Candida auris
現況與感染管制措施介紹

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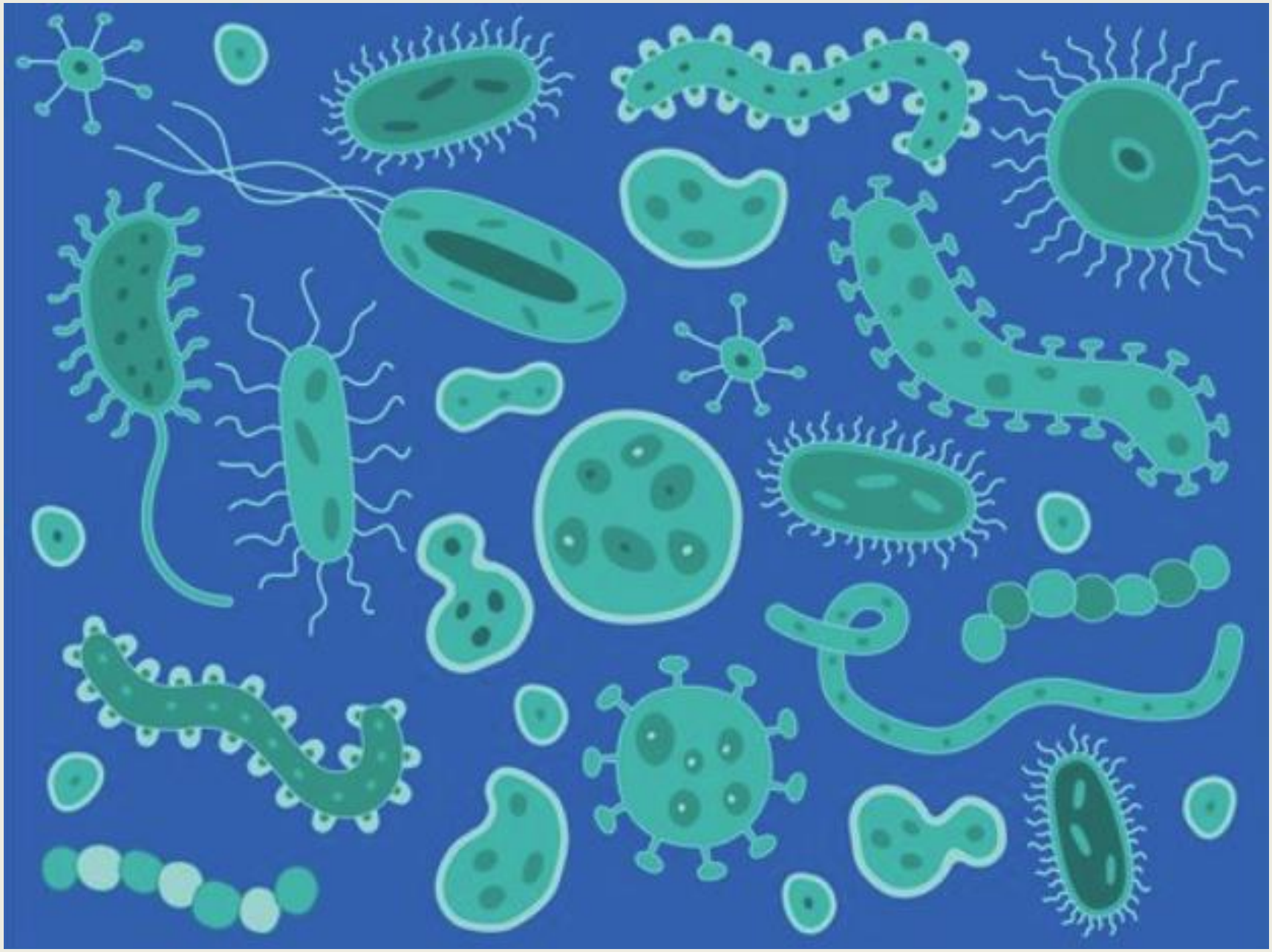
內容

