



**Department
of Health**

***Candida auris* in New York State Healthcare Facilities: An Update for Laboratory Staff**

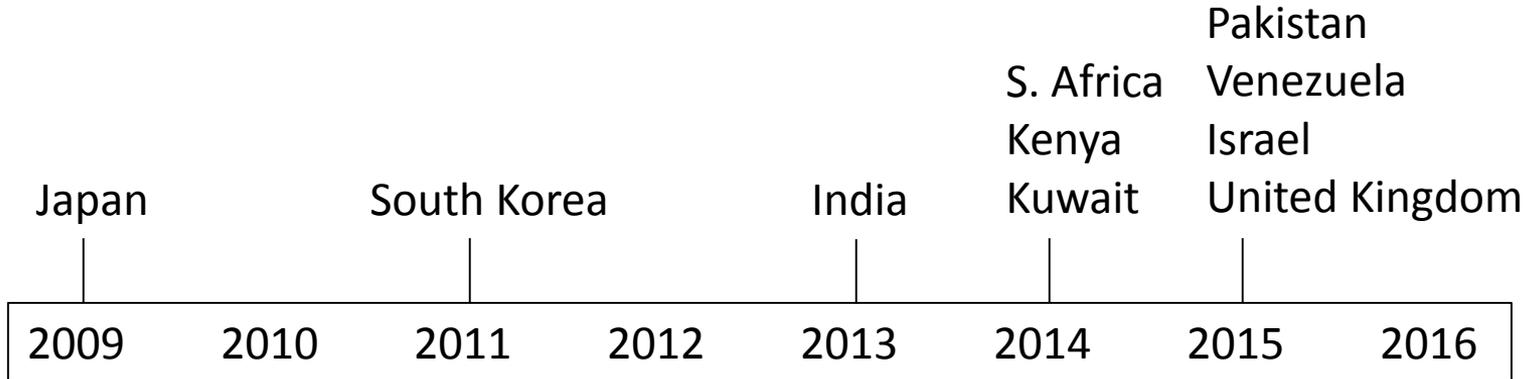
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Director, Bureau of Healthcare Associated Infections
Division of Epidemiology
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Outline

- Background
- Emergence in New York State
- Infection control
- Identifying and reporting *C. auris*
- NYSDOH prevention and control activities

Background

Rapid Emergence Since 2009



C. auris around the World

- Lockhart 2016: 54 isolates from Pakistan, India, South Africa, Venezuela, and Japan
 - Susceptibility testing
 - 93% resistant to fluconazole, 54% to voriconazole, 35% to amphotericin B, 7% to echinocandins, 6% to flucytosine
 - 41% resistant to ≥ 2 classes, 2 isolates resistant to 3 classes
 - Whole genome sequencing
 - 4 clades: South Asia, South Africa, South America, East Asia
 - Minimal differences among isolates within a geographic cluster
 - Suggests simultaneous emergence rather than spread
 - Surveillance
 - SENTRY: 15,271 Candida isolates 2004-2015, four *C. auris* identifications after 2009

Reasons for Concern

- Challenging to identify
 - MALDI-TOF or sequencing required to correctly identify *C. auris*
- Often multi-drug resistant
 - Usually resistant to fluconazole
 - Variable susceptibility to other azoles, amphotericin B, and echinocandins
 - Some have been resistant to all 3 classes of antifungal medications
- Transmitted within healthcare facilities
 - Outbreaks in multiple countries
 - Persistent colonization
 - Survives for long periods in the hospital environment

