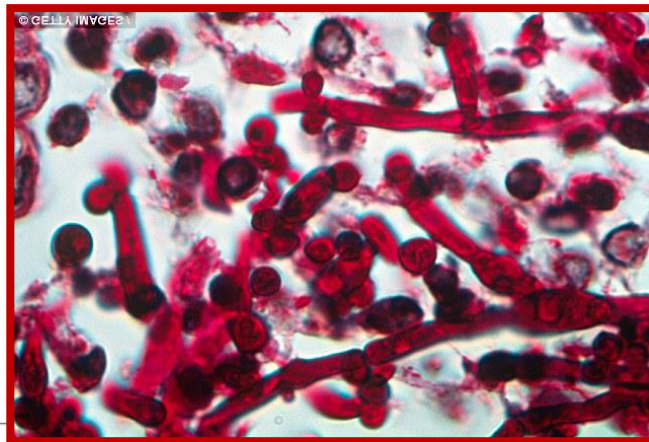


***Candida auris*- Introduction and Current Recommendations for Maintaining A Safe Patient Environment**

Presented by PDI Healthcare

Holly Montejano, MS, CIC, CPHQ



Disclosure

I am a paid employee of the clinical team of PDI Healthcare. The content of this presentation is not representative of the views of PDI or its ownership.

There will be NO discussion of any PDI products and/or solutions in accordance with CE Requirements.

Presentation will incorporate best practices from a variety of information sources that bridge medical disciplines.

Affiliations

Member of the Association for Infection Prevention and Epidemiology (APIC)

Member of Society of Healthcare Epidemiology of America (SHEA)

Program Objectives

- Describe the epidemiology of *Candida auris*
- Cite *Candida auris* case studies and identify issues with fungal resistance and explain the importance of antifungal stewardship
- Outline the different treatment options for *Candida auris* infection
- Outline the difficulties that exist identifying *Candida auris* in the laboratory
- Describe the hierarchy of pathogens for choosing a disinfectant
- Describe the environmental cleaning practices for eradication of *Candida auris* and appropriate infection prevention practices for the healthcare setting
- Outline the CDC recommendation for notifying public health partners

Deadly, drug-resistant *Candida* yeast infection spreads in the US



Candida auris causes multidrug-resistant infections that can result in organ failure
Kateryna Kon/Science Photo Library

Spotlight on Emerging Pathogens

• *Candida auris*

- *C. auris* is a globally emerging pathogen that is often resistant to multiple antifungal agents
 - Fluconazole, azoles, amphotericin, echinocandins
- In several reports, *C. auris* has been recovered from the hospital environment
- CDC has recommended daily and post-discharge disinfection of surfaces in rooms of patients with *C. auris* infection
- At present, CDC recommends an EPA-grade disinfectant effective against *C. difficile* spores

What is *Candida auris*?

- **A yeast, in the same family as *Candida albicans***
- **Resistant to many of the anti-fungal medications used to treat other *Candida* infections**
 - Some strains found to have elevated MICs to drugs in all 3 major classes of antifungals (MMWR 2016)
- **Difficult to identify by many current hospital laboratories' standard practices**
- **Causes bloodstream, wound and ear infections**
- **Also isolated out of urine and lung tissue**
- **Can be the causative agent of outbreaks in healthcare settings**

