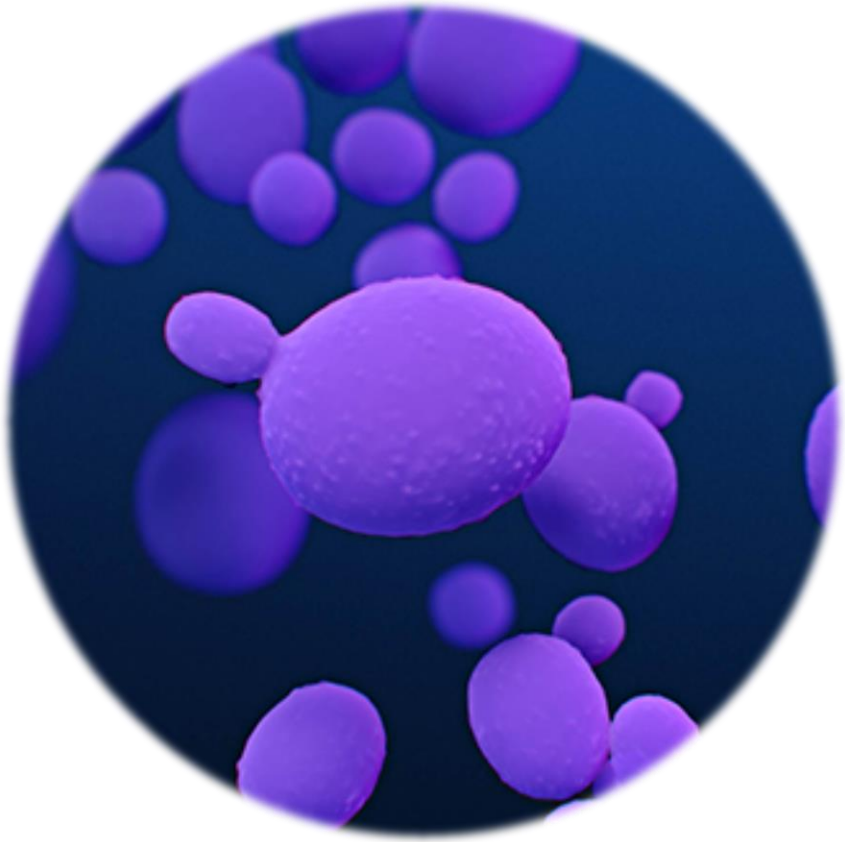
What's up with *Candida auris*?



