



Something wicked this way comes: What health care providers need to know about *Candida auris*

IS Schwartz^{1*}, SW Smith¹, TC Dingle^{2,3}

Abstract

Candida auris is a fungal pathogen that recently emerged and rapidly spread around the globe. It is now in Canada. *C. auris* can cause invasive disease with high mortality rates, is frequently resistant to one or more classes of antifungals, and can be difficult to identify in some clinical microbiology laboratories. *C. auris* can also involve prolonged colonization of patients' skin and contamination of surrounding environments, resulting in nosocomial outbreaks in hospitals and long-term care facilities.

Clinicians, infection prevention and control practitioners and public health officials should be aware of how to mitigate the threat posed by this pathogen. Index cases of *C. auris* should be suspected in patients with invasive candidiasis and recent hospitalization in global regions where *C. auris* is prevalent, as well as in patients who fail to respond to empiric antifungal therapy and from whom unidentified or unusual *Candida* species have been isolated. If a case of *C. auris* infection or colonization is identified or suspected, the following should take place: notification of local public health authorities and infection prevention and control practitioners; placement of colonized or infected patients in single rooms with routine contact precautions; daily and terminal environmental disinfection with a sporicidal agent; contact tracing and screening for *C. auris* transmission; and referral of suspicious or confirmed isolates to provincial laboratories. Patients with symptomatic disease should be treated with an echinocandin pending the results of antifungal susceptibility testing, preferably in consultation with an infectious disease specialist. Through the vigilance of front-line health care workers and microbiologists, robust infection prevention and control practices, and local and national surveillance efforts, *C. auris* can be detected quickly, infections managed and transmissions prevented to protect patients in our health care system.

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Introduction

In July 2017, the first known case of multidrug-resistant *Candida auris* was reported in Canada in an individual who had a two-year history of recurrent ear complaints after returning from a trip to India that was marred by hospitalization for a brain abscess following oral surgery (1). This marked the arrival in Canada of a pathogen that has recently been spreading across the globe. The ability of this fungus to cause invasive disease, its frequent resistance to one or more classes of antifungal agents and its demonstrated potential for nosocomial transmission is of concern to clinicians and public health professionals alike (2,3).

The objective of this article is to summarize what we know about this fungus; outline the challenges of diagnosis, treatment and infection prevention and control, and identify what is being done to track and contain the spread of this pathogen in Canada.

Where in the world is *C. auris*?

C. auris was first described in Japan in 2009; since then, *C. auris* infections have been reported in at least 30 countries



on six continents (4). Whole-genome sequence analyses of global isolates have demonstrated that these cluster into closely related (clonal) geographic clades (5) suggesting the near-simultaneous emergence of *C. auris* on at least three continents. For example, the average genetic distances between the East Asian, South Asian, South African and South American clades were 40,000 to 140,000 single nucleotide polymorphisms (SNPs), whereas on average, fewer than 70 SNPs separated any two isolates within a given clade (3). The reasons for this phenomenon are unknown.

In some countries, *C. auris* has already led to a significant burden of hospital-acquired disease. For example, *C. auris* is the cause of candidemia in 10% of cases nationally in South Africa (6), and 38% of cases in one referral hospital in Kenya (Okinda N et al. *Candidemia at a referral hospital in sub-Saharan Africa: emergence of Candida auris as a major pathogen. Poster presented at: European Congress of Clinical Microbiology and Infectious Diseases; 2014 May 10–13; Barcelona, Spain*). In India, *C. auris* was implicated in 5% of candidemia cases in 27 intensive care units (ICUs), although some Indian centres report proportions of 17.5%–30% (7,8). As of July 31, 2018, the Centers for Disease Control and Prevention (CDC) in the United States (US) reported 361 confirmed clinical cases of *C. auris* in US health care settings; an additional 699 colonized patients were diagnosed in four states with active surveillance (4). In Europe, at least 120 cases of candidemia and 466 cases of colonization occurred from 2013 to 2017 (9).

In Canada, the first two patients reported to be infected with *C. auris* had received health care in India (1,10). In one case, genomic characterization suggested that the infection was imported from the Indian subcontinent (11). Additional imported cases are anticipated. Transmission in Canadian health care facilities is inevitable.

