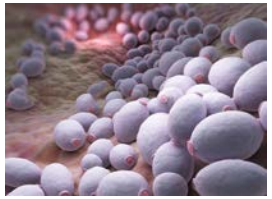
Laboratory Investigations of Multidrug-Resistant *Candida auris* – Impact & Lesson Learned

Sudha Chaturvedi, Ph.D.
Mycology Laboratory
Wadsworth Center

NEW YORK STATE | Department of Health | Wadsworth Center

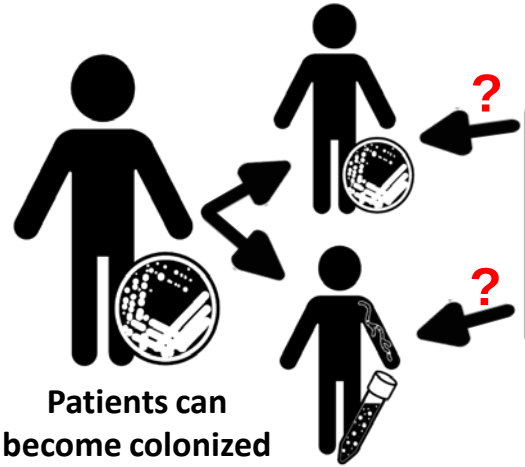
What do we know about *Candida*



***Candida* species**	***Candida auris***
• They are gut bugs	• Skin bug
• Mostly antifungal susceptible	• Mostly resistant to antifungals
• Rarely cause outbreak	• Frequently causing outbreaks

Why are we concerned about *Candida auris*?

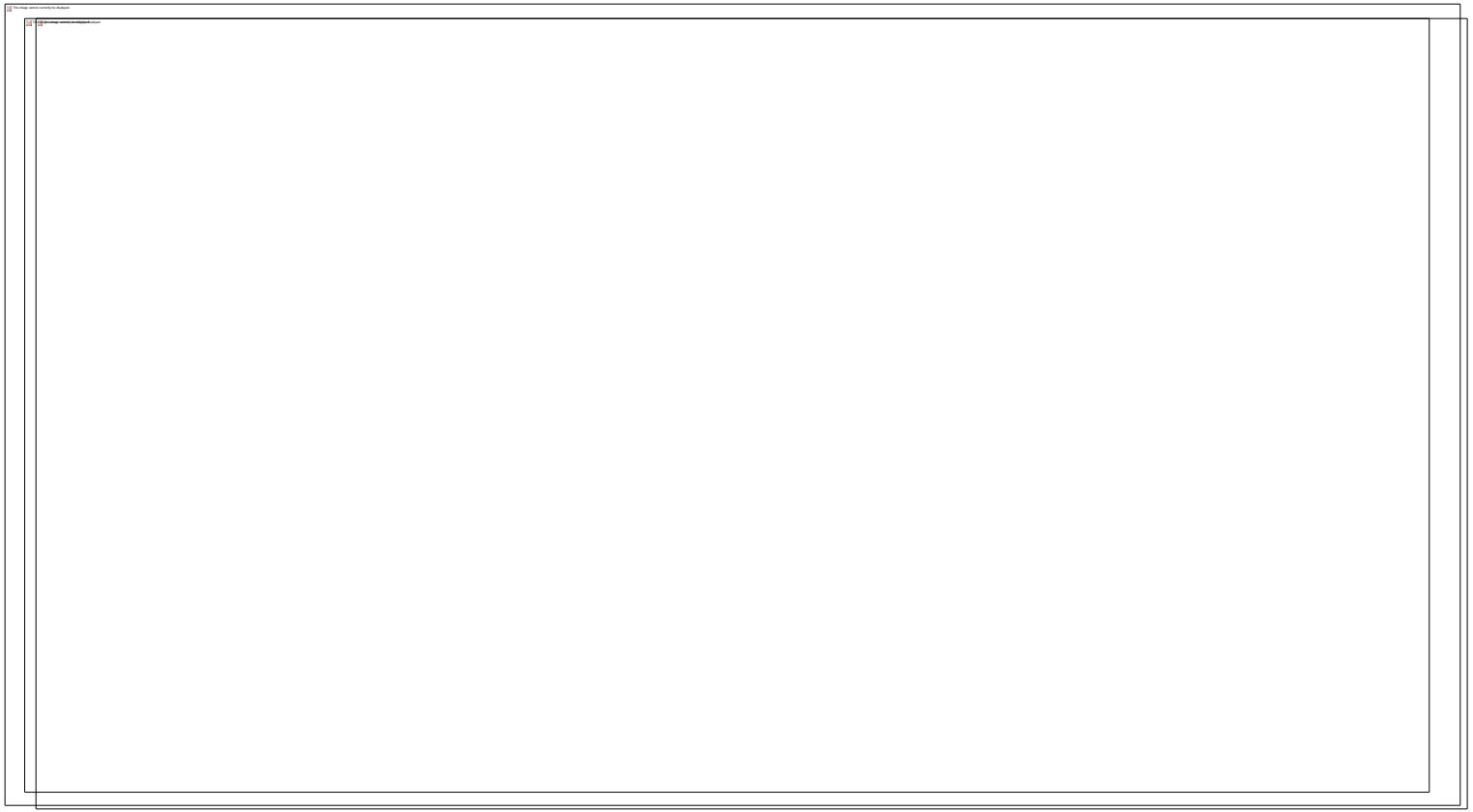
Highly drug-resistant



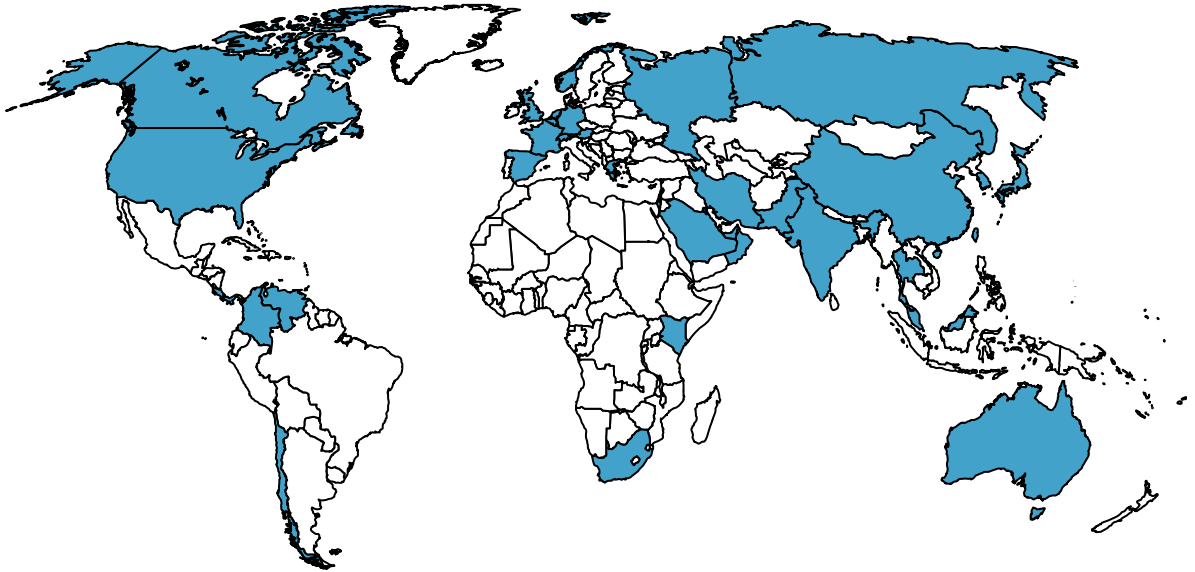
Patients can become colonized and develop invasive infections

