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Review Article

Review Article

Candida auris: The recent emergence of a multidrug-resistant fungal pathogen

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Abstract

Candida auris is an emerging multidrug-resistant yeast that causes serious invasive infections with high mortality. It was first discovered in 2009, and since then, individual cases or outbreaks have been reported from over 20 countries on five continents. Controlling *C. auris* is challenging for several reasons: (1) it is resistant to multiple classes of antifungals, (2) it can be misidentified as other yeasts by commonly available identification methods, and (3) because of its ability to colonize patients perhaps indefinitely and persist in the healthcare environment, it can spread between patients in healthcare settings. The transmissibility and high levels of antifungal resistance that are characteristic of *C. auris* set it apart from most other *Candida* species. A robust response that involves the laboratory, clinicians, and public health agencies is needed to identify and treat infections and prevent transmission. We review the global emergence, biology, challenges with laboratory identification, drug resistance, clinical manifestations, treatment, risk factors for infection, transmission, and control of *C. auris*.

Key words: *Candida*, drug resistance, infection control, fungal, healthcare-associated infections.

Introduction

Candida auris is an emerging multidrug-resistant yeast that can cause invasive infections, is associated with high mortality, and can spread in healthcare settings. This yeast was first described in 2009 and has since been reported in over 20 countries on five continents. *C. auris* poses a global health threat for several reasons:

1. Multidrug resistance is common, and a few isolates are resistant to all three of the main classes of antifungal drugs, severely limiting treatment options.[1]
2. *C. auris* is commonly misidentified in clinical laboratories. Unless laboratories are aware of possible misidentification and have the ability to perform further evaluation, cases of *C. auris* could go undetected.
3. *C. auris* can be transmitted between patients in healthcare settings and cause healthcare-associated outbreaks. *C. auris* can colonize patients, especially on the skin, perhaps indefinitely, and persist for weeks in the healthcare environment. The lack of decolonization methods and suboptimal efficacy of some commonly used hospital environmental disinfectants compounds the challenge of controlling its spread.

The genus *Candida* comprises an array of phenotypically similar yet genetically highly divergent yeasts. *C. auris* differs markedly from common pathogenic *Candida* species like *Candida albicans* and *Candida glabrata*. In healthcare settings, *C. auris* behaves more like transmissible bacterial multidrug-resistant organisms (MDROs), such as methicillin-resistant *Staphylococcus aureus* (MRSA) and carbapenem-resistant Enterobacteriacea (CRE), than other *Candida* species. Unlike other *Candida*

infections, which are generally thought to result from autoinfection from host flora, *C. auris* can be transmitted between patients. Unlike for most other *Candida* species, for which transmission-based precautions are generally not required, *C. auris* requires implementation of specific infection control measures, much like those used for control of MRSA and CRE.

With its multidrug resistance, transmissibility, and severe outcomes, *C. auris* has all the makings of a "superbug." Control of *C. auris* requires better understanding of the organism itself, vigilance and accurate identification, appropriate treatment and infection control measures, and a coordinated public health response. We review the emergence of *C. auris*, examining the global advent, biology, challenges of identification, multidrug resistance, clinical manifestations, treatment, risk factors for infection, transmission, and control of *C. auris*.

Methodology

All articles on PubMed as of March 2018 that contained the phrase "Candida auris" were reviewed ($n = 109$). Citations of these articles were reviewed for additional articles. When articles did not state the date of specimen collection for the earliest *C. auris* isolate in a country, isolate GenBank numbers, if provided, were searched in the Nucleotide database (www.ncbi.nlm.nih.gov/nuccore) to find the collection year. Supplemental governmental documents and conference abstracts were reviewed as needed for details on *C. auris* guidance and case identification by country.

Original data on *C. auris* cases, isolates, or specimens were extracted, including date of first report of cases and of first isolate by country; facility type; number of cases; proportion of cases that were clinical and bloodstream; specimen source; age and sex of patients; proportion of cases with central venous catheters, total parenteral nutrition, antibiotic or antifungal exposure, or other multidrug-resistant organisms; days to onset of *C. auris*; treatment; mortality; transmission; identification methods; resistance by drug; whole-genome sequencing; infection control procedures; and environmental testing. Data from articles describing other *C. auris* topics, like the development antifungal drugs or the microbiology of *C. auris* were summarized.

Emergence

Discovery and earliest cases

C. auris was first reported in 2009 following isolation from the external ear canal of a patient in Japan.[2] The isolate was collected in June 2006 (GenBank accession no. NG055302) from an inpatient in a Tokyo geriatric hospital as part of an antifungal yeast diversity study. Sequencing of the D1/D2 domain of the 26S recombinant DNA (rDNA) and the internal transcribed spacer (ITS) region of rDNA revealed that the isolate was closely related to *Candida haemulonii*, *Candida pseudohaemulonii*, *Candida ruelliae*, and *Candida heveicola,* but was distinct from these previously known species. The organism's unique ability to grow at 42°C and carbon assimilation patterns further confirmed this distinction. Based on these characteristics, the authors proposed a new species, *Candida auris* (Latin for "ear" since this isolate was obtained from the ear canal).

C. auris was subsequently reported in 2011 from 15 patient specimens in South Korea.[3] The cases were identified from ear specimens collected in 2006 at three hospitals as part of a multicenter surveillance study of unusual yeasts.[3,4] The original identification of these isolates occurred before *C. auris* was first given a name, so investigators initially reported these isolates as a novel species closely related to *C. haemulonii*. Through ITS and D1/D2 sequencing performed retrospectively after the first report of *C. auris* was published, the isolates were in fact confirmed to be *C. auris*.[3,4] All patients had chronic otitis media, and seven had persistently positive cultures, including three who had received systemic antifungals.[4] Based on the sequencing results and clustering in three hospitals, the investigators proposed that intra- and interhospital clonal transmission had occurred.[4]

Soon afterward, reports of the first *C. auris* invasive bloodstream infections emerged.[5] Three cases were identified in South Korea during retrospective microbiology reviews of unidentified yeasts, including one isolate collected in 1996, making it the earliest known occurrence of *C. auris*. The other two cases occurred in 2009. All three patients had hospital-onset infection; they had been hospitalized for at least 12 days before their first culture yielding *C. auris*. Isolates were initially misidentified as *C. haemulonii* on VITEK 2 and as *Rhodotorula glutinis* using API 20C and were accurately identified as *C. auris* by ITS and D1/D2 sequencing. The cases occurred in two 1-year-olds and a 74-year-old. Only one child cleared fungemia and survived. This report served as the first indication that *C. auris* was not just confined to the ears, as its name might suggest, but that it could cause serious, even fatal, invasive infections.

In 2013, *C. auris* bloodstream infections began to be reported from India, with the earliest *C. auris* culture dating back to 2009.[6–8] These initial Indian studies identified four affected facilities: a tertiary care general hospital, a pediatric center, a hospital intensive care unit, and a university hospital located in northern and southern India. In subsequent years, cases of *C. auris* were also reported from Kenya and South Africa in 2014 and Kuwait in 2015.[9,10]

In order to determine whether *C. auris* was truly emerging as a cause of human infections, a review of the SENTRY database was conducted. SENTRY is a collection of >15,000 *Candida* isolates collected during 2004–2015 from Asia, Europe, Latin America, and North America. Four isolates between 2004 and 2009, initially identified as *C. haemulonii*, were retrospectively identified as *C. auris*.[1] Unpublished US Centers for Disease Control and Prevention (CDC) reviews of other large-scale isolate collections also confirmed the finding that *C. auris*, as well as

C. haemulonii, were relatively rare before 2009. These findings suggest that *C. auris* emerged as a cause of human infections primarily in the last decade.

Global reach

Since its description in 2009, *C. auris* has been reported from 23 countries spanning five continents (Table 1, Fig. 1). Because clinical laboratories often do not identify *Candida* isolates to the species level, and because *C. auris* is misidentified by commonly available laboratory methods, *C. auris* may be present in other countries, but has not been detected or has not yet been reported.

