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Candida auris: Diagnosis and management

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Candida auris: diagnosis and management

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Outlines

- An emerging yeast
- Painful stories
- Diagnosis
- Management
- Conclusion

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editorial

Stop neglecting fungi

Fungal pathogens are virtually ignored by the press, the public and funding bodies, despite posing a significant threat to public health, food biosecurity and biodiversity.

https://www.nature.com/articles/nmicrobiol2017120

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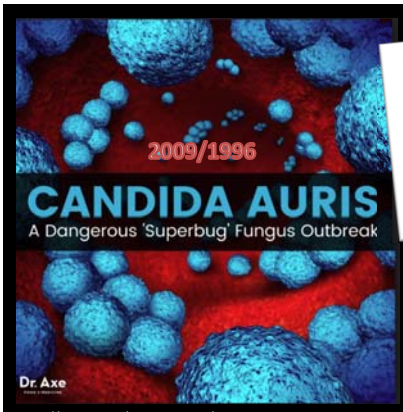
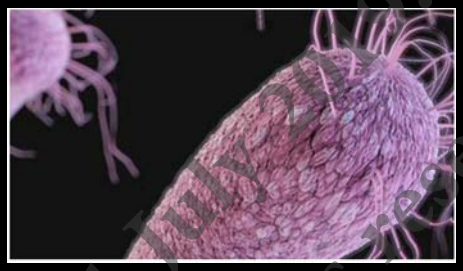


https://draxe.com/candida-auris/

July 9, 2016

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



April 12, 2019

The New York Times

Superbug *C. auris* identified in 617 people, CDC says

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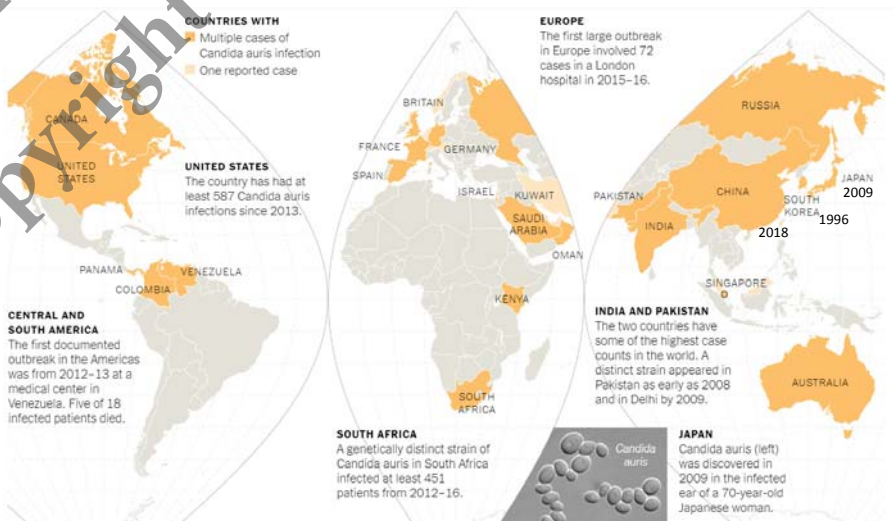
Countries from which *C. auris* cases have been reported



https://www.nytimes.com/2019/04/06/health/drug-resistant-candida-auris.html

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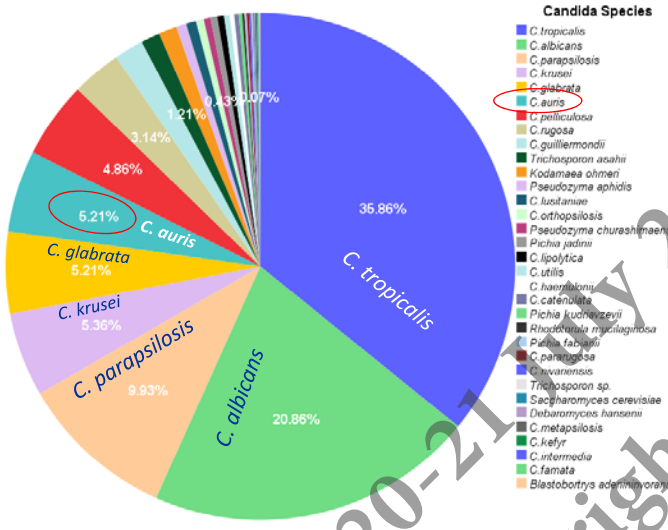
Candidemia, Indian ICUs

