



XLVI Congresso Nazionale AMCLI

11 - 14 Novembre 2017

Palacongressi di Rimini

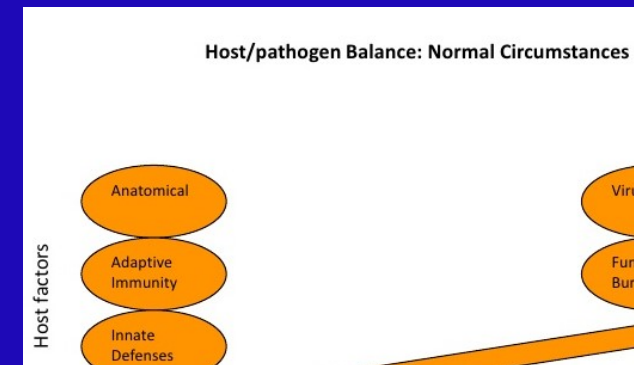
Le infezioni da non dimenticare nel paziente trapiantato

...e non dimentichiamo i funghi

Elena De Carolis



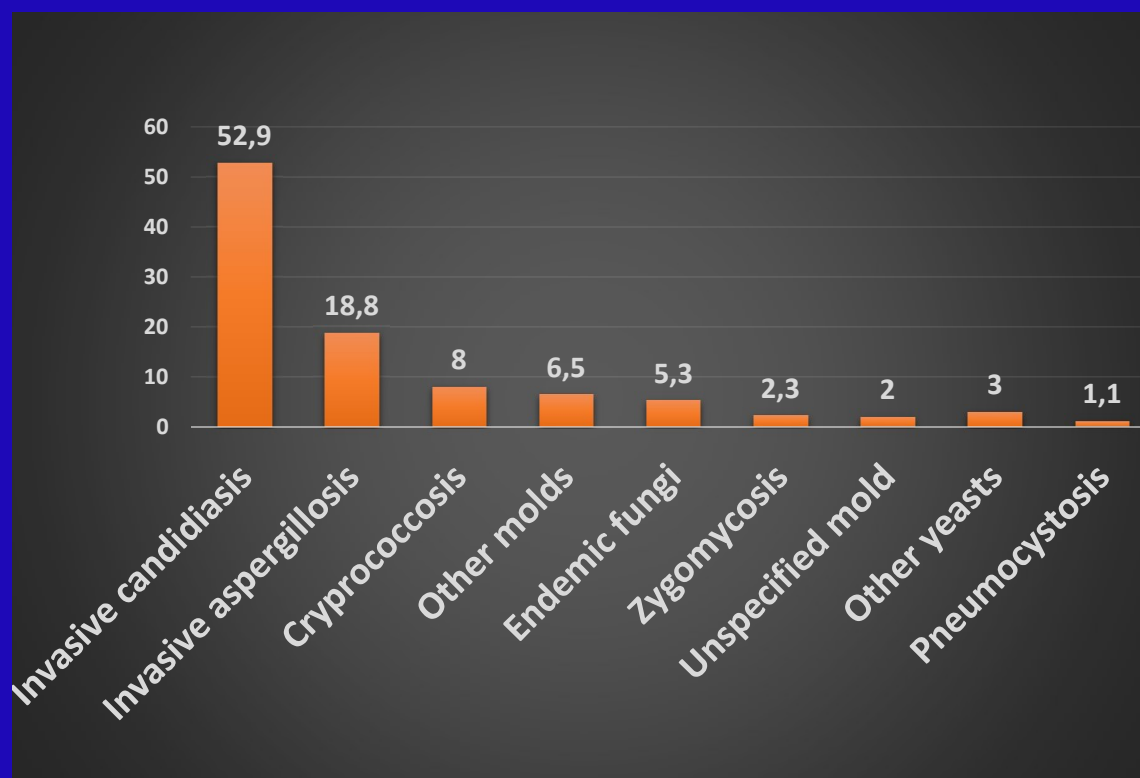
Risk factors for fungal infections



Clin Infect Dis. 2010 Apr 15;50(8):1101-11. doi: 10.1086/651262.

Invasive fungal infections among organ transplant recipients: results of the Transplant-Associated Infection Surveillance Network (TRANSNET).

Pappas PG¹, Alexander BD, Andes DR, Hadley S, Kauffman CA, Freifeld A, Anaissie EJ, Brumble LM, Herwaldt L, Ito J, Kontoyiannis DP, Lyon GM, Marr KA, Morrison VA, Park BJ, Patterson TF, Perl TM, Oster RA, Schuster MG, Walker R, Walsh TJ, Wannemuehler KA, Chiller TM.



