Candida auris (C. auris)
Frequently Asked Questions (FAQs) to Aid Clinical Laboratorians at the Bench

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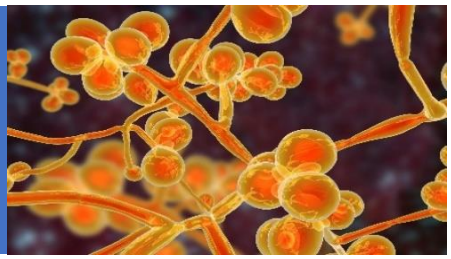

Background

C. auris is an emerging fungal pathogen that is of great concern due to increased antifungal resistance, patient mortality from infection, prolonged skin colonization, environmental contamination, and introduction to healthcare facilities through patient sharing networks. *C. auris* has become widespread in New York, New Jersey, and Illinois, causing hundreds of infections and patient deaths. Based on information from a limited number of patients, 30–60% of people with *C. auris* infections have died. However, many of these people had other serious illnesses that also increased their risk of death. Internationally, *C. auris* has become the dominant fungal pathogen in many facilities in Spain, Kenya, and other regions. Of critical importance, *C. auris* can be misidentified by commercial identification systems utilized in clinical microbiology laboratories resulting in underdiagnoses in infected patients and incomplete infection prevention measures. For example, *C. auris* was frequently misidentified as *Candida haemulonii* by MALDI-TOF until manufacturers of the MALDI instruments updated their software to include *C. auris*.

Starting in February 2019, *C. auris* has been detected in multiple healthcare facilities in Orange County. One colonized patient has been detected in Los Angeles County in June 2019. Los Angeles County has a highly complex and interconnected healthcare system. We face high likelihood of *C. auris* introduction from high burden regions of the world, including regions in the United States.

Early detection is critical to prevent dissemination of *C. auris* through healthcare systems. There are three primary strategies for detecting *C. auris;* 1) identification from clinical infections (e.g. blood cultures), 2) passive surveillance from non-sterile diagnostic specimens (e.g. urine, sputum), and 3) active surveillance (e.g. high-risk patient screening and point prevalence surveys). Each of these early detection strategies have been successfully applied in LA County and more widely in Southern California.

The CDC and Los Angeles County Department of Public Health (LAC DPH) encourage hospitals to develop an effective plan for early identification of *C. auris,* to include reviewing infection prevention strategies and laboratory protocols for yeast recovery and identification.

Scope

The generation of this FAQ document was motivated by discussions amongst the LA County Healthcare-Associated Infections and Antimicrobial Resistance Committee (LAC HAI-ARC). Its intent is to provide resources for clinical microbiology laboratories to potentially expand yeast work up and review yeast identification protocols to enhance detection of *C. auris*. Consideration and further discussion of these FAQs could inform future recommendations and guidelines for clinical microbiology laboratories.

Purpose

The purpose of this FAQ document is to provide laboratory-based questions and answers that could be used as a guidance document to help clinical laboratories determine if they are using reliable methods for recovery and identification of *C. auris.* Additionally, LAC DPH is working to standardize recommendations for yeast workup and identification in both diagnostic and surveillance specimens for which this document could be useful.

A brief summary of *C. auris* for lab workers is located here:
www.cdc.gov/fungal/candida-auris/pdf/C-Auris-Lab-Workers-FactSheet-H.pdf

FAQs

	Question	Answer
	Diagnostic Specimens	
1	From which specimen types should yeast isolates be identified to species level to rule out *C. auris?*	• All sterile site specimens • Select non-sterile site specimens. Work with your Infection Prevention team to develop a protocol for your facility and review below under Passive Surveillance.
2	Which specimen types are most likely to grow *C. auris*?	*Candida auris* has been isolated most commonly from blood and urine but has also been isolated from other specimen types from patients with clinical infection. Visit: www.ncbi.nlm.nih.gov/pmc/articles/PMC6079168/ (See Figure 3)
3	What fungal media/incubation conditions are optimal for *C. auris*?	*C. auris* will grow on Sabouraud Dextrose (Sab-Dex) agar and Candida CHROMagar at 35°C as well as at elevated temps of up to 42°C. **Note**: Check for additional guidance for specific CHROMagar, if used.
4	How long does it take a culture (blood, urine, wound, respiratory) to become positive for *C. auris* on fungal media?	*C. auris* grows on standard fungal media at the same rate (18–24 hours) as other *Candida* species.
5	Is *C. auris* likely to be recovered from routine bacterial cultures (e.g., blood, urine, respiratory, wound)?	Yes. *C. auris* demonstrates colonies similar to those of other yeast on routine bacteriological culture media. However, *C. auris* may be missed if yeast is not identified to the species level.
6	How long does it take a bacterial culture (blood, urine, wound, respiratory) to become positive for *C. auris* on routine blood and chocolate agar?	*C. auris* grows on blood and chocolate agar media at the same rate (18–24 hours) as other *Candida* species.
7	Is there a benefit to adding a fungal medium plate to routine bacterial cultures to enhance recovery of *C. auris*?	*C. auris* will grow on blood and chocolate agars, however, laboratories may elect to subculture yeast recovered on these media to fungal media (e.g., Sabouraud Dextrose). In addition, it would be good practice to include fungal media subcultures when yeast is observed in positive blood culture smears.

