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Candida auris - recommendations on infection prevention and control measures in Switzerland

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Summary

Candida auris, a globally emerging pathogen, has been repeatedly introduced into European healthcare settings, leading to large and long-lasting nosocomial outbreaks. The pathogen has already been isolated in Switzerland, requiring clinicians and microbiologists to become alert. This is the first comprehensive guidance document on prevention and control of C. auris in Swiss acute care hospitals. It brings to light the most recent evidence from published original articles and reviews. We emphasise the importance of quickly identifying this yeast by means of screening in order to prevent an outbreak that could be difficult to contain. Key containment strategies include reinforcing early detection, hand hygiene, application of strict contact precautions for colonised and infected patients, and thorough specific environmental cleaning and disinfection.

Introduction

Candida auris was unknown before 2009. After its first isolation from a Japanese patient's external ear discharge [1], it rapidly spread worldwide [2] and hit several healthcare settings, producing large nosocomial outbreaks that were difficult to contain [3-5]. In clinical studies, C. auris has been isolated from various materials [3, 6], and experiments have shown growth on dry and moist surfaces for several days [7, 8]. Its particular ability to persist in the hospital environment apparently forced one hospital in New York to rip out some ceiling and floor tiles in order to eradicate this tenacious yeast [9]. Most C. auris isolates are resistant to fluconazole and voriconazole, and exhibit variable non-susceptibility rates to other antifungal classes such as amphotericin and echinocandins [2]. Most worrying, however, is that there are already reports of pan-resistant C. auris [10, 11]. This is of major concern since treatment options in the event of invasive infection will be extremely limited. C. auris is more likely to cause invasive infections, including candidaemia, than other species of Candida. Serious infections are observed especially in

patients with severe underlying diseases or immunosuppression and in neonates. Case-fatality rates for C. auris bloodstream infections may exceed 30% [12]. However, attributable mortality is difficult to determine since invasive infections usually occur in severely ill patients with multiple comorbidities [13].

Since the detection of the first case of C. auris in Switzerland in 2018 [14], Swissnoso has become aware through personal communication of two other cases in Switzerland, indicating that this emerging fungus has definitively arrived in Switzerland. Lack of awareness could quickly result in an outbreak if C. auris remains unnoticed or is detected only once a patient has developed invasive infection. Clinicians, hospital epidemiologists and microbiologists therefore need to be prepared for their first case. In this document, we aim to provide a guidance for infection prevention and control of C. auris in Swiss healthcare settings.

Methods

Recommendations issued by the US Centers for Disease Control (CDC) [15], the European Centre for Disease Prevention and Control (ECDC) [16], Public Health England [17], Pan-American Health Organization / World Health Organization [18] and Public Health Ontario [19] were reviewed and, where available, updated with more recent published literature. Eventually, since these guidelines are not harmonised in all aspects, some of the current recommendations rely on consensus opinions from Swissnoso experts, based on their experience and strategies that have proven effective in controlling transmission of other multiresistant pathogens in the hospital setting (e.g., vanmethicillin-resistant comycin-resistant enterococci, Staphylococcus aureus).

Epidemiology

C. auris is spreading around the world and has already been reported from five continents [20]. In Europe, the highest number of cases have been reported in outbreaks in

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Spain and the UK (table 1). However, sporadic cases have occurred in several other countries, including our neighbours France, Germany, Austria and Italy [22]. In view of the fact that some countries still have difficulties in establishing reliable data, either due to problems with microbiological identification or due to the absence of mandatory notification, the actual prevalence in some countries may be underestimated [23].

Mode of transmission

Experience from outbreaks showed that *C. auris* substantially contaminates mobile equipment and the immediate environment of colonised or infected patients [5]. Direct transmission from fomites (such as blood pressure cuffs, axillary temperature probes, ultrasound machines, physical therapy equipment and other utensils in contact with the patient) is a particular risk [17]. Contamination of health-care workers' hands with *Candida* sp. is common [24–26], but it has proved difficult to show that hand contamination is a relevant source of transmission in *C. auris* outbreaks [3, 4, 6].

