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COMMENTARY

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Public health issues with *Candida auris* in COVID-19 patients

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Abstract

The ongoing pandemic of coronavirus disease 2019 (COVID-19) has overwhelmed a number of medical facilities as well as a few entire health-care systems. A novel issue co-incident with the expeditious deployment of specialty care units for COVID-19 inpatients is the worldwide epidemic of *Candida auris* infections. Since its first identification and classification in Japan in 2009, it has spread globally. This threat was predicted as *C. auris* has a high mortality rate, cryptic fomite spread, frequent misidentification since conventional methods do not detect it, and multidrug-resistance. Since the April 2020 warning at the start of the COVID-19 pandemic in the United States, *C. auris* has been delineated as an increasingly consequential source of significant nosocomial infections, emphasizing the added hazard of *C. auris* to COVID-19 inpatients, particularly those in intensive care units.

KEYWORDS

Candida auris, COVID-19, nosocomial infections

INTRODUCTION

The worldwide epidemic of nosocomial *Candida auris* and efforts to interrupt it remain problematic, a threat to overwhelm COVID-19 facilities in high impact areas, with *C. auris* a potentially silent killer unrecognized and neglected (Iguchi et al., 2019; Satoh et al., 2009; Schwartz & Kapila, 2020) (Table 1). Since its first identification and classification in Japan in 2009 (Satoh et al., 2009), this ascomycete yeast has spread globally to more than 40 countries, being easily transmissible. This threat was predicted in early 2020 in an article entitled "Cutaneous Manifestations of a 21st Century Worldwide Fungal Epidemic Possibly Complicating the COVID-19 Pandemic to Jointly Menace Mankind" (Schwartz & Kapila, 2020), as *C. auris*

TABLE 1 *Candida auris*: Global epidemic now!

Multidrug resistant
Requires special equipment to diagnose
Fomite spread rapid: linen, windows, floors
Nosocomial threat
Cryptic killer in ICUs

has a high mortality rate, cryptic fomite spread, frequent misidentification since conventional methods do not detect it, and multidrug-resistance. Since this warning at the start of the COVID-19 pandemic in the United States, *C. auris* has been delineated as an increasingly consequential source of significant nosocomial infections, emphasizing the added hazard of *C. auris* to COVID-19 inpatients. *C. auris* is an unusual pathogenic fungus in that it is a nosocomial environmental colonizer that persists for days to weeks on objects such as dry linen, bedrails, beds, air conditioner ducts, blood pressure cuffs, windows, and floors with risk factors including severe concurrent medical conditions with ICU admission and/or mechanical ventilation (Keighley et al., 2021).

GLOBAL EPIDEMIC

COVID-19/*C. auris* coinfections are now being documented worldwide (Allaw et al., 2021; Chowdhary et al., 2020; Interim Guidance on Management of Coronavirus Disease, 2019; Prestel et al., 2021; Villanueva-Lozano et al., 2021; Yadav et al., 2021). This outcome is unsurprising, given colonization of hospitalized patients, potential for person-to-person spread from colonized and infected patients to facilitate outbreaks, with shedding of viable yeast cells onto environmental surfaces in rooms of those colonized or infected by *C. auris* (Yadav et al., 2021). However, such identification may not be easy, as it usually requires matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS) (Keighley et al., 2021), with some reference databases included in MALDI-TOF devices not providing detection although others are updating their databases (Interim Guidance on Management of Coronavirus Disease, 2019; Yadav et al., 2021). The *C. auris* outbreak in a COVID-19 Specialty Care Unit in Florida, July–August 2020, included 67 patients and found 35 (52%) with *C. auris* (Prestel et al., 2021). The mean age of affected patients was 69 years (range: 38–101 years); 60% were men. However, at this point it is unclear if *C. auris* contributed to the high mortality rate among these COVID-19 patients. Similar outbreaks were recently highlighted in a COVID-19 hospital in Monterrey, Mexico (Villanueva-Lozano et al., 2021). *C. auris* strains belonging to twelve patients and three environmental isolates from their bedrooms were identified by MALDI-TOF MS. *C. auris* strains from 12 patients and three environmental isolates from their bedrooms were identified by the same method and confirmed by multi-locus sequence typing. In New Delhi, India *C. auris* affected 15 critically ill COVID-19 patients, with isolates also identified by MALDI-TOF MS (Chowdhary et al., 2020). Fourteen patients with *C. auris* in a Lebanese tertiary-care center were documented using MALDI-TOF MS, half of whom had COVID-19 before isolation (Allaw et al., 2021). Critically ill COVID-19 patients with *C. auris* were also described in Italy using MALDI-TOF MS (Magnasco et al., 2021). Newly identified *C. auris* cases in southern California more than doubled from 15 in May to 40 in June with 73 in July 2020. In August 2020 the California Department of Public Health issued a health advisory entitled "Resurgence of *C. auris* in Healthcare Facilities in the Setting of COVID-19," emphasizing

TABLE 2 *Candida auris*: Approaches!