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SA PATHOLOGY

Candida auris

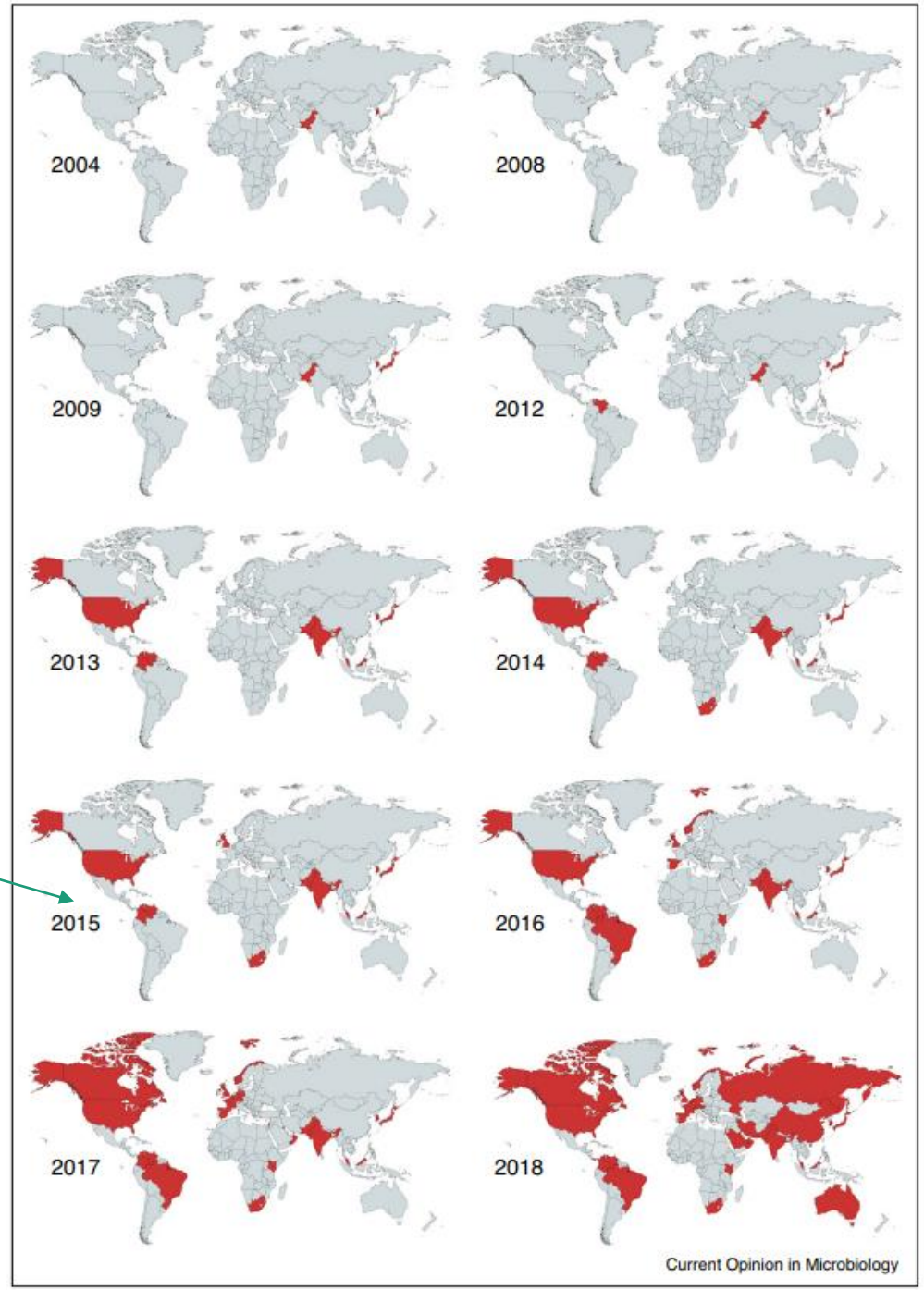
- Yeast-like fungus belonging to the Family Metschnikowiaceae.
  - Most closely related to species within the *Candida haemulonii* complex
- First isolated in Japan, c. 2009, from ear canal discharge
  - Epithet *'auris'* derived from Latin, meaning "of the ear"
  - Korean retrospective study of culture collections found 15 *C. auris* isolates, (misidentified as *C. haemulonii*), from ear samples in 2009, and 1 isolate from 1996
  - Retrospective SENTRY review identified a 2008 isolate from Pakistan
  - No evidence that it existed widely before 2009
- Colonises skin and surfaces, causing invasive disease in at-risk patient groups
- Propensity for nosocomial spread
- Highly resistant to antifungal drugs, esp. fluconazole

Satoh et al., *Microbiol and Immunol* 2009; Ong et al., *Int Med J* 2019

Global emergence

Now reported from all inhabited continents

2015: 1st Australian case
(not reported until 2018)

