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Outbreak of superbug *Candida auris*: Asian scenario and interventions

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ASIA FUNGAL WORKING GROUP
an ISHAM working group

ISHAM
INTERNATIONAL SOCIETY FOR HUMAN AND ANIMAL MYCOLOGY

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Outbreak of superbug *Candida auris*: Asian scenario and intervention required by laboratories

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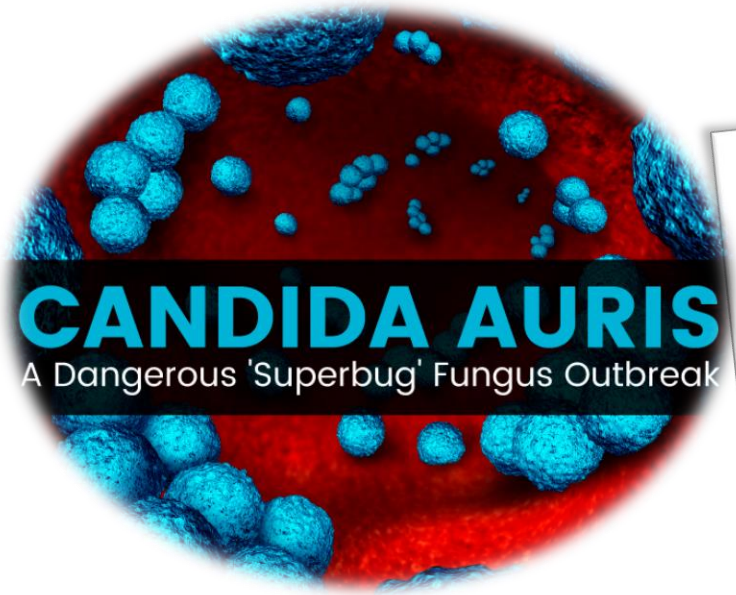
Candida auris will soon reach your hospital



2009-2017….

News

Intensive care unit closed after new deadly superbug emerges in the UK

BMJ 2016;355:i5978 doi: 10.1136/bmj.i5978 (Published 7 November 2016)

Hospital transmitted *Candida auris* infections confirmed in the US

Michael McCarthy

Candida auris: a cause for concern?

Fungus with "super bug" qualities found in 44 cases in New York State

By: Jordan Guerrein

How to Protect Yourself From the Candida Auris Fungal Infection

Cases of this rare yeast superbug are on the rise

By Hallie Levine

Urgent Threats

- *Clostridium difficile*
- Carbapenem-resistant Enterobacteriaceae (CRE)
- Drug-resistant *Neisseria gonorrhoeae*

Serious Threats

- Multidrug-resistant *Acinetobacter*
- Drug-resistant *Campylobacter*
- Fluconazole-resistant *Candida* (a fungus)
- Extended spectrum β-lactamase producing Enterobacteriaceae (ESBLs)
- Vancomycin-resistant *Enterococcus* (VRE)
- Multidrug-resistant *Pseudomonas aeruginosa*
- Drug-resistant Non-typhoidal *Salmonella*
- Drug-resistant *Salmonella* Typhi
- Drug-resistant *Shigella*
- Methicillin-resistant *Staphylococcus aureus* (MRSA)

CDC issued a clinical alert to healthcare facilities – July 2016

Fungal Diseases

Fungal Diseases
Types of Fungal Diseases −
Aspergillosis +
Blastomycosis +
Candidiasis −
Oropharyngeal / Esophageal Candidiasis
Genital / vulvovaginal candidiasis
Invasive candidiasis
Candida auris Q&A
***Candida auris* Alert**
Coccidioidomycosis +
C. neoformans Infection +
C. gattii Infection +
Fungal Eye Infections +

CDC > Fungal Diseases > Types of Fungal Diseases > Candidiasis

Clinical Alert to U.S. Healthcare Facilities

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

Summary: The Centers for Disease Control and Prevention (CDC) has received reports from international healthcare facilities that *Candida auris*, an emerging multidrug-resistant (MDR) yeast, is causing invasive healthcare-associated infections with high mortality. Some strains of *C. auris* have elevated minimum inhibitory concentrations (MICs) to the three major classes of antifungals, severely limiting treatment options. *C. auris* requires specialized methods for identification and could be misidentified as another yeast when relying on traditional biochemical methods. CDC is aware of one isolate of *C. auris* that was detected in the United States in 2013 as part of ongoing surveillance. Experience outside the United States suggests that *C. auris* has high potential to cause outbreaks in healthcare facilities. Given the occurrence of *C. auris* in nine countries on four continents since 2009, CDC is alerting U.S. healthcare facilities to be on the lookout for *C. auris* in patients.

Background

Candida auris is an emerging multidrug-resistant (MDR) yeast that can cause invasive infections and is associated with high mortality. It was first described in 2009 after being isolated from external ear discharge of a patient in Japan [1]. Since the 2009 report, *C. auris* infections, specifically fungemia, have been reported from South Korea [2], India [3], South Africa [4], and Kuwait [5]. Although published reports are not available, *C. auris* has also been identified in Colombia, Venezuela, Pakistan, and the United Kingdom.

It is unknown why *C. auris* has recently emerged in so many different locations. Molecular typing of strains performed by CDC suggests isolates are highly

Public Health England

See more information about this Research and analysis

Research and analysis

Candida auris identified in England

Published 1 July 2016

Notification Whenever there is a suspected or confirmed case of *C. auris* infection or *C. auris*colonization in the hospital, the details should be notified toProf.ArunalokeChakrabarti, Professor and Head, Mycology Reference Laboratory, Department of Medical Microbiology, PGIMER, Chandigarh.

Antifungal resistance is bad, very bad,
C. auris is bad , may be baddder, than bacteria

C. auris: Why reason of concern?

MDR clonal strains that are nosocomially transmitted

More concern

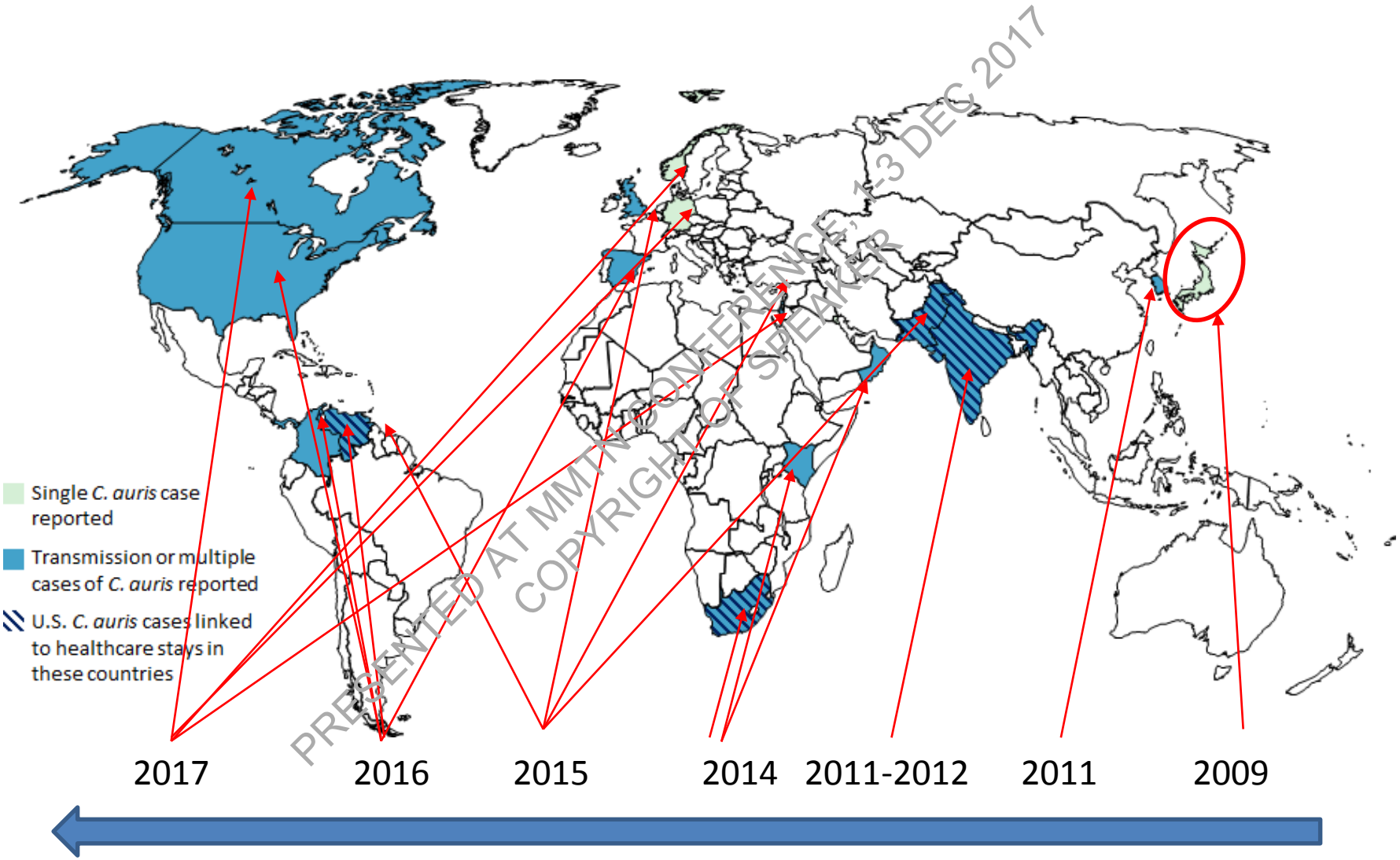
- Not easily identified
- Easily transmitted – colonization, contamination of hospital environment
- Difficult to treat
- Causes severe infections

Challenges !!

