Medical News & Perspectives

On the Rise, Candida auris Outwits Treatments and Travels Incognito in Health Care Settings

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To quote medical mycologist Shawn Lockhart, PhD, Candida auris “is a very clever bug.”

This hardy yeast species can remain viable for at least 2 weeks on plastic surfaces and for months on the skin, and it’s far more likely to resist antifungals than other Candida species are. It’s spread within health care facilities and from one facility to another. And it can travel easily from patient to patient or from a contaminated surface such as a doorknob to a patient.

The fungus is a stealth killer. As many as 90% to 95% of patients colonized with C auris are asymptomatic but can spread the yeast to others and make them sick. The mortality rate from invasive C auris candidiasis—a serious infection in the blood, brain, heart, or other parts of the body—is thought to be as high as 60%, Lockhart said, but pinning that number down is challenging because affected patients typically have a variety of comorbidities that could contribute to their death.

As Lockhart, a senior advisor in the Mycotic Diseases Branch at the US Centers for Disease Control and Prevention (CDC) notes, C auris is “the new kid on the block,” presenting the rare opportunity to observe the emergence of a pathogenic microbe in real time.

In One Ear...

C auris was first identified in 2009 in a specimen taken from the infected ear—the organ for which the species was named—of a patient in Japan 2 years prior. Around the same time, 3 other distinct clades, or populations, of C auris were identified in Africa, South America, and South Asia. The fungus has now been reported in more than 55 countries, Hatim Sati, MD, MPH, technical officer in the Antimicrobial Resistance Division at the World Health Organization (WHO), said in an interview.

It was first identified in the US in 2013. The initial isolates were related to the clades arising in South America, now called clade IV, and South Asia, now clade I, suggesting that patients who’d been treated in health care facilities in those parts of the world had imported C auris to US health care facilities. What appears to be clade V has been seen only in Iran; it was first reported there in 2018 in a 14-year-old girl with an ear infection who had never been out of that country.

“We know that new species don’t just appear,” he said. “We just have not figured out where it was hiding before it started to appear in hospitals worldwide. There’s a lot of speculation.” Lockhart’s best guess is that C auris quietly coexisted with humans in the ear canal—until it didn’t.

Soon after C auris was discovered and named, public health organizations recognized that it was going to be a bad actor. In 2019, the CDC listed it as one of the country’s most urgent “antibiotic resistance threats.” More recently, the WHO in October 2022 categorized C auris as 1 of the 4 most critical fungal pathogens, along with Cryptococcus neoformans, Aspergillus fumigatus, and Candida albicans, on its first-ever priorities list of 19 such microbes.

The WHO report, for which Sati served as the technical lead, noted that “invasive fungal diseases (IFDs) are rising overall and particularly among immunocompromised populations.”

“Despite the growing concern,” the report continued, “fungal infections receive very little attention and resources, leading to a paucity of quality data on fungal disease distribution and antifungal resistance patterns. Consequently, it is impossible to estimate their exact burden.”

Evidence is emerging that climate change is affecting the ecology of fungal pathogens by expanding their habitats, Sati noted, although “the dynamics are not fully understood.” In addition, he said, populations at risk for serious infection by C auris and other disease-causing fungi are increasing because immunocompromised individuals are living longer. This group includes people with HIV or tuberculosis, cancer survivors who’ve undergone chemotherapy, and recipients of solid organ transplants.

The COVID-19 pandemic has also been a factor in increasing numbers of C auris outbreaks. In the second half of 2020, for example, most documented US cases of C auris were in patients with COVID-19, according to the Pan American Health Organization.

Lockhart said he and his colleagues wondered whether C auris had actually been around longer but had been misidentified or overlooked. So they reviewed the literature and queried global microbe collections. The search effort yielded a report of a C auris isolate from a 1996 bloodstream infection in a pediatric surgery patient in Korea. The sample had been stored in a freezer for more than a decade and not recognized as C auris until the new species was identified, Lockhart said. “Japan has also found an isolate from 1997, so it was smoldering somewhere in East Asia before it was discovered and named,” he said.

Lockhart and his colleagues also retrospectively reviewed more than 15 000 Candida isolates in the SENTRY Antimicrobial Surveillance Program’s collection and found only 4 C auris isolates, from 2009, 2013, 2014, and 2015.
“At a community level, we saw a resurgence of C. auris during the original COVID-19 surges,” infectious disease specialist Kavitha Prabaker, MD, said in an interview. Shortages of staff and personal protective equipment and increased numbers of critically ill patients requiring ventilators all likely have contributed to rising numbers of C. auris infections during the COVID-19 pandemic, explained Prabaker, associate director of clinical epidemiology and infection prevention at UCLA Santa Monica.

Lack of awareness about fungal pathogens doesn’t help, Mahmoud Ghannoum, PhD, told JAMA in an interview. “A lot of doctors don’t think of fungus,” said Ghannoum, director of the Center for Medical Mycology at University Hospitals Cleveland Medical Center and Case Western Reserve University.

