

Global epidemiology of emerging *Candida auris*

Johanna Rhodes and Matthew C Fisher

The discovery in 2009 of a new species of yeast, *Candida auris*, heralded the arrival of a novel emerging human infectious disease. This review highlights the unique characteristics of *C. auris* that have led to it being of public health concern worldwide, namely public health concern, namely its global emergence, its ability to cause nosocomial outbreaks in healthcare settings, its innate and emerging resistance to multiple antifungal drugs and its resilience in the face of hygiene and infection control measures. Genomic epidemiology has identified four emergences of *C. auris* marked by four clades of the pathogen. These clades of *C. auris* are genetically dissimilar and are associated with differential resistance to antifungal drugs, suggesting that they will continue to phenotypically diverge into the future. The global emergence of *C. auris* testifies to the unmapped nature of Kingdom Fungi, and represents a new nosocomial threat that will require enhanced infection control across diverse healthcare and community settings.

Address

MRC Centre for Global Infectious Disease Analysis, Imperial College London, London, United Kingdom

Corresponding author: Fisher, Matthew C
(matthew.fisher@imperial.ac.uk)

Current Opinion in Microbiology 2019, 52:84–89

This review comes from a themed issue on **Host-microbe interactions: fungi**

Edited by **Chad A Rappleye** and **Duncan Wilson**

For a complete overview see the [Issue](#) and the [Editorial](#)

Available online 3rd July 2019

<https://doi.org/10.1016/j.mib.2019.05.008>

1369-5274/© 2019 Published by Elsevier Ltd.

Introduction

Since its discovery in 2009 [1], *Candida auris* has been identified in more than 30 countries on six continents [2]. A retrospective SENTRY review identified a 2008 isolation from Pakistan; however, *C. auris* is generally considered rare before 2009 suggesting that it represents a newly emerging human infection. In contrast to other *Candida* species, *C. auris* spreads easily in health-care setting causing nosocomial outbreaks [3,4]. 'This fungus' ability to persist, both on the human host and also on inanimate surfaces, has been well documented [5,6] and is likely a key trait explaining its emergence. Exhibiting intrinsic resistance to fluconazole [7] and variable susceptibility to other azole

antifungal drugs, 5-flucytosine [8], amphotericin B [9], and echinocandins [8,10,11], *C. auris* has been widely acknowledged as multi-drug resistant (MDR) [12,13]. This, along with its ability to persist and easily transmit, alongside its highly proliferative clonal life-history, has led to *C. auris*' pandemic potential by causing an expanding range of nosocomial infections worldwide [1,3,7,14–18].

