Candida auris
The Secret Suberbug

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Gravity Diagnostics

Objectives

- Describe risk factors for *C. auris* infection and colonization
- Discuss testing options for *C. auris*
- Describe evolving treatment options for *C. auris*
- Define steps to take when a case of *C. auris* is suspected or identified

"All the News That's Fit to Print"

The New York Times

Late Edition

Today, sunshine mixing with some clouds, mild, high 64. **Tonight,** cloudy, periodic rain, low 53. **Tomorrow,** a brief shower or two, high 72. Details in SportsSunday, Page 10.

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DADO GALDIERI FOR THE NEW YORK TIMES

A scout discovered Maradoninha, 11, two years ago. His family moved 1,200 miles to enable him to get first-class training.

Fungus Immune to Drugs Quietly Sweeps the Globe

Lethal Infection Adds Alarming Dimension to Dangers of Overusing Medicines

By MATT RICHTEL and ANDREW JACOBS

Last May, an elder[illegible] admitted to the Brooklyn branch of Mount Sinai Hospital for abdominal surgery. A blood test revealed that he was infected with a newly discovered germ as deadly as it was mysterious. Doctors swiftly isolated him in the intensive care unit.

DEADLY GERMS, LOST CURES
A New Public Health Threat

The germ, a fungus called Candida auris, preys on people with weakened immune systems, and it is quietly spreading across the globe. Over the last five years, it has hit a neonatal unit in Venezuela, swept through a hospital in Spain, forced a prestigious British medical center to shut down its intensive care unit, and taken root in [illegible] example of one of the world's most intractable health threats: the rise of drug-resistant infections.

For decades, public health experts have warned that the overuse of antibiotics was reducing the effectiveness of drugs that have lengthened life spans by curing bacterial infections once commonly fatal. But lately, there has been an explosion of resistant fungi as well, adding a new and frightening dimension to a phenomenon that is undermining a pillar of modern medicine.

"It's an enormous problem," said Matthew Fisher, a professor of fungal epidemiology at Imperial College London, who was a coauthor of a recent scientific review on the rise of resistant fungi.

First reported in Japan and now, worldwide

Japan

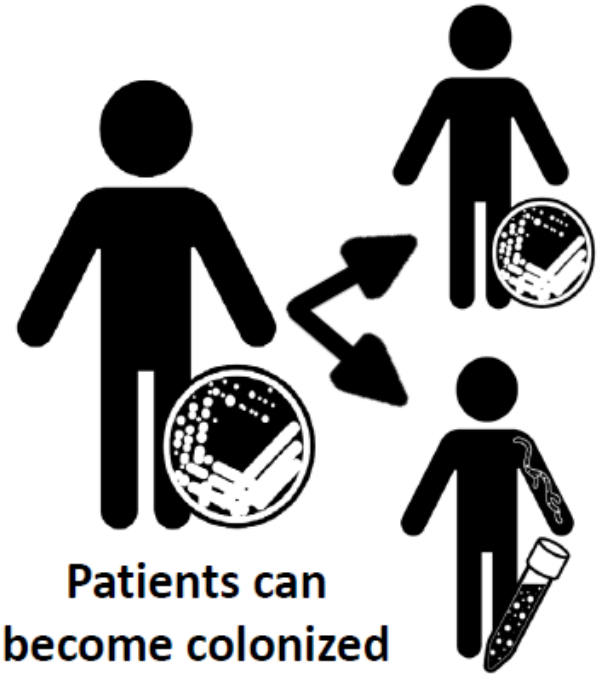
2009

United States

2016

Why are we concerned about *Candida auris*?

Highly drug-resistant

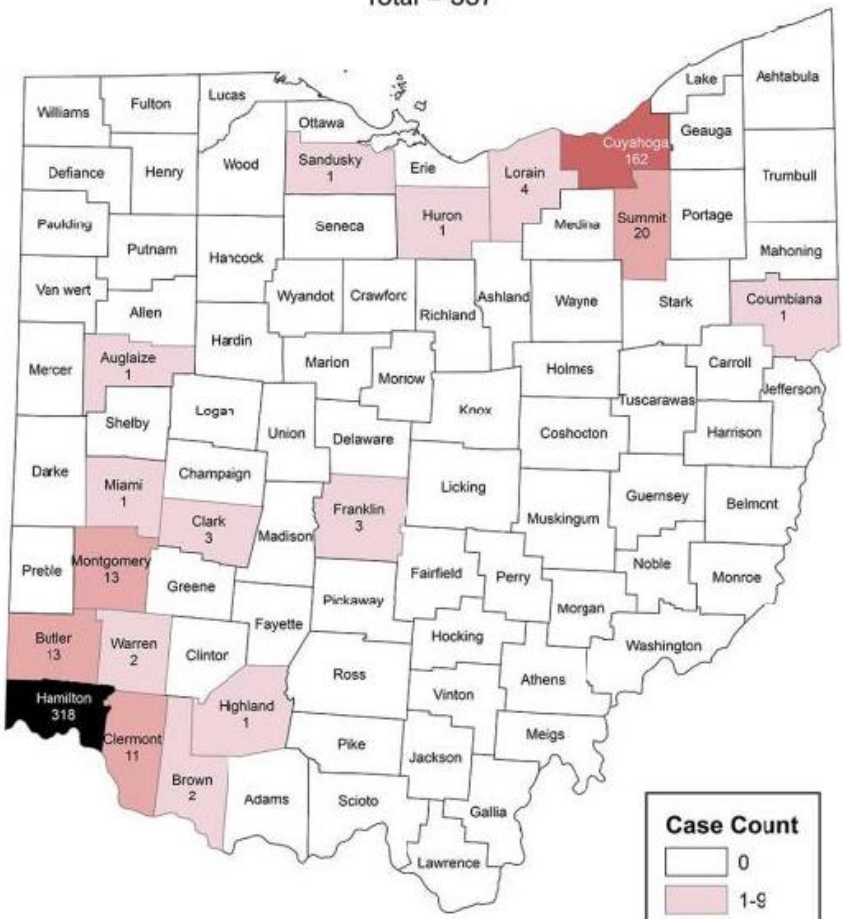


Patients can become colonized and develop invasive infections

Spreads in healthcare settings

Candida auris cases reported in Ohio through July 3, 2023

Total = 557



County reflects county of facility where specimen was collected.
All data are preliminary and subject to change.
Source of disease data: Ohio Disease Reporting System.

A paradigm shift for *Candida* infections
A yeast that acts like a bacteria!