- *Candida* 簡介
- *C. auris*簡介
- *C. auris* 感染管制建議
- *C. auris* 治療建議
- 結論

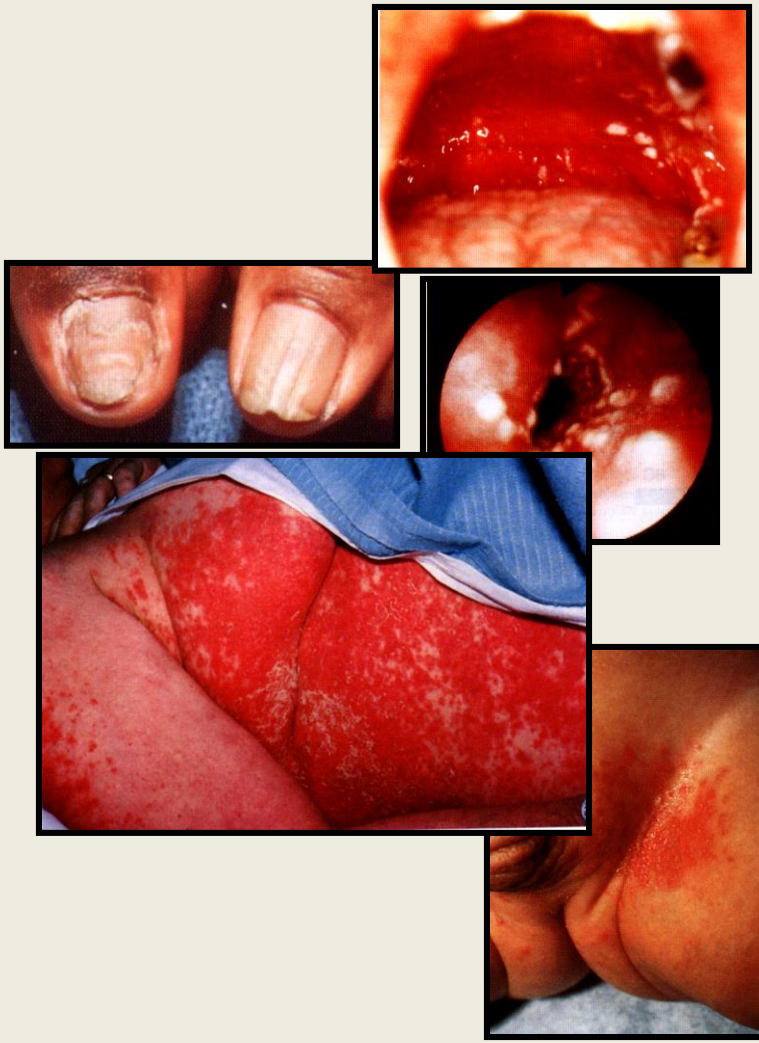


https://www.safespaceco.com/preventing-candida-auris/

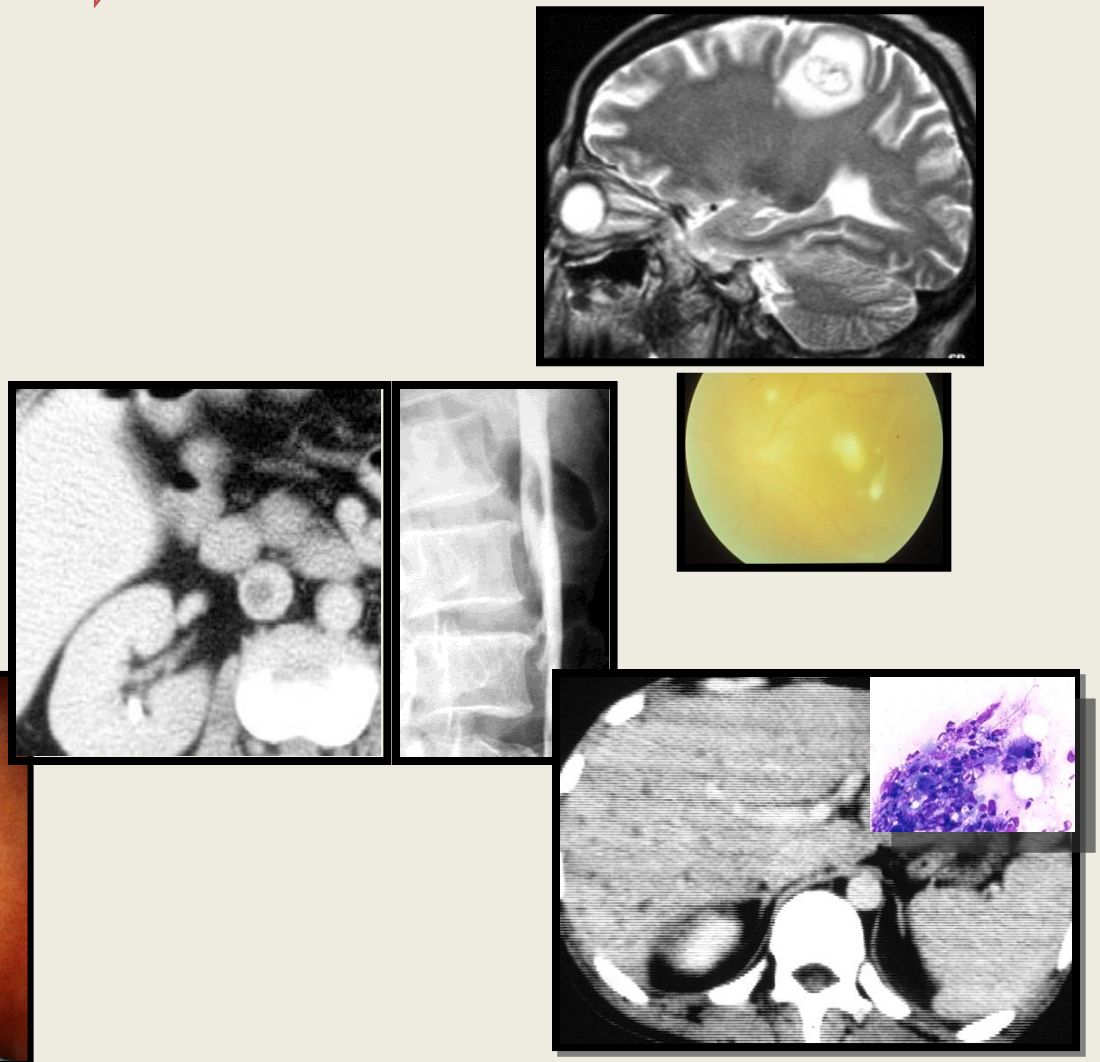
Candida: A Perfect Pathogen

Candida **colonization**

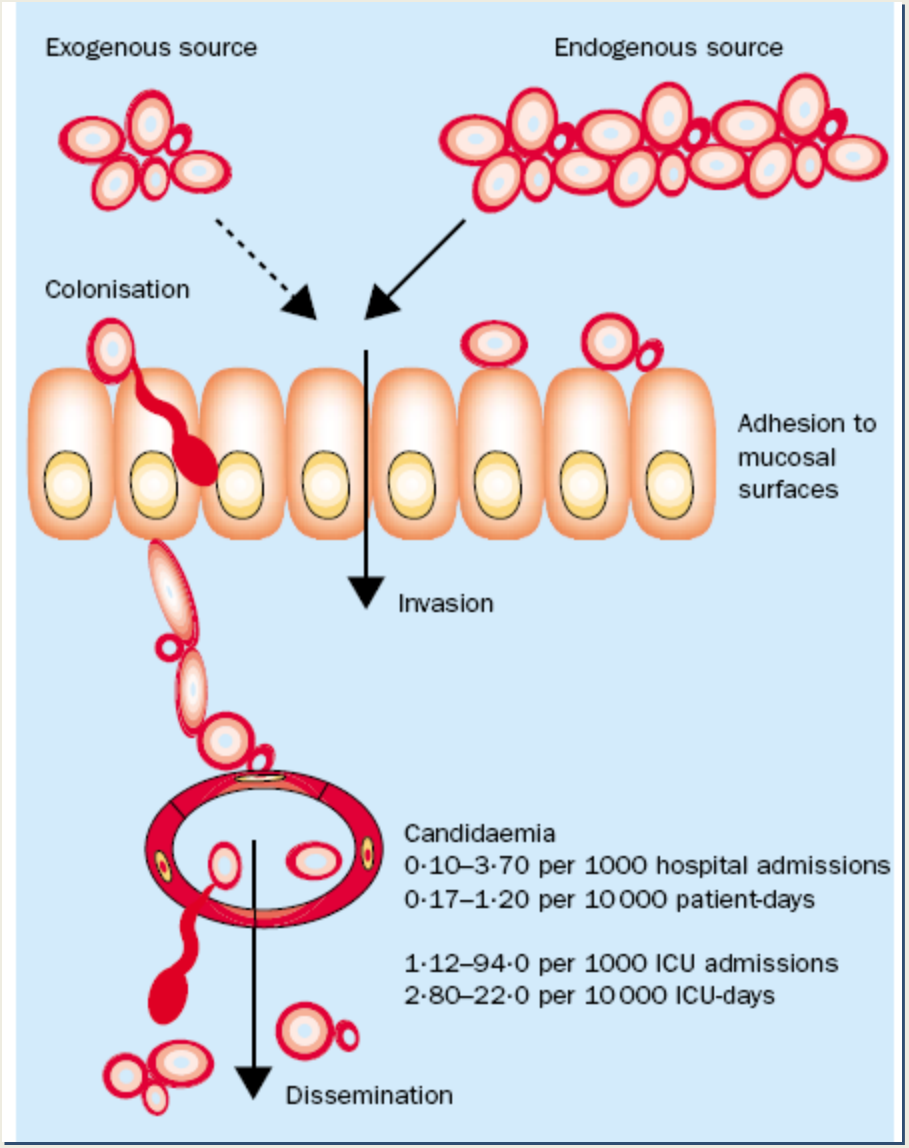
Superficial infection



Systemic infection



Pathophysiology of invasive candidiasis



Endogenous: The organisms are normal commensals of humans and are commonly found on skin, throughout the entire gastrointestinal tract, in expectorated sputum, in the female genital tract, and in the urine of patients with indwelling Foley catheters.

Exogenous: There is a relatively high incidence of carriage on the skin of health care workers.

Lancet Infect Dis 2003; 3: 685–702
http://www.ppidonline.com/content/default.

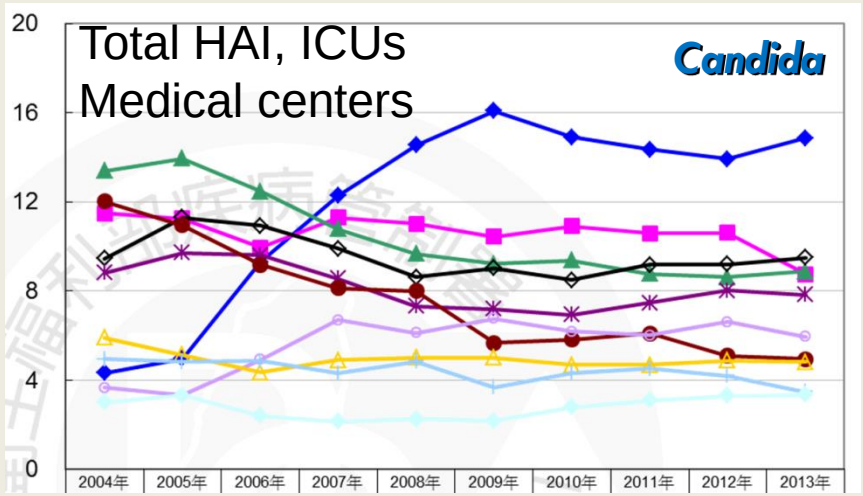
The scope of the problem in Taiwan

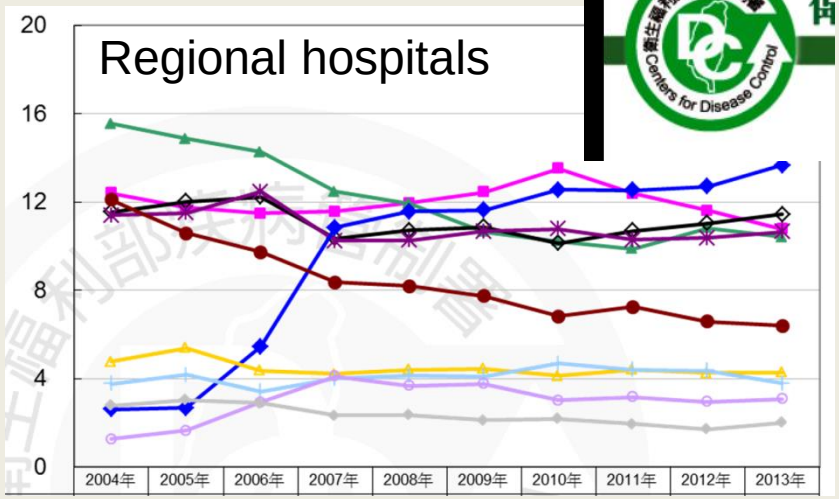
NTUH

- *Candida* were the leading pathogens of healthcare-associated bloodstream infection (HABSI) since 1993 at NTUH.[1]
- Average annual change of *C. albicans* HABSI during 1981-2007 was 13.5% (8.7% -18.4%).[2]

Taiwan

- *Candida* was the **2nd HABSI pathogen** since 2009/2008 and **1st urinary pathogen** since 2007.[3]





[1] Chen YC et al. Infect Control Hosp Epi 1997;18:369-75. [2] Chuang YC et al. J Hosp Infect 2010;76:143
[3] TNIS data, CDC, Taiwan

Journal of Microbiology, Immunology and Infection (2014) 47, 95–103

Available online at www.sciencedirect.com

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journal homepage: www.e-jmii.com

ORIGINAL ARTICLE

Comparison of epidemiology and treatment outcome of patients with candidemia at a teaching hospital in Northern Taiwan, in 2002 and 2010

Pao-Yu Chen [a,b], Yu-Chung Chuang [a,b], Jann-Tay Wang [a,b], Wang-Huei Sheng [a,b], Chung-Jen Yu [a,c,d], Chen-Chen Chu [e], Po-Ren Hsueh [a,f], Shan-Chwen Chang [a,b,c], Yee-Chun Chen [a,b,c,*]

	2002	2010
Incidence, per 1000 patients	2.78	2.88 (p = 0.71)
Incidence density, per 1000 patient-days	0.34	0.41 (p=0.04).

The incidence density of candidemia was high and increased in 2010 compared with 2002, which was at least in part due to the increase in patients at a higher risk of candidemia.

Risk factors associated with candidemia

a hospital-based population study, NTUH, 2010

Parameters	Univariate analysis				Multivariate analysis			
	Odds ratio	95% confidence interval		*p* value	Odds ratio	95% confidence interval		*p* value
		Lower	Upper			Lower	Upper	
Age								
0–12 mo	2.54	1.04	6.17	0.04	3.67	1.50	8.97	0.004
1–19 y	1.08	0.54	2.14	0.82	1.07	0.54	2.13	0.85
20–44 y (as reference)								
45–64 y	2.65	1.73	4.07	<0.001	2.18	1.42	3.30	<0.001
≥65 y	3.70	2.43	5.64	<0.001	2.64	1.72	4.06	<0.001
Sex, male	1.48	1.17	1.88	0.001				
Charlson comorbidity index								
0–1 (as reference)								
2	2.57	1.68	3.92	<0.001				
3	3.94	2.49	6.21	<0.001				
≥4	6.62	4.63	9.47	<0.001				

Chen PY et al. J Microbiol Immunol Infect 2014;47:95

Risk factors associated with candidemia

a hospital-based population study (cont.)

Parameters	Univariate analysis				Multivariate analysis			
	Odds ratio	95% confidence interval		*p* value	Odds ratio	95% confidence interval		*p* value
		Lower	Upper			Lower	Upper	
Underlying diseases/status								
Congestive heart failure	2.24	1.42	3.54	0.001				
Cerebrovascular diseases	1.39	0.86	2.24	0.18				
Chronic pulmonary diseases	2.27	1.52	3.41	<0.001	1.90	1.25	2.89	0.003
Connective tissue diseases	1.12	0.55	2.26	0.76				
Moderate-to-severe liver diseases	1.37	0.83	2.28	0.22				
Moderate-to-severe renal diseases	8.76	6.70	11.46	<0.001	8.08	6.11	10.67	<0.001
Diabetes mellitus without end organ damage	1.46	1.08	1.98	0.01				
Diabetes mellitus with end organ damage	0.95	0.35	2.55	0.92				
Any tumor	1.16	0.91	1.48	0.23				
Lymphoma	3.33	2.11	5.25	<0.001	3.98	2.49	6.35	<0.001
Leukemia	3.68	2.38	5.71	<0.001	4.58	2.90	7.23	<0.001
Gastrointestinal malignancy	3.93	2.83	5.46	<0.001	2.80	1.93	4.05	<0.001
Metastatic solid tumor	2.51	1.93	3.26	<0.001	2.32	1.72	3.14	<0.001
Neutropenia	3.06	1.75	5.35	<0.001				
Acquired immunodeficiency syndrome	2.44	0.78	7.66	0.12				
Solid organ transplant (kidney, liver, heart, pancreas)	1.70	0.63	4.57	0.29				

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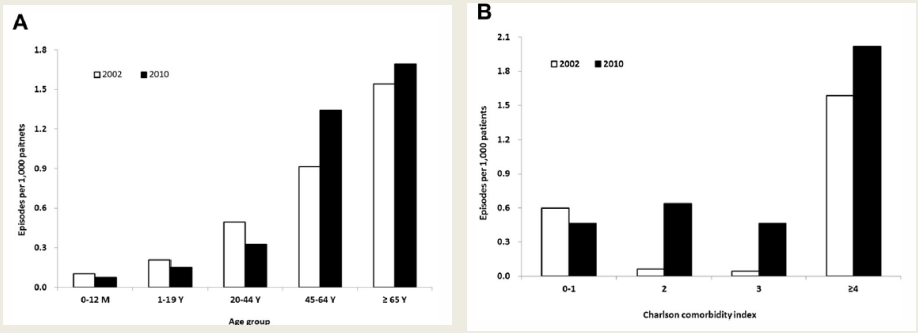
Disease-specific incidence of candidemia



Parameters	2002 (n = 218)	2010 (n = 286)	p value
Congestive heart failure	10 (7.91)	20 (7.71)	>0.99
Cerebrovascular diseases	22 (6.81)	18 (4.89)	0.37
Chronic pulmonary diseases	22 (8.37)	26 (7.71)	0.89
Connective tissue diseases	2 (2.42)	8 (4.00)	0.81
Moderate-to-severe liver diseases	20 (4.91)	16 (4.85)	>0.99
Moderate-to-severe renal diseases	54 (15.13)	73 (23.83)	0.01
Diabetes mellitus without end organ damage	21 (3.86)	52 (4.94)	0.41
Diabetes mellitus with end organ damage	3 (3.27)	4 (3.40)	>0.99
Any tumor	52 (3.90)	104 (3.95)	>0.99
Lymphoma	11 (12.72)	20 (16.99)	0.56
Leukemia	17 (14.33)	22 (12.37)	0.76
Gastrointestinal malignancy	36 (28.80)	42 (12.44)	<0.001
Metastatic solid tumor	53 (11.91)	76 (7.53)	0.01
Neutropenia	11 (11.54)	13 (8.67)	>0.99
Acquired immunodeficiency syndrome	3 (12.10)	3 (10.56)	0.89
Solid organ transplantation (kidney, liver, heart, pancreas)	2 (5.10)	4 (6.04)	>0.99
Hematopoietic stem cell transplantation	0 (0.00)	0 (0.00)	—

Per 1000 patients

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Characteristics of patients hospitalized at NTUH