Epidemiology

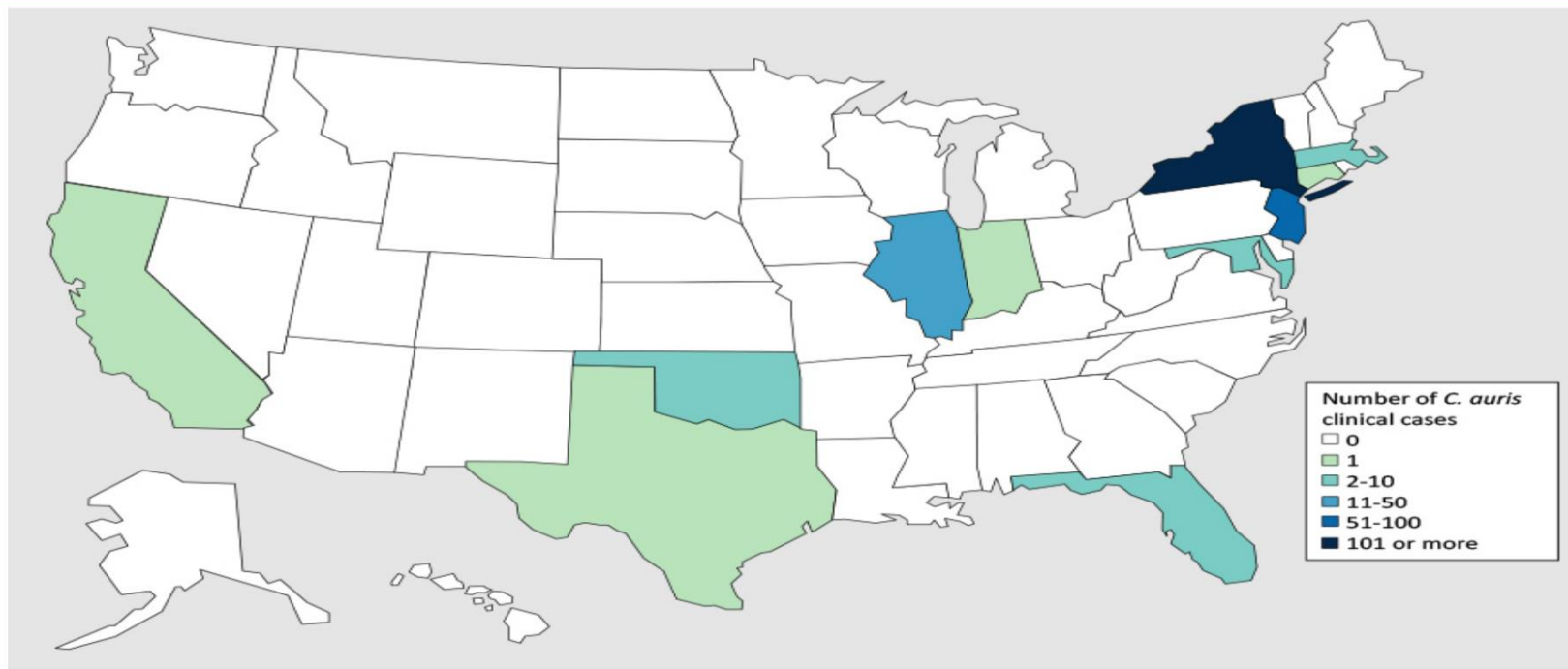
Here and Now: *Candida auris*

- **First identified in 2009**
- **Infections have occurred in several countries across the globe, including Japan, South Korea, India, Pakistan, South Africa, Kenya, Kuwait, Israel, Venezuela, Colombia, the United Kingdom,**
- **Infections have been most recently identified in the United States and Canada**
- **Public reporting: CDC clinical alert (2016) requesting case reporting to local health departments and CDC. (MMWR 2016)**



Current *Candida auris* cases in the U.S.

U.S. Map: Clinical cases of *Candida auris* reported by state, United States, as of May 31, 2018

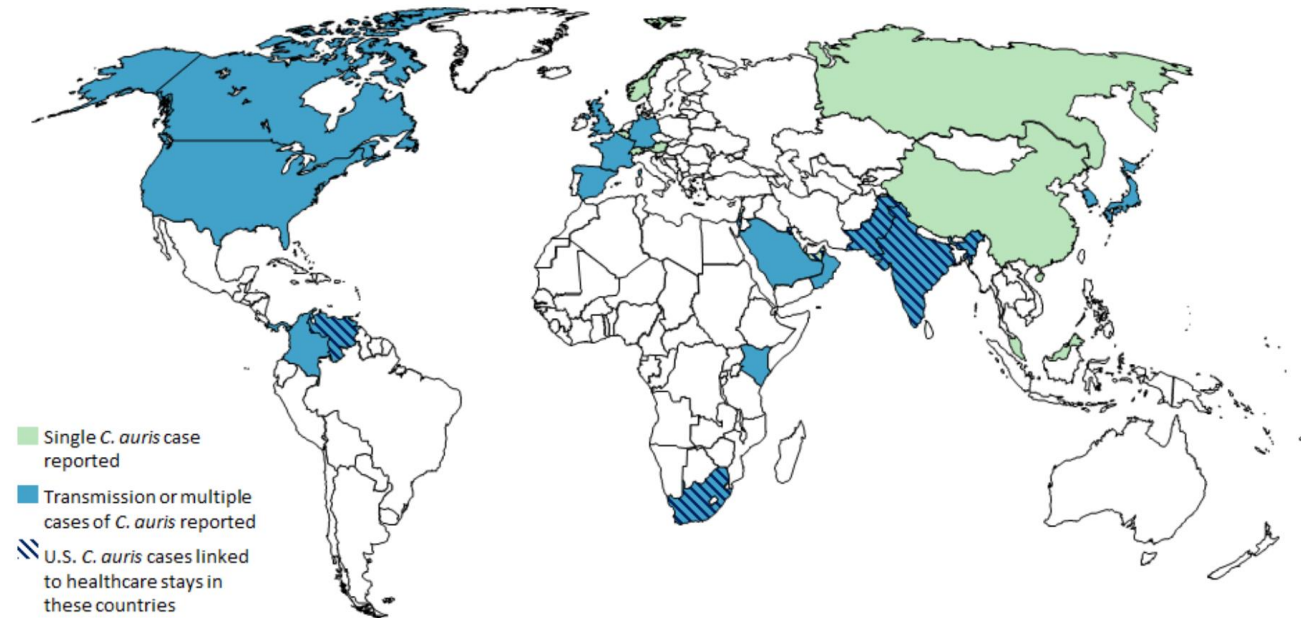


Cases are categorized by the state where the specimen was collected. Most [probable cases](#) were identified when laboratories with current cases of *C. auris* reviewed past microbiology records for *C. auris*. Isolates were not available for confirmation. Early detection of *C. auris* is essential for containing its spread in healthcare facilities.