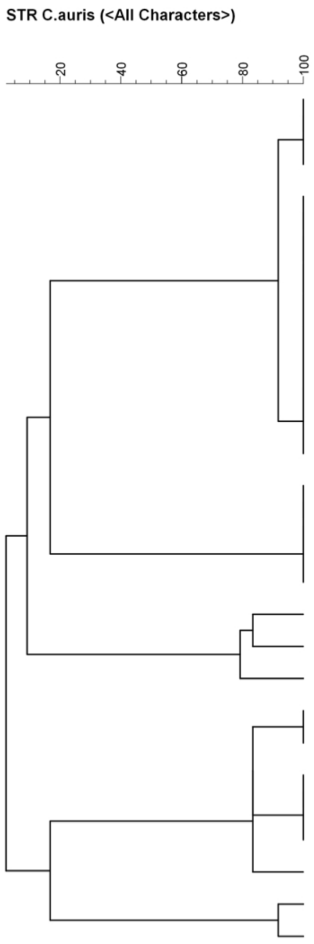


Rhodes & Fisher, *Curr Opin Microbiol*. 2019

Multiple Clades Emerged

HOT OFF THE PRESS

Clade VI "Indo-Malaysian" strain identified in Singapore in April 2023



STR C.auris

2-1	2-2	2-3	3-1	3-2	3-3	3-4	3-5	3-6	9-1	9-2	9-3	Country	Clade
66	19	9	62	10	18	36	29	22	19	11	9	United Kingdom	South-Asia (I)
66	19	9	62	10	18	36	29	22	19	11	9	United Kingdom	South-Asia (I)
66	19	9	62	10	18	36	29	22	19	11	9	United Kingdom	South-Asia (I)
66	19	9	60	10	18	36	29	22	19	11	9	Oman	South-Asia (I)
66	19	9	60	10	18	36	29	22	19	11	9	India	South-Asia (I)
66	19	9	60	10	18	36	29	22	19	11	9	India	South-Asia (I)
66	19	9	60	10	18	36	29	22	19	11	9	India	South-Asia (I)
66	19	9	60	10	18	36	29	22	19	11	9	India	South-Asia (I)
66	19	9	60	10	18	36	29	22	19	11	9	India	South-Asia (I)
66	19	9	60	10	18	36	29	22	19	11	9	India	South-Asia (I)
66	19	9	60	10	18	36	29	22	19	11	9	Oman	South-Asia (I)
66	19	9	60	10	18	36	29	22	19	11	9	Oman	South-Asian (I)
66	20	10	46	9	20	36	43	31	18	13	12	South-Africa	Africa (III)
66	20	10	46	9	20	36	43	31	18	13	12	South-Africa	Africa (III)
66	20	10	46	9	20	36	43	31	18	13	12	South-Africa	Africa (III)
66	20	10	46	9	20	36	43	31	18	13	12	South-Africa	Africa (III)
80	14	9	38	9	50	42	34	23	17	13	8	Korea	East-Asia (II)
80	14	9	38	8	51	42	34	23	17	13	8	Korea	East-Asia (II)
80	14	9	32	8	52	42	34	23	17	13	8	Japan	East-Asia (II)
58	30	24	19	23	16	31	25	7	16	8	6	Colombia	South-America (IV)
58	30	24	19	23	16	31	25	7	16	8	6	Colombia	South-America (IV)
58	30	24	18	27	16	31	25	7	16	8	6	Venezuela	South-America (IV)
58	30	24	18	27	16	31	25	7	16	8	6	Venezuela	South-America (IV)
58	30	24	18	27	16	31	25	7	16	8	6	Venezuela	South-America (IV)
58	30	25	18	23	16	31	25	7	16	8	6	Colombia	South-America (IV)
24	9	9	20	11	14	24	26	6	16	11	6	Iran (Isfahan)	Iran (V)
24	9	8	20	11	14	24	26	6	16	11	6	Iran (Babol)	Iran (V)

Clade I: "South Asian"

Clade III: "African"

Clade II: "East Asian"

Clade IV: "South American"

Clade V: "Iranian"

Safari et al., *Mycopathol* 2022; Suphavilai et al., *medRxiv* preprint Aug 2023

Deadly fungal infection spreading at an alarming rate, CDC says

NEWS

March 21, 2023

A deadly fungus with mysterious origins is raising alarms

NATIONAL GEOGRAPHIC

April 13, 2023

Deadly fungal disease may be linked to climate change, study suggests

July 23, 2019

The Washington Post

WHO fungal priority pathogens

Table 3. WHO fungal priority pathogens list

Critical group	High group	Medium group
Cryptococcus neoformans	*Nakaseomyces glabrata (Candida glabrata)*	*Scedosporium* spp.
Candida auris	*Histoplasma* spp.	*Lomentospora prolificans*
Aspergillus fumigatus	Eumycetoma causative agents	*Coccidioides* spp.
Candida albicans	Mucorales	*Pichia kudriavzeveii (Candida krusei)*
	Fusarium spp.	*Cryptococcus gattii*
	Candida tropicalis	*Talaromyces marneffei*
	Candida parapsilosis	*Pneumocystis jirovecii*
		Paracoccidioides spp.