Emergence in New York State

Case Counts as of August 25, 2017

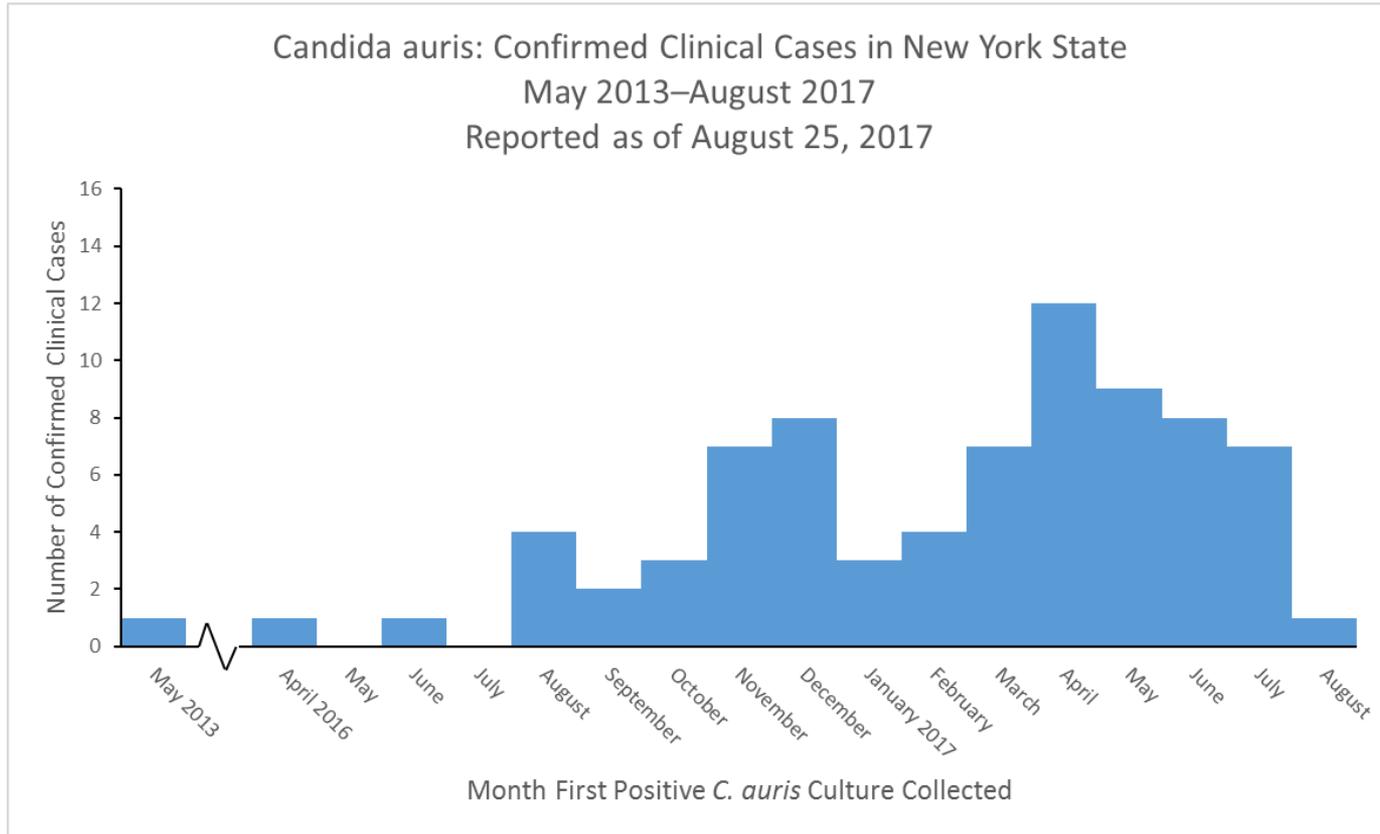
- 78 clinical cases
- 72 screening cases
- 4 probable cases

- All infected persons had other serious medical conditions

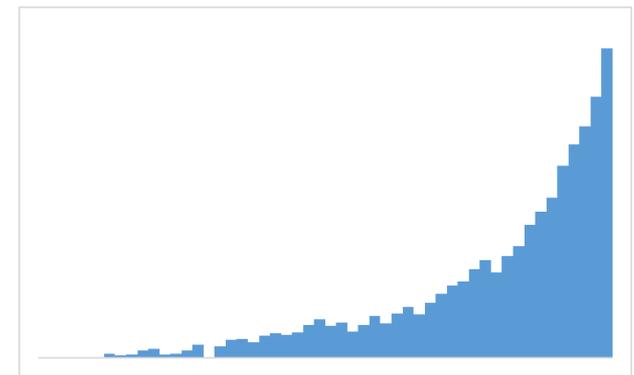
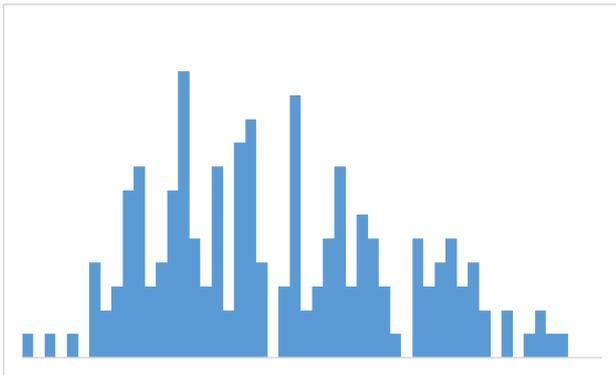
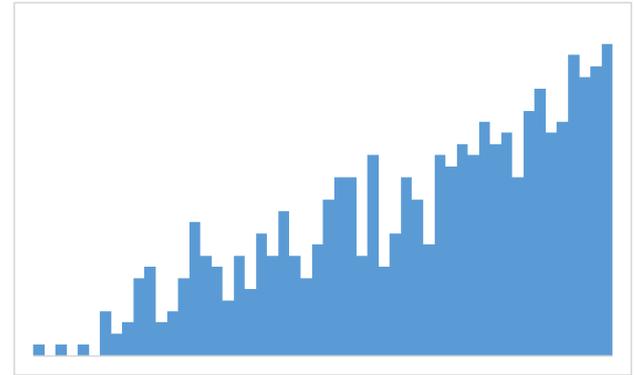
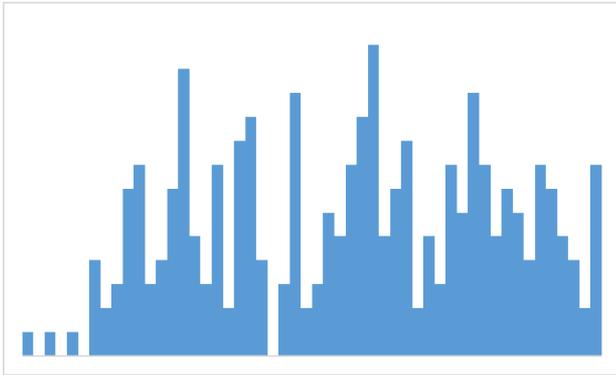
Geographic Distribution