	Species Identification	
8	Are procedures for species identification of *C. auris* available?	Yes. Visit: www.cdc.gov/fungal/candida-auris/recommendations.html This site includes a detailed algorithm: www.cdc.gov/fungal/diseases/candidiasis/pdf/Testing-algorithm-by-Method-temp.pdf Note: Laboratories should be aware of misidentifications that are common for **their** identification platform.
9	How can a laboratory determine if they are utilizing the appropriate software/test version to reliably identify *C. auris* with their test system?	See Question #8 and if necessary, contact your device manufacturer or technical representative to obtain more information about your system, if necessary.
10	What should one do if Vitek or Bruker MALDI TOF result is "No ID"?	The isolate should be sent to the LAC DPH Public Health Laboratory (PHL) for identification. Please call LAC DPH Acute Communicable Disease Control (ACDC) Program at 213-240-7941
	Active Surveillance (colonization)	
11	What criteria might be used to determine which patients should be screened for *C. auris* colonization?	The decision on whom to screen will largely be determined by the infection prevention committee. Admission screening should be done for someone thought to be high risk for *C. auris*. Currently, LAC DPH recommends screening for: • Patients with mechanical ventilator or presence of tracheostomy admitted from an Orange County long-term acute care hospital (LTAC) or skilled nursing facility (SNF) • Patients with an overnight stay in a healthcare facility in New York, New Jersey, and Illinois • Patients with an overnight stay in a healthcare facility outside of the US in the previous 12 months, especially if that country has reported *C. auris* transmission. Countries where *C. auris* transmission has been documented is here: www.cdc.gov/fungal/candida-auris/tracking-c-auris.html • Patients with or history of carbapenemase-producing gram-negative bacillus (e.g., KPC, NDM, IMP, OXA, VIM)
12	What specimen types should be obtained to test for *C. auris* colonization?	Axilla/groin composite swabs (Eswab is acceptable). CDC's recommended procedure for collecting swabs is here: www.cdc.gov/fungal/candida-auris/c-auris-patient-swab.html
13	What culture methods are recommended for *C.auris* colonization testing?	A Salt Sab Dulcitol Broth enrichment protocol located here: jcm.asm.org/content/55/10/2996

		Note: CDC observed that direct plating methods had lower sensitivity than enrichment broth. The CDC does not recommend direct plating.
14	What are the limitations of culture methods for *C. auris* colonization?	The SSD enrichment protocol can have breakthrough growth of non - *C. auris* to include *C. parapsilosis* and some unidentifiable organisms. This breakthrough growth is minimal. TAT for broth enrichment culture is 5–7 days versus PCR at 1–3 days.
15	What molecular methods are recommended for *C. auris* colonization testing?	A real-time PCR protocol located here: www.cdc.gov/fungal/candida-auris/recommendations.html Recent Reference: Leach et al. 2018. J Clin Microbiol. 56: e01223-17 www.ncbi.nlm.nih.gov/pmc/articles/PMC5786737/
16	What are the limitations of molecular methods for *C. auris* colonization??	Some false negatives have been described. The LOD for the CDC PCR assay is low at approximately 1 CFU/PCR. As with many types of molecular assays, false positives (vs culture) can occur due to the presence with nonviable cells. **Note:** If *C. auris* is detected with molecular methods, a culture should be performed to recover the isolate for antifungal susceptibility testing and possible epidemiologic studies.
17	Since the CDC enrichment method or molecular methods described above may not be practical for a clinical laboratory, are there other in-house methods that might be appropriate to screen for *C. auris* from surveillance swabs?	Some have used direct plating to CHROMagar Candida with promising results. Considerable work is being done in this area and more information will be communicated to clinical laboratories when it becomes available.
18	Where can clinical laboratories send surveillance swabs for processing?	Surveillance swabs for patients meeting the criteria in #11 can be sent to the regional Antimicrobial Resistance Laboratory Network (ARLN). Please call LAC DPH ACDC Program at 213-240-7941 to facilitate the submission. LA County is currently unable to provide courier service for submission of swabs.
19	In addition to ARLN Regional Laboratories, what other laboratories (e.g., reference laboratories) perform testing for *C. auris* colonization?	None apparent currently.
	Passive Surveillance	
20	Which diagnostic specimens would be easiest/ most practical to screen?	Urine, however, others could be considered.

