REVIEW ARTICLE

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Candida auris Infections

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CME

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CANDIDA AURIS WAS FIRST IDENTIFIED IN 2009, IN AN ISOLATE FROM THE ear canal of a patient in Japan ("auris" is the Latin word for "ear"),[1] and has rapidly emerged as a serious global public health threat. The species, which has spread across more than 45 countries in six continents, is subdivided into five clades (I through V) with distinct geographic distributions (Fig. 1; and see the interactive graphic, available with the full text of this article at NEJM.org).[2,3] *C. auris* is of particular concern because of its ability to adhere to human skin and inanimate objects and to persist, frequently causing difficult-to-control outbreaks in health care facilities (Table 1). The misidentification of *C. auris* as another candida species, an incomplete understanding of its environmental reservoirs, the high morbidity and mortality associated with invasive infections, and the resistance of *C. auris* to several classes of antifungal agents represent additional challenges to providing effective patient care.[3] The serious risks posed by *C. auris* led the Centers for Disease Control and Prevention (CDC) to classify it as an urgent threat in the 2019 Antibiotic Resistance Threats report.[21] Similarly, the World Health Organization (WHO) recently placed *C. auris* in the "critical" group of human fungal pathogens, indicating an urgent need to prioritize research on improving diagnosis, treatment, and outcomes in patients affected by this opportunistic fungus.

MYCOLOGIC FEATURES

C. auris is a budding yeast closely related to *C. haemulonii* and *C. duobushaemulonii* that, unlike *C. albicans*, rarely forms pseudohyphae or hyphae.[3] Unlike other candida species, *C. auris* thrives in high-salt and high-temperature conditions (as discussed below). This adaptability may account for its persistence in harsh environments and has been postulated to be an environmental adaptation to climate change. Climate change may also explain the simultaneous emergence of *C. auris* in diverse geographic regions worldwide.[22] Thus, global warming may have enabled *C. auris* to break through the human "endothermy barrier," which is a major factor in human resistance to infection by environmental fungi.[22] On the basis of this hypothesis, *C. auris* may be the first pathogenic fungus to have emerged in humans because of climate change, although other factors may have also contributed to its global emergence.[22] Whole-genome sequencing of clinical *C. auris* strains has identified five geographically distinct clades that have different virulence properties, clinical features, and drug-resistance profiles (discussed below): the South Asian clade (I), East Asian clade (II), African clade (III), South American clade (IV), and a more recently reported Iranian clade (V) (Fig. 1).[2,23]

C. auris is particularly adept at colonizing the human skin and abiotic surfaces, including medical devices. Porcine and human ex vivo skin models and mouse models of skin colonization have shown the capacity of *C. auris* to sustain colonization and have highlighted the ability of the organism to form multilayer biofilms when

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KEY POINTS

***CANDIDA AURIS* INFECTIONS**

- Since 2009, when it was first identified, *Candida auris* has rapidly spread across more than 45 countries in six continents; it has been subdivided into five clades with distinct geographic distributions.
- *C. auris* can be misidentified as other candida species on certain microbiologic tests.
- *C. auris* persists for long periods on human skin and inanimate objects, frequently causing difficult-to-control outbreaks in health care facilities.
- Skin colonization by *C. auris* is a risk factor for subsequent candidemia, which can develop in up to 25% of critically ill patients who are colonized with the fungus.
- Most strains of *C. auris* are resistant to fluconazole, and some strains are resistant to all available classes of antifungal drugs.
- Echinocandins are the treatment of choice for patients with invasive *C. auris* infection, but the risk of treatment failure and relapse of infection after antifungal therapy is higher with *C. auris* than with other candida species.

exposed to human sweat and to reside within hair follicles and penetrate deep skin layers, evading clinical detection.[24,25] The recent discovery of the *C. auris*–specific adhesin surface colonization factor (Scf1) has underscored the crucial involvement of this adhesin in biofilm formation, colonization of skin and medical devices, and virulence during invasive infections (Fig. 2),[26] uncovering a promising target for therapeutic intervention.