Distribution of fungal pathogens causing invasive fungal infections in transplant recipients

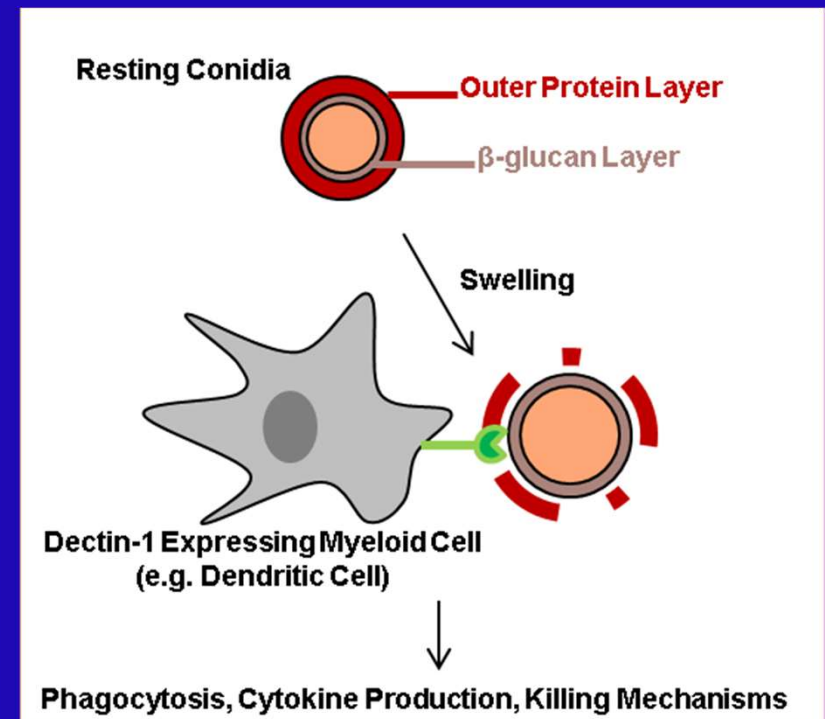
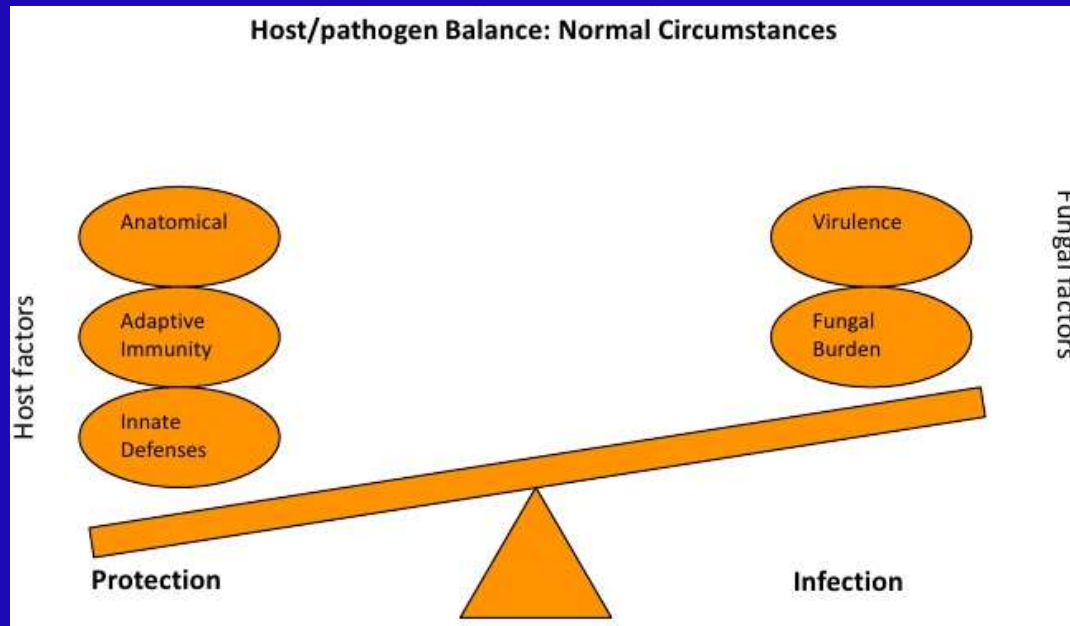
Table 6. Distribution of fungal pathogens causing invasive fungal infections in transp

IFI pathogen	Type of transplantation					
	HSCT (%)	Kidney (%)	Liver (%)	Lung (%)	Pancreas (%)	He
<i>Aspergillus</i>	43–64	11–14	7–11	44–63	5–10	23–
<i>Mucorales</i>	5–8	1–2	2–3	2–3	0	2–
<i>Exophiala</i>	0–0	0–0	0–0	1–1	0–0	0–0