The first largest cases series reported

5.3% (74/1400 candidemia cases), Ranked 5th



Chakrabarti *et al.* Intensive Care Med 2015; 41: 285

(President, International Society for Human and Animal Mycology)

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Unique features from largest series in Indian ICUs

- Significant risk factors in Indian ICUs
  1. prior antifungal exposure (P<0.001)
  2. underlying respiratory illness (P<0.002)
  3. vascular surgery (P<0.048)
  4. multiple interventions (P<0.007)
  5. public-sector hospital (P<0.00

Patients with sepsis, undergoing invasive management for longer periods & exposed to antifungal agents

Rudramurthy S, *et al.* J Antimicrob Chemother 2017; 72: 1794

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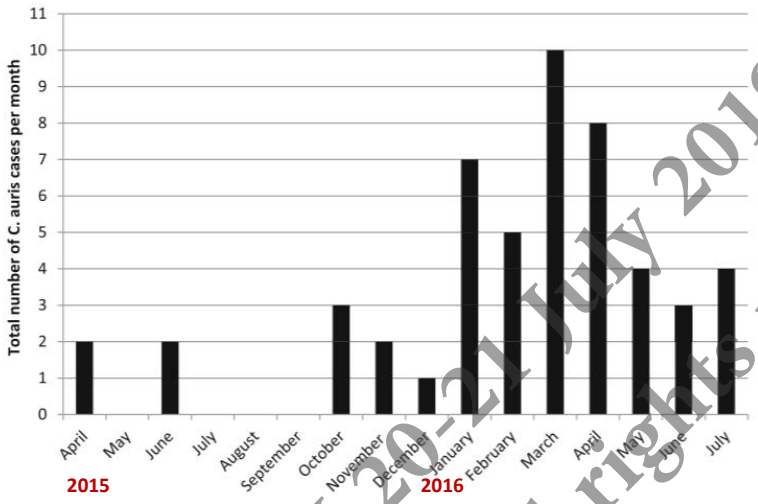
First hospital outbreak *C. auris* in a European hospital



Antimicrob Resist Infect Control 2016;5:35.

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By June 2016, the hospital had seen 72 cases of C. *auris*, and decided to shut down its intensive care unit for 11 days to address the contamination

Royal Brompton Hospital near London, UK - a National Health specialist center for cardio-thoracic surgery with 296 beds that draws wealthy patients from the Middle East and around Europe.

https://www.nytimes.com/2019/04/06/health/drug-resistant-candida-auris.html

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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A *Candida auris* Outbreak and Its Control in an Intensive Care Setting

- Oxford University Hospitals, UK; Feb 2015 and Aug 2017
- 70 patients with *C. auris* colonization/infection (7 patients, 10%)
- 94% admitted to the neuroICU before diagnosis
- Predictors of *C. auris* colonization or infection (multivariate analysis)
  - The use of reusable skin-surface axillary temperature probes (odds ratio, 6.80 , P < 0.001)
  - Systemic fluconazole exposure (odds ratio, 10.34, P = 0.01)
- No attributable mortality

N Engl J Med 2018;379:1322

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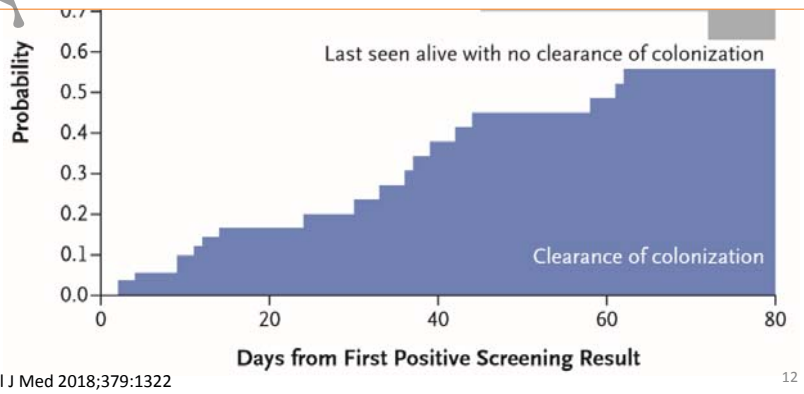
Duration of C. *auris* carriage