IMMUNE RESPONSE

Production of interleukin-17A and interleukin-17F by both innate and adaptive lymphoid cells is critical in decreasing skin colonization and invasion by *C. auris*, which is consistent with the critical role of interleukin-17 signaling in combating candida at mucocutaneous barriers (Fig. 2).[24] Thus, biologic agents that target the interleukin-17 pathway, which are often used to treat psoriasis, may heighten the risk of *C. auris* skin colonization. Although lymphocytes are crucial for controlling skin colonization by *C. auris*, clearance from blood and deep-seated organs relies on phagocytes, primarily monocytes, macrophages, and neutrophils.[27] *C. auris* effectively evades phagocytosis and killing by neutrophils, a feature that is attributed to its mannan structure, which differs significantly from that of *C. albicans*.[28] A vaccine strategy harnessing the fungal adhesin agglutinin-like sequence 3, which was previously found to be effective in reducing vaginitis episodes in women with recurrent vulvovaginal candidiasis,[29] boosted macrophage-dependent killing of fungus and decreased mortality and fungal growth among mice with systemic *C. auris* infection,[30] revealing a promising preventive strategy for vulnerable patients.

EPIDEMIOLOGIC FEATURES

C. auris rapidly spread worldwide within a decade after the initial report in Japan in 2009. Major outbreaks of *C. auris* bloodstream infections have been reported in health care settings worldwide, particularly in India, Pakistan, South Africa, Kenya, the United Kingdom, Spain, Singapore, Venezuela, Colombia, Brazil, and the United States (Table 1). In South Africa and India, *C. auris* has been responsible for up to 25% and 40% of candidemia cases, respectively, in certain health care settings (Fig. 1).[31,32]

Whole-genome sequencing of *C. auris* isolates has shown the simultaneous emergence of genetically unrelated clades in six continents.[2] Three of these clades (I, III, and IV) diverged from a common ancestor over the past 30 years, whereas the oldest clade (II) diverged approximately 400 years ago.[33] Each clade has very few distinct single-nucleotide polymorphisms, which suggests that clonal expansion has occurred within the region. Molecular epidemiologic investigations of *C. auris* outbreaks typically show clustering of closely related isolates, which supports local and ongoing transmission.[34,35] In addition, the detection of isolates from different clades in each of four countries — Germany, the United Kingdom, Singapore, and the United States — suggests that there were multiple introductions into these countries, followed by local transmission.[16,17,36,37]

In the United States, *C. auris* was first reported in 2016, and the number of cases reported each year thereafter has increased, with 95% and 200% increases in clinical and surveillance cases, respectively, occurring in 2021.[5] Although the initial cases of *C. auris* infection in the United

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States were mainly imported, local transmission in health care settings has been responsible for the significant increase in reported cases in recent years. In the United States, colonization in patients and ongoing transmission are mainly reported in long-term care facilities, particularly long-term acute care hospitals and ventilator-equipped skilled-nursing facilities.[38,39] The skin of nursing home residents can be chronically colonized with *C. auris* and serves as an important reservoir for its spread. *C. auris* avidly contaminates hospital floors, bed rails, medical equipment, trolleys, mobile phones, bed trays, air-conditioning wings, and sink surfaces, which contributes to ongoing transmission within health care facilities.[34,40] Furthermore, a possible role of nosocomial transmission through air dispersal has been suggested.[41]

Beyond health care settings, *C. auris* has been isolated from coastal wetlands in the Andaman Islands and Colombia,[42,43] from stored apples,[44] from wastewater during surveillance after an outbreak in Nevada,[45] and from the mouth, ears, and skin of dogs in India and the United States.[46,47] The rapid spread of *C. auris* and its presence in the environment and in animals highlight the public health importance of closely monitoring this fungal pathogen.

RISK FACTORS

The risk factors for colonization and invasive infections by *C. auris* are similar to those for other candida species and for many other multidrug-resistant microorganisms, such as carbapenemase-producing enteric bacteria.[3,48] These factors include advanced age; the presence of indwelling medical devices, such as central venous or urinary catheters; certain coexisting conditions, such as diabetes mellitus and neoplastic or chronic kidney