Parameters	2002	2010	*p* value
Number of acute care beds	2200	2300	—
Total number of admissions	66,763	79,710	—
Total number of patient-days	632,318	691,692	—
Age, y	47.3 ± 23.6	51.2 ± 22.9	<0.001
Sex, male (%)	34,514 (54.58)	39,669 (57.35)	<0.001
Charlson comorbidity index	2.10 ± 3.45	3.18 ± 4.33	<0.001
Underlying disease/status, N (0/00)			
Congestive heart failure	1264 (18.93)	2595 (32.56)	<0.001
Cerebrovascular diseases	3230 (48.38)	3682 (46.19)	0.04
Chronic pulmonary diseases	2629 (39.38)	3372 (42.30)	0.005
Connective tissue diseases	828 (12.40)	2002 (25.12)	<0.001
Moderate-to-severe liver diseases	4076 (61.05)	3302 (41.43)	<0.001
Moderate-to-severe renal diseases	3568 (53.44)	3063 (38.43)	<0.001
Diabetes mellitus without end organ damage	5447 (81.59)	10,530 (132.10)	<0.001
Diabetes mellitus with end organ damage	918 (13.75)	1177 (14.77)	0.10
Any tumor[a]	13,330 (199.66)	26,312 (330.10)	<0.001
Lymphoma	865 (12.96)	1776 (22.28)	<0.001
Leukemia	1186 (17.76)	1779 (22.32)	<0.001
Gastrointestinal malignancy[b]	1250 (18.72)	3377 (42.37)	<0.001
Metastatic solid tumor	4451 (66.67)	10,090 (126.58)	<0.001
Acquired immunodeficiency syndrome	260 (3.89)	346 (4.34)	0.19
Neutropenia	909 (13.62)	1231 (15.44)	0.004
Solid organ transplantation (kidney, liver, heart, pancreas)	392 (5.87)	662 (8.31)	<0.001
Hematopoietic stem cell transplantation	29 (0.43)	106 (1.00)	<0.001
Incidence density of candidemia (per 1000 patient-days)	218 (0.34)	286 (0.41)	0.04

[a] Any tumor is defined as any solid malignancy excluding gastrointestinal malignancy, metastatic malignancy, leukemia and lymphoma.
[b] Gastrointestinal malignancy indicates malignancies involving any part of the following organs: esophagus, stomach, small or large intestines, and rectum.

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Despite more patients in 2010 receiving antifungal therapy earlier, mortality remained high

	2002 (n = 218)	2010 (n = 286)	p value
Time to initiation of antifungal therapy			
Same day	19 (8.72)	31 (10.84)	0.43
1 d later	41 (18.81)	87 (30.42)	0.003
2 d later	33 (15.14)	44 (15.38)	0.94
≥3 d later	38 (17.43)	35 (12.24)	0.10
No treatment	33 (15.14)	30 (10.49)	0.12
Breakthrough candidemia	54 (24.77)	59 (20.63)	0.27
First antifungal agents	185 (84.86)	256 (89.51)	0.12
Fluconazole[a]	162 (87.57)	242 (94.53)	0.009
Voriconazole[a]	0 (0.00)	1 (0.39)	>0.99
Amphotericin B[a]	18 (9.73)	5 (1.95)	<0.001
Lipid formulation amphotericin B[a]	1 (0.54)	0 (0.00)	0.42
Enchinocandins[a]	0 (0.00)	6 (2.34)	0.04
Combination therapy[a]	4 (2.16)	2 (0.78)	0.24
30-day mortality	100 (45.87)	127 (44.41)	0.74
Same day[b]	7/19 (36.84)	14/31 (45.16)	0.56
1 d later[b]	23/41 (56.10)	35/87 (40.23)	0.09
2 d later[b]	15/33 (45.45)	16/44 (36.36)	0.42
≥3 d later[b]	12/38 (31.58)	11/35 (31.43)	0.99
No treatment[b]	13/33 (39.39)	20/30 (66.67)	0.03
Breakthrough candidemia[b]	30/54 (55.56)	31/59 (52.54)	0.75

[a] Percentage by proportion of total patients receiving antifungal therapy.
[b] Mortality stratified by time to initiate antifungal therapy.

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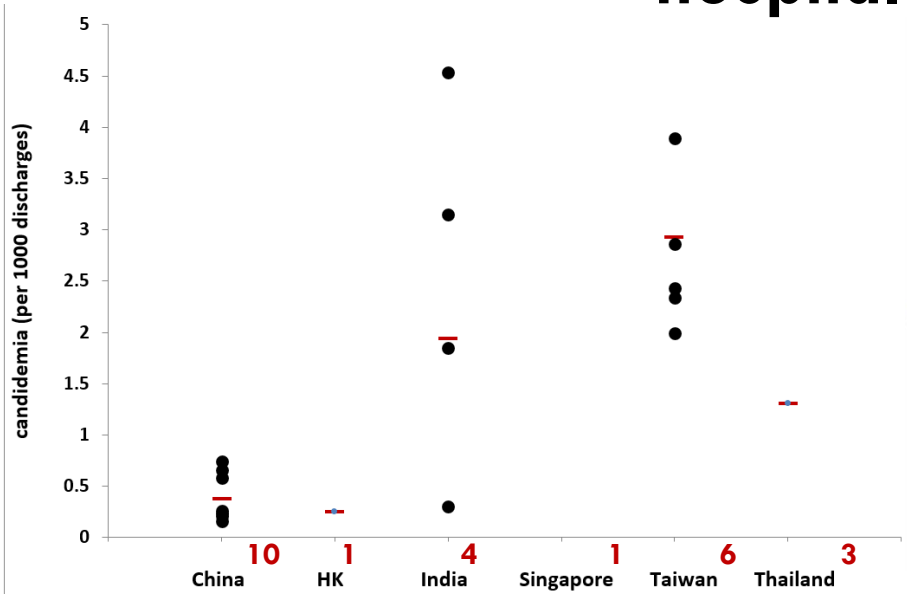
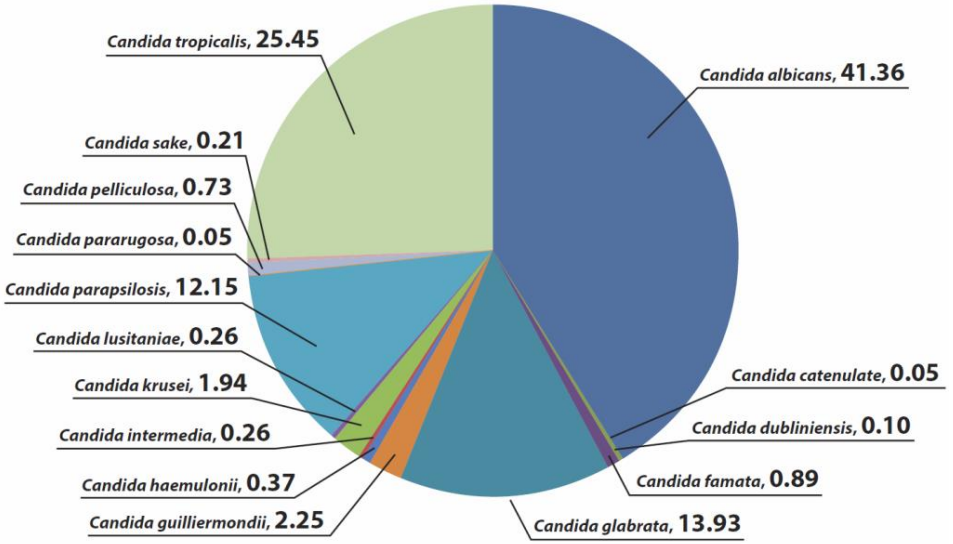
Laboratory-based surveillance of candidaemia, 25 hospitals in Asia



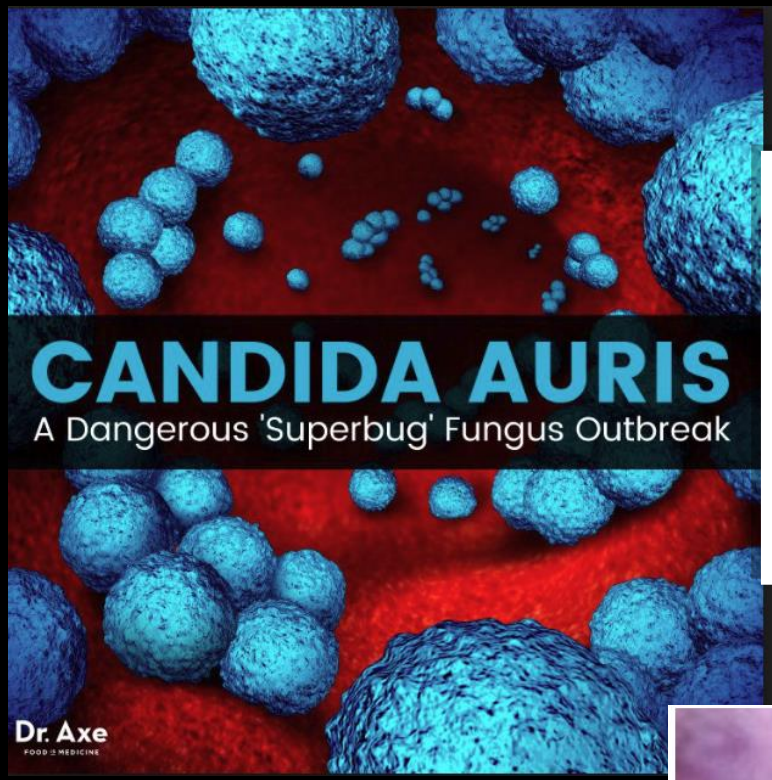


The ICU settings contribute, at least in part, to the incidence variation among hospitals

Among rare *Candida* species, *C. pelliculosa*, also known as *Pichia anomala* or *Hansenula anomala*, is mainly found in plants, fruits and oil. Ten out of 14 episodes in this cohort were reported from a single hospital, clustered in the ICUs. In the preceding year, this hospital identified a monoclonal outbreak of *C. pelliculosa*.

Tan BH, …Chen YC. *Clin Microbiol Infect* 2015;21:946–953.
J Microbiol Immunol Infect 2013;46:456

ICU: intensive care unit.

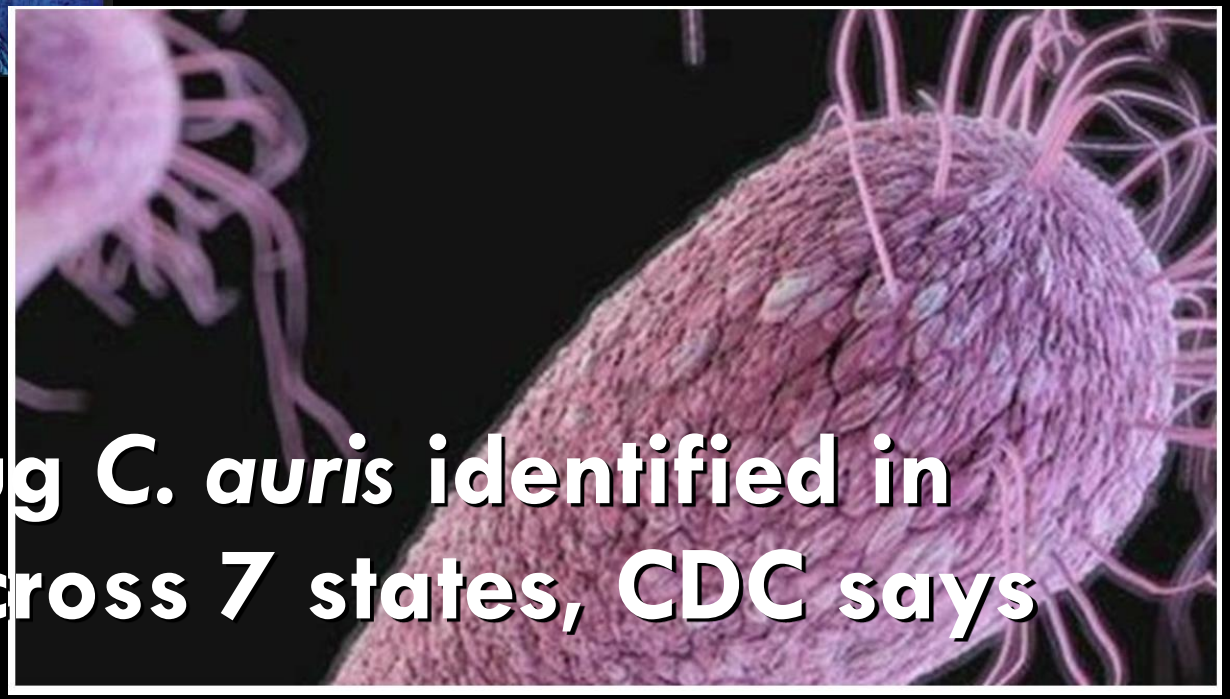


https://draxe.com/candida-auris/

2009-2017….