<https://www.cdc.gov/fungal/candida-auris/tracking-c-auris.html>

Current *Candida auris* Cases Worldwide

Countries from which *Candida auris* cases have been reported, as of June 15, 2018



- Single cases of *C. auris* have been reported from Austria, Belgium, China, Malaysia, Norway, Russia, Switzerland, and the United Arab Emirates.
- Multiple cases of *C. auris* have been reported from Canada, Colombia, France, Germany, India, Israel, Japan, Kenya, Kuwait, Oman, Pakistan, Panama, Saudi Arabia, South Africa, South Korea, Spain, the United Kingdom, the United States (primarily from the New York City Area, New Jersey, and the Chicago area) and Venezuela; in some of these countries, extensive transmission of *C. auris* has been documented in more than one hospital.
- U.S. cases of *C. auris* have been found in patients who had recent stays in healthcare facilities in India, Kuwait, Pakistan, South Africa, the United Arab Emirates, and Venezuela, which also have documented transmission.
- Other countries not highlighted on this map may also have undetected or unreported *C. auris* cases.

Candida auris Case Studies

MMWR 2016: Overview of Retrospectively Identified Cases of *C. auris*

- **Often identified retrospectively due to difficulty with initial confirmation**
 - CDC recommends clinical labs to forward *C. haemulonii* isolates and those isolates not identified beyond *Candida spp.*
- **Patients identified had underlying medical condition/immunocompromised**
 - Hematologic malignancy (1): +blood
 - Hematologic malignancy and bone marrow transplantation (1): +blood
 - Short gut syndrome with TPN and corticosteroid use (1): +blood
 - Paraplegia with chronic urinary catheter (1): +urine
 - Acute respiratory failure requiring high dose corticosteroids (1): blood
 - Brain tumor and recent villous adenoma resection (1): +blood
 - Severe peripheral vascular disease and skull base osteomyelitis (1)*: +ear

Centers for Disease Control and Prevention, MMWR 2016; 65 (44) 1234-1237.

MMWR 2016: Overview of Retrospectively Identified Cases of *C. auris*

- **Median time from inpatient admission to *C. auris* (+): 18 days**
- ***C. auris* (+) blood all from patients with CVC in place at time of culture**
 - All treated with echinocandins, with one patient also receiving amphotericin B
 - All patients cleared *Candida* from blood; one patient with persistent (+) cultures for 10 days despite appropriate bug: drug treatment
 - 2 patients had recurrent candidemia infections 3-4 months post
- **Patient with (+) urine had repeat positives despite appropriate bug: drug treatment**
- **Mortality is high!**
 - 4/7 patients (all with BSI) died in weeks/months after *C. auris* identification

Centers for Disease Control and Prevention, MMWR 2016; 65 (44) 1234-1237.

Spotlight on First Prospectively Identified Case in US

- 89 yo male with 6 month history of ear pain
- H/O: hypertension, Type I DM (poorly controlled), coronary artery disease
- Received oral antibiotics and topical ear drops (ciprofloxacin)
- Multiple inpatient admissions (for ear pain, and other unrelated conditions) in addition to outpatient treatment
- Pneumatic otoscopy= otitis media; CT consistent with otomastoiditis and left nasopharyngeal mass; MRI concerning for skull base osteomyelitis
- OR for biopsy and debridement
 - Purulent material and necrotic tissue discovered.

Yang, et al., First Prospectively identified case of *Candida auris* in the United States. Otolaryngology Case Reports 3 (2017) 6-7.


Spotlight on First Prospectively Identified Case in US, cont'd..

- **Left nasopharyngeal mass (+) *Pseudomonas aeruginosa***
- **Left external ear (+) *C. haemulonii***
 - *MALDI-TOF testing later identified organism as *C. auris**
 - Isolates sent to CDC and NYSDOH for DNA sequencing (and confirmation)
- **Infectious Disease consulted to manage skull base osteomyelitis with IV antibiotics**
 - Antifungals not initiated as patient believed to be colonized (and risks outweighed benefits)

Per CDC: “Management of *C. auris* isolated from noninvasive, non-sterile body sites (e.g. urine, external ear, wounds, and respiratory specimens)

CDC does not recommend treatment of *C. auris* identified from noninvasive sites (such as respiratory tract, urine, and skin colonization) when there is no evidence of infection. Similar to recommendations for other *Candida* species, treatment is generally only indicated if clinical disease is present. ”

Yang, et al., First Prospectively identified case of *Candida auris* in the United States. Otolaryngology Case Reports 3 (2017) 6-7.