Early detection and vigilance

Acute care facilities should have in place a screening policy for early detection of multidrug resistant organisms, including *C. auris*, in order to rapidly identify cases, implement precautionary measures and prevent further transmission within the healthcare facility. Delays in identification, through lack of either screening or availability of a microbiology laboratory on site, can easily lead to clusters or epidemics.

Admission screening

Screening of high-risk patients transferred from a hospital abroad with recent *C. auris* transmission or with endemic *C. auris* is strongly encouraged. According to the recent recommendation issued by the International Society for Antimicrobial Chemotherapy (ISAC) Working Group on Infection Prevention and Control (IPC), patients with a recent stay in an intensive care unit in an endemic country and transfers from hospitals known to have *C. auris* should routinely be investigated [27]. Countries reporting *C. auris* cases are listed in table 1. The epidemiological profile of *C. auris*, however, is evolving. We therefore recommend checking the CDC's report on the global tracking of *C.auris* cases on a regular basis [21].

In view of the global spread, the uncertainty in the identification of laboratories and possible delays in communication, virtually any healthcare facility abroad could be affected without knowing it. Therefore, hospitals may even consider examining all patients referred from a healthcare facility abroad.

In-hospital screening

Patients

Detection of C. auris in a non-isolated patient from a healthcare facility should trigger screening of close contacts, including those who had been sharing the room or equipment. In the absence of firm evidence on the duration (hours/days) of required overlapping exposure between index case and close contacts, screening all close contacts since hospital admission of the index case should be considered. The screening should include all current ward mates if detection was in a non-isolated patient during an intensive care stay or if secondary cases are detected among roommates. All close contacts should be placed under pre-emptive contact precautions either in a single room or grouped together in a multi-bed room. Pre-emptive contact precautions can be discontinued after three consecutive negative screenings at a minimum interval of 24 hours are available [17]. However, the 24-hour interval seems relatively short to safely rule out C. auris colonisation and de-isolated contact patients staying at the hospital should therefore be screened on a weekly basis until their discharge [27].

More intensive actions are required if two or more cases are identified: all current and previous roommates should be tested, and ward-wide screening should include any other patient who had a significant exposure such as sharing the same equipment [19, 27, 28]. We recommend weekly point prevalence screenings on affected wards for at least 3 weeks in a row after the last positive case was detected.

Healthcare workers

Contamination of healthcare workers' hands with *Candida* sp. is common [24–26]. However, whether there is chronic *C. auris* colonisation in healthcare workers that could pose a risk for transmission remains unclear. Screening of healthcare workers is therefore not recommended unless there is substantial evidence suggesting healthcare workers as potential source or if ongoing transmission is identified despite adherence to recommended infection control measures.

Body sites to test for colonisation

Axilla and groin are the body sites most frequently colonised with *C. auris*. The nares, if found positive, usually have a higher load than other sites. Combining these

Table 1: Countries from which C. auris cases have been reported (data as of 31 December 2019 [21]).

	Single cases	Transmissions or multiple cases
Europe	Austria, Belgium, Greece, Italy, Poland, Norway, Switzerland, The Netherlands	France, Germany, Spain, the United Kingdom
Asia and the pacific region	Iran, United Arab Emirates, Taiwan, Thailand	Australia, Bangladesh, China, India, Israel, Japan, Kuwait, Malaysia, Oman, Pakistan, Russia, Saudi Arabia, Singapore, South Korea
Africa	Egypt	Kenya, South Africa
North America		Canada, United States (New York City area, New Jersey, Chicago area)
South America	Chile, Costa Rica	Colombia, Panama, Venezuela

The information in this table has mainly been derived from a Centers for Disease Control and Prevention (CDC) website, which is available free of charge. Please note that the content on the CDC website may be subject to change and its re-use does not imply endorsement by CDC. Other countries not listed in this table may also have undetected or unreported *C. auris* cases.

three sites has been shown to have the highest sensitivity [11]. The sites most frequently considered in targeted multidrug-resistant organisms in Switzerland are nose, throat and groin for multi-resistant *Staphylococcus* aureus, and rectum or perianal site for gram-negative multidrug-resistant organisms and vancomycin resistant enterococci [29]. Relying solely on these anatomical sites, however, may not be sufficient for detection of *C. auris* [30].