- Resistance is the norm
- Thrives on skin
- Contaminates patient rooms
- **CAN SPREAD IN HEALTHCARE SETTINGS**

Typically affects the sickest of the sick

- Tracheostomies
- Ventilator-dependent
- Colonized with other multidrug-resistant organisms
- Recently received antibiotics and antifungals
- Not a threat to general public or healthy individuals

Stays in certain types of post-acute care facilities is a major risk factor: vSNFs and LTACHs

C. auris **prevalence in nursing home units with ventilator beds**

7.7%

C. auris **prevalence in regular nursing homes**

0.7%

Risk Factors for Candidemia ("the other *C. diff*")

- Broad-spectrum antibiotic use
- Immune compromise
- Prolonged ICU stay
- Abdominal surgery
- Central lines

Candida Behavior

Candida albicans

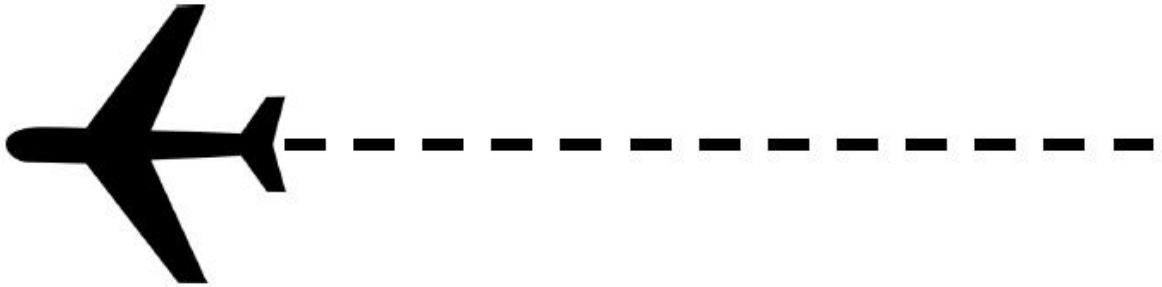
- Not very environmentally persistent
- Easily identified
- Easily killed with Quats
- Colonizes the skin, mouth, gut, vagina
- Causes thrush, bloodstream infections, and candidal vaginitis
- Not resistant
- Transmission not typical

Candida auris

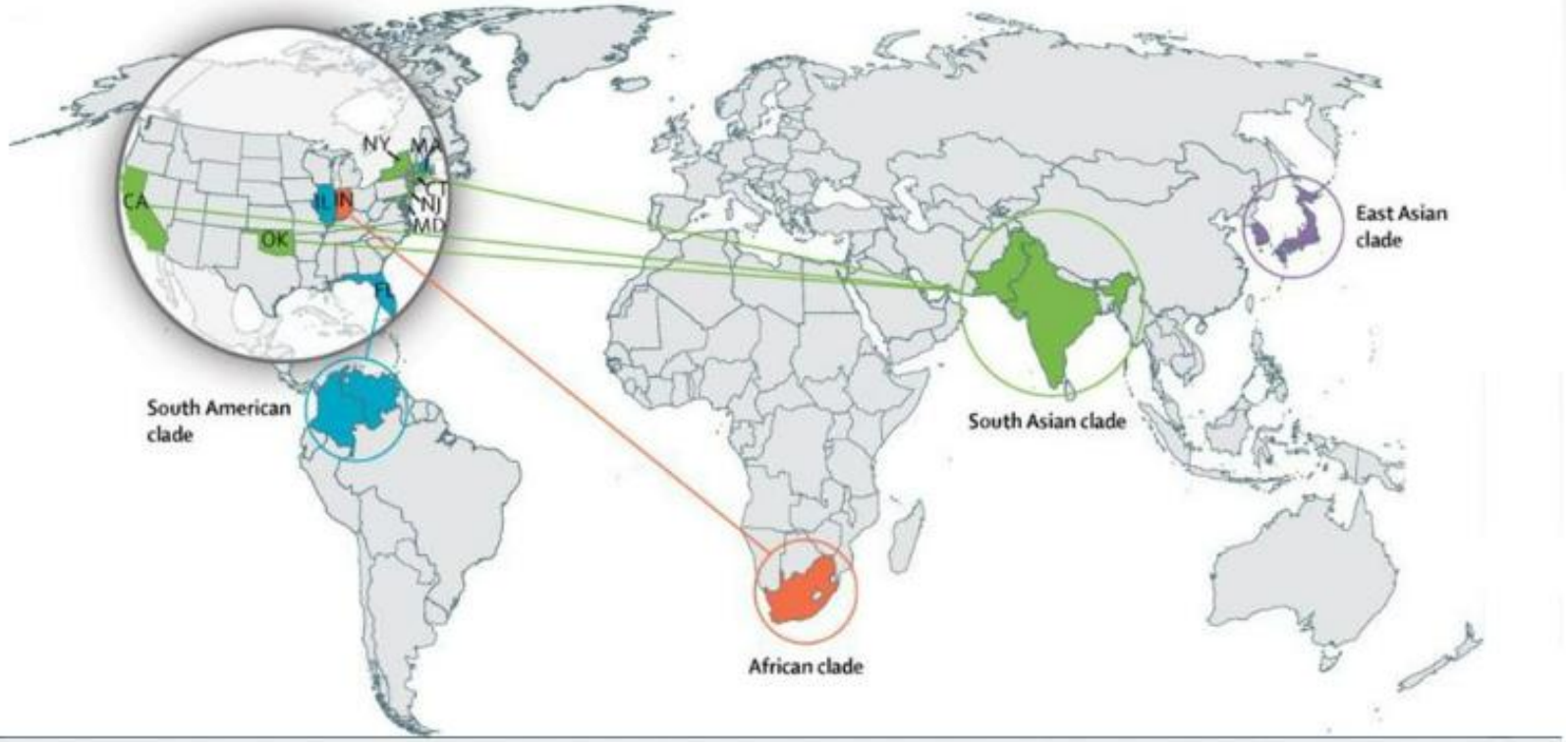
- Very environmentally persistent
- Difficult to identify
- Not easily killed
- Colonizes the groin and axilla
- Opportunistic infections in the blood and other invasive sources
- Very resistant
- Transmitted in healthcare settings via direct contact

Healthcare abroad is risk factor for *C. auris*

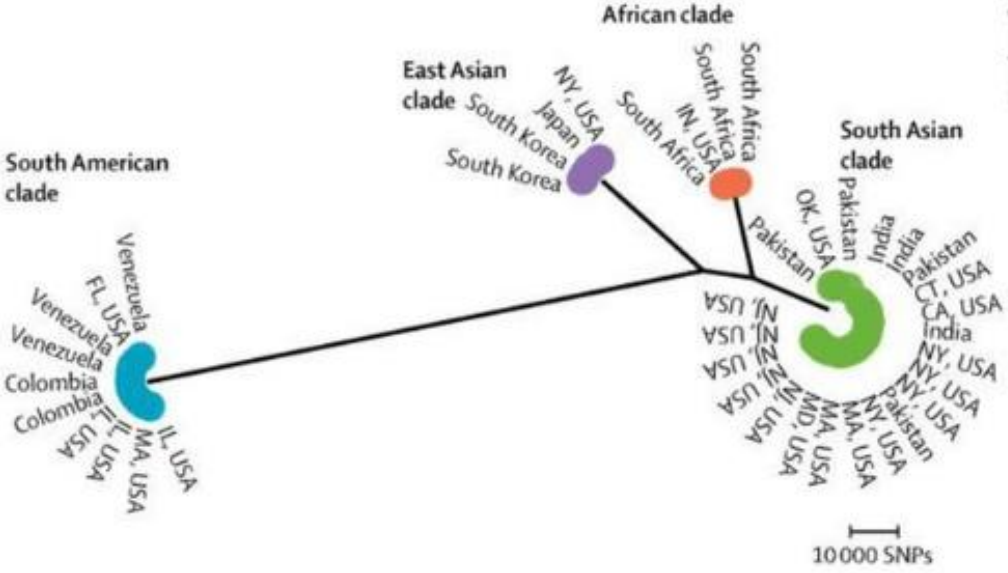
- Patients from India, Pakistan, South Africa, Kenya, Venezuela, UAE, Kuwait
- Identified weeks to two years after hospitalization in that country
- Whole genome sequencing showed isolates were related to those from the countries where patients received healthcare

