Public Health England

Protecting and improving the nation's health

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

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About Public Health England

Public Health England exists to protect and improve the nation's health and wellbeing, and reduce health inequalities. It does this through world-class science, knowledge and intelligence, advocacy, partnerships and the delivery of specialist public health services. PHE is an operationally autonomous executive agency of the Department of Health.

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Introduction: *Candida auris*

Candida auris is a recently identified *Candida* species that has been associated with infection and outbreaks in healthcare settings on five continents. It has been isolated from a range of body sites, including skin (very common), urogenital tract (common), and respiratory tract (occasional), and resulted in invasive infections, such as candidaemia, pericarditis, urinary tract infections and pneumonia. *C. auris* affects both paediatric and adult populations, and has predominantly been identified in critically unwell patients in high dependency settings. As with other organisms associated with nosocomial outbreaks, it appears to be highly transmissible between patients and from contaminated environments, highlighting the importance of instituting effective infection prevention and control practices. Significantly, all *C. auris* isolates from the UK have demonstrated reduced susceptibility to the first line antifungal therapy, fluconazole, and variable susceptibility to other antifungal agents. Difficulties with identification of this organism in the laboratory and uncertainty about routes of transmission have impacted significantly on outbreak detection and management. By the end of July 2017, there have been over 200 patients with *C. auris* initially detected in 20 NHS Trusts and independent healthcare providers (first detection only), and over 35 additional hospitals in the United Kingdom have received patients with a known *C. auris* detection. Approximately one quarter of reported *C. auris* detections are clinical infections, including 27 candidaemias. There have been three large nosocomial intensive care unit outbreaks in England, which despite intensive infection prevention and control measures have been difficult to control. Given limitations in typing methodology these may include several novel introductions, including after periods without any new detections.

Investigation in clinical 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 cornmeal agar. Growth at 42 - 45ºC (used at the Mycology Reference Laboratory) may be useful to help differentiate it from many other *Candida* species,

especially those for which it is most commonly mis-identified such as *Candida haemulonii.* 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. However, chromogenic agars are useful for screening to identify suspicious colonies from mixed cultures including the presence of *C. albicans.* If there is evidence of non–*C. albicans* species on chromogenic agar these should be sub-cultured onto 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, VITEK-2 YST, BD Phoenix and MicroScan, used in many front line diagnostic laboratories can misidentify *C. auris* as a wide range of Candida species and other genera (most commonly as *Candida haemulonii*, *Candida famata*, *Candida lusitaniae*, *Rhodotorula glutinis* or *Saccharomyces cerevisiae*).

Therefore, it is important that any *Candida* spp isolates associated with invasive infections and isolates from superficial sites in patients from high intensity/augmented care settings and those transferred from an affected hospital (UK or abroad) should be analysed to species level. If suspected *Candida* spp 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 Second Generation Surveillance System (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 they investigated, nearly all of 54 isolates were 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. A recent review of 123 global isolates showed that Clinical Laboratory Standard Institute (CLSI) and European Committee for Antimicrobial Susceptibility Testing (EUCAST) MICs are very similar, with 7% resistance to echinocandins and 10% to amphotericin B. Multi-resistant isolates have been reported from South America. Whole genome sequencing of the organism has found resistant determinants to a variety of antifungal agents. Development of resistance to various antifungals has been observed in previously sensitive isolates. Experience to date from the PHE Mycology Reference Laboratory indicates that so far very few multi-drug resistant strains have been found in the UK but all isolates are resistant to fluconazole and often cross-resistant to other azoles, with variable resistance to polyenes (approximately 20% for amphotericin B) and echinocandins (approximately 10%).

Treatment

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 quite 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 bloodstream infections with this organism, although if the urinary tract or central nervous system (CNS) is involved dual therapy may be necessary, and some antifungal classes do not have bio-availability in either urine or CNS. Clinicians are advised to make decisions on

a case by case basis depending on the site of infection. 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.

Colonisation

Colonisation of patients has been reported from affected hospitals around the world. There is no evidence currently that reliably demonstrates whether *C. auris* is susceptible to chlorhexidine. More work is being done in this area. Clinical experience to date has shown that colonisation tends to persist and is difficult to eradicate 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
- prompt removal of venous cannulas if there is any sign of infection
- high standards of aseptic technique when undertaking wound care
- skin decontamination with chlorhexidine washes in critically ill patients.

There is not an evidence base to recommend the following, though these may be considered in individual settings:

- mouth gargles with chlorhexidine
- use of topical nystatin and terbinafine for targeted topical management of key sites such as venous cannula entry sites.