Table 1. Countries where *Candida auris* cases have been reported, as of March 2018.*

Country	Year of first report	Year of earliest isolate reported	Single case or multiple cases reported
Japan[†2,89]	2009	1997	Multiple cases
South Korea[5]	2011	1996	Multiple cases
India[6,7]	2013	2009	Multiple cases
Kenya[‡]	2014	2010	Multiple cases
South Africa[9]	2014	2012	Multiple cases
Kuwait[10]	2015	2014	Single case
Germany[16,90]	2016	2015	Multiple cases
Norway[90]	2016	NR	Single case
Pakistan[§1]	2016	2008	Multiple cases
United Kingdom[39]	2016	2013	Multiple cases
United States[20,91]	2016	2013	Multiple cases
Venezuela[15]	2016	2012	Multiple cases
Canada[28,29]	2017	2017	Multiple cases
Colombia[47,48]	2017	2013	Multiple cases
Israel[37]	2017	2014	Multiple cases
Oman[61]	2017	2016	Multiple cases
Panama[12]	2017	2016	Multiple cases
Spain[50,90]	2017	2016	Multiple cases
Austria[16]	2018	2018	Single case
Belgium[16]	2018	NR	Single case
France[‖16,31]	2018	2017	Multiple cases
Malaysia[71]	2018	NR	Single case
United Arab Emirates[92]	2018	2017	Single case

NR, Not reported.

*References are the earliest publication for each data point. When a country has reported multiple cases by having more than one single case report, the first two single case reports are cited.

†Iguchi S, Mizushima R, Kamata K, et al. *Candida auris* detection from clinical isolates in Japan. 91st Annual Meeting of Japanese Society for Bacteriology, Fukuoka, Japan, March 27–29, 2018, *P*-011.

‡Okinda N, Kagotho E, Castanheira M et al. Candidemia at a referral hospital in sub-Saharan Africa: emergence of *Candida auris* as a major pathogen. European Conference on Clinical Microbiology and Infectious Diseases, Barcelona, May 10–13, 2014, P0065.

§Farooqi JQ, Soomro A, Sajjad S et al. Outbreak of *Candida auris* in a tertiary care hospital in Karachi, Pakistan. International Meeting on Emerging Diseases and Surveillance, Vienna, Austria, November 4–7, 2016, 03.004.

‖GenBank accession no. MG736297

Outbreaks of *C. auris* infections have been reported in healthcare facilities in Colombia,[a] India,[8,11] Pakistan, Panama,[12] Spain,[b] the United Kingdom,[13] the United States,[14] and Venezuela.[15] One European outbreak involved 382 cases.[16]

Several recent reports about *C. auris* describe not just a few sporadic cases or distinct outbreaks, but rather that *C. auris* has become a common cause of *Candida* infection. In South Africa, *C. auris* is now a leading cause of candidemia, having caused hundreds of confirmed cases.[17] In India, a study of 27 intensive care units across the country found 5.7% of candidemia cases from April 2011 to September 2012 were due to *C. auris*.[18] According to a report from Kenya, 38% of candidemia cases during 2010 to 2013 at one hospital were caused by *C. auris*. These changes represent a remarkable shift in species distribution, considering that *C. auris* had rarely been detected before 2009 anywhere in the world.

In the United States, over 250 *C. auris* cases have been identified through specimens collected during routine clinical care as of February 2018.[19] The earliest known case in the United States was from 2013 in a patient who was transferred for care to the United States from a hospital in the United Arab Emirates.[20] All other reported US cases occurred after mid-2015. Cases have been identified in 10 states but have been primarily concentrated in New Jersey and the New York metropolitan area.[19] In New York and New Jersey, most patients have received care at interconnected healthcare facilities in concentrated geographic areas.[14] Epidemiologic links between cases have also been found in Illinois, where one healthcare facility was associated with at least three cases.[14]

Simultaneous emergence in disparate geographic regions

The perplexing and increasing pace of reports of *C. auris* from separate global geographic regions raise questions about how *C. auris* emerged so rapidly around the world. Did the organism emerge in one location and spread to the rest of the world? Did it emerge independently across these different regions? To answer these questions, mycologists turned to whole-genome sequencing (WGS).

WGS of isolates from around the world revealed some remarkable and puzzling results. Genetic sequences of *C. auris* isolates grouped into four geographically distinct clades: South Asia, South Africa, South America, and East Asia.[1] The clades differ by tens of thousands of single-nucleotide polymorphisms

[a] Armstrong PA, Escandon P, Caceres DH et al. Hospital-associated outbreaks of multidrug-resistant *Candida auris* — multiple cities, Colombia, 2016. Epidemic Intelligence Service Conference, Atlanta, April 24-27, 2017, 11:20.

[b] Ruiz A. Epidemiology and clinical features caused by *Candida auris* in the setting of a prolonged outbreak. Trends in Medical Mycology Conference, Belgrade, Serbia, October 6-9, 2017, S18.4.

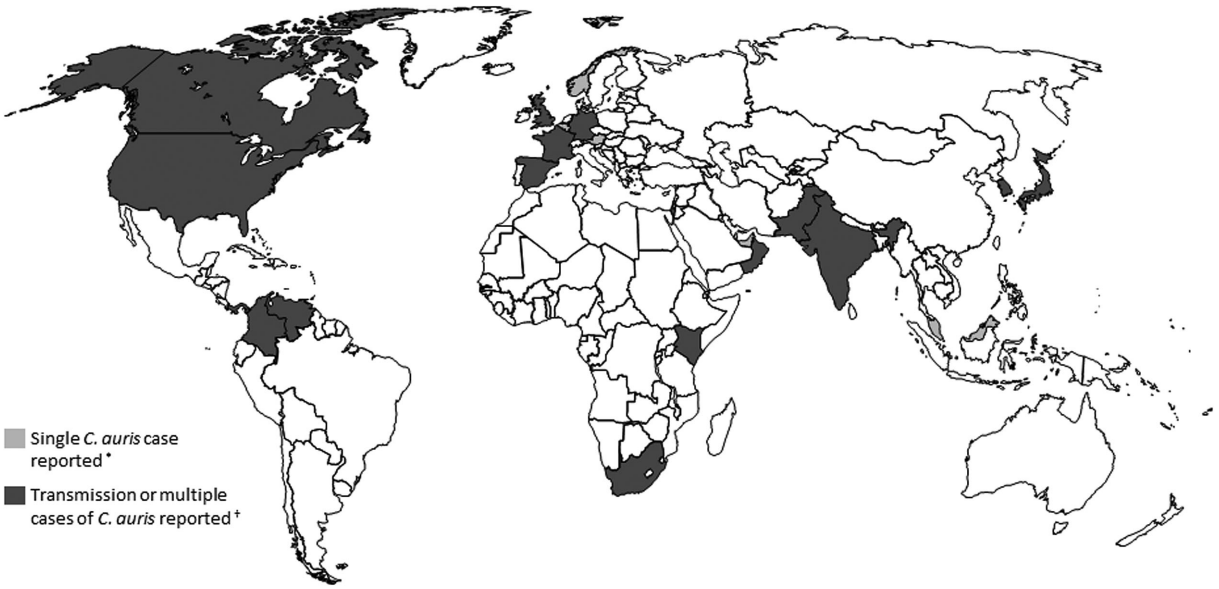

Figure 1. Countries from which *Candida auris* cases have been reported, as of March 31, 2018.‡

*Single cases of *C. auris* have been reported from Austria, Belgium, Kuwait, Malaysia, Norway, and the United Arab Emirates.

†Multiple cases of *C. auris* have been reported from Canada, Colombia, France, Germany, India, Israel, Japan, Kenya, Oman, Pakistan, Panama, South Africa, South Korea, Spain, the United Kingdom, the United States, and Venezuela; in some of these countries, extensive transmission of *C. auris* has been documented in more than one hospital.

‡Other countries not highlighted on this map may also have undetected or unreported *C. auris* cases.

(SNPs), whereas isolates within a clade are highly related and differ by only a few hundred SNPs or less.[1,21] The *C. auris* genome consists of approximately 12.5 million base pairs, hence a difference of a few hundred SNPs within a clade indicates that isolates are almost clonal.[1] To date, these four clades have remained discrete, and all isolates sequenced after the initial assessment have grouped into one of the four clades. This unusual finding suggests that *C. auris* emerged independently and nearly simultaneously in at least four geographic locations.