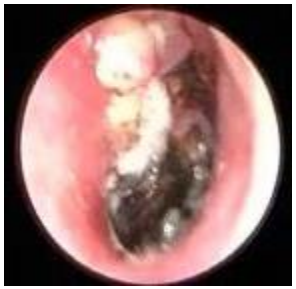
- ?True burden
  - Emerging reports
  - Exact burden unclear
- outbreaks in healthcare settings
  - Nosocomial spread
  - Environmental reservoir unknown
- Identification
  - Misidentified by Vitek 2, API20C-AUX, Auxacolor, Phoenix and Microscan
  - T2 Candida panel may miss its identification
  - Accurate: Molecular sequencing (ITS or LSU region) or MALDI-TOF
- Multidrug resistance
  - ?epidemiological cutoff values (ECVs) or clinical breakpoints not defined
  - High rate of resistance to antifungals
- High mortality rate
  - Persistent candidemia
  - 33-72%

When it appeared? Where? How it spread?

1st report - 2009 from Japan



Candida auris – first appeared

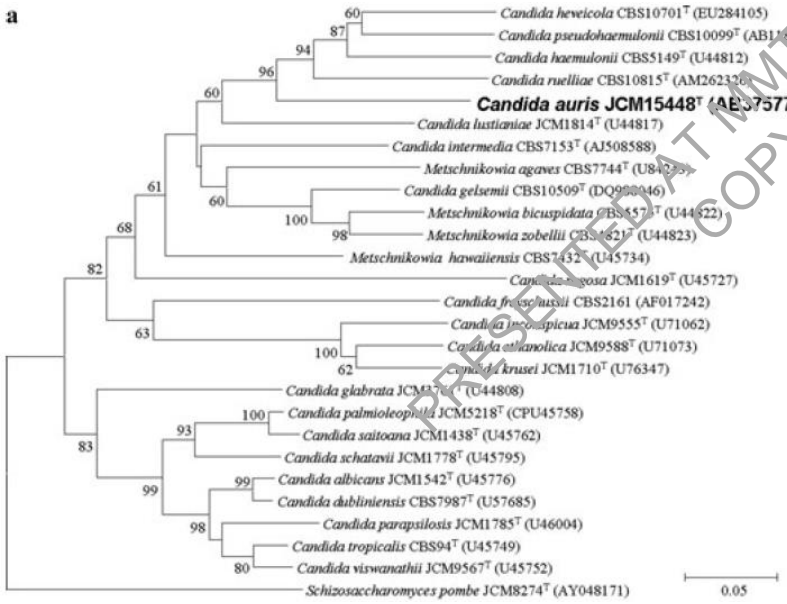


ORIGINAL ARTICLE

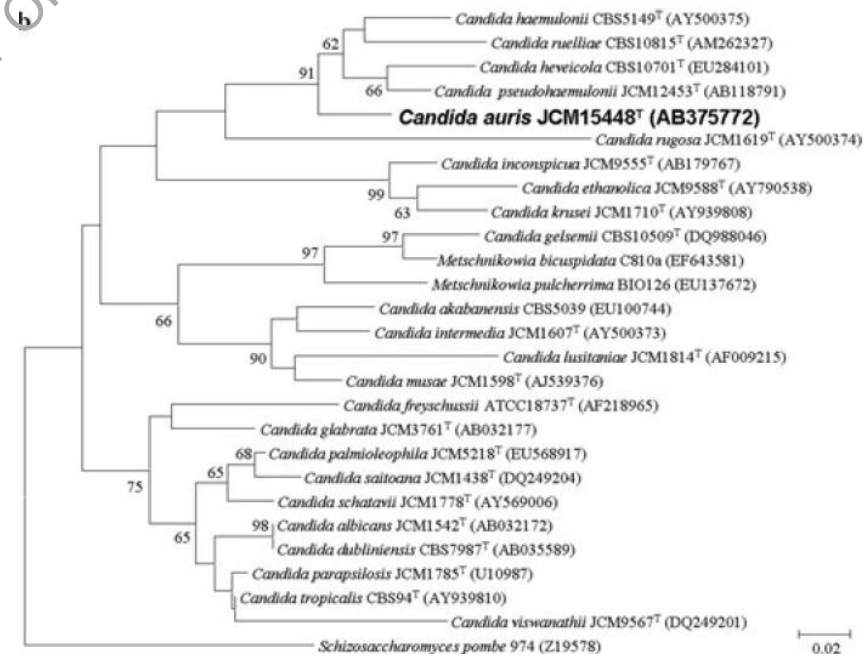
Microbiol Immunol 2009; 53: 41–44

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 Hasumi[1], Yayoi Nishiyama[1], Katsuhisa Uchida[1] and Hideyo Yamaguchi[1]



28s rDNA –D1/D2



18s rDNA

When *C. auris* came?

remain unknown. Multiple independent laboratories with international culture collections subsequently reviewed older isolates to see if *C. auris* had been isolated previously and was either misidentified or not identified at all. While a single isolate from 1996 in Korea had been misidentified and a single isolate from Pakistan in 2008 had been unidentified, no other isolates of *C. auris* were identified from over 30,000 isolates from more than 40 countries that were reviewed [4,9] (CDC, unpublished data). This corroborates the recent clinical emergence of *C. auris* within the last 10 years.

DEADLY DRUG-RESISTANT FUNGUS OUTBREAK STRIKES 200 UK HOSPITAL PATIENTS

Official guidance states that infections are usually minor / *PA*

Candida auris infections that target the immune system have been diagnosed across 20

Drug-resistant Japanese fungus is spreading through British hospitals wards

- A dangerous Japanese fungus is spreading through British hospital wards
- More than 200 patients have been affected or found to carry the fungus
- Hospitals and nursing homes have been ordered to deep clean affected areas
- The fungus, Candida auris, has been resistant to all anti-fungal drug treatment

First reported case of multidrug-resistant *Candida auris* in Canada

IS Schwartz[1*], GW Hammond[1]

Can Commun Dis Rep. 2017;43 (7/8):150-3.

Abstract

Candida auris is a fungal pathogen that has recently emerged as a global threat to public health. It was first described in Japan in 2009 and has since been reported in 17 countries on five continents. This case report describes the first reported case of multidrug-resistant *C. auris* in Canada.

In May 2017, a 64 year-old individual was evaluated for chronic otitis externa. Past medical history included a recent hospitalization in India for elective oral surgery that was complicated by an odontogenic brain abscess. Upon return to Canada, the individual was admitted to a hospital for neurosurgical drainage of the brain abscess and parenteral antibiotics. Early during hospitalization, the patient was identified as a carrier of carbapenem-resistant *Enterobacteriaceae* and was placed on contact precautions. Also early during this hospitalization, a chronic otitis media was managed with placement of a typanostomy tube with drainage of clear fluid from the ear, which continued through the admission and after discharge to a post-neurosurgical rehabilitation facility. During outpatient follow-up, swabs of the ear discharge cultured *C. auris* that was resistant to fluconazole and amphotericin B. There was no clinical response to ototopical antifungal therapy. Surgical evaluation for management of the otomastoiditis is pending.