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Candida auris: Vive la resistance!



***C. auris* and Resistance**

- **Fungus is often multidrug resistant- important to test as levels of resistance can vary widely across isolates.**
 - 90% of isolates resistance to FLU (high MICs suggesting intrinsic resistance)
 - Almost 50% of isolates are MDR (resistant to ≥ 2 antifungal classes)
 - Approximately 4% of isolates show pan resistance to all antifungals

Chowdhary, A. et al. *Candida auris*: A rapidly emerging cause of hospital-acquired multidrug-resistant fungal infections globally. PLOS Pathogens, 2017. 13 (5) 1-10.


- **No established susceptibility breakpoints for *C. auris***
 - *Breakpoints are established for closely related Candida spp- and also based on expert opinion!*
 - *Correlation between susceptibility breakpoints and clinical outcomes are unknown*

<https://www.cdc.gov/fungal/candida-auris/recommendations.html>

C. auris and Resistance, Cont'd

Class/Drug	Tentative MIC Breakpoints (µg/mL)	Comment
Triazoles		
Fluconazole	≥32	Modal minimum inhibitory concentration (MIC) to fluconazole among isolates tested at CDC was ≥256; isolates with MICs ≥32 were shown to have a resistance mutation in the <i>Erg11</i> gene, making them unlikely to respond to fluconazole.
Voriconazole and other second generation triazoles	N/A	Consider using fluconazole susceptibility as a surrogate for second generation triazole susceptibility assessment. However, isolates that are resistant to fluconazole may respond to other triazoles occasionally. The decision to treat with another triazole will need to be made on case-by-case basis.
Polyenes		
Amphotericin B	≥2	Recent pharmacokinetic/pharmacodynamic analysis of <i>C. auris</i> in a mouse model of infection indicates that under standard dosing, the breakpoint for amphotericin B should be 1 or 1.5, similar to what has been determined for other <i>Candida</i> species. Therefore, isolates with an MIC of ≥2 should now be considered resistant. If using Etest for amphotericin B and an MIC of 1.5 is determined, that value should be rounded up to 2.
Echinocandins		
Anidulafungin	≥ 4	Tentative breakpoints are based on the modal distribution of echinocandin MICs of approximately 100 isolates from diverse geographic locations.
Caspofungin	≥ 2	
Micafungin	≥ 4	

<https://www.cdc.gov/fungal/candida-auris/recommendations.html>

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Antifungal Stewardship: Why is *C. auris* so resistant?

- **Large portion of the organism's genome encodes for resistance**
 - ATP-binding cassette (ABC) and major facilitator superfamily (MFS) transporter families and drug transporters may provide *C. auris* with multi-drug resistance
- ***C. auris* has optimal persistence in the environment**
 - Thermotolerance (grows optimally at 37°-42°C), tolerant to salt, aggregates into clusters and form biofilms- making it difficult to kill

Chowdhary, A. et al. *Candida auris*: A rapidly emerging cause of hospital-acquired multidrug-resistant fungal infections globally. PLOS Pathogens, 2017. 13 (5) 1-10.

- **Stewardship becoming increasingly important given resistance of *C. auris***
- **Antifungal prophylaxis (particularly use of fluconazole) benefits may need to be weighed against potential harms created by resistance patterns seen as a result of use**

Chowdhary, A., et al. Multidrug-resistant *Candida auris*: 'new kid on the block' in hospital-associated infections? Journal of Hospital Infection, 94 (2016), 209-212.

C. auris Infection and Treatment Options

- CDC recommends adults and children ≥ 2 months of age:

Echinocandin Drug	Adult dosing	Pediatric dosing
Anidulafungin	loading dose 200 mg IV, then 100 mg IV daily	not approved for use in children
Caspofungin	loading dose 70 mg IV, then 50 mg IV daily	loading dose 70mg/m ² /day IV, then 50mg/m ² /day IV (based on body surface area)
Micafungin	100 mg IV daily	2mg/kg/day IV with option to increase to 4mg/kg/day IV in children 40 kg

- Majority of US strains identified have been echinocandin susceptible
- Patients should be monitored closely for clinical improvement as *C. auris* can develop resistance quickly
 - Follow-up cultures with additional susceptibility testing
- Patients unresponsive to therapy or with persistent fungemia (> 5d) may switch to liposomal amphotericin B
- IDSA 2016 Clinical Practice Guideline:
 - <https://academic.oup.com/cid/article/62/4/e1/2462830>

