

CDC Alert for Hospital Infections due to *Candida Auris* Multiresistant

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Abstract

The Centers for Disease Control and Prevention (CDC) has received reports from international health centers that *Candida auris* multi-drug resistant yeast is causing health-associated invasive infections with high mortality. Some strains of *C. auris* have high minimum inhibitory concentrations (MIC) to the three main classes of antifungals, severely limiting treatment options. *C. auris* requires specialized methods for its identification and could be mistakenly identified as another yeast when the procedure is based on traditional biochemical methods. The CDC is aware that a strain of *C. auris* was detected in the United States in 2013 as part of ongoing surveillance. The experience outside the United States suggests that *C. auris* has a high potential to cause outbreaks in health centers. Given the presence of *C. auris* in nine countries on four continents since 2009, the CDC is alerting health centers in the United States to be on the lookout for *C. auris* infections in patients.

Background

Candida auris is a multi-drug emergent yeast (MDR) that can cause invasive infections and is associated with high mortality. It was first described in 2009 after being isolated in the secretion of the external ear of a patient in Japan¹. Since the 2009 report, *C. auris* infections, specifically fungemia, have been reported in South Korea², 3 India, South Africa⁴, and Kuwait⁵. Although published reports are not available, *C. auris* It has also been identified in Colombia, Venezuela, Pakistan and the United Kingdom. It is unknown why *Candida auris* has recently emerged in so many different places. The molecular typing of the strains carried out by the CDC suggests that the isolated elements are highly related within a country or region, but in different continents⁶.

The earliest known infection with *Candida auris*, based on retrospective tests, occurred in South Korea in 1996. *Candida auris* may not represent a new organism as well as one that has recently appeared in various clinical settings. Although the causes of such an emergency are unknown, they may include new selective or increasing pressures by the use of antifungals in humans, animals or the environment. *Candida auris* infections have been more commonly acquired in the hospital and occurred after several weeks

of hospital stay in a patient. It has been reported that *Candida auris* causes bloodstream infections, wound infections, and otitis². It has also been cultured from the urine and respiratory tract; however, it is unknown whether the isolation of these sites has represented infection or colonization in each case. It has been documented that *Candida auris* can cause infections in patients of all ages. It was found that patients have risk factors similar to those described for infections with other varieties of *Candida* spp.^{6, 7}, including: diabetes mellitus, recent surgery, recent antibiotics, and the presence of central venous catheters.³ Co-infection with another variety of *Candida* spp. Has also been reported. and of *Candida auris* while the patient was being treated with antifungals. Two Although there are no cut-off points for the minimum inhibitory concentration (MIC) established for *Candida auris* at this time, the resistance test of an international collection of isolated microorganisms performed by CDC showed that almost all are highly resistant to fluconazole on the basis of the cut-off points established for other varieties of *Candida* spp. More than half of the *Candida auris* isolates were resistant to voriconazole, one third were resistant to amphotericin B (MIC ≥ 2), and a few were resistant to echinocandins. Some strains have demonstrated high minimum inhibitory concentrations for

the three main azole antifungal classes, including, echinocandins, and polyenes, indicating that treatment options would be limited. *Candida auris* is phenotypically similar to *Candida haemulonii*. Commercially available biochemical-based tests, including API and VITEK-2 strips, which are used in many US laboratories to identify fungi, cannot differentiate *Candida*

auris from other related species. Due to these challenges, clinical laboratories have mistakenly identified the organism as *Candida haemulonii* and *Saccharomyces cerevisiae*. Some clinical laboratories do not fully identify all *Candida* species, and isolation of *Candida auris* has been reported as "another *Candida* spp." Clinicians, the State and public health laboratories must be

aware of the presence of this organism and of the limitations of its identification. At least two countries have already described outbreaks of health infection by *Candida auris* and colonization involving more than 30 patients each. The analysis of the isolates of these groups demonstrates a high degree of clonality within the same hospital, this supports the idea that organisms are transmitted within these health centers. The precise mode of transmission within health care facilities is not known. However, the experience during these outbreaks suggests that *Candida auris* could contaminate the environment of the rooms of colonized or infected patients. Good infection control practices and cleanliness of the environment can help prevent transmission (Figure 1).