Spreads in healthcare settings

NEW YORK STATE | Department of Health | Wadsworth Center

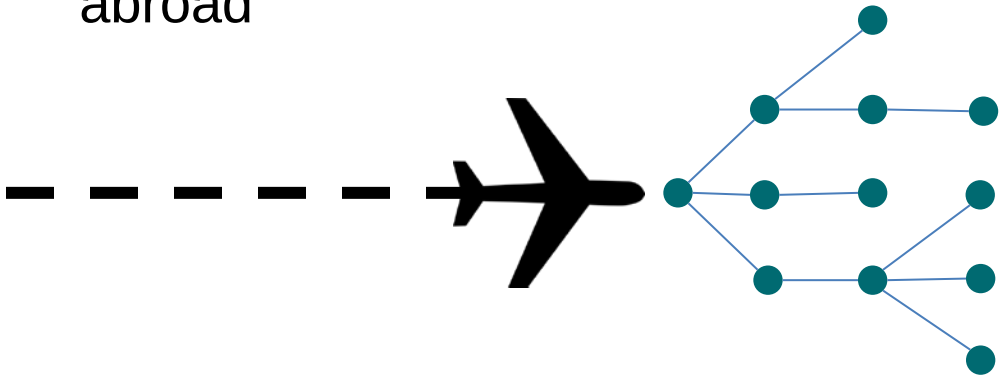


C. auris cases reported in >35 countries

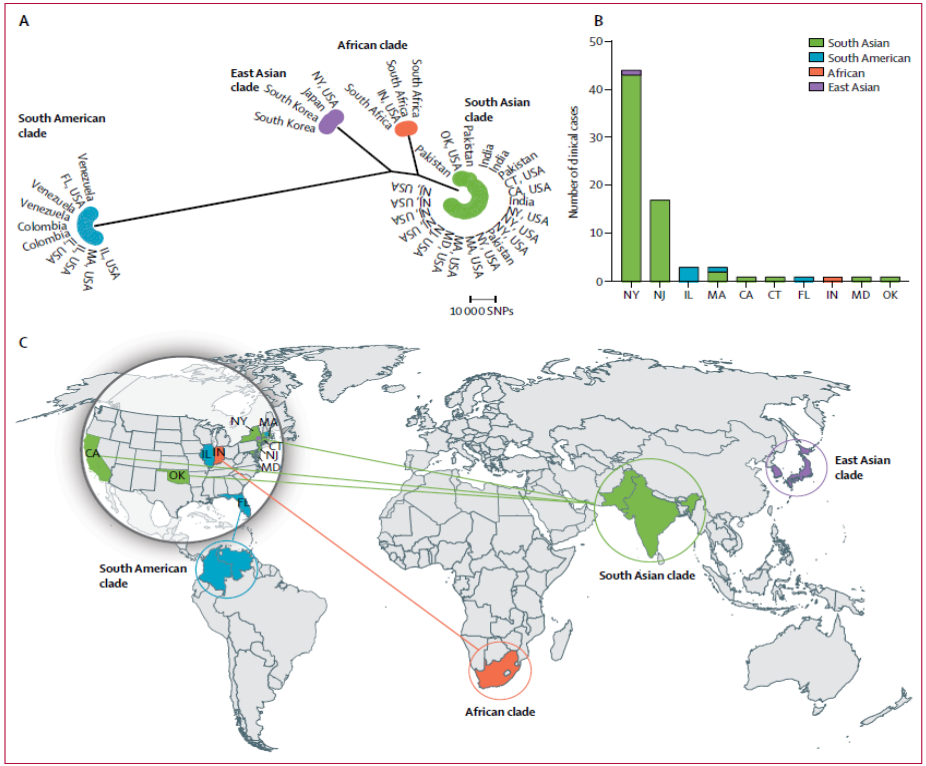


Spreads after introductions from abroad

- Cases are a result of introductions from abroad <u>followed by local transmission</u>
- Majority of cases don't have direct links to healthcare abroad



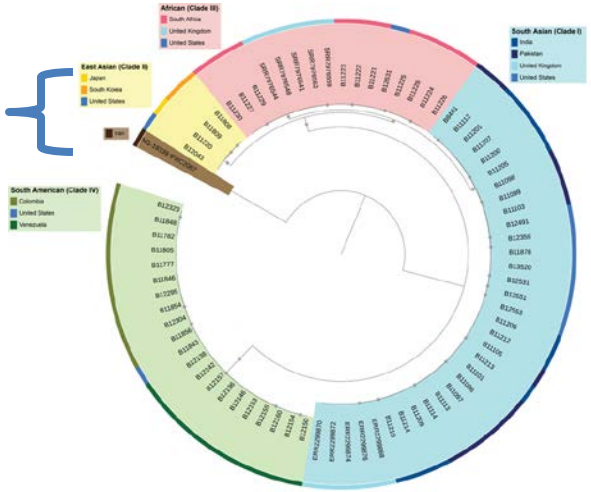
Four Genotypes/Clades



Chow NA et al Lancet ID 2018, 18:1377

Fifth Genotype/Clade

>200,000 SNPs apart



Chow NA et al Emerg Infect Dis 2019, 2019;25(9):1780-1781

NEW YORK STATE | Department of Health | Wadsworth Center

"All the News That's Fit to Print"

The New York Times

Late Edition

VOL. CLXVIII . . No. 58,290 NEW YORK, SUNDAY, APRIL 7, 2019 $6.00

Fungus Immune to Drugs Quietly Sweeps the Globe

Lethal Infection Adds Alarming Dimension to Dangers of Overusing Medicines

By MATT RICHTEL and ANDREW JACOBS

DEADLY GERMS, LOST CURES

A Near Public Health Threat

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

Fire Destroyed 10 Lives, but Not the Illusion

By TARIQ PANJA and MANUELA ANDREONI

RIO DE JANEIRO — Even in death the haggling went on.

Dreams of Soccer Riches Survive Brazil Disaster

SEARCH NEW YORK POST

Democrats' rush to the left is playing into Trump's hands

Breaking down why America hates Tom Brady and Gisele

BETSY MCCAUGHEY

OPINION

New York is Ground Zero for the deadliest super-bug yet

By Betsy McCaughey May 23, 2017 | 7:31pm

A slide with inactive Candida auris taken from a patient.

Patch Your town or ZIP code New York City Post | Advertise Log in

Mon, Feb 4 | 57°F | Nearby | Local News | Neighbor Posts | Lifestyle | Calendar | Real Estate Get Tickets

NEW YORK NEVER STOPS. NEITHER SHOULD ITS ENERGY.

Affordable and reliable. NATURAL GAS is an essential part of New York's energy mix.

ALWAYS ON NY

Health & Fitness

NYC 'Superbug' Outbreak Getting Worse: New Cases Reported At These City Hospitals

Candida auris is a deadly, drug-resistant fungus spreading within NYC hospitals. More than 50 cases have been reported in the past year.

By Simone Wilson, Patch Staff | May 23, 2017 4:12 pm ET | Updated May 24, 2017 12:26 pm ET

DEADLY GERMS, LOST CURES

A Mysterious Infection, Spanning the Globe in a Climate of Secrecy

The rise of Candida auris embodies a serious and growing public health threat: drug-resistant germs.

By Matt Richtel and Andrew Jacobs

April 6, 2019

1635

Leer en español

Last May, an elderly man was 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.