"The new superbug on the block"

"Fungal equivalent of MRSA"

WHO Fungal Priority Pathogen List, 2022

Risk factors and transmission

- Spread via contact with colonised patients and/or contaminated environmental surfaces/equipment
- Outbreaks often due to repeated introductions of novel strains. Failure to control may require closure of the facility to effectively decontaminate.
- Risk factors for colonisation/infection
  - Hospital stay in an area with documented or suspected *C. auris* transmission
  - Prolonged hospital stay
  - Indwelling medical device
  - Mechanical ventilation
  - Impaired immune system
  - Multiple or recent exposures to broad spectrum antibiotics
  - Diabetes mellitus
  - Recent surgery
- Colonised persons should be considered as such indefinitely

https://www.health.vic.gov.au/infectious-diseases/candida-auris-c-auris
https://www.cdc.gov/fungal/candida-auris/

Clinical Aspects

- 5-10% of patients who are colonised will go on to develop BSI.
- Majority of infections occur in ICU setting
  - Mechanical ventilation
- Most reported cases manifest as fungaemia
  - Occasionally meningitis, osteomyelitis, myocarditis
  - Also UTIs, otitis, wounds
- Frequent antifungal drug resistance, inc. multi-drug/pan-resistance.
- Mortality rate 29-53%

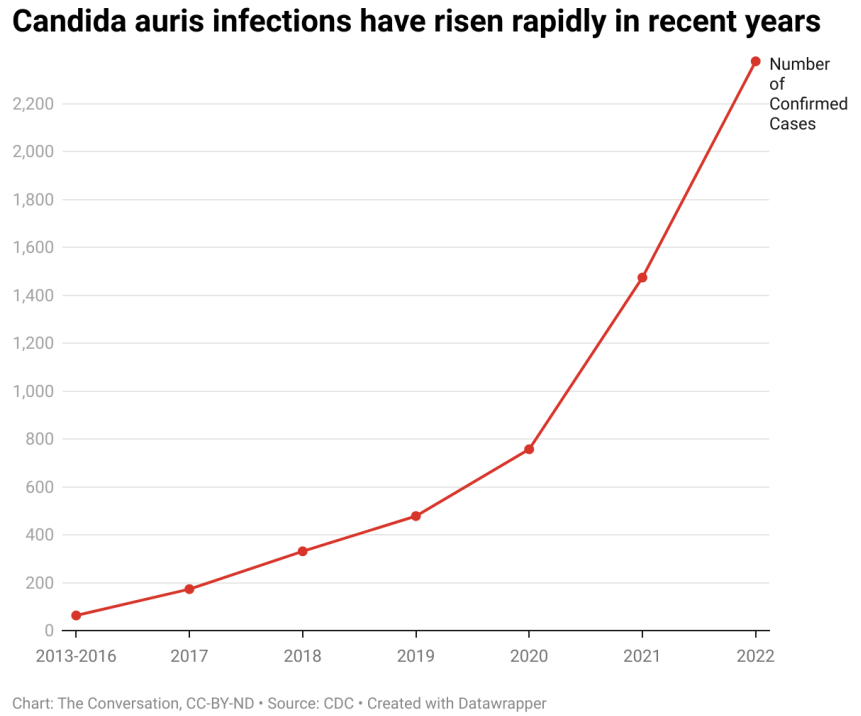
Chowdhary et al., *Annu Rev Microbiol,* 2023; Rossow et al. *Clin Infect Dis,* 2021
Biran et al., *Emerg Infect Dis,* 2023; WHO FPPL 2022

Antifungal susceptibility

- Often multi/pan-resistant to antifungals
  - Fluconazole resistance 87-100%, other azoles variable
  - Amphotericin B resistance 8-35%
  - Echinocandin resistance 0-8%
- Currently recommend susceptibility testing for all infection and colonisation cases using a broth microdilution method (this may change as cases increase)
  - Reliability of other methods unclear (e.g. Vitek 2 AST)
  - Consider referring for confirmatory testing
- No formal breakpoints yet. US CDC has released "tentative breakpoints"
  - Fluconazole R ≥ 32
  - Amphotericin B R ≥ 2
  - Micafungin R ≥ 4
  - Anidulafungin R ≥ 4
  - Caspofungin R ≥ 2