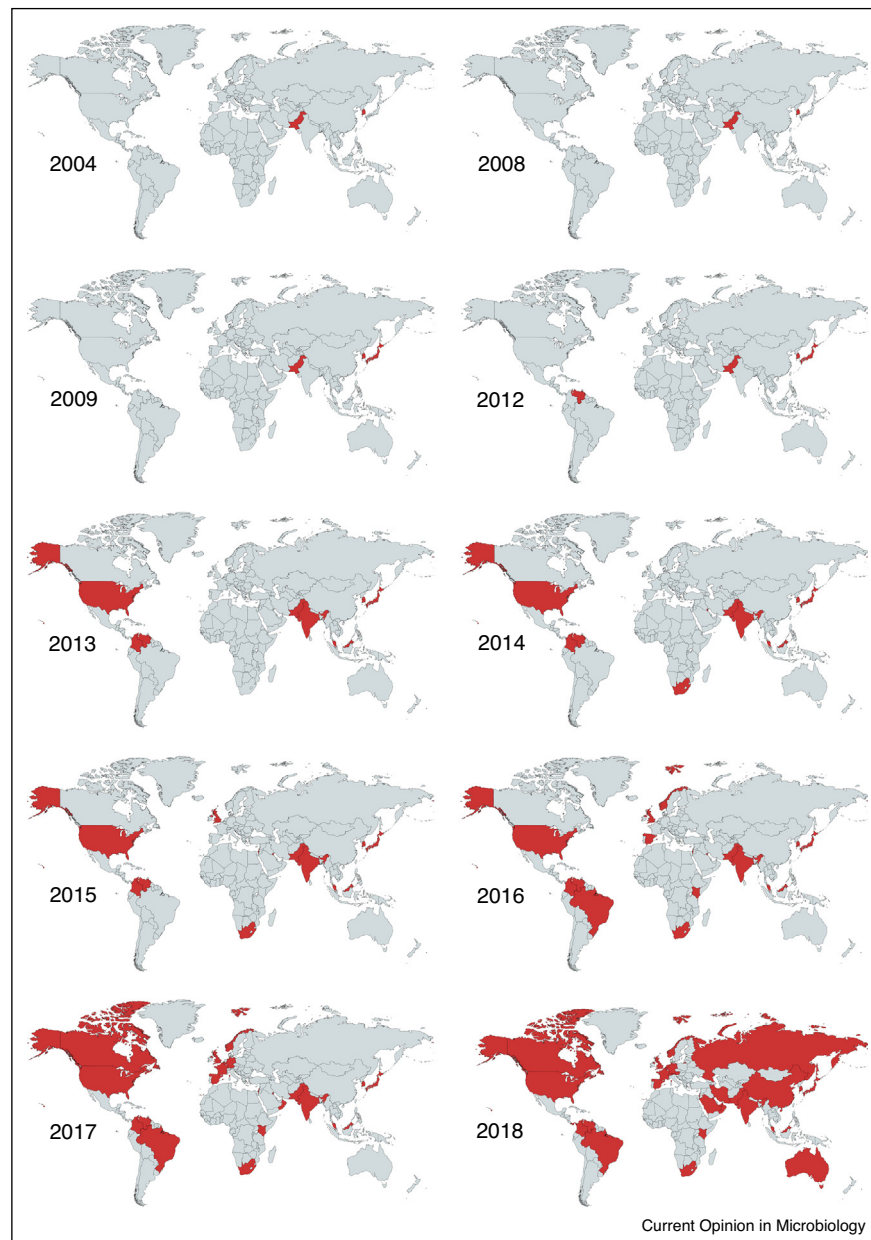
Emergence of *C. auris*

C. auris was first discovered and described in 2009 following isolation from discharge from the ear canal of a patient in Japan [1] and was taxonomically placed as a close relative to the *Candida haemulonii* complex. Since its discovery, *C. auris* has caused a 'stealthy pandemic', emerging across the globe (Figure 1) and is now recorded in all continents except Antarctica (Figure 2). However, *C. auris* is thought to have been misidentified as *C. haemulonii* on a number of occasions [4,13,19], suggesting that *C. auris* has likely been circulating as a human pathogen before 2009. The USA Centers for Disease Control and Prevention (CDC) queried the international surveillance system SENTRY, and discovered four isolates from between 2009 and 2015 that were identified as *C. haemulonii* however were indeed *C. auris* [7]. A study from South Korea, which identified 15 isolates of *C. haemulonii* in 2009 from the ear canals of patients with chronic otitis were later identified to be *C. auris* [20]. In the same year, the first cases of nosocomial infection caused by *C. auris* were also reported in South Korea; this study also queried the South Korean isolate collection, and discovered the earliest isolate of *C. auris* was discovered in 1996 [15]. However, retrospective analysis of over 15 000 isolates from the SENTRY collection show no misidentifications before 2009 [7] and over 5000 archived isolates from Taiwan before 2016 were negative, showing that the currently observed global distribution of *C. auris* is most likely explained by a process of rapid spatial emergence from a small number of foci. This observation is confirmed by ongoing genomic epidemiology showing multiple contemporary introductions and ongoing transmission in the USA as well as other global settings [2].

Genomic epidemiology

Investigation into the *C. auris* genome has shown it to possess over 5000 protein coding genes [7,8,21], and expresses several virulence factors such as biofilm formation and adherence [22,23], although to a lesser extent than *C. albicans* [22,24]. Muñoz *et al.* performed RNA-seq and discovered expansions of entire gene families were linked to drug resistance and virulence [21], which have

Figure 1



Timeline showing the expanding worldwide detection of *C. auris*.

