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First case of *Candida auris* in Switzerland: discussion about preventive strategies

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Introduction

Candida spp. are a major cause of bloodstream infections associated with high mortality. The epidemiology of *Candida* infections is evolving, with a progressive shift from *Candida albicans* to non-albicans *Candida* spp. characterised by decreased susceptibility to azoles [1]. Most concerning is *Candida auris*, a previously unrecognised *Candida* species, which emerged as a novel cause of candidaemia and invasive candidiasis in 2009 [2, 3]. This new fungal pathogen is a serious public health problem because of its potential for nosocomial transmission and its ability to develop resistance to all antifungal drug classes [2, 4]. Outbreaks of strains with different clonal origins have been reported from all continents [2, 4]. *C. auris* has become the fifth most common cause of candidaemia in India and multiple cases have been reported in Pakistan, South Korea, Israel, Kuwait, South Africa, Kenya, United States, Colombia and Venezuela [4, 5]. In Europe, major outbreaks have occurred in London (UK) and Valencia (Spain) [6, 7]. However, *C. auris* has rarely been reported in other European countries, where it has been isolated only from travellers from endemic regions [4]. This epidemiological situation raises important concerns about strategies that should be implemented to prevent the importation and spread of *C. auris* in countries that are currently spared. We present here an update of the situation in Switzerland and our recommended approach in terms of preventive strategies.

Candida auris in Switzerland

In Switzerland, the first case of *C. auris* was documented in Geneva in October 2017. A 74-year-old female who was on vacation in north-eastern Spain was admitted to a local hospital with severe community-acquired pneumonia requiring mechanical ventilation. *C. auris* was isolated from tracheal aspirates and the patient was treated with meropenem and fluconazole. At day 18 of the hospital stay, she was transferred to Geneva with acute respiratory distress syndrome. Screening at various sites (tracheal aspirates, groin, auditory canal, urine) was positive for *C. auris*, whereas multiple sets of blood cultures were negative for yeasts. After initial improvement and antibiotic discontinuation, the patient developed septic shock of unknown origin and ultimately died. *C. auris* was considered as a coloniser and was probably not the cause of this fatal outcome. *C. auris* was identified with MALDI-TOF, with subsequent confirmation by sequencing of the internal transcribed spacer (ITS) region. Antifungal susceptibility testing with Sensititre YeastOne™ (Trek Diagnostics Systems) showed minimum inhibitory concentrations (MICs) of 256, 4, 1, 0.06, 0.12, 0.06 µg/ml for fluconazole, voriconazole, amphotericin B, caspofungin, anidulafungin and micafungin, respectively. The patient was placed on contact precautions, and her room was cleaned with a chlorine-based solution and an active oxygen-based surface disinfectant after discharge. Multiple environmental samples obtained from the room after cleaning were all negative for *C. auris*.

We retrospectively analysed the national cohort of candidaemia of the Fungal Infection Network of Switzerland (FUNGINOS) comprising 2102 *Candida* bloodstream isolates collected from 25 Swiss hospitals between 2004 and 2013. *C. auris* was not recovered during this period. All isolates belonging to species closely related to *C. auris*, which may have been potentially misidentified (four *Candida famata*, two unspecified *Candida* spp. and five *Saccharomyces cerevisiae*), were retrospectively tested by mass spectrometry (matrix-assisted laser desorption ionisation-time of flight, MALDI-TOF) for confirmation.

Recommendations for microbiology laboratories

Accurate and rapid identification of *C. auris* is crucial. *C. auris* is misidentified by classical biochemical methods. Vitek 2 YST (BioMérieux) and Phoenix (BD Diagnostics)

Author contributions
AR and DN contributed equally to the work.
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cannot distinguish it from other *Candida* of the *haemulonii* complex, *C. famata, C. lusitaniae and C. sake.* API-20C AUX (BioMérieux) misidentified it as *Rhodotorula glutinis* [8, 9]. It can be correctly identified by sequencing the D1-D2 region of the 28S rDNA or by a qPCR targeting a specific rDNA region of *C. auris* [10, 11].

Accurate and fast identification is also achieved with MALDI-TOF, either the Biotyper (Bruker) or Vitek-MS (BioMérieux) systems, but only the "research use only" (RUO) libraries contain *C. auris* spectra (the FDA-approved IVD version does not) [8]. Some difficulties in obtaining a high score with direct deposit of *C. auris* on the MALDI plate when using the Biotyper have been reported [9]. Complete extraction following the manufacturer's instructions is needed, and several deposits are recommended to obtain better results. Additionally, the use of a homemade database containing more spectra of *C. auris* significantly improves the identification results [12].