Four cases with history of recent travel

- Countries involved
  - India
  - Pakistan
  - South Africa
  - Venezuela

- Cases involved
  - Urine culture
  - Wound culture

Burden, outbreaks, epidemiology

Prevalence *C. auris* candidemia

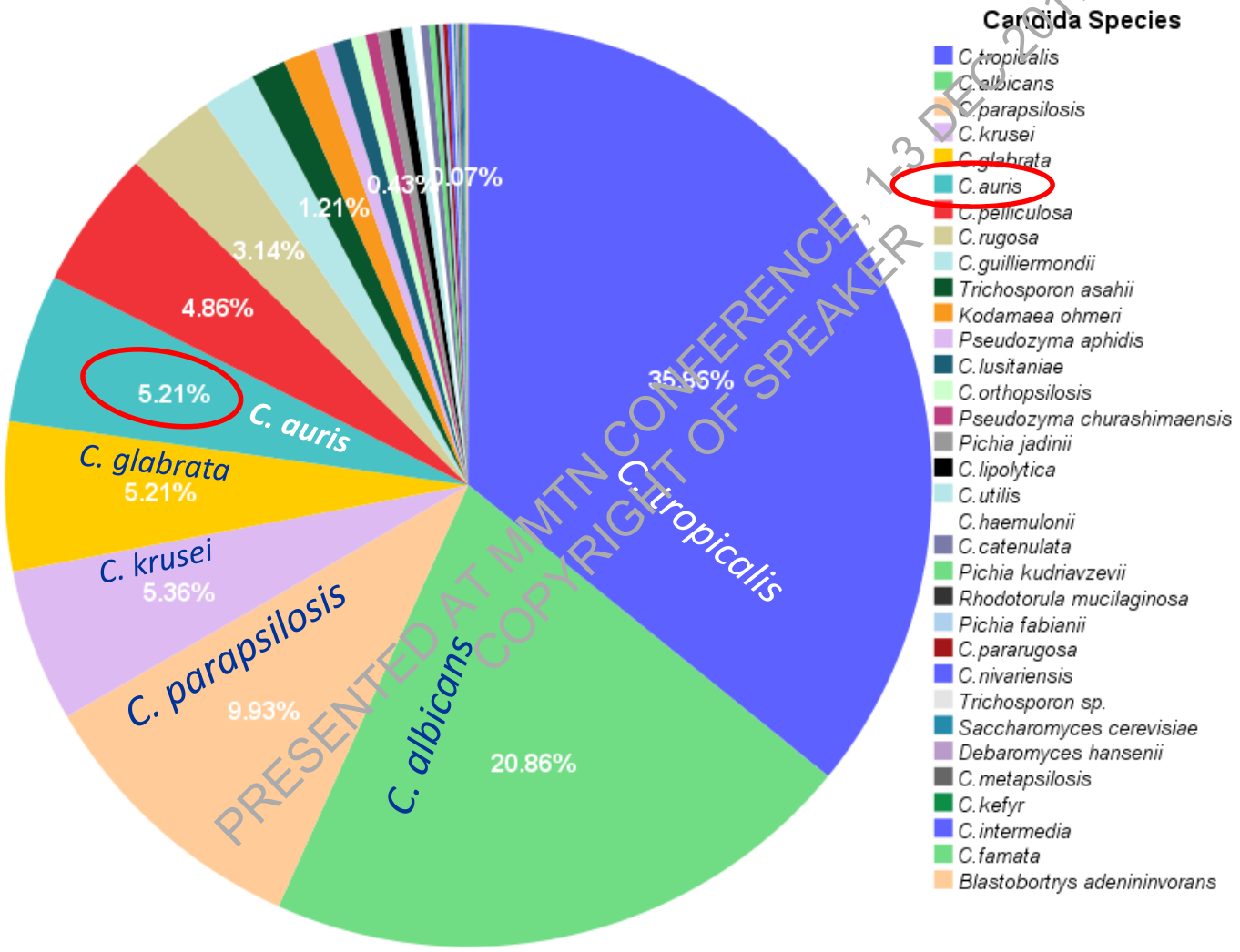
- 0.3% in South Africa (numerator & denominator not known) (Magobo *et al.* Emerg Infect Dis 2014; 20: 1250)
- 38% of Hospital-acquired candidemia in Kenya (Okinda *et al*, ECCMID: May 2014: Barcelona, Spain, Poster)
- 5% (3/60 paediatric), 30% (9/27 adult candidemia) in India (Chowdhary *et al.* Emerg Infect Dis 2013; 19: 1670)

→ small numbers of cases in undefined populations

- 5.3% (74/1400 candidemia cases) in Indian ICUs (5th cause of candidemia in Indian ICUs) (Chakrabarti A, *et al.* Intensive Care Med 2015; 41: 285)

→ Largest number of cases

Candida species isolated during Indian ICU study



Chakrabarti *et al.* Intensive Care Med 2015; 41: 285

Risk factors - Case-control analysis

Rudramurthy S, *et al.* J Antimicrob Chemother 2017; 72: 1794

- Higher in public-sector hospitals (62.2% vs 37.8%; P<0.001)
- Duration of ICU stay prior to candidaemia diagnosis significantly longer (median 25 days vs 15 days, P<0.001)
- High prior antifungal exposure (fluconazole in majority)
- Presence of a central venous line not significantly associated
- Duration of central line in days significantly higher (median 10.5, IQR 5–27 days)

Patients with sepsis, undergoing invasive management for longer periods & exposed to antifungal agents

Investigate for *C. auris* candidemia

C. auris: haven't found it in the environment but relatives have been found in these places:

Outbreak at a UK hospital: 2015-2016

Schelenz et al. Antimicrobial Resistance and Infection Control (2016) 5:35
DOI 10.1186/s13756-016-0132-5

Antimicrobial Resistance and Infection Control

RESEARCH Open Access

First hospital outbreak of the globally emerging *Candida auris* in a European hospital

Silke Schelenz[1,3*], Ferry Hagen[2], Johanna L. Rhodes[3], Alireza Abdolrasouli[1], Anuradha Chowdhary[4], Anne Hall[1], Lisa Ryan[1], Joanne Shackleton[1], Richard Trimlett[5], Jacques F. Meis[2,6], Darius Armstrong-James[1,3] and Matthew C. Fisher[3]

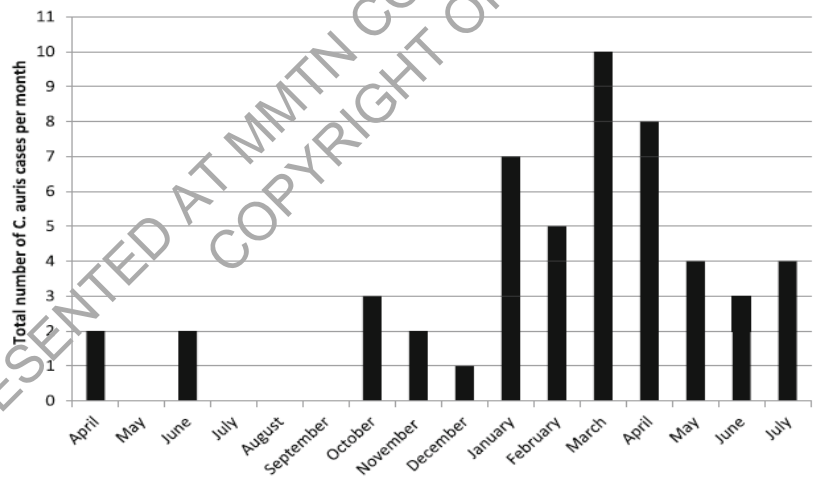
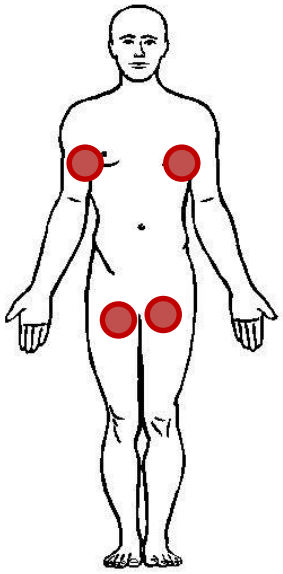


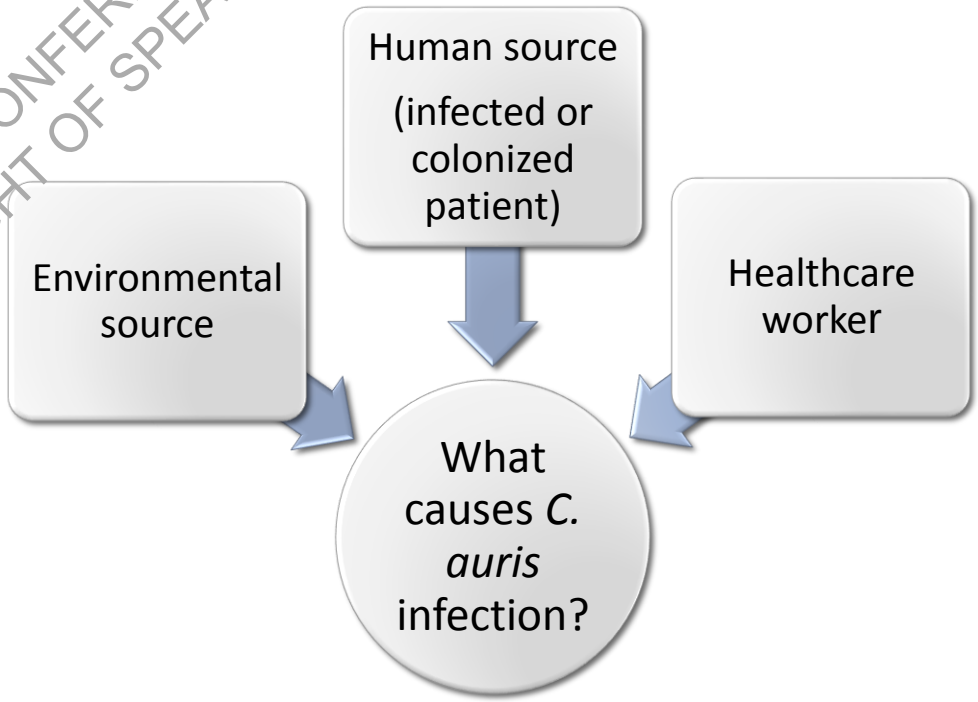
Fig. 1 New cases of *C. auris* per month. Total number of monthly new cases of *C. auris* are listed from the 1 April 2015 to the end of July 2016

- 2246 patients screened at admission
- Only one patient was colonized

Why call it nosocomial spread?