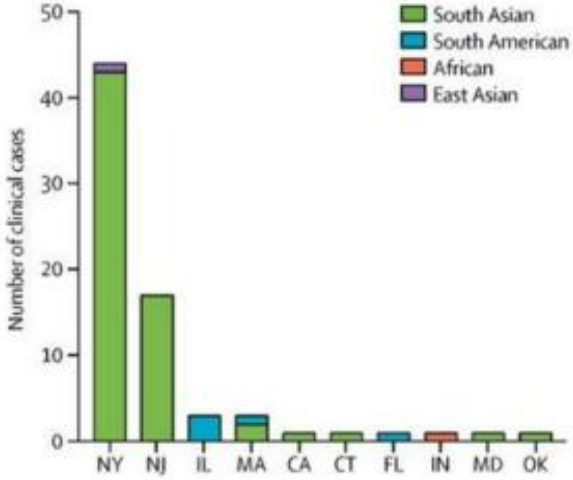


Multiple Global Introductions



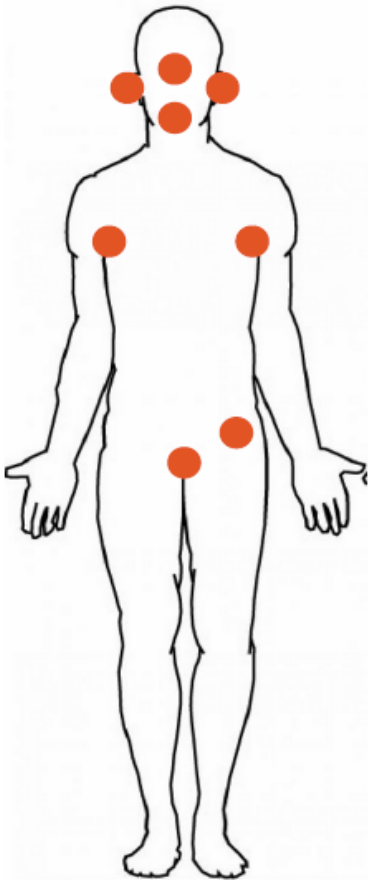
Multiple Global Introductions





Patients are often colonized indefinitely

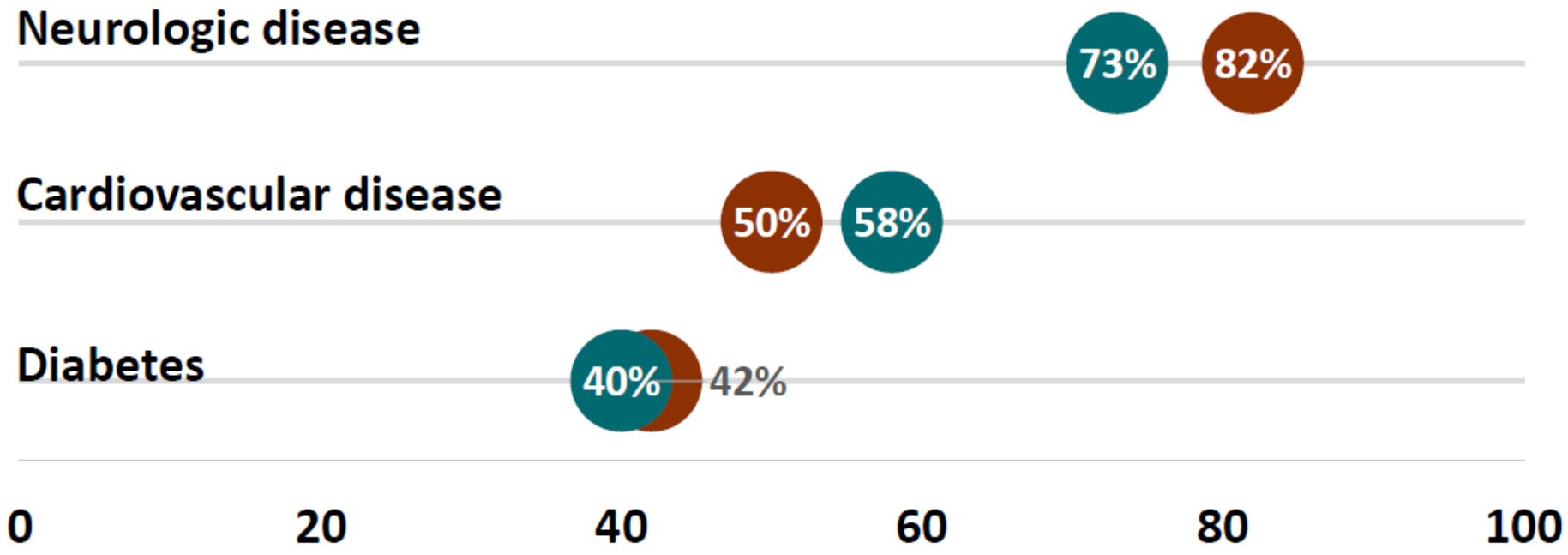
- Primarily on skin, but nares and other body sites also can become colonized
- Persistent, for many months
- No currently known decolonization strategies