The reasons for this simultaneous emergence are not known. Hypotheses have included increasing rates of antifungal use globally, animal reservoirs, and environmental changes. Initial epidemiologic characterization of *C. auris* cases found that many patients with *C. auris* infection had been receiving antifungal drugs at the time *C. auris* was isolated,[1] suggesting that drug pressure could have resulted in emergence of this resistant organism, at least within healthcare settings. An animal or environmental reservoir for *C. auris* has not yet been identified. However, closely related *Candida* species have been isolated from several animal, food, and environmental sources, including fish,[22] cassava roots,[23] and sea water.[22,24] The clade-specific geographic clustering may also offer insight into the reasons for simultaneous emergence. However, strains may have originated in a different location than they were first detected as a human pathogen. The unique attributes of *C. auris*, like its high rates of multidrug resistance, geographic presence, and ability to grow in conditions with high salinity and high temperatures, may provide clues to its origins, which remain unknown.

Whole-genome sequencing as an epidemiological tool

CDC is increasingly using WGS in fungal investigations, and this approach has greatly informed our understanding of *C. auris* transmission. WGS performed on *C. auris* isolates from the United States show that most isolates from New York and New Jersey are related to isolates from South Asia and that Illinois isolates are related to isolates from South America.[14] At least five cases in the United States have been identified in patients who received healthcare in a country with known *C. auris* transmission in the months before their *C. auris* infection.[25] In each case, the patient's isolate closely aligned with isolates from the country where the patient had received care: India, Pakistan, Venezuela, and South Africa. Taken together, WGS provides evidence for multiple introductions of *C. auris* into the United States followed by local transmission.[14]

Additional sequencing techniques have been employed for the investigation of *C. auris*. In the United Kingdom, researchers have begun using the MinION, a nanopore sequencer, to examine the epidemiology of *C. auris*, making this the first time this technology has been used during a fungal outbreak.[26] ITS and 28S rDNA D1/D2 sequencing have shown that the several independent introductions of *C. auris* occurred in the United Kingdom, similar to the WGS results in the United States.[27]

Travel-based introductions continue to be supported through epidemiology as well. Two Canadian patients had recently received care in India,[28,29] an Israeli patient had received care

in South Africa,[30] and a French patient had received care in India and Iran (at this time, Iran has not reported any *C. auris* cases).[31] Travel-related cases and evidence for introduction from abroad have led to guidance in the United States[25] and the United Kingdom[32] on screening or species identification for patients with exposure to healthcare facilities in countries where *C. auris* transmission has occurred.

Biology and morphology

The closest relatives of *C. auris* are *C. ruelliae, C. pseudohaemulonii, Candida duobushaemulonii, Candida vulturna, C. heveicola, Candida konsanensis, Candida chanthaburiensis, C. haemulonii*, and *Candida haemulonis* var. *vulnera*.[33]

C. auris is an ovoid to elongate budding yeast, which seldom forms rudimentary pseudohyphae[6,27,34] and typically appears as pink, but sometimes white or red, colonies on CHROMagar *Candida* or CAN2 chromogenic medium.[31,35] This organism has a high tolerance for salinity and heat.[36] Its unique ability to grow at temperatures up to 42°C[8,37] and to grow in high salt conditions may help to distinguish *C. auris* from other *Candida* species and aid laboratory isolation.[36] However, none of the phenotypic characteristics of *C. auris* are sufficient evidence for definitive identification. Sequencing, mass spectrometry, or a VITEK 2 version 8.01 are needed to accurately distinguish *C. auris* from closely related *Candida* species.

Some strains of *C. auris* have been reported to form aggregations in culture, which may allow the organism to resist penetration by detergents, ultraviolet light, or other cleaning methods.[27] *C. auris* also forms biofilms, which provide a mechanism of adherence to surfaces. However, these biofilms are significantly thinner and less complex than those of *C. albicans*, primarily due to the rarity of pseudohyphae.[34,38] *C. auris* may therefore have reduced ability to attach to surfaces like catheter material as compared to species that can form more robust biofilms.[38]

In animal models, *C. auris* exhibits similar or slightly less virulence as *C. albicans* and *Candida tropicalis* and greater virulence than the closely related species *C. haemulonii*.[37,39,40] Its ability to form biofilms, produce phospholipase and proteinase, and secrete aspartic proteases as well as the presence of oligopeptide transporters and mannosyl transferases may explain some of the virulence seen with *C. auris*, though some of these characteristics have varied by strain.[38,41] Aggregate-forming strains may be less virulent than strains without cell aggregations.[39] Despite these advances in our understanding of *C. auris*, much remains unknown about its cell biology and virulence characteristics.

Missed identification and misidentification

One of the biggest challenges in controlling the spread of *C. auris* is that the organism can "hide in plain sight," going undetected in healthcare facilities. Many clinical laboratories do not perform species identification for *Candida*, and, when identification is attempted, *C. auris* can be misidentified.

Identification often not performed

Many laboratories do not routinely identify *Candida* isolates to the species level. Yeast identification capacity is limited in many laboratories[42–44] and *Candida* species, when identified from non-invasive sites, such as the lungs or urine, may represent colonization and not require antifungal treatment, making information about the specific species seem unnecessary. In some cases, clinicians may not appreciate the need for species-level identification even for invasive *Candida* infection and plan to treat all *Candida* with the same antifungal drug.

However, there are compelling reasons to identify *Candida* species, especially when the infection is in an invasive, sterile site. Many *Candida* species have characteristic antifungal resistance patterns, and knowing the species can assist clinicians in making an effective and appropriate choice for antifungal treatment. For example, *C. albicans* is usually susceptible to antifungals and can be treated with fluconazole, whereas *C. glabrata* has high fluconazole resistance rates and echinocandins should be used as the first-line treatment instead.[45]

Identifying *Candida* species from nonsterile sites should also be considered in certain situations. Unlike for other *Candida* species, which are not thought to be transmitted in the healthcare environment, identification of *C. auris* is critical for preventing transmission through the implementation of infection control measures. Transmission-based precautions are recommended not just for patients with invasive *C. auris* infections, but also for patients with *C. auris* identified from nonsterile body sites who may be colonized rather than infected. Further underscoring the importance of species identification for *Candida* from nonsterile sites is that approximately half of US clinical *C. auris* cases have been identified in non-blood samples, such as urine, wound, respiratory specimens, and bile fluid.[25] Thus, cases may go unrecognized if laboratories do not identify the *Candida* species for non-blood specimens. CDC recommends determining species from nonsterile sites when:

1. Clinically indicated in the care of a patient.
2. A case of *C. auris* colonization or infection has been detected in a unit or facility.
3. A patient has had an overnight stay in a healthcare facility outside the United States in the previous year in a country with documented *C. auris* transmission.[25]

Misidentification of *Candida auris*

Even when species-level identification is performed, *C. auris* may be misidentified by the most commonly used clinical microbiology methods, including biochemical methods and automated testing instruments. The most frequent misidentification

has been *C. haemulonii*, a closely related species.[3] A study of Indian isolates found that ~90% of isolates from five facilities classified by VITEK 2 as *C. haemulonii* were actually *C. auris*.[35] In a test of a panel of 10 *C. auris* isolates by yeast identification systems, *C. auris* was misidentified as *R. glutinis* by API 20C AUX, as *Candida catenulata* and *C. haemulonii* by BD Phoenix, as *C. haemulonii* by VITEK 2, and as *Candida famata*, *Candida lusitaniae*, *Candida parapsilosis*, and *Candida guilliermondii* by MicroScan.[46] Other investigators report that *C. auris* has also been misidentified as *C. albicans*, *C. catenulata*, and *C. tropicalis* on MicroScan,[47,48] as *C. famata* by API Candida and VITEK 2,[6,47] as *C. parapsilosis* on RapID Yeast Plus,[49] and as *Candida sake* by API 20C[6,50] and API/ID32C.[31] *C. auris* should also be suspected when there is an increase in unidentified *Candida* isolates from a patient care unit.