Since admission screening would ideally be combined with screening for other multidrug-resistant organisms, a reasonable approach – on the basis of sensitivity and logistical aspects – includes a composite bilateral swab of axilla and groin and a swab from both nostrils (table 2). Sampling of other sites (throat, rectum, urine from catheterised patients, wounds or catheter exit sites) increases the test yield and can be performed in addition if part of targeted admission screening for other multidrug-resistant organisms or if clinically indicated [17, 27, 31].

Microbiological diagnostics

Laboratories should identify isolates of non-albicans Candida species from invasive infections to the species level. Identification of *Candida* to species level from non-sterile sites should be considered if a C. auris case has been detected in the healthcare facility or if a patient had an overnight stay within the last 12 months in a healthcare facility in a country with documented C. auris transmission [32]. In a previous review [14], our colleagues discussed the diagnostic challenges and the risk of misidentification due to similarity with other Candida spp. such as Candida of the haemulonii complex. In brief, C. auris cannot be identified reliably based on microscopy or growth on chromogenic agar [33]. Matrix assisted laser desorption ionisations time of flight mass spectrometry (MALDI-TOF MS) is a reliable identification method. Frequently used MAL-DI-TOF platforms are MALDI Biotyper (Bruker-Daltonics) and Vitek MS (bioMérieux) [3-5, 34]. Importantly, it must be assured that different C. auris spectra are included in the library and laboratories use the most updated versions [34]. Laboratories performing MALDI-TOF should follow the enrichment broth protocol described in Welsh et al. [7] which is intended for facilitated isolation of C. auris from various clinical specimens.

Molecular-based methods that can rapidly and accurately identify *C. auris* include conventional or real-time PCR assays [35–37]. These assays can be performed directly

from the clinical specimen and do not require prior culture, which is very useful when investigating larger outbreaks.

We are aware that not all laboratories serving healthcare facilities have the means to reliably identify C. auris and test its susceptibility to the whole panel of antifungal agents. It is therefore essential to set up a collaboration with a central laboratory that can provide rapid assistance. All suspicious isolates should be stored, preferably at -80°C, for further analysis.

Case management

The suspicion of a microbiological sample being positive for *C. auris* should trigger immediate reporting to the infection prevention and control team, in order to implement adequate measures aiming at identifying and interrupting transmission (table 3).

Measures upon detection of an incident case in a hospital

Ideally, enforced contact isolation is applied as soon as C. *auris* is suspected in a patient. Upon confirmation of the identification at the latest, the following actions should be taken (adapted from [28]):

- Start contact precautions and place the patient in a single room with dedicated bathroom/toilet.
- Reinforce standard precautions especially hand hygiene with an alcohol-based hand rub.
- Perform a case review: obtain information about previous healthcare facility encounters in the last 3 months in order to evaluate possible transmissions at other healthcare institutions.
- Perform contact tracing, since unrecognised colonised patients pose a risk for transmission identify epidemiologically linked patients, especially current and past roommates and those who shared equipment. These contact patients need to be screened and if already discharged they should be labelled as contacts in order to be screened upon re-admission to the facility. Investigators may even consider as possible contacts patients who are placed into a room that has recently been vacated by a *C. auris* patient.
- Inform healthcare facilities in which the patient stayed before being transferred.

Table 2: Recommended body sites for C. auris screening [15, 17].