- All but 2 diagnosed in New York City facilities
 - Greatest numbers in Brooklyn, Queens
- One diagnosed in Monroe County (Rochester)
 - Recent admission to involved NYC hospital
- One diagnosed in Westchester County
 - No obvious link to NYC facilities

Epidemiologic Curve



The Future



The Future

- India
 - Chowdhary 2013: *C. auris* represented 5% of candidemia in pediatric hospital, 30% of candidemia in tertiary general hospital
 - Chakrabarti 2015: *C. auris* isolated from 19/27 ICUs throughout India, 5.2% of ICU *Candida* isolates
- Kenya
 - Okinda, 2014: *C. auris* accounted for 38% of hospital-acquired candidemia
 - *Candida albicans* 27%

Facility Involvement

- From 90 days before 1st positive culture to the present
 - 34 NYS hospitals
 - 45 NYS nursing homes
 - 1 LTACH, 1 hospice
 - Additionally, 1 hospital outside the US, 1 LTACH in another state, numerous private medical offices, private homes

C. auris in the U.S.

State	Clinical Cases
Connecticut	1
Florida	1
Indiana	1
Maryland	1
Oklahoma	1
Massachusetts	3
Illinois	4
New Jersey	23
New York	78

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

Resistance

- All but one case resistant to fluconazole
 - Variable resistance to other azoles
- Most cases resistant to amphotericin B
- Only one case resistant to echinocandins
 - Recent development, NYC case
 - The resistant case's isolates were initially susceptible to echinocandins but later developed resistance, a known treatment challenge

Identifying and Reporting *C. auris*

When to Suspect *C. auris*

- *C. haemulonii*
- “*Candida* spp.” after identification attempted, especially if infection not responding to treatment
- *Rhodotorula glutinis* or *Candida duobushaemulonii*, *sake*, *catenulata*, *famata*, *guilliermondii*, *lusitaniae*, or *parapsilosis* depending on type of laboratory identification system
- Increase in unidentified *Candida* spp. infections on a patient care unit, including in urine

Reporting

- Mandated reporting under New York State Sanitary Code
- *Candida auris* not explicitly listed

However:

- “In addition to the diseases listed above, any unusual disease (defined as a newly apparent or emerging disease or syndrome that could possibly be caused by a transmissible infectious agent or microbial toxin) is reportable.”

Additionally:

- “...a cluster or outbreak of cases of any communicable disease is a reportable event.”
- Don't assume someone else is reporting

NEW YORK STATE DEPARTMENT OF HEALTH

Communicable Disease Reporting Requirements

Reporting of suspected or confirmed communicable diseases is mandated under the New York State Sanitary Code (10NYCRR 2.10.2.14). The primary responsibility for reporting rests with the physician; moreover, laboratories (PHL 2102), school nurses (10NYCRR 2.12), day care center directors, nursing homes/hospitals (10NYCRR 405.3d) and state institutions (10NYCRR 2.10a) or other locations providing health services (10NYCRR 2.12) are also required to report the diseases listed below.

Anaplasmosis	• Foodborne illness	Influenza	Pittiriasis	Streptococcal infection (invasive disease) ¹
Amebiasis	• Giardiasis	Laboratory-confirmed Legionellosis	• C Fever ²	Group A beta-hemolytic strep
• Animal bites for which rabies prophylaxis is given ³	• Gonococcal infection	Listeriosis	• Rubella	Rocky Mountain spotted fever
• Carbuncle ⁴	Haemophilus influenzae ⁵ (invasive disease)	Lyme disease	• Rubella (including congenital rubella syndrome)	Group B strep
• Carborundum ⁵	• Haemolytic uremic syndrome	Malaria	• Salmonellosis	Staphylococcus pneumoniae
Babesiosis	Hepatitis A	• Measles	• Severe Acute Respiratory Syndrome (SARS)	• Syphilis, specify stage ⁶
• Botulism ⁷	• Hepatitis A in a food handler	• Mumps	Shigatoxin-producing E.coli ⁸ (STEC)	Tetanus
• Brucellosis ⁷	Hepatitis B (specify acute or chronic)	Meningitis	Shigatosis ⁹	Toxic shock syndrome
Campylobacteriosis	Hepatitis C (specify acute or chronic)	• Aseptic or viral meningitis	Staphylococcus aureus ¹⁰ (due to strains showing reduced susceptibility or resistance to vancomycin)	Transmissible spongiform encephalopathies ¹¹ (TSE)
Chancroid	• HIV infection	• Meningococcal meningitis	Staphylococcus aureus ¹⁰ (due to strains showing reduced susceptibility or resistance to vancomycin)	Tuberculosis (current disease (specify site))
Chlamydia trachomatis	• HIV infection	• Meningococcal meningitis	Staphylococcus aureus ¹⁰ (due to strains showing reduced susceptibility or resistance to vancomycin)	Tuberculosis (current disease (specify site))
Chlamydia trachomatis infection	Pregnant hepatitis B carrier	• Meningococcal meningitis	Staphylococcus aureus ¹⁰ (due to strains showing reduced susceptibility or resistance to vancomycin)	Tuberculosis (current disease (specify site))
• Cholera	Herpes infection, infants aged 60 days or younger	• Meningococcal meningitis	Staphylococcus aureus ¹⁰ (due to strains showing reduced susceptibility or resistance to vancomycin)	Tuberculosis (current disease (specify site))
Cryptosporidiosis	Hospital associated infections (as defined in section 2.10 NYCRR)	• Meningococcal meningitis	Staphylococcus aureus ¹⁰ (due to strains showing reduced susceptibility or resistance to vancomycin)	Tuberculosis (current disease (specify site))
Cyclosporiasis		• Meningococcal meningitis	Staphylococcus aureus ¹⁰ (due to strains showing reduced susceptibility or resistance to vancomycin)	Tuberculosis (current disease (specify site))
• Diphtheria		• Meningococcal meningitis	Staphylococcus aureus ¹⁰ (due to strains showing reduced susceptibility or resistance to vancomycin)	Tuberculosis (current disease (specify site))
• E.coli O157:H7 infection ¹²		• Meningococcal meningitis	Staphylococcus aureus ¹⁰ (due to strains showing reduced susceptibility or resistance to vancomycin)	Tuberculosis (current disease (specify site))
Ehrlichiosis		• Meningococcal meningitis	Staphylococcus aureus ¹⁰ (due to strains showing reduced susceptibility or resistance to vancomycin)	Tuberculosis (current disease (specify site))
• Encephalitis		• Meningococcal meningitis	Staphylococcus aureus ¹⁰ (due to strains showing reduced susceptibility or resistance to vancomycin)	Tuberculosis (current disease (specify site))