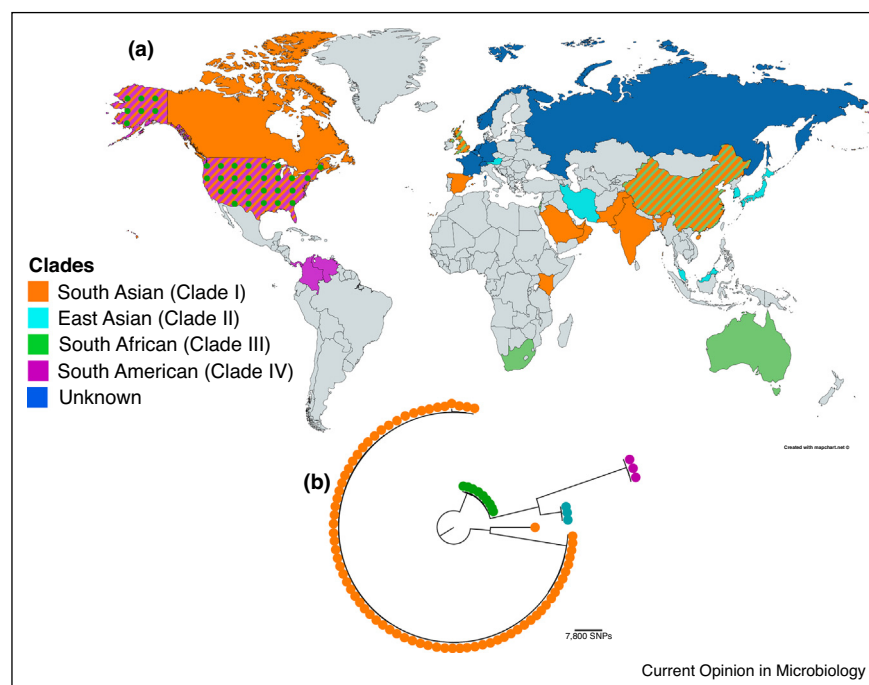
also been described in *C. albicans* [25]. Whilst the roles of specific genes were not characterised as part of the study, Muñoz *et al.* demonstrated that expansions of transporters and lipases within *C. auris* are a likely mechanism of virulence that is shared with other species of *Candida* yeasts [21].

Whilst initially thought to have high virulence, and exhibiting crude mortality rates from *C. auris*-associated candidaemia from between 33–72% [17,26,27], assessment from the UK Brompton outbreak showed no direct

association with mortality [3]. Currently, there is an urgent need to contextualise the virulence of *C. auris* against that observed from other candidaemia-causing yeasts such as *C. albicans* and *Candida glabrata* as there is much uncertainty surrounding the clinical consequences of detecting *C. auris* candidaemia.

Genetic analysis using whole genome sequencing has revealed deep divergence within the *C. auris* species, with large variation between geographic clades separated by thousands of single nucleotide polymorphisms (SNPs)

Figure 2



(a) Global distribution of *Candida auris* clades (as of 28th February 2019) and (b) RAxML phylogeny showing the relationship amongst *C. auris* clades.

[2,7,8*]. This divergence has led to the identification of four distinct geographic clades (I–IV), each with minimal genetic diversity within each clade: South Asian (clade I), South African (clade III), South American (clade IV) and East Asian (clade II; Figure 2). The East Asian clade (containing the type isolate of *C. auris*) appears to infect the ear only, whereas the other clades are known to cause invasive infections, nosocomial transmission and healthcare outbreaks [28]. There appear to be specific drug resistance mutations in the *ERG11* gene (encoding the target of azole antifungal drugs) that are strongly associated with resistance to azoles across the following geographic clades: F126T in South Africa, Y132F in South America, and Y132F or K143R in South Asia [2*,7*,8*]. The appearance of the Y132F and K143R mutations has recently been shown to increase resistance to fluconazole in *C. auris* [29]. There appears to be no [antifungal-resistance mutation in *ERG11* associated with the East Asian clade, which coincides with the higher rate of susceptibility observed in isolates from this clade. Clonal isolates from the South Asian clade have been identified at three hospitals located thousands of miles apart in India, confirming the nation-wide nature of transmission and potential for antifungal-resistance mutations to spread should they evolve [12]. Similarly, isolates from hospitals located approximately 700 km apart in Colombia were found to be genetically identical [30]. Isolates of similar genotypes have also been seen to cluster regionally within

countries, usually around a hospital [2*,31], marking local networks of transmission.