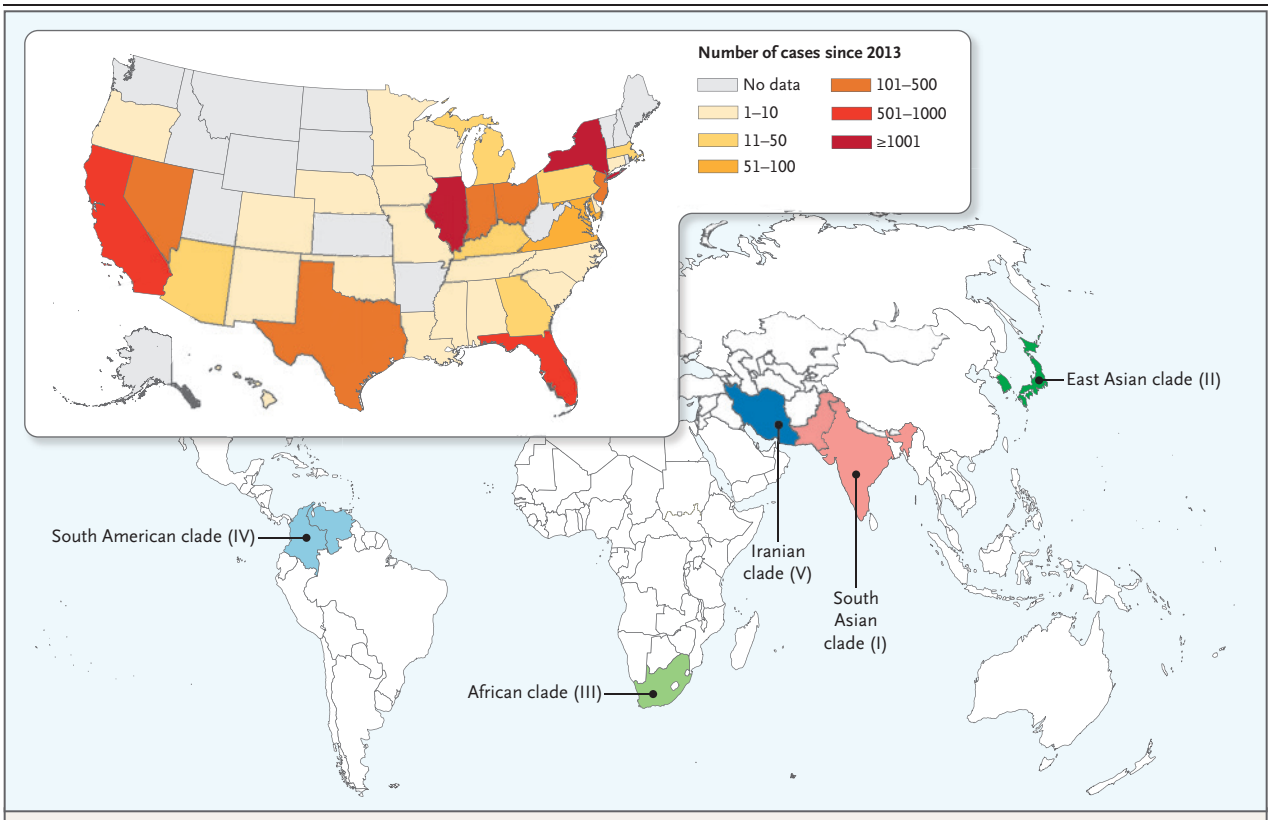

Figure 1. Geographic Origins of *Candida auris* and Clinical Cases in the United States.

Shown are the areas of the globe in which the five *C. auris* clades initially arose. The inset shows the number of *C. auris* clinical cases across the United States from 2013 through 2022 (data are from www.cdc.gov/fungal/candida-auris/tracking-c-auris.html). In South Africa and India, *C. auris* accounts for up to 25% and 40% of candidemia cases, respectively, in certain health care settings.

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disease; total parenteral nutrition; mechanical ventilation; hemodialysis; immunocompromised states, such as neutropenia, glucocorticoid use, or receipt of an organ transplant; recent surgery; severe coronavirus disease 2019 (Covid-19); and recent treatment with broad-spectrum antibiotic or antifungal agents,[2,3,20,39,48] which may enrich conditions for the development of *C. auris*–permissive skin microbial communities.[49] Affected patients typically have prolonged stays in a hospital or intensive care unit, often longer than those for patients with candidemia caused by other candida species, a finding consistent with the hospital-acquired nature of invasive *C. auris* infections.[2,3,50] Moreover, previous skin colonization by *C. auris* is a risk factor for subsequent invasive infections, with candidemia developing in up to 25% of critically ill persons who are colonized.[3]

CLINICAL MANIFESTATIONS

Patients can be colonized with *C. auris* without having clinical signs or symptoms. The most common site of colonization is the skin, primarily in the nares, axilla, and groin.[3] Colonization of the gastrointestinal or urogenital tract occurs less often. This pattern of colonization differs from that observed with other candida species, such as *C. albicans* and *C. glabrata*, which predominantly colonize the human gastrointestinal tract.[48] Mucosal infections, including oral thrush, esophageal candidiasis, and vulvovaginal candidiasis, are infrequent with *C. auris*.