WHO SHOULD REPORT?
Physicians, nurses, laboratory directors, infection control practitioners, health care facilities, state institutions, schools.

WHERE SHOULD REPORT BE MADE?
Report to local health department where patient resides.

Contact Person _____
Name _____
Address _____
Phone _____ Fax _____

WHEN SHOULD REPORT BE MADE?
Within 24 hours of diagnosis:
• Phone diseases in bold type.
• Mail case report, DOH-389 for all other diseases.
• In New York City use form PD-16.

SPECIAL NOTES

- Diseases in bold type require prompt action and should be reported immediately to local health departments by phone followed by submission of the confidential case report form (DOH-389). In NYC, use case report form PD-16.
- In addition to the diseases listed above, any unusual disease (defined as a newly apparent or emerging disease or syndrome that could possibly be caused by a transmissible infectious agent or microbial toxin) is reportable.
- Outbreaks: while individual cases of some diseases (e.g., streptococcal sore throat, head lice, impetigo, scabies and pneumonia) are not reportable, a cluster or outbreak of cases of any communicable disease is a reportable event.
- HIV infection, HIV-related illness and AIDS are reportable on form DOH-4189 which may be obtained by contacting:
Division of Epidemiology and Disease Research
P.O. Box 2073, 53rd Station
Albany, NY 12220-2073
(518) 474-4284

In NYC: New York City Department of Health and Mental Hygiene
For HIV/AIDS reporting, call:
(212) 442-3358

1. Local health department must be notified prior to initiating culture.
2. Diseases that are possible indicators of bioterrorism.
3. Including, but not limited to, infections caused by eastern equine encephalitis virus, western equine encephalitis virus, West Nile virus, St. Louis encephalitis virus, La Crosse virus, Powassan virus, Jamestown Canyon virus, dengue and yellow fever.
4. Positive shigatoxin test results should be reported as presumptive evidence of disease.
5. Only report cases with positive cultures from blood, CSF, joint, peritoneal or pleural fluid. Do not report cases with positive cultures from skin, saliva, sputum or throat.
6. Proposed addition to list.
7. Any non-meningeal test > 1:16 or any positive prenatal or delivery test regardless of titer or any primary or secondary stage disease, should be reported by phone; all others may be reported by mail.
8. Including Creutzfeldt-Jakob disease. Cases should be reported directly to the New York State Department of Health Alzheimer's Disease and Other Dementias Registry at (518) 473-7817 upon suspicion of disease. In NYC, cases should also be reported to the NYCOOHMI.
9. Persons with vaccinia infection due to contact transmission and persons with the following complications from vaccination, eczema vaccinatum, erythema multiforme major or Stevens-Johnson syndrome, fetal vaccinia, generalized vaccinia, inadvertent inoculation, ocular vaccinia, post-vaccinal encephalitis or encephalomyelitis, progressive vaccinia, pyogenic infection of the infection site, and any other serious adverse events.

ADDITIONAL INFORMATION
For more information on disease reporting, call your local health department or the New York State Department of Health Bureau of Communicable Disease Control at (518) 473-4439 or (866) 881-2809 after hours. In New York City, (866) NYC-DOH1. To obtain reporting forms (DOH-389), call (518) 474-0548.