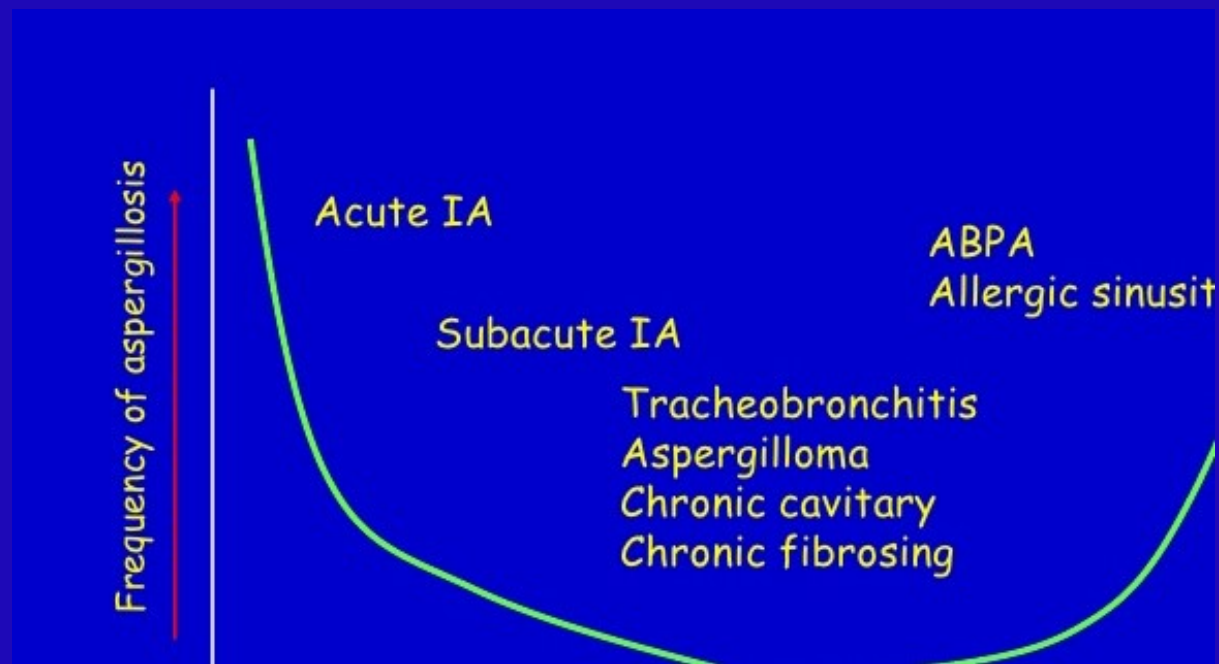
Distribution of fungal infections transplant type



Normal host



Aspergillus-host interaction



IA incidence after HSCT and spore count

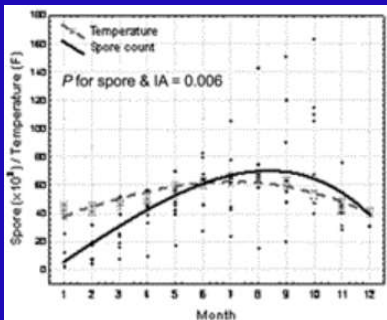
[Clin Infect Dis](#). 2010 Jun 15;50(12):1588-97. doi: 10.1086/652761.

Geoclimatic influences on invasive aspergillosis after hematopoietic stem cell transplantation.

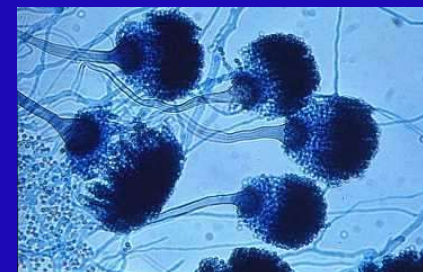
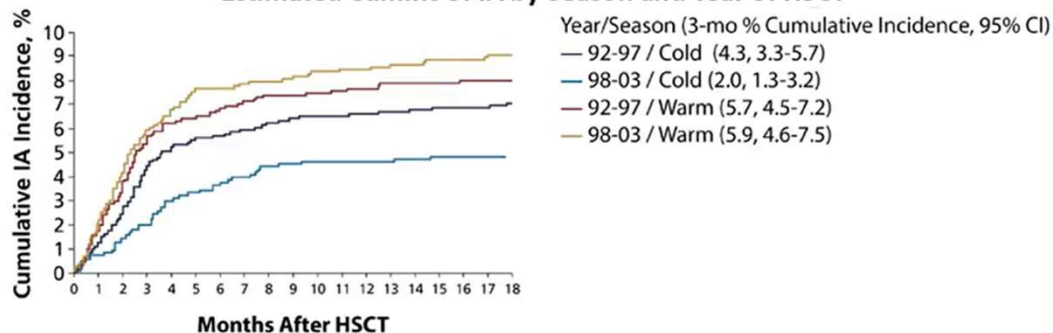
Panackal AA¹, Li H, Kontoyiannis DP, Mori M, Perego CA, Boeckh M, Marr KA.