Recommendations for infection control and prevention

The potential of *C. auris* for inter-human transmission and nosocomial outbreaks is unusual for a fungus, and may be partly explained by its ability to form biofilms and survive on dry or moist surfaces [4]. High rates of candidaemia, persistent patient colonisation and persistence in the environment despite adequate infection control measures were the hallmarks of the *C. auris* outbreaks in the UK and Spain [6, 7]. Therefore, effective infection control strategies are crucial to prevent the emergence and spread of this pathogen, especially in intensive care units. The decision to establish a systematic *C. auris* screening policy should be assessed by each hospital on the basis of the local epidemiology. A listing of preventive measures that can be recommended in a country of very low prevalence, such Switzerland, is presented in table 1. We currently suggest targeted screening of patients with (1) documented *C. auris* infection or colonisation in the past, (2) previous contact with a known *C. auris* case, or (3) a recent stay in a hospital where *C. auris* is endemic. Importantly, each institution should prepare to deal with an emerging *C. auris* outbreak by establishing protocols for screening and disinfection procedures that can be applied as soon as a case of *C. auris* infection or colonisation is detected. Screening should involve swabbing axilla and groin, which have been associated with the highest yield of detection [13], with the optional addition of other sites (e.g., nose and/or clinically relevant sites). Cultures can be performed directly on commercial chromogenic *Candida* agar plates, where *C. auris* produce colonies that usually appear white to rose or light purple (depending on the culture medium) after 48 hours of incubation at 37°C (fig. 1).

In countries with a high prevalence or in the setting of nosocomial outbreaks, pre-culture at 40°C in selective Sabouraud broths with a high-salt content and dulcitol or mannitol as carbon source in accordance with the Centers for Disease Control and Prevention protocol is recommended [14].

Patients with *C. auris* should be isolated in a single-patient room with contact precautions. Strict adherence to hand hygiene is required. Equipment used for the infected/colonised patient should not be shared with other patients. Quaternary ammonium is not active against *C. auris*. Therefore, for surface cleaning, chlorine-based or active oxygen-based products with sporicidal activity (similar to those used against *Clostridium difficile*) should be used [15]. Decontamination of the room and medical equipment with hydrogen peroxide vapour after discharge of the patient has been performed during outbreaks [7].

Recommendations for clinical management of *C. auris* colonisation and infection

Treating *C. auris* colonisation with systemic antifungal agents is not recommended. Persistent skin colonisation is common and there are no well-established decolonisation protocols. Daily chlorhexidine washes are recommended, but their efficacy has not been demonstrated [7, 13]. For documented or suspected cases of *C. auris* infection, echinocandins represent the first-line treatment, with >90% of strains remaining susceptible. Resistance to fluconazole is present in most cases, while voriconazole and amphotericin B have variable activity [2, 10]. According to antifungal susceptibility testing results, these later drugs may be considered as second-line or salvage therapies.

Conclusions

The threat of *C. auris* is a serious consideration because of the virulence of this pathogen, its multi-resistant profile and its potential for nosocomial transmission and prolonged outbreaks, in particular among critically ill patients. Microbiology laboratories should be aware of the diagnos-

Table 1: Recommendations for the prevention and management of *Candida auris*.

Question	Subject	Measures
Which patients should be screened for *C. auris*?	Patients transferred from or with recent stay in hospital with endemic *C. auris* Patients with previous *C. auris* isolation Direct contact (roommate) of *C. auris* case	Composite swab (axilla, groin ± nose ± specific clinical site) Preemptive contact precautions and single room isolation (or patient cohorting) until documented negative screening*
How to manage *C. auris* cases?	Patients with *C. auris* isolated in clinical specimens	Contact precautions and single room isolation (or patient cohorting) until documented negative screening* Decolonisation protocol with daily chlorhexidine washes Avoid or remove catheters if possible or consider protective chlorhexidine disks for catheter exit sites Colonisation only: do not treat with systemic antifungals Infection: treat with an echinocandin as first-line therapy. Reassess treatment according to antifungal susceptibility testing results
Which measures of decontamination should be applied for *C. auris*?	Direct environment of *C. auris* case (room, shared equipment)	Use of chlorine-based or active oxygen-based products with sporicidal activity (daily and at discharge) Consider hydrogen peroxide vaporization at discharge

* Duration of isolation and contact precautions is not well defined. The Centers for Disease Control and Prevention recommends at least two negative screenings at least 1 week apart in the absence of antifungal treatment.