WHO FPPL 2022; https://www.cdc.gov/fungal/candida-auris/

Candida auris in USA



https://www.inverse.com/health/deadly-fungus-candida-auris-us-hospitals

- First case in 2013 (recognised 2016)
- 2019-2021:
  - 3270 clinical cases
    - Annual increases of 44% , 59% and 95%
  - 7413 screening cases 2019-2021
    - 200% increase in positive screenings in 2021
  - 7% ↑ azole resistance
  - Increasing echinocandin- and pan-resistance (but numbers remain low)
- High proportion of cases associated with long-term acute care hospitals (LTACHs) and ventilator-capable skilled-nursing facilities (vSNFs)

Lyman et al., *Ann Intern Med* 2023; Rossow et al., *Clin Infect Dis*. 2021

Candida auris in Australia

Colonisation and infections reportable to public health authorities in some Australian states
Reportable as a CARAlert (AURA) Australia-wide.

State	2019	2020	2021	2022	2023	Total
NSW	2	2		1	1	**6**
VIC	3	3	1	1	1	**9**
QLD				2	1	**3**
SA				3	4	**7**
WA	1			1	9	**11**
NT				1		**1**
ACT						**0**
TAS						**0**
Total	**6**	**5**	**1**	**9**	**16**	**37**

Data from National Alert System for Critical Antimicrobial Resistances (CARAlert) as at Oct 31, 2023.
Excludes pre-2019 cases (approx. 6)

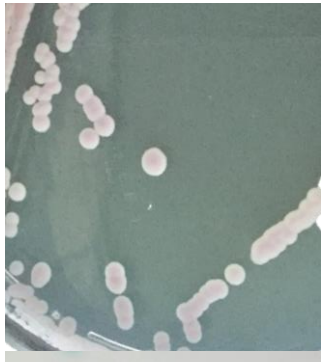
Screening and Surveillance

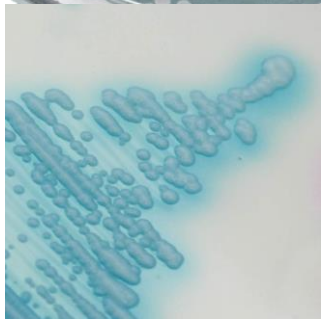
- Colonisation is prolonged (consider all patients as indefinitely colonised)
  - Risk of spread
  - Risk of invasive infection
- Consider any transfer from overseas or area of high endemicity as colonised until proven otherwise
- Screening for all patients with overnight stay in foreign healthcare facility in past 12-18 months
  - Nose/axillae/groin swabs most likely to yield *C. auris* in a colonised patient.
  - Consider also wounds and vascular access sites
- Notifiable/Reportable in NSW, SA, Tas, Vic, WA ~QLD
- Included in CARAlert surveillance program since 2019

Ong et al., *Intern Med J* 2019

Laboratory Aspects

- Avoid colonising laboratory staff and contaminating lab surfaces!
- Cultures require 10 days incubation
- Selective growth of cultured screening swabs
  - 42°C: some but not all isolates grow at 42°C (my experience) – stick to 35°C
  - Dulcitol-salt broth: CDC recommends, but difficult to get in Australia
- Chromogenic agars
  - Traditional *Candida* chromogenic agars – unremarkable appearance (i.e. white to pink colonies)
    - Need to ID all yeast colony types
  - New "Chromagar *Candida* Plus" (available Thermo Scientific, Edwards Group)
    - Colonies have distinctive turquoise halo
    - Need to confirm ID of presumptive *C. auris* colonies





Ong et al., *Intern Med J* 2019; Borman et al., *Med Mycol*, 2021.