- Evaluation for shedding yeast cells from colonized or infected tissue
- Requires matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS) specially programmed to diagnose
- Swab of bilateral axilla and groin for contacts
- Colonized with *C. auris*, possibly indefinitely
- Resistant to fluconazole, often amphotericin B, and sometimes to echinocandins

the need for vigilance and reporting within 1 day (Health and Human Services Agency, 2020). It suggested that personal protective equipment conservation strategies and other practices for COVID-19 status alone might be contributing to this resurgence of *C. auris* and advocated particularly stringent protective methods. Furthermore, it recommended speciating all Candida isolates from normally sterile sites and from non-sterile sites for those at highest risk for *C. auris*. CDC recommends strict isolation of those who are either colonized by or treated for *C. auris* (Infection Prevention and Control for *Candida auris*; Identification of *Candida auris*; Screening for *Candida auris* Colonization https://www.cdc.gov/fungal/candida-auris/c-auris-screening.html). One should employ a composite swab of bilateral axilla and groin in close contacts of those with *C. auris* infection or colonization (Screening for *Candida auris* Colonization) (Table 2). Unfortunately, patients generally remain colonized with *C. auris*, possibly indefinitely. However, the emergence of resistant fungi, such as this multidrug-resistant one, has provided impetus to programs of antifungal stewardship (Capoor et al., 2019; Chowdhary & Sharma, 2020; De Carolis et al., 2021; Kara et al., 2021). Major challenges in the management of *C. auris* infections include the common misidentification of *C. auris* using conventional laboratory techniques and the pathogen's resistance profile, which includes resistance to commonly utilized antifungals. In addition, hospitalization with prolonged use of systemic steroids may also be a predisposing factor (de Almeida et al., 2021). After all, COVID-19 infections can be associated with other invasive candidiasis, other fungi, and other organisms (Al-Hatmi et al., 2020; Lansbury et al., 2020; Salehi et al., 2020).

DIAGNOSING *C. AURIS*

C. auris shares important characteristics with other less dangerous and more common candida species, resulting in frequent misidentification with traditional phenotypic and biochemical methods and rendering under-recognition and limited screening a strongly possibility (Iguchi et al., 2019; Interim Guidance on Management of Coronavirus Disease, 2019; Keighley et al., 2021; Yadav et al., 2021). Unrecognized, *C. auris* may persist on environmental surfaces for weeks, facilitating spread among patients in health care facilities. Thus, if an outbreak occurs, controlling the situation may become extremely difficult. Since conventional methods do not provide the diagnostic speciation, other approaches often not readily available are needed, such as internally transcribed spacers, D1/D2 regions of the 26S rDNA sequencing, and/or MALDI-TOF MS, the latter method the most rapid, reliable, and commercially available (Iguchi et al., 2019; Identification of Candida auris; Interim Guidance on Management of Coronavirus Disease, 2019; Villanueva-Lozano et al., 2021; Yadav et al., 2021). Unfortunately, it is often not employed due to the cost of the mass spectrometer. In California *C. auris* identification and confirmation is available through some

public health laboratories with colonization screening for *C. auris* at no cost through the CDC Antibiotic Resistance Laboratory Network (Health and Human Services Agency, 2020).

There is a significant global health challenge owing to the ability of *C. auris*, which is multi-drug resistant, to colonize and to persist in seemingly inimical environments, leading to nosocomial outbreaks, and thereby endangering already acutely ill individuals due to the high mortality rates associated with *C. auris* itself. Since both *C. auris* and COVID-19 have been found on hospital surfaces including on bedrails, hospital floors, chairs, and mobile phones (Prestel et al., 2021; Schwartz & Kapila, 2020; Villanueva-Lozano et al., 2021; Yadav et al., 2021), one anticipates fomites would also include critical care instrumentation. A recent *Morbidity and Mortality Weekly Report* warning, issued by the U.S. Department of Health and Human Services, is cogent. As a matter of public policy, hospitals must have ready access to the specialized technology needed to diagnosis *C. auris*, which otherwise might be considered a less pernicious species of candida. After all, nosocomial *C. auris* is a threat for a number of reasons, as a serious infection with a high mortality rate, one difficult to identify with standard laboratory methods, challenging to treat, already widespread geographically; it is increasing in prevalence, tends to persist in the environment and is a concern, especially for those with diabetes mellitus, immunosuppression, or chronic kidney disease (Keighley et al., 2021; Schwartz & Kapila, 2020; Yadav et al., 2021).

MOVING FORWARD

We propose a policy that documents the presence or absence of this invasive Candida species in intensive care units during and after this COVID-19 pandemic, with each medical facility undertaking the task of monitoring for the prospectively lethal combination of COVID-19 and *C. auris*, as recommended by the California Department of Public Health (Health and Human Services Agency, 2020). Each medical facility with the potential of infection or colonization with *C. auris* demands close monitoring, as this nosocomial threat is comparable to COVID-19 itself (Schwartz & Kapila, 2020). The identification of *C. auris* compels use of advanced machinery with isolation and other precautions becoming all-important and needed to be documented as readily available.

