Candida auris: MDR Fungus Among Us

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LDH HAI/AR Antimicrobial Stewardship Summit 6/17/2022

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Disclosure

I do not have any relevant financial relationships with any commercial interests

A commercial interest is any entity producing, marketing, re-selling, or distributing health care goods or services consumed by, or used on, patients.

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Objectives

- After participating in this session, attendees should be able to:
  - Describe the epidemiology of *Candida auris* as an emerging pathogen
  - List Infection Prevention and Control and public health measures used to control *Candida auris* outbreaks
  - Discuss antifungal resistance in *Candida auris* isolates and recommendations for empiric therapy

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Outline

- Introduction
  - Epidemiology
    - Worldwide
    - United States
  - Significance
    - Invasive infections
    - Risk factors
- Diagnosis
  - Clinical Laboratory
  - Reference Laboratories
- Antifungal Resistance
  - Resistance mechanisms
  - Antifungal Susceptibility Testing and Interpretation
- Treatment recommendations
  - Infection
  - Colonization
- Infection Prevention and Control
  - Communicability
    - Persists on patients
    - Persists in the environment
  - Contact Precautions
  - Environmental Disinfection
  - Public Health Partnership
    - Guidance
    - Surveillance
- Antimicrobial and Antifungal Stewardship

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INTRODUCTION

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Candida auris was first discovered in:

A. 1959
B. 1979
C. 2009
D. 2019

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Candida auris was first discovered in:

A. 1959
B. 1979
C. <u>2009</u>
D. 2019

Microbiol Immunol 2009; **53**: 41–44
doi:10.1111/j.1348-0421.2008.00083.x

ORIGINAL ARTICLE

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

ABSTRACT

A single strain of a novel ascomycetous yeast species belonging to the genus *Candida* was isolated from the external ear canal of an inpatient in a Japanese hospital. Analyses of the 26S rDNA D1/D2 domain, nuclear ribosomal DNA ITS region sequences, and chemotaxonomic studies indicated that this strain represents a new species with a close phylogenetic relationship to *Candida ruelliae* and *Candida haemulonii* in the Metschnikowiaceae clade. This strain grew well at 40 °C, but showed slow and weak growth at 42 °C. The taxonomic description of *Candida auris* sp. nov. is proposed (type strain JCM15448^T = CBS10913^T = DSM21092^T).

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Candida auris

- First discovered in 2009 – isolated from external ear canal of a patient in a Japanese Hospital
- *Auris* is the Latin word for ear
- Taxonomically placed as close relative to *Candida haemulonii* complex
- Lookback - earliest isolate dates to 1996 in South Korea; 2009 had nosocomial infections in S. Korea; rapid global spread of small # foci

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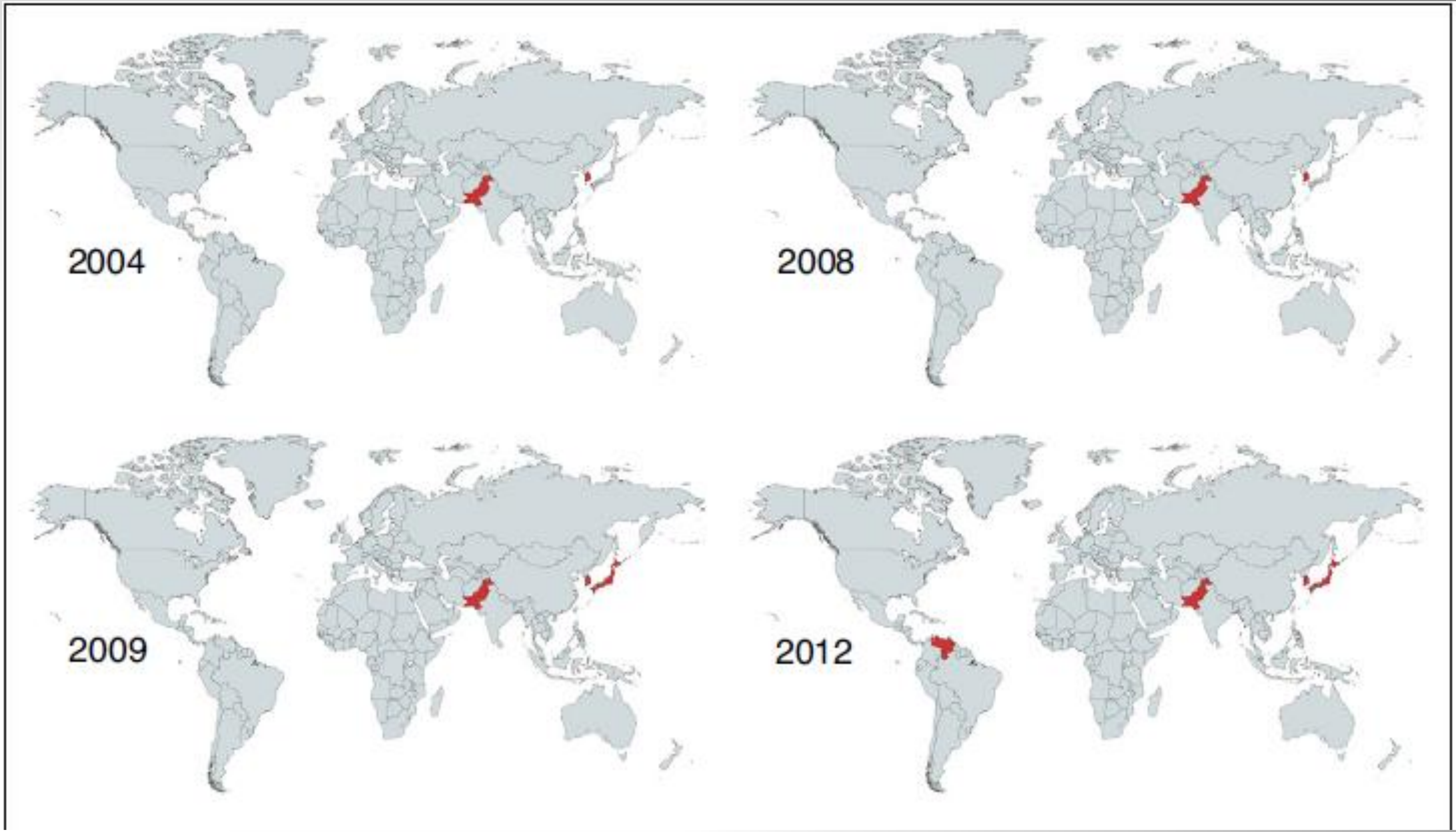
https://www.cdc.gov/fungal/candida-auris/candida-auris-qanda.html

Current Opinion in Microbiology 2019, 52:84–89



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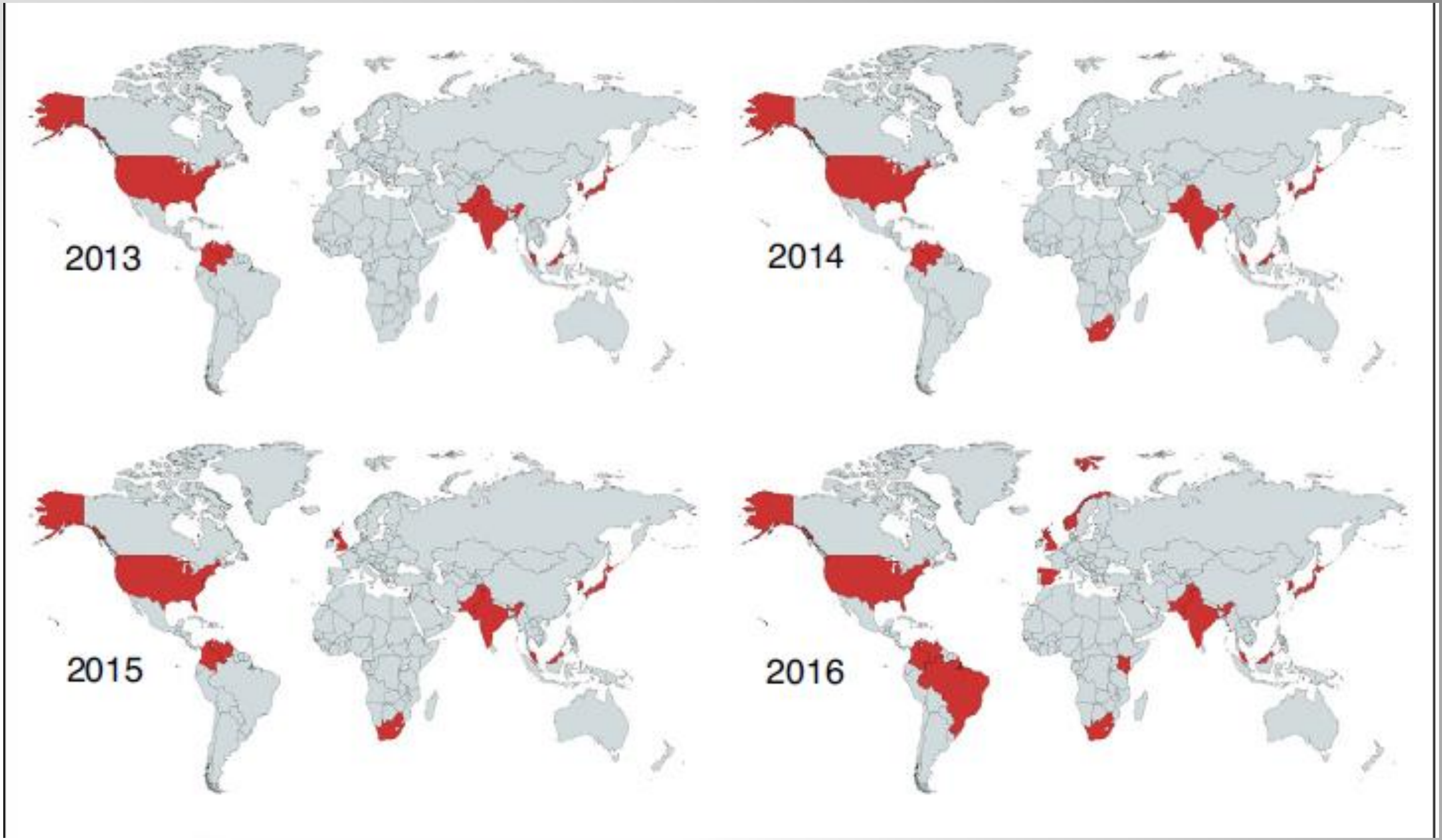
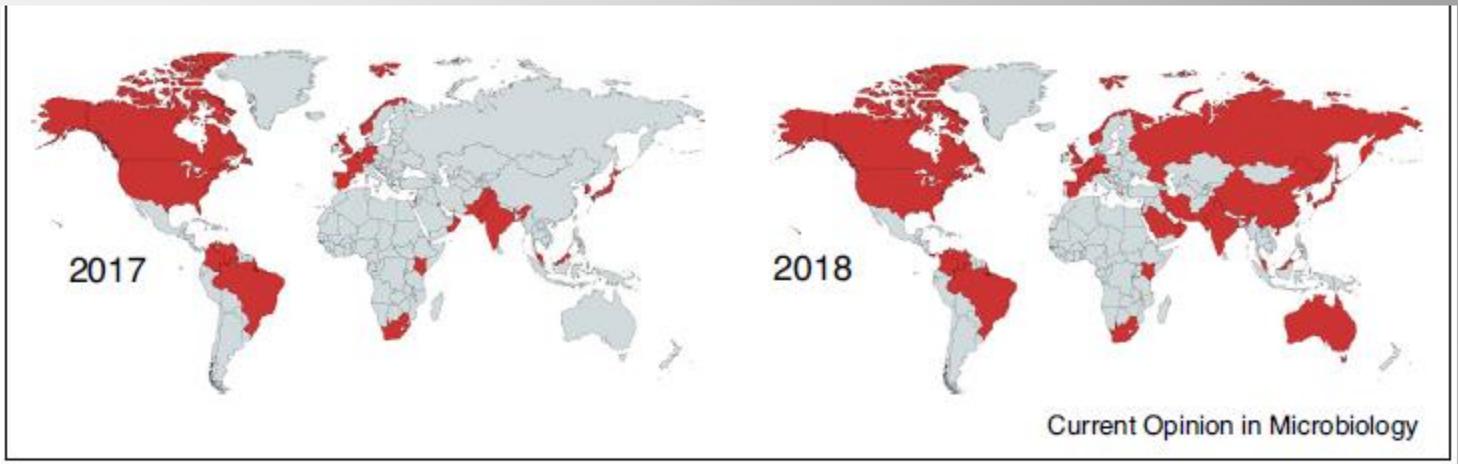
Current Opinion in Microbiology 2019, 52:84–89



Current Opinion in Microbiology 2019, 52:84–89



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Current Opinion in Microbiology 2019, 52:84–89

Countries from which *Candida auris* cases have been reported, as of February 15, 2021

This map is no longer being updated given how widespread *C. auris* has become.