The median duration of carriage among patients remaining alive was
- 61 days when two consecutive negative screening results were used to define clearance of colonization
- 82 days when three consecutive negative results were used



N Engl J Med 2018;379:1322

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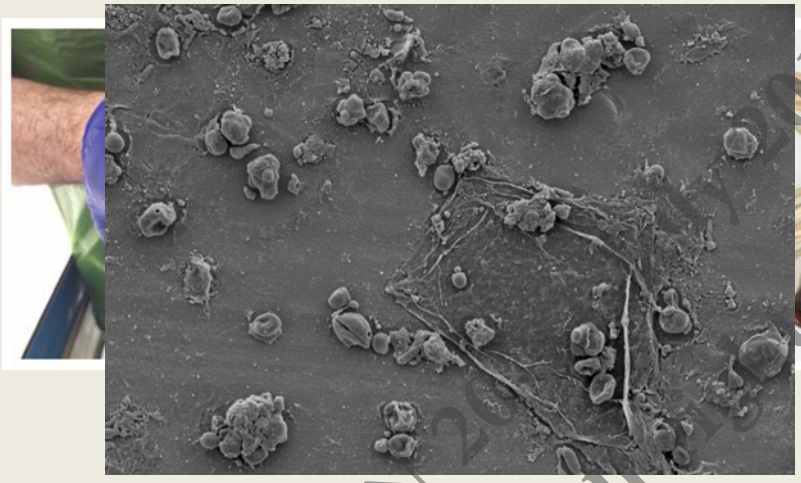
Skin surface temperature probes (axillary), neurolCU, Oxford

Used routinely in ventilated patients for continuous temperature monitoring



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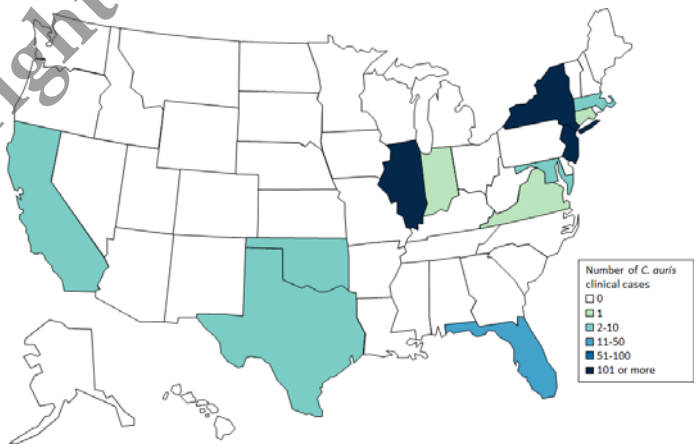
U.S. Map: Clinical cases of *Candida auris* reported by U.S. states, as of May 31, 2019, N=686



An additional 1342 patients have been found to be colonized with *C. auris* by targeted screening in ten states with clinical cases.

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

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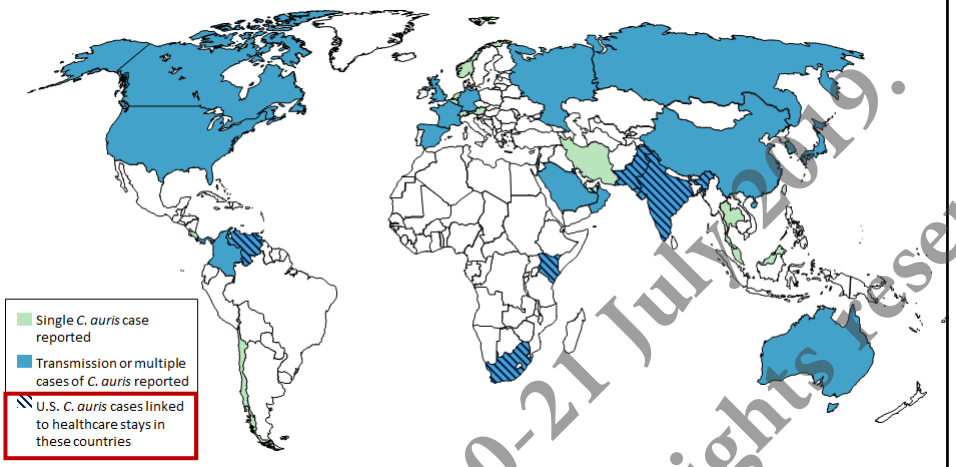
Countries from which *Candida auris* cases have been reported, as of May 31, 2019



