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Investigation of the First Seven Reported Cases of *Candida auris,* a Globally Emerging Invasive, Multidrug-Resistant Fungus—United States, May 2013–August 2016

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What is already known about this topic?

Candida auris is an emerging pathogenic fungus that has been reported from at least a dozen countries on four continents during 2009–2015. The organism is difficult to identify using traditional biochemical methods, some isolates have been found to be resistant to all three major classes of antifungal medications, and *C. auris* has caused health care–associated outbreaks.

What is added by this report?

This is the first description of *C. auris* cases in the United States. *C. auris* appears to have emerged in the United States only in the last few years, and U.S. isolates are related to isolates from South America and South Asia. Evidence from U.S. case investigations suggests likely transmission of the organism occurred in health care settings.

What are the implications for public health practice?

It is important that U.S. laboratories accurately identify *C. auris* and for health care facilities to implement recommended infection control practices to prevent the spread of *C. auris*. Local and state health departments and CDC should be notified of possible cases of *C. auris* and of isolates of *C. haemulonii* and *Candida* spp. that cannot be identified after routine testing.

Introduction

Candida auris, an emerging fungus that can cause invasive infections, is associated with high mortality and is often resistant to multiple antifungal drugs. *C. auris* was first described in 2009 after being isolated from external ear canal discharge of a patient in Japan (1). Since then, reports of *C. auris* infections, including bloodstream infections, have been published from several countries, including Colombia, India, Israel, Kenya, Kuwait, Pakistan, South Africa, South Korea, Venezuela, and the United Kingdom (2–7). To determine whether *C. auris* is present in the United States and to prepare for the possibility of transmission, CDC issued a clinical alert in June 2016 informing clinicians, laboratorians, infection control practitioners, and public health authorities about *C. auris* and requesting that *C. auris* cases be reported to state and local health departments and CDC (8). This report describes the first seven U.S. cases of *C. auris* infection reported to CDC as of August 31, 2016. Data from these cases suggest that transmission of *C. auris* might have occurred in U.S. health care facilities and demonstrate the need for attention to infection control measures to control the spread of this pathogen.

The emergence of *C. auris* raises several serious concerns for public health. First, many isolates are multidrug-resistant, with some strains having elevated minimum inhibitory concentrations to drugs in all three major classes of antifungal medications (9), a feature not

found in other clinically relevant *Candida* species. Second, *C. auris* is challenging to identify, requiring specialized methods such as matrix-assisted laser desorption/ionization time-of-flight or molecular identification based on sequencing the D1-D2 region of the 28s ribosomal DNA. When using common biochemical methods such as analytical profile index strips or the VITEK 2, *C. auris* is often misidentified as other yeasts (most commonly *Candida haemulonii*, but also *Candida famata, Saccharomyces cerevisiae*, and *Rhodotorula glutinis*). Finally, *C. auris* has caused outbreaks in health care settings (*10*). Multidrug resistance and health care–associated transmission are often found with resistant bacteria, such as carbapenem-resistant Enterobacteriaceae, but have been uncommon among *Candida* spp.

To determine whether *C. auris* cases were occurring in the United States, CDC issued a clinical alert (8) in June 2016, requesting that laboratories report *C. auris* isolates to state and local health departments and CDC. Given the challenges of *C. auris* identification, clinical laboratories were encouraged to forward *C. haemulonii* isolates and isolates not identified beyond *Candida* spp. by conventional methods to state public health laboratories and CDC for further characterization. A case was defined as confirmed isolation of *C. auris* in a specimen from a patient at a U.S. health care facility. For all reported cases, patient information and available clinical isolates were obtained for resistance testing and whole-genome sequencing. Among cases in patients who were not deceased, cultures from various patient body sites were obtained to seek evidence of persistent colonization. One patient was hospitalized at the time of the report, allowing for collection of environmental cultures from the hospital room.

Seven *C. auris* cases occurring during May 2013–August 2016 (Table 1) were reported to CDC (one in 2013, one in 2015, and five in 2016). Six of seven cases were identified through retrospective review of microbiology records from reporting hospitals and reference laboratories. Cases were reported from four states: Illinois (n = 2, single hospital), Maryland (n = 1), New Jersey (n = 1), and New York (n = 3, three different hospitals). Recent travel outside the United Stated was documented for only one patient: the 2013 New York patient had been transferred less than 1 week earlier from a hospital in the Middle East. Five patients had *C. auris* initially isolated from blood, one from urine, and one from the external ear canal.

All patients had serious underlying medical conditions, including hematologic malignancies (n = 2), bone marrow transplantation (n = 1), short gut syndrome requiring total parenteral nutrition and corticosteroid use (n = 1), paraplegia with a chronic urinary catheter (n = 1), idiopathic acute respiratory failure requiring high-dose corticosteroids (n = 1), severe peripheral vascular disease and skull base osteomyelitis (n = 1), and brain tumor and recent villous adenoma resection (n = 1). Median time from admission to isolation of *C. auris* was 18 days (range = 0–231). All five patients with *C. auris* bloodstream infections had central venous catheters at the time *C. auris* was identified, and all were treated with echinocandins, a type of antifungal medication; one patient also received liposomal amphotericin B. All patients with bloodstream infections eventually had documented clearance of *C. auris* from the bloodstream, although one patient had persistently positive *C. auris* cultures for 10 days, despite having an isolate that was susceptible to the treatment administered. Two patients had recurrent *C. auris* candidemia episodes 3 and 4 months after the initial episode. *C. auris* was repeatedly isolated from the urine of a patient with a urinary catheter, even after treatment with fluconazole, to which the isolate was susceptible. The patient with the external ear canal isolate was not treated with an antifungal medication. As of August 31, 2016, four of the seven patients, all of whom had bloodstream infections, died during the weeks to months after the identification of *C. auris*.

