

Protecting and improving the nation's health

Guidance for the laboratory investigation, management and infection prevention and control for cases of *Candida auris*

About Public Health England

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Introduction: Candida auris

Candida auris has been reported to cause bloodstream infections, wound infections, and otitis. It has also been cultured from urine and the respiratory tract; however, whether isolation from these sites represents infection versus colonisation in each instance is unknown. *C. auris* appears to be unlike other pathogenic yeast species in its propensity for transmission between hospital patients. Of significance, it is commonly resistant to the first-line antifungal, fluconazole and can develop resistance to other classes of anti-fungal agents.

Investigation in frontline laboratories

C. auris, on microscopy, is indistinguishable from most other Candida species, it is a germ tube test negative budding yeast, however some strains can form rudimentary pseudohyphae on commeal agar. Most *C. auris* isolates are a pale purple or pink colour on the chromogenic agar, CHROMagar Candida, in common with several other non C. albicans species. Growth on this and other chromogenic agars (which may display a different colour) cannot be used as a primary identification method. Chromogenic agars are useful to identify mixed cultures including the presence of C. albicans. If there is evidence of non - albicans on chromogenic agar these should be sub-cultured on Sabouraud's agar and identified according to local laboratory protocols. It is unlikely that any of the currently available biochemical-based tests will include C. auris in their database as it is a newly recognised species so laboratories are advised to check the databases provided for their current methods. According to published data, commercially available biochemical-based tests, including API AUX 20C and VITEK-2 YST, used in many front line diagnostic laboratories can misidentify C. auris as Candida haemulonii, Saccharomyces cerevisiae or Rhodotorula glutinis (the latter species is pink on Sabouraud's agar and is easily distinguished).

Therefore it is important that any *Candida* spp isolates associated with invasive infections and isolates from superficial sites in patients from high intensity settings and those transferred from an affected hospital (UK or abroad) should be analysed to species level. If *Candida haemulonii, Candida famata, Candida sake* or *Saccharomyces cerevisiae* are identified, further work should be undertaken to ensure that they are not *C. auris*. This would involve either molecular sequencing of the D1/D2 domain or MALDI-TOF Biotyper analysis with *C. auris* either already present or added to the database. This facility is available at the PHE Mycology Reference Laboratory. Please send pure isolates on Sabouraud's slopes accompanied by the appropriate form accessed from https://www.gov.uk/government/publications/mycology-identification-and-susceptibility-testing-request-form

Laboratories should also ensure correct mapping of the species code for *C. auris* to facilitate reporting to PHE through SGSS.

Antifungal susceptibility testing: There are no established minimum inhibitory concentration (MIC) breakpoints at present for *C. auris*. Using breakpoints for other *Candida* spp the Centers for Disease Control and Prevention (CDC) demonstrated that of the global outbreaks that they have been investigating, nearly all isolates are highly resistant to fluconazole. In their analysis, more than half of *C. auris* isolates were resistant to voriconazole, one- third were resistant to amphotericin B (MIC ≥ 2 mg/L), and a few were resistant to echinocandins. Some isolates have demonstrated elevated MICs to all three major antifungal classes, including azoles, echinocandins, and polyenes indicating that treatment options would be limited. Whole genome sequencing of the organism has found resistant determinants to a variety of antifungal agents.

Treatment

Experience to date from the PHE Mycology Reference Laboratory indicates that so far no multi-drug resistant strains have been found in the UK but all isolates are resistant to fluconazole and often cross-resistant to other azoles. First-line therapy remains an echinocandin pending specific susceptibility testing which should be undertaken as soon as possible. However, there is evidence that resistance can evolve guite rapidly in this species, ongoing vigilance for evolving resistance is advised in patients who are found to be infected or colonised with C. auris. There is currently no evidence or experience to support combination therapy in invasive infections with this organism and clinicians are advised to make decisions on a case by case basis. The PHE Mycology Reference Laboratory is able to undertake susceptibility testing for amphotericin B, fluconazole, voriconazole, itraconazole, posaconazole, isavuconazole, anidulafungin, caspofungin, and micafungin. If an isolate is found to be resistant to all of these agents the Reference Laboratory will also test for susceptibility to flucytosine, nystatin and terbinafine. Currently UK strains remain susceptible to the topical agents nystatin and terbinafine and it is possible that for the treatment of any future multi-drug resistant strains a regimen incorporating oral terbinafine could be considered.