NEW YORK STATE Department of Health | Wadsworth Center

Wadsworth Center Laboratories
Division of Infectious Diseases

- Arbovirology
- Bacteriology
- Biodefense
- Bloodbore Viruses
- Cellular Immunology
- Diagnostic Immunology
- Mycobacteriology
- Mycology
- Parasitology
- Rabies
- Virology

Hazen & Brown (1955)
NYSTATIN

Morris Gordon

Cryptococcal antigen test
1963

NEW YORK STATE Department of Health | Wadsworth Center

Mycology Laboratory @ Wadsworth Center: Scope

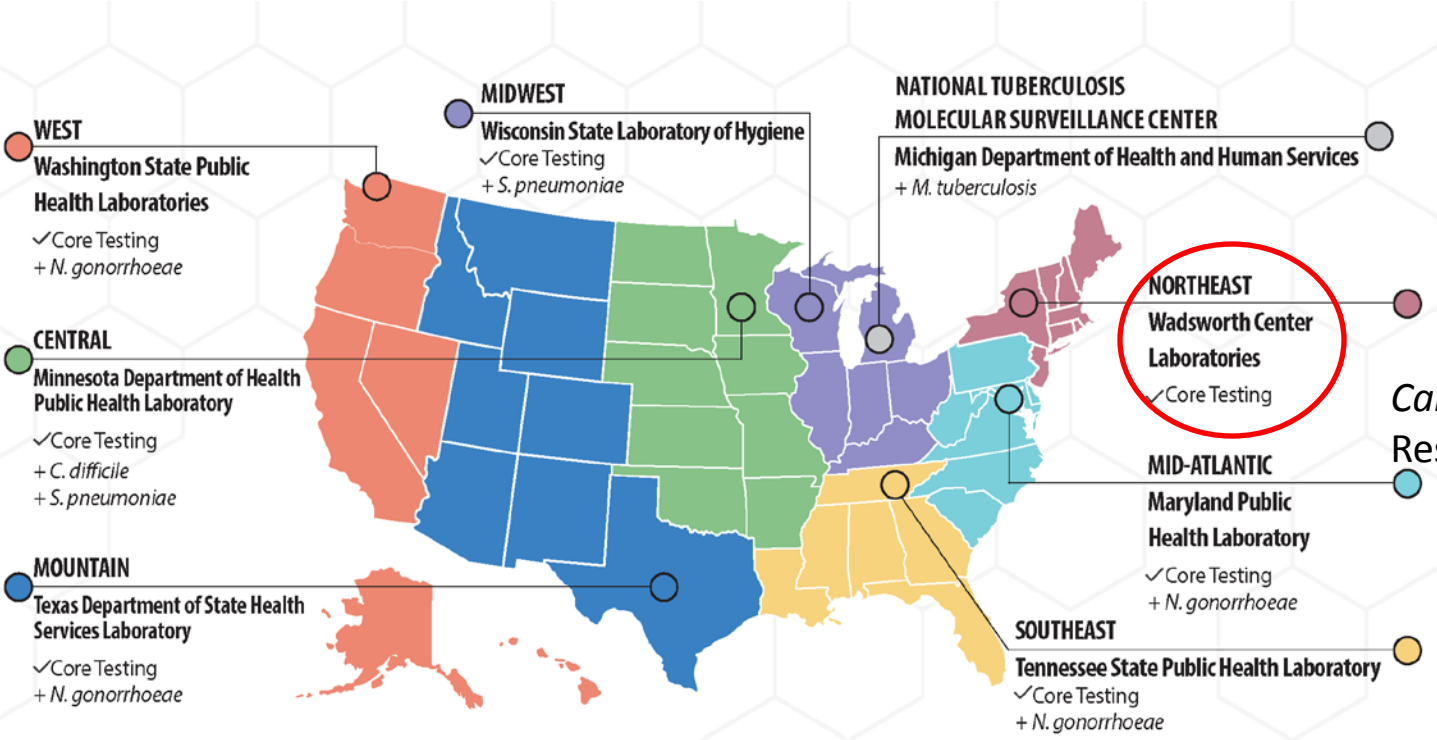
- **Reference Services (Fungal ID)**
  - Culture
  - MALDI-TOF MS (Bruker) - 2013
  - ITS-PCR/Sequencing - 2010
  - Antifungal Susceptibility Testing (2000)
    - E-test (Yeasts)
    - Microbroth Dilution (Yeasts & Molds)
    - YO9 (Yeasts)
  - Real time PCR assays:
    - *Coccidioides immitis/posadasii* (2015)
    - *Histoplasma capsulatum* (2011)
    - *Blastomyces dermatitidis* (2011)
    - *Exserohilum rostratum* (2013)
    - *Candida spp.* (2016)

1,100 to 1,300 Samples/Year (99.9% isolates)

- **Applied Research**
  - Fungal virulence mechanisms (NIH)
  - Antifungal test innovation – (Industry Contracts)
  - Molecular Test Development (WC CLRS)
  - *Pseudogymnoascus* ('Bat White-Nose') (NSF & FWLS)

NEW YORK STATE | Department of Health | Wadsworth Center

CDC–Antibiotic Resistance Laboratory Network (2016…)



Mycology Lab

↓

Candida (glabrata) Resistance Testing

NEW YORK STATE | Department of Health | Wadsworth Center

What did we find?

Unprecedented outbreak of *Candida auris* in NY

What did we do?

180 degree turn around and re-focus

- Writeup of protocols for shipping instructions, sample processing, report release, etc.
- Writeup of advisories with Epi to educate healthcare professionals on *C. auris*
- Enrichment of in-house MALDI library for *C. auris* ID
- Molecular assay development for rapid *C. auris detection* from surveillance samples
- Provid SOPs - *C. auris* culture, MALDI & real-time PCR to Clinical/ Public/Private Laboratories in NY and other states in the US
- Weekly/bi-weekly/monthly conference calls/meetings with NYSDOH Epi/ CDC/WC
- Staff recruitment

Culture/Identification - *C. auris* Surveillance Samples

Laboratory Workflow Pre-PCR Era

Surveillance Samples (Swabs & Sponges)

8/26/16

3/3/17)

Welsh et al, 2017. JCM, 55:2996

Non Selective Agar (SAB+)

Selective Agar (Salt + Dextrose → Dulcitol)

Selective Broth (Salt + Dulcitol)

Growth

Growth

No Growth

Cloudy

MALDI

MALDI

SAB+

***Candida auris* & *Candida* spp.**

Candida auris

Negative culture

No Growth

Growth

MALDI

Candida auris

Sanger Sequencing for Phylogenetic analysis

Antifungal susceptibility testing for resistance profile

Culture + ID = 4 to 14 days

Total Number of Samples Processed (August 2016 to April 2019)

Clinical Isolates suspected of *C. auris*	= 746
Surveillance (Patient)	= 9,676
Surveillance (Environmental)	= 4,123
Admission Screening	= 4,871
Total	= 15,453

Swabs

Sponges

NEW YORK STATE Department of Health | Wadsworth Center

Surveillance Sample Testing Strategies

Axilla, Groin, Nares (August 2016)
Axilla/Groin & Nares (November 2016)
Nares/Axilla/Groin (January 2018)