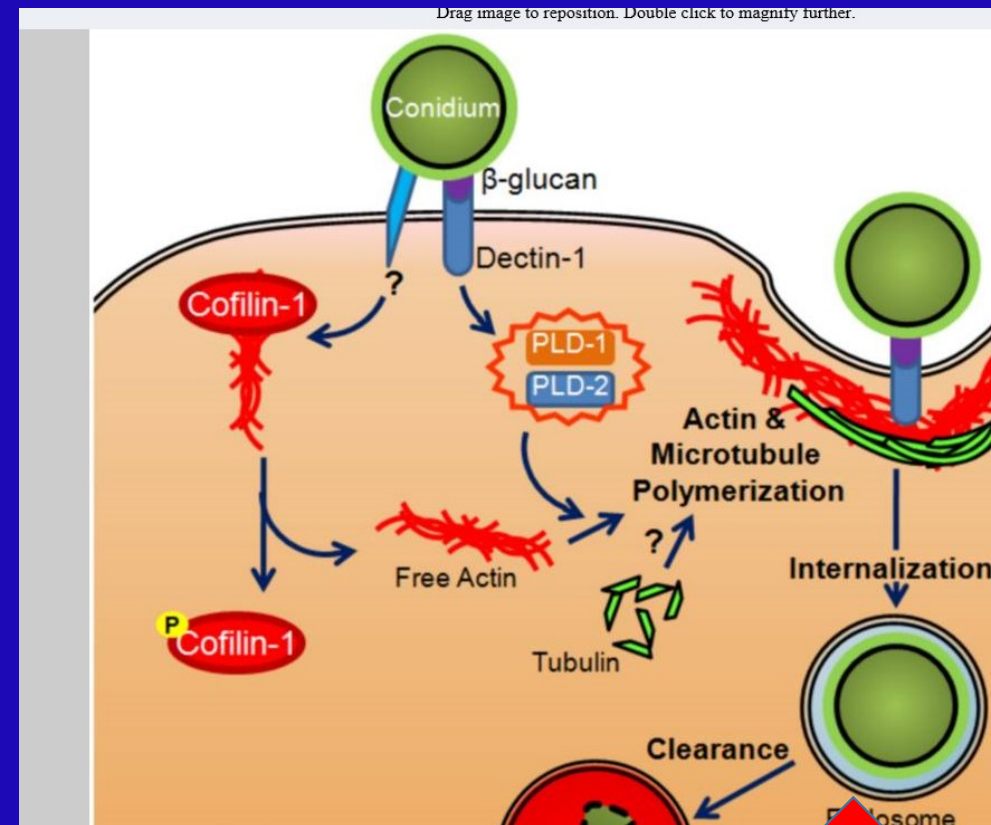
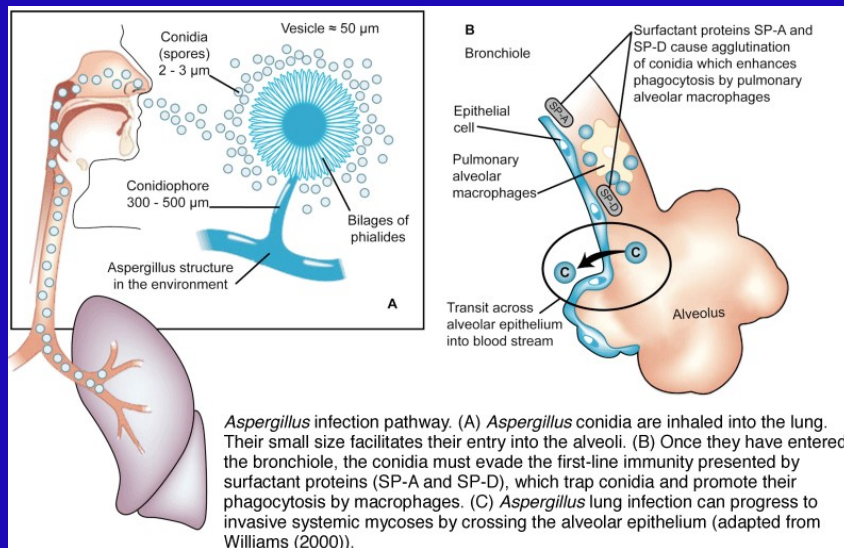
Summers in Seattle¹

- Seattle cohort: 4,213 patients (1992-2003)
- Variability according to season, in all years