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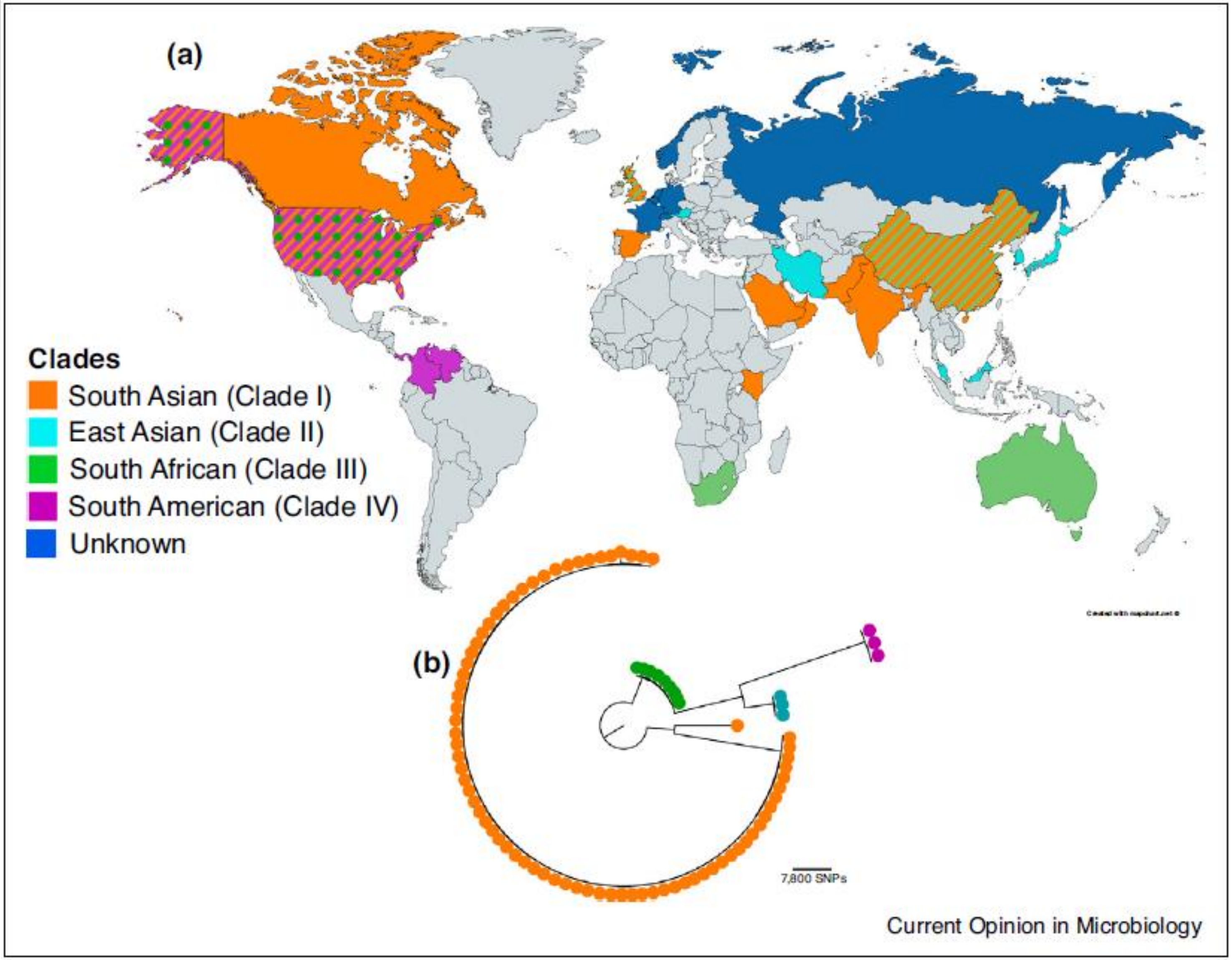
https://www.cdc.gov/fungal/candida-auris/tracking-c-auris.html



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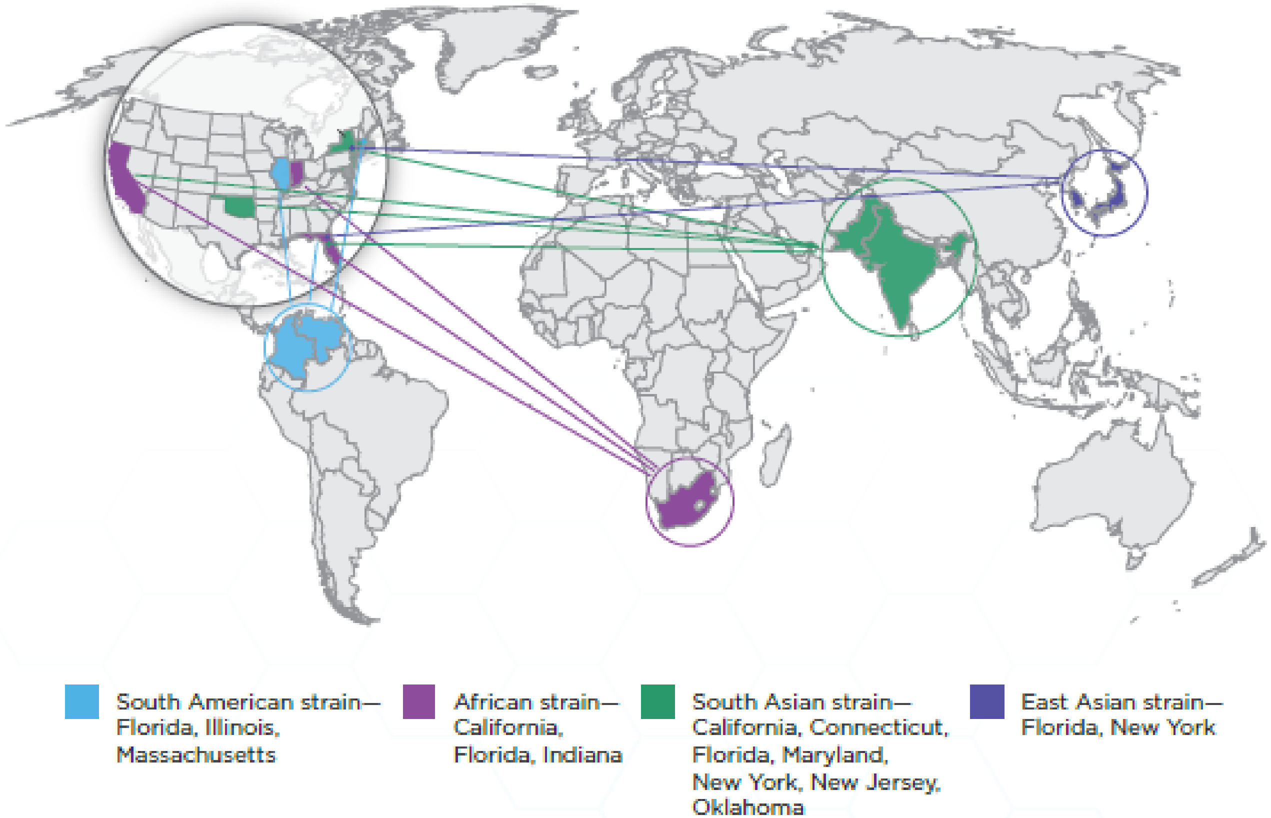
(a) Global distribution of *Candida auris* clades (as of 28th February 2019) and
(b) RAxML phylogeny showing the relationship amongst *C. auris* clades.

Current Opinion in Microbiology 2019, 52:84–89

A GLOBAL THREAT

Investigators still do not know why four different strains of *C. auris* emerged around the same time across the globe. All four strains have been found in the United States, likely introduced through international travel and subsequent spread in U.S. healthcare facilities.



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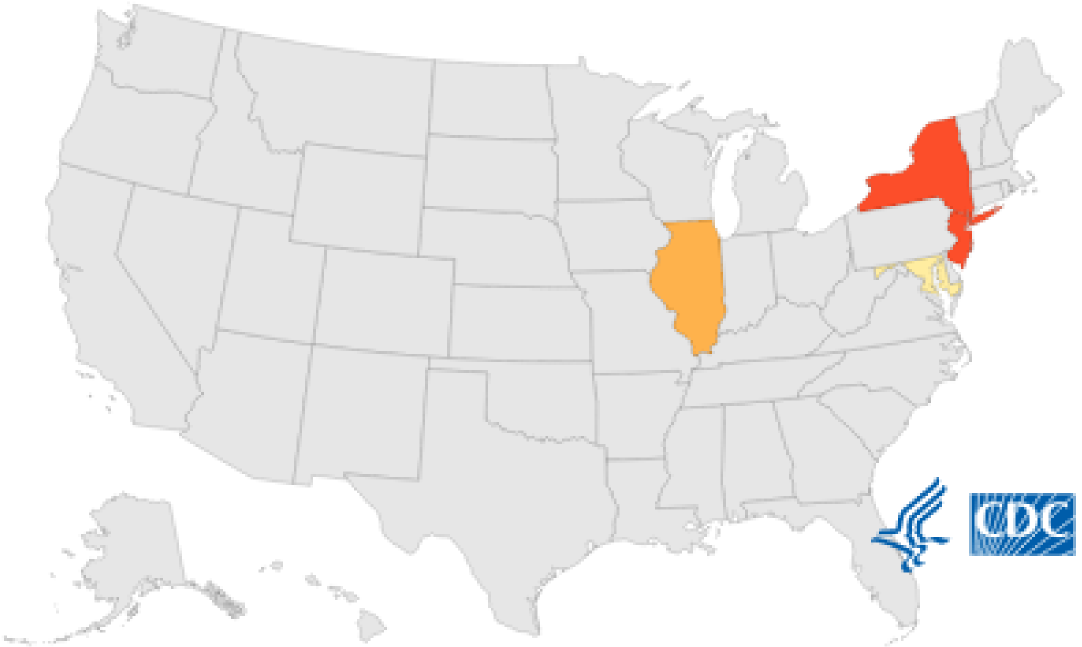
CDC. Antibiotic Resistance Threats in the United States, 2019. Atlanta, GA: U.S. Department of Health and Human Services, CDC; 2019. DOI: http://dx.doi.org/10.15620/cdc:82532

Reported clinical cases of *Candida auris*, 2013-2016



Location	Number of clinical cases
Illinois	6
Maryland	1
New Jersey	25
New York	31

Total 63

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

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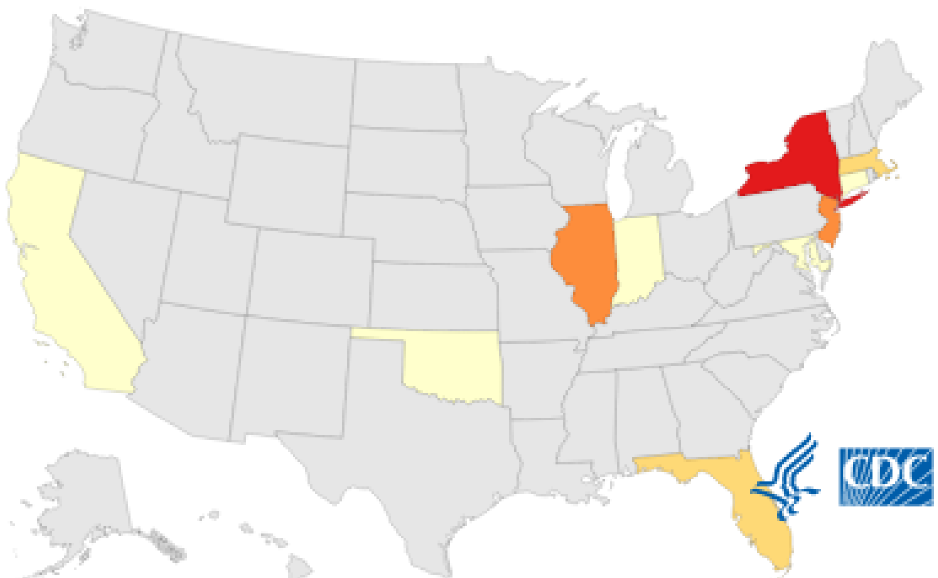
Reported clinical cases of *Candida auris*, 2017



Location	Number of clinical cases
California	1
Connecticut	1
Florida	2
Illinois	11
Indiana	1
Maryland	1
Massachusetts	7
New Jersey	46
New York	99
Oklahoma	1

Total 170

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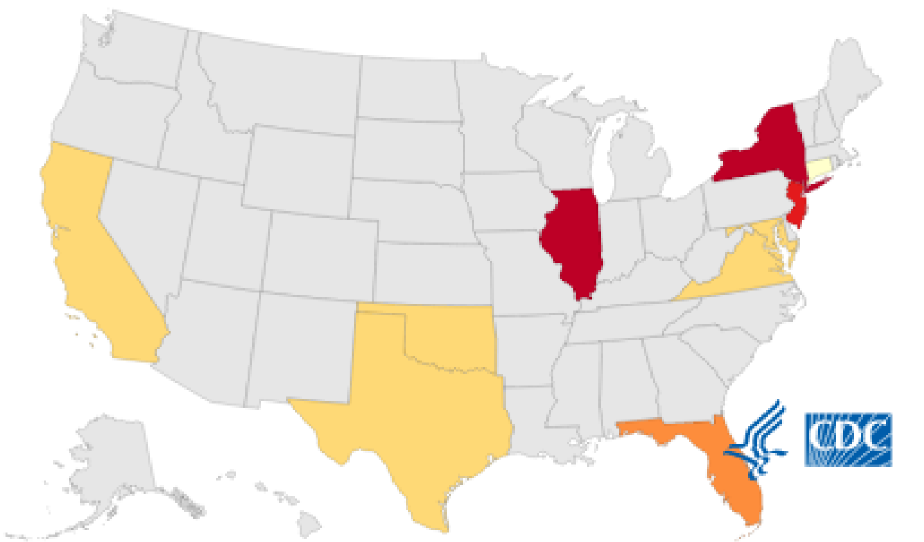
https://www.cdc.gov/fungal/candida-auris/tracking-c-auris.html