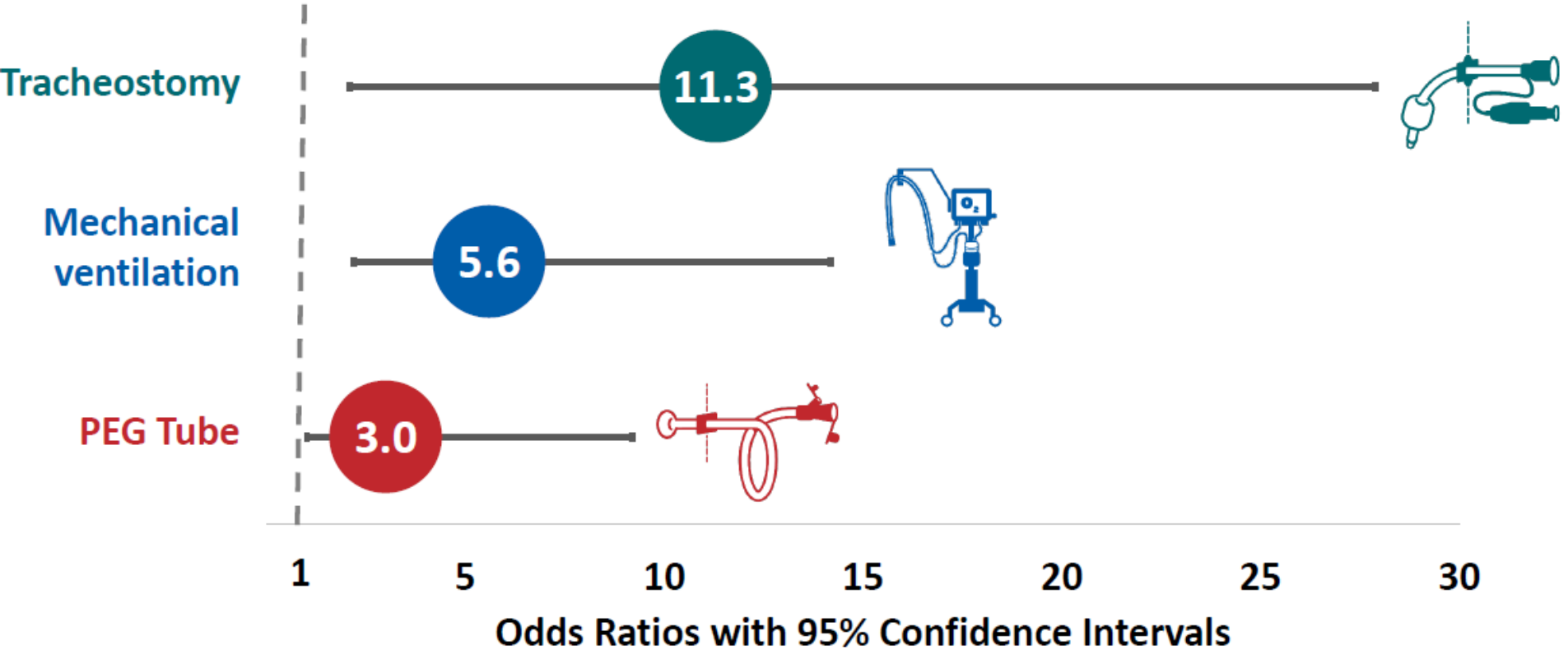
- Leads to:
  - Invasive infection
  - Transmission to others

Case control study for *C. auris* colonization risk factors in vSNFs in NY

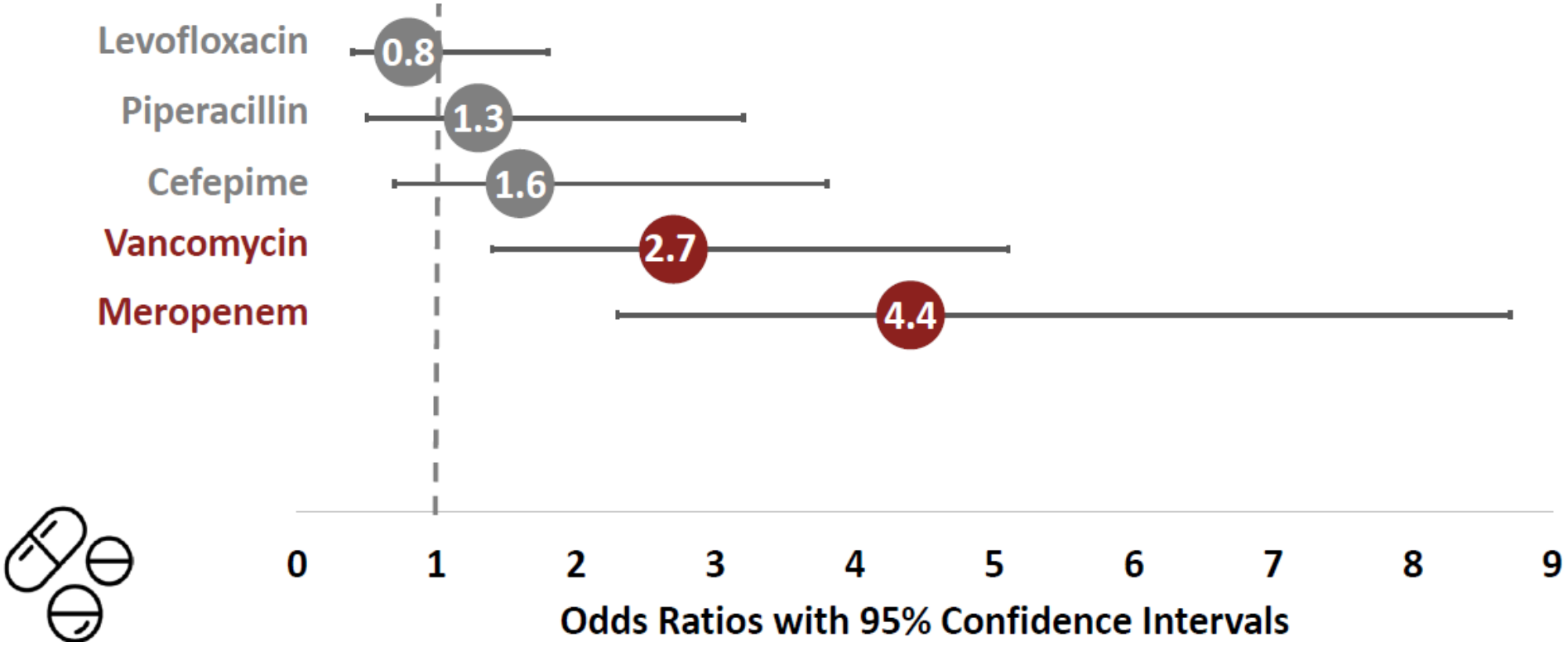
Both cases and controls had lots of comorbidities



Tracheostomy, ventilation, and PEG tubes were associated with colonization.