Candida auris: Fooling the Lab



C. auris and Laboratory Misidentification

Identification Method	Organism <i>C. auris</i> can be misidentified as
Vitek 2 YST	<i>Candida haemulonii</i> <i>Candida duobushaemulonii</i>
API 20C	<i>Rhodotorula glutinis</i> (characteristic red color not present) <i>Candida sake</i>
BD Phoenix yeast identification system	<i>Candida haemulonii</i> <i>Candida catenulata</i>
MicroScan	<i>Candida famata</i> <i>Candida guilliermondii</i> * <i>Candida lusitaniae</i> * <i>Candida parapsilosis</i> *
RapID Yeast Plus	<i>Candida parapsilosis</i> *

***Candida auris* Identification: Laboratory Technology**

- **Diagnostic devices using matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) allow for differentiation of *C. auris* from other *Candida* spp.**
 - Unfortunately, not all of the reference databases supplied to MALDI-TOF devices allow for the differentiation.
- Bruker Biotype brand MALDI-TOF using their “research use only” database
- FDA-approved and updated CA system database
- VITEK (MALDI-TOF) MS RUO (with Saramis Version 4.14 database and Saccharoycetaceae update)
- CDC Resource link
 - <https://www.cdc.gov/fungal/diseases/candidiasis/pdf/Testing-algorithm-by-Method-temp.pdf>

The Importance of Environmental Cleaning

Choosing an Effective Cleaner and Disinfectant



Keeping Patients Safe from the Environment

Patient(s) contaminate surfaces or medical equipment



Environmental surfaces/inanimate objects are reservoirs (fomites)



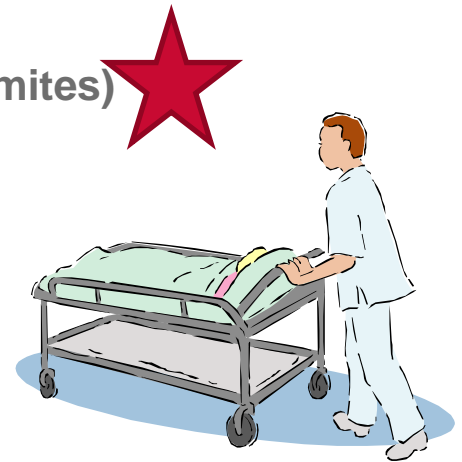
Healthcare workers contact contaminated surface & patients



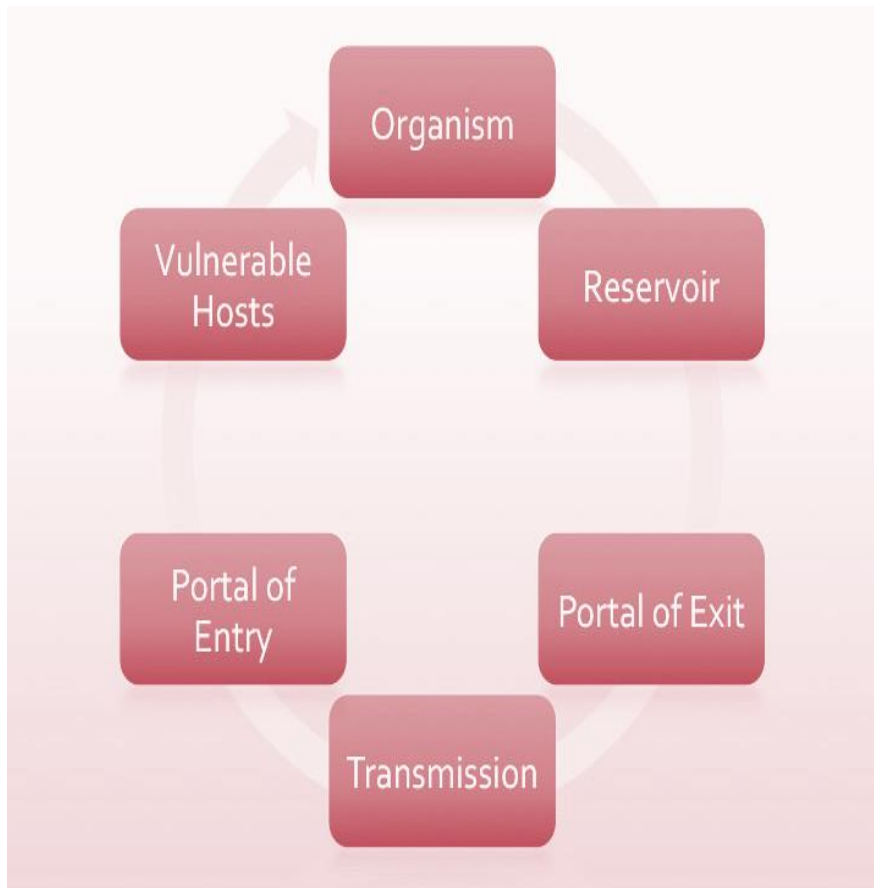
Environmental Contamination + Poor Hand Hygiene