Reported clinical cases of *Candida auris*, 2018



Location	Number of Clinical Cases
California	1
Connecticut	0
Florida	3
Illinois	109
Maryland	1
New Jersey	54
New York	158
Oklahoma	1
Texas	1
Virginia	1

Total 329

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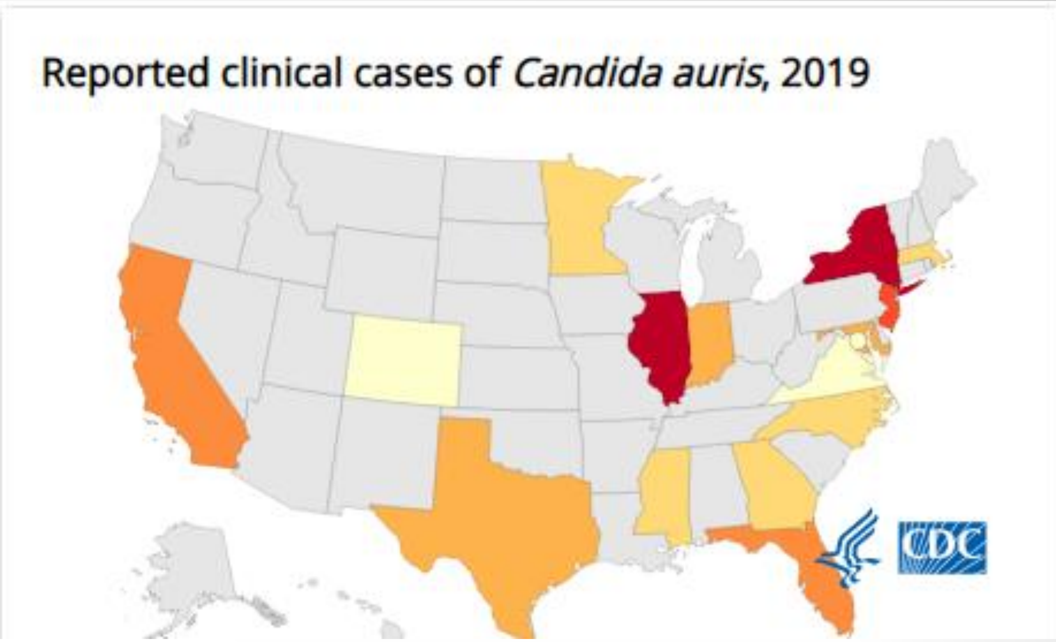
https://www.cdc.gov/fungal/candida-auris/tracking-c-auris.html



Location	Number of Clinical Cases
California	24
Colorado	0
District Of Columbia	0
Florida	26
Georgia	1
Illinois	172
Indiana	3
Maryland	6
Massachusetts	1
Minnesota	1
Mississippi	1
New Jersey	52
New York	178
North Carolina	1
Texas	5
Virginia	0

Total 471

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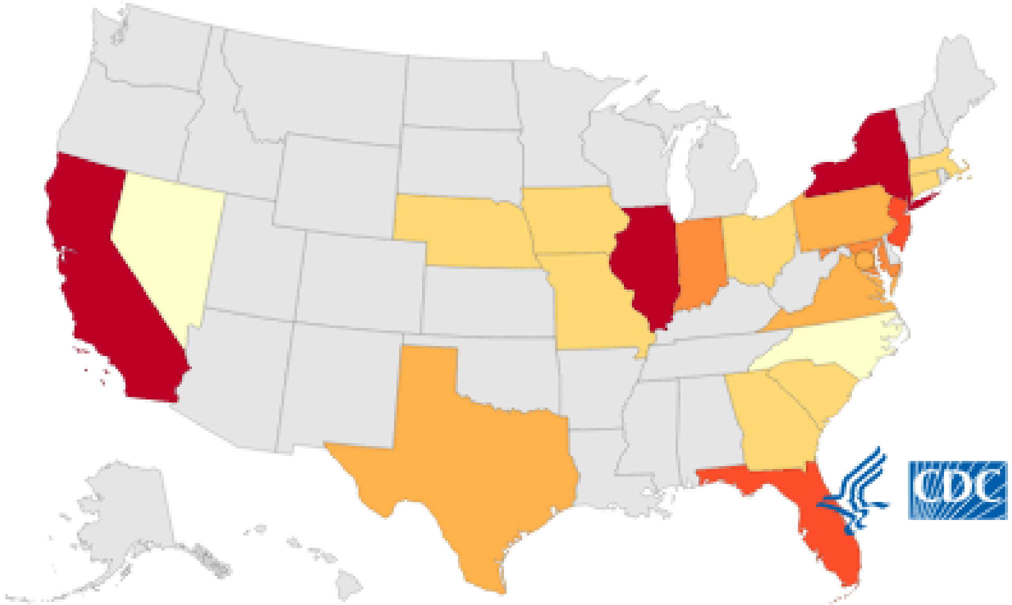
https://www.cdc.gov/fungal/candida-auris/tracking-c-auris.html

Reported clinical cases of *Candida auris*, 2020



Location	Number of Clinical Cases
California	117
Connecticut	1
District Of Columbia	4
Florida	84
Georgia	1
Illinois	181
Indiana	23
Iowa	1
Maryland	13
Massachusetts	1
Missouri	1
Nebraska	1
Nevada	0
New Jersey	59
New York	248
North Carolina	0
Ohio	1
Pennsylvania	4
South Carolina	1
Texas	3
Virginia	5

Total 749

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

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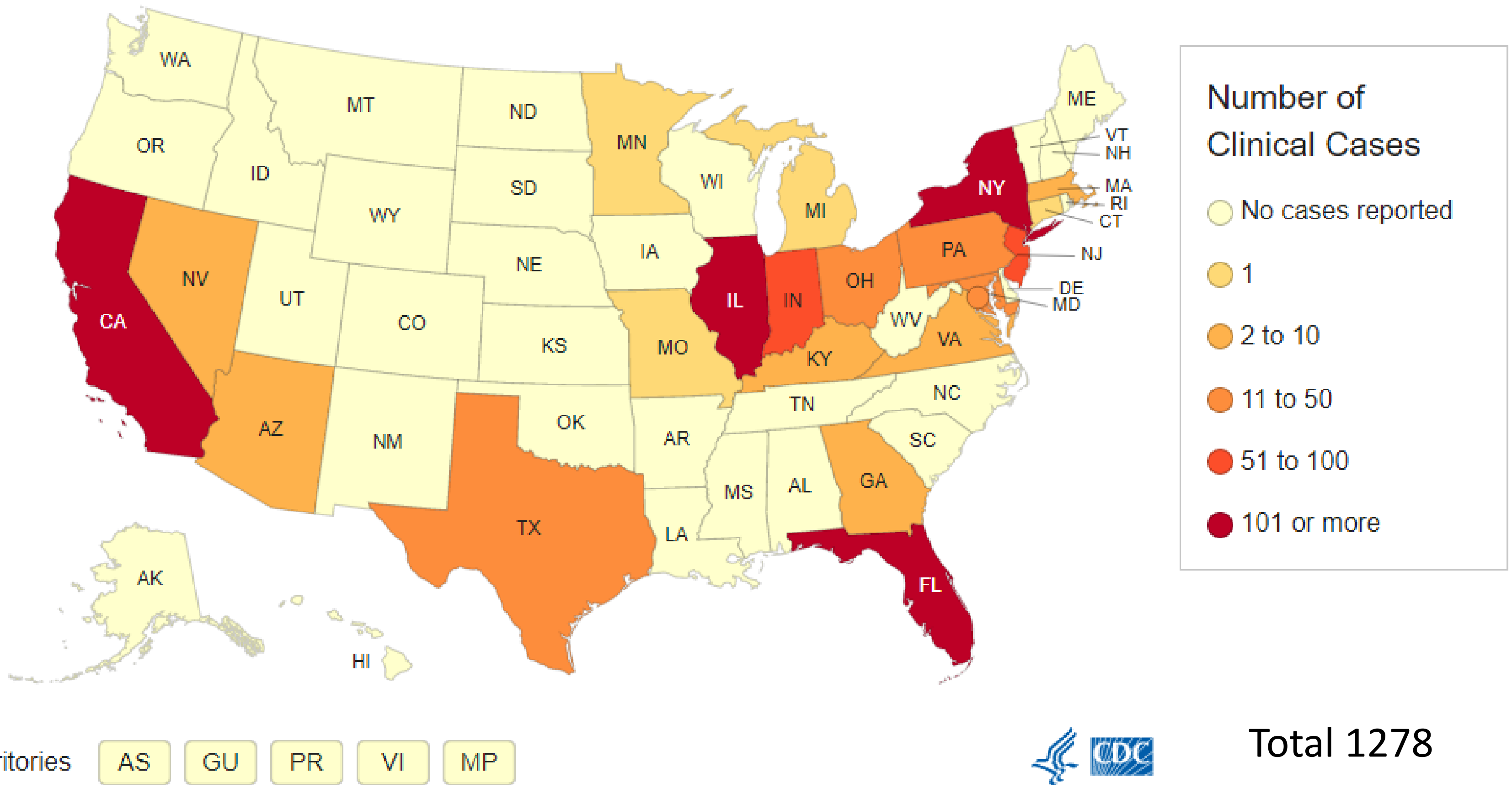
Reported clinical cases of *Candida auris*, January 01, 2021-December 31, 2021



Clinical cases include both confirmed and probable cases. In addition to these clinical cases, targeted screening has identified 3,772 patients colonized with *C. auris*.

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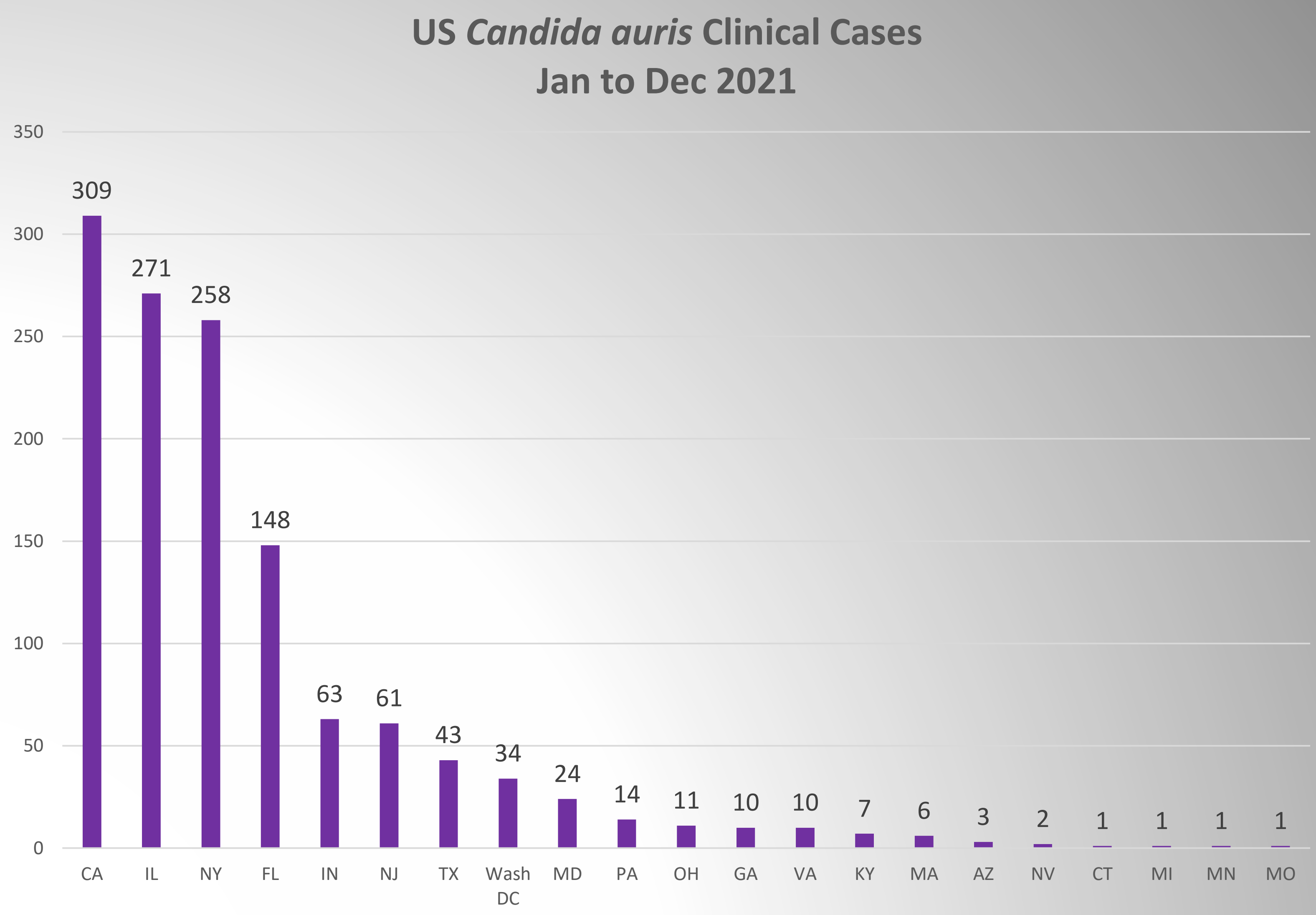
https://www.cdc.gov/fungal/candida-auris/tracking-c-auris.html