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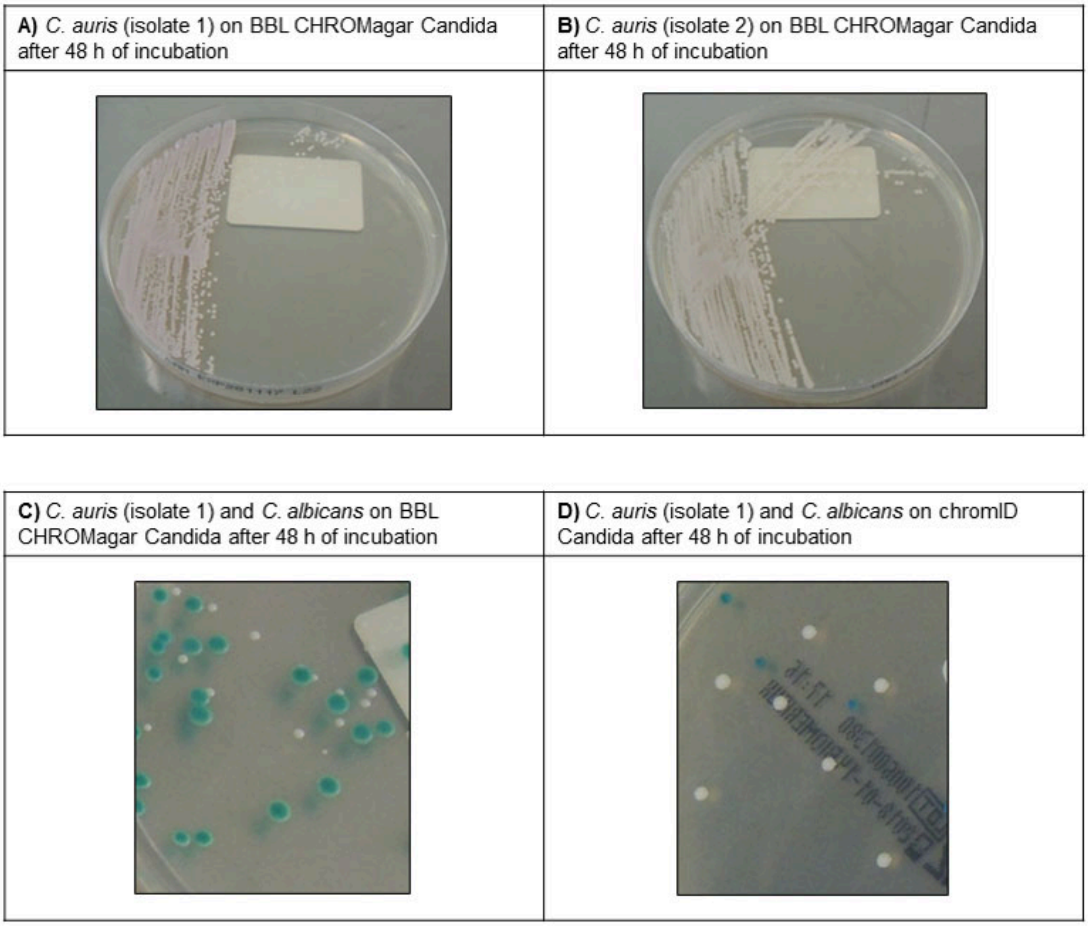
Figure 1: Typical white to pale pink aspect of two different *C. auris* isolates named isolate 1 (panel A) and isolate 2 (panel B) after 48 h of growth on BBL CHROMagar Candida medium (Becton Dickinson Diagnostics Systems).Differentiation between *C. auris* (white to pale pink colonies) and *C. albicans* (green to blue colonies) on BBL CHROMagar Candida (panel C) and chromID Candida (bioMérieux) (panel D).



tic challenges related to the identification of this pathogen. Infection control protocols for screening and management of *C. auris* infection/colonisation should be planned in order to anticipate outbreaks, which can rapidly become overwhelming and difficult to eradicate.

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