Contributes to the spread of resistant pathogens



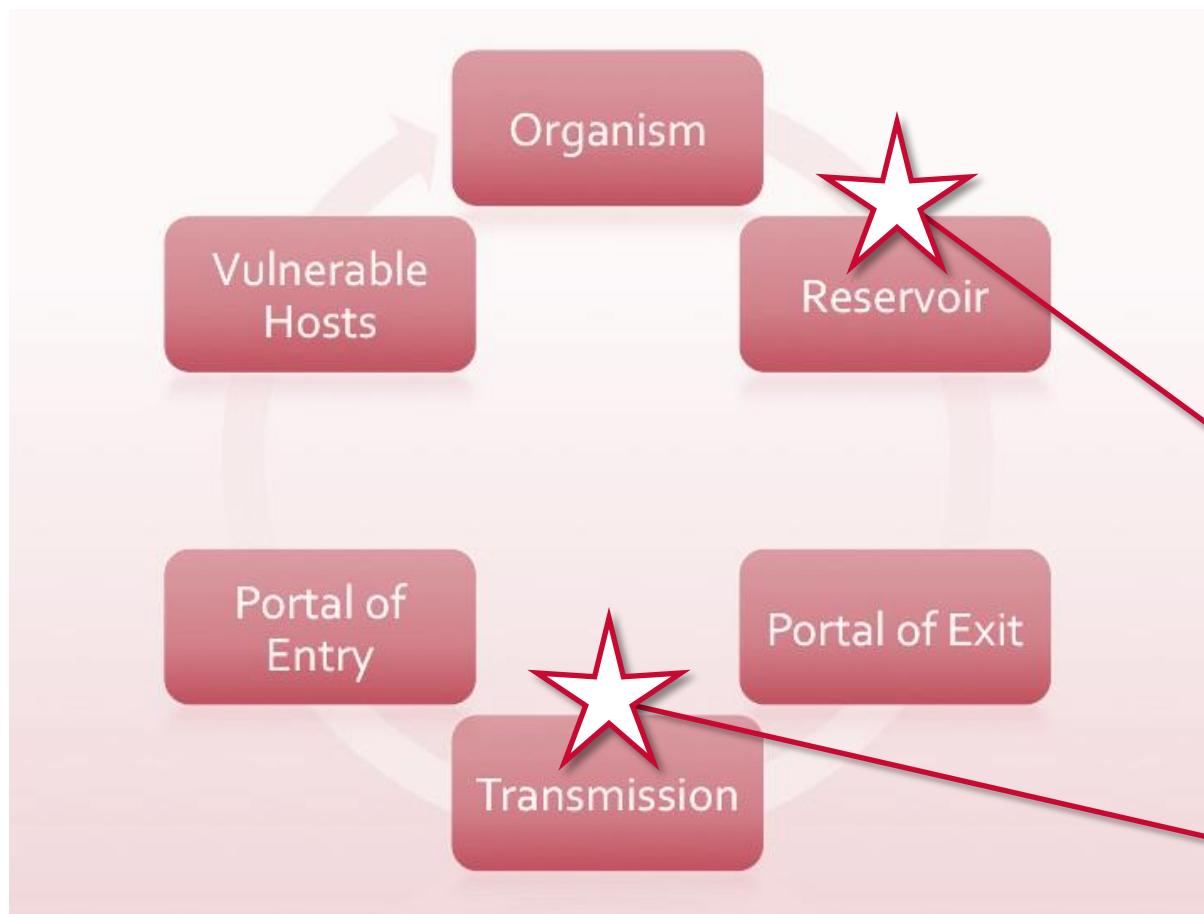
What is Chain of Infection?



In order for infection to occur, each link of the chain must be present:

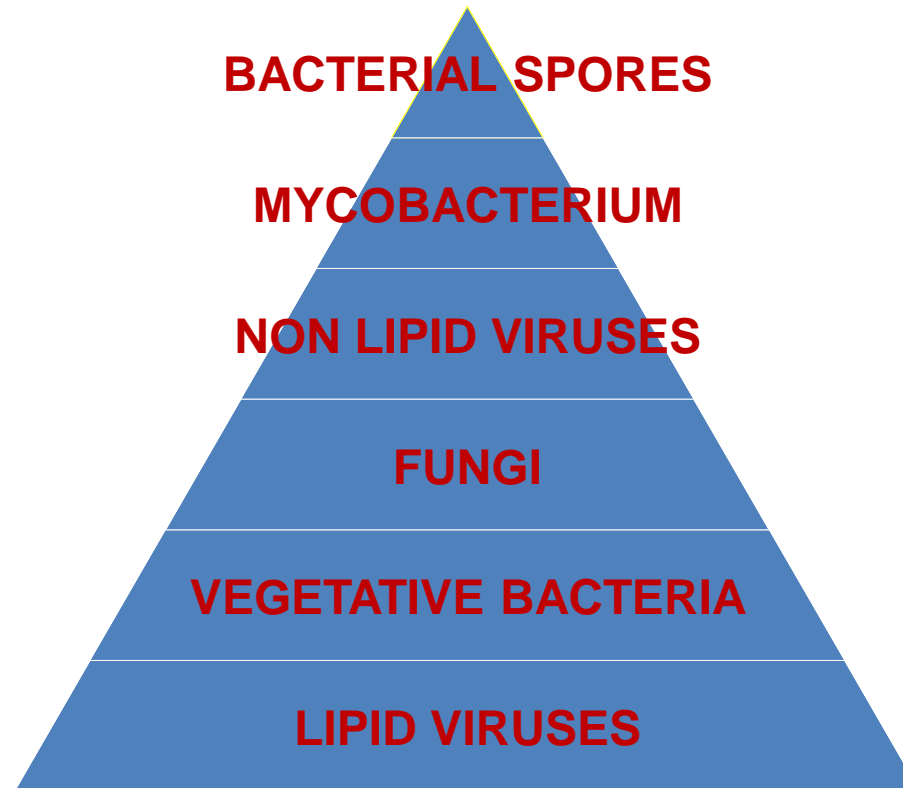
- ✓ An organism is present
 - Bacteria, virus, fungus or parasite
- ✓ It is on or in reservoir where it can survive/thrive
- ✓ It has portal of exit from reservoir
- ✓ It has an appropriate mode of transmission
- ✓ It must have portal of entry
- ✓ It must have a vulnerable/susceptible host to infect

Breaking the Chain



Because transmission and reservoirs are easier to control than the host!

APIC HIERARCHY OF PATHOGENS



Descending Order of Resistance to Germicidal Chemicals

NEW CONCEPT FOR ORGANISM LIST

Difficult

Prions

Bacterial spores (C. difficile)

Protozoan oocysts

Helminth eggs

Small, non-enveloped viruses (Norovirus)

Mycobacteria

Protozoan cysts

Fungal spores

Gram negative bacilli (Acinetobacter, ESBL E. Coli, KPC)

Vegetative fungi and algae

Large, non-enveloped viruses

Easier

Gram positive bacilli (MRSA, VRE)

Enveloped viruses



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***C. auris* and the Environment**

- ***C. auris* can survive on surfaces for weeks**
- **CDC recommends thorough daily and terminal cleaning and disinfection of patient room**
- **CDC recommends the cleaning and disinfection of areas outside of the patient room (e.g. physical therapy, radiology)**
- **Shared equipment should be cleaned and disinfected prior or use by another patient**

<https://www.cdc.gov/fungal/candida-auris/c-auris-infection-control.html#disinfection>

***Candida auris* and disinfection practices**

- **Abstract that performed a retrospective review of 217 patients during a *C. auris* outbreak in a critical care unit**
- **Disinfection of patient's rooms was performed using a chlorine solution followed by hydrogen peroxide vapor system**
- **30 patients found to be positive after sharing an environment with a patient with a *C. auris* infection**
 - 16 of those patients occupied the room directly after a positive *C. auris* case
 - 11 out of 16 (69%) patients acquired *C. auris* even after the room had been disinfected using a two step disinfection process
- **Highlights the ineffectiveness of the cleaning agents and two step process used**

Shackleton, J., Schelenz, S., Rochon, M., Hall, A., Ryan, L., & Cervera-Jackson, R. (2016, November). The impact of environmental decontamination in a *Candida auris* outbreak [Abstract]. *The Journal of Hospital Infection*, 94(S1), 588.

Efficacy of Disinfectants and Antiseptics against *C. auris*

Efficacy of Disinfectants and Antiseptics against *Candida auris*

Rutala, Kanamori, Gergen, Sickbert-Bennett, Weber, 2017 ID Week Poster

- $\geq 3 \log_{10}$ reduction (*C. auris*, 1m, 5% FCS, QCT)
 - 0.20% peracetic acid
 - 2.4% glutaraldehyde
 - 0.65% hydrogen peroxide, 0.14% peroxyacetic acid
 - 0.5% Quat, 55% isopropyl alcohol
 - Disinfecting spray (58% ethanol, 0.1% QUAT)
 - 28.7% isopropyl alcohol, 27.3% ethyl alcohol, 0.61% QAC
 - 0.07% o-phenylphenol, 0.06% p-tertiary amylphenol
 - 70% isopropyl alcohol
 - ~5,250 ppm chlorine
 - Ethanol hand rub (70% ethanol)
 - Accelerated hydrogen peroxide, 1.4%
 - Accelerated hydrogen peroxide, 2%