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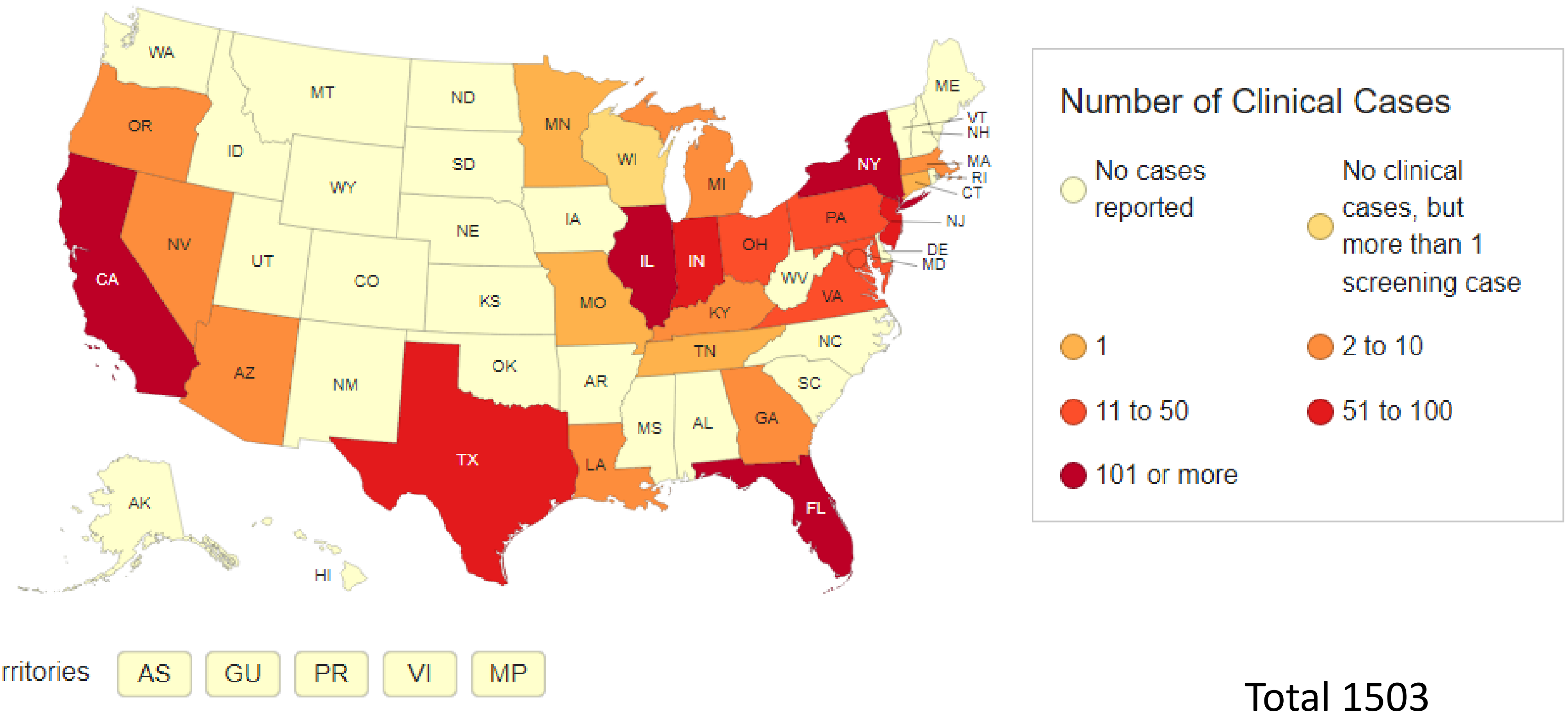
https://www.cdc.gov/fungal/candida-auris/tracking-c-auris.html

Reported clinical cases of *Candida auris*, March 1, 2021-February 28, 2022



Total 1503

Clinical cases include both confirmed and probable cases. In addition to these clinical cases, targeted screening has identified 3,958 patients colonized with *C. auris*.

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

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CDC. Antibiotic Resistance Threats in the United States, 2019. Atlanta, GA: U.S. Department of Health and Human Services, CDC; 2019. DOI: http://dx.doi.org/10.15620/cdc:82532

C. auris Superpowers include all <u>EXCEPT</u>:

A. Able to colonize skin and body sites for prolonged periods
B. Able to leap tall buildings in a single bound
C. Able to persist in healthcare environments
D. Able to resist antifungal drugs
E. Able to evade some clinical laboratory detection

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C. auris Superpowers include all <u>EXCEPT</u>:

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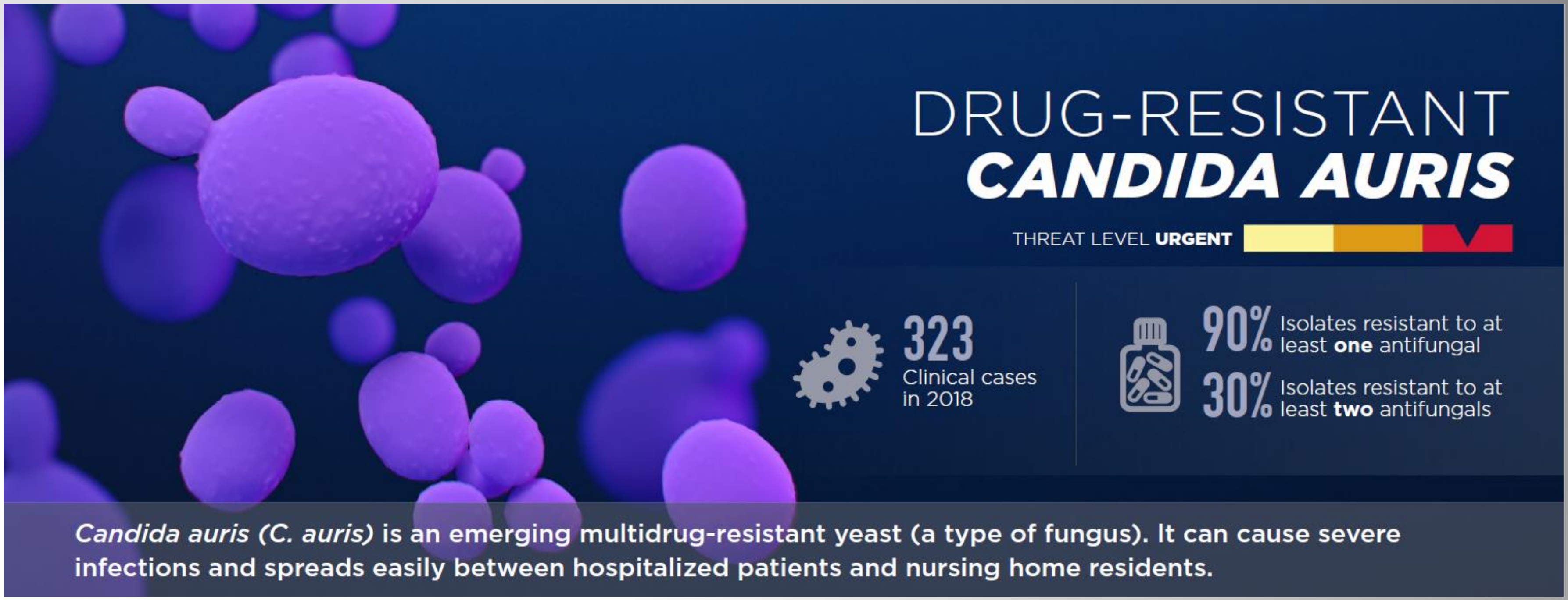

CANDIDA AURIS SIGNIFICANCE

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CDC. Antibiotic Resistance Threats in the United States, 2019. Atlanta, GA: U.S. Department of Health and Human Services, CDC; 2019. DOI: http://dx.doi.org/10.15620/cdc:82532

Candida auris Superpowers

- **Invasive** – causes fungemia and other infections
- **Stealth** – diagnostic challenges
- **Drug-resistant** – to one or more antifungals, often **Multidrug-resistant (MDR)** and can be resistant to all 3 antifungal classes
- **Communicable** – persists on patients, environment, and medical equipment

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Morbidity and Mortality Weekly Report

Investigation of the First Seven Reported Cases of *Candida auris*, a Globally Emerging Invasive, Multidrug-Resistant Fungus — United States, May 2013–August 2016

TABLE. Characteristics of the first seven cases of *Candida auris* identified in the United States—May 2013–August 2016

Patient	Isolation month/ year	State	Site of *C. auris* isolation	Underlying medical condition(s)	Outcome*
1	May 2013	New York	Blood	Respiratory failure requiring high-dose corticosteroids	Died
2	July 2015	New Jersey	Blood	Brain tumor and recent villous adenoma resection	Died
3	April 2016	Maryland	Blood	Hematologic malignancy and bone marrow transplant	Died
4	April 2016	New York	Blood	Hematologic malignancy	Died
5	May 2016	Illinois	Blood	Short gut syndrome requiring total parenteral nutrition and high-dose corticosteroid use	Survived
6	July 2016	Illinois	Urine	Paraplegia with long-term, indwelling Foley catheter	Survived
7	August 2016	New York	Ear	Severe peripheral vascular disease and skull base osteomyelitis	Survived

* Mortality was not necessarily attributable to *C. auris* infection.

To determine whether cases were occurring in U.S.,
CDC issued clinical alert in June 2016 requesting *C. auris* cases be reported to health departments and CDC; labs encouraged to send isolates of *C. haemulonii* and those not identified beyond *Candida* species.

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MMWR / November 11, 2016 / Vol. 65 / No. 44

Invasive Infections

- *C. auris* has been identified from many body sites including bloodstream, urine, respiratory tract, biliary fluid, wounds, and external ear canal. Approximately half of clinical cases in the United States have been in the bloodstream and the remainder have been found in non-invasive body sites.

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

ISHAM
INTERNATIONAL SOCIETY FOR HUMAN AND ANIMAL MYCOLOGY

Medical Mycology, 2019, 57, 1–12
doi: 10.1093/mmy/myy054
Advance Access Publication Date: 31 July 2018
Review Article

Review Article

Candida auris: The recent emergence of a multidrug-resistant fungal pathogen

Kaitlin Forsberg[1,2], Kate Woodworth[3], Maroya Walters[3], Elizabeth L. Berkow[1], Brendan Jackson[1], Tom Chiller[1] and Snigdha Vallabhaneni[1,*]

[1]Mycotic Diseases Branch, Centers for Disease Control and Prevention, Atlanta, Georgia, USA, [2]IHRC, Inc., Atlanta, Georgia, USA and [3]Division of Healthcare Quality and Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

C. auris candidemia is associated with mortality rates of about 30 – 60%, depending on the setting

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Medical Mycology, 2019, Vol. 57, No. 1

Risk Factors for *Candida auris* Infection

- Most common in older persons (can infect neonates and children)
- Underlying medical conditions – cancer, DM
- Recent abdominal surgery
- Presence of central venous catheter, tracheostomies, gastrostomy tubes, total parenteral nutrition, or other invasive devices

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Medical Mycology, 2019, Vol. 57, No. 1

Risk Factors for *Candida auris* Infection

- Recent antibiotic exposure
- Nearly half had been receiving antifungals at the time of or immediately before *C. auris* diagnosis
- Most U.S. cases have extensive exposure to healthcare in the preceding months
  - Particularly in higher acuity long-term care facilities, such as LTACs and SNFs that support patients who are chronically vent dependent
- Recent exposure to healthcare in a country with *C. auris* transmission

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Medical Mycology, 2019, Vol. 57, No. 1

Clinical Infectious Diseases

MAJOR ARTICLE

IDSA Infectious Diseases Society of America · hivma hiv medicine association · OXFORD

Factors Associated With *Candida auris* Colonization and Transmission in Skilled Nursing Facilities With Ventilator Units, New York, 2016–2018

John Rossow,[1,2] Belinda Ostrowsky,[3] Eleanor Adams,[4] Jane Greenko,[4] Robert McDonald,[1,5] Snigdha Vallabhaneni,[2,3] Kaitlin Forsberg,[2] Stephen Perez,[1] Todd Lucas,[1] Karen A. Alroy,[1] Kara Jacobs Slifka,[3] Maroya Walters,[3] Brendan R. Jackson,[2] Monica Quinn,[5] Sudha Chaturvedi,[6,7] and Debra Blog[5,7]; for the New York *Candida auris* Investigation Workgroup

- NYSDOH intensively tracked cases of *C. auris* infection and conducted contact tracing at facilities where case residents resided in the 90 days prior to the *C. auris* infection
- Point prevalence studies (PPS) – swabbed in nares, groin, axilla for PCR and culture
- Case-control investigation to assess factors associated with *C. auris* colonization in vSNFs; 60 cases and 218 controls from 6 vSNFs

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Candida auris in Ventilator-capable SNFs • CID 2021:72 (1 June)

Factors Associated with *C. auris* Colonization

Table 3. Multivariable Logistic Regression Models for Assessing Factors for Association With *Candida auris* Colonization, New York, 2016–2018

		95% Confidence Interval	
Factors	aOR	Lower	Upper
Mechanically ventilated[a]	5.88	2.25	15.37
Any ACH visit in the 6 months prior to PPS[b]	4.23	1.87	9.60
Received a carbapenem in the 90 days prior to PPS[c]	3.52	1.62	7.63
Received systemic fluconazole in the 90 days prior to PPS[d]	5.98	1.58	22.64
Received vancomycin in the 90 days prior to PPS[e]	1.65	.75	3.67
Any MDRO in the 90 days prior to PPS[f]	1.25	.56	2.76
Room with a colonized roommate[g]	.37	.12	1.16
Room type at time of screening[h]			
In a room with 1 bed	Ref	Ref	Ref
In a room with 2 beds	1.44	.55	3.80
In a room with 4 beds	2.04	.54	7.70