- Persistent colonization of *C. auris* multiple body-sites of patients, carriage by healthcare workers, & presence in environment leading to high transmissibility & protracted outbreaks

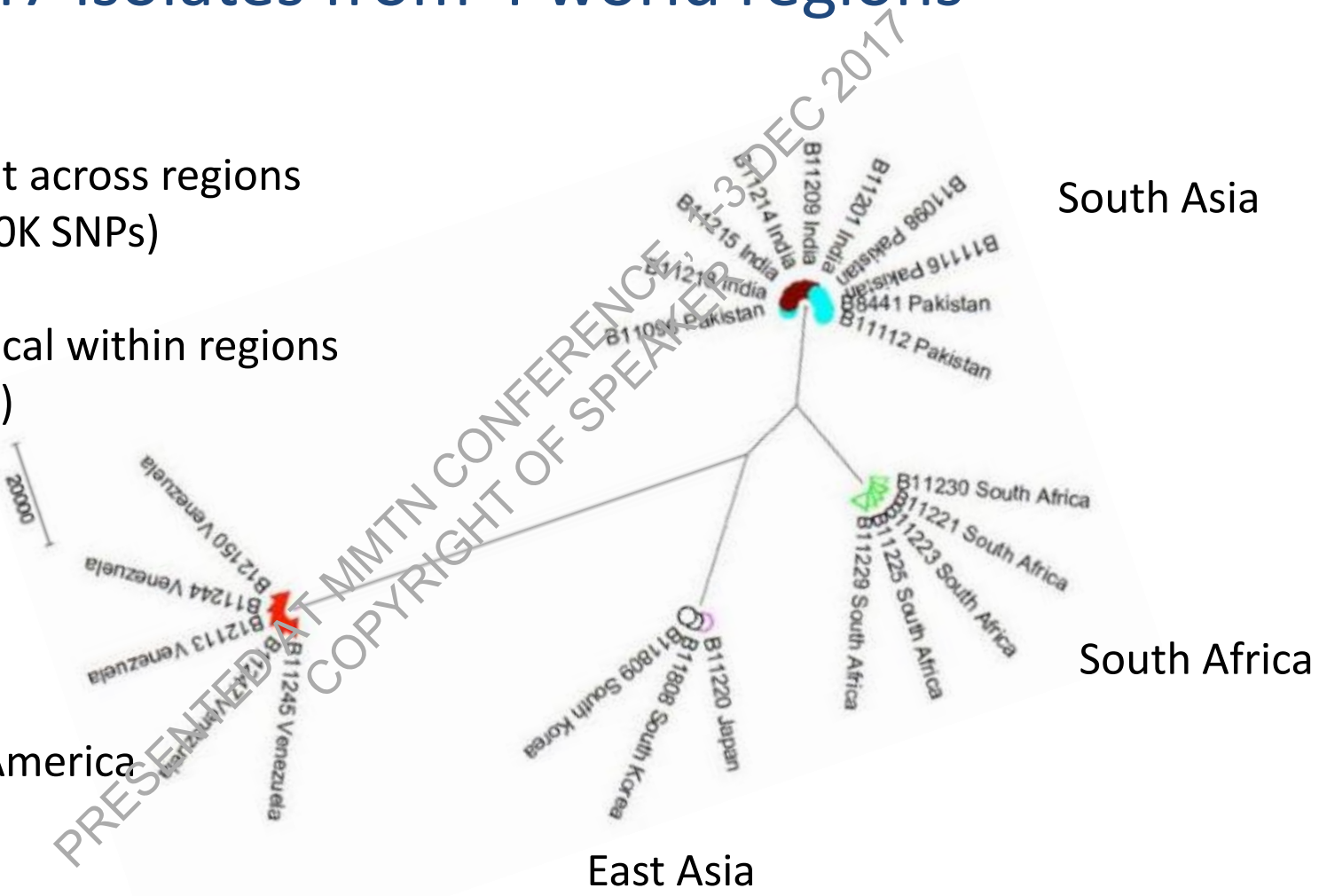




But, we do not know where the organism thrive in the hospital

WGS of 47 isolates from 4 world regions

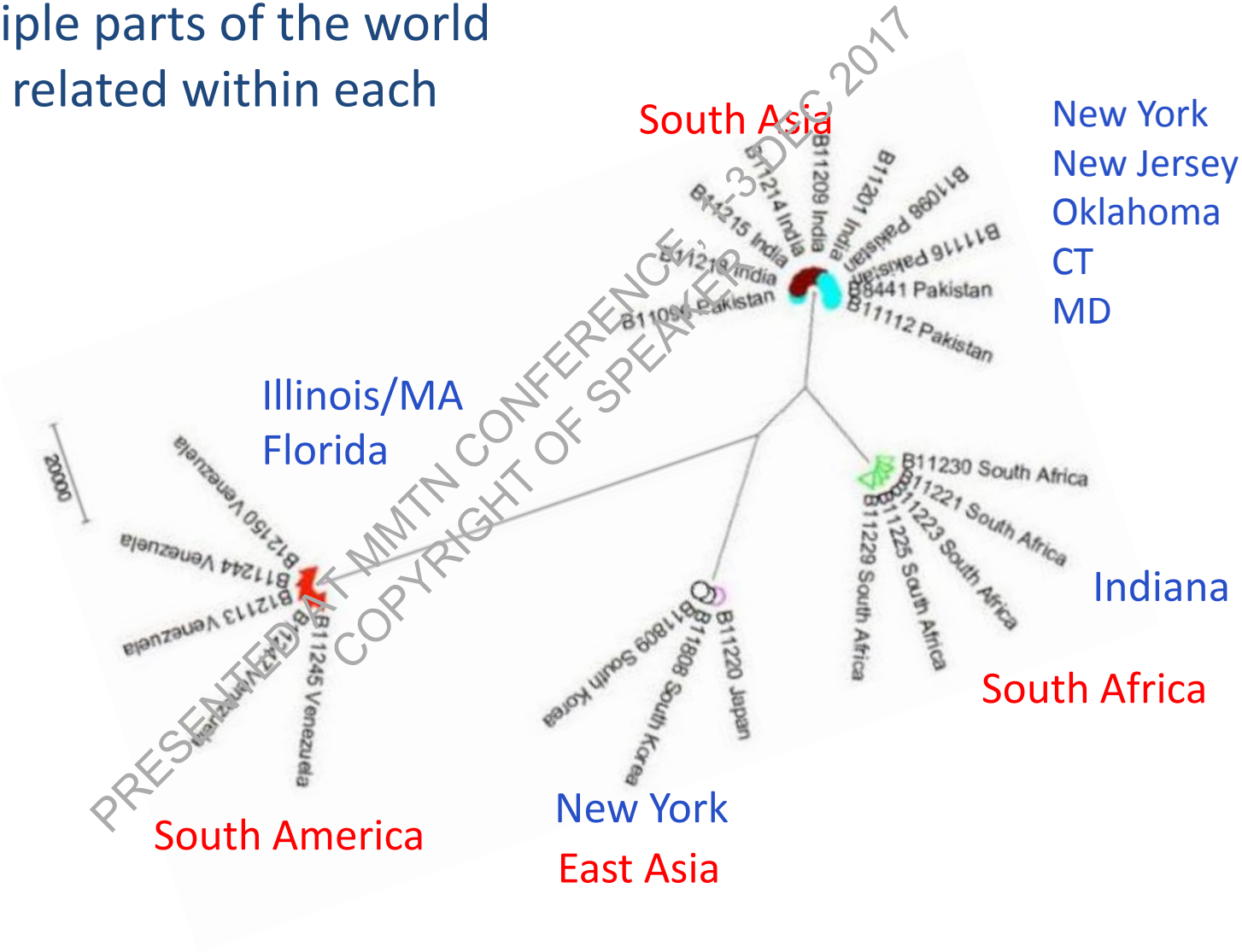
- Very different across regions
  - (>40K-400K SNPs)
- Nearly identical within regions
  - (<70SNPs)



Countries from which *Candida auris* cases have been reported, as of August 31, 2017