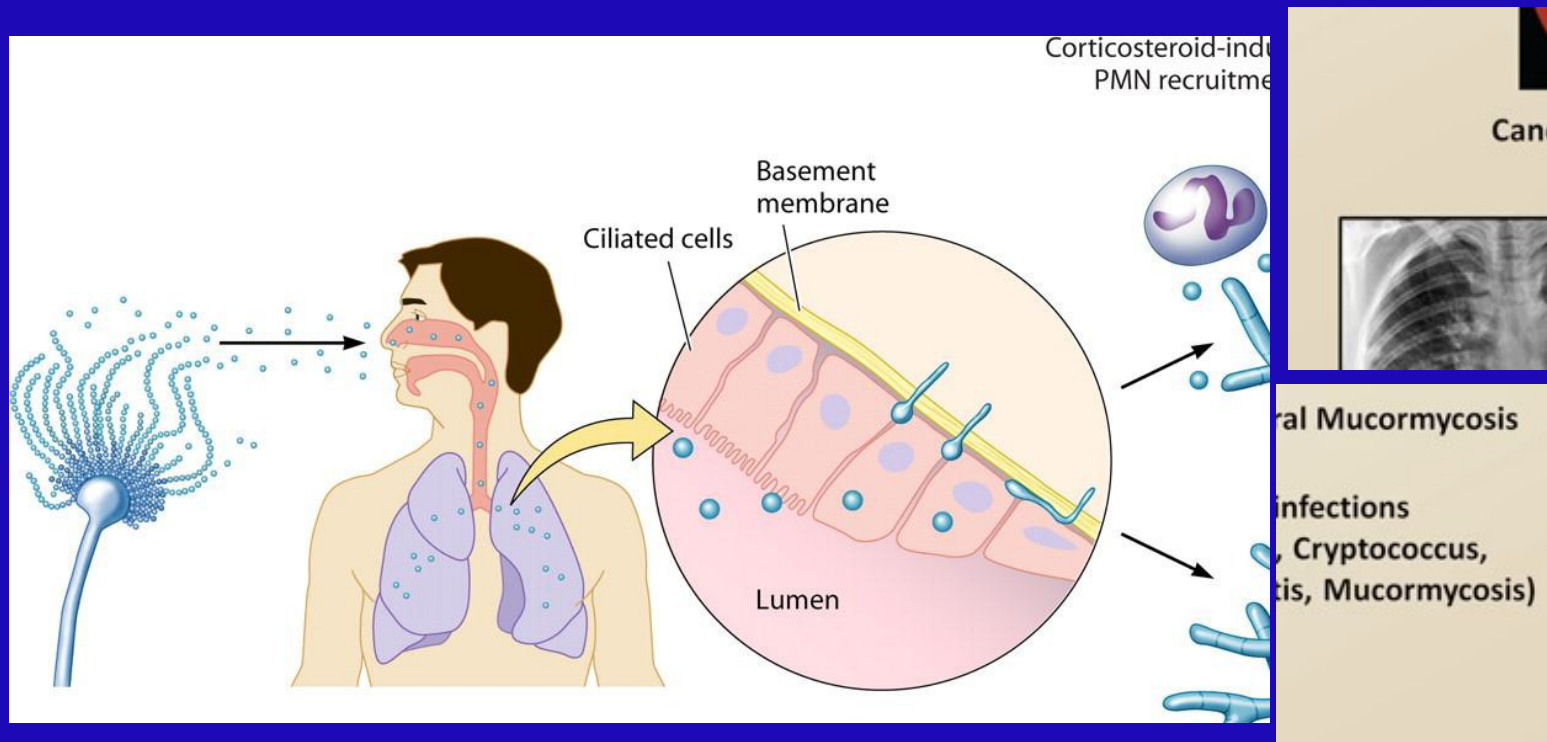


Estimated CumInc of IA by Season and Year of HSCT





Host with immune dysfunction



GM and BDG in clinical practice

The management of invasive fungal infections begins with a high index of suspicion and prompt diagnosis

Can I Tell Bacterial From Fungal Pneumonia by the I

Favors Mold

Macronodule

Halo sign

Cavity

Favors Bacterial

Airspace
consolidation

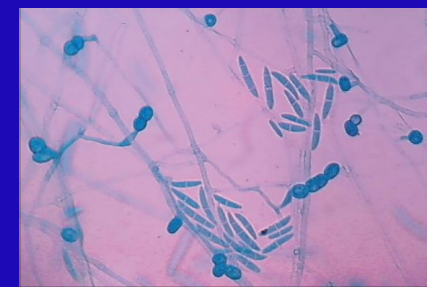
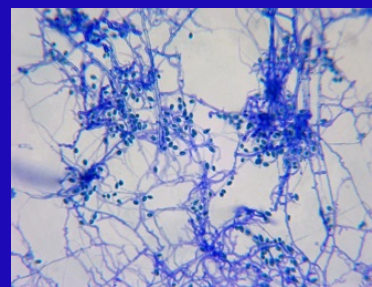
Pre-test probability		BDG / GM testing (serum)	Post-test probability
IA Prevalence	Clinical suspicion		
Hematologic cancer / Neutropenia / HSCT	Lung nodules with halo or air- crescent sign	High (++)	+++ + to ++
Solid-organ transplantation	Aspecific lung nodules	Moderate (+)	+ to ++ + / -

Clinical characteristics of emerging fungi

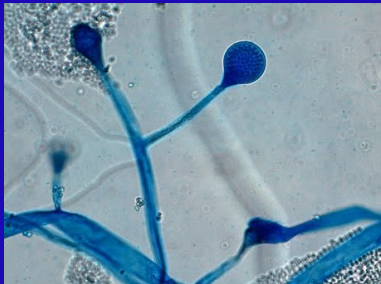
Table 3

Clinical Characteristics of Emerging Fungi

Infection	Characteristic transplant recipient	Median time to infection	Typical site
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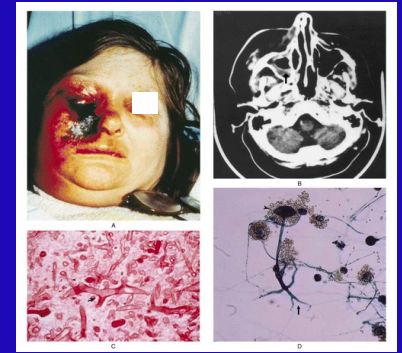


Is mucormycosis or Aspergillosis more likely?