What are clinical features of disease caused by *C. auris*?

The clinical spectrum of *C. auris* infection ranges from asymptomatic colonization to invasive candidiasis, most commonly in the form of healthcare-associated candidemia (12). Bloodstream infections can be protracted and difficult to treat, and crude mortality rates of approximately 30%–60% have been reported (5,13,14). Metastatic complications, such as spondylodiscitis, endocarditis and ventriculitis, have been described (13). Other frequently reported clinical syndromes include otomycosis and otomastoiditis (15,16): in fact, the etymology of the fungus reflects the anatomic origin of the first identified isolate, which was collected from a patient's ear (17). Involvement of other sites, including respiratory, urogenital, abdominal, and skin and soft tissue, has also been reported (18).

Who becomes infected by *C. auris* and how?

Patients who develop candidemia caused by *C. auris* usually have risk factors in common with patients with disease caused by other *Candida* species (6,13,14,19). These include hospitalization and, in particular, admission to an ICU, use of central venous catheters, abdominal surgery and exposure to broad-spectrum antibiotics or antifungals (20).

There are several ways in which the pathogenesis of *C. auris* appears to differ from classically encountered *Candida* species (Table 1) (21). With the exception of *C. parapsilosis*, a skin colonizer, the majority of clinically important non-*auris* *Candida* species are commensals of the human gastrointestinal tract (21). The pathogenesis of candidemia caused by these species typically involves gut translocation of yeasts (21,22); although nosocomial transmission of *Candida* is occasionally reported, disease is most commonly caused by strains that are part of the patient's endogenous flora (23).

Table 1: Differences between *Candida auris* and classical pathogenic *Candida* species

Feature	<i>Candida auris</i>	Classical <i>Candida</i> species ^a
Habitat	Commensal of the skin	Commensals of the gastrointestinal tract ^b
Pathogenesis of infection	Exogenous	Endogenous
Healthcare-associated infections	Common	Uncommon
Environmental contamination	Common	Uncommon
Multidrug resistance	Common	Uncommon

^a Other *Candida* species most commonly encountered clinically include *C. albicans*, *C. glabrata*, *C. parapsilosis*, *C. krusei* and *C. tropicalis*

^b With exception of *C. parapsilosis*, which is a commensal of skin

C. auris is primarily carried on the skin of colonized patients, and this can lead to contamination of the patient's environment and spread to health care workers and other patients. Moreover, *C. auris* isolates implicated in healthcare-associated outbreaks have been clonally related, suggesting disease is caused by exogenous strains that are nosocomially spread (5,13,24,25).

What are the diagnostic challenges?

C. auris can be difficult to detect by routine laboratory testing. This may lead to delays in identifying and isolating colonized or infected patients. Commercial biochemical identification systems commonly used in clinical microbiology laboratories are unreliable for *C. auris* identification (26). For example, *C. auris* can be misidentified by VITEK-2 (bioMérieux, Marcy-l'Étoile,



France) (typically as *C. haemulonii*) (26) and by API20CAUX (usually as *Rhodotorula glutinis*, *C. sake* or *Saccharomyces cerevisiae*) (27). This may change as biochemical identification system databases are updated; for example, VITEK-2 YST card v. 8.01 now includes *C. auris*.

C. auris can be identified accurately using matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF) mass spectrometry instruments with databases that include *C. auris* (these include the most recent Bruker MALDI Biotyper CA and Research Use Only [RUO] databases, and the bioMérieux VITEK MS RUO database [v4.14 with *Saccharomycetales* package]) and by molecular-based sequencing methods.

What are the treatment challenges?

In general, *C. auris* isolates are less susceptible to antifungals than other *Candida* species, although patterns of susceptibility appear to be related to the geographic clade. Resistance to fluconazole is widespread, albeit not universal as was initially feared (2), and fluconazole resistance is now thought to be an acquired rather than a shared trait (21). Rates of fluconazole resistance have ranged from 14% among isolates from Colombia (25) to >90% among isolates belonging to the South Asian clade (14,28). Resistance to amphotericin B and the echinocandins also appear to be heterogeneous. Several studies have found amphotericin B resistance rates around 30% (5,14,25); alternatively, Chowdhary et al. reported amphotericin B resistance in 27/350 (8%) of Indian isolates (28). Significant variation in rates of amphotericin B resistance were encountered between regions in Columbia (25). Echinocandin resistance occurs in approximately 2%–5% of isolates (5,28,29). Resistance to two antifungal classes occurred in 41% of global isolates tested (5). In rare cases, isolates can be resistant to all three major classes of antifungal agents (5).

