

Interim guidance for management of *Candida auris* infections in South African hospitals

What is *Candida auris*?

Candida auris is an emerging fungal (yeast-like) pathogen which has caused invasive infections and hospital outbreaks on several continents. The fungus is difficult to identify in the routine laboratory setting, is associated with a high in-hospital mortality among patients with invasive infection and may be difficult to “eradicate” from the hospital environment.

Of most concern, *C. auris* is often multi-drug resistant; almost all tested *C. auris* isolates are resistant to fluconazole, an important first-line antifungal agent¹⁻⁷, and in a recent global study, more than 40% of isolates were resistant to two or more major classes of antifungals¹.

What is the current global epidemiology?

Since *C. auris* was first described in Japan in 2009, cases have subsequently been reported in South Korea, India, Kuwait, Kenya, South Africa and more recently in Colombia, Venezuela, Pakistan, the United Kingdom and the United States²⁻¹⁴. It is possible that *C. auris* has emerged in other resource-limited countries but has remained undetected owing to a limited capacity for case detection. A whole genome sequencing study documented recent, near-simultaneous and independent emergence of *C. auris* clones on three different continents (Africa, Asia and South America), rather than spread of a single “clone” across the globe¹. To date, infections with *C. auris* have been largely acquired in a hospital setting and horizontal spread of the pathogen has been demonstrated through clonality of isolates within a hospital. Healthcare-associated outbreaks of *C. auris* have been reported in at least three countries to date^{1, 6, 7}.

What infections does it cause?

C. auris has been reported to cause bloodstream infections (including central venous catheter-associated bloodstream infections), meningitis, bone infections and wound infections (incl. colonisation and infection of burns). The fungus has also been isolated from urine (sometimes implicated in a catheter-associated urinary tract infection), skin and mucosal membranes, tracheal aspirates and other sites.

What is the current situation in South Africa and why is there concern?

C. auris was the second most common cause of candidaemia in the South African private sector in 2016 based on current active, laboratory-based surveillance for candidaemia, with most cases occurring in Gauteng province. In public-sector hospitals, *C. auris* was the fourth most common species of *Candida* causing candidaemia, again with most cases in Gauteng province. Overall, there have been over 1500 cases in South Africa to date (Govender NP, et al. unpublished data), with 70-80 new cases

every month since April 2016. Large on-going outbreaks have occurred at several Johannesburg and Pretoria hospitals, with most cases occurring in private-sector facilities.

Healthcare facilities are requested to **notify the NICD urgently** if a new outbreak in a hospital or long-term care facility is suspected. To date, no outbreaks have been reported from South African paediatric or neonatal units – all personnel are requested to maintain high levels of vigilance for such an occurrence.

How is this fungal pathogen identified in the laboratory?

C. auris is often misidentified in the routine diagnostic laboratory using commercially-available biochemical methods. If *Candida haemulonii*, *Saccharomyces cerevisiae*, *Rhodotorula glutinis*, *Candida sake* or *Candida famata* are identified, further confirmatory testing should be done to determine if the isolate is *C. auris*, especially if the fungus is fluconazole resistant. The identification of this yeast-like fungus can be currently confirmed by molecular methods or mass spectrometry, including MALDI Biotyper system (Bruker Corporation, Billerica, MA, USA) and Vitek MS (bioMerieux, Marcy l'Etoile, France). Refer to laboratory algorithm below (Figure 1). Note: The Vitek-2 YST identification database will be updated to include *C. auris* in early 2017 (personal communication, bioMerieux). Species-level identification and antifungal susceptibility testing (AST) of isolates is essential to guide patient management. There are no agreed-upon interpretive breakpoints for *C. auris* and any antifungal agent; however, conservative breakpoints, developed for other *Candida* species, have been applied to *C. auris* for epidemiological purposes. *C. auris* exhibits resistance to fluconazole in over 90% of isolates. In addition, 35% of isolates are resistant to amphotericin B, 7% resistant to echinocandins and 41% multi-drug resistant (MDR) (i.e. resistant to at least 2 classes of antifungals)¹. Isolates found to be resistant to an echinocandin or amphotericin B should promptly be referred to the NICD. In addition, referral of all MDR isolates is required.