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Candida auris in Ventilator-capable SNFs • CID 2021:72 (1 June)

Candida auris

DIAGNOSIS

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Clinical Microbiology Labs

- Usually identify to species level yeast only from sterile site and significate isolates
  - Many candida isolates from sputum, urine, or wounds are not routinely speciated
- Traditional phenotypic methods frequently misidentify *Candida auris*
- Have varying technology capable of identifying *Candida auris* – CDC Lab Algorithm

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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*
API ID 32C	*Candida intermedia* *Candida sake* *Saccharomyces kluyveri*
BD Phoenix yeast identification system	*Candida haemulonii* *Candida catenulata*
MicroScan	*Candida famata* *Candida guilliermondii*** *Candida lusitaniae*** *Candida parapsilosis***
RapID Yeast Plus	*Candida parapsilosis***

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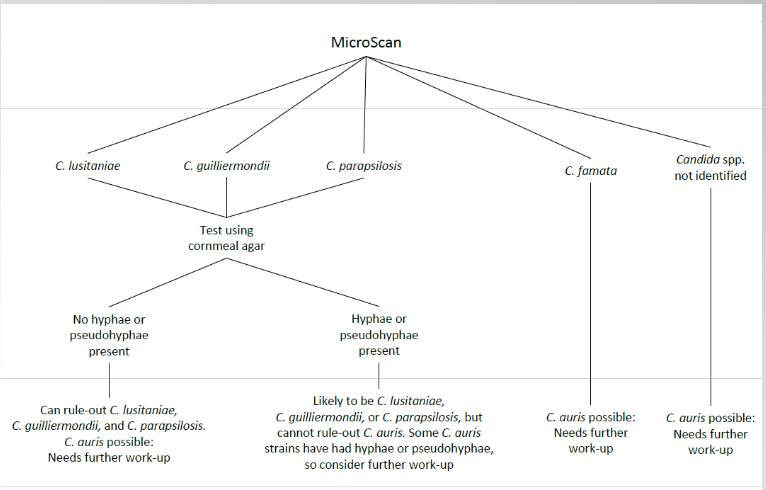
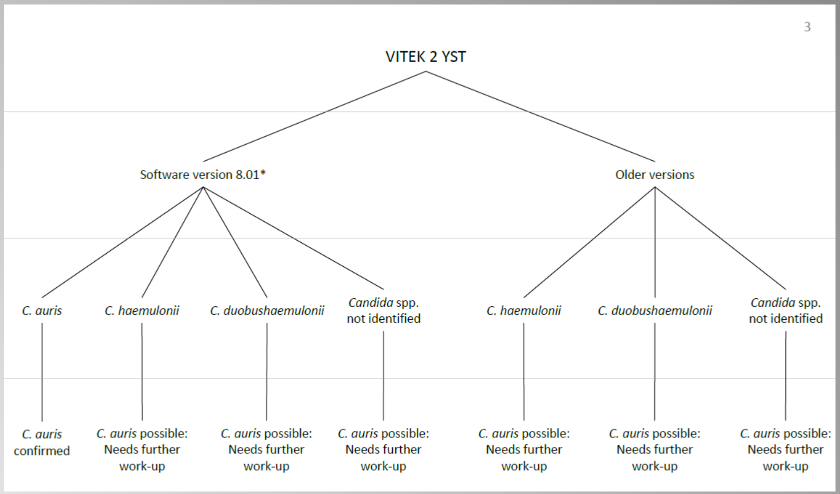
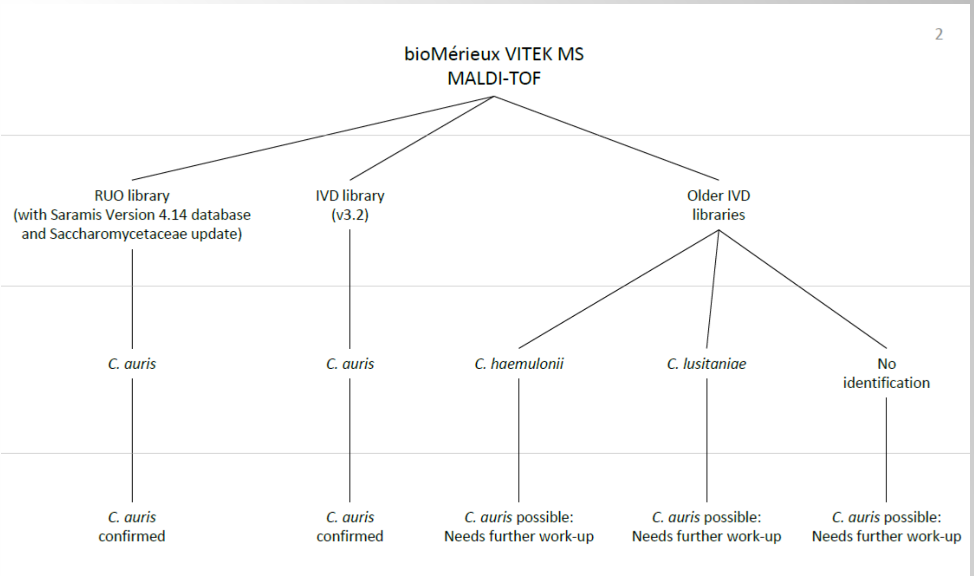
https://www.cdc.gov/fungal/candida-auris/identification.html







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

Identification Method	Database/Software, if applicable	*C. auris* is confirmed if initial identification is *C. auris.*	*C. auris* is possible if the following initial identifications are given. Further work-up is needed to determine if the isolate is *C. auris.*
Bruker Biotyper MALDI-TOF	RUO libraries (Versions 2014 [5627] and more recent)	*C. auris*	n/a
	CA System library (Version Claim 4)	*C. auris*	n/a
bioMérieux VITEK MS MALDI-TOF	RUO library (with Saramis Version 4.14 database and Saccharomycetaceae update)	*C. auris*	n/a
	IVD library (v3.2)	*C. auris*	n/a
	Older IVD libraries	n/a	*C. haemulonii* *C. lusitaniae* No identification
VITEK 2 YST	Software version 8.01*	*C. auris*	*C. haemulonii* *C. duobushaemulonii* *Candida* spp. not identified
	Older versions	n/a	*C. haemulonii* *C. duobushaemulonii* *Candida* spp. not identified
API 20C		n/a	*Rhodotorula glutinis* (without characteristic red color) *C. sake* *Candida* spp. not identified
API ID 32C		n/a	*C. intermedia* *C. sake* *Saccharomyces kluyveri*
BD Phoenix		n/a	*C. catenulata* *C. haemulonii* *Candida* spp. not identified
MicroScan		n/a	*C. lusitaniae*** *C. guilliermondii*** *C. parapsilosis*** *C. famata* *Candida* spp. not identified
RapID Yeast Plus		n/a	*C. parapsilosis*** *Candida* spp. not identified
GenMark ePlex BCID-FP Panel		*C. auris*	n/a

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

MALDI-TOF

Matrix-assisted laser desorption/ionization-time of flight

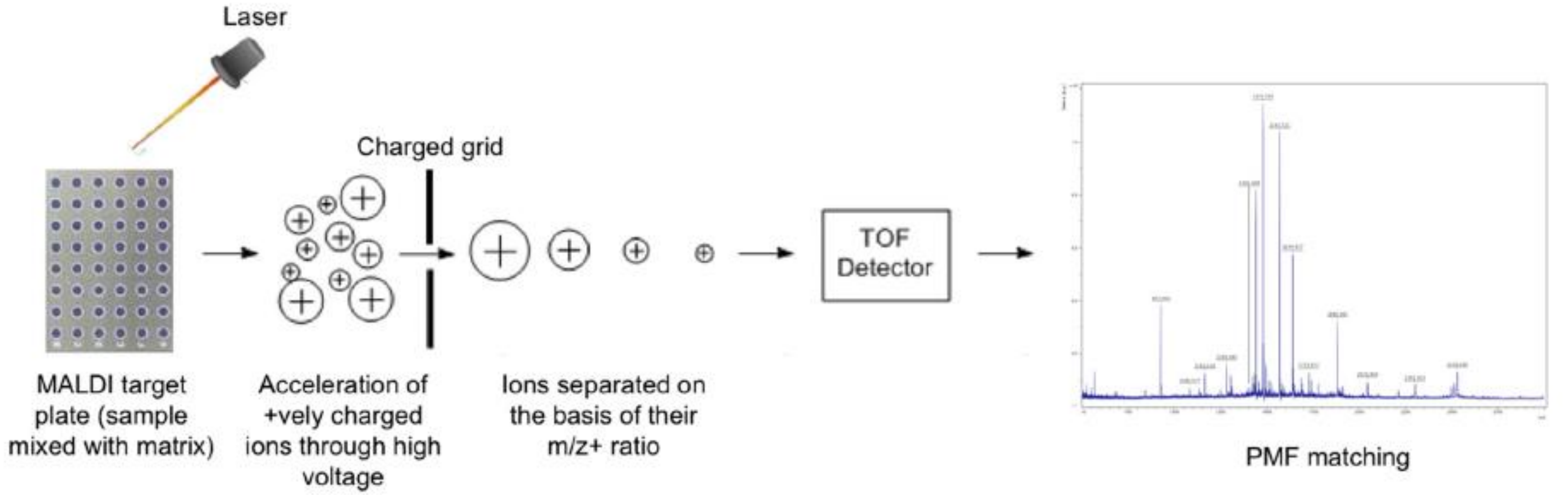

FIGURE 1 | Schematic diagram showing the work-flow in a MALDI-TOF MS.

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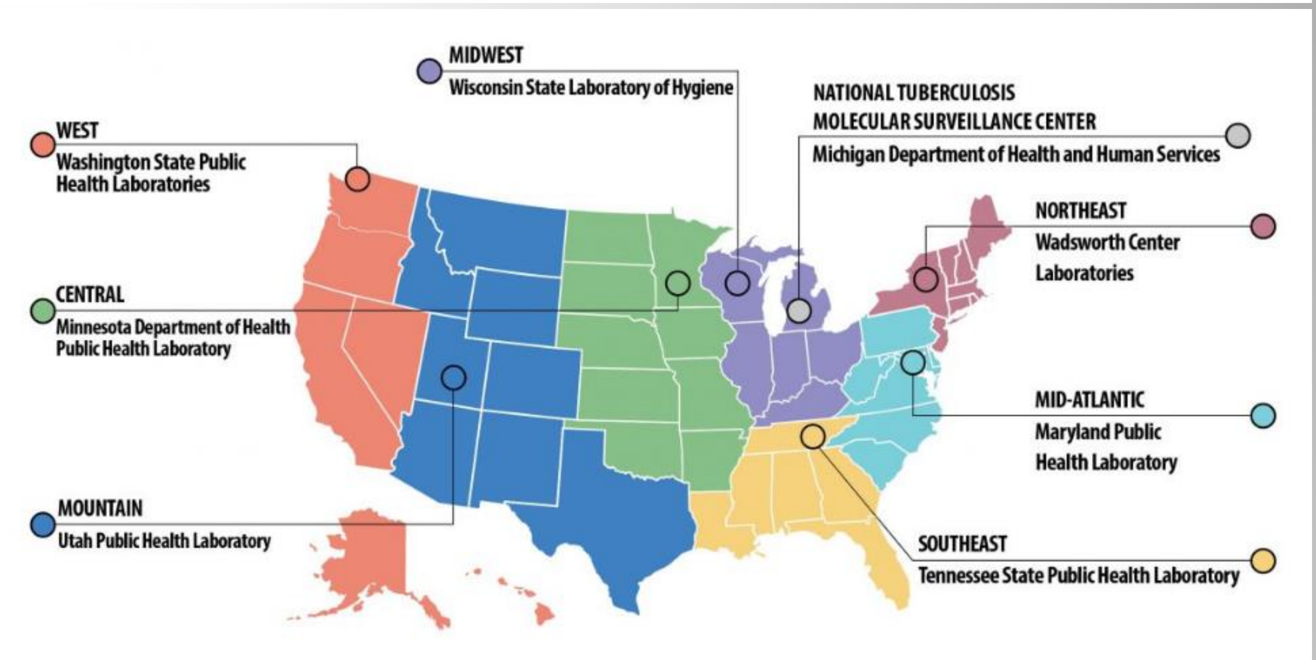
Reference Labs



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https://www.cdc.gov/drugresistance/ar-lab-networks/domestic.html

ARLABnetwork

- Louisiana’s reference lab is in Tennessee
- Verifies identification of *Candida auris*
- Performs whole genome sequencing of strains
- Performs “home brew” PCR (not FDA approved) for *Candida auris* on surveillance swabs
  - For indeterminate results – they culture for identification

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Candida auris

ANTIFUNGAL RESISTANCE

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Antifungal Classes

- **Polyenes** – bind with ergosterol in fungal cell membrane
  - Amphotericin B (AMB)
- **Azoles** – inhibits conversion of lanosterol to ergosterol
  - **Triazoles**
    - Fluconazole
    - Isavuconazole
    - Itraconazole
    - Posaconazole
    - Voriconazole
- **Echinocandins** – inhibit creation of glucan in fungal cell wall by inhibiting 1,3-Beta-glucan synthase
  - Anidulafungin
  - Caspofungin
  - Micafungin
- **Antimetabolite** – pyrimidine analog
  - 5-Fluorocytosine (5-FC) (Flucytosine)
    - Always used in combination; never alone

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antibiotics

MDPI

Review

Antifungal Resistance in *Candida auris*: Molecular Determinants

María Guadalupe Frías-De-León [1], Rigoberto Hernández-Castro [2], Tania Vite-Garín [3], Roberto Arenas [4], Alexandro Bonifaz [5], Laura Castañón-Olivares [3], Gustavo Acosta-Altamirano [1] and Erick Martínez-Herrera [1,*]

Table A1. Main resistance mechanisms of action to polyene, triazoles and echinocandins in *C. auris*.