News

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



CNN: Superbug C. *auris* identified in 122 people across 7 states, CDC says

為什麼要重視C. auris ？

多重抗藥性 + 在醫療照護機構傳播 + 困難診斷

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

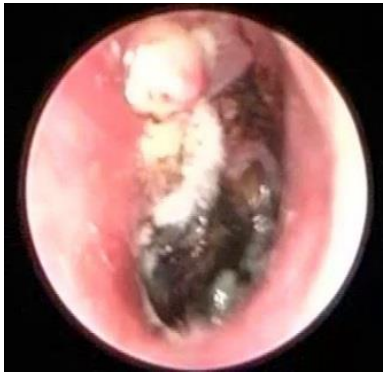
C. auris重要性及獨特性

1. 可造成**血流**感染、傷口感染及耳部感染，甚或死亡， 特別是在有嚴重疾病或醫療處置的病人身上。
2. 常具有多重**抗藥**性，其對多種常用於治療念珠菌症的 抗黴菌藥抗藥（大多對 fluconazole 抗藥），嚴重限制了 C. *auris* 感染之治療選擇。有些菌株對 3 類主要的抗黴菌藥均抗藥， 此種多重抗藥性在其他念珠菌種非常罕見。
3. 傳統的檢驗方法難以**鑑定** C. *auris*，若沒有特定技術，C. *auris* 會被誤認為其他菌種，導致不適當的處理。
4. C. *auris* 於 2009 年在日本首次被發現，但其已於歐洲、亞洲、 美洲、非洲十餘國迅速傳播並造成感染。
5. C. *auris* 以外的念珠菌種之感染多為散發性、內源性菌株之感 染，然而C. *auris* 則較易在醫療照護機構中經由人傳人傳播 /感染，並已在醫療照護機構中引起**群突發**，且難以控制。

C. *auris* infection

- First isolation of C. *auris* was from the external ear canal of a 70-year-old woman in Japan (Microbiol Immunol 2009; 53: 41)
- Chronic otitis media - in Korea (2004-2006) reported 15 cases (Clin Infect Dis 2009; 48: e57)
- Vulvovaginitis -a young woman in India (J Infect Dev Countries 2015; 9: 435)
- Fatal pericarditis in an Indian patient with end stage liver disease (JMM Case Rep doi:.10.1099/jmmcr.0.T00018)
- In London outbreak – isolated from sternal wound (Antimicob Res Infect Control 2016; 5: 35)
- Candidemia

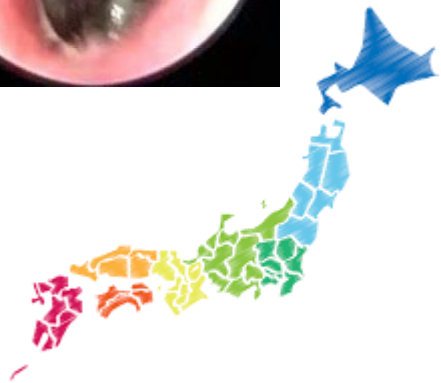
2009年在日本首次被發現

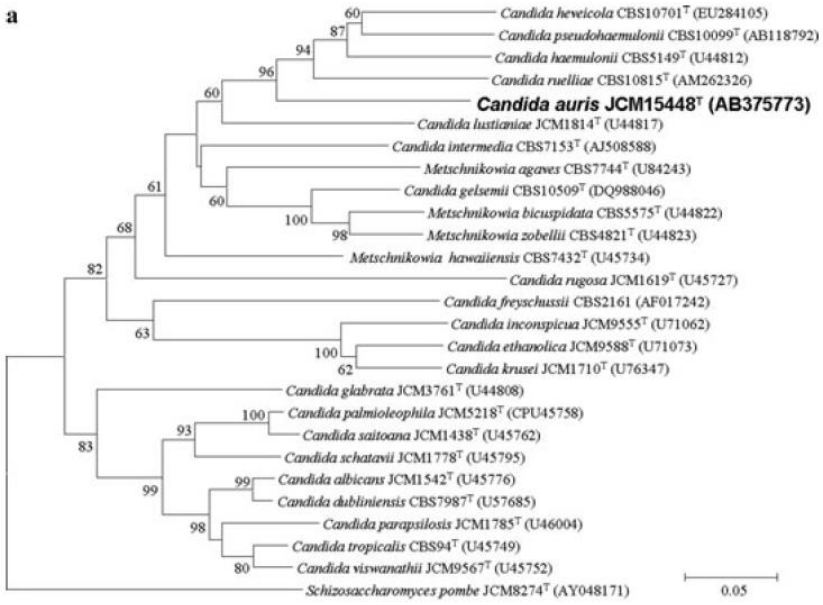


ORIGINAL ARTICLE *Microbiol Immunol* 2009; 53: 41–44

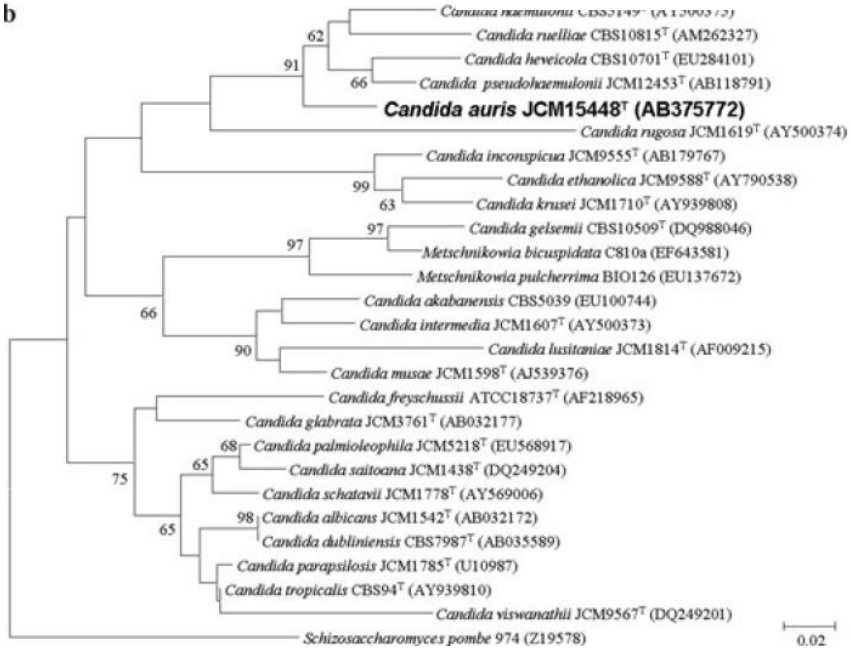
Candida auris sp. nov., a novel ascomycetous yeast isolated from the external ear canal of an inpatient in a Japanese hospital

Kazuo Satoh[1,2], Koichi Makimura[1,3], Yayoi Hasumi[1], Yayoi Nishiyama[1], Katsuhisa Uchida[1] and Hideyo Yamaguchi[1]