Molecular methods or matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS) are required for species identification. *C. auris* can be identified by sequencing the D1/D2 region of the 28S rDNA or ITS of rDNA.[5] Bruker Biotyper and bioMérieux VITEK MS MALDI-TOF MS identification currently requires the use of a "research use only" database that contains *C. auris*. Without this database, the systems will provide no species identification ("No ID")[46] or the VITEK MS system may misidentify *C. auris* as *C. haemulonii* or *C. lusitaniae*.[50] Other databases with *C. auris* identification available have also been created, including Quest Diagnostics's CMdb[51] and CDC's MicrobeNet.[52] VITEK 2 with the 8.01 software update may also correctly identify *C. auris*, though independent studies demonstrating this have not yet been published. These methods for *C. auris* identification are often not available in laboratories. For example, the European Centre for Disease Prevention and Control found over a quarter of the European Union/European Economic Area countries did not have the laboratory capabilities needed to identify *C. auris*.[16]

Rapid culture-independent diagnostic tests are under development, including polymerase chain reaction (PCR) and real-time PCR techniques.[53] Such techniques will greatly enhance capacity to identify patients who are colonized with *C. auris*. Rapid identification will support infection control by allowing healthcare facilities to quickly screen patients to identify new cases and swiftly implement infection control measures.

Multidrug resistance

C. auris is a highly concerning pathogen because it can be resistant to multiple antifungal drugs, with some isolates resistant to all three major antifungal classes (azoles, polyenes, and echinocandins). The Clinical and Laboratory Standards Institute (CLSI) and the European Committee for Antimicrobial Susceptibility Testing (EUCAST) have not established clinical susceptibility minimum inhibitory concentration (MIC) breakpoints for *C. auris*. In the interim, CDC has proposed the following tentative breakpoints, conservatively based on those established for other species: ≥32 for fluconazole, ≥2 for amphotericin B (or ≥1.5 if using Etest), ≥4 for anidulafungin and micafungin, and ≥2 for caspofungin.[54]

In a collection of 54 isolates from India, Pakistan, South Africa, and Venezuela, 93% of isolates were resistant to fluconazole, 35% were resistant to amphotericin B, and 7% were resistant to echinocandins using the following breakpoints: ≥32 for fluconazole, ≥2 for amphotericin B, and ≥8 for echinocandins.[1] Forty-one percent of isolates were resistant to at least two drug classes and two isolates were pan-resistant.[1]

In the largest study of *C. auris* resistance, on 350 isolates from India, 90% of isolates were resistant to fluconazole by the tentative breakpoints described above, 2% to anidulafungin, 2% to micafungin, and 8% to amphotericin B.

In the United States, about 90% of isolates have been resistant to fluconazole, 30% have been resistant to amphotericin B, and 5% have been resistant to echinocandins.[54] Public Health England has reported that all UK isolates have been resistant to fluconazole, approximately 20% have been resistant to amphotericin B, and about 10% have been resistant to echinocandins.[32] Taking data from around the world into account, *C. auris* has been generally resistant to fluconazole, and a substantial portion of isolates has been resistant to amphotericin B and echinocandins.

Most other species of *Candida* identified in clinical specimens exhibit high *in vitro* susceptibility to antifungal drugs. One of the other drug-resistant *Candida* of high concern has been *C. glabrata*, in which approximately 10% of isolates in the United States exhibit fluconazole resistance and 0–10% exhibit echinocandin resistance.[56,57] In comparison, the level of drug resistance observed in *C. auris* is unprecedented. Molecular mechanisms underlying this resistance are currently under investigation. Twelve *Erg11* mutations, which have been found in fluconazole-resistant but not wild-type *C. albicans*, have been found in *C. auris*.[1,55] Three of these mutations have been directly linked to drug resistance in *C. albicans*, suggesting that they contribute to the resistance observed in *C. auris* as well.[58] Efflux pump activity contributes to azole resistance in other *Candida* species and may contribute to resistance in *C. auris*, though the extent of this contribution is unknown.[37] None of these mechanisms alone can account for the high levels of resistance seen in *C. auris*, so multiple mechanisms are likely involved. Elevated echinocandin MICs are likely the result of *FKS* mutations observed in *C. auris* isolates, such as the S639F mutation observed in isolates from India.[55] These mutations correspond to known mutations in other *Candida* species, which have been directly linked to echinocandin resistance.[59] Finally, while resistance to amphotericin B is rare in the most common

Candida species, it is observed in approximately 30% of US isolates of *C. auris*. Though unconfirmed at this time, it is suspected that this is likely due to a reduction in ergosterol content in the cellular membrane—specifically a mutation in a gene involved in ergosterol biosynthesis.[60]

Clinical manifestations

Similar to other *Candida* species, *C. auris* can cause severe invasive infections or colonize patients without infection. *C. auris* has been isolated from normally sterile body sites, including blood, bone, and cerebrospinal fluid, indicating invasive infection.[39,47] Infections may be severe, and persistently positive blood cultures for >5 days or recurrent candidemia in those with *C. auris* candidemia have been reported.[20] *C. auris* candidemia is associated with mortality rates of about 30–60%, depending on the setting.[5,6,8,15,37,47,50,61,62] Other clinical sources found in the course of routine patient care have been bile fluid, the ear, jejunal biopsy, ocular secretion, peritoneal fluid, pleural fluid, the respiratory tract, urine, vaginal fluid, and wounds; some of these represent sites of colonization rather than infection. Patients can also be asymptomatically colonized with *C. auris* on the skin, nares, and other body sites.

Treatment

Only three major classes of antifungal drugs are available to treat invasive fungal infections. *C. auris* poses a real treatment challenge because of high rates of antifungal drug resistance. As reported above, most *C. auris* isolates are resistant to fluconazole, the most widely available antifungal treatment for candidiasis. The alternatives, echinocandins and amphotericin B, are expensive and are not easily available in countries with more limited resources.[17] Amphotericin B is also known for causing severe side effects.

Although studies have reported therapeutic outcomes,[1,8,15] no systematic study has assessed effectiveness of various antifungals against *C. auris* infections in humans. However, in a mouse model, micafungin was more efficacious at killing *C. auris* than fluconazole and amphotericin B.[63] An *in vitro* study examining combinations of treatment with echinocandins and azoles found a synergistic interaction between micafungin and fluconazole and did not find any antagonistic interactions between micafungin or caspofungin and fluconazole or voriconazole.[64] Research is also being conducted on activity of new drugs like SCY-078,[38,65] APX001A/APX001,[66] and CD101[67] against *C. auris*, but these options are not yet available for clinical use in most settings.

Based on the most frequent resistance profiles, echinocandins are the recommended first-line treatment for most *C. auris* infections in adults.[25] Antifungal susceptibility testing is advised to inform treatment and patients should be closely monitored for treatment failure. Acquired resistance while on treatment is a concern. Echinocandin resistance has developed in patients with *C. auris* infection while receiving echinocandin treatment.[25] For neonates and infants under 2 months of age, CDC recommends amphotericin B deoxycholate (1 mg/kg daily) as the first line treatment, with consideration of liposomal amphotericin B (5 mg/kg daily) if unresponsive to amphotericin B deoxycholate.[68] Echinocandin treatment in neonates and infants under 2 months of age should only be considered in rare circumstances and only after checking that the central nervous system has not been affected. Removal of catheters and lines and surgical debridement have been used alongside antifungal drugs when clinically indicated.[5,8,15,30,61,69,70]

Risk factors for *Candida auris* infection

Case reports and descriptive studies of *C. auris* have provided insights on the populations most likely at risk for *C. auris* infections. *C. auris* can infect people of all ages; *C. auris* candidiasis is most common in older persons, and infections in neonates and children have occurred.[6,15] Many of the risk factors for *C. auris* infection are similar to risk factors for other types of *Candida* infections and include underlying medical conditions like cancer and diabetes, as well as recent history of abdominal surgery, presence of central venous catheters, and recent antibiotic exposure.[1,8] Nearly half of patients with *C. auris* infection had been receiving antifungals at the time of or immediately before *C. auris* infection was diagnosed, indicating that previous antifungal therapy may be a risk factor for *C. auris* infection.[1,6,8,30,47,61,62] Patients with *C. auris* infection often have catheters, tracheostomies, gastrostomy tubes, total parenteral nutrition, or other invasive devices.[8,12,15,30,47,48,62,70,71]

Most patients with *C. auris* infection in the United States have had extensive exposure to healthcare in the months preceding the *C. auris* infection, particularly in higher acuity long-term care facilities, such as long-term acute care hospitals and skilled nursing facilities that support patients who are chronically ventilator dependent.[14] Exposure to long-term care facilities has been a known risk factor for acquiring several bacterial MDROs, such as CRE;[72] in contrast, other *Candida* infections have historically been in associated with care in intensive care units. Recent exposure to healthcare in countries with extensive *C. auris* transmission is also an emerging risk factor.