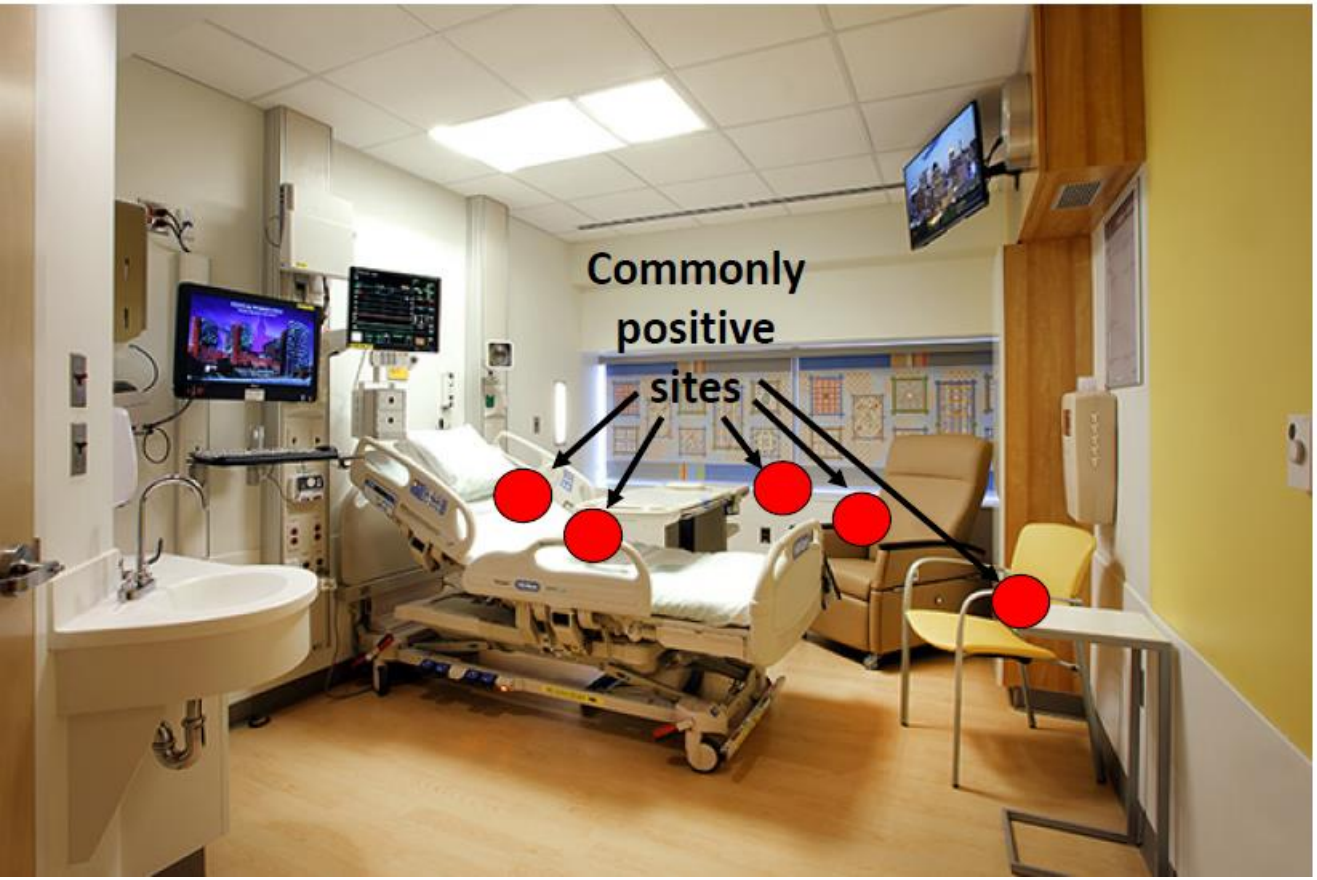
Certain broad-spectrum antibiotics were associated with *C. auris* colonization.



Contact Precautions

- Single patient room using contact precautions
  - If cohorting is necessary, place patients with similar MDROs together
- Duration of colonization is unknown
  - Months to indefinite

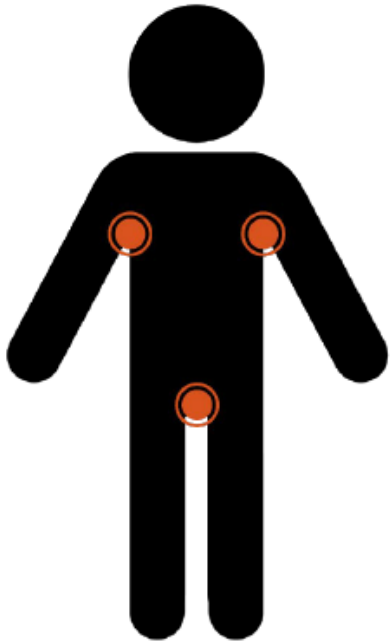
C. auris persists in the environment

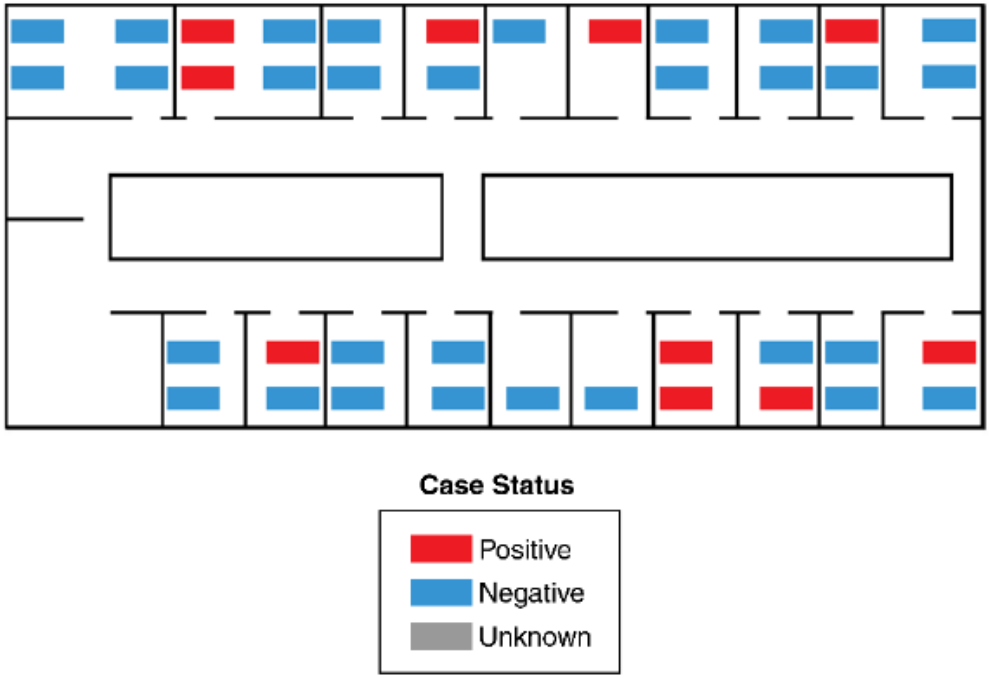


- Can survive over a month
- Some common disinfectants (quaternary ammonia compounds) don't work

Mobile equipment has been heavily implicated in transmission

C. auris colonization doesn't just get passed to roommates—others on the unit also seem to be at risk





C. auris detection has been challenging

But, its getting better!