Point Prevalence Screening

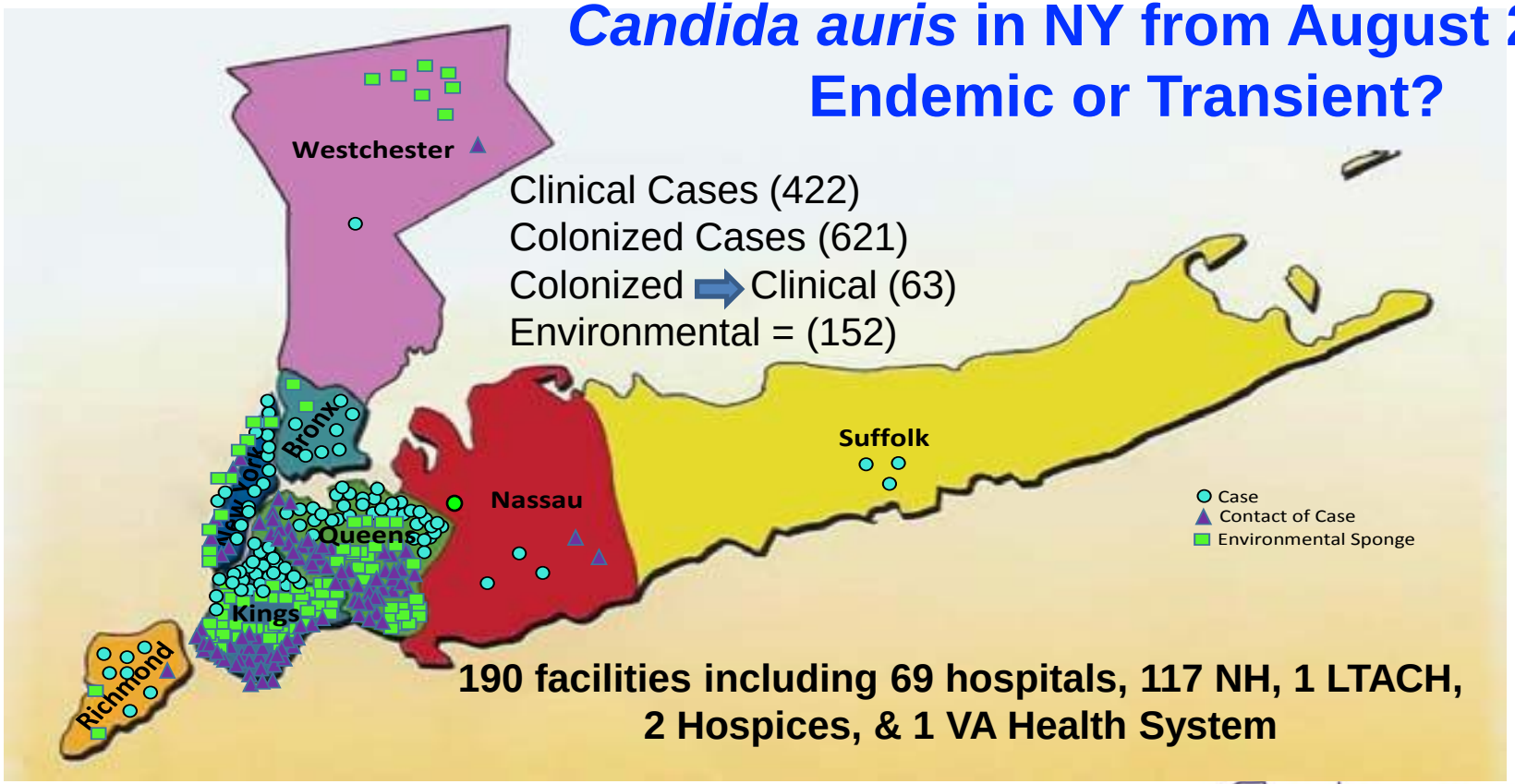
Swabs

Surveillance Samples (11,035)

931+ve for *C. auris* (8.4%)

NEW YORK STATE Department of Health | Wadsworth Center

Candida auris in NY from August 2016... Endemic or Transient?

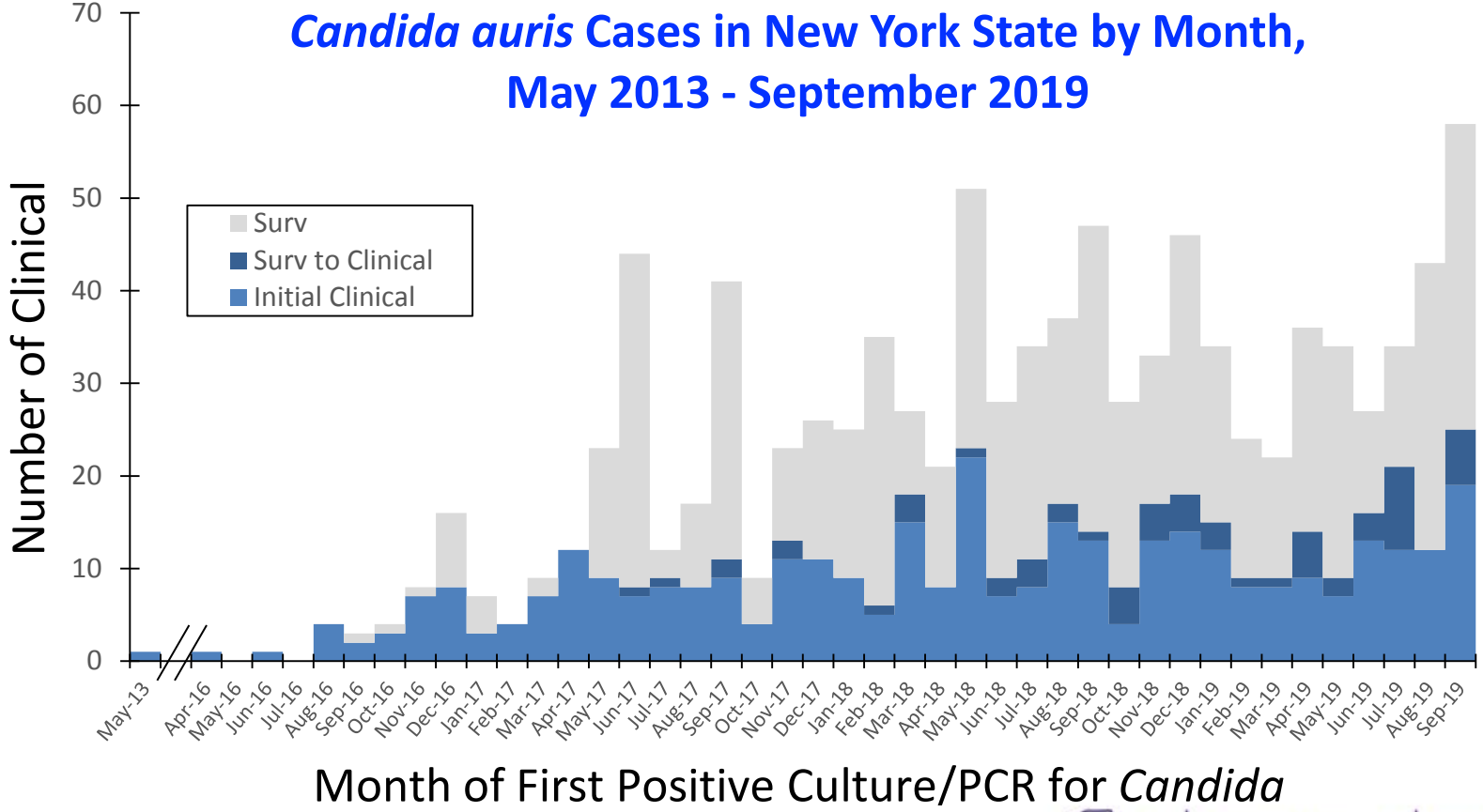


Clinical Cases (422)
Colonized Cases (621)
Colonized ➡ Clinical (63)
Environmental = (152)

190 facilities including 69 hospitals, 117 NH, 1 LTACH, 2 Hospices, & 1 VA Health System

NEW YORK STATE | Department of Health | Wadsworth Center

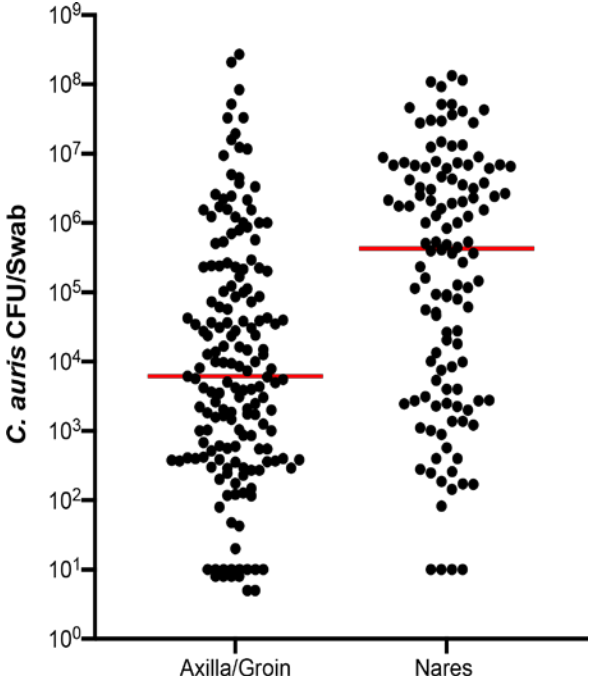
Candida auris Cases in New York State by Month, May 2013 - September 2019