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

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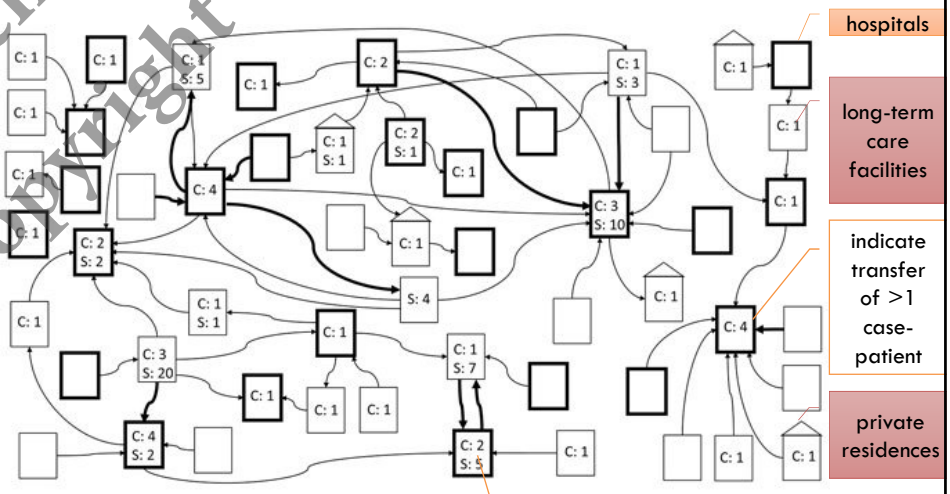
Epidemiologic links between healthcare facilities affected by *C. auris*, New York, USA, 2013–2017



Emerg Infect Dis 2018;24:1816
572 cases

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Environmental contamination with C. *auris* in healthcare facilities, New York, USA

Category, object or surface	No. samples negative by culture & PCR/No. samples evaluated (%)
Near-patient surfaces and objects in rooms	145/178 (82)
Other surfaces and objects in rooms	163/187 (87)
Equipment in room	30/35 (86)
Equipment outside of room	243/260 (94)

Emerg Infect Dis 2018;24:1816

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Everything was positive

- Colonization at axilla, groins, etc.
- Environmental Contamination
- Not limited in the acute-care hospitals
- Persistent carriage

N Engl J Med 2018;379:1322; Emerg Infect Dis 2018;24:1816

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Invisible and Unexpected

Invisible	unaware
What the mind does not know, the eye does not see	Misidentification

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Species-level identification

- All yeast isolates obtained from a normally sterile site (e.g., bloodstream, cerebrospinal fluid) be identified to the species level so that appropriate initial treatment can be administered based on the typical, species-specific susceptibility patterns.
- When *Candida* is isolated from non-sterile sites
  - When clinically indicated in the care of a patient.
  - Close contact of those with C. *auris* colonization/infection
  - Patients from healthcare settings or countries with known outbreaks

Modified from https://www.cdc.gov/fungal/candida-auris/c-auris-surveillance.html

Mixed culture on CHROMagar Candida

https://www.cdc.gov/fungal/candida-auris/recommendations.html

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Candida auris on CHROMagar Candida, displaying multiple color morphs

https://www.cdc.gov/fungal/candida-auris/recommendations.html

C. auris is a budding yeast, which almost never forms short pseudohyphae and does not form germ tubes.

Unlike most other *Candida*species, it grows well at 40–42º C on CHROMagar.