What are the challenges in infection prevention and control?

Nosocomial outbreaks are anticipated because patients can remain colonized and/or their environments can remain contaminated for weeks to months after infection (14,24,25,30). Large-scale hospital outbreaks in the United Kingdom (UK) have been associated with multi-use axillary thermometers (31); and in Spain with the use of blood-pressure cuffs (31). Moreover, *C. auris* has been recovered from a wide range of fomites from patient environments (13,14,24,25). Surface cationic-active disinfectants and quaternary ammonium disinfectants are ineffective against *C. auris* (13,33,34). *C. auris* is also relatively resistant to killing by ultraviolet light (35). Chlorhexidine gluconate, iodinated povidone, chlorine bleach and H₂O₂ vapour appear to be effective against *C. auris* (36).

The role of health care workers in spreading *C. auris* is still unknown. During investigation of the outbreak in the UK, *C. auris* was isolated from the nares of 1/258 health care workers, a nurse who was providing care for a patient who was heavily colonized (24). Moreover, an outbreak investigation in Colombia isolated *C. auris* from the hands of two health care workers and the groin of one out of six health care workers. Whole-genome sequencing established that these were genetically identical to strains isolated from a patient and his or her environment (25).

Tracking and containing *C. auris* can be particularly challenging due to interfacility transfer of infected or colonized patients in whom this status may not yet be recognized, potentiating spread of *C. auris* between facilities (14). For example, in New York, 112 patients in hospitals and long-term care facilities were affected: 61 had candidemia and 51 additional patients were found to be colonized on screening. Infected or colonized patients were transferred between a total of 24 hospitals and 24 long-term care facilities in the 90 days before their infection or colonization status was recognized (14).

Implications for clinical care

The prompt identification, management and containment of patients infected or colonized with *C. auris* require collaboration by hospitalists/intensivists, microbiologists, infectious disease experts, and infection control and prevention practitioners.

Clinicians should be aware of the yeast identification methods used by their local microbiology laboratory and consider *C. auris* when unidentified or unusual *Candida* species are isolated from patients who fail to respond to empiric antifungal therapy (37). Consultation with a microbiologist is recommended when *C. auris* is suspected. Isolates that are suspicious for or confirmed as *C. auris* should be referred to provincial laboratories for further testing. Given the challenges in predicting antifungal susceptibility patterns, antifungal susceptibility testing is recommended for all clinical *C. auris* isolates. Treatment of disease should be guided by antifungal susceptibility testing results, although echinocandins are appropriate for empiric therapy pending these results. Early consultation with an infectious disease expert is advised. Treatment of asymptomatic colonization is not recommended.

The identification of patients in whom infection or colonization with *C. auris* is suspected or confirmed should prompt consultation with local infection prevention and control practitioners. Infected or colonized patients should be isolated in private rooms; routine practices and contact precautions should be taken; and rooms should be cleaned daily with sporicidal disinfectants. Whether and when to discontinue isolation precautions is still being debated. The CDC currently recommends that infected or colonized patients be tested periodically with composite groin and axillary swabs for fungal culture to test for persistent colonization, with the proviso that



patients can be de-isolated after two consecutive screening swabs (38). In practice, few reported patients have met such criteria (14). Alternatively, Public Health England recommends that isolation precautions be continued for the duration of a patient's admission to hospital (39). This recommendation is in part because patients can become re-colonized after testing negative (*Silke Schelenz, "Management of Candida auris outbreaks at a national level". 20th Congress of the International Society for Human and Animal Mycology, Amsterdam, The Netherlands July 2018*).

Table 2 shows a summary of how to detect, assess and manage *C. auris*. Further infection prevention and control guidelines are available from the CDC (39).