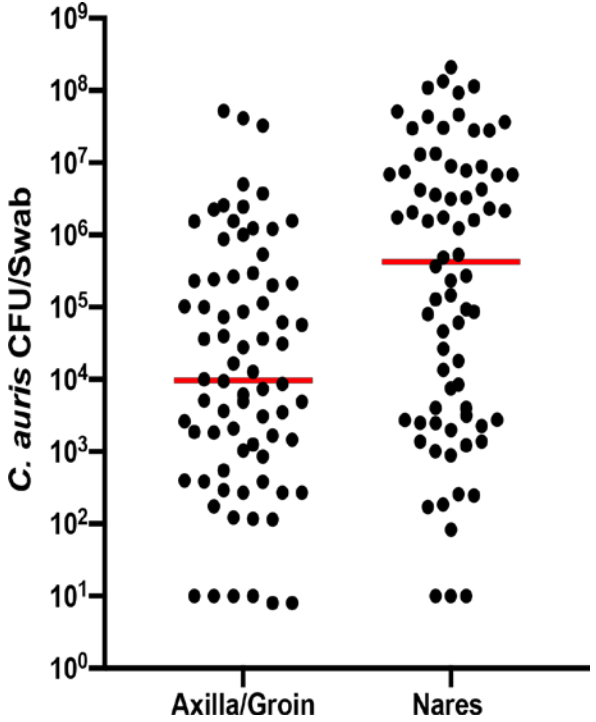
C. haemulonii → *C. auris*

NEW YORK STATE Department of Health | Wadsworth Center

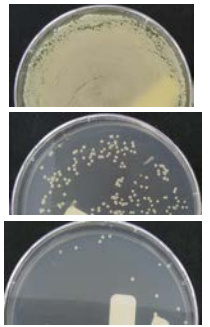
Heavy Colonization of Skin & Mucosa of 350 Colonized Cases