PLEASE POST THIS CONSPICUOUSLY

DOH-389 (2/11) p2 of 2

Reporting

- Notify facility infection preventionists and patient's clinical team
- As described in previous NYSDOH health alert to laboratories, report to and coordinate with regional epidemiologist to forward suspicious isolates to Wadsworth Center

Infection Control

General

- Applies to both infected and colonized patients
- Standard and Contact Precautions
 - Generally, gown and gloves
- Hand hygiene
- Environmental cleaning and disinfection

Persistent Colonization

- Affected persons remain colonized for undefined but usually lengthy durations
- Remain under Standard and Contact Precautions indefinitely unless clearance documented
- Need at least 2 rounds of negative surveillance cultures (not on antifungals) at least 1 week apart before a person can be considered “cleared” – discuss with your NYSDOH regional epidemiologist
- No data and no recommendations for decolonization

Healthcare Personnel

- NYS - several healthcare personnel hands cultured – all negative
- Schelenz, 2016: UK hospital outbreak
 - Cultured 258 healthcare personnel
 - Hands, nose, axilla, groin, throat
 - Only 1 positive in nose
- *C. auris* is not generally considered a risk for healthcare personnel

NYSDOH Prevention and Control Activities

Goals

- Prevent transmission and further spread in affected facilities
- Define the extent of the problem
- Delay and blunt the impact of this organism in New York and the US

When We Find a Case

- NYSDOH regional epidemiologists contact facility
- Ensure appropriate infection control measures are in place
- Case investigation (e.g. medical record review, location tracking)
- Surveillance cultures of contacts (e.g. roommates)
- Point prevalence surveys of affected units
- Environmental cultures of surfaces
- Site visit

Acknowledgements

- NYSDOH

- Eleanor Adams
- Sudha Chaturvedi
- Richard Erazo
- Rafael Fernandez
- Rosalie Giardina
- Jane Greenko
- Ronald Jean Denis
- Sarah Kogut
- Rutvik Patel
- Monica Quinn
- Karen Southwick

- CDC

- Karlyn Beer
- Tom Chiller
- Nancy Chow
- Janet Glowicz
- Brendan Jackson
- Alex Kallen
- Ana Litvintseva
- Shawn Lockhart
- Abimbola Ogundimu
- Eugenie Poirot
- Sharon Tsay
- Snigdha Vallabhaneni
- Rory Welsh



References

1. Borman AM, Szekely A, Johnson EM. Comparative pathogenicity of United Kingdom isolates of the emerging pathogen *Candida auris* and other key pathogenic *Candida* species. mSphere. 2016;1:e00189–16.
2. Calvo B, Melo ASA, Perozo-Mena A, et al. First report of *Candida auris* in America: clinical and microbiological aspects of 18 episodes of candidemia. J Infect. 2016;73:369–74.
3. Chakrabarti A, Sood P, Rudramurthy SM, et al. Incidence, characteristics and outcome of ICU-acquired candidemia in India. Intensive Care Med. 2015;41:285–95.
4. Chowdhary A, Kumar VA, Sharma C, et al. Multidrug-resistant endemic clonal strain of *Candida auris* in India. Eur J Clin Microbiol Infect Dis. 2014;33:919–26.
5. Chowdhary A, Sharma C, Duggal S, et al. New clonal strain of *Candida auris*, Delhi, India. Emerg Infect Dis. 2013;19:1670–3.
6. Chowdhary A, Voss A, Meis JF. Multidrug-resistant *Candida auris*: 'new kid on the block' in hospital-associated infections? J Hosp Infect. 2016;94:209–12.
7. Emara M, Ahmad S, Khan Z, et al. *Candida auris* candidemia in Kuwait, 2014. Emerg Infect Dis. 2015;21:1091–2.
8. Kathuria S, Singh PK, Sharma C, et al. Multidrug-resistant *Candida auris* misidentified as *Candida haemulonii*: characterization by matrix-assisted laser desorption/ionization-time of flight mass spectrometry and DNA sequencing and its antifungal susceptibility profile variability by Vitek 2, CLSI broth microdilution, and Etest method. J Clin Microbiol. 2015;53:1823–30.
9. Kim M-N, Shin JH, Sung H, et al. *Candida haemulonii* and closely related species at 5 university hospitals in Korea: identification, antifungal susceptibility, and clinical features. Clin Infect Dis. 2009;48:e57–61.
10. Lee WG, Shin JH, Uh Y, et al. First three reported cases of nosocomial fungemia caused by *Candida auris*. J Clin Microbiol. 2011;49:3139–42.
11. Lockhart SR, Etienne KA, Vallabhaneni S, et al. Simultaneous emergence of multidrug resistant *Candida auris* on three continents confirmed by whole genome sequencing and epidemiological analyses. Clin Infect Dis. Advance access, published October 20, 2016, accessed December 15, 2016.
12. Magobo RE, Corcoran C, Seetharam S, et al. *Candida auris*-associated candidemia, South Africa. Emerg Infect Dis. 2014;20:1250–1.
13. Oh BJ, Shin JH, Kim M-N, et al. Biofilm formation and genotyping of *Candida haemulonii*, *Candida pseudohaemulonii*, and a proposed new species (*Candida auris*) isolates from Korea. Med Mycol. 2011;49:98–102.
14. Okinda N, Kagotho E, Castanheira M, et al. Candidemia at a referral hospital in sub-Saharan Africa: emergence of *Candida auris* as a major pathogen. European Congress of Clinical Microbiology and Infectious Diseases. Barcelona, 2014. Poster presentation.
15. Sarma S, Kumar N, Sharma S, et al. Candidemia caused by amphotericin B and fluconazole resistant *Candida auris*. Indian J Microbiol. 2013;31:90–1.
16. Satoh K, Makimura K, Hasumi Y, et al. *Candida auris* sp. nov., a novel ascomycetous yeast isolated from the external ear canal of an inpatient in a Japanese hospital. Microbiol Immunol. 2009;53:41–4.
17. Schelenz S, Hagan F, Rhodes JL, et al. First hospital outbreak of the globally emerging *Candida auris* in a European hospital. Antimicrob Resist Infect Control. 2016;5:eCollection.
18. Centers for Disease Control and Prevention. *Candida auris* interim recommendations for healthcare facilities and laboratories. Available at: <https://www.cdc.gov/fungal/diseases/candidiasis/recommendations.html> Accessed 12/15/2016.