One such a cluster was observed in the UK in 2015. An initial case of *C. auris* was reported in the Royal Brompton Hospital, a specialist cardio-thoracic centre in London, in April 2015 in a 20 bed mixed adult intensive care unit (ICU) [3]. The following week, a patient in the adjacent bed to the index case was identified as *C. auris* culture positive from a sputum sample, and they subsequently developed an intravascular line infection. Formal outbreak measures were introduced in November 2015 when nine cases were identified, some with candidaemia. The number of cases within the Royal Brompton Hospital rose rapidly at the start of 2016. As healthcare associated transmission was a possibility within the ICU, environmental sampling of areas surrounding colonised patients was carried out, which showed contamination with *C. auris*. It was also observed during the outbreak that once patients were skin colonised, daily washes with the recommended 2% chlorhexidine wash cloth did not eradicate *C. auris* [5]. Therefore, due to the uncertainty over the time and source of the introduction of *C. auris* into the hospital, rapid development of molecular epidemiological tools was required. The handheld MinION nanopore sequencing device from Oxford Nanopore Technologies, UK (ONT) and Illumina was used to whole genome sequence (WGS) multiple isolates with a diverse

temporal range over the outbreak to describe the genetic epidemiology of the outbreak, both within the hospital and in the global context. Temporal analysis of the sequences placed the introduction of *C. auris* into the hospital as March 2015, one month before the index case, and placed the outbreak globally within the South Asian clade [8[•]]. Similar patterns of introduction and local spread have recently been described in other settings, notably the USA, where isolates from all known lineages of *C. auris* have been reported (Figure 2), and including a number of cases where patients are thought to have acquired infections from exposures in other countries [2[•]].

Antifungal resistance and transmission in *C. auris*

Currently, candidaemia infections caused by *C. albicans* are widely managed via the use of echinocandin therapy, and in some cases in combination with amphotericin B [17,32]. Intravenous amphotericin B not in combination with another drug has resulted in treatment failure [15]; however, the mechanistic nature of this resistance is not yet understood. Whilst there are currently no established breakpoints for antifungal susceptibility in *C. auris*, it is generally accepted that most isolates are multi-drug resistant, based on applying *C. albicans* breakpoints (both CLSI and EUCAST) [33].

Reduced susceptibility to fluconazole, which displays high MICs in many cases (>64 mg/l) have been seen in over 90% of cases [3,7[•],34], and reduced susceptibility to voriconazole, itraconazole, posaconazole, and isavuconazole have also been demonstrated [3,8[•],12]. Varying susceptibility to amphotericin B has also been shown [7,11,16,17,34,35], with Escandon *et al.* presenting four novel non-synonymous mutations that may be associated with resistance [30]. However, Muñoz *et al.* demonstrated that there was a transcriptional response to voriconazole and amphotericin B, with a small number of differentially expressed genes post-exposure to both drugs, suggesting that the mechanism of resistance to these drugs may be epigenetic rather than mutation-based [21]. Data on susceptibility to 5-flucytosine (5FC) are limited, but reports from India and the UK have shown raised MICs [3,7[•],8[•],36]. Because of the varying susceptibility of *C. auris* to azoles and amphotericin B, public health recommendations have led to the use of echinocandins as front-line therapy for infections [27,37]. Despite this, however, reduced susceptibility to echinocandins associated with polymorphisms in the *FKSI* gene has been identified [8[•],10,11] suggesting that, here too, antifungal resistance has evolved and may be of clinical significance. In a small percentage of cases, elevated MIC's were found against all of the three major classes of antifungals. Increasing the copy numbers of *ERG11* has recently been suggested as a mechanism of drug resistance in *C. auris* [21], similar to that seen in *C. albicans* [38] and *Cryptococcus neoformans* [39]. Clearly, the ongoing evolution of *C. auris*

in the face of antifungal therapies needs to be closely monitored.