Decolonisation:

Colonisation of patients has been reported from affected hospitals around the world. There is no evidence currently that can establish whether *C. auris* is susceptible or resistant to chlorhexidine. More work is being done in this area. Clinical experience to date has shown that colonisation is difficult to eradicate and colonisation tends to persist making infection prevention and control strategies particularly important. However it is still recommended that strategies to prevent and/or treat colonisation include:

- strict adherence to central and peripheral catheter care bundles, urinary catheter care bundle and care of the tracheostomy site
- skin decontamination and mouth gargles with chlorhexidine washes
- use of topical nystatin and terbinafine would be options for targeted topical management of key sites such as venous cannula entry sites

Screening

All Trusts are encouraged to develop a screening policy after local risk assessments are undertaken. Screening is recommended in units that have ongoing cases or colonisations. Screening is also advised for patients coming from other affected hospitals / units in the UK and abroad. Currently hospital outbreaks have been reported from India, Pakistan, Venezuela and Colombia; although UK and worldwide prevalence is still to be established due to problems with laboratory diagnosis.

Suggested screening sites, based on the predilection of Candida species to colonise the skin and mucosal surfaces ie genitourinary tract, mouth and respiratory tract, are:

- nose, throat, groin
- urine / urethral swab
- perineal or low vaginal swab if appropriate
- sputum / endotracheal secretions
- drain fluid (abdominal/pelvic/mediastinal)
- cannula entry sites if clinically indicated
- wounds

Routine wound swabs may be used to collect the screening sample.

All screen positive patients should be isolated or cohorted as described below. As for other healthcare associated infections, a series of three negative screens taken 24 hours apart are needed to de-isolate the patient. As there is clinical experience of recurrence of colonisation, the need for ongoing vigilance in the form of weekly screens in certain clinical environments should be considered by performing local risk assessments.

Infection, prevention and control (IPC)

Reports from India, Pakistan and Venezuela (CDC, personal communication) have described healthcare outbreaks of *C. auris* infection and colonisation involving more than 30 patients. The precise mode of transmission within the healthcare environment is not known. However, experience during these outbreaks suggests that *C. auris* might substantially contaminate the environment of rooms of colonised or infected patients. Transmission directly from fomites (such as blood pressure cuffs, stethoscopes and other equipment in contact with the patient) is a particular risk, however this does not

preclude transmission via hands of healthcare workers and hand hygiene needs to be strictly adhered to. Where possible equipment used for the infected/colonised patient should not be shared with other patients on the ward unless between-patient cleaning can be assured. It is essential that all healthcare providers work in a multi-disciplinary team with their Clinical Microbiologists and under the direction of their specialist IPC team.

The patient

Key infection prevention and control measures should include:

- isolation of all patients colonised or infected with the organism in a single room with *ensuite* facilities wherever possible
- isolation of all patients who have been transferred from an affected UK hospital or a hospital abroad until screening results are available
- strict adherence to standard precautions including hand hygiene using soap and water followed by alcohol hand rub
- personal protective equipment in the form of gloves and aprons (or gowns if there is a high risk of soiling with blood or body fluids)
- these should be donned after hand washing and before entering the room and removed and discarded in the room followed by a thorough hand wash and application of alcohol hand rub
- visors and masks are not routinely required and should be worn only if there is a procedural risk of spillage or splashes
- visitors of infected or colonised patients need to be briefed about the infection and infection prevention and control precautions reinforced; including the need for robust hand hygiene and use of protective aprons

The environment and fomites

A chlorine releasing agent is currently recommended for cleaning of the environment at 1000 ppm of available chlorine. Individual Trusts should adopt a local cleaning policy and regimen depending on the level of contamination and case load. Domestic staff will require training and supervision until declared competent.

<u>Terminal clean</u>: once the patient has left the environment a terminal clean should be undertaken preferably using hydrogen peroxide vapour, all equipment should be cleaned in accordance with manufacturer's instructions and where relevant returned to the company for cleaning. Particular attention should be paid to cleaning of multiple-use equipment (eg BP cuffs, thermometers, computers on wheels, ultra-sound machines) from the bed space of an infected/colonised patient.

If a patient needs to be taken out of the side room or bay to theatre or for imaging, they should be scheduled last on the list for the day and the environment cleaned as described above.

Waste and linen disposal

Trusts should follow their current waste and soiled linen policies as for any other multiresistant healthcare-associated organism.

- attention should be paid to appropriate bagging and isolation of soiled linen and waste so that the environment is not contaminated
- in paediatric and neonatal units, specific attention should be paid to disposal of soiled nappies
- at no time should infected / soiled material be discarded / washed in the clinical hand wash sinks

Further reading

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Useful contact details

- 1. Clinical Mycology advice and referral of candida isolates to PHE Mycology Reference Laboratory or contact elizabeth.johnson@phe.gov.uk
- 2. Advice about decontamination, environmental screening / cleaning of high intensity units contact jimmy.walker@phe.gov.uk