Antifungal	Genes Associated with Resistance	Effect on *C. auris*	References
Polyenes	*ERG1, ERG2, ERG3, ERG5, ERG6, ERG11, ERG13*	- Ergosterol biosynthesis path - Overexpression of genes - Alterations in ergosterol composition - Decrease or absence in ergosterol levels	[1,2,21,24,25,32–36,38,39]

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Antibiotics **2020**, *9*, 568; doi:10.3390/antibiotics9090568

Resistance to each antifungal is closely related to the type of clade to which the strain belongs

Antifungal	Genes Associated with Resistance	Effect on *C. auris*
Triazoles	*ERG11*	- Mutations that alter the shape of the lanosterol 14-α its affinity with triazole - Overexpression of the gene - Duplications on the chromosome containing the gene.
Triazoles	*HSP90*	- Promotes cellular response to stress. - Regulates signaling on the cell wall. - Involved in morphogenesis or the fungus. - Involved in fluconazole tolerance
Echinocandins	*FKS1*	- Changes in amino acids in the catalytic subunit of the β-1,3-D-glucan synthase - Mutation in *HS1* - Presence of serine in place of phenylalanine in S639F - Substitution of amino acids in S639P - Mutation in *HS1* in *S639Y*
Polyenes	Efflux pumps	- Identification of orthologous genes in ABC and MFS-type efflux pumps
Triazoles	Efflux pumps	- Transcriptional overexpression and overregulation of *CDR1*. - Resistant strains genome present multiple genes for ABC transporters
Polyenes	OPT1, CSA1, MET15, ARG1, *MVD, SIT1, PGA7, RBT*	- Ergosterol biosynthesis path - Intrinsic transcription of multidrug transporters - Overexpression of genes in transcriptional response - Increased transcription in *CDR4a*
Polyenes	*FLO8*	- Mutation in transcription factor for biofilm formation - Single-nucleotide polymorphism
5-FC	*FUR1*	- Mutation at the F211I position causes phenylalanine substitution with isoleucine

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Antibiotics **2020**, *9*, 568; doi:10.3390/antibiotics9090568

C. auris Antifungal Susceptibility Testing Interpretation

- Currently no established *C. auris*-specific susceptibility breakpoints
- Breakpoints are defined based on those established for closely related *Candida* species and on expert opinion
- Correlation between microbiologic breakpoints and clinical outcomes is not known at this time
  - For this reason, the information below should be considered as a general guide and not as definitive breakpoints for resistance
- Please note that a finding of an elevated minimum inhibitory concentration (MIC) for an antifungal drug should not necessarily preclude its use, especially if the use of other antifungal drugs for the patient has been ineffective

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

Triazole Class Drugs	Tentative MIC Breakpoints (μg/mL)	Comment
Fluconazole	≥32	Modal minimum inhibitory concentration (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, making them unlikely to respond to fluconazole.
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.

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

Polyene Class Drug	Tentative MIC Breakpoints (μg/mL)	Comment
Amphotericin B	≥2	Recent pharmacokinetic/pharmacodynamic 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. Therefore, **isolates with an MIC of ≥2** should now be considered resistant. **If using Etest for amphotericin B and an MIC of 1.5 is determined, that value should be rounded up to 2.**

Echinocandin Class Drugs	Tentative MIC Breakpoints (μg/mL)	Comment
Anidulafungin	≥ 4	Tentative breakpoints are based on the modal distribution of echinocandin MICs of approximately 100 isolates from diverse geographic locations.
Caspofungin	≥ 2	
Micafungin	≥ 4	

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

U.S. *C. auris* Isolates Resistance Patterns

- Based on these MIC breakpoints, many isolates are MDR
- Some U.S. *C. auris* isolates have been found to be resistant to all three classes of antifungal drugs
  - Pan-resistance
- In the United States
  - About 90% of *C. auris* isolates resistant to fluconazole
  - About 30% resistant to amphotericin B
  - Less than 5% resistant to echinocandins
  - These proportions may include multiple isolates from the same individuals and may change as more isolates are tested

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

Louisiana *Candida auris* Clinical Isolates Antifungal Susceptibility Testing Results MIC (mcg/mL) With CDC Tentative MIC Breakpoints Applied

				Polyene	Azole				Echinocandin			Antimetabolite
Pt	Specimen Date	Source	Lab	Ampho B	Fluconazole	Itra	Posa	Vori	Anidulafungin	Caspo	Mica	5-flucytosine
# 1	1/5/22	Blood	Mayo	1	64	0.12	0.06	0.25	0.12	0.03	0.12	0.25
# 1	1/5/22	Blood	ARLN	1.5	128	0.5	0.125	0.5	0.5	0.125	0.125	
# 2	1/10/22	Urine	ARUP	1	64	0.25	0.12	0.25	0.06	0.03	0.06	0.25
# 2	1/10/22	Urine	ARLN	1	32	0.25	0.25	0.5	0.125	0.125	0.125	
# 2	2/10/22	Urine	Mayo	2	32	0.12	0.03	0.12	0.12	0.03	0.06	0.12
# 3	2/15/22	Blood	Mayo	2	32	0.12	0.03	0.06	0.12	0.06	0.12	</= 0.06
# 4	2/23/22	Wound	Mayo	2	32	0.06	0.03	0.06	0.12	0.06	0.06	</= 0.06

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

Morbidity and Mortality Weekly Report

Candida auris Isolates Resistant to Three Classes of Antifungal Medications — New York, 2019

- *C. auris* first detected in New York in July 2016
- As of June 28, 2019 – total of 801 patients with C. auris in NY – both clinical cultures and surveillance swabs
- 3 patients found to have pan-resistant *C. auris* that developed after receipt of antifungals – including echinocandins
  - All 3 with multiple comorbidities; no travel
  - No transmission detected to other patients or environment

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MMWR / January 10, 2020 / Vol. 69 / No. 1

Morbidity and Mortality Weekly Report

Candida auris Isolates Resistant to Three Classes of Antifungal Medications — New York, 2019

- As of June 28, 2019 – 801 pts with *C. auris* in NY
  - Testing of first available clinical isolate
    - 276/277 (99.6%) Fluconazole Resistant
    - 170/277 (61.3%) Amphotericin B Resistant
    - 0 Echinocandin Resistant
  - Testing of subsequent isolates
    - 330/331 (99.7%) Fluconazole Resistant
    - 210/331 (63.4%) Amphotericin B Resistant
    - 13/331 (3.9%) Echinocandin Resistant
    - 3 were pan-resistant

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MMWR / January 10, 2020 / Vol. 69 / No. 1

Notes from the Field

Transmission of Pan-Resistant and Echinocandin-Resistant *Candida auris* in Health Care Facilities — Texas and the District of Columbia, January–April 2021

- ARLN detected independent clusters of pan-resistant OR echinocandin-resistant cases in Texas and District of Colombia (DC) in 2021
- Each cluster involved common health care encounters and no known previous echinocandin exposure, suggesting transmission of pan- and echinocandin-resistant strains for the first time in the US

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MMWR / July 23, 2021 / Vol. 70 / No. 29

Notes from the Field

Transmission of Pan-Resistant and Echinocandin-Resistant *Candida auris* in Health Care Facilities — Texas and the District of Columbia, January–April 2021

- DC - 101 clinical and screening cases during January–April 2021
  - 3 pan-resistant (LTAC patients)
- Texas - 22 clinical and screening cases of during the same period
  - 2 pan-resistant
  - 5 resistant to both echinocandins and fluconazole
  - These seven cases – at two facilities that share patients in the same city
    - 2 at LTAC; 3 three at short-term acute care hospital, and 2 at both facilities
    - 4 were identified through colonization screening, 3 three clinical isolates (2 blood, 1 wound)
- No known epidemiologic links were identified between the Texas and DC clusters. No patients with pan- or echinocandin-resistant isolates in either cluster had received echinocandins before *C. auris* specimen collection
- Thirty-day mortality in both outbreaks combined was 30%, but the relative contribution of *C. auris* was unclear

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MMWR / July 23, 2021 / Vol. 70 / No. 29

Candida auris

TREATMENT RECOMMENDATIONS

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Treatment

- Consult Infectious Diseases!!!
- **DO NOT** Treat Colonization
- Echinocandin first line agent
- Carefully monitor on treatment – follow-up cultures with repeat susceptibility testing
- Could consider switching to Liposomal Amphotericin B if clinical failure or persistent fungemia > 5 d on echinocandin

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

Echinocandin Drug	Adult dosing	Pediatric dosing
Anidulafungin	loading dose 200 mg IV, then 100 mg IV daily	not approved for use in children
Caspofungin	loading dose 70 mg IV, then 50 mg IV daily	loading dose 70mg/m^2/day IV, then 50mg/m^2/day IV (based on body surface area)
Micafungin	100 mg IV daily	2mg/kg/day IV with option to increase to 4mg/kg/day IV in children at least 40 kg

Dose information for neonates and infants <2 months of age

Echinocandin Drug	Neonatal dosing
Caspofungin	25 mg/m^2/day IV (based on body surface area)
Micafungin	10mg/kg/day IV

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

Candida auris Colonization

- Candida auris isolated from noninvasive, non-sterile body sites
  - (e.g., urine, external ear, wounds, respiratory specimens and skin colonization)
- Do not treat colonization when there is no evidence of infection
- This includes surveillance swabs

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

Pan-resistant *C. auris* Treatment

- Data lacking about most appropriate therapy
- Combination antifungal treatment – promising in laboratory settings but have not been evaluated in clinical settings
- Investigational drugs have been tried and may be considered for patients with echinocandin-resistant isolates

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

Disclosure of Off-Label Use of FDA Approved Medications

- **Note – some antifungal combinations may be considered** "off label" use of the medications
  - Flucytosine – is FDA approved for use in combination with amphotericin B for the treatment of systemic candidiasis and cryptococcosis because of the emergence of resistance to Flucytosine
- **Note – Ibrexafungerp** is FDA approved for the treatment of vulvovaginal candidiasis (VVC) in adult and post-menarchal pediatric females

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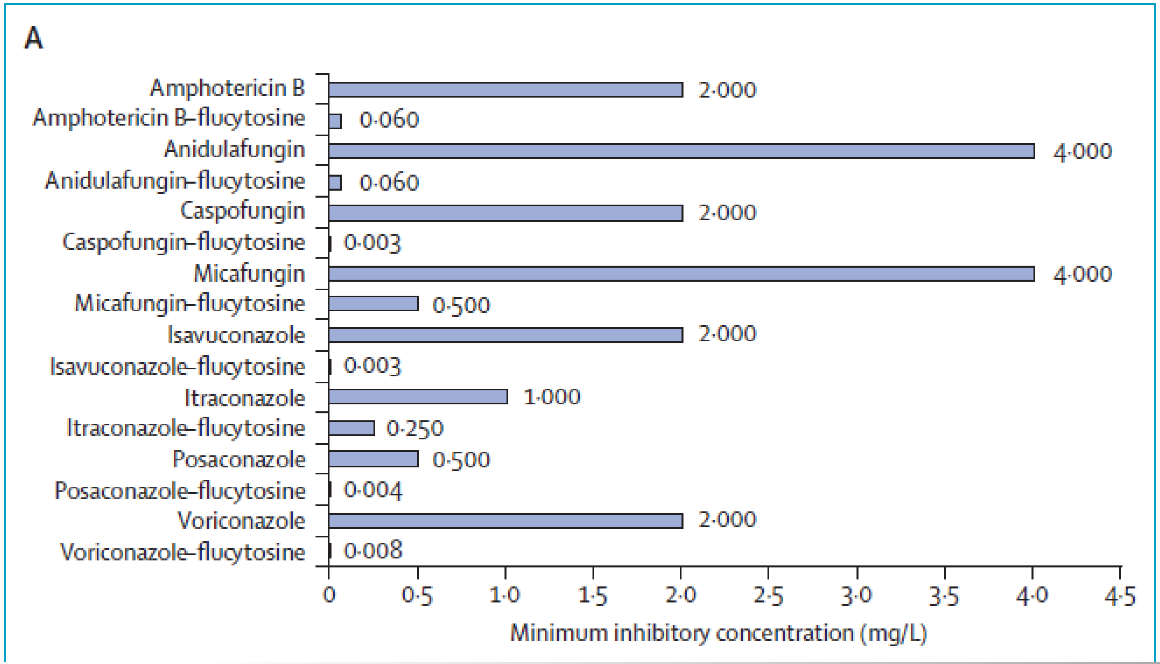
Pan-resistant *Candida auris*: New York subcluster susceptible to antifungal combinations

- 4 pan-resistant isolates were 100% inhibited in vitro by combinations of 2 antifungal drugs using fixed concentrations achievable in vivo
- Flucytosine combinations most effective
- > 2 log reduction in cfu with combo – suggesting fungicidal



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www.thelancet.com/microbe Vol 1 September 2020

antibiotics

MDPI

Review

Ibrexafungerp: A Novel Oral Triterpenoid Antifungal in Development for the Treatment of *Candida auris* Infections

Mahmoud Ghannoum [1], Maiken Cavling Arendrup [2,3,4], Vishnu P. Chaturvedi [5], Shawn R. Lockhart [6], Thomas S. McCormick [1], Sudha Chaturvedi [5], Elizabeth L. Berkow [6], Deven Juneja [7], Bansidhar Tarai [7], Nkechi Azie [8], David Angulo [8,*] and Thomas J. Walsh [9]

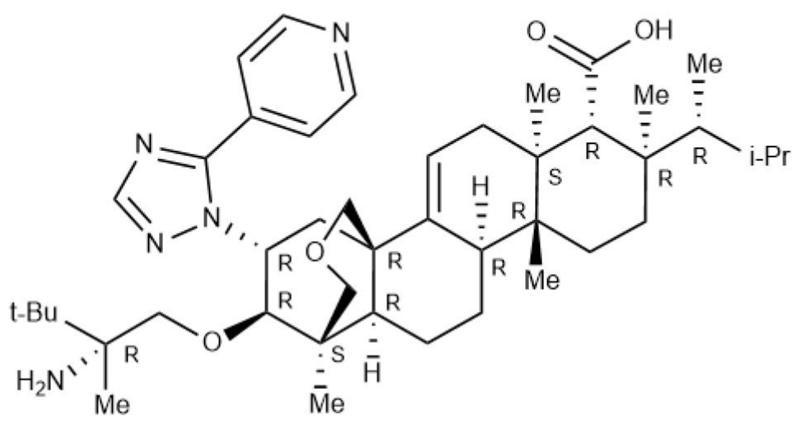

Figure 1. Structure of ibrexafungerp.