Table 2: What to do to detect and manage *Candida auris*

What to do	How
Keep a high index of suspicion	Consider <i>C. auris</i> in patients who: <ul style="list-style-type: none"> received health care in countries (or US states) where <i>C. auris</i> is prevalent, as tracked by the CDC (4) have a clinical syndrome consistent with candidiasis and fail to respond to empiric antifungal therapy and from whom an atypical or unidentified yeast is isolated
Assess for <i>C. auris</i> specifically	Consult with a microbiologist and/or infectious disease specialist Refer suspicious or confirmed isolates to relevant provincial laboratory for further testing or for referral to the National Microbiology Laboratory
Manage <i>C. auris</i> with a robust clinical infection control and public health response	Notify the institutional infection prevention and control team Notify local public health officials, who will notify their provincial/territorial counterparts (who will notify the Public Health Agency of Canada) Place patient in single room with contact precautions in addition to routine practices In case of symptomatic disease, begin treatment, preferably with guidance from an infectious disease specialist (treatment of asymptomatic colonization is not recommended) Order daily and terminal cleaning of the patient's environment with sporicidal disinfectant Enable local public health officials to initiate contact tracing and screening to assess for <i>C. auris</i> transmission Order composite swab of axilla and groin when indicated for patient screening

Abbreviations: *C. auris*, *Candida auris*; CDC, Centers for Disease Control and Prevention; US, United States

Gaps and next steps

Many questions remain unanswered about how to best detect *C. auris* and limit its spread within and between Canadian health care facilities. Knowledge gaps regarding the optimal laboratory detection and identification of *C. auris* should be addressed by bolstering existing biochemical and MALDI-TOF identification databases and by developing simple, rapid and sensitive laboratory screening protocols. Uncertainties that affect infection prevention and control practices for *C. auris* include the duration that patients remain colonized (and thus how long patients should be isolated after first detection) and optimal screening

strategies. For example, should screening be reserved for patients with documented contact with a known case or used for all patients who have travelled to or received health care in areas where *C. auris* is prevalent? Because the geographic distribution of *C. auris* will change over time, and in light of incomplete surveillance data from many regions, identifying patients at high risk for colonization can be challenging for front-line health care workers.

To better understand the epidemiology of *C. auris* in Canada, the Canadian Nosocomial Infection Surveillance Program is conducting national surveillance for infections in representative hospitals across the country. (*Garcia Jeldes F, Mitchell R, Bharat A, McGeer A for the CNISP C. auris Interest Group. Preparedness for Candida auris in Canadian Nosocomial Infection Surveillance Program [CNISP] Hospitals, 2018. IDWeek 2018. October 3–7, 2018. San Francisco, California*). In addition, a point prevalence study is planned to identify the prevalence of both colonization and infection in Canadian tertiary care hospitals (*Dr. Allison McGeer, September 2018, personal communication*). The surveillance and point prevalence data will provide evidence needed to guide the development of infection prevention and control policies surrounding this emerging pathogen.

Conflict of Interest

None.

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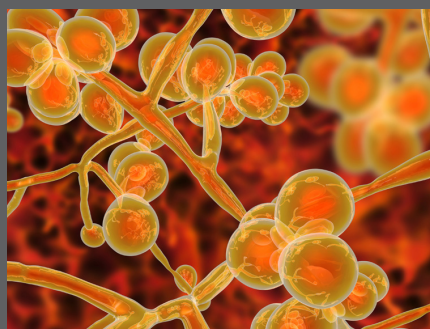
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 VISUAL ABSTRACT

CANDIDA AURIS WHAT HEALTH CARE PROVIDERS NEED TO KNOW

C. auris is an emerging multidrug resistant fungus

It is now in Canada

- can cause invasive disease
- is difficult to detect
- can spread easily in health care environments



Who is at risk?



Those who don't respond to antifungal therapy and have a history of:

- travel-associated healthcare
- a lab result with unidentified/unusual candida species
- a central venous line
- abdominal surgery
- exposure to broad-spectrum antibiotics or antifungals

Best Practices

Transfer the patient to a private room and consult:

- infectious disease specialist
- infection prevention and control
- public health



Reference: Schwartz IS, Smith SW, Dingle TC. Something wicked this way comes: What health care providers need to know about *Candida auris*. Can Commun Dis Rep 2018;44(11):271–6. <https://doi.org/10.14745/ccdr.v44i11a01>