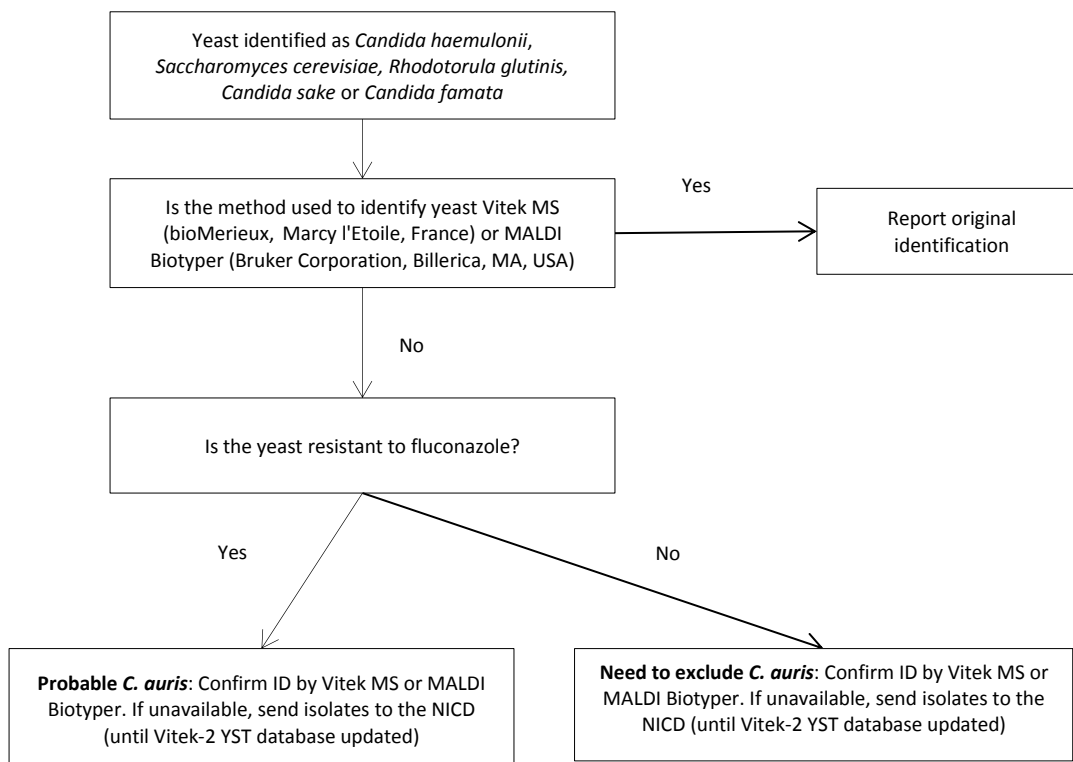


Figure 1: Laboratory algorithm to confirm commonly-misidentified yeasts as *Candida auris*

How is a case identified?

A case of *C. auris* can be defined as follows:

A case of <i>C. auris</i> infection	<p>Any patient with confirmed or suspected <i>C. auris</i> infection identified by a diagnostic laboratory from <u>any sterile body site</u>:</p> <ul style="list-style-type: none"> • Blood • Central venous catheter (CVC) tip • Cerebrospinal fluid (CSF) • Tissue • Fluid from a sterile site • Urine (NB: to consider clinical picture and the presence of cells or casts in the urine – see treatment recommendations for urinary tract infections below) <p>Patients may or may not have evidence of sepsis or altered biomarkers.</p>
A case of <i>C. auris</i> colonisation	<p>Any patient with confirmed or suspected <i>C. auris</i> from <u>any “non-sterile” body site</u>:</p> <ul style="list-style-type: none"> • Skin • Tracheal aspirate/ respiratory secretions • Rectal swab • Nasal swab • Urine (NB: to consider clinical picture and the presence of cells or casts in the urine – see treatment recommendations for urinary tract infections below)

How should a case of *Candida auris* infection be managed?

An echinocandin (i.e. caspofungin, micafungin or anidulafungin) or amphotericin B deoxycholate should be used as first-line therapy, depending on availability. Treatment should be adjusted, based on AST results, as soon as available. Where feasible, every effort should be made to remove devices such as CVCs and urine catheters. Antifungal treatment duration is standard as for infections caused by other *Candida* species; treatment for candidaemia should be continued for 14 days after documented clearance of *Candida* from the bloodstream (one blood culture per day until negative) and resolution of symptoms attributable to candidaemia^{15, 16}. There is no evidence for combination antifungal therapy at present for *C. auris* infections.

The following is recommended for the treatment of patients where *C. auris* is isolated from urine:

Condition	Recommended treatment
Asymptomatic candiduria	<ul style="list-style-type: none"> • No antifungal therapy indicated, except if patients are at high risk for dissemination (very low birth weight (VLBW) neonates, patients with neutropenia, urologic surgery pending) • Removal of urine catheter
Symptomatic lower urinary tract infection (UTI)	<ul style="list-style-type: none"> • Antifungal treatment: consider amphotericin B IV or amphotericin B bladder irrigation. Echinocandins do not achieve high urine concentrations and are thus not ideal agents • Removal of urine catheter
Urinary fungal ball	<ul style="list-style-type: none"> • Surgical removal
Pyelonephritis	<ul style="list-style-type: none"> • Antifungal treatment, as for candidaemia

What infection prevention and control measures are appropriate to limit transmission?