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Common misidentifications based on the identification method used

Identification Method	Organism C. auris can be misidentified as
Vitek 2 YST	*Candida haemulonii* *Candida duobushaemulonii*
API 20C	*Rhodotorula glutinis* (characteristic red color not present) *Candida sake*
BD Phoenix yeast identification system	*Candida haemulonii* *Candida catenulata*
MicroScan	*Candida famata* *Candida guilliermondii** *Candida lusitaniae** *Candida parapsilosis**
RapID Yeast Plus	*Candida parapsilosis**

**C. guilliermondii*, *C. lusitaniae*, and *C. parapsilosis* generally make pseudohyphae on cornmeal agar. If hyphae or pseudohyphae are not present on cornmeal agar, this should raise suspicion for *C. auris* as *C. auris* typically does not make hyphae or pseudohyphae. However, some *C. auris* isolates have formed hyphae or pseudohyphae. Therefore, it would be prudent to consider any *C. guilliermondii*, *C. lusitaniae*, and *C. parapsilosis* isolates identified on MicroScan or any *C. parapsilosis*isolates identified on RapID Yeast Plus as possible *C. auris* isolates and forward them for further identification.

https://www.cdc.gov/fungal/candida-auris/recommendations.html. Page last reviewed: June 13, 2019 23

How to identify C. *auris*

- Matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF)
  - the Bruker Biotyper brand MALDI-TOF using the updated Bruker FDA-approved MALDI Biotyper CA System library (Version Claim 4) or their "research use only" libraries (Versions 2014 [5627] and more recent)
  - the bioMérieux VITEK (MALDI-TOF) MS using the FDA-approved IVD v3.2 or their "research use only" libraries (with Saramis Ver 4.14 database and Saccharomycetaceae update).
- Molecular methods: sequencing the D1-D2 region of the 28s rDNA or the Internal Transcribed Region (ITS) of rDNA

https://www.cdc.gov/fungal/candida-auris/recommendations.html

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Antifungal Susceptibility Testing and Interpretation

- All *Candida auris* isolates should undergo antifungal susceptibility testing according to CLSI guidelines.
- Although C. *auris* is commonly multidrug resistant, levels of antifungal resistance can vary widely across isolates.
- There are currently no established C. *auris*-specific susceptibility breakpoints.
- In the United States, 90% of C. *auris* isolates have been resistant to fluconazole, about 30% have been resistant to amphotericin B, and less than 5% have been resistant to echinocandins. These proportions may include multiple isolates from the same individuals and may change as more isolates are tested.

https://www.cdc.gov/fungal/candida-auris/c-auris-antifungal.html

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Tentative MIC Breakpoints (µg/mL)

Antifungal	Breakpoints (µg/mL)	Comment
Fluconazole	≥32	Modal MIC to fluconazole among isolates tested at CDC was ≥256; isolates with MICs ≥32 were shown to have a resistance mutation in the *Erg11* gene
Voriconazole and other second generation triazoles	N/A	Consider using fluconazole susceptibility as a surrogate for second generation triazole susceptibility assessment. However, isolates that are resistant to fluconazole may respond to other triazoles occasionally. The decision to treat with another triazole will need to be made on case-by-case basis.
Amphotericin B	≥2	Recent PK/PD analysis of C. *auris* in a mouse model of infection indicates that under standard dosing, the breakpoint for amphotericin B should be 1 or 1.5, similar to what has been determined for other *Candida* species.
Anidulafungin	≥ 4	based on the modal distribution of echinocandin MICs of ~ 100 isolates from diverse geographic locations.
Caspofungin	≥ 2	
Micafungin	≥ 4	https://www.cdc.gov/fungal/candida-auris/c-auris-antifungal.html

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Call for Action

Infection prevention and control	Be award and increase in vigilance
Diagnostic and antimicrobial stewardship	Strengthen capability and capacity for medical mycology

Need for a One Health strategy

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Journal of the Formosan Medical Association (2018) 117, 462–470 2017 online published

Available online at www.sciencedirect.com
ScienceDirect
journal homepage: www.jfma-online.com

Review Article

Are we ready for the global emergence of multidrug-resistant *Candida auris* in Taiwan?