As a result, when a patient goes to the hospital with symptoms of an infection, physicians are likely to assume the cause is bacterial and treat them with one antibiotic after another to no avail, Ghannoum said. In fact, the most common signs of invasive Candida infection are fever and chills that don’t respond to antibiotics, according to the CDC.

“Mycology is neglected in the training of medical professionals,” Sati acknowledged. “Where there are no trained mycologists, there is no mycosis.”

**Look, and You Shall Find**

From October 1, 2021, to September 30, 2022, the most recent year for which data are available, 28 states and the District of Columbia reported at least 1 clinical case of C. auris infection, for a total of 1994 cases nationwide, according to the CDC.

But just because states didn’t identify any cases doesn’t mean they didn’t have any.

“In infection control...the big adage is if you don’t look for it, you won’t find it,” infectious disease specialist Natasha Bagdasarian, MD, MPH, the state of Michigan’s chief medical executive, noted in an interview.

Compared with the 3 years prior, Michigan has seen a big spike in C. auris cases in 2022, Bagdasarian acknowledged. “It looks like the cases have exploded.” What’s more likely, though, is that many cases went undetected in 2019, 2020, and 2021, when public health laboratories were overwhelmed by COVID-19 and chronic underfunding didn’t have the bandwidth to look for C. auris, she explained. “This is an insidious organism that likely has been introduced to the state many, many times.”

C. auris can survive in warmer and saltier environments than other fungal pathogens. Screening high-risk patients by swabbing their armpits and groin, common sites of colonization, is one key to stopping its spread in health care facilities, according to the CDC.

High-risk patients include those who’ve been in close contact with someone newly identified with C. auris colonization or infection, such as roommates in nursing homes, or those who’ve had an overnight stay in a health care facility outside the US in the previous year, especially if they were hospitalized in a country with documented C. auris or have an infection or colonization with carbapenemase-producing gram-negative bacteria, the CDC notes. C. auris co-colonization is regularly seen with these bacteria.

To reduce the risk of spreading C. auris, health care facilities might cohort colonized and infected patients, instruct health care personnel or other caregivers to wear gowns and gloves when providing care to them, clean their rooms with different products than usual, and encourage family members and others who come in contact with them to wash their hands often, the CDC explains in a fact sheet for patients. “We assume family members can carry it on their hands and spread it to other patients,” Lockhart explained.

**A Sticky Situation**

Sticky might not exactly be a scientific term, Bagdasarian acknowledged, but it’s an apt description for C. auris.

The pathogen exhibits a capacity for colonization well beyond that of C. albicans, the most frequently isolated Candida species, a 2020 study found. For reasons that aren’t fully understood, the majority of colonized patients don’t become sick with invasive C. auris infections. As for why, “I think that’s the million-dollar question,” CDC Mycotic Diseases Branch medical officer Meghan Lyman, MD, said in an interview.

There is no protocol for decolonizing patients, Lockhart noted, but regular bathing can reduce C. auris growth. Chlorhexidine, a broad-spectrum biocide, is commonly used.

Patients can remain colonized with C. auris months after being discharged from a health care facility, and if they seek care in a different facility, they can be a source of nosocomial transmission, noted researchers from the New York City Department of Health and Mental Hygiene in another study published in 2020. At the time, about half of all US cases were found in New York City hospitals and nursing homes. To guide infection control practices, the researchers developed a case management pilot program for 75 patients who had a history of a positive C. auris culture and had been discharged from a hospital or nursing home to the community.

Case managers tried to coordinate C. auris colonization assessments every 3 months with the patients’ outpatient clinicians, although in practice the screening frequency varied. Most study participants no longer had detectable C. auris by a year after it was first identified. The study was too small to identify clinical factors associated with persistent colonization, the authors wrote.

Although health care workers can carry C. auris on their skin or gloves or other protective gear, they don’t appear to be colonized by it, Lockhart said. One explanation he offered is that colonized patients’ skin microbiome could differ from that of healthy individuals. Long-term antibiotic use could disrupt the skin microbiome, as could the stringent soaps used to bathe hospitalized patients. The question remains, however: Does C. auris take advantage of a disrupted skin microbiome, or does colonization change the skin microbiome? “We just don’t know what the normal interaction is,” Lockhart said.

In New York, studies have shown that 5% to 10% of colonized patients eventually go on to develop invasive C. auris infection, he said. “We know that patients who have multiple [venous] lines are at a higher risk,” Lockhart explained, noting that undergoing surgery is another risk factor.

**Too Little, Too Late**

Unfortunately, health care facilities typically don’t begin screening high-risk patients for C. auris until they’ve identified an infection, Lyman said. “At that point they’re already kind of behind,” she noted.

Nebraska has been dealing with concurrent outbreaks of 2 different C. auris clades, but some health care facilities “have been reluctant to consistently and appropriately screen patients,” Dawn Cribb, a spokesperson for the Nebraska Department of Health and Human Services wrote in an emailed response to questions from JAMA. Implementing consistent and clear commu-
Communications about patients’ *C auris* status when they are transferred from one facility to another has also been challenging, Cribb said.