21	Are there any tricks to identify colonies more likely to be *C. auris* on routine fungal or bacteriological media?	No. There is no reliable way to visually identify *C. auris* on routine fungal or bacteriological media. The color of *C. auris* on many commercial CHROMagar media looks identical to other species of *Candida*.

	Antifungal Susceptibility Testing:	
22	If a *C. auris* is isolated from a diagnostic or surveillance specimen, should it be subjected to antifungal susceptibility testing?	Yes.
23	What antifungal susceptibility testing methods (reference and commercial) are reliable for *C. auris*?	Broth microdilution is used and Etest has been used selectively. However, there are currently no CLSI breakpoints or epidemiologic cutoff values (ECVs) specific for *C. auris*. Correlation between antifungal susceptibility test results and clinical outcomes is not known at this time. Tentative breakpoints used by the CDC for broth microdilution testing of agents recommended for testing are located here: www.cdc.gov/fungal/candida-auris/c-auris-antifungal.html
24	If antifungal susceptibility testing as recommended by CDC cannot be performed in-house, where can the isolate be sent for testing?	If the reference laboratory used by your facility can perform the recommended testing, you can send the isolate to that laboratory. Alternatively, you can send the isolate to your ARLN laboratory. Please call LAC DPH ACDC Program at 213-240-7941 to facilitate the submission. *C. auris* recovered by the ARLN laboratory from surveillance specimens submitted to them are automatically tested for susceptibility.
25	What are the expected susceptibility profiles of *C. auris*?	*C. auris* are often more resistant to antifungal agents than other *Candida* species. Approximately 90% of isolates are resistant to fluconazole and 30% to amphotericin B. Some isolates have also been resistant to echinocandins (i.e., caspofungin, anidulafungin, micafungin). Unpublished data, CDC.
	***C. auris* Prevalence**	
26	How many patients have been identified in California (and beyond) with *C. auris* infections?	Updated case counts can be found here: www.cdc.gov/fungal/candida-auris/tracking-c-auris.html
	Safe Handling of *C. auris*	
27	Are there any special recommendations for handling *C. auris* in the laboratory?	CDC recommendations for handling and disposing of *C. auris* are found here: www.cdc.gov/fungal/candida-auris/c-auris-lab-safety.html
	ARLN Submission	
28	Will submitting laboratories be charged for testing performed at ARLN?	No.

29	What information is required and where are forms available for submitting isolates or swab specimens to ARLN?	Minimum information is required unless a *C. auris* is definitively recovered from a diagnostic or surveillance specimen. Please call LAC DPH ACDC Program at 213-240-7941 to facilitate the submission and obtain the test request form.
30	Where can I find more information about ARLN?	A description of ARLN can be found here www.cdc.gov/drugresistance/solutions-initiative/ar-lab-network.html
	Other	
31	Are there guidelines for clinicians for management of *C. auris* when reported from non-sterile sites (e.g., in settings where yeast previously was not identified to species level)? How should such reports be handled?	There are no specific guidelines at this time, however, since *C. auris* can be a colonizer when recovered from nonsterile sites, the best strategy would be to suggest an Infectious Diseases consult.

Definitions	
Diagnostic specimens	specimens obtained to confirm or rule out the etiologic agent of a suspected infection.
Active surveillance specimens	specimens obtained to confirm or rule out colonization; for *C. auris*, axilla/groin composite specimens are recommended.
Passive surveillance	identification of organisms from diagnostic specimens that may or may not otherwise be identified.

References and Resources

1. Best Practices for Candida Testing in a Clinical Laboratory: an ASM-APHL-CDC Sponsored Training Webinar. (January 2019) www.pathlms.com/asm/courses/10247
2. Brooks RB, Walters M, Forsberg K, Vaeth E, Woodworth K, Vallabhaneni S. *Candida auris* in a U.S. Patient with Carbapenemase-Producing Organisms and Recent Hospitalization in Kenya. MMWR Morb Mortal Wkly Rep 2019; 68:664–666.
3. *Candida auris*: Is it here to stay? APHL webinar. (September 2019)
4. CDC Website *Candida auris:* www.cdc.gov/fungal/candida-auris/index.html
5. Jeffery-Smith, A et al. 2018. *Candida auris*: A Review of the Literature. Clin Microbiol Rev. 31: e00028–17.
6. Spivak, ES and KE Hanson. 2018. *Candida auris*: An Emerging Fungal Pathogen. J Clin Microbiol. 56: e01588–17. www.aphl.org/training/Pages/public-health-webinars.aspx