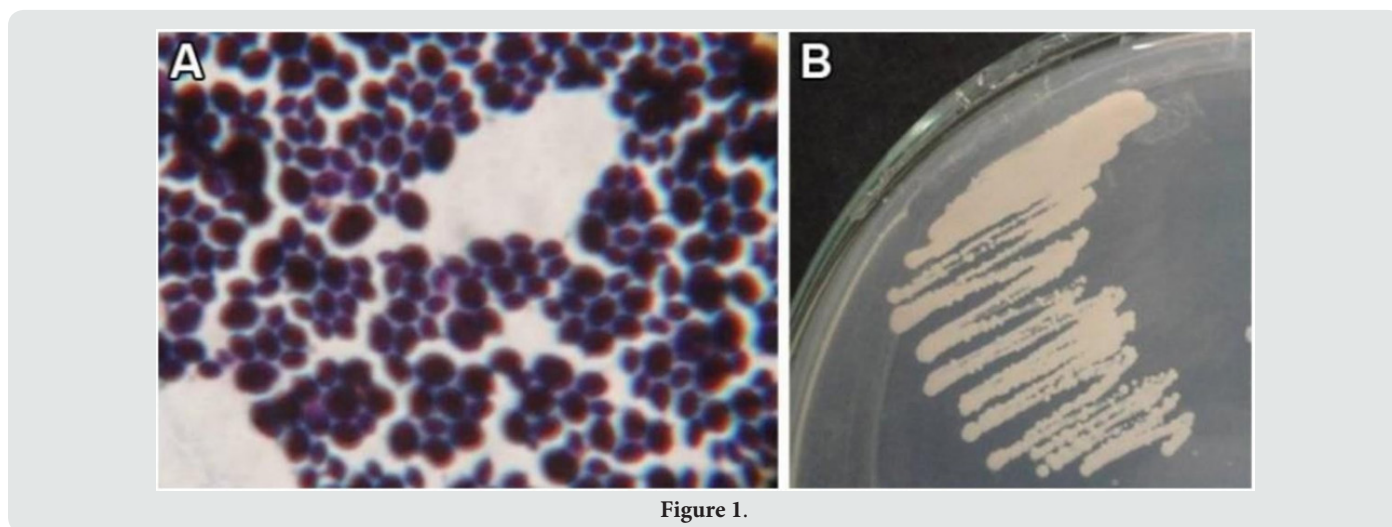


Figure 1.

Interim Recommendations

The CDC is concerned that *Candida auris* will appear in new places, including the United States. The CDC and its partners continue to work closely, and new information will be provided as soon as it becomes available. CDC recommends the following actions for installation and United States health laboratories: Health centers that suspect that they have a patient with *Candida auris* infection should contact the state / local public health authorities and the CDC (candidaauris@cdc.gov) - Reporting. Laboratory diagnosis: Diagnostic devices based on the desorption / ionization laser-assisted matrix or MALDI-TOF can differentiate *Candida auris*, but not all devices currently include the *Candida auris* in their reference database to allow detection. Molecular methods based on the sequencing of the D1-D2 region of 28S rDNA can also identify *Candida auris*. The CDC made requests to laboratories that identify *Candida auris* in the United States to notify their state or local health departments and the CDC (candidaauris@cdc.gov). Infection Control: Until more information becomes available, health centers should place patients with colonization or *Candida auris* infection in individual rooms and health personnel should use standard precautions for contact precautions. In addition, state or local health authorities and CDC should be consulted about the need for additional interventions to prevent transmission. The CDC is working with national and international partners to develop a

definitive infection control guide. Cleanliness of the environment: Anecdotal reports suggest that *Candida auris* can persist in the environment. Health centers that have patients with infection or colonization by *Candida auris* should guarantee the daily cleaning in depth and the disinfection of the rooms of these patients using a disinfectant for hospital use registered by the EPA with a warning for fungi.

Conclusion

Antifungal resistance of *C. auris*: There are still no cut-off points for the susceptibility of *C. auris* to antifungals. This species is highly resistant to fluconazole (MIC 90 > 64 mg / L) and one third of the isolates have an elevated MIC to voriconazole (≥ 2 mg / L) and amphotericin B. Few strains have high MICs to echinocandins. Its profile of resistance to the three large families of antifungals limits the therapeutic alternatives. This species is genetically related to *C. haemulonii*, which has intrinsic resistance to amphotericin B and fluconazole. So far, the mechanisms of resistance are not clearly known. Apparently, it would be inducible by selection pressure producing rapid mutational changes. A recent genetic study showed that this species would have unique copies of several genes related to resistance to antifungals such as ERG3, ERG11, FKS1, FKS2 and FKS3 as well as a higher proportion of genes from families of transporters ABC and MSF (efflux pumps), that could

explain multiresistance. It is probable that the unmediated use of antifungals has resulted in the emergence of *C. auris* as a successful multi-resistant pathogen. Given the high MICs to amphotericin B, echinocandins should be used as first line therapy, with antifungal susceptibility test. In addition, antifungal susceptibility should be monitored in patients infected or colonized by this agent. The potentially devastating impact of invasive infections by this multi-resistant species in both patients and clinical services should not be underestimated. It is necessary to continue contributing

information to the knowledge of the global epidemiology of this emerging infection and how to prevent it.

References

1. Shawn Lockhart, an expert on fungal infections at the Centers for Disease Control and Prevention with a microscope slide of *Candida auris*.
2. National Center for Emerging and Zoonotic Infectious Diseases.
3. Matthew Fisher, Professor of Epidemiology of Fungal Diseases at Imperial College London (London Imperial School).
4. Ilie Vasiliev, Vice President WAMS.



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