Laboratory Aspects

- Can be difficult to identify, depending on lab resources
  - Until ~2018 *C. auris* very difficult to identify by routine methods, frequently misidentified.
  - MALDI-ToF now generally accurate
  - Vitek 2 database v8.01 identifies some, but not all clades
  - Still can not be identified by: BD Phoenix, API Biochemical strips, Microscan, RapID Yeast Plus – not represented in databases
    - Misidentified as *C. haemulonii, C. duobushaemulonii, C. famata, C. lusitaniae, C. sake, C. intermedia, Saccharomyces spp., Rhodotorula glutinis*
    - 'Identifications' above should be confirmed using MALDI-ToF or DNA sequencing, and/or referred to reference lab

Misuwaza et al., *JCM* 2017; Forsberg et al., *Med Mycol* 2018; Desoubeaux et al., *J Mycol Med* 2018; Ambaraghassi et al., *JCM* 2019

Candida auris PCR screening

- Safer than culture-based methods
  - Inactivate with lysis buffer
  - Reduced handling – risk of laboratory acquired colonisation or infection
- Rapid turn around time (24-48h) vs. culture-based screening (10 days)
- High throughput
  - Can manage clusters/outbreaks
  - Reduced scientist workload compared with culture-based methods
- High sensitivity [0.94 (95% CI: 0.92-0.95)] and specificity [0.99 (95% CI: 0.99-0.99)]
- Positive results → reflex culture for susceptibility testing, genomic characterisation

Crawford et al., *Med Mycol.*, 2022; Lin et al., *Clin Lab*. 2022

Infection Control Recommendations

Most Aus states have specific guidelines

Not currently necessary to routinely screen all patient admissions.
Screen all patients who have been treated in overseas healthcare facilities.

Interventions	Recommended actions
Identification of cases of *C. auris* (colonization or infection)	Swabs from axillae, groin, nose and, depending on the clinical situation, throat, urine, stool, wound drainage fluid, venous catheter insertion site, and respiratory tract; for patients who are not receiving antifungals, two or more evaluations, one week apart, with negative culture results. In case of healthcare-associated infections, notify the Hospital Infection Control Committee
Contact precautions or enhanced barrier precautions	In addition to individualized personal protective equipment (aprons; if necessary mouth-nose mask), isolate whenever possible (single or cohort). Special precautions must be taken if there is a high risk of contact with the body or body fluids while disinfecting exposed *C. auris* areas (details in [42]; if the patient must leave her/his room for diagnostics or therapy, it should be scheduled last for the shift, followed by environmental disinfecting cleaning
Hand hygiene	Use of alcohol-based hand rubs, monitoring compliance with the 5 WHO indications for hand rub
Environmental disinfecting cleaning	Minimal daily running disinfecting cleaning and after discharge terminal room disinfection; avoid QAC-based surface disinfectants because of uncertain effect and switch to sporocidal disinfectants (oxidants, pescetic acid, hypochlorite); to keep track of the disinfecting cleaning, keep a diary that includes date and time; follow disinfection preparation and storage guidelines, check the concentrations, and adhere to the manufacturer's declared contact time
Disinfection of mobile and reusable equipment	Proper disinfection after usage, before contact with next patient with alcohol-based or sporocidally active disinfectants
Staff allocation	Minimize the number of staff who care for *C. auris* patient. If several *C. auris* patients are present in a facility, consider cohorting staff for these patients
Patient electronic alert	Flag the patient's record to immediately start infection control measures in case of re-admission
Patients, visitors and family members	Should be informed of the importance of hand hygiene and encouraged to use protective aprons
Periodic re-assessment of patient	e.g., checking every 3 months for presence of *C. auris* in a patient with known *C. auris* colonization or infection could help determine the duration of infection control measures
Ongoing education and training	Education of all staff involved, including those working with environmental cleaning services, about *C. auris* and requirements for proper precautions, antibiotic and antifungal administration

Candida auris: a novel emerging nosocomial pathogen – properties, epidemiological situation and infection control