Following the 'Brompton experience', guidelines from Public Health England report that colonisation by *C. auris* is highly persistent and is difficult to eradicate [40]. Specifically, reusable items of medical equipment, specifically axillary skin-surface temperature probes, are known to be predictors of colonisation by *C. auris* [41[•]]. Withdrawal of temperature probes following an outbreak in an Oxford (UK) hospital was shown to reduce the incidence of infection [41[•]]. Further, daily skin decolonisation of patients with 2% aqueous chlorhexidine wipes was shown to be effective during an outbreak in a tertiary care hospital in Spain [32]. Overall, experience in attempting to contain the emergence of *C. auris* is showing that a one-size-fits-all approach to *Candida* infection control cannot be assumed.

Future directions

Currently, nothing is known about the origins and initial emergence of *C. auris*; its propensity to survive on inanimate objects within the hospital alongside resistance to disinfection protocols suggests the existence of an unknown non-human environmental reservoir. However, similar to other *Candida* species, the true nature of *C. auris*' ancestral reservoirs currently remains elusive [42–44]. The detection of clonal *C. auris* isolates on multiple continents simultaneously with distinct geographical antifungal resistance mechanisms suggests at least four independent emergence events followed by clonal expansion and the ongoing evolution of resistance in response to antifungal therapy [8[•]]. Recent comparative genomic analysis has shown that most of the *Candida* mating and meiosis genes are present, and that each of the *C. auris* clades are fixed for either the *MTLa* or *MTLα* mating loci as follows: South Asian clade I, *MTLa*; South African clade III, *MTLα*; South American clade IV, *MTLa*; and East Asian clade II, *MTLα* [21]. These findings suggest that recombination is possible if clades of opposite mating types encounter one another. A recent study confirmed that *C. auris* is capable of efficient recombination [45]; such mating, if it occurs, could lead to the spectre of more complex genotypic and phenotypic diversity evolving in the future with potentially novel antifungal and virulence characteristics.

Given the difficulties in identifying *C. auris*, there is a need for not only species level identification, but also clade-specific identification if the antifungal resistance characteristics of the clades continue to diverge [46]. There is a need to develop global surveillance tools, similar to those seen in the Ebola and Zika outbreak response [47], not only for *C. auris*, but for other human emerging fungal pathogens, such as *Rasamsonia* and *Exophiala* species. These surveillance tools need to be open access, web-based, and be available to all parts of the globe, especially in places where there is limited funding

for healthcare. These tools should be able to differentiate between the geographic clades; standard molecular typing techniques have proven unsuccessful or incomparable between laboratories. It is essential that these tools also rapidly identify *C. auris*; the use of the WGS and the MinION sequencer from ONT has demonstrated that outbreak-specific references can be generated rapidly for the use of single nucleotide polymorphism (SNP) changes and phylogenetic analyses [8*,41]. As sequencing technology develops, it is likely rapid sequencing of *C. auris* isolates can be achieved in 48 hours or less leading to the potential for bedside diagnostics twinned with molecular epidemiology of nosocomial patterns of transmission. Currently, it is not often known when patients become colonised – whether from the hospital environment or endogenous carriers [27] – and the extent of carriage in the community remains largely unexamined. Therefore, epidemiological studies that incorporate WGS to investigate the genetic diversity of environmental and clinical isolates are needed more widely. There is also a need for studies that examine the genetic diversity of clinical isolates from multiple body sites in patients. This is because the differential exposure to antifungal drugs for isolates from mucosal sites versus systemic infections is likely to lead to the differential evolution of resistance, which may lead to downstream clinical complications.

As echinocandins are the front-line therapy for *C. auris* infection treatment, new drugs may be needed to combat high-grade echinocandin resistance if it evolves. New drug options, such as rezafungin (previously called CD101), and the β -glucan synthesis inhibitor SCY-078, have already shown promise [22,48]. More broadly, there is a need for novel antifungal chemistries as the worldwide emergence of resistance to antifungal drugs continues to challenge human health and food security [49*].

Acknowledgements

JR and MCF were supported by UK NERC (NE/P001165/1) and the UK MRC (MR/R015600/1). MCF is a Canadian CIFAR Fellow in the 'Fungal Kingdom' program.