As with other candida species, invasive *C. auris* infections manifest primarily as candidemia, with or without associated sepsis, but *C. auris* can spread hematogenously to distal anatomical sites.[2,3,48] *C. auris* has been isolated from cerebrospinal, pleural, pericardial, biliary, and peritoneal fluids and has been reported to cause myocarditis, pericarditis, meningitis, hepatosplenic infection, osteomyelitis, urinary tract infections, endophthalmitis, ear infections, and wound infections, as well as donor-derived disease after lung transplantation.[2,3,51] *C. auris*–associated candidemia and invasive candidiasis can be life-threatening, with reported crude case fatality rates ranging between 30 and 60%.[2,3] However, attributable mortality is difficult to quantify precisely because of concurrent acute and chronic conditions.

DIAGNOSIS

Culture-based testing of specimens obtained for clinical or screening purposes is the cornerstone of the laboratory diagnosis of *C. auris* infection. Isolation of *C. auris* in culture is important for reporting antifungal susceptibility patterns. *C. auris* can be readily cultured from blood, urine, sputum, other bodily fluids, and tissue on routine laboratory and mycologic media such as Sabouraud dextrose agar. Morphologically, *C. auris* cannot be distinguished from other candida species. However, unlike most other candida species, *C. auris* grows well at 40 to 42°C. On traditional chromogenic media, *C. auris* colonies usually appear white or pink. A new chromogenic agar, CHROMagar Candida Plus, allows rapid identification of *C. auris* and differentiation from other candida species.

C. auris appears as pale-cream colonies with a blue halo visible within 48 hours on CHROMagar Candida Plus medium. *C. diddensiae* and *C. vulturna* may show similar coloration, although these species are clinically rare.[52,53] However, a recent study evaluating the use of CHROMagar Candida Plus in a large number of fungal isolates did not report false positive results with these rare species.[54] Moreover, another chromogenic medium — HardyCHROM Candida+, which is used to detect *C. auris* on the basis of colony morphologic features, color, and ultraviolet fluorescence — is available for easy differentiation of *C. auris* from other candida species. When this medium is used, *C. auris* produces white colonies with teal or teal-green "bull's-eye" centers that are positive for ultraviolet fluorescence. The CDC currently recommends the use of a high-salt, high-temperature enrichment medium (10% salt Sabouraud Dulcitol broth) for reliable isolation of *C. auris* from clinical skin swabs and environmental surveillance samples. Conventional phenotypic yeast-identification systems such as VITEK-2 YST, API 20C, BD Phoenix, and MicroScan may misidentify *C. auris* isolates as *C. haemulonii*, *C. sake*, *Rhodotorula glutinis*, or other candida species.[55,56] However, several of these systems have recently been updated to include *C. auris*. Although widely used in resource-constrained laboratories worldwide, the updated systems still have limited ability to correctly identify *C. auris* from the African and East Asian clades.

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Table 1. Major *Candida auris* Outbreaks across the Globe.*