Is Mucormycosis or Aspergillosis More Likely?¹

Site of Infection	Mucormycosis, n (%) (n = 21)	
Sinus	4 (19%)	
Sinopulmonary	4 (19%)	
Rhino(orbito)cerebral	2 (10%)	
Pneumonia	7 (33%)	
Disseminated	2 (10%)	



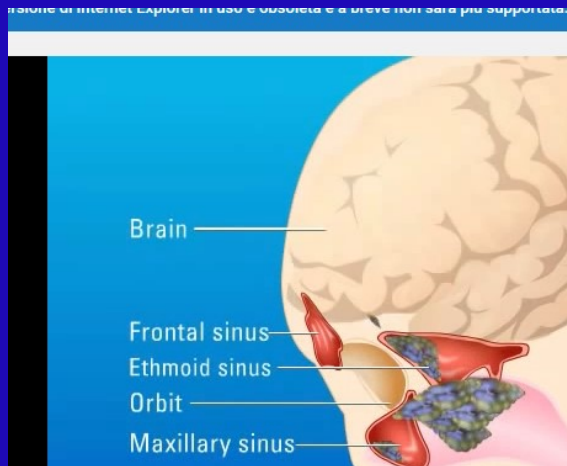
MUCORMYCOSIS

Overall mortality rate in organ transplant recipients with zygomycosis is approximately 38% to 48%

Lung infections with the fungus can cause fever and cough.

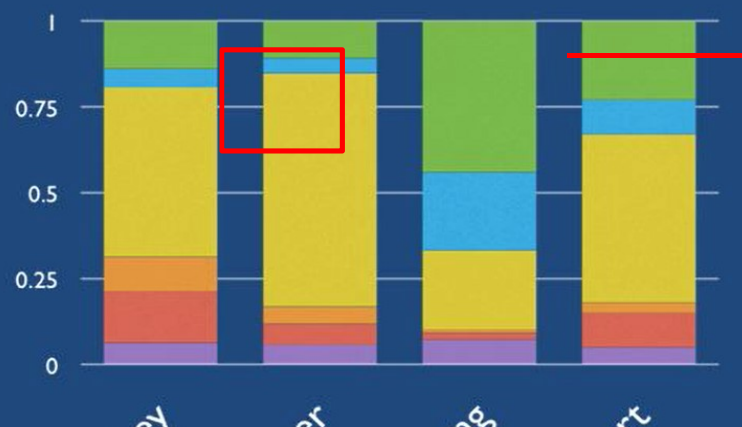
A skin infection can look like blisters or ulcers, and the infected tissue may turn black

Symptoms of sinus infections include fever, headache, and sinus pain.



Rhinocerebral disease represents one-third to one-half of all cases of zygomycosis mortality 70-100%

Distribution of fungal infection by transplant type



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Table 3

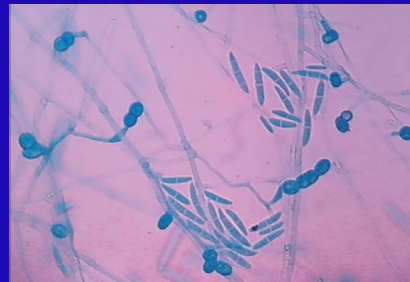
Clinical Characteristics of Emerging Fungi

Infection	Characteristic transplant recipient	Median time to infection	Typical site
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Fusariosis

The most frequent pattern of disseminated disease:
is a combination of **cutaneous lesions and positive blood cultures**,

typical clinical presentation
patient with **prolonged (>10 days) and profound (<100/mm³) neutropenia**
persistently febrile and develops disseminated and characteristic skin lesions, with a positive blood culture for a mold

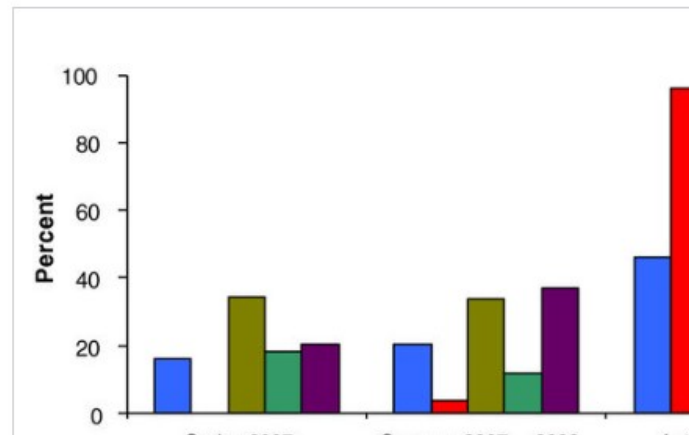


- Fusarium solani*
- *Fusarium verticillioides*
- *Fusarium oxysporum*
- *Fusarium proliferatum*
- *Fusarium dimerum*

Nosocomial waterborne fusariosis

ORIGINAL ARTICLE

Removal of waterborne pathogens from liver transplants
prevention of healthcare-associated infections: a prospective
cost-effective, prospective infection control strategy
CMI 2014



- *Fusarium* species were recovered from a hospital water system (water, water storage tanks, shower)
- **Showering and other water-related activities** appeared to be an efficient mechanism for the dispersion of airborne fusarial conidia and transmission to the **immunocompromised host**

Format: Abstract ▼

Transpl Int. 2014 Oct;27(10):e99-e101. doi: 10.1111/tri.12365. Epub 2014 Jun 21.