Las Vegas news outlets, citing the state health department, reported that 774 cases of *C auris* colonization or infection and 63 associated deaths had been identified in Nevada in 2022 as of late November. The cases were found in 33 facilities, including both long-term care homes and hospitals.

The first case in the current Nevada outbreaks was reported in August 2021, Cribb said. “The origination of *C auris* in Nevada is currently unknown,” she told JAMA, because neither the clade I cases nor the clade III cases match anything seen in current US databases. Plus, she added, a specimen identified in northern Nevada in early 2020 wasn’t closely related to organisms in the 2 current outbreaks.

“Nevada is an interesting case,” Lyman said. As in some other states, she explained, a patient who’d been colonized out-of-state probably introduced *C auris*, which had likely already circulated widely before it finally was identified. “At this point, most of our cases are locally acquired,” she added.

Even when health care facilities are willing to screen for *C auris*, some patients won’t provide consent, Bagdasarian said. Obtaining consent wasn’t a problem before the COVID-19 pandemic. But now, she said, some patients don’t want to be screened for *C auris* because it’s not directly related to their care, just as some people refuse to be tested for COVID-19 because they don’t see any personal benefit in doing so.

Screening every high-risk patient can still miss some cases, suggested a recent study coauthored by UCLA Santa Monica’s Prabaker. The study was the first to characterize many clade III *C auris* cases in the US, according to the authors. From late 2019 to early 2022, they identified 45 patients with *C auris* at UCLA Santa Monica and UCLA Ronald Reagan, the 2 main UCLA health system sites. Most of those patients had a tracheostomy and had been transferred from a skilled nursing facility with a known *C auris* outbreak. Invasive candidiasis was identified in 13 of the patients, 9 of whom had bloodstream infections.

The researchers used both active surveillance, which entailed screening every patient who fit the CDC’s definition of high risk, and passive surveillance, which involved working up all *Candida* isolates that had grown in cultures from nonsterile sources such as urine. Before her hospital’s *C auris* outbreak began, its laboratory would “not spend the extra time and money to identify the species of *Candida* unless specifically requested by the doctor,” Prabaker explained.

Using passive surveillance, the study identified *C auris* in 4 patients who wouldn’t have been targeted by active surveillance of high-risk individuals. Two of the patients came from facilities not known to have *C auris*, one a skilled nursing facility and the other a hospital, Prabaker said.

Toward the end of the study, she noted, the hospital began screening patients transferred from any skilled nursing facility because it had become too complicated to keep track of the ever-changing list of which ones had *C auris* outbreaks.

**Most Likely to Resist Antifungals**

Before *C auris*, the most-feared yeast species was *Candida glabrata*, Lockhart said. *C albicans*—which, like *C auris*, sits atop the WHO’s fungal priorities list—is associated with more cases of invasive candidiasis than *C glabrata*. However, *C glabrata* was the yeast species most likely to be resistant to antifungals, Lockhart explained.

Among *C glabrata* isolates, 1% or 2% are resistant to amphotericin B, a commonly used antifungal, he said. But *C glabrata* is easy prey for antifungals compared with *C auris*. In the US, about 30% of *C auris* isolates are resistant to amphotericin B, about 90% are resistant to fluconazole, and less than 5% have been resistant to echinocandins, according to the CDC, which notes that some isolates are resistant to all 3 classes of antifungal drugs. The problem, Sati said, is that lower-income countries can’t afford echinocandins, which are newer and more expensive than the other antifungals.

To top it off, becoming resistant to treatment doesn’t come at a cost for *C auris*, Lockhart added. Usually, treatment-resistant yeast don’t grow as well as susceptible yeast, but, surprisingly, that’s not been the case with *C auris*, he said.

And yet, relatively few new antifungals are in the pipeline, Sati noted.

The US Food and Drug Administration approved ibrexafungerp (marketed as Brexafemme) in 2021 to treat vaginal yeast infections, which are most commonly caused by *C albicans*. The prescribing information mentions that ibrexafungerp, a first-in-class antifungal drug, has in vitro activity against *C auris* and 8 other yeast species, but that the clinical significance is unknown.

New Jersey–based Scynexis is conducting a multicenter open-label phase 3 clinical trial of ibrexafungerp among patients with documented *C auris* infections, and the National Institutes of Health recently awarded Ghannoum’s team at Case Western a $3 million, 5-year grant to evaluate and enhance a second-generation version of the drug. In the laboratory, the novel drugs show good fungicidal activity against *C auris* isolates resistant to current antifungals, Ghannoum said.

Meanwhile, Lockhart said, “It’s very important for us as a health care community to support resource-limited settings, where they’re really struggling.”

As Sati pointed out, many countries can’t afford the antifungal of choice for treating *C auris*. But the pathogen knows no borders, which means that *C auris* “is not a US problem,” Lockhart emphasized. “It’s a global problem.”

Published Online: December 28, 2022.

doi:10.1001/jama.2022.17760

**Conflict of Interest Disclosures:** Dr Ghannoum reported receiving research contracts from and acting as an advisor to Pfizer, Gilead, Scynexis, Mycova, and Cidara. No other disclosures were reported.

**Note:** Source references are available through embedded hyperlinks in the article text online.