References

- Sato 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 Blackwell Publishing, Asia.
- Research describing the discovery, description and naming of *C. auris* from the ear-canal of a patient in Japan.
- Chow NA, Gade L, Tsay SV, Forsberg K, Greenko JA, Southwick KL et al.: **Multiple introductions and subsequent transmission of multidrug-resistant *Candida auris* in the USA: a molecular epidemiological survey.** *Lancet Infect Dis* 2018, **18**:1377-1384.
- Key molecular epidemiology study from the US CDC showing that *C. auris* has been introduced into the USA several times. The study goes on to conclude that local and ongoing transmission is widely occurring.
- Schelenz S, Hagen F, Rhodes JL, Abdolrasouli A, Chowdhary A, Hall A et al.: **First hospital outbreak of the globally emerging *Candida auris* in a European hospital.** *Antimicrob Resist Infect Control* 2016:1-7.
- Chowdhary A, Sharma C, Meis JF: ***Candida auris*: a rapidly emerging cause of hospital-acquired multidrug-resistant fungal infections globally.** *PLoS Pathog* 2017, **13**:e1006290 Hogan DA (editor), Public Library of Science.
- 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.
- Welsh RM, Bentz ML, Shams A, Houston H, Lyons A, Rose LJ et al.: **Survival, persistence, and isolation of the emerging multidrug-resistant pathogenic yeast *Candida auris* on a plastic health care surface.** *J Clin Microbiol* 2017, **55**:2996-3005 Diekema DJ (editor) American Society for Microbiology Journals.
- Lockhart SR, Etienne KA, Vallabhaneni S, Farooqi J, Chowdhary A, Govender NP et al.: **Simultaneous emergence of multidrug resistant *Candida auris* on three continents confirmed by whole genome sequencing and epidemiological analyses.** *Clin Infect Dis* 2017, **64**:134-140 Oxford University Press.
- A key US CDC study describing the four-clade structure of the global *C. auris* population using genomics. The study details the near-simultaneous worldwide emergence of these four clades across three continents alongside patterns on antifungal resistance.
- Rhodes J, Abdolrasouli A, Farrer RA, Cuomo CA, Aanensen DM, Armstrong-James D et al.: **Genomic epidemiology of the UK outbreak of the emerging human fungal pathogen *Candida auris*.** *Emerg Microbes Infect* 2018, **7**:43.
- First use of rapid nanopore sequencing to characterise a *C. auris* outbreak and to identify the geographical region of origin as the Indian subcontinent. The study uses molecular clock dating to time the introduction of the infection into the hospital.
- Escandon P, Chow NA, Caceres DH, Gade L, Berkow EL, Armstrong P et al.: **Molecular epidemiology of *Candida auris* in Colombia reveals a highly related, countrywide colonization with regional patterns in amphotericin B resistance.** *Clin Infect Dis* 2019, **68**:15-21.
- Berkow EL, Lockhart SR: **Activity of CD101, a long-acting echinocandin, against clinical isolates of *Candida auris*.** *Diagn Microbiol Infect Dis* 2017, **90**(3):196-197.
- Chowdhary A, Prakash A, Sharma C, Kordalewska M, Kumar A, Sarma S 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, **13** e1006290–9.
- Chowdhary A, Anil Kumar V, Sharma C, Prakash A, Agarwal K, Babu R et al.: **Multidrug-resistant endemic clonal strain of *Candida auris* in India.** *Eur J Clin Microbiol Infect Dis* 2013, **33**:919-926 Springer, Berlin Heidelberg.
- Kathuria S, Singh PK, Sharma C, Prakash A, Masih A, Kumar A 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 Warnock DW (editor), American Society for Microbiology.
- Chowdhary A, Sharma C, Duggal S, Agarwal K, Prakash A, Singh PK et al.: **New clonal strain of *Candida auris*, Delhi, India.** *Emerg Infect Dis* 2013, **19**:1670-1673.
- Lee WG, Shin JH, Uh Y, Kang MG, Kim SH, Park KH et al.: **First three reported cases of nosocomial fungemia caused by *Candida auris*.** *J Clin Microbiol* 2011, **49**:3139-3142 American Society for Microbiology.
- Vallabhaneni S, Kallen A, Tsay S, Chow N, Welsh R, Kerins J 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* 2016, **17**:296-299.