Candida auris: An Emerging Threat

Laboratory testing

Ron Limberger Ph.D.
Wadsworth Center

Sudha Chaturvedi Ph.D.
Wadsworth Center

First Reported from Japan, 2009

***Candida auris* sp. nov., a novel ascomycetous yeast isolated from the external ear canal of an inpatient in a Japanese hospital**

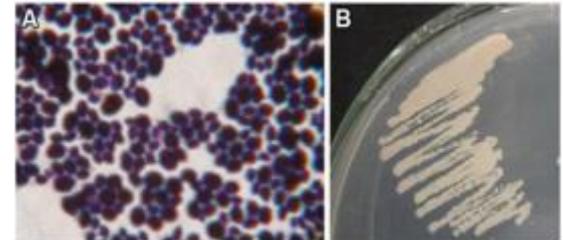
Kazuo Satoh^{1,2}, Koichi Makimura^{1,3}, Yayoi Hasumi¹, Yayoi Nishiyama¹, Katsuhisa Uchida¹ and Hideyo Yamaguchi¹

¹Teikyo University Institute of Medical Mycology, 359 Otsuka, Hachioji, Tokyo 192-0395, ²Japan Health Sciences Foundation, 13-4 Nihonbashi-Kodenmacho, Chuo-ku, Tokyo 103-0001 and ³Genome Research Center, Graduate School of Medicine and Faculty of Medicine, Teikyo University, Otsuka 359, Hachioji, Tokyo 192-0395, Japan

- High temperature tolerance (45°C)
- High salt tolerance (10%)
- No specific features e.g. chlamydospore, hyphae, pseudohyphae, etc.
- Unique sugar assimilation profile



Chrome agar



Gram Stain

What methods can detect *C. auris*?

- Culture and identification of isolate
- PCR - currently only available at the Wadsworth Center

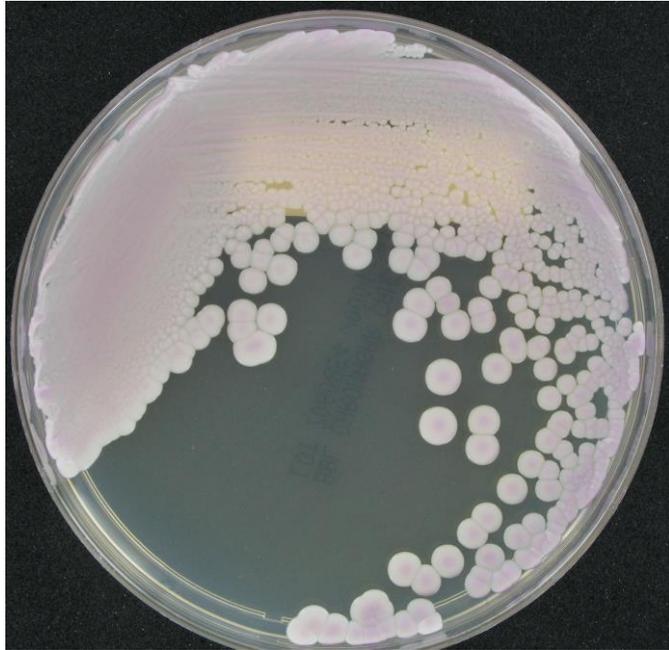
C. auris culture

- Can be grown on selective medium that contains 2% dulcitol & 10% salt at 40° C and CHROMagar Candida at 37° C.