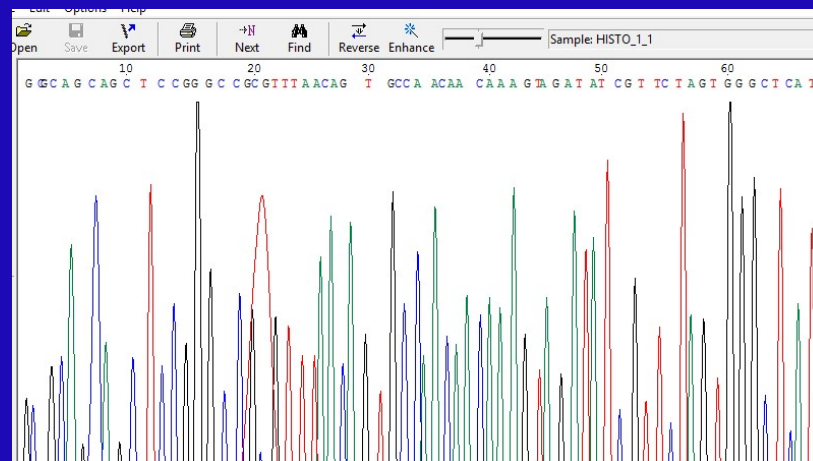
Letter to the editors

Table 1. Review of published cases of histoplasmosis in lung transplant recipients and summary of current

Source	Age/Sex	Time post-LT (months)	Country	Regimen	Urine/ Serology	Histo Cult
Cuellar-Rodriguez <i>et al.</i> [5]	41/M	10	OH (US)	CyA, Pr, MMF	+/-	+/ND
	52/M	47	OH (US)	SIR, Pr, MMF	-/ND	+/ND
	64/M	83	OH (US)	AZA, Pr, CyA	+/+	+/+
Shah <i>et al.</i> [7]	43/M	10*	OH (US)	ND	-/-	+/+
Assi <i>et al.</i> [6]	59/M	23	AL (US)	CyA, MMF, Pr	+/ND	+/+
	29/M	84	MN (US)	CyA, MMF, Pr	+/ND	+/+
	59/F	57	IN (US)	MMF, Pr	+/ND	ND/-
	49/F	144	IN (US)	SIR, Pr	+/-	ND/-

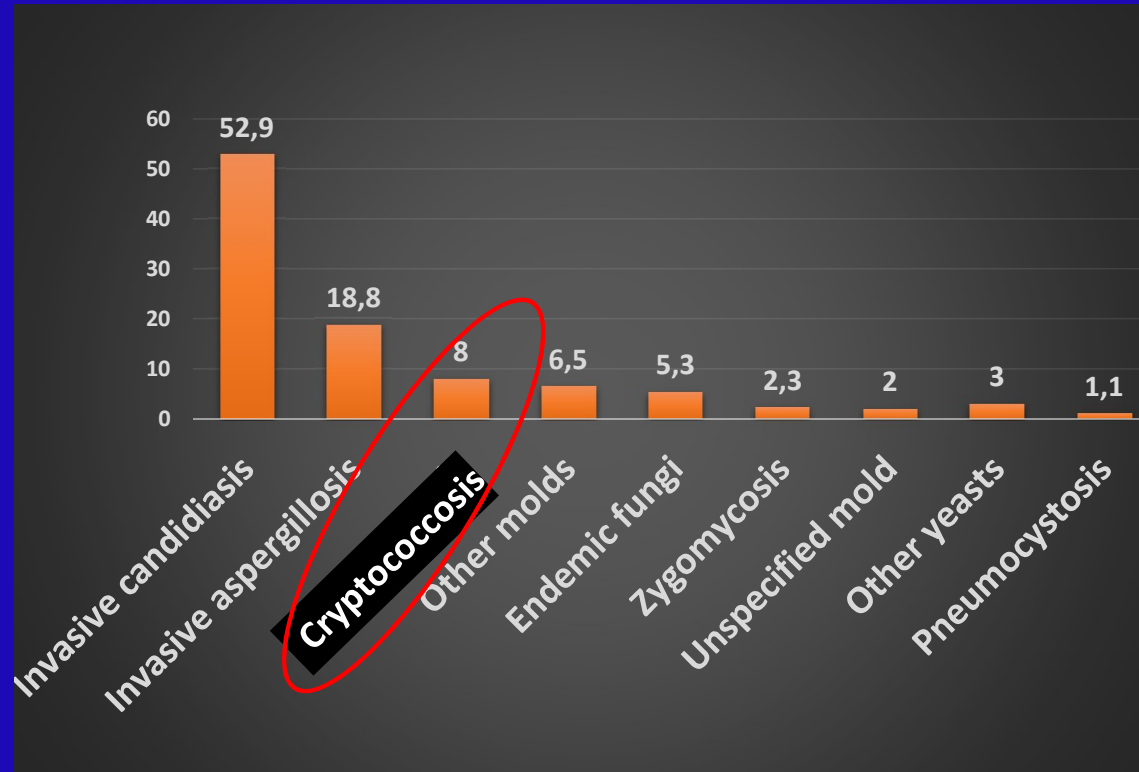
Format: Abstract ▼

Transpl Int. 2014 Oct;27(10):e99-e101. doi: 10.1111/tri.12365. Epub 2014 Jun 21.