Po-Liang Lu [a,b,c], Wei-Lun Liu [d,e], Hsiu-Jung Lo [f,g], Fu-Der Wang [h,i], Wen-Chien Ko [j,k], Po-Ren Hsueh [l,m], Mao-Wang Ho [n], Chun-Eng Liu [o], Yen-Hsu Chen [a,b,c], Yee-Chun Chen [f,m,*], Yin-Ching Chuang [p], Shan-Chwen Chang [m]

[a] *Division of Infectious Diseases, Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan*
[b] *School of Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan*
[c] *Department of Biological Science and Technology, College of Biological Science and Technology,*

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Prevalence of *C. auris* among 5064 clinical isolates based on multicenter surveillance in Taiwan

Investigator(s)	Source of isolates	Specimens types	Year	Results
HJ Lo	TSARY National surveillance[b]	Randomly collected *Candida* clinical isolates (1999) or *Candida* isolates from sterile sites and non-sterile sites (2002, 2006, 2010, and 2014)	1999 2002 2006 2010 2014	0/660 0/945 0/1015 0/1130 0/1168
WL Liu, FD Wang, MW Ho, YH Chen, CE Liu	CMMC, VGH-TPE, CMUH, KMUH, CCH	Blood isolates, hospital wide, rare *Candida* species[c]	January 2011–June 2014	0/52[d]
YC Chen, PR Hsueh	NTUH	Blood isolates, hospital wide, rare *Candida* species[c]	2011–2016	0/57[d]
WL Liu	CMMC, Liouying campus	Blood isolates, hospital wide, rare *Candida* species[c]	2007–2014	0/21[d] [37]
MC Li WC Ko	NCKUH	Blood isolates, hospital wide, rare *Candida* species[c]	2011–2016	0/37

Abbreviation: TSARY, Taiwan Surveillance of Antimicrobial Resistance of Yeasts; CMMC: Chi Mei Medical Center; VGH-TPE: Taipei Veterans General Hospital; CMUH: China Medical University Hospital; KMUH: Kaohsiung Medical University Hospital; CCH: Changhua Christian Hospital; NTUH, National Taiwan University Hospital; NCKUH, National Cheng Kung University Hospital.

[a] Data from personal communication with the principal investigators at each hospital or research site. These data are generated based on DNA sequencing of the internal transcribed spacer regions of the nuclear rRNA gene operon and the D1/D2 domain of the large ribosomal subunit of 26S rDNA.

[b] Multicenter in different geographic location of Taiwan.[36]

[c] *Candida* species other than *C. albicans*, *C. tropicalis*, *C. parapsilosis*, *C. glabrata*, and *C. krusei*.

[d] One isolate per patient.

Lu P-L, et al., Are we ready for the global emergence of multidrug-resistant Candida auris in Taiwan?, Journal of the Formosan Medical Association (2017), https://doi.org/10.1016/j.jfma.2017.10.005

Recommendations for treatment of *Candida auris* infections

- Consultation with an infectious disease specialist
- Infection prevention and control measures: Even after treatment for invasive infections, patients generally remain colonized with C. *auris* for long periods, and perhaps indefinitely.
- Based on the limited data available to date, an echinocandin drug is recommended initial therapy for treatment of C. *auris* infections.

https://www.cdc.gov/fungal/candida-auris/c-auris-treatment.html

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Management of C. *auris* isolated from noninvasive, non-sterile body sites

- Treat infection, not colonization
- Prevention of invasive candidiasis:
  - Infection prevention and control: hand hygiene, bundle cares (BSI, UTI, VAP, SSI)
  - Risk assessment and modification
  - Antibiotic stewardship
- Prevention of spread and contamination

Modified from https://www.cdc.gov/fungal/candida-auris/c-auris-treatment.html 31

Infection Prevention and Control for *Candida auris*

- Emphasizing adherence to standard precaution for every patient: hand hygiene, environment cleaning, etc.
- Using standard and contact precaution for patient with C. *auris* colonization/infection
  - Single-patient room isolation
  - Cleaning and disinfecting patient care environment and reusable equipment (daily and terminal cleaning) with recommended products.
- Inter-facility communication about patient's C. *auris* status at transfer to another healthcare facility
- Screening contacts of newly identified case patients to identify C. *auris* colonization.
- Conduct surveillance for new cases to detect ongoing transmission.

https://www.cdc.gov/fungal/candida-auris/c-auris-infection-control.html. 32

C. *auris* - an emerging fungus that presents a serious global health threat

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

Invisible and unexpected

Think fungus

Call for action

1. Is often multidrug-resistant
2. Is difficult to identify
3. Has caused outbreaks in healthcare settings (delayed diagnosis, prolonged carriage, environment contamination)

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