In essence there are two concerns: identification of *C. auris* and enhanced transmission in health-care settings, as documented in the Florida outbreak (Prestel et al., 2021). Fundamentally, effective measures need to be instituted to reduce or prevent the transmission of *C. auris* in COVID-19 ICUs. Ultimately, the conquest of both COVID-19 and *C. auris* probably depends on effective global vaccination programs, with the former an accomplished fact and the latter showing potential promise in murine models (Infection Prevention and Control for *Candida auris*). Hopefully, a rapid and inexpensive method will be developed for *C. auris* detection, facilitating matters. The goal is to render this COVID-19 pandemic and the *C. auris* epidemic into history (Identification of *Candida auris*https://www.cdc.gov/fungal/candida-auris/identification.html). However, hospitalizations with *C. auris* colonized patients for extended periods seem likely, with multiple genotype monitoring of *C. auris* a good idea (de Almeida et al., 2021). High occupancy burdens with limited resources for infection control plus prolonged usage of personal protective equipment due to shortages or monetary costs, will likely facilitate spread and *C. auris* colonization and/or infection.

The threat of *C. auris* for COVID-19 patients in intensive care units requires emphasis. The transmission of *C. auris* in COVID-19 facilities has been enhanced by difficulty in grouping of these patients and inability to provide routine surveillance in COVID-19 patients. Furthermore, lack of best options for compliance with hospital infection prevention policies have resulted in repeated hospitalization and continued *C. auris* colonization. Additionally,

TABLE 3 *Candida auris:* Future prospects

- CHROMagar™ Candida Plus: a novel chromogenic agar for rapid identification
- NDV-3A vaccine protects mice from *C. auris*, hopefully human soon
- Rapid identification using MALDI-TOF Mass Spectrometry
- Prompt antifungal resistance detection using MALDI-TOF Mass Spectrometry

multiple genotypes of *C. auris* colonize patients in post COVID facilities (Yadav et al., 2021). Whole genome sequencing and microsatellite typing revealed that multiple strains contaminated the fomites and colonized different body sites of patients. Notably, 10% of fomite samples contained *C. auris* in rooms about 8.5 days after *C. auris* colonized patients were admitted and 37% of *C. auris* isolates were resistant to amphotericin B. *C. auris* is typically resistant to fluconazole, often to amphotericin B, and sometimes to echinocandins, leaving physicians with few therapeutic options (Chowdhary & Sharma, 2020; Chowdhary et al., 2020; de Groot et al., 2021; Giacobbe et al., 2021). An echinocandin is recommended initial therapy for infection with *C. auris* (Infection Prevention and Control for *Candida auris*). Topical antifungals should be considered too, particularly for cutaneous erosions or skin colonized with *C. auris*. *C. auris* is susceptible to medical-grade honey and local unprocessed honey in vitro, which may represent be a promising therapeutic option (de Groot et al., 2021).

FUTURE PROSPECTS

Future prospects for addressing this fungus, whose natural environmental habitats may include coastal wetlands (Arora et al., 2021), include a new and novel chromogenic agar for rapid identification of *C. auris* (Borman et al., 2021; Keighley et al., 2021), a vaccine that protects humans from *C. auris* (Singh et al., 2019), and rapid identification and antifungal resistance detection using MALDI-TOF MS (De Carolis et al., 2021) (Table 3). Certainly, once this fungus is diagnosed, aggressive screening efforts plus vigorous hand hygiene, use of single-patient room isolation, contact precautions, and elimination of *C. auris* from both patients and environment are mandatory for infection control (Carlton et al., 2020; de Groot et al., 2019; Infection Prevention and Control for *Candida auris*; Identification of *Candida auris*; Pearlmutter et al., 2021; Prestel et al., 2021; Schwartz & Kapila, 2020; Screening for *Candida auris* Colonization). Determining the clade of the *C. auris* infection may have practical value, emphasized by preliminary findings that isolates from clades III and IV were less susceptible to ultraviolet-C (UV-C) than clade I and II isolates utilizing relatively low-cost UV-C devices (Pearlmutter et al., 2021). After patient discharge, room turnover procedures should include cleaning of all surfaces and floors plus ultraviolet disinfection. We strongly favor good ventilation and UV-C decontamination for both COVID-19 and for *C. auris* (Allaw et al., 2021; Chowdhary et al., 2020; Infection Prevention and Control for *Candida auris*; Identification of *Candida auris*; Schwartz & Kapila, 2020; Screening for *Candida auris* Colonization https://www.cdc.gov/fungal/candida-auris/c-auris-screening.html), which should constitute an important adjunct to vigorous fomite cleaning. Pandemics are here to stay (Schwartz & Kapila, 2021), as is *C. auris*, with their impacts hopefully minimized with effective responses.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

ETHICS STATEMENT

Ethics approval was not required for this scoping review. This article is entirely the authors' own work, which has not been previously published in any form elsewhere.

AUTHOR CONTRIBUTIONS

Conceptualization and writing: Edmund J. Janniger and Rajendra Kapila

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