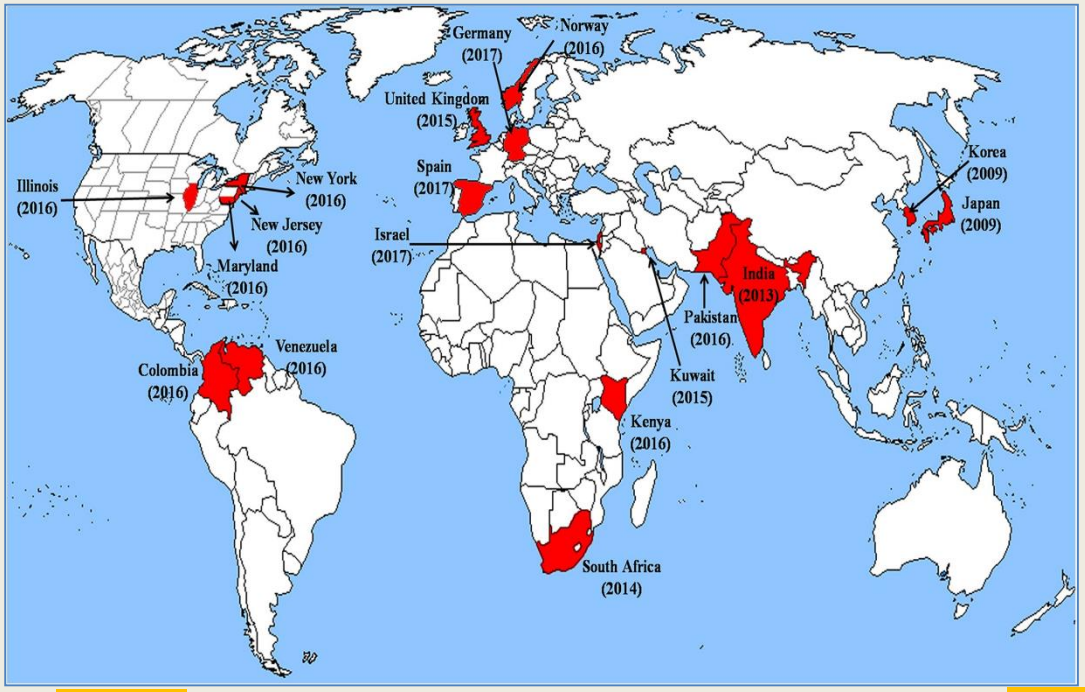


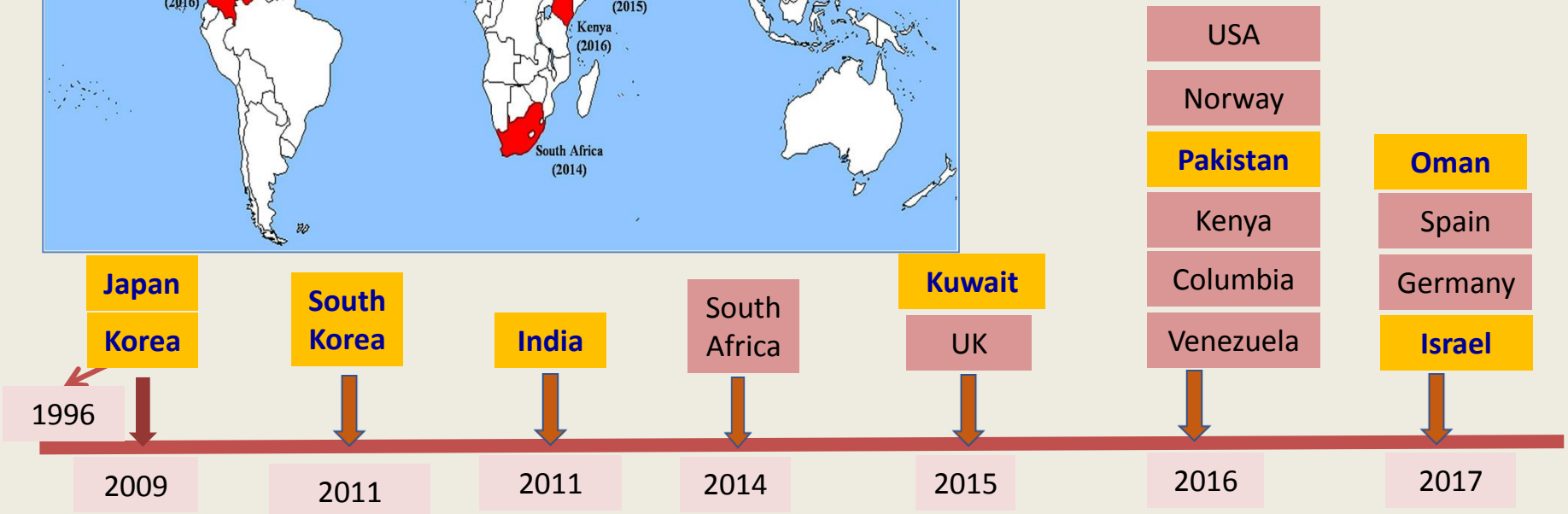
28s rDNA –D1/D2



18s rDNA

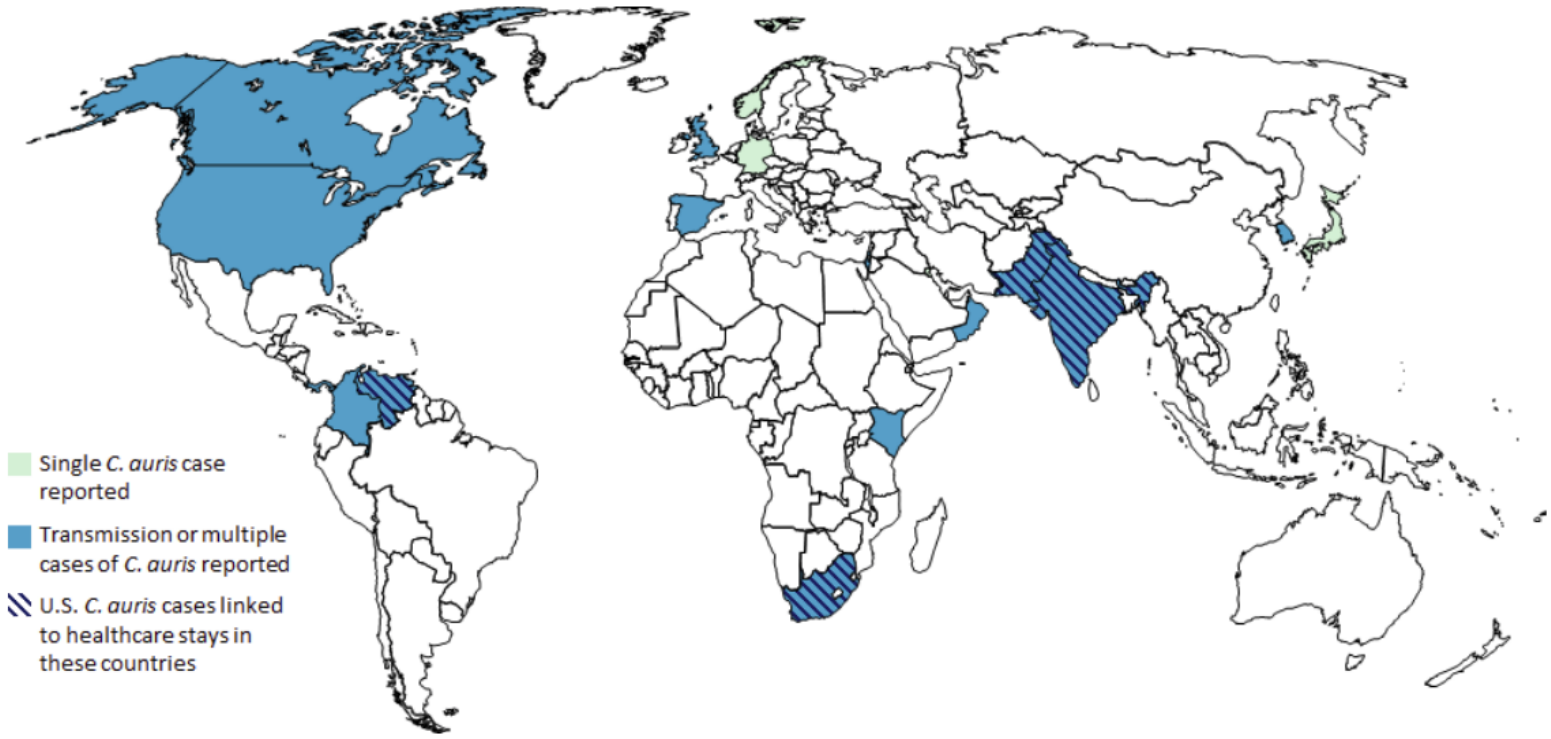
最早已知的菌株來自於1996 年的南韓，已於歐、亞、美、非十餘國迅速傳播並造成感染





Chakrabarti A, *et al.* Intensive Care Med 2015; 41: 285
Chowdhary A, *et al.* J Hosp Infect 2016; 94: 209

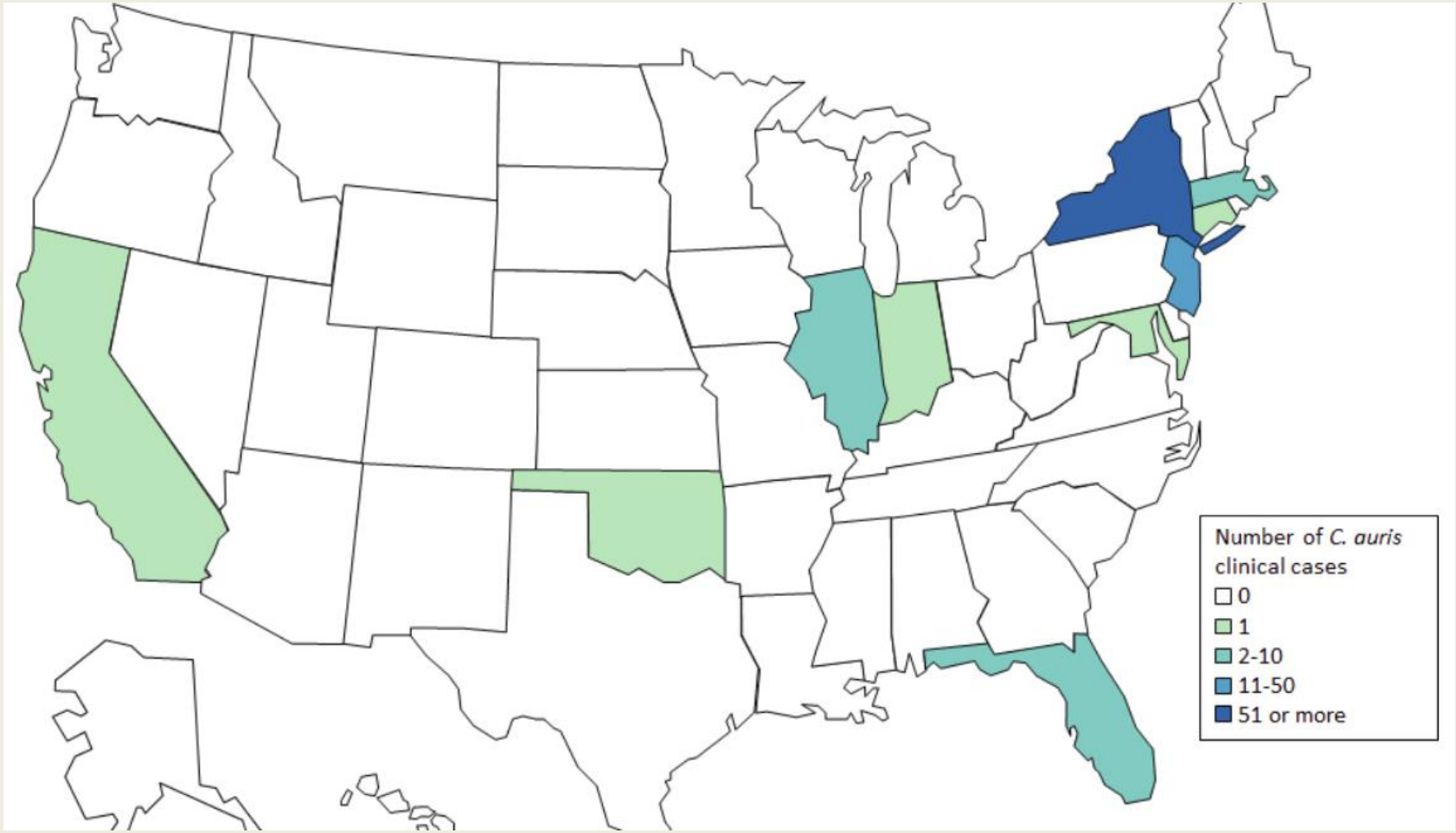
Countries from which *Candida auris* cases have been reported, as of September 30, 2017



- Single cases of *C. auris* have been reported from Germany, Japan, Kuwait, and Norway.
- Multiple cases of *C. auris* have been reported from Canada, 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 in more than one hospital.
- U.S. cases of *C. auris* have been found in patients who had recent stays in healthcare facilities in India, Pakistan, South Africa and Venezuela, which also have documented transmission.
- Other countries not highlighted on this map may also have undetected or unreported *C. auris* cases.

https://www.cdc.gov/fungal/diseases/candidiasis/tracking-c-auris.html

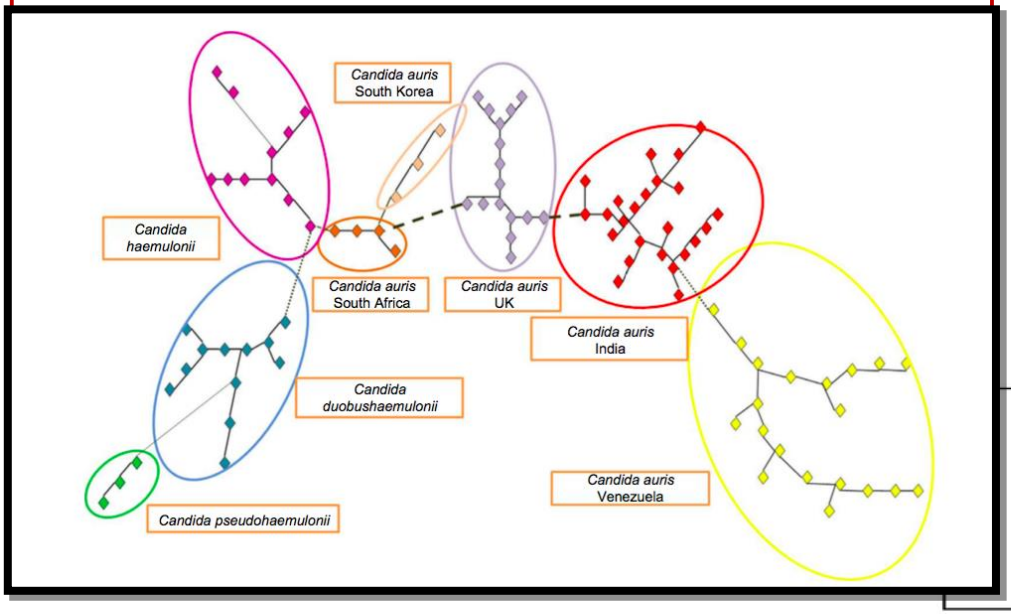
U.S. Map: Clinical cases of *Candida auris* reported by state, United States, as of September 30, 2017