Area	Outbreak Duration	No. of Cases	Risk Factors and Patient Characteristics	*C. auris* Clade or Clades	Source
China	2018–2023	312 *C. auris*–associated hospitalizations and 4 outbreaks of infection in health care settings	Lung infections, hypertension, liver disease, diabetes mellitus, cancer	I–IV; multiple origins or introductions	Bing et al.[4]
United States	2019–2021	3270 Clinical cases (blood or urine samples) and 7413 colonizations	Delays in early identification of cases and implementation of infection prevention and control measures	NA	Lyman et al.[5]
Virginia	October 2020–June 2021	28 Cases in two ventilator-equipped nursing facilities: 3 clinical cases (blood or urine samples) and 25 screening cases	Respiratory failure and previous colonization or infection with a carbapenemase-producing organism; no recent health care stays abroad or in other regions	I (5 cases) and III (3 cases)†	Waters et al.[6]
Colombia	January 2015–September 2016	40 Cases of candidemia in 4 acute care hospitals	ICU stay of ≥15 days, severe sepsis, diabetes mellitus	NA	Caceres et al.[7]
Pakistan	October 2014–March 2017	38 Cases of candidemia and 27 non-candidemia infections; 27 colonizations	Surgery, antibiotic use, ICU stay, indwelling lines, isolation of another multidrug-resistant organism	NA	Sayeed et al.[8]
Venezuela	March 2012–July 2013	18 Cases of candidemia	Antibiotic use, invasive medical procedure, ICU admission, prolonged hospital stay	NA	Calvo et al.[9]
Brazil	December 2020	3 Cases of candidemia in patients with Covid-19; 9 colonization cases	Colonized digital thermometer, central venous catheter, mechanical ventilation, hemodialysis	I	Nobrega de Almeida et al.[10]
Kenya	October 2010–December 2016	77 Cases of candidemia	Central venous catheter, critical illness	NA	Adam et al.[11]
Italy	June 2020–January 2021	77 *C. auris* infections (bloodstream, lung, and urinary tract)	ICU stay, surgery, transplantation	NA	Piatti et al.[12]
India	August 2020–January 2021	14 Cases of candidemia in patients with Covid-19 in the ICU	Hypertension, diabetes mellitus, renal infection	NA	Rajni et al.[13]
South Africa	October 2012–November 2016	451 Cases of invasive candidiasis, 1128 colonizations (622 in urine, 288 on central venous catheter tips, 173 in respiratory tract, and 45 on skin, mucosal, or wound swabs)	Fluconazole prophylaxis and treatment, suboptimal adherence to infection prevention and control practices	NA	Govender et al.[14]
Kuwait	January 2018–June 2019	17 Cases of candidemia, 54 colonizations	Hypertension, diabetes mellitus, coexisting cardiovascular conditions	NA	Alfouzan et al.[15]
Germany	2015–2017	7 *C. auris* cases of infection	Previous health care exposure in the Middle East, Asia, Africa, or United States	I (6 cases) and III (1 case)	Hamprecht et al.[16]

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Singapore	2012–2018	4 Cases of candidemia, 3 noncandidemia infections	NA	Tan et al.[17]
Spain	October 2017–June 2020	47 Cases of candidemia, 287 colonizations	Diabetes mellitus, cancer, surgery within 30 days before occurrence of candidemia, mechanical ventilation, central venous catheter, Covid-19	Mulet Bayona et al.[18]
United Kingdom	February 2015–August 2017	70 Cases of *C. auris* colonization or infection; 7 invasive infections (4 with candidemia, and 3 with central nervous system device–associated meningitis)	Reusable axillary temperature probes, systemic fluconazole exposure	Eyre et al.[19]
Israel	May 2014–May 2022	209 Cases of *C. auris* colonization or infection	Covid-19, mechanical ventilation	Biran et al.[20]

* Covid-19 denotes coronavirus disease 2019, ICU intensive care unit, and NA not available.
† Clade information is available for 8 cases only.

Accurate identification of *C. auris* is accomplished with matrix-assisted laser desorption ionization–time-of-flight (MALDI-TOF) mass spectrometry. The two most common MALDI-TOF systems, the Bruker Biotyper and the VITEK MS, include *C. auris* in their databases for research use only and in certain versions of their Food and Drug Administration (FDA)–approved system databases. In addition, a CDC-curated database, MicrobeNet, includes *C. auris* spectra and is freely available as a supplement to the Bruker database. Laboratories can also reliably identify *C. auris* by sequencing the D1–D2 region of the 28S ribosomal DNA (rDNA) or the internal transcribed spacer regions of rDNA. Real-time polymerase-chain-reaction (PCR) assays are sensitive and specific methods of directly identifying *C. auris* nucleic acids in clinical samples, with a detection threshold as low as 1 to 10 colony-forming units. TaqMan quantitative PCR (qPCR), SYBR Green qPCR, and the T2 Magnetic Resonance assay are promising tools for screening patients colonized with *C. auris*, with results available within hours.[57] These assays have higher sensitivity and specificity than culture-based methods and provide same-day results. The GenMark ePlex blood culture identification (BCID) fungal pathogen panel and the BioFire FilmArray BCID2 are FDA-approved molecular tests for identification of *C. auris* in positive blood cultures.[58,59] However, no FDA-approved tests are currently available for colonization swabs.