Efficacy of Disinfectants and Antiseptics against *C. auris*

Efficacy of Disinfectants and Antiseptics against *Candida auris*

Rutala, Kanamori, Gergen, Sickbert-Bennett, Weber, 2017 ID Week Poster

- $\leq 3 \log_{10}$ (most $< 2 \log_{10}$) reduction (*C. auris*, 1m, 5% FCS, QCT)
 - 0.55% OPA
 - 3% hydrogen peroxide
 - Quat, (0.085% QACs)
 - 10% povidone-iodine
 - ~1,050 ppm chlorine
 - 2% Chlorhexidine gluconate-CHG
 - 4% CHG
 - 0.5% triclosan
 - 1% CHG, 61% ethyl alcohol
 - 1% chloroxylenol

Infection Prevention

Stopping the Spread of *Candida auris*



Recommended Infection Control Practices

- Patients with suspected *Candida auris* infections or colonization should be placed in private rooms and on Standard and Contact precautions
- Patients should remain on Contact precautions indefinitely or until multiple rounds of surveillance cultures are negative
 - Daily and terminal cleaning of the patient room should be done with an EPA registered hospital grade disinfectant effective against *C. difficile* spores



Recommended Infection Control Practices: Hand Hygiene

- **HH is paramount where infection/colonization is present!!**
- **Alcohol-based hand rub OR soap and water HH when hands visibly soiled.**
- **Wearing gloves is not a substitute for HH!!**
- **Following contact precautions, HCW should:**
 - Always wear gloves to reduce contamination to hands
 - Avoid touching surfaces outside of the immediate “patient zone” while wearing gloves
 - Perform HH before donning gloves and after doffing

<https://www.cdc.gov/fungal/candida-auris/c-auris-infection-control.html>

CDC Recommendations: *C. auris* Specimen Collection

- **Candida isolates should be obtained from a sterile site (e.g. bloodstream, CSF) for species-level identification to start effective therapy (based on species specific susceptibility patterns)**
- **53% *C. auris*- blood; 46% *C. auris*- other body sites**
- **When identified from a non-sterile site, some labs do not speciate Candida because thought to be colonization (thus not requiring treatment)**
 - Important to ID isolate species from a non-sterile site because it can represent broader body colonization (increased risk of transmission)
- **Species identification critical:**
 - Clinically indicated in care of patient
 - Known case of *C. auris* identified and need to ID additional cases- species Identification can be continued for up to a month until no evidence of transmission found
 - Patient with known travel history to areas where US cases have been linked- if being admitted

Re-assessment of *C. auris* Colonization:

- **Periodic reassessments of colonization status to inform duration of infection control measures**
 - Axilla, groin, and any other sites previously positive
 - Should not be on current anti-fungal treatment (CDC recommends at least 1 week after treatment complete)
 - If CHG bathing performed, wait 48 hours for colonization testing
- **If patient swab positive, no repeat sampling for at least 3 months**
- **If patient swab negative, at least one more negative swab at least one week later needed to d/c *C. auris* specific infection control precautions**

Recommended Screening for *Candida auris*

- **Patients are often colonized long (months) prior to *C. auris* being detected**
 - Potential for transmission to other patients when specific control measures not implemented
 - Important to identify prior healthcare exposures and contact those facilities
- **Screen to identify colonization among epi-linked patients:**
 - Point-prevalence to identify those colonized on units/floors where index case resided
 - Initially limit to those patients who were present on unit with index case for 3+ days, or those patients who required higher levels of care (e.g. ventilated)
 - Ring strategy: screen those closest to index case- and if positives identified, move out from there
- **Collect specimen from the axilla or groin- these areas found to be common and consistent sites of colonization**

<https://www.cdc.gov/fungal/candida-auris/recommendations.html#suspect>

When to Suspect *C. auris* in Your Facility and WHAT TO DO

- Increase in unidentified *Candida* species infections in the inpatient setting (including increases in *Candida* from urine specimens)
- Review patient record to identify previous healthcare exposures- particularly overnight stays
 - Previous facilities (including current, those in which patient stayed 7+ days within prior 3 months, LTACH, NH) should be targeted for contact investigation and a review of microbiology reports to identify other cases
- Notify DOH to assist with contact investigation
- Educate HWC/EVS on *C. auris* cleaning and disinfection practice- and monitor adherence!
- Ensure adequate supplies for IP precautions
- Flag patient record for subsequent admissions

<https://www.cdc.gov/fungal/candida-auris/recommendations.html>

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Bring in your Public Health Partners!

Build and Nurture Relationships



CDC Recommendations for Public Health Reporting

- Suspected *C. auris* infections should be reported to the local public health department and CDC
- Laboratories should forward suspect specimens to their state public health laboratory for further identification



CDC Resources for Patient Education

- **FAQs for *Candida auris* screening: helping the patient to understand why they are being screened**
- **Template for verbal consent of patient for *Candida auris* colonization screening**
- **Resources available here: <https://www.cdc.gov/fungal/candida-auris/c-auris-screening-info.html>**

