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Candida auris: Emergence of a multidrug resistant fungus

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 - CNISP

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Learning Objectives:

By the end of this session, participants will be able to:

- a) Describe the epidemiology and clinical significance of *C. auris*.
- b) Implement interventions to prevent the emergence of *C. auris*

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Clinical Infectious Diseases
MAJOR ARTICLE

Simultaneous Emergence of Multidrug-Resistant *Candida auris* on 3 Continents Confirmed by Whole-Genome Sequencing and Epidemiological Analyses

Shovan R. Lockhart, Kiron A. Etsema, Sanjitha Vallabhakann, Javeria Farooq, Anuradha Choudhury, Rishabh P. Grewal, Anshu Lagan Girdhari, Rishika Ghosh, Christian A. Gomez, Christopher A. Desjardins, Elizabeth K. Berling, Marissa Castellanos, Hindolran E. Mupfema, Kausar Johana, Hans J. Anghar, Jacques F. Meis, Brandon Jackson, Sam Chiller, and Anastasia P. Livintseva*

Whole Genome Sequencing

- 4 clades identified:
 - South Asian, South African, South American & East Asian
- Between these clades there are thousands of SNP differences
- Within clade – almost clonal

PublicHealthOntario.ca CID 2017;64 (15 January) Lockhart et al 7

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CDC Centers for Disease Control and Prevention
2016
CDC 24/7: Saving Lives, Protecting People™

Clinical Alert to U.S. Healthcare Facilities - June 2016

Global Emergence of Invasive Infections Caused by the Multidrug-Resistant Yeast *Candida auris*

- Rapid global emergence
- Often drug resistant or multi-drug resistant
- Often misidentified
- High mortality (crude mortality ~ 30-60%)
- Highly transmissible between patients and environment
- Nosocomial infections/outbreaks

PublicHealthOntario.ca <https://www.cdc.gov/fungal/candida-auris/candida-auris-alert.html> 8

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Candida auris & the Challenge of Resistance

% Resistant* (N=54)

Azole Resistance
Known mutations in ERG11 not spot

- V132F
- K143R
- F126T

*Using breakpoints for other *Candida* species in lieu of actual breakpoints

PublicHealthOntario.ca CID 2017;64 (15 January) Lockhart et al 9

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Microbiological Diagnosis of *C. auris*

| Yeast Identification System | |
|---|--|
| bioMérieux VITEK 2 version 8.01 | <i>C. auris</i> is able to be identified <i>Misidentifications still possible</i> |
| bioMérieux VITEK MS, RUO Saramis Ver 4.14 and Saccharomycetaceae update | <i>C. auris</i> is able to be identified <i>Misidentifications still possible</i> |
| Bruker MALDI Biotyper, FDA -approved CA system (version claim 4) | <i>C. auris</i> is able to be identified |
| Bruker MALDI Biotyper, RUO libraries version 2014 [5627] and beyond | <i>C. auris</i> is able to be identified |
| ITS &/D1D2 sequencing | <i>C. auris</i> is able to be identified |

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The American Experience

2013 -2016: 7 cases
Current case count (April 30, 2019):
 - **643 clinical cases**
 - **1143 colonized**

Identified *C. auris* in 5 hospitalized patients who were recently hospitalized in other countries (India, Pakistan, South Africa, and Venezuela)

WGS & Epi → majority of cases are the result of local transmission following introduction from other countries

In the US:

- Majority of isolates South Asian Clade
- Approximately:
 - 90% resistant to fluconazole
 - 30% resistant to amphotericin B
 - 5% resistant to echinocandins

Candida auris now nationally notifiable in the USA - 2019
Council for State and Territorial Epidemiologists (CSTE) Annual Conference - 2018

Lancet ID 2018; 18(12):1377-1384
<https://www.cdc.gov/fungal/candida-auris/tracking-c-auris.html#world>

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Tracking & containing *C. auris* is challenging

- New York, 112 affected

- Infected/colonized patients were transferred between **24 hospitals and 24 LTCF in the 90 days** before their infection/colonization status recognized

Epidemiologic links between healthcare facilities affected by *C. auris*, New York, USA, 2013–2017
 Adams E et al. *Candida auris* in Healthcare Facilities, New York, USA, 2013–2017. *Emerg Infect Dis* 2018 Oct;24(10):1816–24

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Tracking and containing *C. auris* is challenging