--Awareness of the organism
--Improved access to MALDI-TOF
--Ability to confirm at reference and public health labs

Update on lab methods for detecting *C. auris*

- FDA approvals
  - VITEK MS MALDI
  - Bruker Biotyper MALDI
  - GenMark ePlex BCID-FP panel blood culture test
- VITEK 2 8.01 update
- rt-PCR

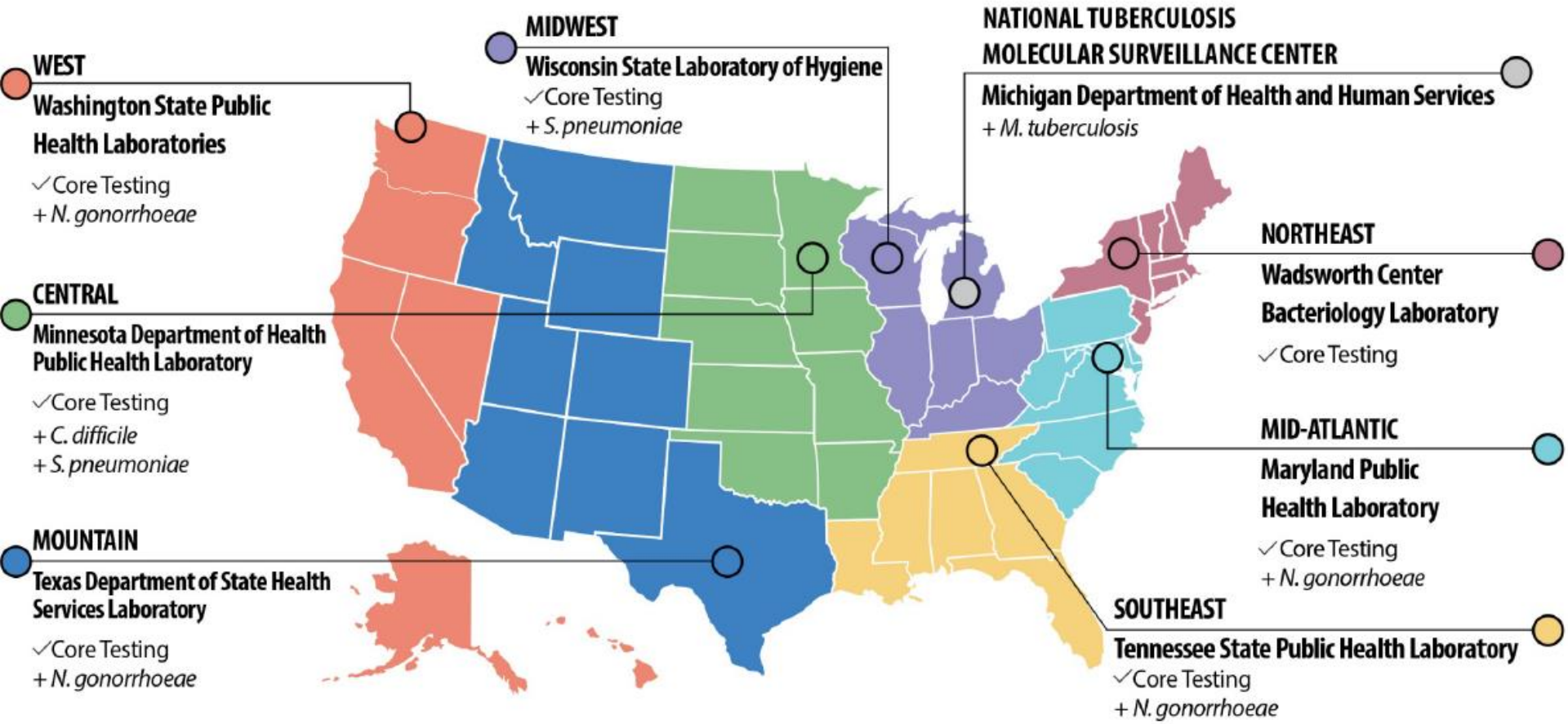
Misidentification

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

Candida from urine and other non-sterile body sites

- Yeast from urine usually tossed out because not considered an infection
- Long-term acute care hospital network decided to determine species of any yeast identified in urine
- Within 5 months, detected first case of *C. auris* in their region

ARLN Labs – *Candida auris* identification services available



Colonization screening presents challenges

- PCR or culture-based methods are available through CDC and public health labs
- Few clinical labs now conducting screening using PCR

Testing Methodology Background

CDC Recommended Protocol

No FDA-approved tests for colonization swab analysis, but there is a Real-time PCR protocol recommended by the CDC.

Modified from:

Leach L, Zhu Y, Chaturvedi S. Development and Validation of a Real-Time PCR Assay for Rapid Detection of Candida auris from Surveillance Samples. J Clin Microbiol. 2018 Jan 24;56(2):e01223-17. doi: 10.1128/JCM.01223-17. PMID: 29187562; PMCID: PMC5786737.

Scott Licardi

Senior Manager of Laboratory Development

Performance Measures

365 patient swabs compared to culture.

Sensitivity 89% [C.I. 77-96%]

Specificity 99% [C.I. 97-100%]

C. auris Target: *ITS2*

Primer and probes designed to detect *ITS2* gene due to high specificity to *C. auris* compared to other yeast species.

Optimization Studies

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Ensuring protocol can work on Gravity's equipment and able to fit within our current molecular microbiology workflows.

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Assay Optimization

Multiple reaction volumes and concentrations were tested to determine the appropriate PCR conditions for the QuantStudio 12K instrument.

Isolation Techniques

Different vendor solutions for isolating *C. auris* DNA from contrived liquid amies specimens were tested. Our current workflow for other molecular microbiology tests provided equivalent results to other isolation methodologies.

Range Finding Limit of Detection

Dilution series to determine if LoD matches those of published studies.

Validations

Validation Studies Conducted

Analytical Accuracy

Precision Studies

Analytical Sensitivity (Limit of Detection)

Reportable Range

Interference Studies

Stability Studies

- Burd EM. Validation of laboratory-developed molecular assays for infectious diseases. Clin Microbiol Rev. 2010 Jul;23(3):550-76. doi: 10.1128/CMR.00074-09. PMID: 20610823; PMCID: PMC2901657.
- CLSI. User Protocol for Evaluation of Qualitative Test Performance; Approved Guideline-Second Edition. CLSI document EP12-A2. Wayne, PA: Clinical and Laboratory Standards Institute; 2008.
- College of American Pathologist. Accreditation checklist COM.40350 Validation of Test Performance Specifications – Modified FDA – cleared/approved Tests and LDTs
- Association of Molecular Pathologist. Molecular Diagnostics Assay Validation – September 2017 AMP White Paper
- Food and Drug Administration. In Vitro Diagnostics EUA for COVID-19 Molecular Diagnostics Template (October 6, 2021)

Analytical Specificity

Accuracy Studies

25 paired patient specimens (1 positive and 24 negatives) 100% concordance of results

Analytical Specificity

CDC Panel from Antibiotic Resistance bank for *C. auris*.

Interference Studies

Added 1% volume/volume or weight/volume of expected substances, (i.e., normal skin flora, blood, deodorant, etc.)

THREE CLASSES OF ANTIFUNGALS

1

Azoles

2

Polyenes

3

Echinocandins

Resistance in the U.S.

1

87.6%
Azoles

2

33.7%
Polyenes

3

1.7%
Echinocandins

- 33% multidrug resistant
- 2 pan-resistance found in 2019

CDC *C. auris* management guidance

- Echinocandins are first line treatment
- AFST on every isolate
- Repeat cultures until documented clearance for invasive sites

Decolonization

- Active area of investigation

Echinocandin Treatment of *Candida auris* infection

- Anidulafungin (*Eraxis*) 100 mg IV daily ($41)
- Caspofungin (*Cancidas*) 50 mg IV daily ($70)
- Micafungin (*Mycamine*) 100 mg IV daily ($69)

C. auris isolated from noninvasive, nonsterile body sites

- Respiratory tract, skin, urine.
- CDC does NOT recommend treatment when there is no evidence of infection.
- Similar to recommendations for other *Candida* species
- Prevention of invasive infections
- May be increased risk for surgical site infections

Antibiotic stewardship may be important in the prevention of *C. auris* colonization.