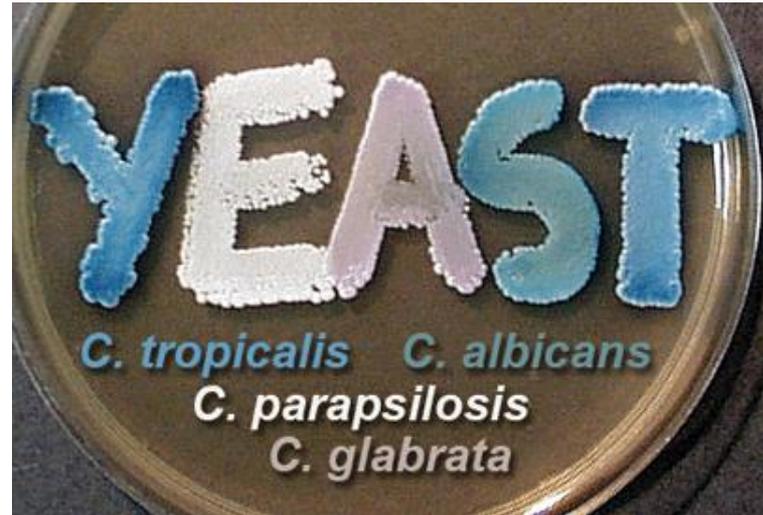
Limitations

- Dulcitol is fairly selective but occasional growth of other yeasts seen (i.e. *C. parapsilosis*, *C. guilliermondii*).
- CHROMagar Candida is selective in terms of color for some *Candida* spp. but cannot differentiate *C. auris* from *C. parapsilosis* and *C. glabrata*.

C. auris on CHROMagar Candida



C. auris

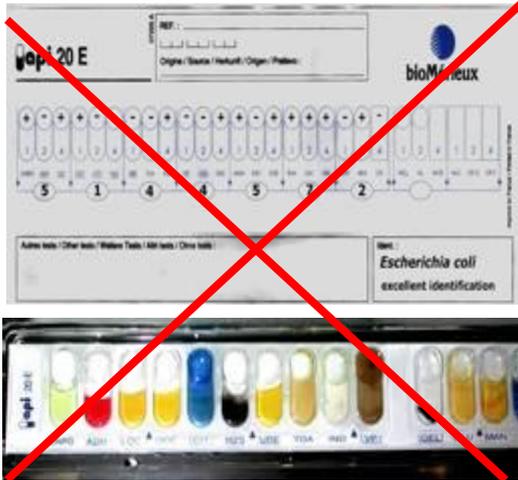


Culture (cont.)

- Wadsworth can share the CDC recipe for dulcitol medium.
- After isolation, the suspect *C. auris* colonies must be further tested.

Culture confirmation

- **Current diagnostic methods** used in the majority of clinical labs are inadequate for *C. auris* ID



API



Vitek 2



Microscan

***Candida auris* can be misidentified as**

<i>Candida haemulonii</i>	VITEK2 YST
<i>Rhodotorula glutinis</i> (absence of red pigment) <i>Candida sake</i>	API 20C
<i>Candida haemulonii</i> <i>Candida catenulata</i>	BD Phoenix yeast identification system
<i>Candida famata</i> <i>Candida guilliermondii</i> <i>Candida lusitaniae</i> <i>Candida parapsilosis</i>	Microscan

These and all *C. auris* isolates should be sent to the Wadsworth Center Mycology Laboratory for confirmation. Also, any yeast that cannot be identified to the species level, should be sent for ID.

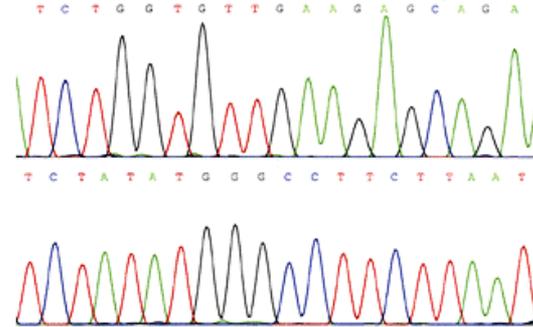
Culture confirmation of *Candida auris*

MALDI & Sequencing



(1) MALDI-TOF-MS BRUKER

(2) VITEK 2 YST with Ver 8.01 software
(BIOMERIEUX)



(3) Sequencing-Ribosomal gene

How do I validate MALDI-TOF for *C. auris*?

- If already CLEP-approved for using MALDI-TOF for yeast then just validate in-house. No need to submit validation to CLEP.
- If not CLEP-approved for using MALDI-TOF for yeast, then follow guidelines at <https://www.wadsworth.org/regulatory/clep/clinical-labs/obtain-permit/test-approval/submission-checklists> and submit to CLEP.

How do I validate ITS sequencing for *C. auris*?

If already CLEP approved for yeast identification by sequencing then just validate in-house. No need to submit to CLEP

If not CLEP approved for yeast identification by sequencing then follow guidelines at <https://www.wadsworth.org/regulatory/clep/clinical-labs/obtain-permit/test-approval/submission-checklists> and submit to CLEP

How do I validate the Wadsworth *C. auris* PCR in my laboratory?

- Request the *C. auris* PCR protocol from Wadsworth Mycology Laboratory
- Perform a streamlined in-house validation

Streamlined Validation

- Perform a limit of detection using 10-fold dilutions in matrix
- Perform a blinded accuracy study of 20 positive samples and 10 negatives for each matrix
- Submit above data and the SOP to CLEP

More on validation

NOTE: as of 8/30/2017 the Wadsworth PCR has only been approved for skin and nares swabs

If you intend to perform the testing using other matrices, a validation must be submitted to CLEP for the modification of this test

Yeast DNA extraction

The Wadsworth *C. auris* PCR has a fairly cumbersome DNA extraction process. We are working to improve this part of the assay and open to collaboration.