One Indian study investigated risk factors for *C. auris* candidemia compared to non-*C. auris* candidemia.[62] This analysis found that geographic region, admission to public sector hospitals (compared with private sector hospitals), underlying respiratory illness, vascular surgery, prior antifungal exposure, and low APACHE II scores were significantly associated with *C. auris* candidemia.

Transmission of *Candida auris*

With the exception of documented outbreaks of *C. parapsilosis* in intensive care units, *Candida* have not historically been thought to spread in healthcare settings.[73–75] *C. auris* appears distinct among yeast in that it readily spreads in healthcare settings. The sections below elaborate on the various aspects of *C. auris* that contribute to its ability to spread in healthcare settings. Interventions to limit the spread of *C. auris* are similar to those used for multidrug-resistant bacteria, which traditionally have been the focus of healthcare-associated transmission research and infection control.

Patients can be colonized with *Candida auris*

Many *Candida* species are commensals of the gastrointestinal tract, although they have also been isolated from other body sites, such as skin and nails.[76] *C. auris* seems to have a special predilection for the skin. Data from swabs taken to assess patients for *C. auris* colonization show that the axilla and groin are the highest yield sites to detect colonization, followed by nares. Specimens from urine, stool, vagina, and rectum have also yielded *C. auris*.[36] Patients with clinical infection with *C. auris* were typically found to be colonized in noninvasive sites, like skin, long after resolution of invasive infection.[77] Patients may also become colonized with *C. auris* without active infection.

Although asymptomatic colonization with *C. auris* does not require antifungal treatment, it is important to identify individuals who are colonized. Colonization can lead to invasive infections; patients who were colonized with *C. auris* developed an invasive bloodstream infection days to months after becoming colonized. The candidemia usually occurs after an event, such as placement of a new line or tube, which provides the opportunity to introduce the organism from the skin into the bloodstream. Patients colonized with *C. auris* can also be a source of transmission to other patients. Unlike the management of almost any other *Candida* species, a patient known to be colonized with *C. auris* should be placed in a single room with contact precautions to prevent spread in the healthcare facility.

For many patients in long-term healthcare settings, colonization with *C. auris* persists for many months, and possibly indefinitely.[11,25,32] To date, few patients followed in the United States have cleared colonization, and there are no known decolonization regimens. Whether some topical antiseptics might reduce the burden of *C. auris* on the skin, and therefore provide a potentially valuable tool for infection control, is unclear. *In vitro* testing has shown 10% povidone-iodine, a skin antiseptic, to be effective in reducing *C. auris*.[78] Chlorhexidine gluconate solutions containing isopropyl alcohol, usually used for catheter placement and maintenance, may also be effective, but a diluted 4% chlorhexidine gluconate wash did not sufficiently reduce *C. auris* burden.[78] Chlorhexidine body washes have been used in healthcare facilities with *C. auris* outbreaks settings, but patients have remained colonized with *C. auris* even after repeated washes.[11,13] Whether chlorhexidine plays any role in source control (reducing burden of *C. auris* rather than eradication) remains to be studied. Other potential decolonization strategies could include use of topical antifungal drugs but have not been studied.

Transmission between patients

C. auris can be transmitted between patients in healthcare settings. In the United States, 12% of close healthcare contacts of index patients (e.g., persons who shared a room with an index patient or had an overlapping stay in a healthcare facility with an index patient), who were screened for *C. auris*, primarily in long-term healthcare settings, were colonized.[14] In India, 21% of screened patients (mainly those in the same ward as the index patients) were colonized with *C. auris*.[11] Studies have suggested that colonization can occur rapidly, after just a few hours or a few days of exposure.[11,13] Transmission of *C. auris* has also been documented through solid organ transplantation.[14,79]

Healthcare personnel may play a role in transmitting *C. auris* from one patient to another, particularly with inadequate hand hygiene and contact precautions and through the movement and use of contaminated equipment. In a study of a north Indian tertiary hospital, *C. auris* was detected on the hands of four healthcare workers (2.8%); this was likely due to inadequate hand hygiene as opposed to long-term colonization.[11] In a *C. auris* outbreak investigation in the United Kingdom, of >250 healthcare personnel who were screened with nose, axilla, groin, and throat swabs, only one, a nurse, was found to be transiently colonized with *C. auris*.[13]

Although transmission of *C. auris* in healthcare settings has been well-documented, less is known about transmission in the community. A report of screening on admission to the hospital (potentially reflecting burden of *C. auris* in the community) in the United Kingdom found that just one in over 2200 of admitted patients were positive for *C. auris*. However, this screening was performed in a low prevalence country, and the patient's prior healthcare exposures were not reported, limiting interpretation about whether *C. auris* colonization was acquired in the community or in the healthcare setting.[13] A smaller admission screening program at a trauma intensive care unit in India, a country with more documented transmission, did not find any patients with *C. auris* colonization at admission.[11] In the United States, nearly all patients have had recent healthcare exposure. Community-based studies are necessary to understand the risk of transmission outside healthcare settings.

Environmental spread

C. auris may spread through contact with contaminated environmental surfaces and fomites. People infected or colonized with *C. auris* shed the organism. Environmental sampling for

C. auris has found the organism in several places in rooms of patients and hallways outside patient rooms, including beds, chairs, windowsills, countertops, trolleys, electrocardiogram leads, blood pressure monitoring cuffs, infusion pumps, and ventilators.[11,14,26,70] Shared and mobile equipment, like temperature probes, have also tested positive for *C. auris* and provide a potential transmission route for patients placed in single rooms.[11,80]

To make matters worse, *C. auris* persists on surfaces. In laboratory studies, *C. auris* has been shown to survive on moist surfaces for at least 7 days,[81] on dry linen for up to 7 days,[11] on dry steel disks for at least 7 days,[81] and on dry plastic coupons for at least 14 days.[36] *C. auris* cells remain viable on plastic surfaces for at least 4 weeks, or 2 weeks after they are no longer culturable.[36] It is not yet known if viable but nonculturable cells are able to cause infection or colonization. The ability of *C. auris* to remain culturable on surfaces appears to be greater than that of *C. albicans* but less than that of *C. glabrata* or *C. parapsilosis*.[36,81]

Infection control

Recommendations for infection control measures for *C. auris* have been adapted from strategies used for other pathogens, such as CRE and *Clostridium difficile*, which readily spread in the healthcare environment. Improved infection control measures have been shown to decrease transmission of other MDROs in healthcare settings.[82,83] These methods are novel for a *Candida* species as, historically, transmission was not a concern for most *Candida* species. Recommendations for infection control are the same for a patient infected or colonized with *C. auris* since both pose a risk for transmission.

Hand hygiene and contact precautions

Hand hygiene is one of the most basic components of infection control. Hand hygiene can be performed with soap and water, alcohol-based hand rubs, or alcohol and chlorhexidine hand rubs.

To contain transmission, patients with *C. auris* should be placed in a single room on contact precautions with dedicated, noncritical equipment.[32,84] Patients with *C. auris* may be cohorted in the same room if single rooms are not available. However, patients with *C. auris* and other MDROs should not be placed in the same room as patients with *C. auris* with no other or different MDROs.