Unpaired Samples

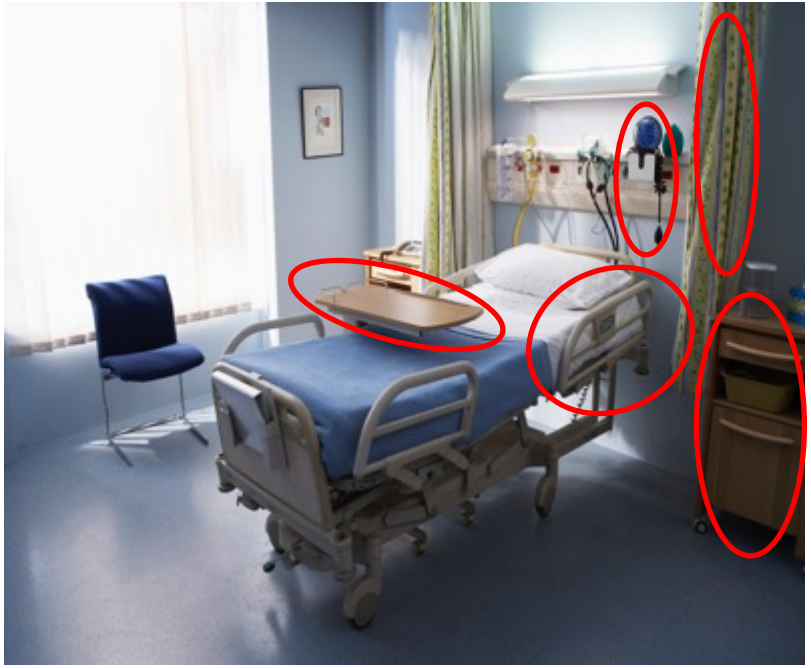


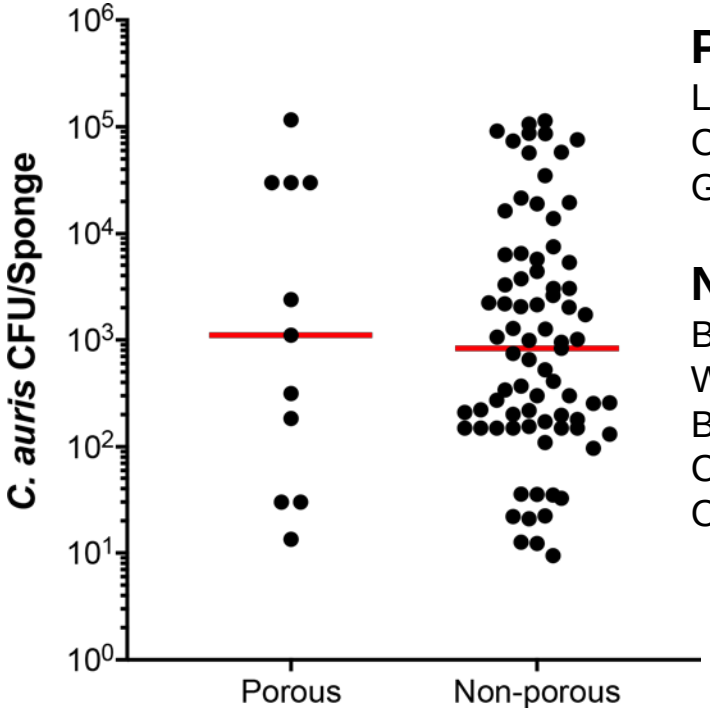
Paired Samples



NEW YORK STATE Department of Health | Wadsworth Center

Heavy Colonization of Hospital Surfaces

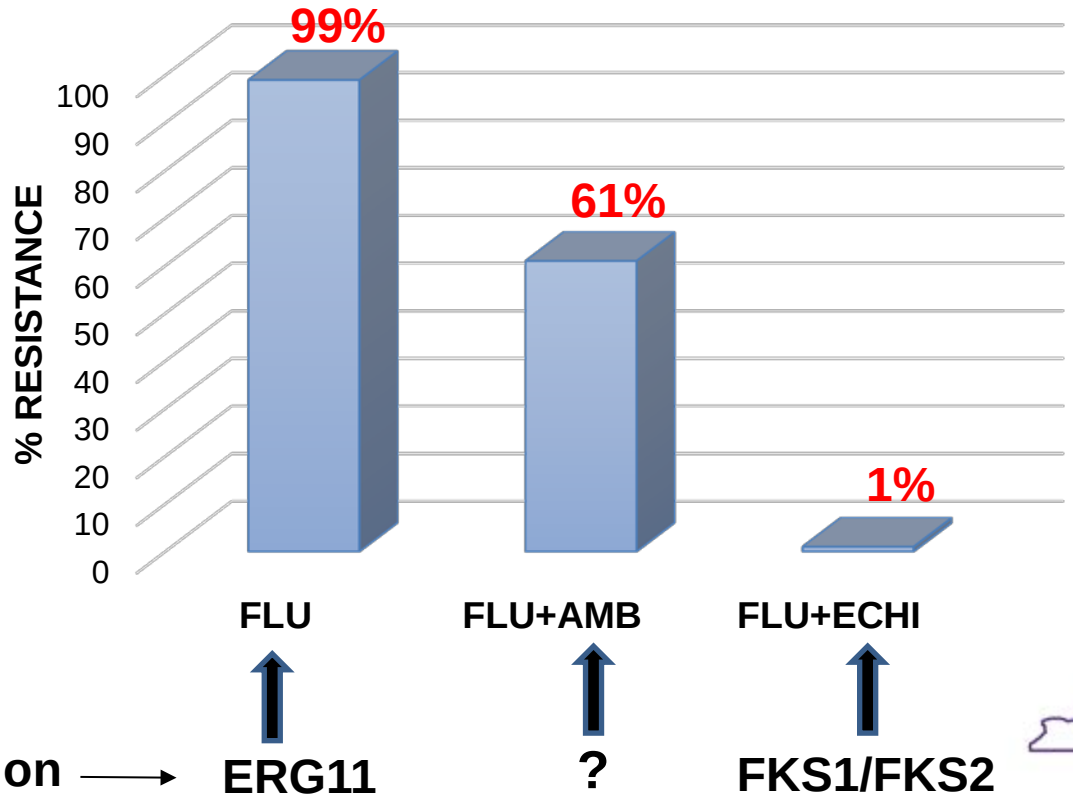




Porous
Linen
Carpet
Gowns

Non-porous
Bed rail
Window sill
Bathroom surface
Call bell
Counter top

Antifungal Resistance Pattern of NY *C. auris* isolates



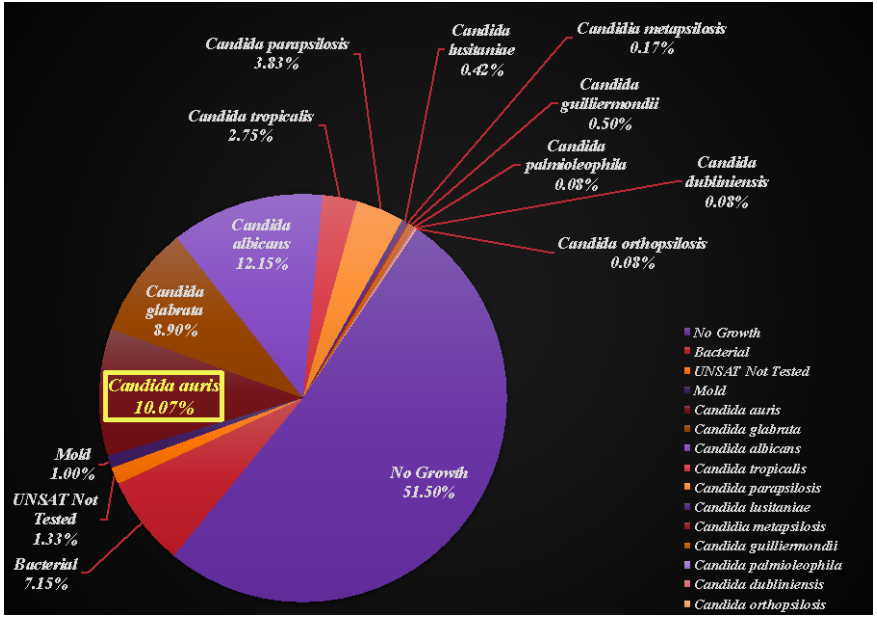
FLU = Fluconazole
AMB = Amphotericin B
ECHI = Echinocandins

Pan Resistant Isolates = 3

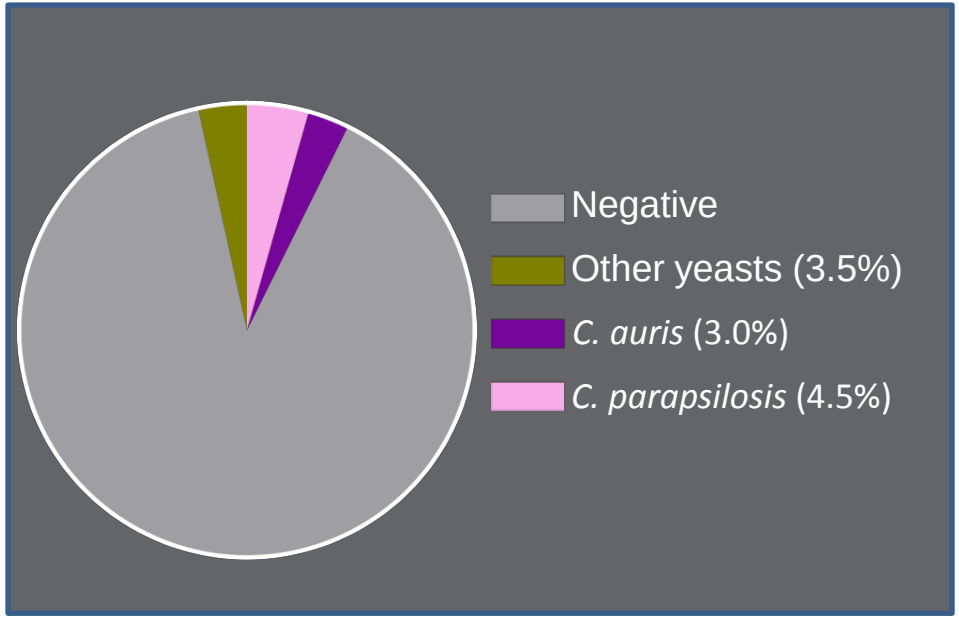
NEW YORK STATE Department of Health | Wadsworth Center

Candida auris Prevalence

Patients



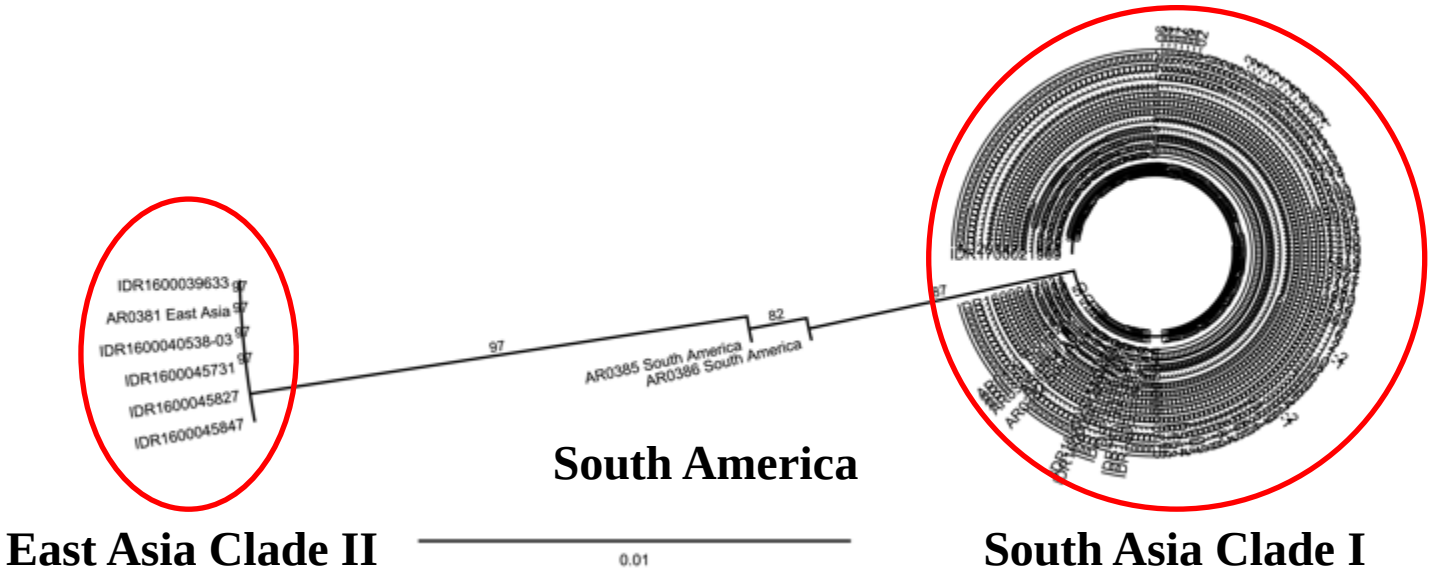
Environment



NEW YORK STATE Department of Health | Wadsworth Center

NY Outbreak is dominated by South Asia Clade I

Sanger Sequencing of Ribosomal genes



AMERICAN SOCIETY FOR MICROBIOLOGY | Journal of Clinical Microbiology®

MYCOLOGY

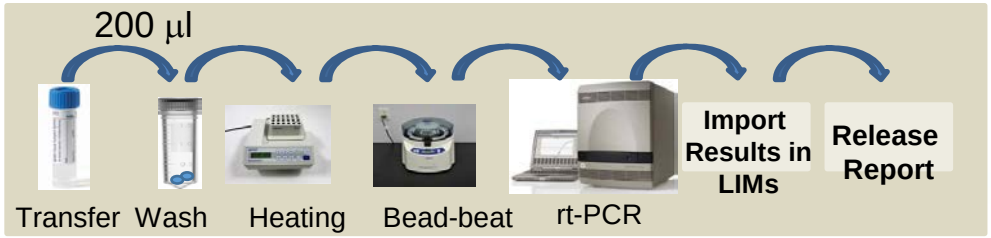
Development and Validation of a Real-Time PCR Assay for Rapid Detection of *Candida auris* from Surveillance Samples