In two separate circumstances, two patients were hospitalized in the same hospital. The first instance included

Table 1: Characteristics of the first seven cases of *Candida auris* identified in the United States—May 2013–August 2016

Patient	Isolation month/year	State	Site of *C. auris* isolation	Underlying medical condition(s)	Outcome[1]
1	May 2013	New York	Blood	Respiratory failure requiring high-dose corticosteroids	Died
2	July 2015	New Jersey	Blood	Brain tumor and recent villous adenoma resection	Died
3	April 2016	Maryland	Blood	Hematologic malignancy and bone marrow transplant	Died
4	April 2016	New York	Blood	Hematologic malignancy	Died
5	May 2016	Illinois	Blood	Short gut syndrome requiring total parenteral nutrition and high-dose corticosteroid use	Survived
6	July 2016	Illinois	Urine	Paraplegia with long-term, indwelling Foley catheter	Survived
7	August 2016	New York	Ear	Severe peripheral vascular disease and skull base osteomyelitis	Survived

[1]Mortality was not necessarily attributable to *C. auris* infection.

the two patients from Illinois who were admitted to the same hospital on three separate occasions but were on different floors or wings of the hospital. These two patients were subsequently also admitted to a long-term acute care hospital within days of one another, although their admission dates did not overlap. The second instance involved the patients identified in Maryland and New Jersey. The patient identified in Maryland was a resident of New Jersey and had been hospitalized at the same time as the New Jersey patient, in the same New Jersey hospital, but on a different ward. This overlapping admission occurred approximately 6 months before *C. auris* was identified in the Maryland hospital.

Specimens for surveillance cultures to evaluate patients for colonization were taken from the three living patients (one with *C. auris* in the blood, one in urine and one in the external ear canal). In all three cases, cultures yielded *C. auris* from at least one body site, including groin, axilla, nares, and rectum, 1–3 months after initial detection of *C. auris*. Environmental cultures of the hospital room were collected during a subsequent hospitalization of one of the Illinois patients who had a *C. auris* bloodstream infection 3 months earlier, and who remained persistently colonized in multiple body sites; samples taken from the mattress, bedside table, bed rail, chair, and windowsill all yielded *C. auris*. *C. auris* was not detected in this patient's hospital room after terminal cleaning with sodium hypochlorite solution and ultraviolet light.

Five of seven reported isolates were either misidentified initially as *C. haemulonii* or not identified beyond *Candida* spp. at the institution's microbiology laboratory and were later identified as *C. auris* at a reference laboratory. Five of seven isolates were resistant to fluconazole; one of these isolates was resistant to amphotericin B, and another isolate was resistant to echinocandins. No isolate was resistant to all three classes of antifungal medications.

Whole-genome sequencing was performed on isolates from six patients. Isolates identified in Maryland, New Jersey, and New York were closely related to one another (differing by approximately 70 single nucleotide polymorphisms [SNPs]); the isolates from Maryland and New Jersey (the patients admitted to the same New Jersey hospital) differed by <10 SNPs, which was on same order of magnitude as the 6-SNP differences identified among multiple isolates from specimens obtained over a 10-day period from the Maryland patient. These U.S. isolates were related to isolates from South Asia (<60 SNPs apart). Isolates from the two Illinois patients were nearly identical (<10 SNPs apart) and were most closely related to isolates from South America (<150 SNPs apart). Furthermore, differences of ≤5 SNPs were identified between the environmental and patient isolates in Illinois. As a point of reference, isolates from different continents are tens of thousands of SNPs apart (9). None of the patients from which isolates were sequenced, including the patient from the 2013 case in the Middle East, had known travel or other direct links to South Asia or South America.

Discussion

C. auris is an emerging cause of *Candida* infections in the United States. Although the cases of *C. auris* described in this report appear related to isolates from South Asia and South America, available epidemiologic information suggests that most were acquired in the United States. Although transmission to patients in U.S. health care settings has not been definitively documented, several findings suggest that transmission occurred. First, whole-genome sequencing results demonstrate that isolates from patients admitted to the same hospital in New Jersey were nearly identical, as were isolates from patients admitted to the same Illinois hospital. The number of SNPs differentiating isolates from the same hospital is comparable to that detected among the multiple isolates from same patient or patient and the environment. Second, patients were colonized with *C. auris* on their skin and other body sites weeks to months after their initial infection, which could present opportunities for contamination of the health care environment. Third, *C. auris* was isolated from samples taken from multiple surfaces in one patient's health care environment, which further suggests that spread within health care settings is possible. To decrease the risk for transmission, health care personnel in acute care settings should use Standard and Contact Precautions (http://www.cdc.gov/hicpac/pdf/isolation/Isolation2007.pdf) for patients colonized or infected with *C. auris*. In nursing homes, providers should consider the level of patient care being provided and the presence of transmission risk factors when deciding on the level of precautions. If such patients are transferred to other health care facilities, receiving facilities should be notified of the presence of this multidrug-resistant organism to ensure appropriate precautions are continued. Facilities should ensure thorough daily and terminal cleaning of rooms of patients with *C. auris* infections, including use of an EPA-registered disinfectant with a fungal claim. Facilities and laboratories are requested to continue to report cases and forward isolates of *C. haemulonii* and *Candida* spp. that are not identified further after using common laboratory identification methods to state or local health authorities and CDC, who can provide consultation about the need for additional interventions to prevent transmission.*

CDC continues to work with domestic and international partners to conduct epidemiologic studies on the emergence of this organism, risk factors for infection, and transmission mechanisms, and to evaluate the effectiveness of current infection control guidance to make additional recommendations.

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Note

*https://www.cdc.gov/fungal/diseases/candidiasis/recommendations.html.

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