Contact tracing and active surveillance

After a facility identifies a *C. auris* case, contact tracing should be performed to identify other patients who may have been exposed to *C. auris* and screen them for asymptomatic colonization. The patients of highest priority for screening are patients who are currently sharing a room with the index patient or who had shared a room with them in the month preceding identification of *C. auris*. These high priority patients include patients at other facilities where the index patient was admitted during this period and who have since been discharged. Point prevalence surveys to screen additional contacts, such as patients in the same unit as the index patient, should be strongly considered, particularly if the patient was not under contact precautions for his or her entire stay or if the patient was under contact precautions but there was suboptimal adherence. If transmission is identified, periodic point prevalence surveys are indicated to assess whether infection control interventions have stopped transmission. Facilities should consider prospective surveillance for additional cases by performing species identification on all clinical cultures in which *Candida* is detected until there is no evidence of ongoing transmission, including cultures from non-sterile sites such as urine or wounds.[77]

Disinfection

Evidence to date indicates that several commonly used hospital disinfectants are not effective against *C. auris*. An *in vitro* study of the effectiveness of commercial cleaning products and white distilled vinegar found that quaternary ammonium products were not effective against *C. auris;* however, sodium hypochlorite and topical hydrogen peroxide-based products have been shown to be effective *in vitro* and in environmental sampling surveys of *C. auris* in rooms thoroughly cleaned with a sodium hypochlorite disinfectant.[11,14,78,85] UK investigators reported that cleaning patient rooms with chlorine products three times a day and performing terminal cleaning with chlorine detergent and hydrogen peroxide vapor was anecdotally effective.[13] Early *in vitro* research suggests that hydrogen peroxide vapor may be effective on some strains, but further research is needed to evaluate its effectiveness in real-world settings.[86] Ultraviolet light room decontamination devices do not appear to be as effective for disinfecting *C. auris* in patient rooms as they are for vegetative bacterial pathogens, though these devices may be useful as a supplemental cleaning method and when using longer exposure times.[87] CDC has recommended daily and terminal cleaning for rooms of patients with a US Environmental Protection Agency-registered disinfectant effective against *C. difficile* spores.[25]

In less than a decade since its discovery, the multidrug-resistant yeast *C. auris* has emerged globally, causing severe infections and outbreaks. *C. auris* has brought about a paradigm shift in the way we think about *Candida*. Its high rates of multidrug resistance and transmissibility are unlike those of other pathogenic *Candida* species. Its emergence is a reminder that the genus *Candida* can include species with vastly different characteristics.[88] Knowing that an invasive infection is caused by "*Candida*" is not enough; the species name is important because of the different antifungal susceptibility patterns and different propensities for transmission in healthcare settings of different

species. Healthcare transmission of *C. auris* should motivate us to reexamine our assumptions about infections from other *Candida* species arising from autoinfection from host flora and consider whether transmission may play a role with other *Candida* species as well. The rise of *C. auris* has also made clear the need for a wider antifungal armamentarium given the resistance observed to all three major classes of systemic antifungals. *C. auris* is proof that multidrug-resistant, infectious fungal pathogens are possible, and we need to be prepared to detect, prevent, and treat them.

Prevention of *C. auris* will be more effective and efficient than reactive efforts, as *C. auris* is difficult to eliminate from healthcare facilities once established. Clinicians need to know when to expect *C. auris* infection or colonization in a patient based on known risk factors, how to treat infections, and how to implement strict infection control measures and contact precautions to prevent transmission. Laboratorians need to provide accurate species identification and alert clinicians and public health departments to suspected or confirmed cases. Public health departments, healthcare facilities, and other related health networks need to raise awareness about *C. auris* through communication and education and oversee a regional approach to prevent transmission of *C. auris* and other healthcare associated infections. Such a coordinated response is essential for identifying, treating and controlling the spread of *C. auris*, a first-of-its-kind fungal pathogen.

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Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and the writing of the paper. The findings and conclusions in this report are those of the author(s) and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

References

1. Lockhart SR, Etienne KA, Vallabhaneni S et al. Simultaneous emergence of multidrug-resistant *Candida auris* on 3 continents confirmed by whole-genome sequencing and epidemiological analyses. *Clin Infect Dis*. 2017; 64: 134–140.
2. Satoh K, Makimura K, Hasumi Y, Nishiyama Y, Uchida K, Yamaguchi H. *Candida auris* sp. nov., a novel ascomycetous yeast isolated from the external ear canal of an inpatient in a Japanese hospital. *Microbiol Immunol*. 2009; 53: 41–44.
3. Oh BJ, Shin JH, Kim MN et al. Biofilm formation and genotyping of *Candida haemulonii*, *Candida pseudohaemulonii*, and a proposed new species (*Candida auris*) isolates from Korea. *Med Mycol*. 2011; 49: 98–102.
4. Kim MN, Shin JH, Sung H et al. *Candida haemulonii* and closely related species at 5 university hospitals in Korea: identification, antifungal susceptibility, and clinical features. *Clin Infect Dis*. 2009; 48: e57–61.
5. Lee WG, Shin JH, Uh Y et al. First three reported cases of nosocomial fungemia caused by *Candida auris*. *J Clin Microbiol*. 2011; 49: 3139–3142.
6. Chowdhary A, Sharma C, Duggal S et al. New clonal strain of *Candida auris*, Delhi, India. *Emerg Infect Dis*. 2013; 19: 1670–1673.
7. Sarma S, Kumar N, Sharma S et al. Candidemia caused by amphotericin B and fluconazole resistant *Candida auris*. *Indian J Med Microbiol*. 2013; 31: 90–91.
8. Chowdhary A, Anil Kumar V, Sharma C et al. Multidrug-resistant endemic clonal strain of *Candida auris* in India. *Eur J Clin Microbiol Infect Dis*. 2014; 33: 919–926.
9. Magobo RE, Corcoran C, Seetharam S, Govender NP. *Candida auris*-associated candidemia, South Africa. *Emerg Infect Dis*. 2014; 20: 1250–1251.
10. Emara M, Ahmad S, Khan Z et al. *Candida auris* candidemia in Kuwait, 2014. *Emerg Infect Dis*. 2015; 21: 1091–1092.
11. Biswal M, Rudramurthy SM, Jain N et al. Controlling a possible outbreak of *Candida auris* infection: lessons learnt from multiple interventions. *J Hosp Infect*. 2017; 97: 363–370.
12. Arauz AB, Caceres DH, Santiago E et al. Isolation of *Candida auris* from nine patients in Central America: importance of accurate diagnosis and susceptibility testing. *Mycoses*. 2017; 61: 44–47.
13. Schelenz S, Hagen F, Rhodes JL et al. First hospital outbreak of the globally emerging *Candida auris* in a European hospital. *Antimicrob Resist Infect Control*. 2016; 5: 35.
14. Tsay S, Welsh RM, Adams EH et al. Notes from the field: ongoing transmission of *Candida auris* in health care facilities—United States, June 2016–May 2017. *MMWR Morb Mortal Wkly Rep*. 2017; 66: 514–515.
15. Calvo B, Melo AS, Perozo-Mena A et al. First report of *Candida auris* in America: clinical and microbiological aspects of 18 episodes of candidemia. *J Infect*. 2016; 73: 369–374.
16. Kohlenberg A, Struelens MJ, Monnet DL, Plachouras D. *Candida auris*: epidemiological situation, laboratory capacity and preparedness in European Union and European Economic Area countries, 2013 to 2017. *Eurosurveillance*. 2018; 23: 18–00136.
17. Britz E, Govender NP. Global emergence of a multi-drug resistant fungal pathogen, *Candida auris*. *South Afr J Infect Dis*. 2016; 31: 3–4.
18. Chakrabarti A, Sood P, Rudramurthy SM et al. Incidence, characteristics and outcome of ICU-acquired candidemia in India. *Intensive Care Med*. 2015; 41: 285–295.
19. Division of Foodborne, Waterborne, and Environmental Diseases, National Center for Emerging and Zoonotic Infectious Diseases, Centers for Disease Control and Prevention. Tracking *Candida auris*. 2018; https://www.cdc.gov/fungal/candida-auris/tracking-c-auris.html. Accessed July 19, 2018.
20. Vallabhaneni S, Kallen A, Tsay S et al. Investigation of the first seven reported cases of *Candida auris*, a globally emerging invasive, multidrug-resistant fungus—United States, May 2013-August 2016. *Am J Transplant*. 2017; 17: 296–299.
21. Sharma C, Kumar N, Pandey R, Meis JF, Chowdhary A. Whole genome sequencing of emerging multidrug resistant *Candida auris* isolates in India demonstrates low genetic variation. *New Microbes New Infect*. 2016; 13: 77–82.
22. Van Uden N Kolipinski M. *Torulopsis haemulonii* nov. spec. a yeast from the Atlantic Ocean. *Antonie Van Leeuwenhoek*. 1962; 28: 78–80.
23. Ferreira N, Belloch C, Querol A, Manzanares P, Vallez S, Santos A. Yeast microflora isolated from Brazilian cassava roots: taxonomical classification based on molecular identification. *Curr Microbiol*. 2010; 60: 287–293.
24. Antony SP, Singh IS, Sudheer NS, Vrinda S, Priyaja P, Philip R. Molecular characterization of a crustin-like antimicrobial peptide in the giant tiger shrimp, *Penaeus monodon*, and its expression profile in response to various immunostimulants and challenge with WSSV. *Immunobiology*. 2011; 216: 184–194.
25. Division of Foodborne, Waterborne, and Environmental Diseases, National Center for Emerging and Zoonotic Infectious Diseases, Centers for Disease Control and Prevention. *Candida auris* clinical update: September 2017. 2017; https://www.cdc.gov/fungal/candida-auris/c-auris-alert-09-17.html. Accessed July 19, 2018.
26. Rhodes J, Abdolrasouli A, Farrer RA et al. Genomic epidemiology of the UK outbreak of the emerging human fungal pathogen *Candida auris*. *Emerg Microbes Infect*. 2018; 7: 43.

