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Research Letter

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Evaluation of *Candida auris* acquisition in US international travellers using a culture-based screening protocol[1]

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First isolated in 2009, *Candida auris* has emerged as a global health threat.[1,2] As of February 2021, *C. auris* has been identified in 47 countries, with mortality rates up to 60%.[1–3] Whole-genome sequencing of *C. auris* isolates within the USA revealed both global and local transmission, with healthcare facility contamination and skin colonization serving as reservoirs for acquisition.[3,4] International travel has been implicated in the spread of this pathogen[5] but, to date, little is known about *C. auris* acquisition during travel. The goal of this study was to establish the feasibility of a culture-based screening protocol for *C. auris* acquisition in a cohort of US international travellers.

We recruited participants presenting for a pretravel visit from the Travelers' Advice and Immunization Clinic at the Massachusetts General Hospital (MGH). Participants self-collected single composite axillary-inguinal groin swabs using the collection method and transport system recommended by the Centers for Disease Control and Prevention (CDC).[6] Samples were collected within 2 weeks before and after international travel and sent through the US postal system to the MGH Microbiology Laboratory for processing. If a traveller was found to be colonized with *C. auris*, further swabs were to be collected at 3, 6 and 12 months after travel. At the time of recruitment through the Global TravEpiNet system,[7] travellers recorded select medical history, demographic and travel information, which was confirmed at the pretravel visit. Upon travel return, participants completed a post-travel questionnaire assessing behaviours associated with potential *C. auris* acquisition (e.g. antibiotic use or contact with the healthcare). This study was approved by the Partners Healthcare institutional review board; participants provided written informed consent and each was provided a small monetary compensation for every sample returned.

At enrolment, participants were trained in proper collection technique that involved rubbing a swab over bilateral axillary and inguinal areas. Self-collected swabs were screened for *C. auris* using a culture-based protocol developed by the Centers for

[1]Interim analysis presented at ASM Microbe 2020, Chicago, IL.

Disease Control and Prevention (CDC) Infectious Diseases Laboratories Mycotic Diseases Branch.[8] Specifically, self-collected nylon flocked swabs placed in liquid transport medium (BD Eswab collection and transport system; Becton Dickinson and Company, Sparks, MD) were vortexed before transferring 100 μl into 2.0 ml of salt sabouraud dulcitol broth (SSD) containing gentamicin and chloramphenicol.[8] Each inoculated SSD broth was incubated at 40°C using a shaking incubator at 250 rpm. Any visible growth was sub-cultured onto a BBL CHROMagar Candida plate (Becton Dickinson and Company, Sparks, MD) for further identification. In addition, after 7 days of incubation, 100 μl of inoculated SSD broth was plated to CHROMagar Candida and incubated for another 7 days. Any cream, pink, purple or red colony growth on CHROMagar Candida was sub-cultured to BBL™ Sabouraud Dextrose Agar (Becton Dickinson and Company, Sparks, MD) and underwent identification using a custom-designed Vitek MS matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF) database that had been internally validated for *C. auris* identification [VITEK MS v4.14 Saramis (RUO) database with the Saccharomycetaceae update, bioMerieux, Durham, NC, USA]. Positive and negative quality controls were performed concurrently with subject samples.[8]

From January 2019 to February 2020, we enrolled 132 participants; 105 (80%) submitted swabs for evaluation. Of the 105 participants, 11 (10%) were excluded from analysis, leaving 94 (71%) evaluable subjects. Reasons for exclusion included no pre-travel sample received (N = 1); no post-travel sample received (N = 9) and participant did not fill out the post-travel questionnaire (N = 1). Reasons for the nine without post-travel samples included: trip cancellation (N = 4); lost to follow up (N = 1) and study halted due to the COVID-19 pandemic (N = 4). Patient characteristics are listed in Table 1. Of the 94 evaluable travellers, 42 (45%) were male; the average age was 52 years (SD ±15). Two (2%) travellers were immunosuppressed: one reported a history of asplenia and the other reported taking mercaptopurine for ulcerative colitis. No travellers were pregnant or breastfeeding.

Travelers often travelled to only one geographic region, with a mean travel duration of 15 days (SD ±9). Prevalence of *C. auris* in these geographic regions at the time of travel was unknown. The most common region visited was eastern Africa (33%); the most common reason for travel was leisure (76%). Five (5%) travellers travelled to provide medical care; no participants travelled to receive medical care. More than half (58%) of travellers reported taking malaria prophylaxis during travel. Only four (4%) travellers reported seeking medical attention during travel: two visited emergency departments; one visited a clinic and one did not provide information regarding the visit setting. Reasons for seeking medical care included diarrhoea, cellulitis and trauma-related injuries; none of these travellers reported receiving antibiotics at these visits. Four (4%) travellers reported taking antibiotics during travel; in all cases, participants took azithromycin but did not seek medical attention.