Minimum standard			
Axilla and groin bilaterally, a composite (pooled) swab is acceptable			
Nose (both nostrils)			
Consider additional sites if clinically relevant			
Wounds			
Catheter entry site			
Sputum / endotracheal secretions			
Throat			
Drain fluid			
Rectum or stool sample			
Urine, if catheterised			
Vaginal swab			

Contact precautions and isolation

Contact isolation is recommended for all microbiologically confirmed cases and close contacts. Single rooms should have a dedicated or en-suite bathroom. We recommend using dedicated items, preferably single-use items or equipment and discarding them immediately after use. Proper re-processing according to the manufacturer's instructions is crucial for any re-usable item; for example, we strongly discourage using wipes containing disinfectants if the re-usable item is in fact difficult to clean with wipes.

Staff and visitors should wear gowns, gloves and surgical masks upon entry to the room. Swissnoso is aware that many Swiss hospitals have dropped this procedure for other multidrug resistant organisms and apply personnel protective equipment as for standard precautions. However, due to the high environmental burden of *C. auris*, this approach might be insufficient. Importantly, the infection prevention and control team must ensure regular training on correct donning and doffing of personal protective equipment.

Data on transmission by droplets is not known, but *C. auris* has been isolated from patients' nostrils [38]. Wearing a surgical mask is therefore recommended for staff and vis-

itors when entering a patient's room and is required for the patient when exiting the room for a medical procedure. Medical personnel should inform the patient about not leaving the room otherwise and communicate any medically necessary movement outside the room to the infection control team.

Clearly, proper hand hygiene as recommended by the World Health Organization remains the most important measure to prevent transmission of known or unrecognised pathogens. After leaving the patient's room it is of utmost importance to carry out thorough hand hygiene using alcoholic hand-rub immediately after removing gowns and gloves.

Transmission via droplets is unlikely unless a patient has symptoms of respiratory tract infection and presence of *C. auris* in the respiratory tract. After contact with potentially contaminated respiratory secretions, correct hand hygiene must be carried out as for standard precautions. To the extent possible, the number of healthcare workers and other personnel who care for the *C. auris* patient should be kept to a minimum. Since the duration of colonisation remains largely unknown but can last several months, and no effective decolonisation scheme is available, colonised or in-

Table 3: Overview of infection prevention and control measures for C. auris single cases and outbreaks. Adapted from Kenters et al. [27]*.

	Single/sporadic case(s)	Outbreak
Hand hygiene	Use an alcohol based [†] compound	Use an alcohol based [†] compound
Contact isolation		
Gloves	Single-use, non-sterile Use per patient when entering the room Discard when visibly soiled or when leaving the patient and immediately perform hand hygiene	Single-use, non-sterile Use per patient when entering the room Discard when visibly soiled or when leaving the patient and immediately perform hand hygiene
Gown	Staff wears a gown for any direct patient contact Discard when leaving the patient and immediately per- form hand hygiene	Staff wears a gown for any direct patient contact and per patient in co- hort Discard when leaving the patient and immediately perform hand hy- giene
Surgical mask	Staff wear a mask for any direct patient contact Required for the patient when exiting the room	Staff wear a mask for any direct patient contact Required for the patient when exiting the room
Room	Single room	Single room or cohort positive cases in an area clearly separated from confirmed negative patients
Ventilation	Normal	Normal
Toilet / commode / bedpan	Dedicated toilet, commode and/or bedpan En-suite bathroom (if available)	Dedicated toilet, commode, bedpan or en-suite bathroom (if available) Bathroom can be shared with other cases if cohort area
Bathroom/washbasin	Dedicated	Dedicated/shared with other cases
Bedding	Check pillow and mattresses (when linen is removed) for damage and discard if damaged	Single use pillows or check pillows and mattresses (when linen is removed) for damage and discard if damaged
Cleaning and disinfection		
Cleaning material	Single use cloths	Single use (microfibre) cloths
Frequency of environmental decontamination	Twice daily (affected rooms, at least high-touch surfaces)	Twice daily (wards, at least high-touch surfaces)
Small surfaces	70% ethanol or alcohol-based disinfectants and follow manufacturers' direction	70% ethanol or alcohol-based disinfectants and follow manufacturers' direction
Alcohol-sensitive or large surfaces	Use disinfectant compound with fungicidal activity Follow all manufacturers' direction	Use disinfectant compound with fungicidal activity Follow all manufacturers' direction
Surveillance		
Index case was not isolated	Test current and previous roommates (since hospital admission of the index case), extend screening to all current ward mates if secondary cases are identified	Not applicable
Screening frequency	Weekly point prevalence testing on intensive care units (other units, e.g., oncology, to be considered in individual risk assessment)	Perform weekly point prevalence testing on outbreak wards In case of ongoing transmission increase frequency from weekly to twice or thrice weekly point prevalence testing Alternatively continue weekly prevalence testing and perform additional screening on admission and at discharge
Inter-hospital transfers		
Communication	Notify receiving hospital in advance if a <i>C. auris</i> -positive patient is transferred Inform healthcare institutions where a patient has stayed before being transferred	Notify receiving hospitals in advance about the current epidemiological situation and the perceived risk of any transferred patient of being colonised or infected with <i>C. auris</i> (room-/ward-mates of a <i>C. auris</i> positive patient) and any (pending) screening result