27. Borman AM, Szekely A, Johnson EM. Isolates of the emerging pathogen *Candida auris* present in the UK have several geographic origins. *Med Mycol*. 2017; 55: 563–567.
28. Schwartz I, Hammond G. First reported case of multidrug-resistant *Candida auris* in Canada. *Canada Communicable Disease Report*. 2017; 43: 150.
29. British Columbia Centre for Disease Control. Case reports of public health significance: first *Candida auris* case identified in BC. *Laboratory Trends*. October 2017; 2017: 4.
30. Belkin A, Gazit Z, Keller N et al. *Candida auris* infection leading to nosocomial transmission, Israel, 2017. *Emerg Infect Dis*. 2018; 24: 801–804.
31. Desoubeaux G, Bailly E, Guillaume C et al. *Candida auris* in contemporary mycology labs: a few practical tricks to identify it reliably according to one recent French experience. *J Mycol Med*. 2018; 28: 407–410.
32. Bishop L, Cummins M, Guy R et al. Guidance for the laboratory investigation, management and infection prevention and control for cases of *Candida auris*. August 2017 v2.0. Vol v 2.0. London: Public Health England, 2017.
33. Sipiczki M, Tap RM. *Candida vulturna* pro tempore sp. nov., a dimorphic yeast species related to the *Candida haemulonis* species complex isolated from flowers and clinical sample. *Int J Syst Evol Microbiol*. 2016; 66: 4009–4015.
34. Sherry L, Ramage G, Kean R et al. Biofilm-forming capability of highly virulent, multidrug-resistant *Candida auris*. *Emerg Infect Dis*. 2017; 23: 328–331.
35. Kathuria S, Singh PK, Sharma C et al. Multidrug-resistant *Candida auris* misidentified as *Candida haemulonii*: characterization by matrix-assisted laser desorption ionization-time of flight mass spectrometry and DNA sequencing and its antifungal susceptibility profile variability by Vitek 2, CLSI broth microdilution, and Etest method. *J Clin Microbiol*. 2015; 53: 1823–1830.
36. Welsh RM, Bentz ML, Shams A et al. Survival, persistence, and isolation of the emerging multidrug-resistant pathogenic yeast *Candida auris* on a plastic healthcare surface. *J Clin Microbiol*. 2017; 55: 2996–3005.
37. Ben-Ami R, Berman J, Novikov A et al. Multidrug-resistant *Candida haemulonii* and *C. auris*, Tel Aviv, Israel. *Emerg Infect Dis*. 2017; 23: 195–203.
38. Larkin E, Hager C, Chandra J et al. The emerging pathogen *Candida auris*: growth phenotype, virulence factors, activity of antifungals, and effect of SCY-078, a novel glucan synthesis inhibitor, on growth morphology and biofilm formation. *Antimicrob Agents Chemother*. 2017; 61: e02396–16.
39. Borman AM, Szekely A, Johnson EM. Comparative pathogenicity of United Kingdom isolates of the emerging pathogen *Candida auris* and other key pathogenic *Candida* species. *mSphere*. 2016; 1: e00189–16.
40. Fakhim H, Vaezi A, Dannaoui E et al. Comparative virulence of *Candida auris* with *Candida haemulonii*, *Candida glabrata* and *Candida albicans* in a murine model. *Mycoses*. 2018; 61: 377–382.
41. Chatterjee S, Alampalli SV, Nageshan RK, Chettiar ST, Joshi S, Tatu US. Draft genome of a commonly misdiagnosed multidrug resistant pathogen *Candida auris*. *BMC Genomics*. 2015; 16: 686.
42. Barnes RA, Denning DW, Evans EG et al. Fungal infections: a survey of laboratory services for diagnosis and treatment. *Commun Dis Rep CDR Rev*. 1996; 6: R69–75.
43. Goodwin SD, Fiedler-Kelly J, Grasela TH, Schell WA, Perfect JR. A nationwide survey of clinical laboratory methodologies for fungal infections. *J Med Vet Mycol*. 1992; 30: 153–160.
44. Rosner ER, Reiss E, Warren NG, Shadomy HJ, Lipman HB. Evaluation of the status of laboratory practices and the need for continuing education in medical mycology. *Am J Clin Pathol*. 2002; 118: 278–286.
45. Pappas PG, Kauffman CA, Andes DR et al. Clinical practice guideline for the management of candidiasis: 2016 update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2016; 62: e1–50.
46. Mizusawa M, Miller H, Green R et al. Can multidrug-resistant *Candida auris* be reliably identified in clinical microbiology laboratories? *J Clin Microbiol*. 2017; 55: 638–640.
47. Morales-Lopez SE, Parra-Giraldo CM, Ceballos-Garzon A et al. Invasive infections with multidrug-resistant yeast *Candida auris*, Colombia. *Emerg Infect Dis*. 2017; 23: 162–164.
48. Parra-Giraldo CM, Valderrama SL, Cortes-Fraile G et al. First report of sporadic cases of *Candida auris* in Colombia. *Int J Infect Dis*. 2018; 69: 63–67.
49. Snayd M, Dias F, Ryan RW, Clout D, Banach DB. The misidentification of *Candida auris* using RapID Yeast Plus, a commercial, biochemical enzyme-based manual rapid identification system. *J Clin Microbiol*. 2018; 56: e00080–18.
50. Ruiz Gaitan AC, Moret A, Lopez Hontangas JL et al. Nosocomial fungemia by *Candida auris*: first four reported cases in continental Europe. *Rev Iberoam Micol*. 2017; 34: 23–27.
51. Bao JR, Master RN, Azad KN et al. Rapid, accurate identification of *Candida auris* by using a novel matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS) database (library). *J Clin Microbiol*. 2018; 56: e01700–17.
52. Lockhart SR, Berkow EL, Chow N, Welsh RM. *Candida auris* for the clinical microbiology laboratory: not your grandfather's *Candida* species. *Clin Microbiol Newsl*. 2017; 39: 99–103.
53. Kordalewska M, Zhao Y, Lockhart SR, Chowdhary A, Berrio I, Perlin DS. Rapid and accurate molecular identification of the emerging multidrug resistant pathogen *Candida auris*. *J Clin Microbiol*. 2017; 55: 2445–2452.
54. Division of Foodborne, Waterborne, and Environmental Diseases, National Center for Emerging and Zoonotic Infectious Diseases, Centers for Disease Control and Prevention. Recommendations for identification of *Candida auris*. 2017; https://www.cdc.gov/fungal/candida-auris/recommendations.html. Accessed July 19, 2018.
55. Chowdhary A, Prakash A, Sharma C et al. A multicentre study of antifungal susceptibility patterns among 350 *Candida auris* isolates (2009-17) in India: role of the ERG11 and FKS1 genes in azole and echinocandin resistance. *J Antimicrob Chemother*. 2018; 73: 891–899.
56. Vallabhaneni S, Cleveland AA, Farley MM et al. Epidemiology and risk factors for echinocandin nonsusceptible *Candida glabrata* bloodstream infections: data from a large multisite population-based candidemia surveillance program, 2008–2014. *Open Forum Infect Dis*. 2015; 2: ofv163.
57. Lockhart SR, Iqbal N, Cleveland AA et al. Species identification and antifungal susceptibility testing of *Candida* bloodstream isolates from population-based surveillance studies in two U.S. cities from 2008 to 2011. *J Clin Microbiol*. 2012; 50: 3435–3442.
58. Flowers SA, Colon B, Whaley SG, Schuler MA, Rogers PD. Contribution of clinically derived mutations in ERG11 to azole resistance in *Candida albicans*. *Antimicrob Agents Chemother*. 2015; 59: 450–460.
59. Perlin DS. Mechanisms of echinocandin antifungal drug resistance. *Ann N Y Acad Sci*. 2015; 1354: 1–11.
60. Pfaller MA, Espinel-Ingroff A, Canton E et al. Wild-type MIC distributions and epidemiological cutoff values for amphotericin B, flucytosine, and itraconazole and *Candida* spp. as determined by CLSI broth microdilution. *J Clin Microbiol*. 2012; 50: 2040–2046.
61. Al-Siyabi T, Al Busaidi I, Balkhair A, Al-Muharrmi Z, Al-Salti M, Al'Adawi B. First report of *Candida auris* in Oman: clinical and microbiological description of five candidemia cases. *J Infect*. 2017; 75: 373–376.
62. Rudramurthy SM, Chakrabarti A, Paul RA et al. *Candida auris* candidaemia in Indian ICUs: analysis of risk factors. *J Antimicrob Chemother*. 2017; 72: 1794–1801.
63. Lepak AJ, Zhao M, Berkow EL, Lockhart SR, Andes DR. Pharmacodynamic optimization for treatment of invasive *Candida auris* infection. *Antimicrob Agents Chemother*. 2017; 61: e00791–17.
64. Fakhim H, Chowdhary A, Prakash A et al. In vitro interactions of echinocandins with triazoles against multidrug-resistant *Candida auris*. *Antimicrob Agents Chemother*. 2017; 61: e01056–17.
65. Berkow EL, Angulo D, Lockhart SR. In vitro activity of a novel glucan synthase inhibitor, SCY-078, against clinical isolates of *Candida auris*. *Antimicrob Agents Chemother*. 2017; 61: e00435–17.
66. Hager CL, Larkin EL, Long L, Zohra Abidi F, Shaw KJ, Ghannoum MA. In vitro and in vivo evaluation of the antifungal activity of APX001A/APX001 against *Candida auris*. *Antimicrob Agents Chemother*. 2018; 62: e02319–17.
67. Berkow EL, Lockhart SR. Activity of CD101, a long-acting echinocandin, against clinical isolates of *Candida auris*. *Diagn Microbiol Infect Dis*. 2018; 90: 196–197.
68. Division of Foodborne, Waterborne, and Environmental Diseases, National Center for Emerging and Zoonotic Infectious Diseases, Centers for Disease Control and Prevention. Recommendations for treatment and prevention of *Candida auris*. 2017; https://www.cdc.gov/fungal/candida-auris/c-auris-treatment.html. Accessed July 19, 2018.