New York experience:

- 51 invasive infections (candidemia n=31; 61%)
 - 23 (45%) died within 90 days (all had co-morbidities)
- 61 additional patients colonized on screening (11% of screened patients +)
- Environmental cultures were positive for samples from 15/20 facilities
- 50 (98%) were resistant to fluconazole
- 13 (25%) were resistant to fluconazole & amphotericin B
- No initial isolates were resistant to echinocandins
- **Subsequent isolates obtained from 3 individuals who had received an echinocandin acquired resistance to it**

April 17, 2019: CDC reported the first 2 pan-resistant U.S. cases

PublicHealthOntario.ca Adams E et al. Emerg Infect Dis 2018 Oct;24(10):1816-24 <https://www.cdc.gov/fungal/candida-auris/index.html> 13

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What is happening in Canada?

- 2017 Manitoba reported the first multi-drug resistant isolate in a patient
 - previous hospitalization & procedure in India (brain abscess following oral surgery)
 - Chronic otitis externa (2 years)
 - Isolate from ear fluid – **resistant to fluconazole and Ampho B**

PublicHealthOntario.ca Schwartz & Hammond. Can Commun Dis Rep. 2017;43 (7/8):150-3. 15


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July 6, 2017

Public Health Agency of Canada Communication Notice
Emerging Global Healthcare Associated Infection
Antimicrobial Resistant Issue
Candida auris

Reporting

To better monitor the current situation with respect to this emerging fungal infection, PHAC would appreciate being informed of any additional cases of confirmed *C. auris* infection (whether drug resistant or not) via e-mail sent to CARSS-SCSRAd@phac-aspc.gc.ca.

 Public Health Agency of Canada Agence de santé publique du Canada


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What is happening in Canada?

Canada


- 19+ known cases (2013-present)
- Several isolated cases
- One confirmed outbreak
- Sixth case in Ontario identified recently via admission screening of patient hospitalized in South Asia; isolate is MDR (J. Kus, personal communication)



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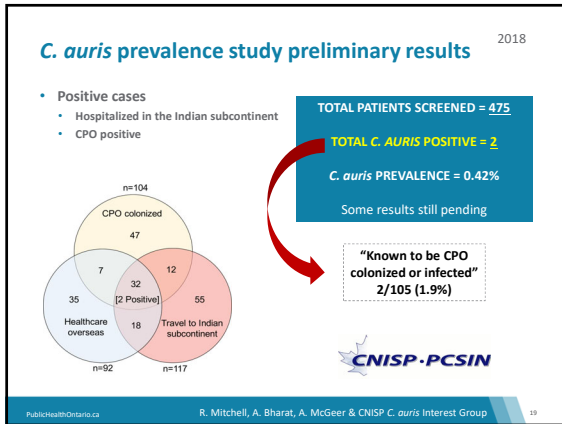
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Canadian Nosocomial Infection Surveillance Program

- National Point Prevalence Study 2018 
- 6 provinces, 21 hospitals
- Screening of patients at 'high' risk of *C. auris* to assess extent of problem in Canada
 - Patients hospitalized outside of Canada (35)
 - Patients traveling to the Indian Subcontinent (53)
 - Patients colonized with CPO (105)
 - Patients on a hospital unit with high anti-fungal usage (282)
 - Patients directly exposed to a case of *C. auris* in Canada (0)

PublicHealthOntario.ca R. Mitchell, A. Bharat, A. McGeer & CNISP *C. auris* Interest Group 18

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Hospital Outbreaks

- Many hospital outbreaks of *C. auris* have been reported
- Outbreaks are difficult to control and have resulted in
 - Development of endemic disease within the facility
 - Dissemination of *C. auris* to other facilities
 - Regional and country-wide spread within healthcare facilities
- "Although control measures were implemented, we were not able to control the outbreak"
 - Alba Ruiz-Gaitan et al. Mycosis 2018;61(498-505)
- Transmission (patient to patient, environment to patient) documented with exposures of only 4 hours
 - Schlenz S. Antimicrob Resist Infect Control. 2016.5:35