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fected patients should be placed under contact isolation for the duration of the entire hospital stay. After discharge, patients should remain labelled in an electronic alert system for early detection and immediate contact isolation upon readmission.

Five consecutive negative screenings at least one week apart may allow discontinuation of contact precautions and isolation. However, we advise the first control swabs to be taken only after a period of 3–6 months and to maintain flagging of patients for at least 1 year after the first negative culture [27].

Communication

Microbiologists should inform the local infection and control team as soon as C. auris is suspected (e.g., when non-C. albicans isolates with fluconazole resistance are found) to allow rapid implementation of necessary infection control measures. Colonised and infected patients, as well as close contacts, without at least three consecutive negative screenings 1 week apart should be (electronically) labelled in their patient file. Patients and their family should be informed about the importance of contact isolation measures and what they can do to prevent C. auris from spreading. A communication standard for inter-facility transfers must be in place. After discharge the general practitioner must be informed. Since reporting of a single C. auris case to the Federal Office of Public Health is not mandatory, we strongly advise at least informing colleagues and collaborators about such an epidemiologically important finding.

Environmental decontamination

Survival in the hospital environment, particularly on plastic [7] and moist surfaces [8] facilitates persistence of C. auris. However, it is not commonly found in the general environment or air [5]. Thorough cleaning and disinfection of patient equipment and the surrounding area is critical to prevent spreading of this organism and to break the chain of transmission. Daily environmental cleaning and disinfection should be intensified to a minimum twice daily for at least all high-touch surfaces on wards with C. auris positive patients [27]. Thoroughness of terminal environmental decontamination after discharge of a C. auris positive patient should be reinforced using a compound with adequate fungicidal efficacy. International guidelines recommend using high-strength (1000 ppm) chlorine-based or hydrogen-peroxide-containing disinfectants. However, any surface disinfectant with approved fungicidal and sporicidal activity (e.g., effective against Clostridioides difficile) is effective provided the recommended contact time is followed [3, 6]. The exception are water-based quaternary ammonium compounds, which seem to have poor activity against C. auris, and their use is therefore discouraged [39, 40]. Efficacy of no-touch disinfectant technologies such as ultraviolet light on killing of C. auris on surfaces depends largely on contact time and distance of the surfaces from the light source, but data are still limited. Ultraviolet light disinfection is recommended as an adjunctive disinfecting method for terminal cleaning if available, after the surface has been thoroughly cleaned and disinfected [41, 42]. Everything that cannot be cleaned must be discarded (e.g., porous materials, etc.).