Although the dynamics of transmission of *C. auris* are not clearly established, *C. auris* is known to contaminate the immediate environment of infected or colonised patients with hypothesised onward transmission on the hands of healthcare workers or on fomites (such as shared equipment).

It is essential to have commitment from hospital management, infection prevention and control (IPC) teams and clinical teams, in order to curb the spread of this pathogen. Facilities should update internal IPC policies and ensure that recommendations are appropriately implemented.

In order to limit transmission within a facility, the following measures are recommended:

- Patients with *C. auris* infection or colonisation should be isolated in single rooms with en suite facilities, side rooms or cohorted, wherever possible.
- Standard precautions should be strictly adhered to, including hand hygiene using soap and water (especially with visible soiling) followed by alcohol hand rub. Between care activities, alcohol hand rub can be used if hands are not visibly soiled
- In addition, contact precautions are recommended: these include the donning of appropriate personal protective equipment (PPE) (gloves and aprons) before touching a patient or the patient's immediate surroundings (bed linen, bed rails, personal belongings, invasive devices). PPE should be donned after application of alcohol hand rub and hands should be cleaned with soap and water followed by alcohol hand rub, after removal of PPE
- Improved adherence to bundles of care for venous and urinary catheters, as well as tracheostomy care is essential
- Hand hygiene practices among staff members should also be evaluated and adherence emphasised
- Clinicians and ancillary health professionals (including dietitians, radiographers, physiotherapists, phlebotomists etc.) should also be trained regarding IPC recommendations
- Affected patients, visitors and family members should be briefed about the importance of hand hygiene and visitors encouraged to use protective aprons
- If a patient needs care or investigations in another department within a facility (including radiology, theatre, outpatient clinic etc.), the receiving department should be notified of the patient's *C. auris* status and advised on what precautionary measures to take prior to and during the transfer/ procedure. These patients should also be scheduled last on the list for the day, if feasible.
- If a patient needs to be transferred to another healthcare facility, including a long-term care facility, the referring facility should ensure that the receiving facility is appropriately notified of the patient's *C. auris* infection or colonisation status.

Should screening be performed in routine clinical care?

Routine screening for *C. auris* at the time of hospital admission is not currently recommended owing to limited evidence.

How should a case of *Candida auris* colonisation be managed?

Patients known to be colonised with *C. auris* should be isolated in side rooms or cohorted, wherever possible. If a patient has to be transferred to another healthcare facility, including a long-term care facility, the referring facility should ensure that the receiving facility is appropriately notified by clearly documenting “*Candida auris* colonisation” as a diagnosis on the referral letter and/ or discharge summary. Decolonisation procedures (such as chlorhexidine skin wipes, mouth washes, etc.) are not currently recommended owing to limited evidence.

How should the patient’s immediate environment be cleaned?

Regular cleaning with a chlorine-releasing agent with a strength of 1000 ppm (i.e. higher than that routinely used) is recommended. Terminal cleaning and disinfection of the bed space should be performed after the patient has left the environment, using a chlorine-releasing agent (1000 ppm). Also consider a terminal clean with hydrogen peroxide vapour, where feasible. Multi-use equipment (including BP cuffs, thermometers, computers/ equipment on wheels, ultrasound machines etc.) should be thoroughly cleaned during a terminal clean. If a patient needs care or investigations in another department within a facility, they should be scheduled last on the list for the day, followed by thorough cleaning of the environment in the relevant department, as described above. Standard waste and linen disposal procedures should be followed. Facilities should ensure buy-in from housekeeping services or outsourced cleaning service providers and ensure that cleaning staff are appropriately trained with regard to cleaning recommendations.

References and further reading:

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Where can I find more information?

If you require any additional information, please contact NICD:

- To notify the NICD if a new outbreak is suspected:
 - Nelesh Govender: 011-555-0353 / neleshg@nicd.ac.za OR
 - Kerrigan McCarthy: 011-555-0542 / kerriganm@nicd.ac.za OR
 - Erika van Schalkwyk: 011-386-6452 / erikab@nicd.ac.za OR
 - **After-hours:** NICD Doctor-on-call: 082 883 9920.
- Please contact NICD before any isolates are referred:
 - Ruth Mpembe: 011-555-0325/ ruthm@nicd.ac.za OR
 - Gloria Zulu: 011-555-0323 / gloriaz@nicd.ac.za OR
 - NICD-COHI mycology reference laboratory 011-555-0381