- Single cases of *C. auris* have been reported from Canada, Germany, Japan, Kuwait, and Norway.
- Multiple cases of *C. auris* have been reported from Colombia, India, Israel, Kenya, Oman, Pakistan, Panama, South Korea, South Africa, Spain, the United Kingdom, the United States (primarily from New York City Metropolitan Area and New Jersey) and Venezuela; in some of these countries, extensive transmission of *C. auris* has been documented

U.S. case isolates related to those from multiple parts of the world
→ Closely related within each state



Emergence of *C. auris*

- simultaneous yet independent

Identification & characteristics of *C. auris*

Laboratory testing & misidentification – *C. auris*

Method	Comment
API-20C	Identify as *Rhodotorula glutinis, Candida sake, Saccharomyces cerevisiae*
Vitek - 2	Identify as *Candida haemulonii, Candida famata* (updated database may able to identify)
BD Phoenix	Identify as *Candida haemulonii*
Microscan	Identify as *C. famata, C. guilliermondii, C. lusitaniae, C. parapsilosis*
MALDI	**Can identify *C. auris* after improvement of data base** Before improvement – we updated the data base on our own (Ghosh *et al.* Clin Microbiol Infect. 2015; 21: 372-378)
DNA sequencing	**D1-D2 domain** of large subunit can identify correctly

C. auris could grow at 42˚ C, but failed to grow in presence of 0.01% or 0.1% cycloheximide. Utilization of dextrose, dulcitol & mannitol may help

JCM Accepted Manuscript Posted Online 26 July 2017
J. Clin. Microbiol. doi:10.1128/JCM.00921-17

Molecular diagnosis

JCM Accepted Manuscript Posted Online 29 November 2017
J. Clin. Microbiol. doi:10.1128/JCM.01223-17

Development and validation of a real-time PCR assay for rapid detection of *Candida auris* from surveillance samples

L. Leach, Y. Zhu, S. Chaturvedi

- TaqMan based real-time PCR assay targeting the internal transcribed spacer 2 (*ITS2*) region of the ribosomal gene
- 365 patient swabs & 258 environmental sponges
- Real-time PCR yielded positive results from 49 swab & 58 sponge samples, with 89% and 100% clinical sensitivity to their respective culture-positive results
- real-time PCR also detected C. auris DNA from 1% & 12% of swab & sponge samples with culture-negative results

J Clin Microbiol. 2017; 55: 2445

Rapid and Accurate Molecular Identification of the Emerging Multidrug-Resistant Pathogen *Candida auris*

Primer	Sequence	Specificity
CauF	5′-CGCACATTGCGCCTTGGGGTA-3′	*C. auris*
CauR	5′-GTAGTCCTACCTGATTTGAGGCGAC-3′	
CauRelF	5′-GCGATACGTAGTATGACTTGCAGACG-3′	*C. auris* and related species (*C. duobushaemulonii*, *C. haemulonii*, and *C. lusitaniae*)
CauRelR	5′-CAGCGGGTAGTCCTACCTGA-3′	

In vitro properties

- Thermotolerance, growing optimally at 37°C & viability up to 42°C, salt tolerance, & cell aggregation into large, difficult-to-disperse clusters (hyphae absent)

- Adhere to polymeric surfaces, form biofilms, & resist antifungal agents

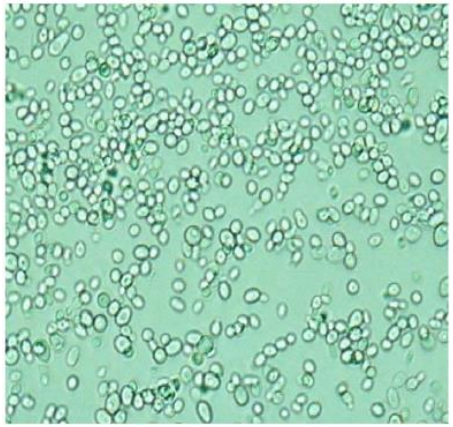
- *C. auris* biofilms significantly thinner (50% thickness of *C. albicans* biofilm) (Larkin E, *et al.* Antimicrob Agents Chemother. 2017 Apr 24, online)

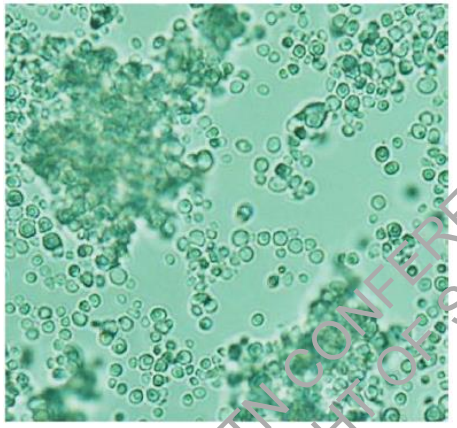
- Minimal ability to adhere to silicone elastomer (a representative catheter material) relative to *C. albicans*

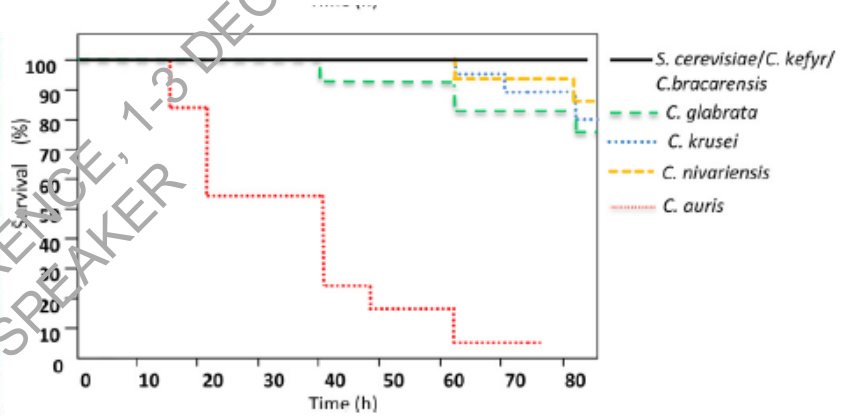
mSphere. 2016 Jul-Aug; 1(4): e00189-16.

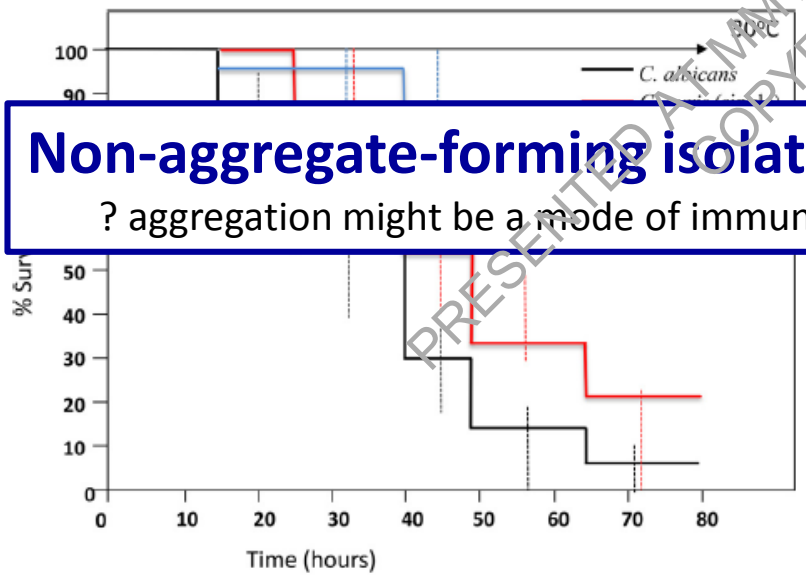
Comparative Pathogenicity of United Kingdom Isolates of the Emerging Pathogen *Candida auris* and Other Key Pathogenic *Candida* Species

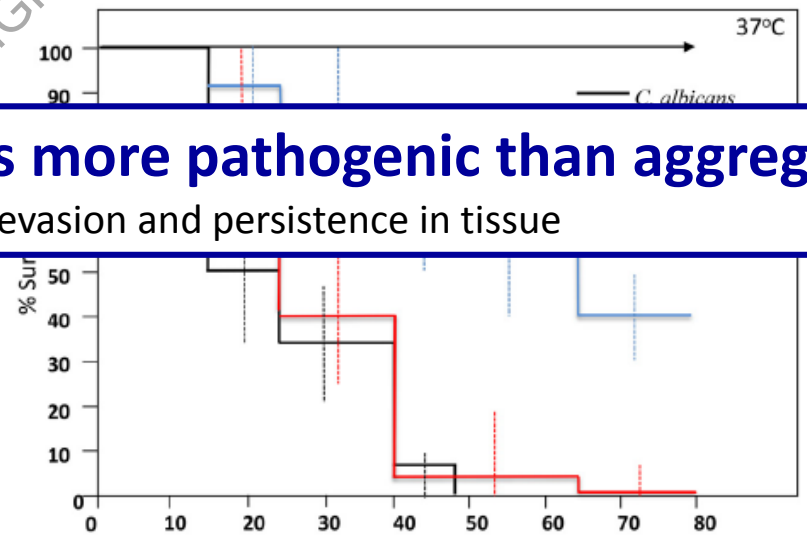
Andrew M. Borman,✉ Adrien Szekely, and Elizabeth M. Johnson