17. Calvo B, de Azevedo Melo AS, Perozo-Mena A, Hernandez M, Francisco EC, Hagen F *et al.*: **First report of *Candida auris* in America: clinical and microbiological aspects of 18 episodes of candidemia.** *J Infect* 2016;1-24. Elsevier Ltd..
18. Morales-López SE, Parra-Giraldo CM, Ceballos-Garzón A, Martínez HP, Rodríguez GJ, Álvarez-Moreno CA *et al.*: **Invasive infections with multidrug-resistant yeast *Candida auris*, Colombia.** *Emerg Infect Dis* 2017, **23**:162-164.
19. Magobo RE, Corcoran C, Seetharam S, Govender NP: ***Candida auris*-associated candidemia, South Africa.** *Emerg Infect Dis* 2014, **20**:1250-1251.
20. Kim M-N, Shin JH, Sung H, Lee K, Kim E-C, Ryoo N *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-e61.
21. Muñoz JF, Gade L, Chow NA, Loparev VN, Juieng P, Berkow EL *et al.*: **Genomic insights into multidrug-resistance, mating and virulence in *Candida auris* and related emerging species.** *Nat Commun* 2018, **9**:5346 Nature Publishing Group.
22. Larkin E, Hager C, Chandra J, Mukherjee PK, Retuerto M, Salem I *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**:41 2nd ed. American Society for Microbiology Journals.
23. Sherry L, Ramage G, Kean R, Borman A, Johnson EM, Richardson MD *et al.*: **Biofilm-forming capability of highly virulent, multidrug-resistant *Candida auris*.** *Emerg Infect Dis* 2017, **23**:328-331.
24. 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**:9 Mitchell AP (editor), 3rd ed. American Society for Microbiology Journals.
25. Butler G, Rasmussen MD, Lin MF, Santos MAS, Sakthikumar S, Munro CA *et al.*: **Evolution of pathogenicity and sexual reproduction in eight *Candida* genomes.** *Nature* 2009, **459**:657-662 Nature Publishing Group.
26. Saris K, Meis JF, Voss A: ***Candida auris*.** *Curr Opin Infect Dis* 2018, **31**:334-340.
27. Chowdhary A, Voss A, Meis JF: **Multidrug-resistant *Candida auris*: "new kid on the block" in hospital-associated infections?** *J Hosp Infect* 2016, **94**:209-212 W.B. Saunders.
28. Welsh RM, Sexton DJ, Forsberg K, Vallabhaneni S, Litvintseva A: **Insights into the Unique Nature of the East Asian clade of the emerging pathogenic yeast, *Candida auris*.** *J Clin Microbiol* 2019:1-10. American Society for Microbiology Journals.
29. Healey KR, Kordalewska M, Jimenez-Ortigosa C, Singh A, Berrio I, Chowdhary A *et al.*: **Limited ERG11 mutations identified in isolates of *Candida auris* directly contribute to reduced azole susceptibility.** *Antimicrob Agents Chemother Am Soc Microbiol* 2018, **1062**(10) pii: e01427-18.
30. Escandon P, Chow NA, Caceres DH, Gade L, Berkow EL, Armstrong P *et al.*: **Molecular epidemiology of *Candida auris* in Colombia reveals a highly related, countrywide colonization with regional patterns in Amphotericin B resistance.** *Clin Infect Dis* 2018, **13** 3rd ed., e1006290-7.
31. Escandón P, Chow NA, Caceres DH, Gade L, Berkow EL, Armstrong P, Rivera S, Misas E, Duarte C, Moulton-Meissner H *et al.*: **Molecular epidemiology of *Candida auris* in Colombia reveals a highly-related, country-wide colonization with regional patterns in Amphotericin B resistance.** *Clin Inf Dis* 2018, **68**:15-21.
32. Ruiz-Gaitan A, Moret AM, Tasiar-Pitarch M, Aleixandre López AI, Martínez-Morel H, Calabuig E *et al.*: **An outbreak due to *Candida auris* with prolonged colonization and candidemia in a tertiary care European hospital.** *Mycoses* 2018:1-19.
33. Arendrup MC, Prakash A, Meletiadis J, Sharma C, Chowdhary A: **Comparison of EUCAST and CLSI reference microdilution MICs of eight antifungal compounds for *Candida auris* and associated tentative epidemiological cutoff values.** *Antimicrob Agents Chemother* 2017, **61** American Society for Microbiology. e00485-17.