There is limited evidence that in *in vitro* settings, shorter contact times with chlorhexidine (without alcohol) may not be as effective as povo-iodine based topical

applications in reducing *C. auris* colonisation – this may be considered when performing invasive procedures such as line insertions or surgical procedures in colonised patients.

Screening policies

All Trusts are encouraged to develop a screening policy after local risk assessments are undertaken. Screening is recommended in units that have ongoing cases and/or colonisations, or identification of a new infected or colonised patient, as follows:

- any novel detection in a Trust should be an indicator to screen close contacts if on an intensive care setting
- if the patient has been isolated during admission on a ward other than an intensive care setting, Trusts are advised to speciate all candida isolates from the same unit to the species level using an appropriate method that will detect *C. auris* for the subsequent four weeks
- in all cases, in the four weeks prior to diagnosis in the index patient, hospitals should look back to see if there has been an increase in detection of *Candida* spp in the same intensive care setting or ward as this may represent unrecognised transmission
- if the index patient was not isolated, close contacts who have been in the same bay with an affected patient in the 48 hours prior to first identification should be isolated or cohorted with other contacts, and cared for with enhanced infection prevention and control measures as detailed below for cases. Close contacts can be de-isolated after three consecutive negative screens at least 24 hours apart.

Screening is advised for patients coming from other affected hospitals/units in the UK and abroad. Currently hospital outbreaks have been reported from the United States, India, Pakistan, Venezuela, Columbia, Israel, Oman, South Africa, and Spain, although UK and worldwide prevalence is still to be established due to problems with laboratory diagnosis. An updated PHE briefing note was disseminated in March 2017 to all Trusts

listing UK Trusts with evidence of sustained outbreaks[1]. Time from initial exposure to colonisation as low as four hours have been reported by several affected hospitals.

Suggested screening sites, based on the predilection of *Candida* spp to colonise the skin and mucosal surfaces i.e. genitourinary tract, gastrointestinal, mouth and respiratory tract, are:

- groin and axilla (the most persistently positive in Trusts that have conducted screening)
- urine (there have been several cases of persistent urinary colonisation in catheterised patients)
- nose and throat
- perineal swab
- rectal swab or stool sample.

Other sites that may be considered if clinically indicated are:

- low vaginal swab
- sputum / endotracheal secretions
- drain fluid (abdominal/pelvic/mediastinal)
- cannula entry sites
- wounds.

Routine wound swabs may be used to collect screening samples. Rectal swabs have been shown to be intermittently positive – they may be more useful to detect incident colonisation rather than transmission in hospital environments, but the role of gastrointestinal carriage is as yet unclear.

All screen positive patients should be isolated or cohorted as described below. There is currently no evidence to support the de-isolation of patients found to be colonised or infected with *C. auris* as the length of carriage is unknown. As there is clinical

[1] Please write to candidaauris@phe.gov.uk if you need this resent

experience of recurrence of colonisation, the need for ongoing vigilance in the form of weekly (or more frequent) screens in clinical environments where *C. auris* colonised patients have been managed should be considered by performing local risk assessments.

All newly positive screens or clinical samples from patients unknown to be colonised should be reported to the local PHE Centre Health Protection Team (HPT) – a detailed Standardised Operating Procedure has been developed for HPTs to utilise which details specifics of cases definitions, isolation of cases and contacts, and ward screening for both single sporadic cases and potential outbreak scenarios.

Isolation and rescreening of patients known to be previously colonised is recommended on readmission as there is not enough evidence yet to exclude lifelong colonisation. De-isolation is not recommended apart from in units with experience of managing *C. auris*.

Infection, prevention and control (IPC)

Reports from India, Pakistan, Venezuela, Spain, UK, South Africa, Israel, and Colombia (CDC, personal communication) have described large healthcare outbreaks of *C. auris* infection and colonisation. The precise mode of transmission within the healthcare environment is not known, and is likely to be multifactorial. However, experience during these outbreaks suggests that *C. auris* might substantially contaminate the environment and equipment 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 decontamination can be assured. *C. auris* has been detected on settle plates around patient bedsides and on monitoring devices within the UK. Hospitals must ensure that the bed space requirements between patients comply with the Health Building Note regulations in order to minimise the likelihood of transmission. Adherence to hand hygiene needs to be consistently high and sustained. It is essential that all healthcare staff work in a multi-disciplinary team with their Clinical

Microbiologists and under the direction of their IPC team when dealing with care of patients colonised with *C. auris*.