Non-aggregate-forming isolates more pathogenic than aggregating

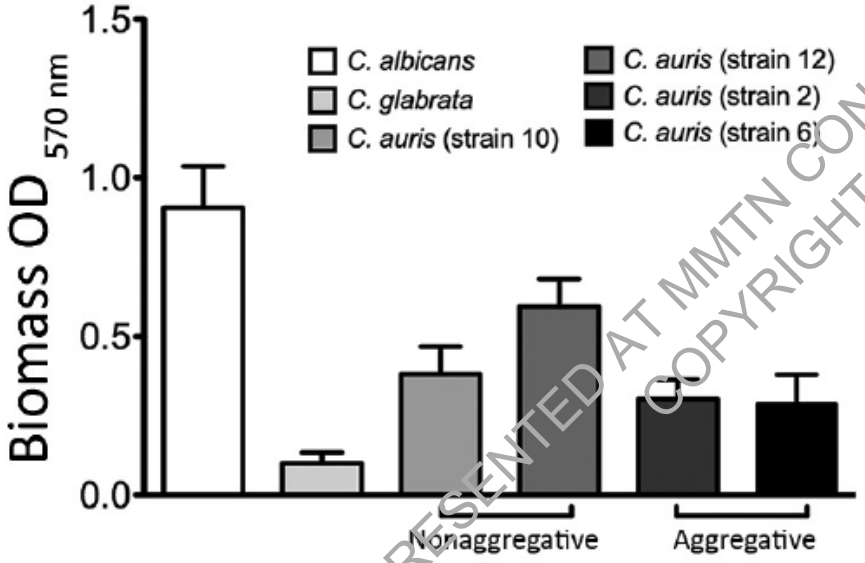
? aggregation might be a mode of immune evasion and persistence in tissue

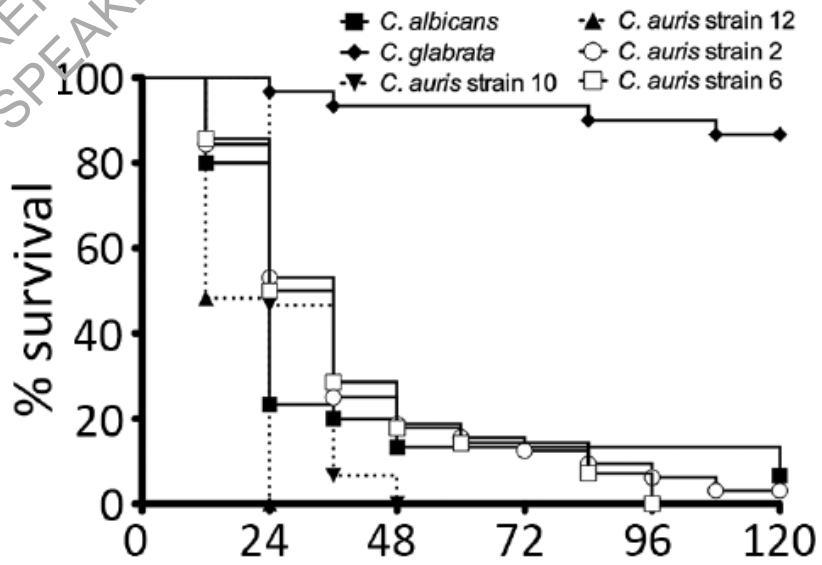
virulence of *Candida* species in *Galleria mellonella* larvae at 37°C

Biofilm-Forming Capability of Highly Virulent, Multidrug-Resistant *Candida auris*

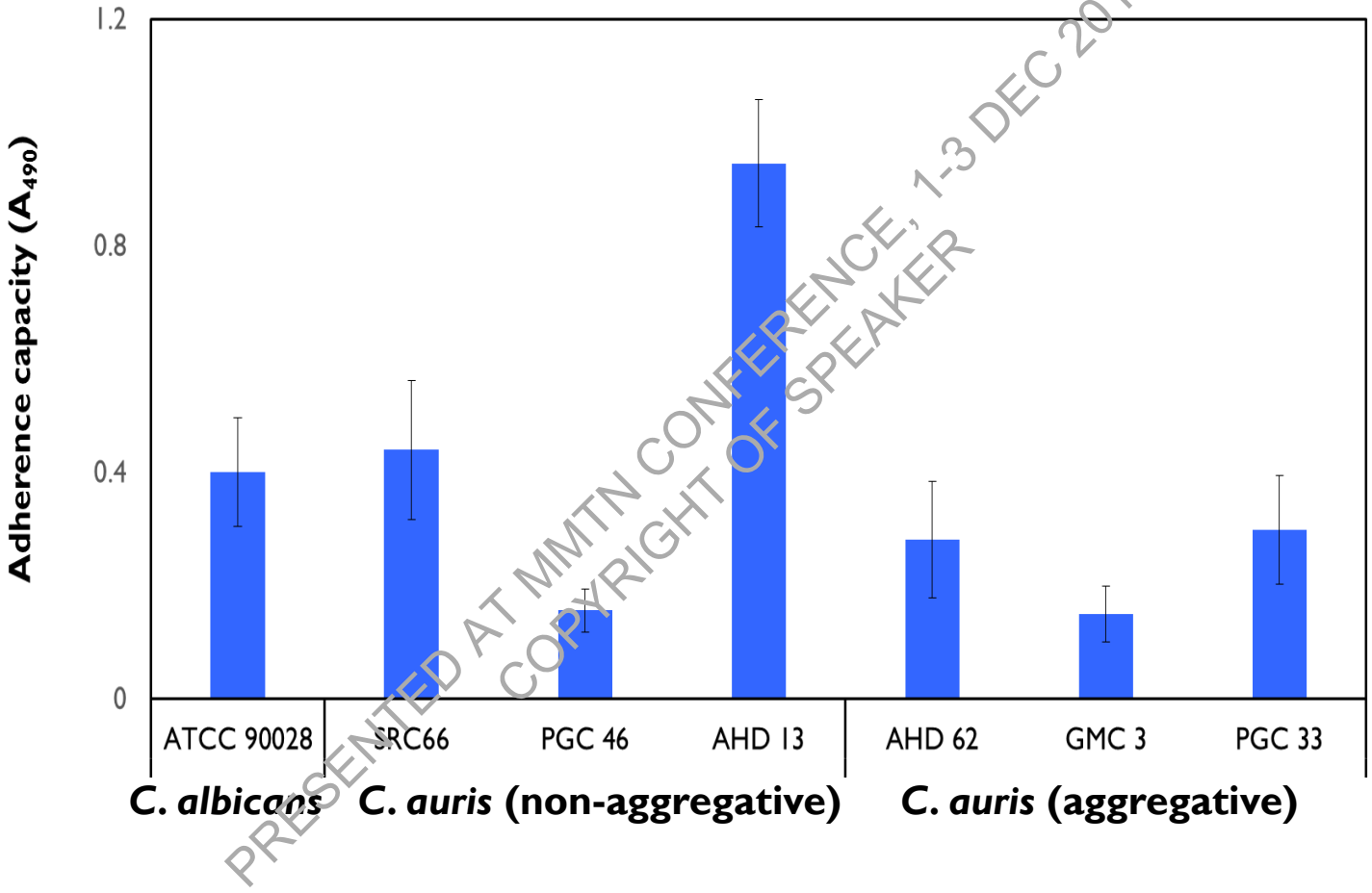
Leighann Sherry, Gordon Ramage, Ryan Kean,
Andrew Borman, Elizabeth M. Johnson,
Malcolm D. Richardson,
Riina Rautemaa-Richardson

Emerging Infectious Diseases
Vol. 23, No. 2, February 2017 328





Biofilm formation of *C. auris*



Genome

- Size approximately **12.3 Mb**
- Large percentage of genes **devoted to central metabolism**
- Genes for cell wall modelling & nutrient acquisition, histidine kinase-2 component systems, iron acquisition, tissue invasion, enzyme secretion, **multidrug efflux**
- ATP-binding cassette **(ABC)** & major facilitator superfamily **(MFS)** transporter families along with drug transporters
- Weak phospholipase activity (majority of isolates being non-phospholipase producers)

Chatterjee S, *et al*. BMC Genomics 2015; 16:686
Sharma C, *et al*. Genome Announc. 2015; 3:pii: e00722

