant *Acinetobacter*
  - ***Candida auris***
  - *Clostridioides difficile*
  - Carbapenem-resistant Enterobacteriaceae
  - Drug-resistant *Neisseria gonorrhoeae*

Centers for Disease Control and Prevention. Antibiotic Resistance Threats in the United States, 2019.  
<https://www.cdc.gov/drugresistance/biggest-threats.html>. Accessed July 30, 2020.



# C. auris Antifungal Resistance

Antifungals	India, Pakistan, South Africa, and Venezuela (54 isolates)	U.S. (reported to CDC)
Fluconazole	93 %	90 %
Amphotericin B	35 %	30 %
Echinocandins	7 %	5 %

Lockhart SR, Etienne KA, Vallabhaneni S, et al. Simultaneous Emergence of Multidrug-Resistant *Candida auris* on 3 Continents Confirmed by Whole-Genome Sequencing and Epidemiological Analyses. *Clin Infect Dis* 2017; 64:134-140. Centers for Disease Control and Prevention. *Candida auris*. <https://www.cdc.gov/fungal/candida-auris/index.html>12. Accessed July 30, 2020.



# *C. auris* Proposed Resistance Mechanism

- Twelve *Erg11* mutations
- Efflux pump activity contributes to azole resistance
- *FKS* mutations
- Amphotericin B resistance?

Hata DJ, Humphries R, Lockhart SR., and for the College of American Pathologists Microbiology Committee. *Candida auris*: An emerging yeast pathogen posing distinct challenges for laboratory diagnostics, treatment, and infection prevention. *Archives of Pathology & Laboratory Medicine* 2020; 144:107-114.



# *C. auris* Antifungal Susceptibility

Drug Class	Drugs	Tentative MIC Breakpoints (µg/mL)
Triazole	Fluconazole	≥32
	Voriconazole and other second generation triazoles	N/A
Polyene	Amphotericin B	≥ 2
Echinocandin	Anidulafungin	≥ 4
	Caspofungin	≥ 2
	Micafungin	≥ 4

Centers for Disease Control and Prevention. *Candida auris*. <https://www.cdc.gov/fungal/candida-auris/index.html>12. Accessed July 30, 2020.





# Treatment Recommendations

- Echinocandin first line treatment
- Other options are still in development
  - Antifungal combinations
  - New drugs like Ibrexafungerp (SCY-078)

Bidaud AL, Botterel F, Chowdhary A, Dannaoui E. *In vitro* antifungal combination of flucytosine with amphotericin B, voriconazole, or micafungin against *Candida auris* shows no antagonism. *Antimicrob Agents Chemother* 2019; 63(12):e01393-19.

Scoreaux B, Angulo D, Borroto-Esoda K, Ghannoum M, et al. SCY-078 is fungicidal against *Candida* species in time-kill studies. *Antimicrob Agents Chemother* 2017; 61:e01961-16.



# In Summary...

- Sudden emergence globally
- Colonization and transmission in healthcare settings
- Mis-identification from many systems
- Potential to gain pan resistance to antifungals



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9. Scorneaux B, Angulo D, Borroto-Esoda K, Ghannoum M, et al. SCY-078 is fungicidal against *Candida* species in time-kill studies. *Antimicrob Agents Chemother* 2017; 61:e01961-16.

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