The patient

Key infection prevention and control measures include:

- isolation of all patients colonised or infected with the organism in a single room, ideally 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 on dry hands
- 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, or likely physical contact with patient's skin)
- these should be donned after hand washing and before entering the room or patient area and removed and discarded in the room or patient environment followed by a thorough hand wash and application of alcohol hand rub on dry hands before exit
- visors and masks are not routinely required and should be worn only if there is a procedural risk of spillage or splashes
- patients and visitors of infected or colonised patients need to be briefed about the infection (possibly using the patient information leaflet) and infection prevention and control precautions reinforced; including the need for robust hand hygiene and use of protective aprons
- single-patient use items such as blood pressure cuffs and pillows should be considered, especially in outbreak situations.

Some Trusts have found the introduction of chlorhexidine impregnated protective disks for long lines useful in preventing invasive infection.

Terminal clean

Once the patient has left the environment a terminal clean should be undertaken. For terminal cleaning of a bedspace or room vacated by a *C. auris* colonised/infected patient, disinfection, preceded by cleaning, of horizontal surfaces plus all items that may have come into contact with the patient or staff hands should occur. The disinfectants used should be those for each item in compliance with the hospital's policy. A hypochlorite is currently recommended for cleaning of the environment at 1000 ppm of available chlorine. As different staff groups may be responsible for different items, attention should be focused on all relevant items going undecontaminated. Application of disinfectant should be thorough ensuring good contact before the disinfectant dries. Privacy curtains should be changed. Consideration should be given to discarding less expensive items that are difficult to decontaminate, or using single-patient use devices such as blood pressure cuffs. Stocks of single use items in the immediate patient environment should be discarded.

If any non-contact disinfection is used (e.g. gaseous hydrogen peroxide or UV), full cleaning and disinfection preceding it should still occur. 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. Cleaning staff should change gloves and aprons with appropriate hand decontamination after cleaning each *C. auris* area. There should be appropriate decontamination of dynamic mattresses.

If a patient needs to be taken out of the side room or bay to theatre, procedure room, or for imaging, they should be scheduled last on the list for the day and the environment cleaned as described above. Several hospitals have reported favourable use of gaseous hydrogen peroxide, following preparatory protocols.

Cleaning and decontamination of equipment

All equipment (including patient monitoring devices and mobility aids) 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 reusable

equipment (e.g. pulse oximeters, thermometer probes, computers on wheels, ultrasound machines) from the bed space of an infected/colonised patient.

Waste and linen disposal

Trusts should follow their current waste and used linen policies as for any other multi-resistant healthcare-associated organism:

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

Further Infection control guidance in community care setting can be accessed from https://www.gov.uk/government/publications/candida-auris-infection-control-incommunity-care-settings

Communications

An information leaflet for affected patients and relatives is available and can be accessed from https://www.gov.uk/government/publications/candida-auris-a-guide-for-patients-and-visitors.

C. auris colonisation information should be included in any discharge summary or patient transfer documents, ideally with direct communication to IPC representatives at receiving hospitals. If positive results become available after discharge or transfer, information should be relayed to the receiving hospital/GP for further communication to the patient and for relevant public health action.

If a patient dies and the cause of death is attributable to *C. auris*, this must be included in the death certificate and should be relayed to the National Incident Team (Contact Details 6). To date there has been no attributable *C. auris* mortality within the UK.

Systems permitting, each hospital should label colonised patients with an infection control flag on the patient electronic case record, so healthcare professionals are immediately alerted to the *C. auris* status if or when that patient is readmitted in future.

Useful contact details

1. For mycology advice, and referral of candida isolates to PHE Mycology Reference Laboratory, please contact elizabeth.johnson@phe.gov.uk and andrew.borman@phe.gov.uk
2. For advice about decontamination, environmental screening, and cleaning please contact peter.hoffman@phe.gov.uk, jimmy.walker@phe.gov.uk and ginny.moore@phe.gov.uk
3. For clinical management advice, please contact s.schelenz@rbht.nhs.uk, a.hall@rbht.nhs.uk, surabhi.taori@nhs.net, and katie.jeffery@ouh.nhs.uk
4. For IPC advice, please contact the above and bharat.patel@phe.gov.uk, rohini.manuel@phe.gov.uk, and martina.cummins@phe.gov.uk
5. Trusts should contact their local Health Protection Team (HPT), however for HPTs who require advice from colleagues with *C. auris* experience, please contact yimmy.chow@phe.gov.uk, janice.lo@phe.gov.uk, louise.bishop@phe.gov.uk, and clare.humphreys@phe.gov.uk
6. For national incident advice please contact colin.brown@phe.gov.uk, rebecca.guy@phe.gov.uk, and PHE.candidaauris@nhs.net or candida.auris@phe.gov.uk

Further reading

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