ANTIFUNGAL RESISTANCE

Resistance of *C. auris* to antifungal agents is clade-specific, with clades I, III, and IV responsible for multidrug-resistant invasive infections worldwide.[33,60] In contrast, clade II (the East Asian clade) predominantly causes ear infections and is uniformly susceptible to antifungal drugs.[61] Resistance of *C. auris* to fluconazole appears to be acquired, and approximately 90% of strains from all clades except for clade II are fluconazole-resistant.[61,62] The most common mechanism of azole resistance in *C. auris* involves mutations in *ERG11*, which encodes the drug target lanosterol 14α-demethylase enzyme (Fig. 2). The most commonly reported *ERG11* mutations result in the amino acid substitutions F126L, Y132F, and K143R, which are clade-specific.[63,64] In addition, mutations in genes encoding zinc-cluster transcription

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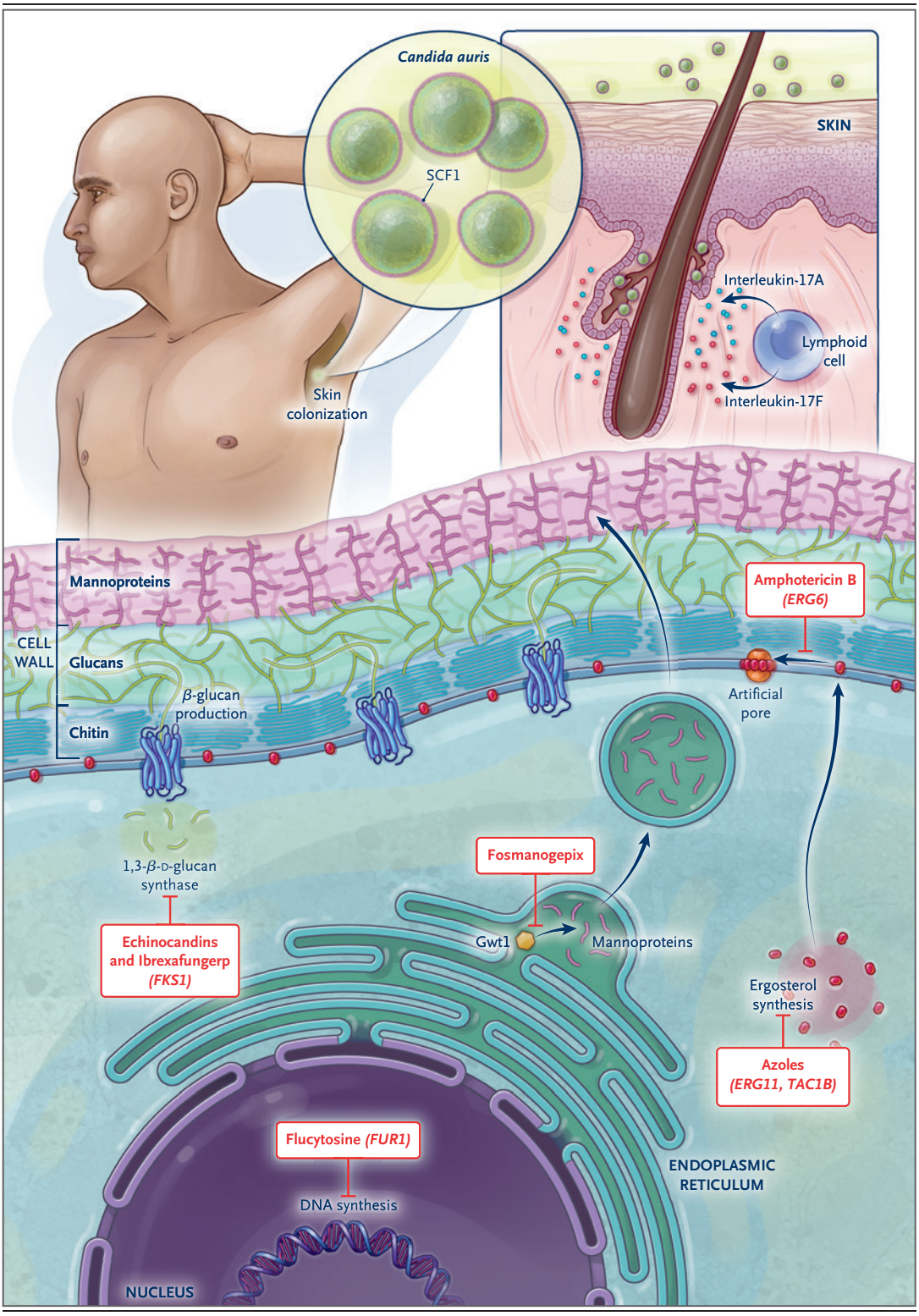