In total, we screened 94 paired (pre-travel and post-travel) self-collected axillary-inguinal groin swabs for the presence of *C. auris*. Mean swab transport time was 4 days (SD ±3). No *C. auris* was isolated from any samples (Table 1).

Table 1. Patient and sample characteristics

Patient characteristics	N = 94
Age-yr[¥]	52 ± 15
Male sex-No. (%)	42 (45)
Immunosuppressed[#]-No. (%)	2 (2)
Pregnant or breastfeeding-No. (%)	0 (0)
Reason for travel-No. (%)	
Leisure	71 (76)
Business	12 (13)
Visiting friends and relatives	1 (1)
Adoption	0 (0)
Provide medical care	5 (5)
Receive medical care	0 (0)
Research and education	9 (10)
Service	2 (2)
Missionary service	5 (5)
Military	0 (0)
Adventure	13 (14)
Mass gathering	3 (3)
Geographic regions travelled[*]-No. (%)	
South America	17 (18)
Eastern Africa	31 (33)
Southern Africa	12 (13)
Southern Asia	15 (16)
Southeastern Asia	11 (12)
Other[§]	41 (44)
Number of geographic regions travelled-No. (%)	
One	65 (69)
Two	25 (27)
Three	4 (4)
Duration of trip-days[¥]	15 ± 9
Malaria prophylaxis during travel-No. (%)	
Atovaquone proguanil	43 (46)
Unknown medication	11 (12)
None	40 (42)
Sought medical attention during travel[**]-No. (%)	4 (4)
Took antibiotics during travel[†]-No. (%)	4 (4)
Sample characteristics	N = 188
Sample transport time-days[¥]	4 ± 3
Candida auris isolated-No. (%)	
Pre-travel	0 (0)
Post-travel	0 (0)

[¥] Plus-minus values are means ± standard deviation.
[#] One traveller was asplenic and the other reported taking mercaptopurine for ulcerative colitis.
[*] Reported travel destinations grouped into geographic regions using definitions from the United Nations Statistics Division.
[§] Represents geographic regions where <10% of participants travelled. Central America: 4 (4%); Northern Europe: 6 (6%); Western Europe: 5 (5%); Southern Europe: 4 (4%); Northern Africa: 2 (2%); Western Africa: 4 (4%); Africa (not further specified): 1 (1%); Eastern Asia: 7 (7%); Western Asia: 5 (5%) and Caribbean: 3 (3%).
[**] One subject sought medical attention for diarrhoea, one for cellulitis, one for a head injury and one for a fractured fifth metatarsal.
[†] All four subjects took azithromycin.
Abbreviations: Yr, year; No., number.

In this small study of US international travellers, we did not detect *C. auris* using a culture-based screening protocol. Of note, the majority of travellers did not take antibiotics or seek medical attention during travel, both of which have been implicated as risk factors for *C. auris* colonization and infection.[9] Few travellers (5%) reported providing or receiving medical care while traveling, indicating a low incidence of contact with healthcare systems during travel.

Limitations to our study include its small sample size, reducing our ability to detect lower rates of *C. auris* transmission. In addition, quality control for swab self-collection was not performed. Finally, we employed a culture-based strategy for *C. auris* screening; since this study, molecular methods have been developed, which may improve detection.[10]

In conclusion, we demonstrated the acceptability and laboratory feasibility of evaluating travellers for *C. auris* acquisition, a first step in assessing the risk of *C. auris* transmission during international travel. *Candida auris* was not identified in this small cohort of healthy travellers; further study is needed to determine the overall risk of travel-associated *C. auris* acquisition, especially among individuals who receive in-patient medical care while abroad.

Author's Contributions

SET co-conceived and co-designed the study, performed data acquisition and statistical analyses, and wrote the initial manuscript draft. MB and EO performed data collection and acquisition, database management and statistical analyses. BB, MK and LD performed data collection and acquisition. JAB co-conceived and co-designed the study and contributed to database development. MW and ATW co-conceived the study and contributed to discussion and interpretation of results. RL and ETR co-conceived and co-designed the study, performed database management and co-wrote the manuscript. All authors have read and approved the final manuscript.

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