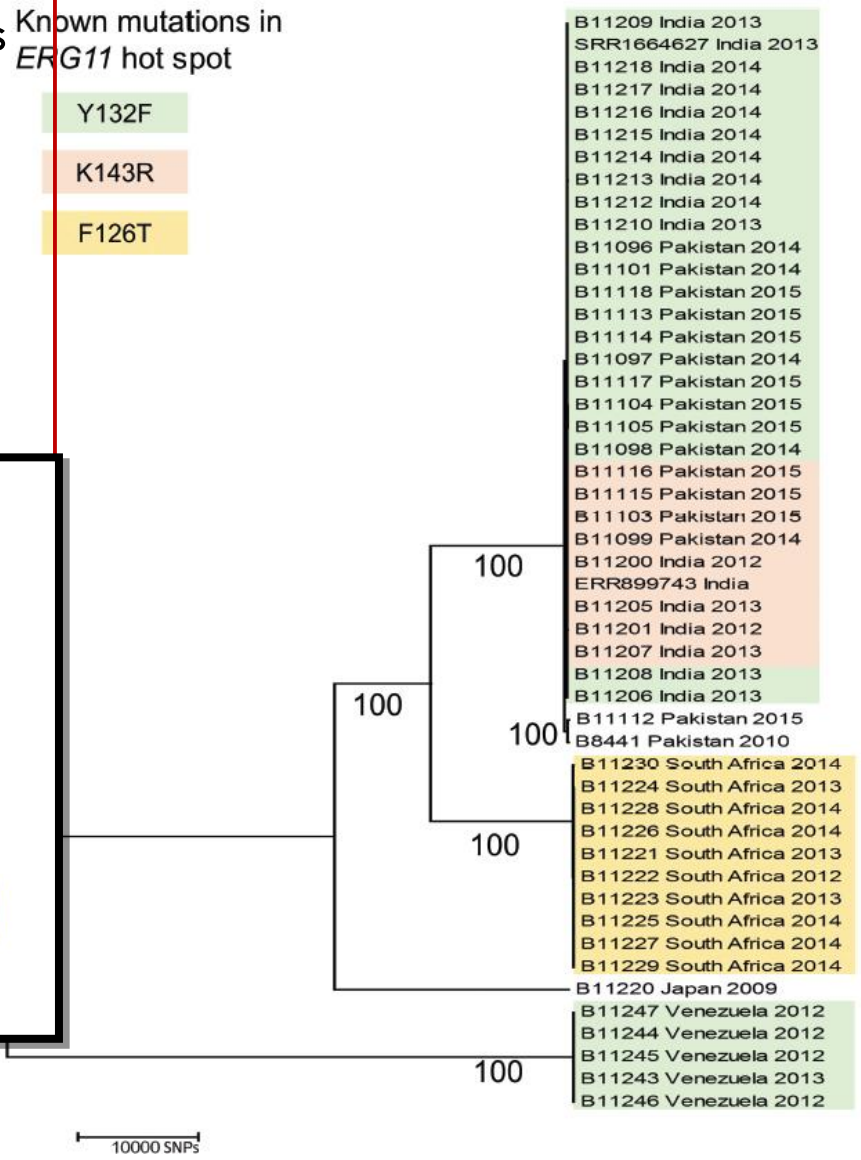


https://www.cdc.gov/fungal/diseases/candidiasis/tracking-c-auris.html

C. auris 如何在國際間散播

- Whole genome sequencing of 54 isolates
- 4 clades: South Asia, South Africa, South America, East Asia
- Minimal difference within same geographical region
- Suggest simultaneous emergence, rather than spread



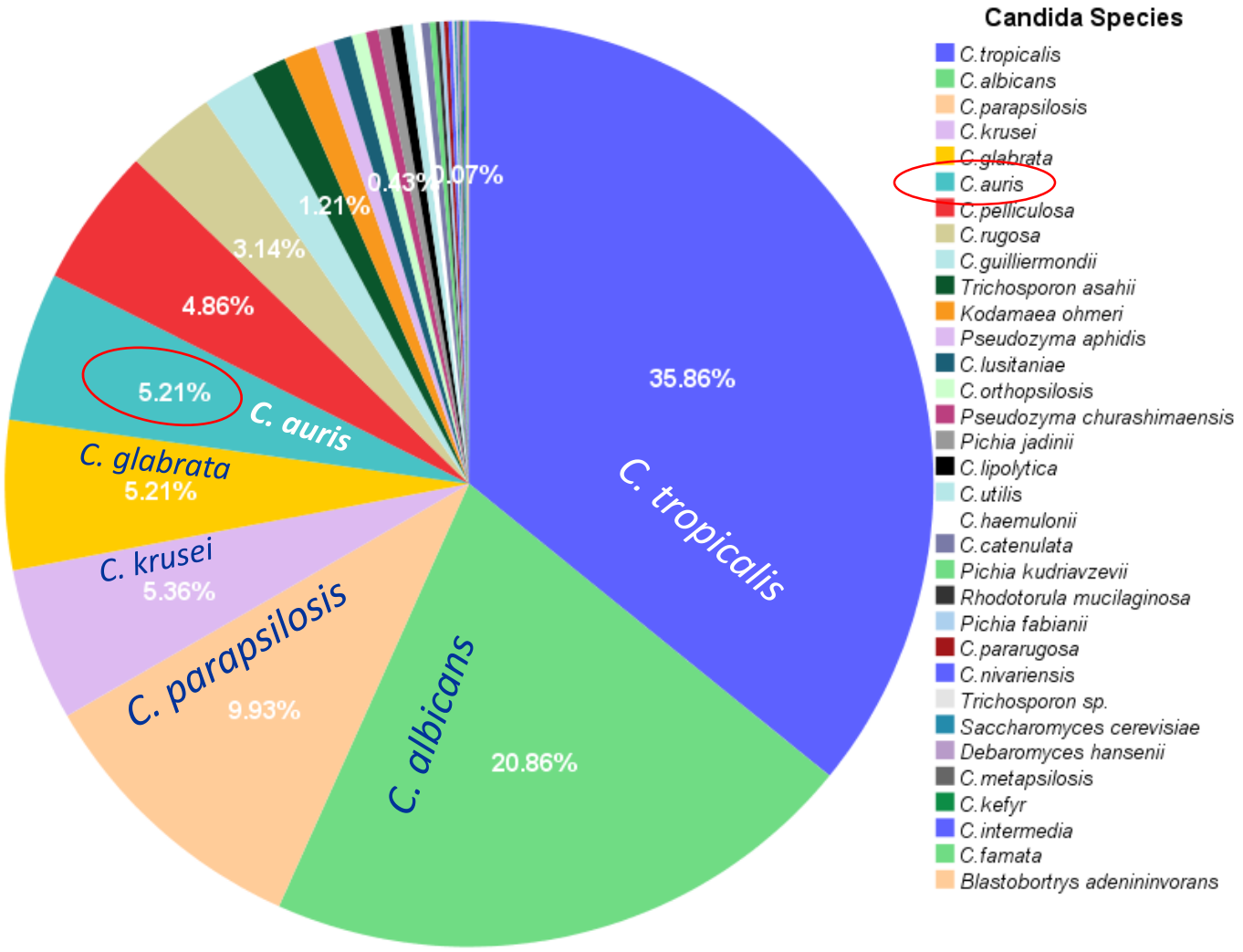


Lockhart SR, *et al.* Clin Infect Dis 2017; 64: 134
Sharma & Upadhyay. Infect Drug Resist 2017; 10: 155

危險因子

- 依據有限的資料顯示，C. *auris* 感染之危險因子大致與其他 念珠菌症相似，包括：近期手術、糖尿病、使用廣效抗生素及抗 黴菌藥物及加護病房病人。近期入住護理之家且有使用侵入性管 路（如：呼吸管及鼻胃管等）的人，感染 C. *auris* 之風險似乎最 高。
- 感染發生在各年齡層的病人，從早產兒到老年人都有。關於 C. *auris* 感染之危險因子尚需更進一步的研究。

Candida species isolated during Indian ICU study



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

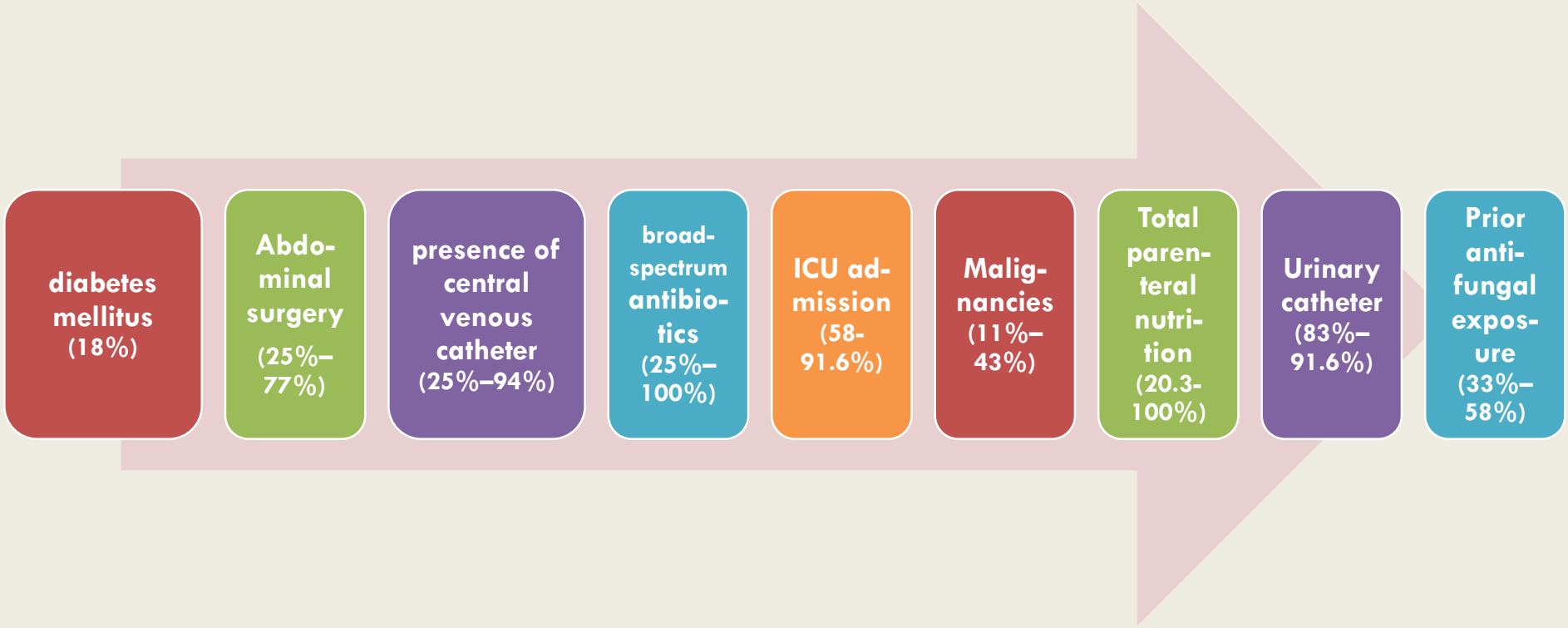
Unique features from largest series in Indian ICUs

- Significant risk factors in Indian ICUs
  1. prior antifungal exposure (P<0.001)
  2. underlying respiratory illness (P<0.002)
  3. vascular surgery (P<0.048)
  4. multiple interventions (P<0.007)
  5. public-sector hospital (P<0.006)

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

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

Risk factors in other studies



J Hosp Infect 2016;94:209
South Af J Infect Dis 2016;31:69

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Review Article

Are we ready for the global emergence of multidrug-resistant *Candida auris* in Taiwan?

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Candida auris is a recently identified multi-resistant *Candida* species, first reported in Japan in 2009, and poses a serious global health threat. Lack of awareness of this new *Candida* species and difficulties with laboratory identification have impacted significantly on outbreak detection and management, and compromised patient outcome. Accordingly, there is an urgent need to raise awareness of healthcare personnel to this emerging pathogen and determine its prevalence, impact, and challenges to the Taiwan healthcare system. Enhanced laboratory testing strategies are needed to differentiate *C. auris* from other *Candida* species to provide accurate diagnosis and implement control measures early enough to prevent hospital outbreaks. In this report, we review the key epidemiological, microbiological and clinical characteristics of *C. auris* and provide the results of a multicenter surveillance study of *C. auris* in Taiwan. We also conducted a web-based survey to determine awareness of the medical community to *C. auris* and the capability of Taiwanese hospital laboratories to identify this microorganism. *C. auris* has not yet been isolated from humans in Taiwan, but the unique features of this microorganism and its ability to reach across international boundaries justify the importance of these initiatives in Taiwan.