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Figure 2 (facing page). Pathogenesis of *C. auris*, Therapeutic Targets, and Genes Conferring Drug Resistance.
The top part of the illustration shows *C. auris* yeasts colonizing the skin, including the hair follicles, a process that is promoted by the fungal adhesin surface colonization factor (Scf1). *C. auris* colonization is counteracted by interleukin-17 produced by lymphoid cells. The lower part shows therapeutic targets of antifungal drugs against *C. auris*. Echinocandins and ibrexafungerp inhibit the production of β-glucans in the fungal cell wall. Azoles and amphotericin B target ergosterol in the fungal cell membrane. Fosmanogepix targets fungal mannoprotein transport, and flucytosine inhibits DNA synthesis. Genes involved in the resistance of *C. auris* to the corresponding antifungal drugs are shown in parentheses.

factors can promote fluconazole resistance. An example is a mutation in *TAC1B* that increases the expression of efflux pumps such as Cdr1p.[65]

The echinocandins act by inhibiting the synthesis of a major constituent of the fungal cell wall, 1,3-β-glucan. Overall, resistance to echinocandins is uncommon, with approximately 5% of *C. auris* isolates reported to be echinocandin-resistant.[63,66] However, resistance can develop during echinocandin therapy and is caused by mutations at amino acid S639 (S639Y, S639F, or S639P) in hotspot 1 of the drug target 1,3-β-D-glucan synthase, which is encoded by *FKS1* (Fig. 2).[63,66] In addition, a newly discovered mutation outside the hotspot 1 region that confers echinocandin resistance has been observed in clinical *C. auris* isolates.[67] These mutations substantially decrease the sensitivity of glucan synthase to inhibition by echinocandins. Alarmingly, the CDC reported that rates of echinocandin resistance tripled in 2021 relative to the previous 2 years.[5]

Clinical resistance to amphotericin B is rare among fungi. However, amphotericin B resistance has been reported in approximately 30% of *C. auris* isolates, mainly from clades I and IV, on the basis of a tentative susceptibility breakpoint of 2 μg per milliliter for amphotericin B against *C. auris*.[2,68] A single case report showed that a mutation in *ERG6* within the ergosterol biosynthetic pathway was associated with amphotericin B resistance in a clinical *C. auris* isolate (Fig. 2).[69] Amphotericin B–resistant *C. auris* isolates have reduced permeability of membrane lipids, which may also contribute to resistance.[70] The most worrisome issue with respect to *C. auris* infections is the transmission, in the United States, of some isolates that are resistant to echinocandins and others that are resistant to all available classes of antifungal drugs, which suggests that drug-resistant clones are spreading within health care settings.[71]

TREATMENT

Randomized clinical trials evaluating the management of *C. auris* infections and the efficacy of specific antifungal therapies are lacking. Current CDC recommendations advise against antifungal treatment in patients with *C. auris* colonization if there is no evidence of clinical infection. However, for patients with *C. auris* candidemia or invasive candidiasis, prompt initiation of antifungal treatment is required and consultation with an infectious-disease specialist is advised, because this strategy is associated with improved outcomes for patients with invasive infections with other candida species.[72,73]

For *C. auris* infection in adults and in children 2 months of age or older, the CDC recommends the use of echinocandins as empirical or initial therapy pending the results of susceptibility testing, given the potent in vitro activity of these agents and the relatively low rates of primary echinocandin resistance (Fig. 2).[73] The preferred echinocandins for children 2 months of age or older are caspofungin and micafungin because of the limited pharmacokinetic and pharmacodynamic data on anidulafungin in this age group. For neonates and infants younger than 2 months of age, amphotericin B deoxycholate is the recommended treatment, with a switch to a lipid formulation of amphotericin B if there is no clinical response (Fig. 2).[73] This recommendation stems from the propensity of invasive candidiasis to cause disseminated disease, including meningoencephalitis, in this age group and from the limited penetration of echinocandins in the cerebrospinal fluid.[73]

Patients should be monitored closely to ensure an invasive infection resolves, because primary echinocandin resistance can occur, albeit infrequently,[2,5] and because the emergence of secondary

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resistance has been documented in serial *C. auris* strains after echinocandin treatment.[74] Follow-up blood culture should be performed to establish the clearance of candidemia, and any subsequent fungal strains should undergo repeat susceptibility testing. Two weeks of antifungal therapy after clearance of blood cultures is recommended for patients who do not have metastatic foci.[73] Switching to a lipid formulation of amphotericin B can be considered if a patient has persistently positive blood cultures for 5 days or more with no clinical response to echinocandin therapy. Amphotericin B deoxycholate is the preferred treatment in resource-scarce countries where echinocandins and in vitro susceptibility testing are not available. Because *C. auris* is often resistant to azole antifungal agents (Fig. 2), oral treatment options are limited for patients with *C. auris* infection. Azoles, such as fluconazole, voriconazole, or posaconazole, should be considered only as step-down treatment after successful initial therapy with an echinocandin in selected patients who are infected with susceptible strains.[73]