Caliman Sato et al., *GMS Hyg Infect Cont* 2023

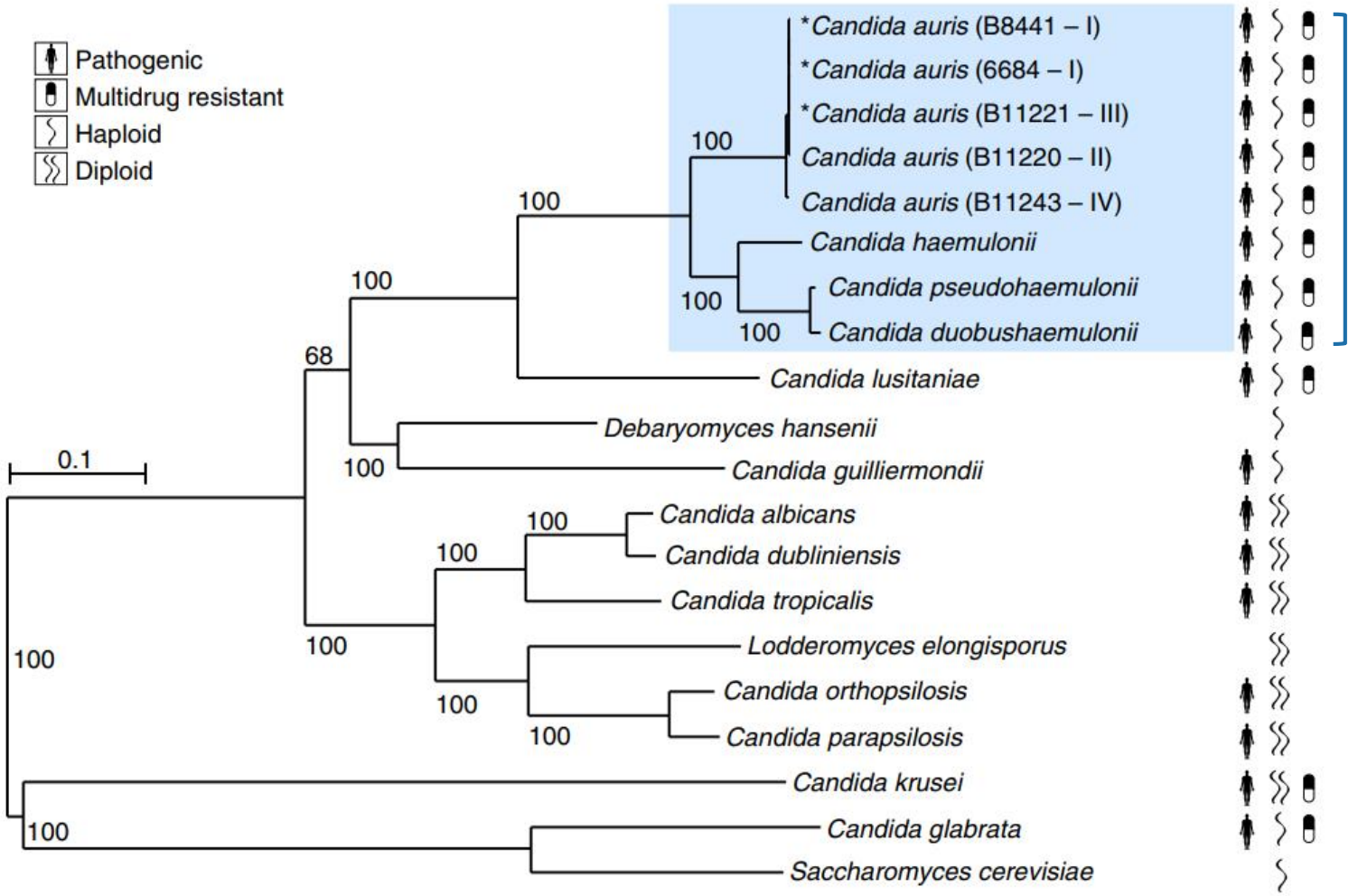
Final thoughts

Candida auris is an alarming reminder that new fungal pathogens will continue to emerge, likely in response to climate change, selective pressure from agricultural fungicide use and medical antifungals.

Think Fungus!