69. Choi HI, An J, Hwang JJ, Moon SY, Son JS. Otomastoiditis caused by *Candida auris*: case report and literature review. *Mycoses*. 2017; 60: 488–492.
70. Lesho EP, Bronstein MZ, McGann P et al. Importation, mitigation, and genomic epidemiology of *Candida auris* at a large teaching hospital. *Infect Control Hosp Epidemiol*. 2018: 39: 53–57.
71. Mohd Tap R, Lim TC, Kamarudin NA et al. A fatal case of *Candida auris* and *Candida tropicalis* candidemia in neutropenic patient. *Mycopathologia*. 2018; 183: 559–564.
72. Lin MY, Lyles-Banks RD, Lolans K et al. The importance of long-term acute care hospitals in the regional epidemiology of *Klebsiella pneumoniae* carbapenemase-producing Enterobacteriaceae. *Clin Infect Dis*. 2013; 57: 1246–1252.
73. Magobo RE, Naicker SD, Wadula J et al. Detection of neonatal unit clusters of *Candida parapsilosis* fungaemia by microsatellite genotyping: results from laboratory-based sentinel surveillance, South Africa, 2009–2010. *Mycoses*. 2017; 60: 320–327.
74. Pinhati HM, Casulari LA, Souza AC, Siqueira RA, Damasceno CM, Colombo AL. Outbreak of candidemia caused by fluconazole resistant *Candida parapsilosis* strains in an intensive care unit. *BMC Infect Dis*. 2016; 16: 433.
75. Lupetti A, Tavanti A, Davini P et al. Horizontal transmission of *Candida parapsilosis* candidemia in a neonatal intensive care unit. *J Clin Microbiol*. 2002; 40: 2363–2369.
76. Richardson MD, Warnock DW. *Fungal Infection: Diagnosis and Management*. New York: John Wiley & Sons, 2012.
77. Tsay S, Kallen A, Jackson BR, Chiller TM, Vallabhaneni S. Approach to the investigation and management of patients with *Candida auris*, an emerging multidrug-resistant yeast. *Clin Infect Dis*. 2018; 66: 306–311.
78. Moore G, Schelenz S, Borman AM, Johnson EM, Brown CS. The yeasticidal activity of chemical disinfectants and antiseptics against *Candida auris*. *J Hosp Infect*. 2017; 97: 371–375.
79. Azar MM, Turbett SE, Fishman JA, Pierce VM. Donor-derived transmission of *Candida auris* during lung transplantation. *Clin Infect Dis*. 2017; 65: 1040–1042.
80. Madder H, Moir I, Moroney R et al. Multiuse patient monitoring equipment as a risk factor for acquisition of *Candida auris*. *bioRxiv*. 2017; 149054.
81. Piedrahita CT, Cadnum JL, Jencson AL, Shaikh AA, Ghannoum MA, Donskey CJ. Environmental surfaces in healthcare facilities are a potential source for transmission of *Candida auris* and other *Candida* species. *Infect Control Hosp Epidemiol*. 2017;38: 1107–1109.
82. Munoz-Price LS, Hayden MK, Lolans K et al. Successful control of an outbreak of *Klebsiella pneumoniae* carbapenemase-producing *K. pneumoniae* at a long-term acute care hospital. *Infect Control Hosp Epidemiol*. 2010; 31: 341–347.
83. Borer A, Eskira S, Nativ R et al. A multifaceted intervention strategy for eradication of a hospital-wide outbreak caused by carbapenem-resistant *Klebsiella pneumoniae* in Southern Israel. *Infect Control Hosp Epidemiol*. 2011; 32: 1158–1165.
84. Division of Foodborne, Waterborne, and Environmental Diseases, National Center for Emerging and Zoonotic Infectious Diseases, Centers for Disease Control and Prevention. Recommendations for infection control for *Candida auris*. 2017; https://www.cdc.gov/fungal/candida-auris/c-auris-infection-control.html. Accessed July 19, 2018.
85. Cadnum JL, Shaikh AA, Piedrahita CT et al. Effectiveness of disinfectants against *Candida auris* and other *Candida* species. *Infect Control Hosp Epidemiol*. 2017; 38: 1240–1243.
86. Abdolrasouli A, Armstrong-James D, Ryan L, Schelenz S. In vitro efficacy of disinfectants utilised for skin decolonisation and environmental decontamination during a hospital outbreak with *Candida auris*. *Mycoses*. 2017; 60: 758–763.
87. Cadnum JL, Shaikh AA, Piedrahita CT et al. Relative resistance of the emerging fungal pathogen *Candida auris* and other *Candida* species to killing by ultraviolet light. *Infect Control Hosp Epidemiol*. 2018; 39: 94–96.
88. de Hoog GS, Chaturvedi V, Denning DW et al. Name changes in medically important fungi and their implications for clinical practice. *J Clin Microbiol*. 2015; 53: 1056–1062.
89. Iguchi S, Mizushima R, Kamada K et al. The second *Candida auris* isolate from aural discharge in Japan. *Jpn J Infect Dis*. 2018; 71: 174–175.
90. European Centre for Disease Prevention and Control. *Candida auris in Healthcare Settings – Europe – 19 December 2016*. Stockholm: ECDC, 2016.
91. Division of Foodborne, Waterborne, and Environmental Diseases, National Center for Emerging and Zoonotic Infectious Diseases, Centers for Disease Control and Prevention. Clinical alert to US healthcare facilities: June 2016. 2016; https://www.cdc.gov/fungal/candida-auris/candida-auris-alert.html. Accessed July 19, 2018.
92. Alatoom A, Sartawi M, Lawlor K et al. Persistent candidemia despite appropriate fungal therapy: first case of *Candida auris* from the United Arab Emirates. *Int J Infect Dis*. 2018; 70: 36–37.