Additional approaches to the management of *C. auris* infection are the same as those for infections with other candida species, as outlined in the 2016 Infectious Diseases Society of America clinical practice guidelines.[73] These approaches include prompt removal of central venous catheters, when feasible, and ophthalmologic examination to rule out intraocular involvement, given the poor penetration of echinocandins at this anatomical site. On the basis of a systematic literature review showing a low frequency of concordant endophthalmitis among patients with candidemia, the American Academy of Ophthalmology recommends funduscopic examination only in patients with signs or symptoms suggestive of ocular infection.[75,76] Cost-effective, evidence-based protocols, endorsed by both infectious disease and ophthalmologic professional societies, are needed for identifying patients with candidemia and ocular involvement. Patients with candidemia caused by *C. auris* have a higher risk of treatment failure and microbiologic recurrence after completion of antifungal therapy than patients with candidemia caused by other candida species.[2,3,77]

PREVENTION

In health care settings, transmission of *C. auris* among patients can occur within 3 to 4 hours after contamination of the environment or equipment. Therefore, rapid identification of the presence of *C. auris* and timely infection-control measures are warranted to prevent nosocomial outbreaks.[78] Although screening on admission is a valuable tool in identifying and controlling the introduction of *C. auris* into health care facilities, this approach does not assess spread among persons within a facility. Therefore, admission screening should be accompanied by regular point-prevalence surveys to control the spread of *C. auris*. Contact precautions or enhanced barriers, including universal use of gowns and gloves during contact with patients or their environment, placement of individual patients in single rooms or grouping of patients with *C. auris* colonization or infection, and preemptive isolation of patients who have come in contact with *C. auris*–carrying patients, are recommended.[79,80] Dedicated medical equipment and switching to single-use or single-patient-use alternatives (e.g., blood-pressure cuffs) and assigning nursing staff to care for patients in the same designated area, wherever possible, can be implemented. Equipment that must be shared should be thoroughly cleaned between uses. During isolation, daily disinfection and cleaning of the floor and surfaces near patients is required. Disinfectants that are routinely used in health care settings, such as quaternary ammonium compounds, are not effective against *C. auris*. Therefore, the CDC recommends the use of an Environmental Protection Agency (EPA)–registered (under EPA List P), hospital-grade disinfectant against *C. auris*, which is also effective against *Clostridioides difficile* spores.

CONCLUSIONS AND FUTURE PERSPECTIVES

The rapid emergence and global spread of multidrug-resistant *C. auris* underscore the urgent need to ramp up control measures against this opportunistic fungal pathogen. A deeper understanding of the virulence traits of *C. auris* and the molecular factors that promote immunity could lead to the discovery of new antifungal drug targets, adjunctive immune-based therapies, or vaccines. Improving non–culture-based diagnostic tests, such as qPCR, could facilitate timely and accurate identification of *C. auris* colonization and infection. The use of effective infection-control measures can help reduce or eradicate

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colonization and transmission, improve environmental disinfection, and reduce the risk of nosocomial outbreaks of *C. auris* infection. The precise delineation of environmental reservoirs is another important step in enhancing strategies for infection prevention and control for vulnerable patients.

Echinocandins are the preferred treatment for *C. auris* infections. The roles of rezafungin, a newly approved long-acting echinocandin,[81] and ibrexafungerp, a newly approved oral triterpenoid compound that also inhibits fungal glucan synthesis,[81] warrant further investigation (Fig. 2). For patients infected with echinocandin-resistant or multidrug-resistant strains, determining the antifungal drug regimen that should be used is critical. Fosmanogepix, which inhibits the fungal enzyme Gwt1 and impairs cell-wall mannoprotein synthesis (Fig. 2), has shown promise in early studies and is being evaluated in phase 3 clinical trials.[81] Additional work is needed to further characterize the molecular mechanisms underlying intrinsic and acquired antifungal drug resistance of strains from different clades and to better understand the clade-specific strain differences in antifungal resistance and virulence. Defining the most effective strategies for the diagnosis, prevention, and treatment of *C. auris* infections may curb its spread and improve clinical outcomes.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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