Drug resistance & therapy

Drug resistance reported till 2016

Sharma & Upadhyay. Infect Drug Resist 2017; 10: 155

Reference	No of isolates tested	Method of susceptibility	MIC Range (µg/mL)				
			FLU	VRC	AMB	CAS	5-FC
Satoh et al[11] (2009)	1	Not mentioned	2	0.03	–	–	0.5
Kim et al[9] (2009)	15	Etest method	2–128	0.03–2	0.38–1.5	0.125–0.25	–
Lee et al[27] (2011)	6	CLSI (2008)	2–128	0.03–1	0.5–1	0.06	–
Sarma et al[13] (2012)	15	Vitek 2 compact YST (MIC50/90)	64/64	1/2	8/16	–	1/1
Chowdhary et al[14] (2013)	12	CLSI (2008)	16–64	0.125–0.25	0.25–1	0.125–0.5	0.06–0.125
Chowdhary t al[14] (2013)	15	CLSI (2008)	64	0.5–4	0.25–1	0.25–1	0.25–64
Khillan et al[15] (2014)	4	CLSI (2008)	>64	0.06–0.125	0.125–0.5	1	0.125–4
Shallu Kathuria et al[33] (2016)	90	CLSI (2008)	1–>64	<0.03–16	0.125–8	0.125–8	<0.125–>64
Schelenz et al[20] (2016)	50	Sensititre YeastOne	>256	–	0.5–2	0.06–0.25	0.06–0.12
Sharma et al[34] (2016)	5	CLSI (2008)	≥64	0.125–16	0.25–4	0.25–8	0.125–64

Drug resistance reported in 2017

Antifungal	MIC Range, µg/mL	MIC_{50}, µg/mL	MIC_{90}, µg/mL
Fluconazole	4–256	128	256
Voriconazole	0.03–16	2	8
Itraconazole	0.125–2	0.5	1
Posaconazole	0.06–1	0.5	1
Caspofungin	0.03–16	0.25	1
Anidulafungin	0.125–16	0.5	1
Micafungin	0.06–4	0.25	2
Flucytosine	0.125–128	0.125	0.5
Amphotericin B	0.38–4	1	2

- **Resistance to fluconazole – 93%, voriconazole - 54%, AmB – 35%, Echinocandins – 7%**
- **41% ≥ 2 classes**

Lockhart SR, *et al.* Clin Infect Dis 2017; 64: 134

Drug resistance menace in Asian countries

Fluconazole	• 90% resistant
Voriconazole	• Elevated MICs in 50% of isolates
Amphotericin B	• variable susceptibility; 15%–30% of the isolates exhibit high (>2 µg/ml) MICs
Echinocandin	• 2%–8% resistant
MDR	• 50% resistant to ≥2 antifungal classes
All classes resistant	• 4%
Indian ICUs	• Fluconazole 58.1% (R), amphotericin B (13.5%), Caspofungin 9.5% (high MIC);16.2% MDR

Rudramurthy *et al.* J Antimicrob Chemother 2017; 72: 1794

Chowdhary *et al.* PLoS Pathog 2017 13(5): e1006290.

Chakrabarti *et al.* Intensive Care Med 2015; 41: 285

Mechanism of drug resistance

- Resistance probably **inducible under antifungal pressure with rapid mutational changes**
  - Single copies of ERG3, ERG11, FKS1, FKS2and FKS3 genes present
  - Alterations at azole-resistance codons of ERG11 (strongly associated with country-wise–specific geographic clades)
  - Significant portion of genome encodes ABC and MFS transporter families along with drug transporters

Chatterjee S, *et al*. BMC Genomics 2015; 16:686
Sharma C, *et al*. Genome Announc. 2015; 3:pii: e00722

Therapeutic options

- No consensus exists for optimal treatment
- Echinocandins remain the first-line therapy for *C. auris* infection
  - Caspofungin shown to be inactive against *C. auris* biofilms
- Flucytosine (MIC50, 0.125–1 µg/ml) in renal tract or UTI
- Posaconazole (range, 0.06–1 µg/ml) & isavuconazole (range, <0.015–0.5 µg/ml) show excellent in vitro activity against *C. auris*
- New drugs- SCY-078 & pulmocide exhibit potent antifungal activity against *C. auris* isolates

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Pharmacodynamic Optimization for Treatment of Invasive *Candida auris* Infection

Lepak AJ, Zhao M, Berkow EL, Lockhart SR, Andes DR.

Table. Nine select *Candida auris* strains used in the studies including country of origin, antimicrobial susceptibility results, and 24-hour total drug PK/PD target exposures in the murine invasive candidiasis model.

Strain	Country of Origin	96 h Growth in Untreated Controls (CFU/kidney)	Fluconazole		Micafungin			Amphotericin B	
			MIC (mg/L)	24 h Stasis AUC/MIC	MIC (mg/L)	24 h Stasis AUC/MIC	24 h 1 log kill AUC/MIC	MIC (mg/L)	24 h Stasis Cmax/MIC
B11804	Colombia	2.17	2	51.2	0.5	48.1	120.3	0.5	0.87
B11801	Colombia	2.86	16	26.3	1	32.9	49.9	2	NA
B11799	Colombia	2.08	16	36.3	2	18.5	92.1	0.5	1.29
B11221	South Africa	1.85	128	6.3	1	47.6	140.6	0.38	0.52
B11211	India	1.97	256	NA	4	NA	NA	1.5	0.69
B11785	Colombia	2.32	8	34.1	0.5	59.4	119.2	1.5	1.50
B11220	Japan	1.04	4	5.0	0.125	286.5	674.4	0.38	NA
B11203	India	2.13	256	NA	0.25	117.0	376.4	4	0.51
B11104	Pakistan	1.71	256	4.1	0.25	134.3	536.8	1	2.13
Median				**26.3**		**53.7**	**130.5**		**0.87**
Std dev				**18.5**		**87.9**	**235.3**		**0.60**

NA, endpoint not achieved

was a fluconazole AUC/MIC of 26, amphotericin B Cmax/MIC of 0.9, and micafungin AUC/MIC of 54. The micafungin PD targets for *C. auris* were ≥20-fold lower than other *Candida* species in this animal model. Clinically relevant micafungin exposures produced the most killing among the three classes.

In vitro interaction between echinocandins & azoles

- **Synergistic interactions between micafungin & voriconazole** with fractional inhibitory concentration index (FICI) values of 0.15 to 0.5
- **Indifferent interactions between micafungin & fluconazole** (FICI, 0.62 to 1.5)
- **Indifferent interactions between caspofungin & fluconazole or voriconazole**

	MFG + FLU[c]				MFG + VRC[c]			
	MIC (μg/ml)				MIC (μg/ml)			
Strain no.	MFG	FLU	MFG/FLU	FICI/INT	MFG	VRC	MFG/VRC	FICI/INT
VPCI 482/P/13[a]	0.25	≥64	0.25/64	1.5/IND	0.25	2	0.016/0.5	0.31/SYN
VPCI 1132/P/13[a]	0.5	32	0.25/4	0.62/IND	0.5	0.5	0.016/0.125	0.28/SYN
VPCI 1133/P/13[a,b]	8	≥64	4/32	0.75/IND	8	1	2/0.25	0.5/SYN
VPCI 265/P/14[a]	0.5	32	0.5/8	1.25/IND	0.5	8	0.063/1	0.25/SYN
VPCI 1510/P/14[a]	0.125	32	0.063/8	0.75/IND	0.125	4	0.016/0.25	0.19/SYN
VPCI 1514/P/14[a,b]	8	≥64	8/16	1.1/IND	8	0.5	1/0.125	0.37/SYN
VPCI 266/P/14[a]	0.25	≥64	0.25/32	1.25/IND	0.25	0.5	0.008/0.125	0.28/SYN
VPCI 267/P/14[a,b]	8	32	8/8	1.25/IND	8	0.5	1/0.125	0.37/SYN
VPCI 487/P/14[a]	4	≥64	4/32	1.25/IND	4	1	0.5/0.125	0.25/SYN
VPCI 518/P/14[a]	0.5	≥64	0.25/64	1/IND	0.5	1	0.016/0.125	0.15/SYN

	CAS + FLU[b]				CAS + VRC[b]			
	MIC (μg/ml)				MIC (μg/ml)			
Strain no.	CAS	FLU	CAS/FLU	FICI/INT	CAS	VRC	CAS/VRC	FICI/INT
VPCI 482/P/13[a]	2	≥64	1/32	0.75/IND	2	2	1/0.5	0.75/IND
VPCI 1132/P/13[a]	2	32	1/8	0.75/IND	2	0.5	1/0.063	0.62/IND
VPCI 1133/P/13[a]	4	≥64	2/64	1/IND	4	1	2/0.25	0.75/IND
VPCI 265/P/14[a]	4	32	2/32	1.5/IND	4	8	2/0.25	0.75/IND
VPCI 1510/P/14[a]	0.5	32	0.5/32	2/IND	0.5	4	0.5/4	2/IND
VPCI 1514/P/14[a]	1	≥64	0.5/32	0.75/IND	1	0.5	1/0.25	1.5/IND
VPCI 266/P/14[a]	2	≥64	1/32	0.75/IND	2	0.5	1/0.25	1/IND
VPCI 267/P/14[a]	2	32	1/8	0.75/IND	2	0.5	2/0.063	0.62/IND
VPCI 487/P/14[a]	1	≥64	0.5/8	0.56/IND	1	1	0.5/0.125	0.62/IND
VPCI 518/P/14[a]	0.5	≥64	0.25/8	0.56/IND	0.5	1	0.25/0.25	0.75/IND