L. Leach,[a] Y. Zhu,[a] S. Chaturvedi[a,b]

[a]Mycology Laboratory, Wadsworth Center, New York State Department of Health, Albany, New York, USA
[b]Department of Biomedical Sciences, School of Public Health, University at Albany, Albany, New York, USA

Jan 2018

- Highly Sensitive (one *C. auris* CFU/PCR reaction)
- Highly Specific (No cross-reaction to yeasts/molds/bacteria/parasites)
- Rapid (4 h)
- Drawback- Manual nature of the assay

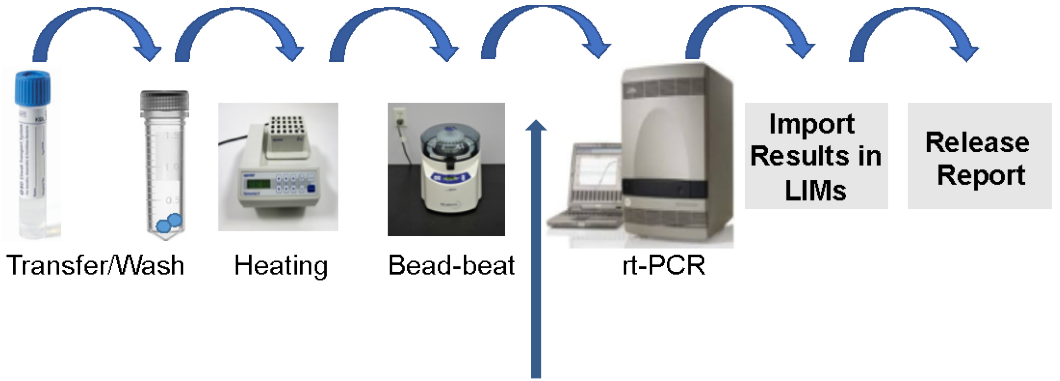


NEW YORK STATE Department of Health | Wadsworth Center

Bruker Expands Portfolio for Testing of Candida Auris, an Emerging, Multidrug-Resistant Pathogen in Human Healthcare

July 2018

Fungiplex *Candida Auris* RUO Real-Time PCR Kit



Leach et al 2018, JCM, 56:E01223-17

NEW YORK STATE Department of Health | Wadsworth Center

Mycoses. 2019 Feb 23. doi: 10.1111/myc.12907. [Epub ahead of print]

CDC

A high-throughput and rapid method for accurate identification of emerging multidrug-resistant Candida auris.

Ahmad A[1], Spencer JE[1], Lockhart SR[2], Singleton S[2], Petway DJ[1], Bagarozzi DA Jr[1], Herzegh OT[1].

MagNa Pure
DNA automation

Heating

Bead-beat

rt-PCR

Import Results in LIMs

Release Report

NEW YORK STATE Department of Health | Wadsworth Center

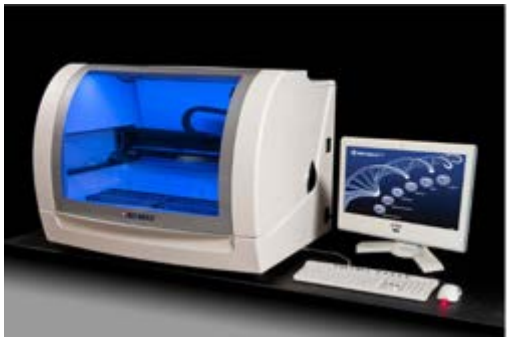
AMERICAN SOCIETY FOR MICROBIOLOGY | Journal of Clinical Microbiology®

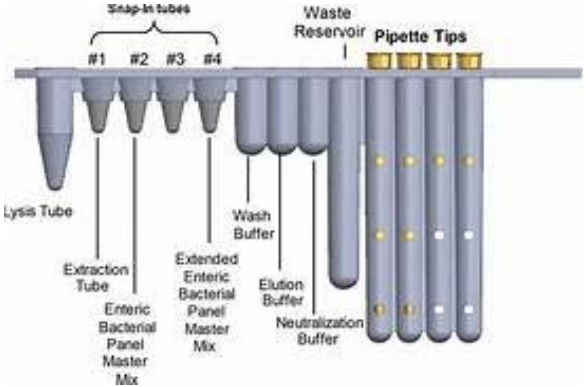
Sept 2019

Mycology

A Rapid and Automated Sample-to-Result *Candida auris* Real-Time PCR Assay for High-Throughput Testing of Surveillance Samples with the BD Max Open System

L. Leach, A. Russell, Y. Zhu, S. Chaturvedi, V. Chaturvedi





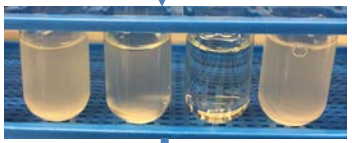
Sensitivity = One *C. auris* CFU/PCR Reaction
TAT = 2 h
Total samples = 100-150 samples/Day

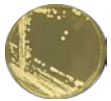
NEW YORK STATE | Department of Health | Wadsworth Center

Modified Workflow Post PCR Era

PCR

- **Negative** → No Further Test
- **Positive** → Culture (Dulcitol Broth)





MALDI

C. auris

Significant cut down on

- **Efforts**
- **Supplies**
- **$ amount**

NEW YORK STATE | Department of Health | Wadsworth Center

Testing doesn't end with real-time PCR assay!

- Need *C. auris* isolate with confirmed ID to do antifungal susceptibility testing, genotyping, etc.

Bruker MALDI-TOF MS – FDA approved database April 2018
http://www.cidrap.umn.edu/news-perspective/2018/04/fda-approves-rapid-diagnostic-test-candida-auris

bioMérieux VITEK MS - FDA approved database December 2018
https://www.rapidmicrobiology.com/news/new-fda-clearance-for-vitek-ms-expanded-id-for-challenging-pathogens

Continuing Challenges

- Mycology training/re-training needed in Clinical, Public Health & Commercial Laboratories
- Availability of selective medium (Dulcitol) is restricted to one vendor https://s2cm.com/product/salt-sabouraud-dulcitol-broth-ssdb/
- LDT for *C. auris* is not FDA approved
- MALDI-TOF MS expensive technology-not easily available
- AST – 50% inhibition by naked eye –need extensive practice

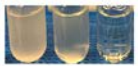
NEW YORK STATE OF OPPORTUNITY | Department of Health | Wadsworth Center


ARLABnetwork


Antimicrobial Resistance Laboratory Network

Northeast Regional *Candida auris* Training Workshop

Wadsworth Center – Mycology Laboratory
Albany, NY
November 4 - 5, 2019

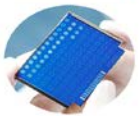



Swab and Sponge Testing
by PCR and Culture

Antifungal Susceptibility Testing
by Microbroth and E-test

MALDI-TOF MS Identification of Yeasts

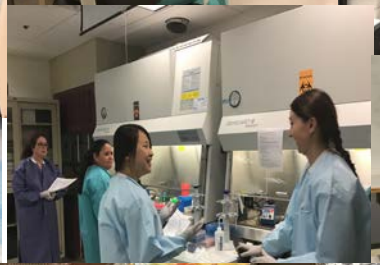
Packaging and Shipping of Surveillance Samples










Offered by: New York State Department of Health-Wadsworth Center Mycology Laboratory
And: Association of Public Health Laboratories (APHL)

This project was funded with federal funds from a federal program. This training material was supported by Cooperative Agreement # NU50CK000516 from Centers for Disease Control and Prevention (CDC) and Association of Public Health Laboratories (APHL). Its contents are solely the responsibility of the authors and do not necessarily represent the official views of CDC.