Contact Precautions are recommended for patients colonized/infected with *C. auris*

- Gown and gloves must be worn on every room entry

Removal of Contact Precautions

1. Wait 3 months since last identification
2. Wait until patient is off antifungal medications for at least one week
3. Wait at least 48 hours after administration of topical antiseptic (e.g., chlorhexidine)
4. Culture the axilla and groin
5. In addition, culture and sites previously positive (e.g., urine)

- If positive, remain in contact precautions and re-evaluate in 3 months
- If negative, wait at least one week and repeat process.
  - Consider removing patient from contact precautions after 2 consecutive negative screenings

Focus on High-Touch Areas

- Bed and chair rails
- Sink and toilet
- Bedside tables
- Call light
- Remote control and phone

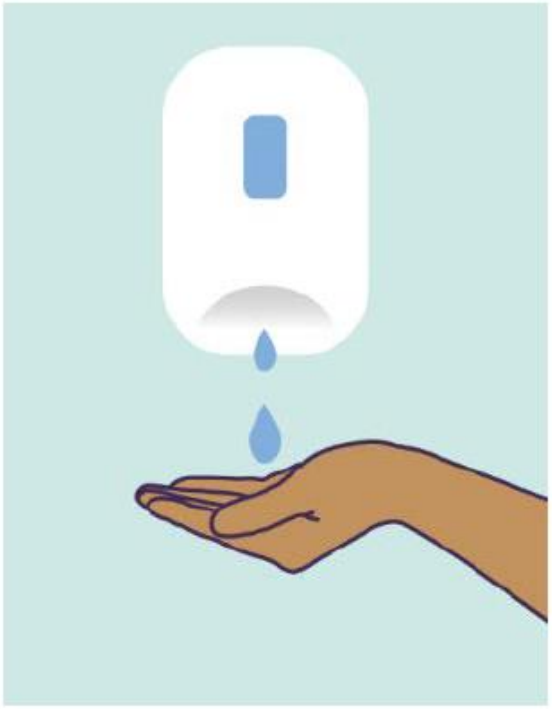
Recommended Infection Control Practices

- Standard and Contact Precautions
- Single room
- Daily and terminal cleaning of patient rooms with EPA-registered disinfectants effective against ***Clostridium difficile*** **spores**
- On transfer to another facility, notify and communicate level of precautions

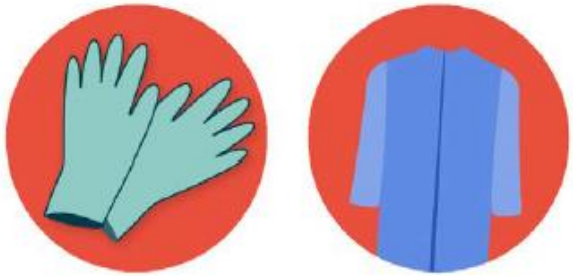
Colonization Screening: Close healthcare contacts

- Close healthcare contacts include:
  - Roommates
  - Patients whose care overlapped on the same unit with the index patient for at least three days
  - High acuity patients in the same unit
- Healthcare facilities should collaborate with public health as needed to conduct colonization screening

Facility Level Prevention Strategies: Back to Basics



Hand Hygiene



Personal Protective Equipment & Precautions

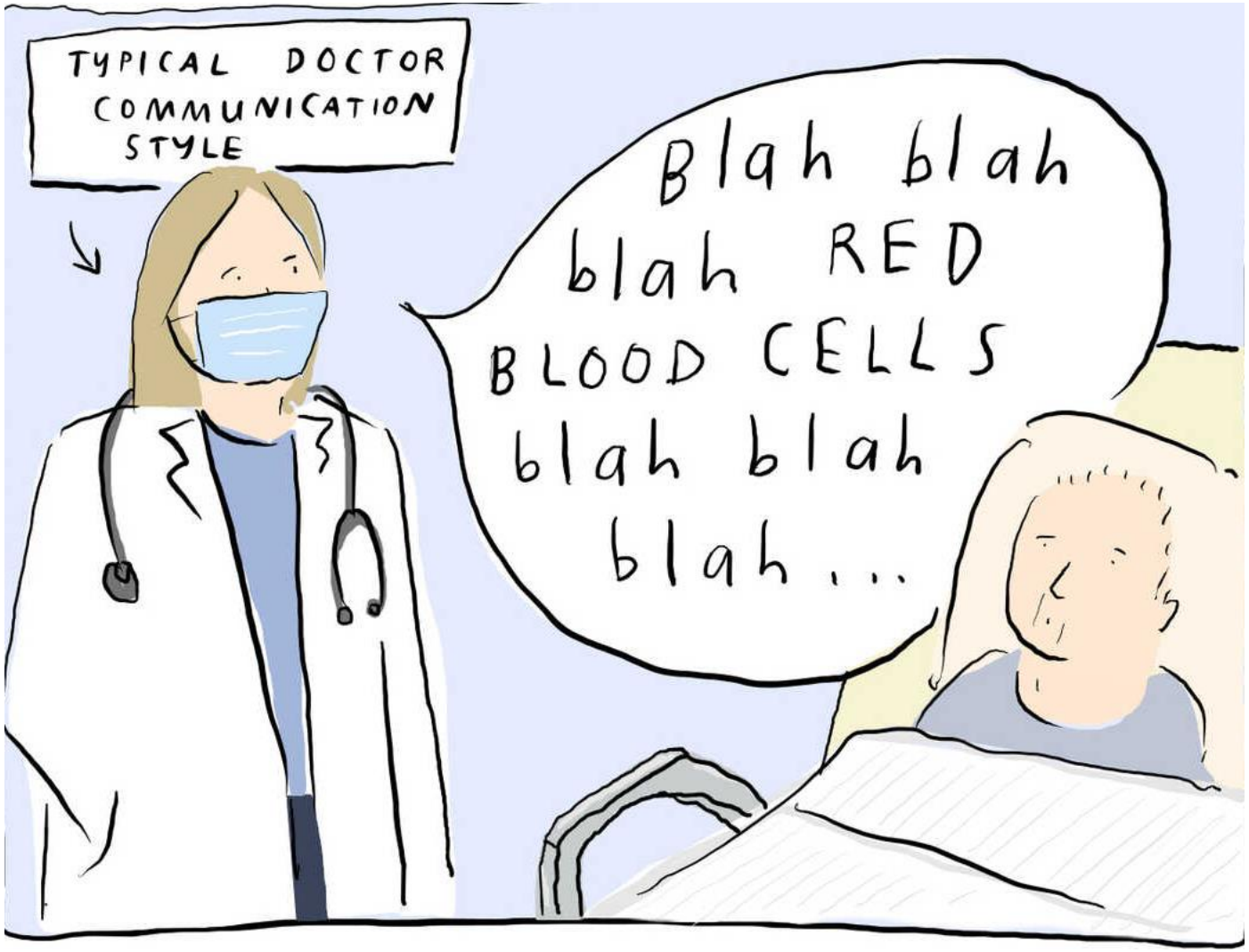
Environmental Cleaning & Disinfection

Environmental Cleaning and Disinfection

- Product must be active against *C. difficile* spores

- List K: EPA's Registered Antimicrobial Products Effective against *C. difficile* Spores: https://www.epa.gov/sites/production/files/2018-01/documents/2018.10.01.listk_.pdf