Waste management

Bedding, towels and cloths should be replaced when visibly soiled and/or after patient discharge, and machine washed. We recommend following the "Minimum standards for handling contaminated laundry in the healthcare sector" issued by the Swiss Society of Hospital Hygiene [43].

Decolonisation of patients

There is no established decolonisation regimen. Chlorhexidine gluconate and povidone iodine are effective in killing C. auris in vitro [44, 45]. Chlorhexidine gluconate combined with topical mupirocin have shown some effect on reducing candiduria in patients in intensive care when universally applied [46]. However, the prolonged C. auris outbreaks in the UK and Spain showed that despite decolonisation efforts using daily chlorhexidine gluconate washes patients continued to be colonised or developed new candidaemia episodes [3, 4]. This may be explained by recolonisation from the contaminated environment (e.g., bedlinen, mattresses), insufficient contact time and the relatively low chlorhexidine gluconate concentration of 2% commonly used in clinical practice [44]. Therefore, as a validated and published decolonisation regimen is lacking, no firm recommendation can be made until further studies are available.

Additional measures for outbreaks

- Assess for potential causes of transmission: most critical are inadequate hand hygiene performed by healthcare providers and lack of appropriate cleaning and disinfection of mobile equipment or the environment.
- Reinforce adherence with hand hygiene including proper hand hygiene techniques and contact precaution measures.
- Promptly initiate an epidemiological investigation and perform cross-sectional screening of contact patients for *C. auris* carriage.
- Ensure that the microbiology laboratory stores all specimens for further investigations.
- Cohort C. auris positive patients in a dedicated area and, if possible, with dedicated nursing staff.
- Separate contact patients under investigation for C. auris carriage from confirmed negative cases.
- Reinforce importance of thoroughly decontaminating the environment, by means of educational sessions and observation of appropriate implementation.
- Consider ceasing new admissions to affected rooms/ wards if the outbreak cannot be contained.
- Perform weekly ward-wide surveillance cultures.
- If significant transmission is identified on weekly point prevalence testing despite implementation of infection control measures enhance frequency (e.g., 2–3 times per week) and/or add admission and discharge screening
- Environmental screening is not recommended unless epidemiological investigation points towards a specific environmental source or if ongoing transmission occurs despite adherence to recommended interventions. Consider regular (e.g., daily) audit monitoring by using

- adenosine triphosphate detectors or a fluorescent marker substance, to ensure appropriate environmental hygiene.
- Hospital management support is required to provide adequate resources.
- Obtain guidance from an experienced outbreak management team and liaise with national infection control experts.
- Adjust empirical treatment regimens for suspected fungal infections, in close coordination with the infectious diseases service.

When to declare an outbreak terminated

An outbreak can be considered over if no new patient has been identified on clinical or screening specimens over a 3-week period, and at least three unit-wide point prevalence studies are negative [19].

Summary

Why C. auris is a problem

- Healthcare-associated infections: C. auris causes serious infections, mainly bloodstream infections.
- Limited treatment options: C. auris is often resistant to several antifungal drug classes; especially azoles are often not active. Some C. auris infections have been resistant to all three types of antifungal drugs (azoles, echinocandins and polyenes).
- It is difficult to identify: C. auris can be misidentified as other types of fungi unless specialised laboratory technology (MALDI-TOF or PCR) is used.
- Potential for spread: C. auris can spread silently in hospitals and nursing homes. Outbreaks in healthcare facilities have been difficult to control. It can spread through contact with affected patients and contaminated surfaces or equipment.

What can we do?

- Be alert and know the pathogen as epidemiologically important.
- Inform colleagues and collaborators about this new emerging pathogen.
- Screen patients at risk on admission and take swabs from axilla, groin and nose.
- Immediately isolate newly detected cases and investigate contacts around the index case.
- Perform good hand hygiene and reinforce thorough disinfection in healthcare facilities.

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Potential competing interests

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