Prevalence of *C. auris* among 5064 clinical isolates based on multicenter surveillance in Taiwan

Investigator(s)	Source of isolates	Specimens types	Year	Results
HJ Lo	TSARY National surveillance[b]	Randomly collected *Candida* clinical isolates (1999) or *Candida* isolates from sterile sites and non-sterile sites (2002, 2006, 2010, and 2014)	1999 2002 2006 2010 2014	0/660 0/945 0/1015 0/1130 0/1168
WL Liu, FD Wang, MW Ho, YH Chen, CE Liu	CMMC, VGH-TPE, CMUH, KMUH, CCH	Blood isolates, hospital wide, rare *Candida* species[c]	January 2011—June 2014	0/52[d]
YC Chen, PR Hsueh	NTUH	Blood isolates, hospital wide, rare *Candida* species[c]	2011—2016	0/57[d]
WL Liu	CMMC, Liouying campus	Blood isolates, hospital wide, rare *Candida* species[c]	2007—2014	0/21[d] [37]
MC Li WC Ko	NCKUH	Blood isolates, hospital wide, rare *Candida* species[c]	2011—2016	0/37

Abbreviation: TSARY, Taiwan Surveillance of Antimicrobial Resistance of Yeasts; CMMC: Chi Mei Medical Center; VGH-TPE: Taipei Veterans General Hospital; CMUH: China Medical University Hospital; KMUH: Kaohsiung Medical University Hospital; CCH: Changhua Christian Hospital; NTUH, National Taiwan University Hospital; NCKUH, National Cheng Kung University Hospital.

[a] Data from personal communication with the principal investigators at each hospital or research site. These data are generated based on DNA sequencing of the internal transcribed spacer regions of the nuclear rRNA gene operon and the D1/D2 domain of the large ribosomal subunit of 26S rDNA.

[b] Multicenter in different geographic location of Taiwan.[36]

[c] *Candida* species other than *C. albicans*, *C. tropicalis*, *C. parapsilosis*, *C. glabrata*, and *C. krusei*.

[d] One isolate per patient.

Lu P-L, et al., Are we ready for the global emergence of multidrug-resistant Candida auris in Taiwan?, Journal of the Formosan Medical Association (2017), https://doi.org/10.1016/j.jfma.2017.10.005

Awareness, source of information of *C. auris* and capability of identification in the routine microbiology laboratories or research laboratories based on a web-based survey, August 26-27, 2017

Question	Answer	Response, no. (%)
Awareness		
Ever heard of *C. auris*	Yes	31/51 (60.8%)
	No	20/51 (39.2%)
Source of information (multiple choice)	Academic publications	20/31 (64.5%)
	Academia conference	15/31 (48.4%)
	Government news	10/31 (32.3%)
	News media	4/31 (12.9%)
Do you know what Taiwan CDC has done? (Select all that apply)	Has announced in the CDC web[b]	10/51 (19.6%)
	Has established a standard procedure for report and submit clinical isolate for identification[b]	10/51 (19.6%)
	Has sent an official letter to healthcare settings	15/51 (37.3%)
	No, I do not know	30/51 (58.8%)
Capability		
Hospital Laboratory with ability to identification *C. auris*	Yes	13/51[c] (25.5%)
	No or not sure	38/51 (74.5%)
What *Candida* isolates will submit for molecular identification in order to detect *Candida auris*?	Yes[d]	13/51 (25.5%)
	Such practice is under development and not implement yet.	4/51 (7.8%)
	No such practice yet or unknown	29/51 (66.7%)

[a] This web-based survey was conducted along with the annual symposium of Taiwan Medical Mycology Training Network. Among 51 respondents, 27 are medical technicians (52.9%), 20 are physicians (39.2%), others are research scientists or academic personnel; 26 involve in routine microbiology laboratories, 5 involve in microbiologic experiments occasionally for research, 20 do not involve in laboratories.

[b] Taiwan CDC announced on July 7, 2016 that *C. auris* caused outbreak in UK; announced how to report and submit clinical isolates for further identification on July 10, 2016.

[c] All the 13 respondents' hospital applied MALDI-TOF as the method for *C. auris*. Among them, four respondents answered that subsequent DNA sequencing is possible for uncommon yeast in their hospital or research laborator respondents answered that subies.

[d] All *Candida* species other than *C. albicans*, *C. tropicalis*, *C. glabrata*, *C. parapsilosis*, *C. krusei* (2 respondents), low score in MALDI-TOF (5), or multidrug resistant rare *Candida* species (2).

Lu P-L, et al., Are we ready for the global emergence of multidrug-resistant Candida auris in Taiwan?, Journal of the Formosan Medical Association (2017), https://doi.org/10.1016/j.jfma.2017.10.005


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自訂搜尋
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首頁 > 傳染病介紹 > 感染管制及生物安全 > 抗生素抗藥性管理 > 抗微生物製劑相關管制措施 > Candida auris感染管制建議
傳染病介紹
傳染病介紹
第一類法定傳染病
第二類法定傳染病
第三類法定傳染病
第四類法定傳染病
第五類法定傳染病
其他傳染病
人畜共通傳染病
感染管制及生物安全
抗微生物製劑相關管制措施
Candida auris感染管制建議 (2017-11-02) 讚 0
壹、 前言
貳、 背景
參、 Candida auris 之發現及鑑定
肆、 防治作業與感染管制建議
伍、 Candida auris 之治療建議

傳播方式

- *C. auris* 可於環境表面存活數週之久，可經由接觸 *C. auris* 帶菌病人及汙染的環境表面或設備傳播，故平日落實標準防護措施很重要，尤其是**手部衛生**及**環境清潔**。
- **即早發現**住院之 *C. auris* 帶菌（移生或感染）個案尤其重要，有利於醫療照護機構採取適當的防護措施，並進行相關調查及處理，以防止其傳播。

何時應懷疑 *Candida auris*

1. **流行病學**：來自有 C. *auris* 之醫院或長期照護機構的病人。
2. **臨床**：疑似念珠菌感染治療失敗之病人。
3. **實驗室**： 當使用傳統的生化方法（如：VITEK 2 YST, API 20C, BD Phoenix 酵母菌鑑定系統及 MicroScan 等）鑑定出表 1 所列之 菌種時。
4. **監測**：

依傳統的生化鑑定系統 C. auris 可能被錯誤鑑定之菌種

鑑定系統	*C. auris* 可能被錯誤鑑定之菌種
Vitek 2 YST	●*Candida haemulonii* ●*Candida duobushaemulonii*
API 20C	●*Candida famata* ●*Rhodotorula glutinis* (characteristic red color not present) ●*Candida sake* ●*Saccharomyces cerevisiae*
BD Phoenix yeast identification system	●*Candida haemulonii* ●*Candida catenulata*
Microscan	●*Candida famata* ●*Candida guilliermondii* (no hyphae/pseudohyphae present on cornmeal agar) ●*Candida lusitaniae* (no hyphae/pseudohyphae present on cornmeal agar) ●*Candida parapsilosis* (no hyphae/pseudohyphae present on cornmeal agar)

註：此表係依目前有關 *C. auris* 錯誤鑑定之知識而訂，可能會隨新的資訊而更新。

何時應懷疑 *Candida auris*

就**監測**之面向：有下列情形時，應懷疑 *C. auris*：

1. 非 *C. albicans* 之念珠菌菌株數或案例異常增加。
2. 少見的念珠菌（請參閱表 1） 菌株數或案例異常增加。
3. 不明念珠菌菌種菌株數或案例異常增加。
4. 多重抗藥之念珠菌菌株數或案例異常增加。
5. 念珠菌感染治療失敗案例異常增加。

實驗室鑑定

鑑定至菌種（species）之時機

- 自血液等原本無菌部位分離之念珠菌菌株建議鑑定至菌種層級，以利初始治療藥物選擇之參考。
- 其他部位分離之念珠菌菌株在下列情況下亦需考慮菌種鑑定。

1. 病人臨床照護需要。
2. 當機構內有偵測到 C. *auris* 感染或移生病人時，為偵測其 他病人之移生情形，可考慮菌種鑑定。可持續至證據顯示無 C. *auris* 傳播後 1 個月。
3. 病人於 1 年內曾入住有 C. *auris* 傳播之國家的醫療照護機 構。

實驗室鑑定

- **如何鑑定 *Candida auris***

  1. MALDI-TOF (matrix-assisted laser desorption ionization-time of flight) 可鑑別 C. *auris* 和其他念珠菌菌種，但並非所有的 MALDI-TOF 儀器其包含之 參考資料庫均可偵測 C. *auris*。
  2. DNA 定序。
  3. 送疾管署鑑定。

- 抗黴菌藥物之藥敏試驗：
  - 所有的 C. *auris* 分離菌株均應進行藥敏試驗。

通報及送驗

- 醫療照護機構或實驗室若懷疑有病人有 C. *auris* 帶菌(移生或 感染)，需要疾管署協助鑑定， 可經由傳染病通報系統中「其他傳染病」項下勾選「其他」欄並 註明「*Candida auris*」，辦理疑似菌株之通報及送驗
- 將疑似 C. *auris* 純化之菌株以拭子沾滿一圈後，置入 Cary-Blair 輸送培養基，以常溫運送至疾管署進行鑑定。
- 送驗相關事項請參閱疾管署傳染病檢體採檢手冊。
- 個案資料則於台灣院內感染監視資訊系統（TNIS）/通報系統/特殊 MDRO 個案通報項下進行通報。

Candida auris 之監測及調查

- 所有的醫療照護機構或實驗室，特別是未具備 C. *auris* 鑑定能力之醫療照護機構，應持續執行或強化例行的監測。
- 有「參、 *Candida auris* 之發現及鑑定」項下「二、何時應懷疑 *Candida auris*」之情形，建議進行調查及處理。
- 所有的醫療照護機構或實驗室，特別是已有 C. *auris* 帶菌(移生或感染)個案之機構，應執行下列事項：

1. 回顧指標病人陽性培養前1個月內曾入住的單位之所有病人的微生物學紀錄，以找出C. *auris*確定或疑似病例
2. 持續監測以找出未來的 C. *auris* 病例。
3. 考慮針對C. *auris*病人之密切接觸者進行C. *auris*之篩檢。

住院單位之感染管制建議

- 將 C. *auris* 病人安置於單人病房，並採取**標準及接觸防護措施**。
- 強調手部衛生之遵從性。
- 使用建議的產品清潔及消毒病人照護環境（每日及終期清潔）。
- 進行**病人接觸者之篩檢**以找出 C. *auris* 移生病人。因 C. *auris* 移生病人可以是傳播源，這些病人應採取與 C. *auris* 感染病人相同的感染管制措施。

解除接觸防護措施

- 目前建議只要病人仍有 C. *auris* 感染/移生，就應持續採取接觸防護措施。
- 有關 C. *auris* 移生持續期程的資訊有限，定期（如每 3 個月）評估帶菌狀態，可以輔助接觸防護措施持續期程之決策。
- 採檢部位：應至少包含腋窩、鼠蹊，及先前 C. *auris* 培養陽性部位（如：尿液及痰液等）。
- 移生之病人：證據顯示病人可能持續移生數個月甚至更久。若病人 C. *auris* 檢驗陽性，3 個月內不需再重複採檢。

解除接觸防護措施

- 感染之病人：使用治療 C. *auris* 的抗黴菌藥物時不宜評估病人之帶菌狀態。雖然理想的停藥期尚未建立，但停藥 1 週後再評估是合理的；若使用外用的抗菌劑（ 如：chlorhexidine），則應停藥至少 48 小時。
- 解除接觸防護措施之條件：連續 2 次（間隔至少 1 週）培 養陰性或連續 3 次不同天培養陰性，即可考慮解除 C. *auris* 感染管制防護措施。
- 另需注意的是，病人轉介之決定應依據臨床準則及接收機構提供照護之能力而定，而不是以有無移生狀況而定。

環境清潔與消毒

- C. *auris* 可持續存在於醫療照護環境之表面。常規用於消毒的四級銨類（quaternary ammonium）產品可能對 C. *auris* 無效，
- 建議使用醫院等級抗 *Clostridium difficile* 的殺孢劑，如：1000 PPM 的次氯酸鈉、4.5%過氧化氫強效配方（hydrogen peroxide enhanced action formulation, HP-EAF）等，並遵照使用說用使用產品，包括正確的接觸時間。

環境清潔與消毒

- 落實病人房間的每日及終期清潔消毒及病人於房間外接 受照護（如：放射科及物理治療等）區域的清潔消毒是必要 的。
- 照護儀器/設備應盡可能供 C. *auris* 單一病人使用（如： 壓脈帶、聽診器等），特別是在群突發流行期間。
- 若為共用的儀器/設備（如：呼吸器、物理治療器材等），應於使用後經 適當清潔消毒，才可供下一位病人使用。