- Consider using across entire unit or facility if multiple residents screen positive for *C. auris*

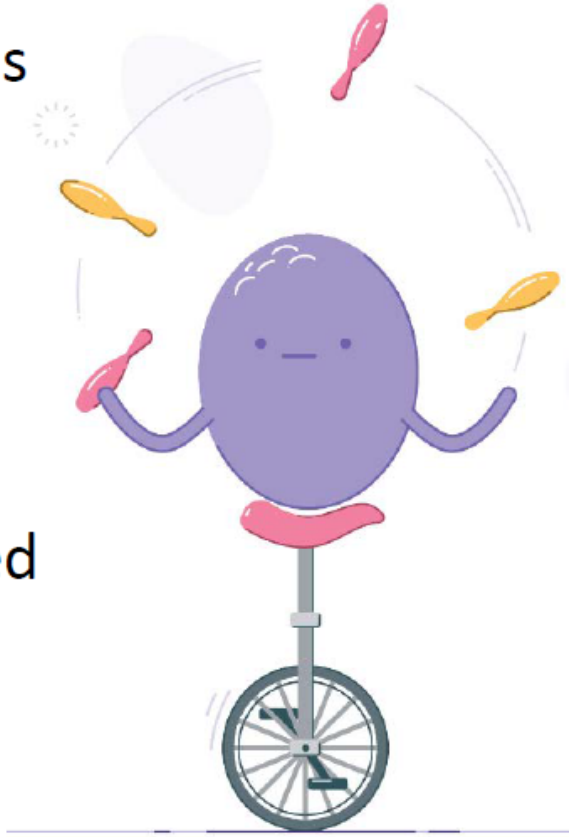

TYPICAL DOCTOR COMMUNICATION STYLE
Blah blah blah RED BLOOD CELLS blah blah blah...

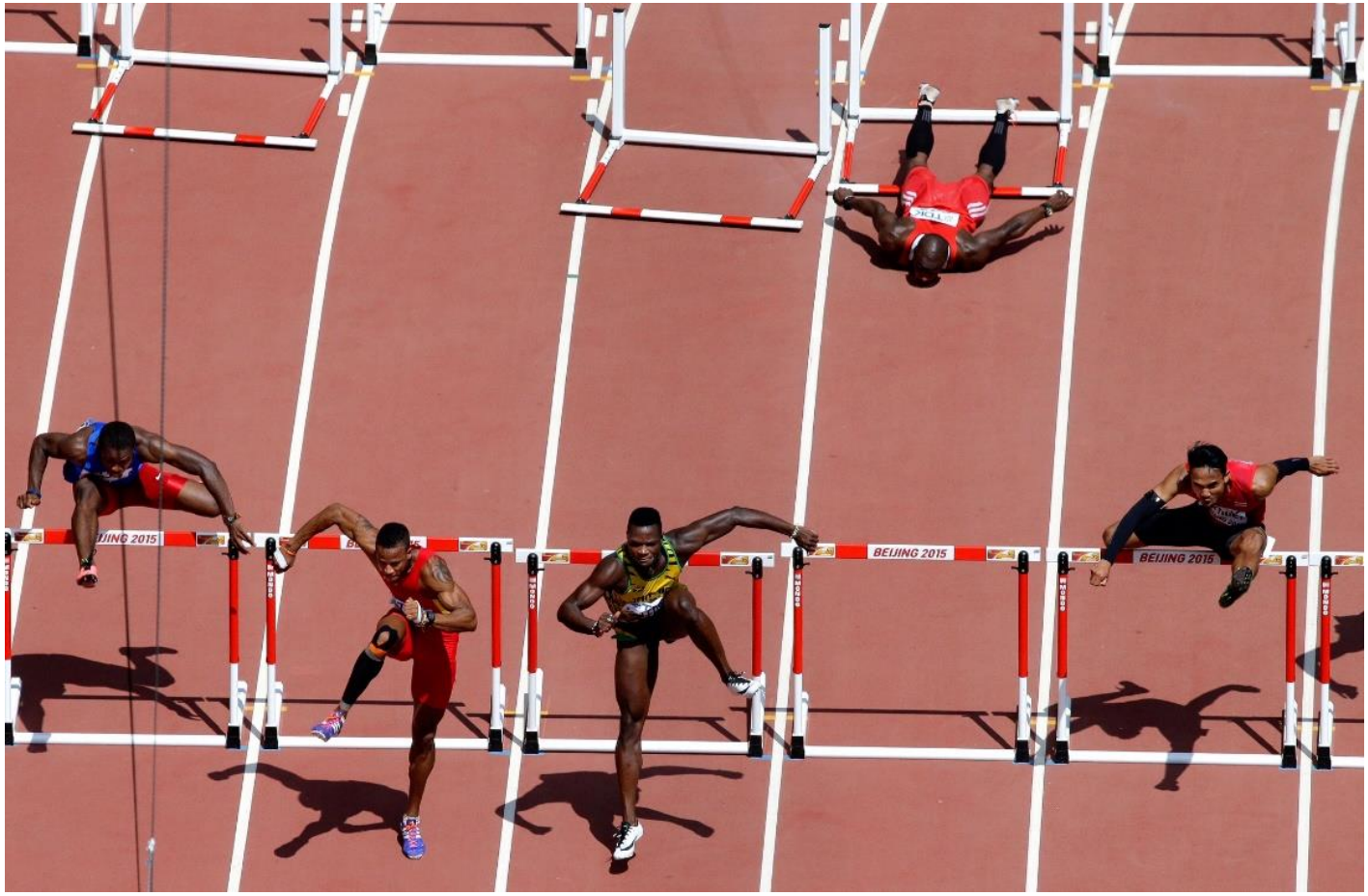
Containment steps when a case of *C. auris* is found

- Report the case to your local/state health department
- With health department, screen other patients who were in contact with the index patient to identify asymptomatically colonized individuals
- Infection control assessments to minimize transmission
- Meticulous prospective surveillance
- Health departments should assess other high risk facilities for patients asymptomatically colonized with *C. auris.*

It's new bug using old tricks

- Drug resistant, makes people sick, and spreads
- Similar to CRE, VRE, MRSA, and other drug resistant bugs
- We are still learning a lot about *C. auris*, but we also know how to control the spread of other similar germs
  - Many of the same principles can be applied to *C. auris*

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