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Hospital Outbreaks

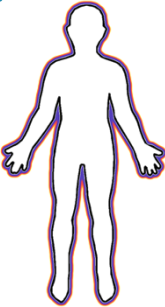
- Outbreaks have been associated with persistent environmental contamination with *C. auris* despite routine cleaning and disinfection
 - Schlenz S. Antimicrob Resist Infect Control. 2016.5:35
 - Adams E. EID 2018;24(10)
- Contaminated medical equipment has contributed to outbreaks (e.g. axillary thermometer probes, neurosurgical equipment) as have other fomites
 - Eyre DW. NEJM 2018;379(14)
- Quaternary ammonium compounds may not be effective for disinfection
 - Cadnum JL. ICHE 2017;38

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Isolated from a range of body sites

- Skin colonization – common – ?different from other candida?
- Invasive infections – similar to other candida



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Interim Guide for Infection Prevention and Control of *Candida auris*
November 2018

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Facility Preparedness

All health care facilities should develop policies and procedures for the recognition, investigation and care of patients or residents colonized or infected with *C. auris*.

Many cases in the US – almost no cases here – now is the time to prepare!

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Microbiology Laboratories

- Microbiology laboratories should be capable of identifying *C. auris* from appropriate specimens or should forward specimens to a reference laboratory
- Labs should be capable of identification of *C. auris* from
 - All sterile site specimens
 - Appropriate screening specimens from patients at high risk for *C. auris* infection or colonization

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Admission Screening – who to test?

- Test patients or residents with known exposure to a *C. auris* patient
- Test patients or residents transferred from a facility with a *C. auris* outbreak or endemic *C. auris*
- (Consider) testing patients or residents admitted to a healthcare facility outside of Canada within the prior 12 months
- [Based on CNISP data, testing patients with CPO is also appropriate]

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How to test for colonization

- Collect a nasal swab and combined bilateral axillary and groin swab
- Test other sites if indicated (e.g. wound, urine, exit site)
- Testing more sites (e.g. throat, rectal) will increase the sensitivity of detection
- If risk is high, retest if negative – for example repeat testing at 7 and 14 days to maximize sensitivity

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Immediate Case Management

- A single case is a sentinel event – notify IPAC
- Contact Precautions and isolation in a private room with dedicated toileting facilities
- Enhanced Environmental Cleaning
 - Dedicated equipment (disinfected daily)
 - Avoid QAC for disinfection
 - Use bleach or improved hydrogen peroxide
 - Consider twice daily room cleaning
 - Consider no touch disinfection (although *C.auris* relatively resistant to UV – HPV may be preferred).

• Cadnum JL. ICHE 2017;39

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Case Investigation

- Every *C. auris* case requires an investigation to determine the source of *C. auris* and to assess the risk of transmission
- Notify transferring facility when applicable
- Assess risk factors
- Put roommates in Contact Precautions and test for *C.auris* (regardless of exposure duration)
- Do a point prevalence study on all exposed wards

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How do you define an outbreak?

- Outbreak = more cases than would be expected of a given infectious diseases in a give place over a given period of time
- Has your facility ever had a case of *C.auris*? If not → one nosocomial case is an outbreak!

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Outbreak Management

- Isolation and Contact Precautions
- Contact the experts
- Case finding – immediate point prevalence study for all affected areas
- Close ward to new admissions
- Minimize external and internal transfers
- Communicate clearly to receiving facility/unit and to IPAC team for any medically essential transfer
- Education, Adherence to RPAP

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Who to Screen in an Outbreak

- All patients or residents on the affected ward
- Discharged roommate contacts
- Consider testing room contacts
- Anyone else with a significant exposure

- Flag all positive or exposed patients for isolation and screening on re-admission

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What was the cause of the outbreak?

- Look for epidemiological links between cases
 - Direct contact?
 - Overlapping stays?
 - Common procedures or equipment?
 - Shared staff
- Consider case-control study

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Outside the Box

- Standard IPAC approaches may not work for *C.auris*
- We may need to do more – but what?
 - ? Compliance monitoring
 - ? Enhanced environmental cleaning
 - ? More frequent point prevalence studies
 - ? Post-outbreak monitoring

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Conclusions

- *Candida auris* is an emerging fungal pathogen that
 - Can cause invasive disease associated with high mortality
 - Rapidly develop multidrug resistance
 - Cause large and difficult to control outbreaks in healthcare facilities
- Develop a plan for *C. auris*
- Ensure your facility is capable of identifying *C. auris*
- Treat each case as a sentinel event
- Screen patients hospitalized outside of Canada for *C.auris*
- **Watch for updates!**

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