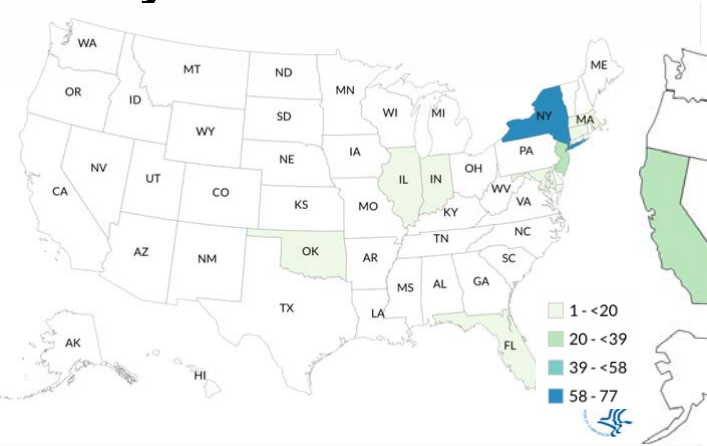
NEW YORK STATE | Department of Health | Wadsworth Center

SUMMARY

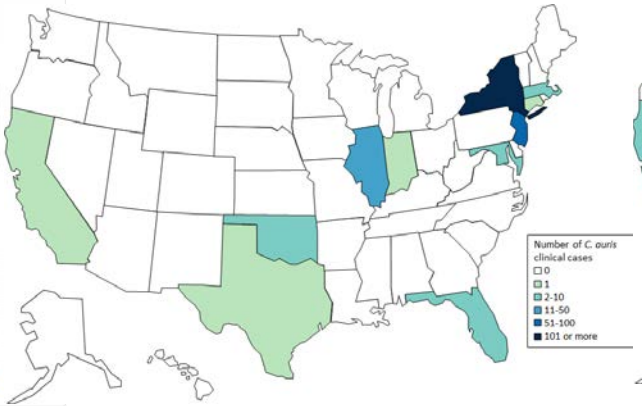
- Total Surveillance samples tested 20, 661 including 15, 026 point prevalence (10,521 swabs & 4,505 sponges), & 5,635 admission screening
- Clinical cases 422 & colonized cases 623 as of November 5, 2019. Approximately 10% of colonized cases converted into clinical, a major concerning factor.
- Successful use of one swab of Nares/Axilla/Groin for all PPS (January 2018)
- Development of PCR assays (manual & automated) and their impact on infection control practices
- Relatively heavier colonization of nares than axilla/groin
- Predominance of South Asia Clade I
- Isolation of three Pan-resistant isolates

Candida auris in the U.S.

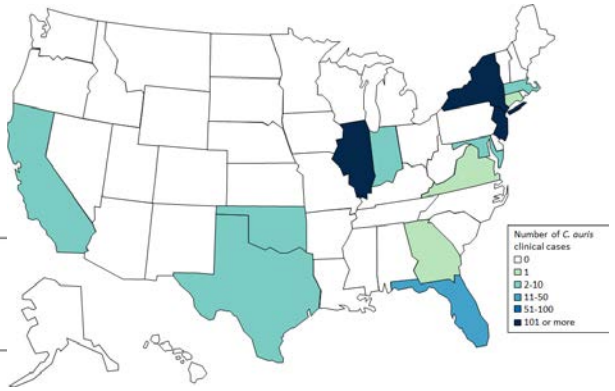
May 2017



July 2018

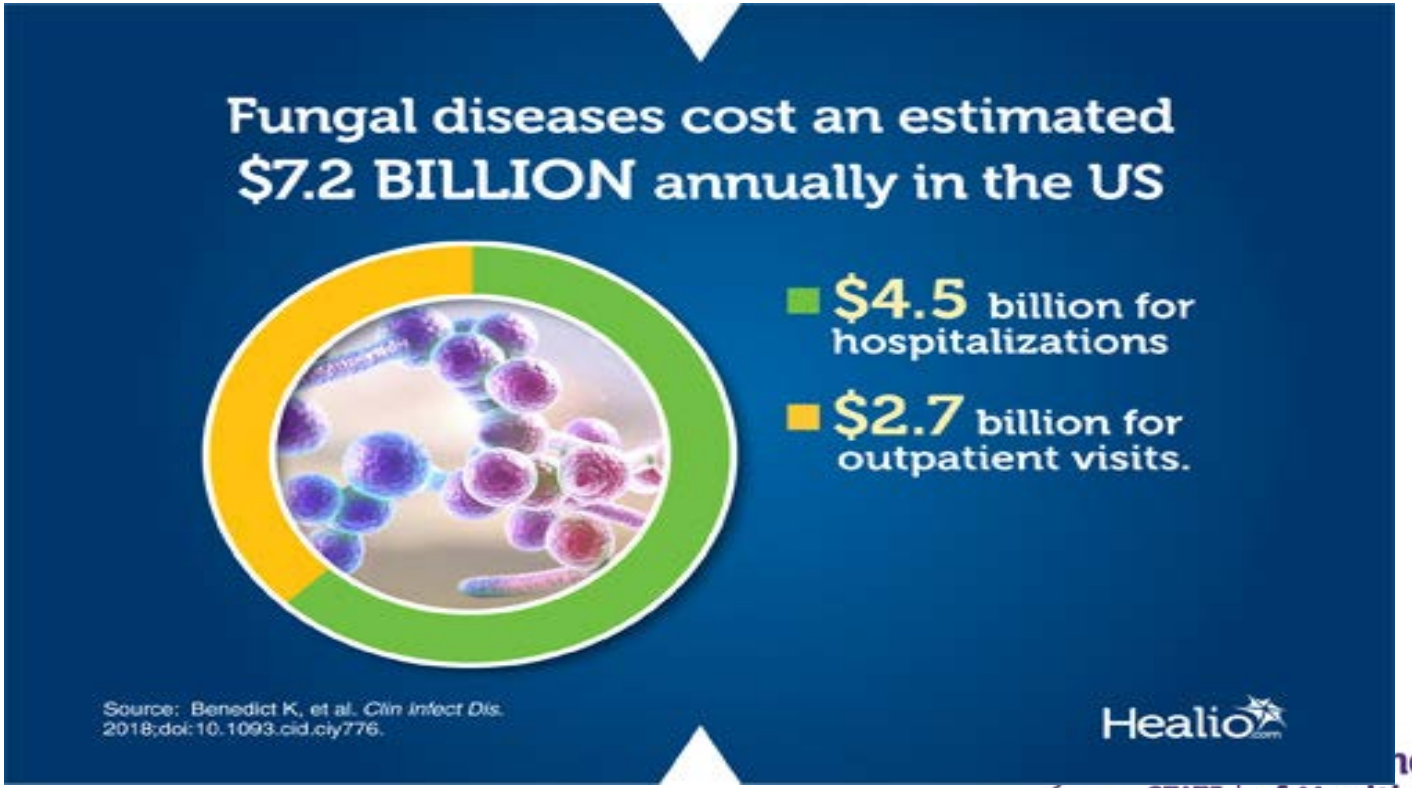


July 2019



NEW YORK STATE | Department of Health | Wadsworth Center

Think Fungus



Acknowledgements

WC Mycology Lab Staff

Current

YanChun Zhu
Lynn Leach
Brittany O'Brien
Rokebul Anwar
Jiali Liang

Dr. Vishnu Chaturvedi

Past

Alexis Russell
Samantha Frye (MLS student)
Alexandra Clarke
Ayodele Ojebode (APHLFellow)
Dr. Amanpreet Singh

Other Staff

Geetha Nattanmai
Tom Miller
Sara Griesemer
Amy Chiefari
Mark Meola

HAI (NYSDOH)

Ms. Monica Quinn
Dr. Eleanor H. Adams
Dr. Emily C. Lutterloh
Dr. Elizabeth Dufort
Dr. Karen Southwick
Ms. Coralie Bucher
Mr. Brad Hutton
Dr. Nina Ahmad
Dr. Belinda Ostrowsky
MARO Staff

CDC

Dr. Sharon Tsay
Dr. Snigdha Vallabhaneni
Dr. Shawn Lockhart
Dr. Tom Chiller
Dr. Rory Welch

Funding

CDC-ARLN
WC-CLRS

Dr. Ron Limberger
Dr. Jill Taylor

Media, Tissue Culture & Sequencing Cores

NEW YORK STATE | Department of Health | Wadsworth Center