Susceptibility testing

Can be done using microbroth dilution and E-test methods as per the guidelines of Clinical Laboratory Standard Institute (CLSI).

No need to submit validation data to CLEP.

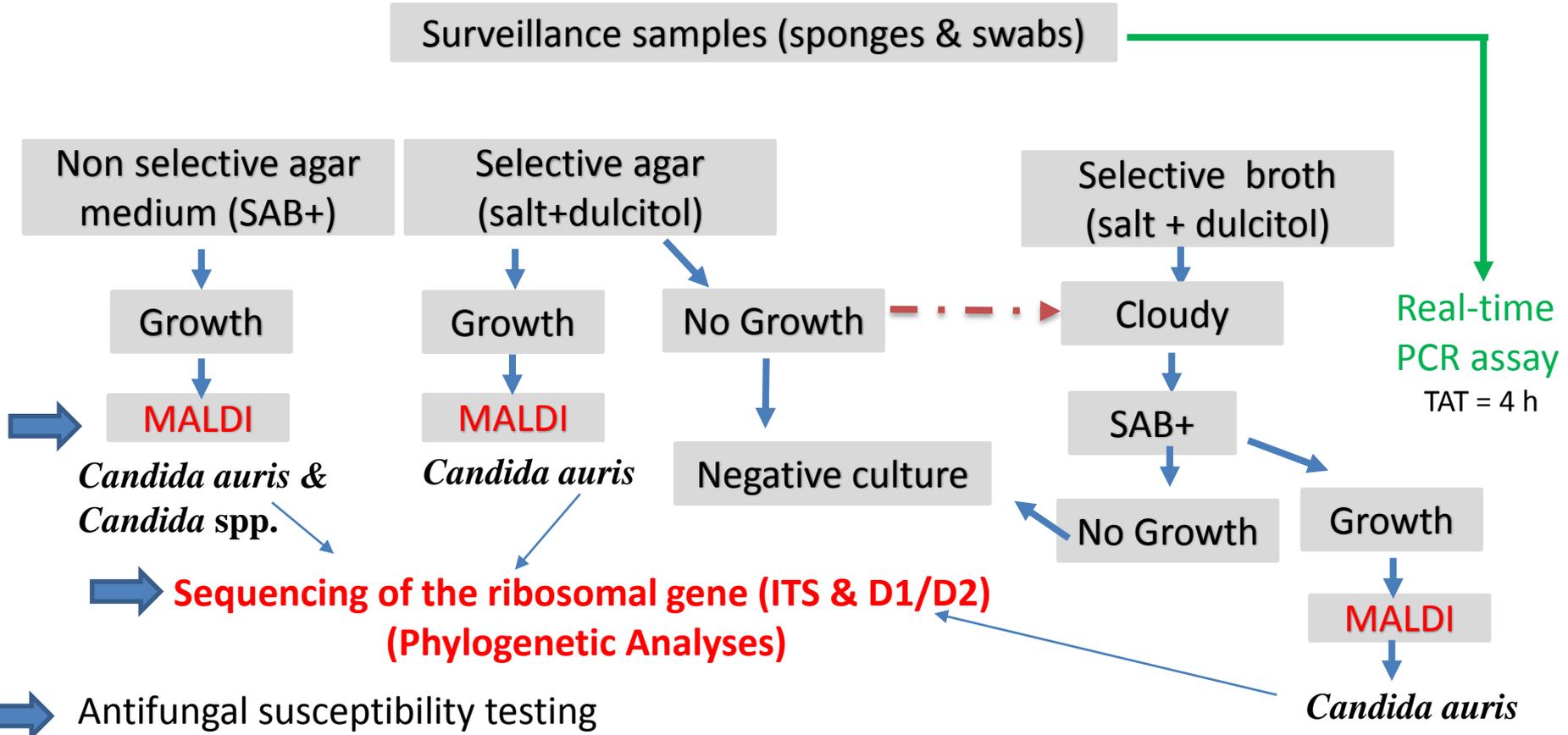
Reporting

- As described in a previous NYSDOH health alert to laboratories, report to and coordinate with regional epidemiologist to forward suspicious isolates to Wadsworth Center

Sending specimens to Wadsworth

- Fill out ID requisition form (available on wadsworth.org)
- Pack and ship appropriately for infectious agents (category B). Ship at room temperature.
- For commercial carrier, send to Mycology Laboratory, Wadsworth Center, Axelrod Institute, 120 New Scotland Ave, Albany, NY 12208
- If using USPS, send to the above at PO Box 22002, Albany, NY 12201

Laboratory Workflow



Lab Contact information

For Mycology test details: sudha.chaturvedi@health.ny.gov

For CLEP guidance: clep@health.ny.gov

Unsure or general questions: ronald.limberger@health.ny.gov

Web resource for validation guidance:

<https://www.wadsworth.org/regulatory/clep/clinical-labs/obtain-permit/test-approval/submission-checklists>

Epi Contact Info

NYSDOH Regional and Central Office Contact Information:

Western Regional Office (716) 847-4503

Central New York Regional Office (315) 477-8166

Metropolitan Area Regional Office (914) 654-7149

Capital District Regional Office (518) 474-1142

Central Office (518) 474-1142

General questions or comments can be sent to icp@health.ny.gov