Fakhim H, *et al*. Antimicrob Agent Chemother 2017; 61: e01056-17

Prevention & control of outbreak

Prevention of spread

- Problem – we do not know the source
- Admission screening for yeast carriage
- Isolation or cohorting of patients with dedicated nursing staff in separate areas, contact precaution & notify any positive case
- Epidemiological investigation, complemented by cross-sectional patient screening & environmental sampling
- Skin decontamination and oral gargles with chlorhexidine-containing mouth wash, & use of topical nystatin & terbinafine for cannula entry sites
- Environmental cleaning - chlorine & hydrogen peroxide products
- Hand hygiene compliance, maximal sterile barriers upon insertion & use of chlorhexidine for skin disinfection

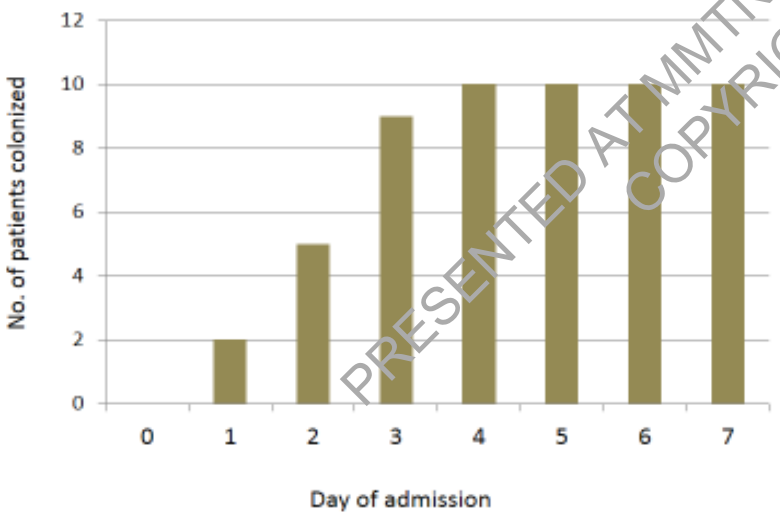
CDC recommendation

- **Contact precautions** with a single room
- **Reinforce hand washing** - alcohol-based hand rub or soap & water
- **Daily and terminal cleaning** of patient rooms and equipment with an EPA-registered disinfectant active against *C. difficile*
- **Weekly screens** for recurrence of colonization for patients admitted for prolonged duration
- First-line therapy remains an **echinocandin** although susceptibility testing is recommended

http://www.cdc.gov/fungal/diseases/candidiasis/candida-auris-alert.html

Surveillance of *C. auris* in hospital

- Colonization of the patients in trauma ICU
  - None of the patients are colonized at the time of admission



Days of acquisition of *C. auris*

- Persistence of *C. auris* in hospital environment
  - **Hands** of healthcare workers
  - Contamination of bed surface, certain equipment like ventilator, temperature probes & ECG leads
  - *C. auris* can **persist on blankets or linen at least 7d**

Biswal M, *et al.* J Hosp Infect 2017 (online)

How to get rid of *C. auris* from hospital environment?

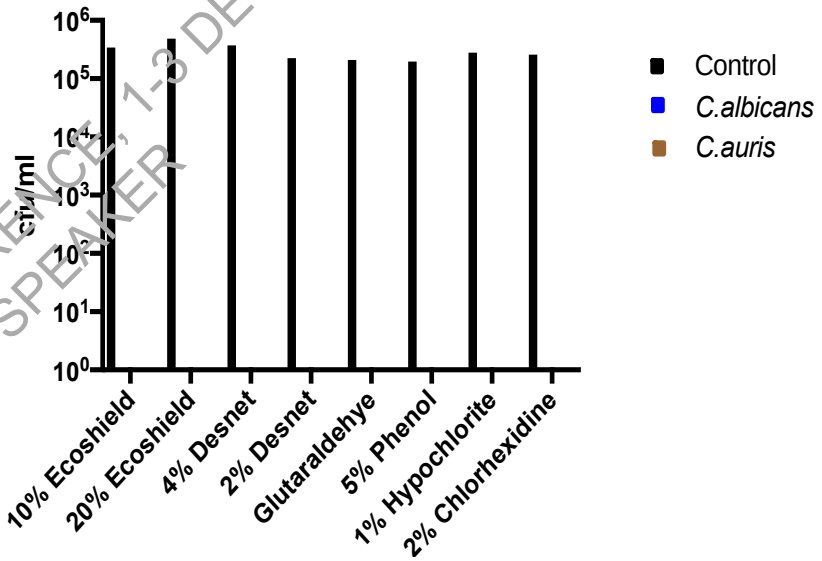
- **Colonization of patients**
  - Chlorhexidine body wash
  - Oral nystatin tablets

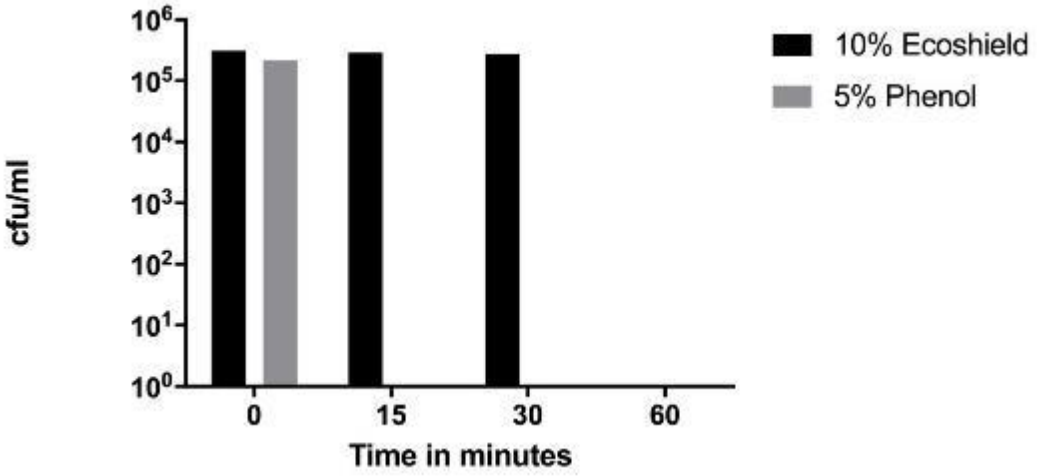
- **Hand wash**

S. no	Group 1 (control)	Group-2 (Soap & water)	Group-3 (Alcohol + chlorhexidine)	Group-4 (70% Alcohol)
1	Confluent growth	2 colonies	No growth	No growth
2	Confluent growth	No growth	No growth	No growth
3	Confluent growth	No growth	No growth	No growth

Biswal M, *et al.* J Hosp Infect 2017 (online)

- **Disinfectant**





When you should think you are dealing with *C. auris*?

- If the patient is from ICU or high-dependency area
- Transferred from another hospital after a long stay
- Multiple intervention & prior antifungal exposure
- If one identify in a commercial system -*Candida haemulonii, Candida famata, C. guilliermondii, C. lusitaniae, C. parapsilosis, Rhodotorula glutinis, Candida sake, Saccharomyces cerevisiae*
- If the *Candida* appears to be resistant to fluconazole & high MIC to voriconazole

***C. auris* could grow at 42˚ C, but failed to grow in presence of 0.01% or 0.1% cycloheximide. Ferment dextrose, dulcitol, mannitol**

A paradigm shift for *Candida* infections

The yeast that acts like a bacteria!

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

Gaps in knowledge

Is it a jump from Japan & Korea to India or we missing the isolates in other Asian countries?

Why it is independently, almost simultaneously, emerged in so many places worldwide?

Why it exhibits high level of antifungal resistance?

Need to study source of agent & transmission mechanism

Best therapeutic options

Take home message

- *C. auris* – a new agent, multi-drug resistant, ?clonal
- Emerged in several countries across globe within short period
- Comes in crop, disappear, again comes
- Hospital is the major source - ?where it thieves
- Identification is challenge – microbiologist should be vigilant
- Vigilance of the clinicians for any ICU patient with long stay
- Should be reported to reference centre of your country
- Disinfectants (hypochlorite, hydrogen peroxide, phenol, iodine providone, & alcohols) are effective for environmental surfaces; quaternary ammonium compounds not effective
- For decolonization of skin, 2% chlorhexidine gluconate sponging or paint with 1% providone iodine

THANK YOU