Spare slides

Taxonomic position



Candida haemulonii complex

Munoz et al., *Nature Comm* 2018

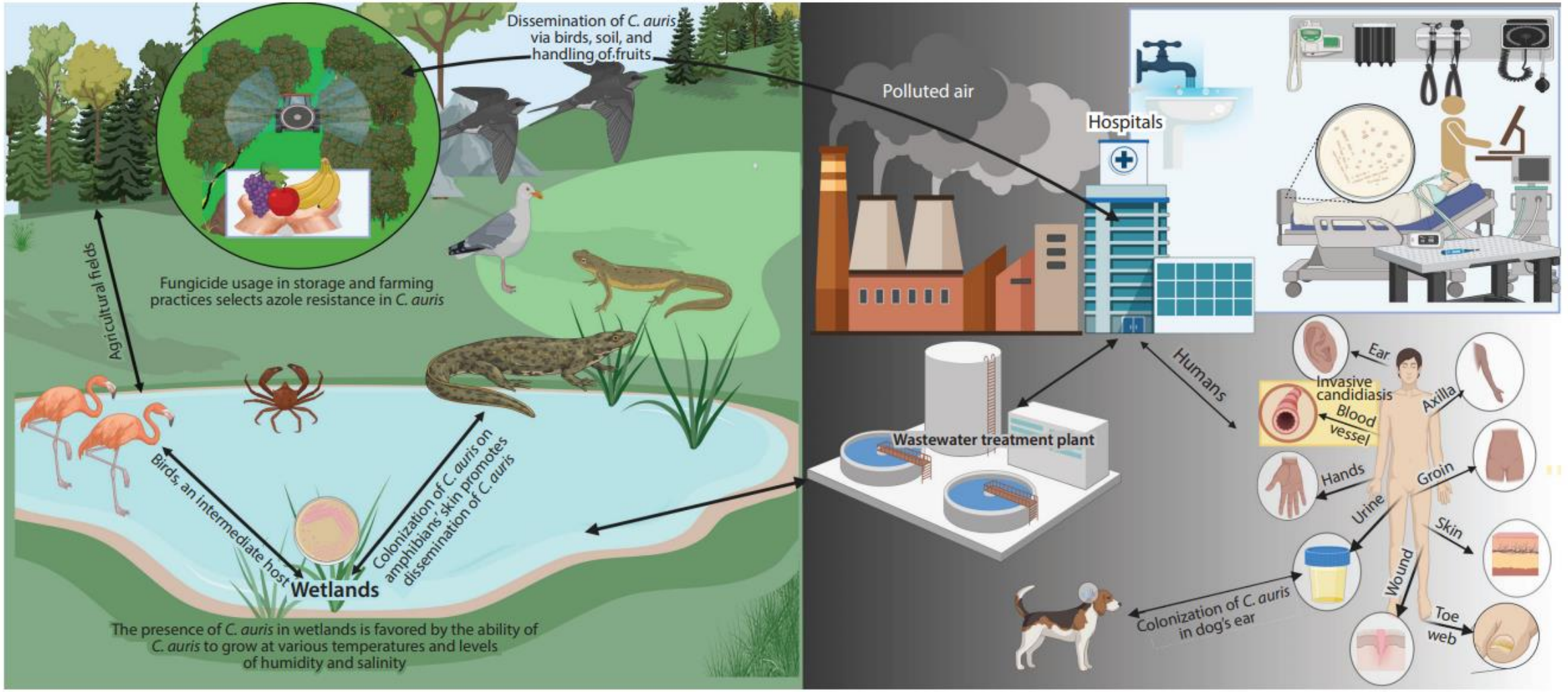


Figure 3

Schematic diagram of the possible ecological niches of *Candida auris* and its transmission to humans. *C. auris* can survive in wetlands because of its unique ability to grow at various temperatures and levels of humidity and salinity, which may have contributed to its emergence in humans. Amphibians, including species of newts, colonized with *C. auris* facilitate its transmission to other intermediate hosts, such as birds, that then spread *C. auris* within the ecosystem. Important drivers of acquisition of antifungal resistance include wide application of fungicides, which have structures similar to those of medical azoles, in stored fruits and agriculture fields. Figure adapted from images created with BioRender.com.

Chowdhary et al., *Annu Rev Microbiol,* 2023.