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Antibiotics **2020**, *9*, 539; doi:10.3390/antibiotics9090539

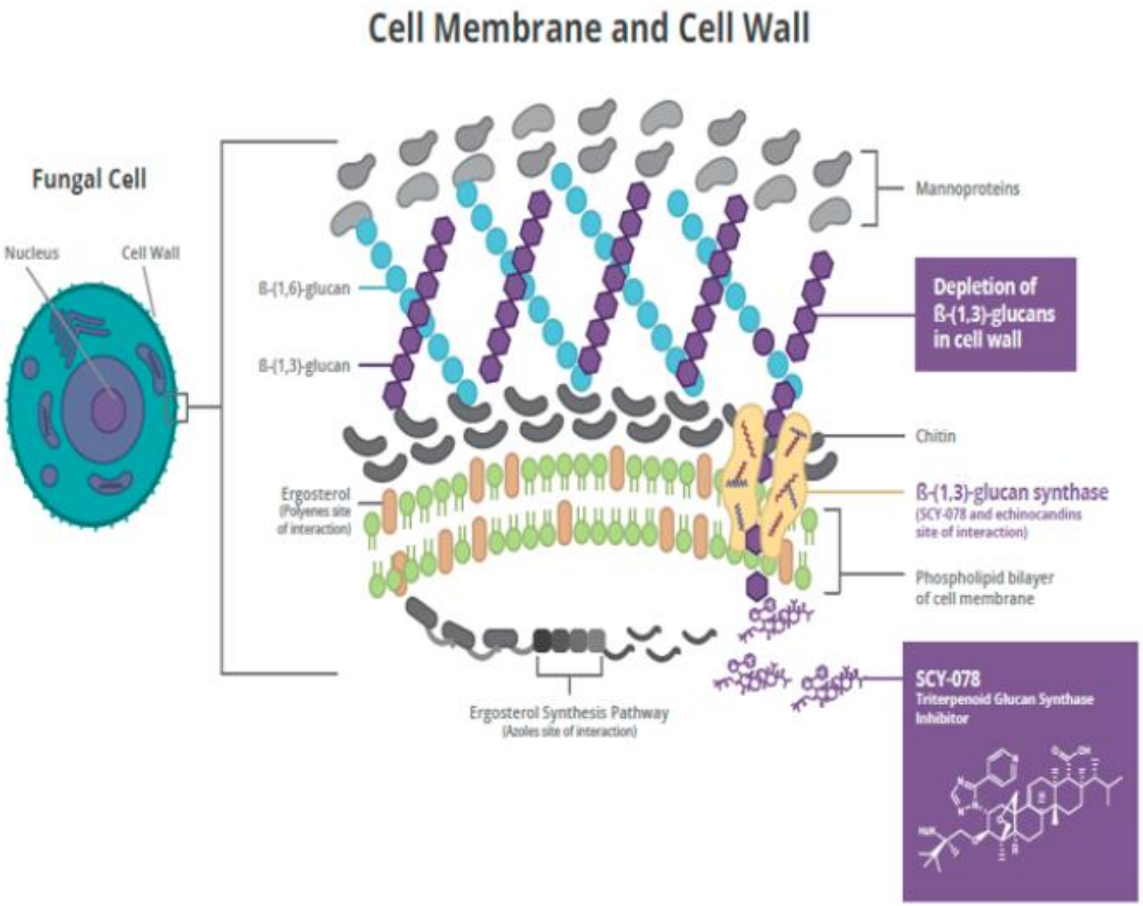

Figure 2. Mechanism of action for ibrexafungerp.

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Antibiotics **2020**, *9*, 539; doi:10.3390/antibiotics9090539

Ibrexafungerp

- First-in-class triterpenoid antifungal agent
- Similar to echinocandins – inhibits (1 ->3)-Beta-D-glucan synthase, a key component of the fungal cell wall, resulting in fungicidal activity against *Candida* spp.
- Minimum inhibitory concentration (MIC_{50} and MIC_{90}) values in >400 C. auris isolates were 0.5 g/mL and 1.0 g/mL, respectively

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Antibiotics **2020**, *9*, 539; doi:10.3390/antibiotics9090539

Candida auris

INFECTION PREVENTION AND CONTROL

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Candida auris Requires What Isolation Precautions in Acute Care Hospitals?

A. None
B. Airborne Isolation Precautions
C. Droplet Isolation Precautions
D. Contact Isolation Precautions
E. Airborne and Contact Isolation Precautions

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Candida auris Requires What Isolation Precautions in Acute Care Hospitals?

A. None
B. Airborne Isolation Precautions
C. Droplet Isolation Precautions
D. Contact Isolation Precautions
E. Airborne and Contact Isolation Precautions

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Communicability

- Persists on patients
  - Patients colonized for several months after infection is resolved
  - Don't know maximum time of colonization
  - No data on efficacy of decolonization – CHG or topical antifungals
- Persists in the environment – for weeks
- Persists on medical equipment

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

Infection Prevention and Control of *Candida auris*

- **Hand Hygiene**
  - Alcohol-based hand sanitizer (ABHS) is effective against C. auris and is the preferred method for cleaning hands when they are not visibly soiled
  - If hands are visibly soiled, wash with soap and water
  - Wearing gloves is not a substitute for hand hygiene

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

Contact Precautions

- Hand Hygiene before and after PPE
- Gown and gloves before entry into room
- Dedicated equipment – BP cuff, thermometer, stethoscope
- Private room **PREFERRED**
- Environmental cleaning

- If MUST share rooms:
  - Separate 3 feet apart
  - Use privacy curtains
  - Clean and disinfect any shared reusable equipment
  - Clean and disinfect environment more frequently
  - HCW change PPE and HH between roommates

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

Duration of Contact Precautions

- Entire duration of stay in the facility and indefinitely thereafter
  - For Clinical Cases **AND** Colonized Patients
  - Flag chart
  - Colonization persists for a long time
  - Repeat swabs may be positive then negative then positive again
  - Reassessment of colonization to be done with Health Department, no sooner than 3 months from last positive test

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

Accessible version: https://www.cdc.gov/hai/containment/PPE-Nursing-Homes.html

Implementation of Personal Protective Equipment in Nursing Homes to Prevent Spread of Novel or Targeted Multidrug-resistant Organisms (MDROs)

Updated: July 29, 2019

Enhanced Barrier Precautions in Nursing Homes

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https://www.cdc.gov/hai/containment/PPE-Nursing-Homes.html

Implementation of Personal Protective Equipment in Nursing Homes to Prevent Spread of MDROs

Precaution	Applies to:	PPE used for these situations:	Required PPE	Room restriction
Enhanced Barrier Precautions	All residents with *any of the following*: • Infection or colonization with a novel or targeted MDRO *when Contact Precautions do not apply*. • Wounds and/or indwelling medical devices (e.g., central line, urinary catheter, feeding tube, tracheostomy/ventilator) *regardless of MDRO colonization status* who reside on a unit or wing where a resident known to be infected or colonized with a novel or targeted MDRO resides.[4] Facilities may consider applying Enhanced Barrier Precautions to residents infected or colonized with other epidemiologically-important MDROs based on facility policy.	During high-contact resident care activities: • Dressing • Bathing/showering • Transferring • Providing hygiene • Changing linens • Changing briefs or assisting with toileting • Device care or use: central line, urinary catheter, feeding tube, tracheostomy/ventilator • Wound care: any skin opening requiring a dressing	Gloves and gown prior to the high-contact care activity (change PPE before caring for another resident) (Face protection may also be needed if performing activity with risk of splash or spray)	None

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https://www.cdc.gov/hai/containment/PPE-Nursing-Homes.html

C. auris Persists in Environment

- Has been cultured from multiple locations in patient rooms, including both high-touch surfaces, such as bedside tables and bedrails, and general environmental surfaces farther away from the patient, such as windowsills
- Has been identified on mobile equipment that is shared between patients, such as glucometers, temperature probes, blood pressure cuffs, ultrasound machines, nursing carts, and crash carts

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

Environmental Disinfection

- Perform **thorough daily and terminal cleaning and disinfection** of patients' or residents' rooms and other areas where they receive care (e.g., radiology, physical therapy) using an appropriate disinfectant
- Shared equipment (e.g., ventilators, physical therapy equipment) should also be cleaned and disinfected before being used by another patient
- It is important to **follow all manufacturers' directions** for use of surface disinfectants and applying the product for the **correct contact time**
- Some products with *C. albicans* or fungicidal claims may not be effective against *C. auris,* and accumulating data indicate that products solely dependent on quaternary ammonia compounds (QACs) are **NOT** effective

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

United States Environmental Protection Agency

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Pesticide Registration

List P: Antimicrobial Products Registered with EPA for Claims Against Candida Auris

List P: Antimicrobial Products Registered with EPA for Claims Against Candida Auris

Registration	Active Ingredient	Product Brand Name	Company	Contact Time (minutes)	Formulation Type	Surface Types	Use sites
10324-214	Hydrogen Peroxide and Paracetic Acid	MAGUARD 5626	MASON CHEMICAL COMPANY	2	Dilution	Hard Nonporous Surfaces	Healthcare, Institutional and Residential
1677-226	Hydrogen Peroxide, Paracetic Acid and Octoanoic Acid	Virasept	Ecolab Inc.	4	Ready to Use	Hard Nonporous Surfaces	Healthcare and Institutional
1677-237	Hydrogen Peroxide and Paracetic Acid	Oxycide™ Daily Disinfectant Cleaner	Ecolab Inc.	3	Dilution	Hard Nonporous Surfaces	Healthcare and Institutional
1677-262	Dodecylbenzenesulfonic acid	Disinfectant 1 Spray	Ecolab Inc.	1	Ready to Use	Hard Nonporous Surfaces	Healthcare and Institutional
1677-263	Dodecylbenzenesulfonic acid	Disinfectant 1 Wipe	Ecolab Inc.	1.25 (75 seconds)	Ready to Use/Wipe	Hard Nonporous Surfaces	Healthcare and Institutional
37549-1	Sodium Hypochlorite	Micro-Kill Bleach Germicidal Bleach Wipes	Medline Industries Inc.	2	Ready to Use/Wipe	Hard Nonporous Surfaces	Healthcare, Institutional and Residential
71847-6	Sodium dichloro-s-triazinetrione	KLORSEPT	Medentech LTD.	2	Dilution	Hard Nonporous Surfaces	Healthcare, Institutional and Residential
8383-13	Hydrogen Peroxide and Paracetic Acid	PERIDOX RTU	CONTEC, INC.	1	Ready to Use	Hard Nonporous Surfaces	Healthcare and Institutional
9480-10	Ethanol, Isopropyl Alcohol and DDAC	Wonder Woman Formula B Spray	Professional Disposables International	1	Ready to Use	Hard Nonporous Surfaces	Healthcare and Institutional
9480-12	Ethanol, Isopropyl Alcohol and DDAC	Wonder Woman Formula B Germicidal Wipes	Professional Disposables International	1	Ready to Use/Wipe	Hard Nonporous Surfaces	Healthcare and Institutional
9480-14	Hydrogen Peroxide	PROJECT FLASH SPRAY	Professional Disposables International	1	Ready to Use	Hard Nonporous Surfaces	Healthcare and Institutional
9480-16	Hydrogen Peroxide	PROJECT FLASH WIPES	Professional Disposables International	1	Ready to Use/Wipe	Hard Nonporous Surfaces	Healthcare and Institutional
9480-4	Isopropyl Alcohol and Quaternary Ammonium Compounds	SANI-CLOTH® GERMICIDAL WIPES	PROFESSIONAL DISPOSABLES INTERNATIONAL, INC.	2	Ready to Use/Wipe	Hard Nonporous Surfaces	Healthcare and Institutional

Continued

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https://www.epa.gov/pesticide-registration/list-p-antimicrobial-products-registered-epa-claims-against-candida-auris

Communication Between Facilities

- **When transferring a patient to another facility - make sure to notify the receiving facility of patient's *C. auris* infection or colonization status**
  - including recommended Infection Control precautions – see tool

Inter-Facility Infection Control Transfer Form for States Establishing HAI Prevention Collaboratives

Available from: https://www.cdc.gov/hai/prevent/prevention_tools.html

This example Inter-facility Infection Control patient transfer form can assist in fostering communication during transitions of care. This concept and draft was developed by the Utah Healthcare-associated Infection (HAI) working group and shared with Centers for Disease Control and Prevention (CDC) and state partners courtesy of the Utah State Department of Health.