密切接觸者之移生篩檢

- 由於 C. *auris* 病人可能在偵測出 C. *auris* 前已移生數個月，部份感染管制措施未落實，C. *auris* 可能傳播至該病人周遭的其他病人。因此，確認該病人先前的健康照護史及接觸者是重要的。
- 針對高風險之接觸者（如：目前或1 個月內同病室之病人等）或近期曾入住有 C. *auris* 傳播之國家的醫療照護機構之病人，在未確認陰性前，可考慮進行適當的**預先隔離**措施。
- 移生篩檢可採取**環形策略**：先篩檢與指標病人最密切接觸的病人，若證實有傳播，可考慮擴大篩檢範圍。
- 篩檢對象：至少應包含與指標個案具下列流行病學相關性之病人：

  1.目前與指標個案同病室的病人。

  2.指標病人陽性培養前 1 個月曾同病室之病人或同房之機構 服務對象，即使是已經出院之病人/服務對象亦需確認及篩 檢。

密切接觸者之移生篩檢

- 若欲偵測傳播情形應考慮進行更大規模的篩檢，如：針對指標病人目前或先前入住的單位或樓層進行點盛行率調查。可從最高風險之接觸者開始調查，包含：和指標病人住同一病房或單位 3 天以上的病人或需要較高層次照護的病人（如：呼吸器）；若證據顯示或疑似有持續傳播之情形（如： 從篩檢中檢出多名 C. *auris* 病人），則進行更大規模的調查。
- C. *auris* 之篩檢應以拭子就病人的腋窩及鼠蹊部位採檢。雖然在病人的鼻內、外耳道、口咽、尿液、傷口及直腸 中亦有發現 C. *auris* 移生，然而，腋窩和鼠蹊為最常見且一致的移生部位。一旦確認病人有 C. *auris* 移生，應採取與 C. *auris* 感染病人相同的感染管制措施。

主動監測培養

- 若發生難以控制的群突發時，可針對新入住及已入住感染病房之病人進行常規的主動監測培養，作為強化的措施之一。

疫情調查

醫療照護機構種類	調查對象	調查期間
指標病人目前入住的醫院	指標病人陽性培養前 1 個月內曾入住單位之所有病人	指標病人陽性培養前 1 個月至指標病人進行隔離前
指標病人陽性培養前 1 個月內曾入住的其他醫院/機構	指標病人於該醫院/機構入住期間同一單位內之所有病人/機構服務對象	指標病人於該醫院/機構入住前 1 個月至指標病人出院之期間
指標病人陽性培養前 3 個月內曾入住超過 7 天之其他醫院/機構		
其他經風險評估認定之醫院/機構		

經調查後若發現有符合「(五)密切接觸者之移生篩檢」之接觸者，依其建議進行移生之篩檢。

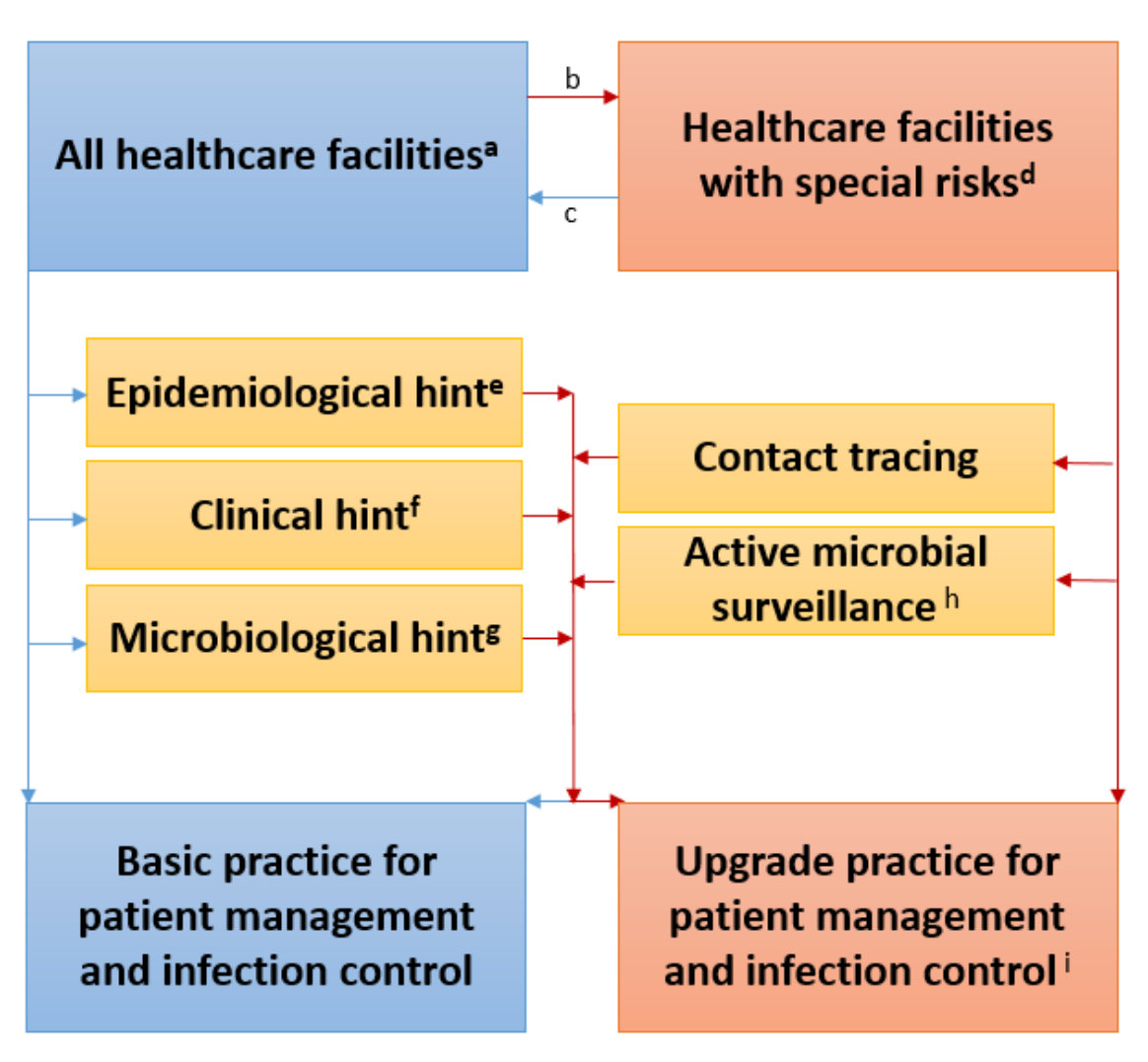
預防院際間之傳播

- 建議考慮針對來自有 C. *auris* 案例之醫院/機構服務對象，進行**入院篩檢**及採取**預先隔離**措施，以降低因 C. *auris* 傳入而引發群突發的風險。

抗黴菌藥物管理

- 雖然沒有證據顯示抗黴菌藥物管理對 C. *auris* 之興起及傳播的效果，但抗黴菌藥物大量使用之環境可能有利於多重抗藥性酵母菌（如 C. *auris*）之興起，因此，仍建議進行抗黴 菌藥物管理。
- 在有 C. *auris* 傳播的單位中，應避免 fluconazole 預防性用藥。

防治作業與感染管制建議



Lu P-L, et al., Are we ready for the global emergence of multidrug-resistant Candida auris in Taiwan?, Journal of the Formosan Medical Association (2017), https://doi.org/10.1016/j.jfma.2017.10.005

[a] include hospitals, long-term care facilities, nursing homes, etc.

[b] Upgrade practice under the suspicion or confirmed increase risk of C. *auris* cases or outbreaks.

[c] Deescalate to basic practice once the risk has been cleared.

[d] Healthcare facilities with special risks are those with a suspicion of increased incidence of invasive infection by *non-albicans* C*andida* species

[e] Patients transferred from countries/regions/facilities reporting C. *auris* outbreaks or those with special risks.

[f] Treatment failure, particularly for rare C*andida* species or yeasts (Table 1).

[g] A positive result of screen tests; rare C*andida* species or yeasts (Table 1), no or low score in MDALD-TOF.

[h] Targeting patients at high risk for carriage of C. *auris*

[H] Include modification of selection of initial antifungal agent based on recent local epidemiology, presumptive contact isolation precaution , single room isolation or patient cohorting, and dedicated nursing staff for patients who are colonized or infected with C. *auris*.

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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

Abbreviations: MIC, minimum inhibitory concentration; MIC_{50}, MIC for 50% of isolates; MIC_{90}, MIC for 90% of isolates.

- **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 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

Antifungal susceptibility testing for *Candida auris*

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

https://www.cdc.gov/fungal/diseases/candidiasis/recommendations.html

What we can do

Category	Response
Hospital	• Establish integrated algorithm for early detection and response to *Candida auris* (Figure 1 is a proposed template.).
Laboratory personnel	• Establish or update yeast identification schema to include C. *auris*[a] • Isolates of *Candida* species from invasive infections should be identified to species level. • C. *auris* is able to grow at temperatures in excess of 42 °C, a characteristic which has potential as a quick screening test. • Further testing must be undertaken if biochemical tests identify yeast isolates from blood cultures as C. *haemulonii*, C. *sake*, *Rhodotorula glutinis*, *Saccharomyces cerevisiae* or other non-*albicans Candida species*. • Update MALDI-TOF identification library if available. • Prompt notification of the clinical team and the infection control team is essential to implement infection control precautions in a timely manner.

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What we can do

Category	Response
Physicians	• Be familiar with the risk factors associated with invasive candidiasis. • Be aware of occurrence of *Candida* infection in high-risk patients and diagnose and treat accordingly. • Be alert and suspect C. *auris* colonization/infection and response accordingly. • Antifungal susceptibility testing is recommended on all isolates from invasive disease and should be repeated on later isolates if infection persists despite treatment.

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What we can do

Category	Response
Healthcare personnel	• Enforce compliance of standard precaution to all patients at any time. Good standard infection control, including environmental cleaning, adequate reprocessing of medical devices and adequate capacity of microbiological laboratories as well as sufficient capacity of healthcare facilities for patient isolation, are the basis for the prevention of transmission of any pathogen, including C. *auris*, in healthcare settings • Be alert to early identify patients with C. *auris* carriage and initiate contact precaution accordingly.

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HEALTH ALERT

What we can do

Category	Response
Government	Update and evaluate global situation. Periodic monitor national status, identify the gap and response accordingly. Strengthen capability or capacity of reference laboratory or conduct special program to combating C. *auris* and other multidrug resistant organisms with high transmissibility, high morbidity/mortality and difficulty with detection/identification in daily practice.
Everyone	Follow update information Taiwan Centers for Disease Control. http://www.cdc.gov.tw/rwd/professional Centers for Disease Control and Prevention. General Information about *Candida auris*. Available at: https://www.cdc.gov/fungal/diseases/candidiasis/candida-auris-qanda.html. Centers for Disease Control and Prevention. Recommendations for Identification of *Candida auris*. Available at: https://www.cdc.gov/fungal/diseases/candidiasis/recommendations.html. Centers for Disease Control and Prevention. Recommendations for Treatment of *Candida auris*. Available at: https://www.cdc.gov/fungal/diseases/candidiasis/c-auris-treatment.html. Centers for Disease Control and Prevention. Recommendations for Infection Control for *Candida auris*. Available at: https://www.cdc.gov/fungal/diseases/candidiasis/c-auris-infection-control.html. Public Health England. Guidance for the laboratory investigation, management and infection prevention and control for cases of *Candida auris* (v2.0). Available at: https://www.gov.uk/government/publications/candida-auris-laboratory-investigation-management-and-infection-prevention-and-control. Public Health England. *Candida auris*: infection control in community care settings. Available at: https://www.gov.uk/government/publications/candida-auris-infection-control-in-community-care-settings. European Centre for Disease Prevention and Control. *Candida auris* in healthcare settings –Europe. Available at: https://ecdc.europa.eu/sites/portal/files/media/en/publications/Publications/Candida-in-healthcare-settings_19-Dec-2016.pdf.

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CANDIDA AURIS