34. Prakash A, Sharma C, Singh A, Kumar Singh P, Kumar A, Hagen F *et al.*: **Evidence of genotypic diversity among *Candida auris* isolates by multilocus sequence typing, matrix-assisted laser desorption ionization time-of-flight mass spectrometry and amplified fragment length polymorphism.** *Clin Microbiol Infect* 2016, **22**:277.e1-277.e9.
35. Belkin A, Gazit Z, Keller N, Ben-Ami R, Wieder-Finesod A, Novikov A *et al.*: ***Candida auris* infection leading to nosocomial transmission, Israel, 2017.** *Emerg Infect Dis* 2018, **24**:801-804.
36. Sarma S, Kumar N, Sharma S, Govil D, Ali T, Mehta Y *et al.*: **Candidemia caused by amphotericin B and fluconazole resistant *Candida auris*.** *Indian J Med Microbiol* 2013, **31**:90-91 Medknow Publications.
37. Kim Hutchings UKE: ***Candida auris* in Healthcare Settings – Europe.** 2016:1-8. December 20.
38. Selmecki A, Gerami-Nejad M, Paulson C, Forche A, Berman J: **An isochromosome confers drug resistance in vivo by amplification of two genes, ERG11 and TAC1.** *Mol Microbiol* 2008, **68**:624-641 John Wiley & Sons, Ltd (10.1111).
39. Sionov E, Lee H, Chang YC, Kwon-Chung KJ: ***Cryptococcus neoformans* overcomes stress of azole drugs by formation of disomy in specific multiple chromosomes..** Filler SG (editor) *PLoS Pathog* 2010, **6**:e1000848.
40. PHE: **Guidance for the Laboratory Investigation, Management and Infection Prevention and Control for Cases of.** 2017:1-16. August 14.
41. Eyre DW, Sheppard AE, Madder H, Moir I, Moroney R, Quan TP • *et al.*: **A *Candida auris* outbreak and its control in an intensive care setting.** *N Engl J Med* 2018, **379**:1322-1331.
Study describing the nosocomial nature of transmission in a hospital outbreak. The study identified the reuse of axillary temperature probes as a key determinant of transmission.
42. Pfaller MA: **Nosocomial candidiasis: emerging species, reservoirs, and modes of transmission.** *Clin Infect Dis* 1996, **22** (Suppl. 2):S89-S94.
43. Finkelstein R, Reinhertz G, Hashman N, Merzbach D: **Outbreak of *Candida tropicalis* fungemia in a neonatal intensive care unit.** *Infect Control Hosp Epidemiol* 1993, **14**:587-590.
44. Sarvikivi E, Lyytikäinen O, Soll DR, Pujol C, Pfaller MA, Richardson M *et al.*: **Emergence of fluconazole resistance in a *Candida parapsilosis* strain that caused infections in a neonatal intensive care unit.** *J Clin Microbiol* 2005, **43**:2729-2735.
45. Grahl N, Demers EG, Crocker AW, Hogan DA: **Use of RNA-protein complexes for genome editing in non-albicans *Candida* species.** *mSphere* 2017, **2** Mitchell AP (editor), American Society for Microbiology Journals. e00218-17.
46. Lockhart SR, Jackson BR, Vallabhaneni S, Ostrosky-Zeichner L, Pappas PG, Chiller T: **Thinking beyond the common *Candida* species: need for species-level identification of *Candida* due to the emergence of multidrug-resistant *Candida auris*.** *J Clin Microbiol* 2017, **55**:3324-3327 Kraft CS (editor), American Society for Microbiology.
47. Gardy JL, Loman NJ: **Towards a genomics-informed, real-time, global pathogen surveillance system.** *Nat Rev Genet* 2018, **19**:9-20 Nature Publishing Group.
48. Lepak AJ, Zhao M, Andes DR: **Pharmacodynamic evaluation of rezafungin (CD101) against *Candida auris* in the neutropenic mouse invasive Candidiasis model.** *Antimicrob Agents Chemother* 2018, **62**:352 American Society for Microbiology Journals.
49. Fisher MC, Hawkins NJ, Sanglard D, Gurr S: **Worldwide emergence of resistance to antifungal drugs challenges human health and food security.** *Science* 2018, **60**:739-742.
Review describing the rapid global emergence of multidrug-resistant pathogenic fungi, and potential routes to combating their emergence.