This tool can be modified and adapted by facilities and other quality improvement groups engaged in patient safety activities.

https://www.cdc.gov/hai/prevent/prevention_tools.html

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

Combat *Candida auris* Superpowers

- **Invasive** – Remove devices (central lines, urinary catheters, ventilators) ASAP when not needed - assess daily; use aseptic technique for insertion and maintenance
- **Stealth -** Have micro lab improve diagnostics, be aware of CDC algorithm, work up all candida isolates to species level
- **Drug-resistance** – Antimicrobial stewardship – both antibiotic and antifungal stewardship; echinocandin empiric therapy

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Combat *Candida auris* Superpowers

- **Communicable** –
  - Educate on importance of good technique – PPE Hand Hygiene, separate clean and dirty
  - Use Contact Precautions – monitor compliance and educate
  - Environmental Cleaning – enhance daily cleaning and have protocol for terminal room clean and monitoring – such as ATP testing
  - Communicate with other facilities on patient transfer

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Combat *Candida auris* Superpowers

- **Communicable** –
  - Partner with Health Department
    - notify them ASAP upon identification of *C. auris* in facility
    - Guidance from Office of Public Health (OPH) and CDC extremely helpful
    - Conduct weekly surveillance
      - Use ARLN resources for PCR surveillance
      - Discuss next steps with OPH

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ANTIMICROBIAL/ANTIFUNGAL STEWARDSHIP

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scientific reports

Check for updates

OPEN

Impact of antifungal stewardship interventions on the susceptibility of colonized *Candida* species in pediatric patients with malignancy

Ali Amanati[1,2], Parisa Badiee[1]✉, Hadis Jafarian[1], Fatemeh Ghasemi[1], Samane Nematolahi[3], Sezaneh Haghpanah[4] & Seyedeh Sedigheh Hamzavi[1]✉

Study in pediatric oncology patients identifying antifungal susceptibility of candida colonization before and after implementing antifungal stewardship (AFS) program Shiraz University of Medical Sciences, Amir Medical Oncology Center (AMOC), Shiraz, Iran

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Scientific Reports | (2021) 11:14099 | https://doi.org/10.1038/s41598-021-93421-3

Methods

- Cross-sectional study of susceptibility patterns of colonized *Candida* species in children with malignancy
- Samples from oral/nasal secretions and urine/stool specimens
  - no oral/nasal specimens from children with severe thrombocytopenia or bleeding
- Regular weekly sampling of patients after admission until discharge
- Used AMOC baseline data from 2011 – 2012 which was conducted before the AFS program started

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Scientific Reports | (2021) 11:14099 | https://doi.org/10.1038/s41598-021-93421-3

Antifungal Stewardship Program Components

Appropriate treatment of the suspected IFDs
Disposition to targeted therapy (by diagnostic driven approach) instead of empiric treatment
Adherence to current evidence-based guidelines in the treatment of the IFDs instead of individual decision making
Appropriate antifungal prescription
Appropriate antifungal selection
Appropriate duration
Appropriate administration route
Appropriate dosage
Limited use of azoles for prophylaxis of the IFDs (only for secondary prophylaxis in patients with a previous history of IFDs)
Regular epidemiologic surveillance to estimate of fungal infection incidence and detection of any epidemiologic shift
Regular surveillance of the susceptibility pattern to antifungal drugs
Appropriate use of new diagnostic modalities (implementation of routine GM test, twice/week during prolonged and profound neutropenic phase (ANC < 500 cells/mm^3)
Improving mycological diagnostic approach with judicious use of bronchoalveolar lavage and ultrasound/CT scan guided lung biopsy (or other organs as needed)
Time-sensitive automatic stop orders for specified antifungal prescriptions
Switching from intravenous to oral antifungal, when appropriate and confirmed by the infectious disease consultant
Full-time laboratory services (24-h, 7 days per week coverage) and strategies for reducing lab turnaround time (establishing a "hotline" for contributors to call about the lab test results)
Non-medical approach to prevent fungal infections
Applying modalities to reduce the nosocomial infections (for example, diminished colonization by the appropriate use of an indwelling catheter)
Surveillance of the possible environmental roots of infection (for example, surveillance of indoor spore load in the hospital's wards)

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AFS – Antifungal Stewardship; IFDs – invasive fungal diseases; IMDs – invasive mold diseases; GM – galactomannan; ANC – absolute neutrophil count

Scientific Reports | (2021) 11:14099 | https://doi.org/10.1038/s41598-021-93421-3

AFS Program in AMOC

- Began in 2015
- Changed from empiric therapy to pre-emptive antifungal treatment strategies using non-culture based methods, such as galactomannan antigen, mannan, and PCR
- Since 2016 - Therapeutic drug monitoring (voriconazole) and antifungal susceptibility testing
- Since 2015 - Switched from fluconazole to liposomal amphotericin b for antifungal prophylaxis

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Results

Antifungal agent	Susceptibility	Period 1	Period 2[a]	p-value
Fluconazole	Sensitive	53 (67.1)	102 (100)	< 0.001**
	Resistant	26 (32.9)	0	
Caspofungin	Sensitive	94 (89.5)	101 (99.1)	< 0.001**
	Resistant	11 (10.9)	1 (0.9)	
Amphotericin B	Sensitive	83 (100)	95 (93.1)	< 0.001**
	Resistant	0	7 (6.9)	

Table 5. The susceptibility of isolated *C. albicans* against fluconazole, caspofungin, and amphotericin B, during 2011–12 (period 1) and 2017–2018 (period 2). [a]Number (%) of children colonized with *C. albicans*. [a]No fluconazole-resistant isolates of *C. albicans* was found during period 2 (2017–2018). **Statistically significant by Fisher's exact test.

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Results

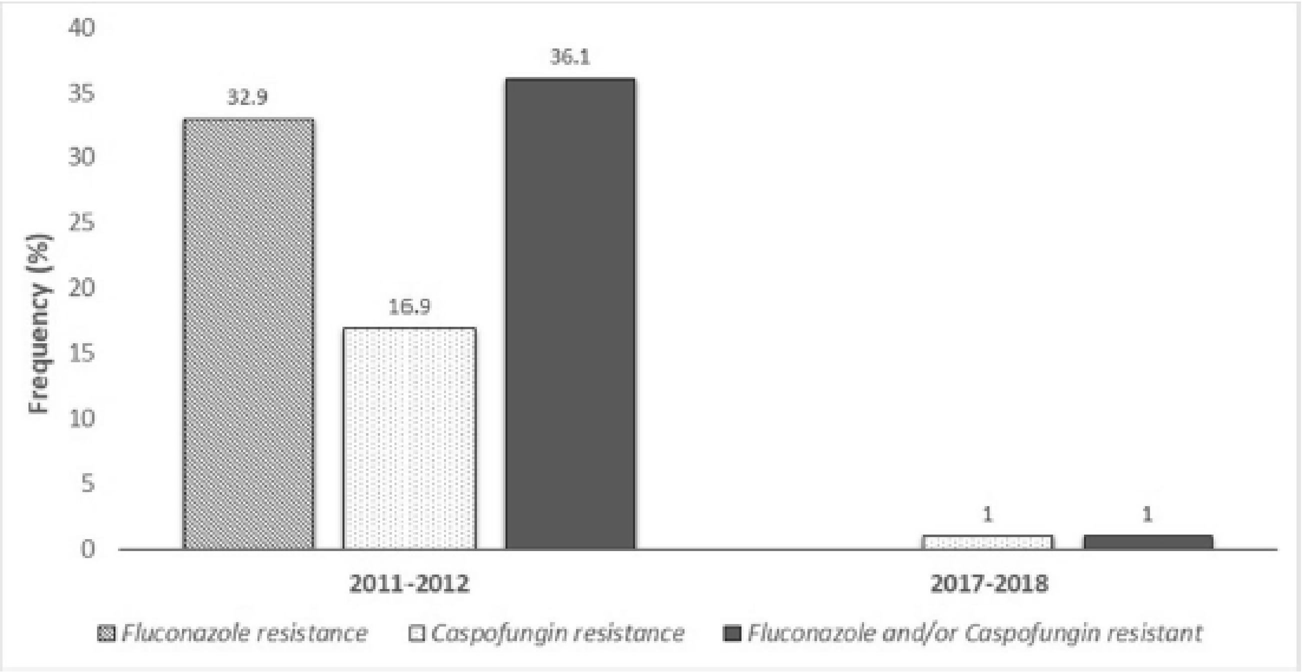

Figure 3. Frequency of fluconazole-resistant, caspofungin-resistant and fluconazole and/or caspofungin-resistant strains of *C. albicans* during the two study periods.

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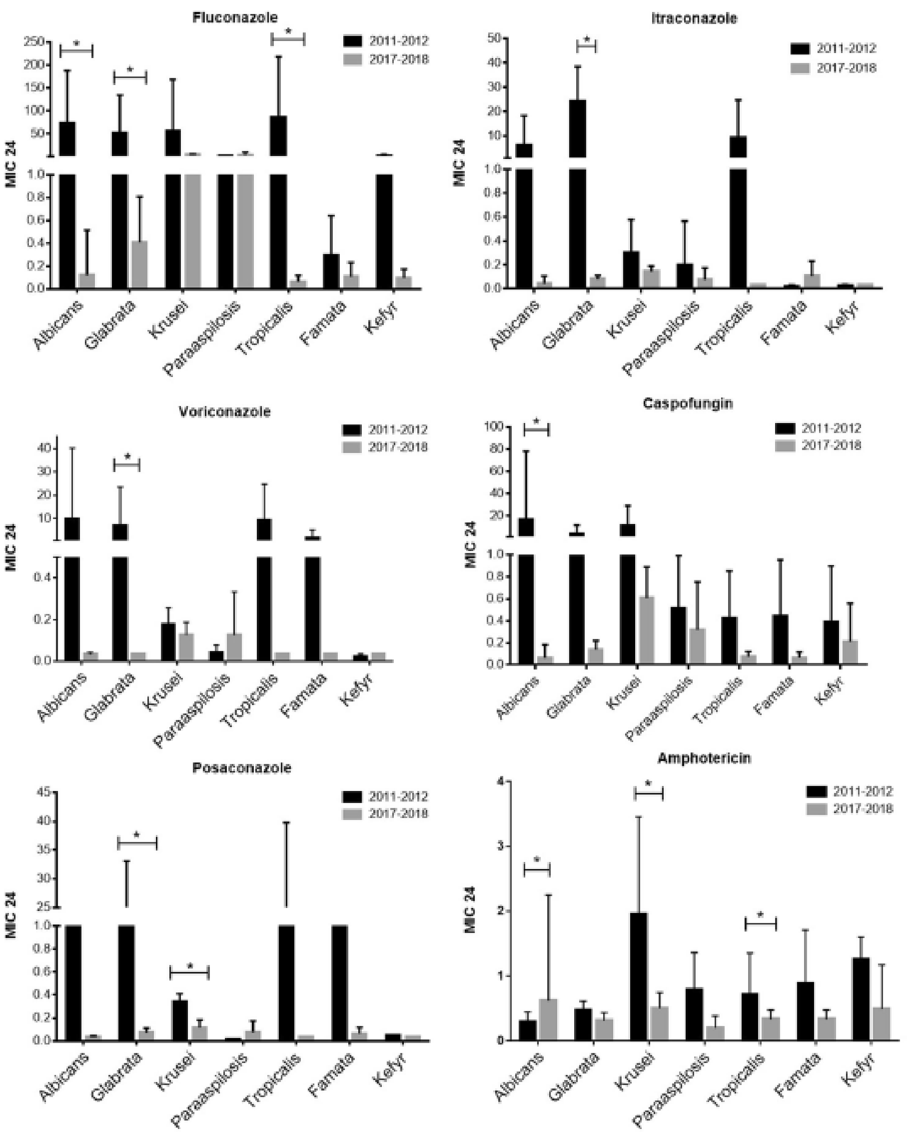

Figure 4. The mean MIC value (24-h) of *C. albicans*, *C. glabrata*, *C. krusei*, *C. parapsilosis*, *C. tropicalis*, *C. famata*, and *C. kefyr* for fluconazole, itraconazole, voriconazole, caspofungin, posaconazole, and amphotericin B, during the two study periods. Error bars represent standard deviations. $^*P \leq 0.05$ by the two-way ANOVA test.

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Antimicrobial and Antifungal Stewardship

- Many pts with *C. auris* infection/colonization have received broad-spectrum antibacterial and antifungal medications in the weeks before their first culture yielding *C. auris*
- Assessing the appropriateness of antibiotics, especially antifungals, and discontinuing them when not needed may help prevent *C. auris* colonization and infection

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