H. capsulatum M antigen amplification

PCR Assay for Identification of *Histoplasma capsulatum* Based on the Nucleotide Sequence of the M Antigen



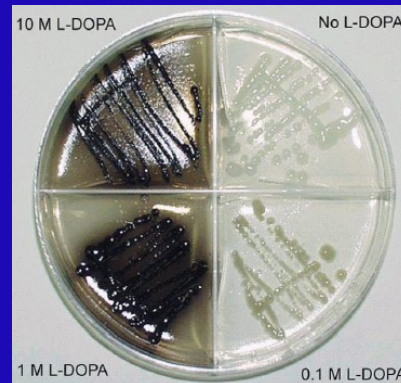
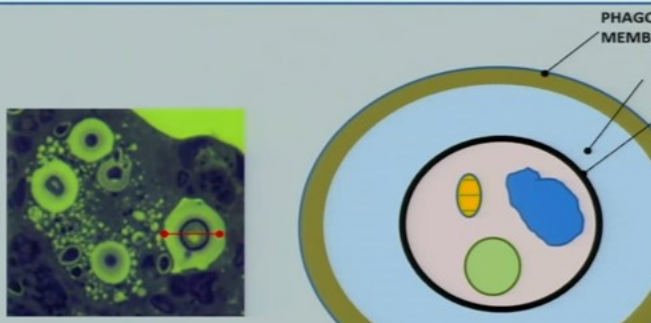
Cryptococcosis

Unrecognized Pretransplant and Donor-Cryptococcal Disease in Organ Transplant

Hsin-Yun Sun,^{1,22} Barbara D. Alexander,³ Olivier Lortholary,²³ Francoise Dromer,²⁴ et al.

Approximately 53-72% of the solid organ transplant recipients with cryptococcosis have disseminated disease or CNS involvement

C. NEOFORMANS EVADES INTRACELLULAR KILLING THROUGH TWO MAJOR MECHANISMS

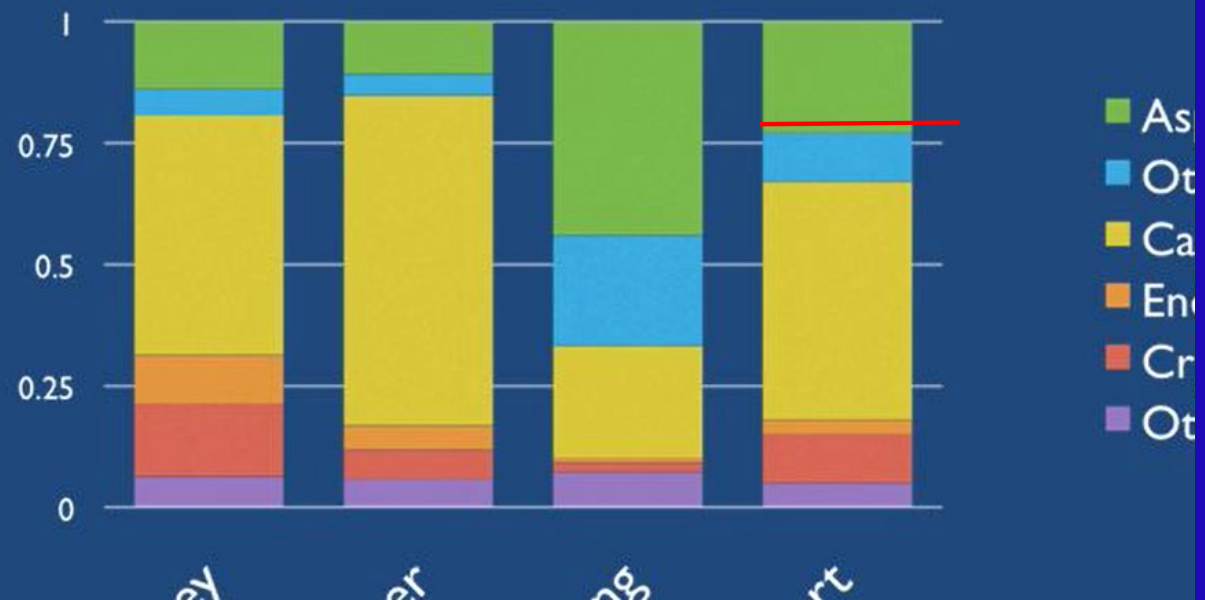


Associated with its ability to utilize catecholamines for melanin synthesis

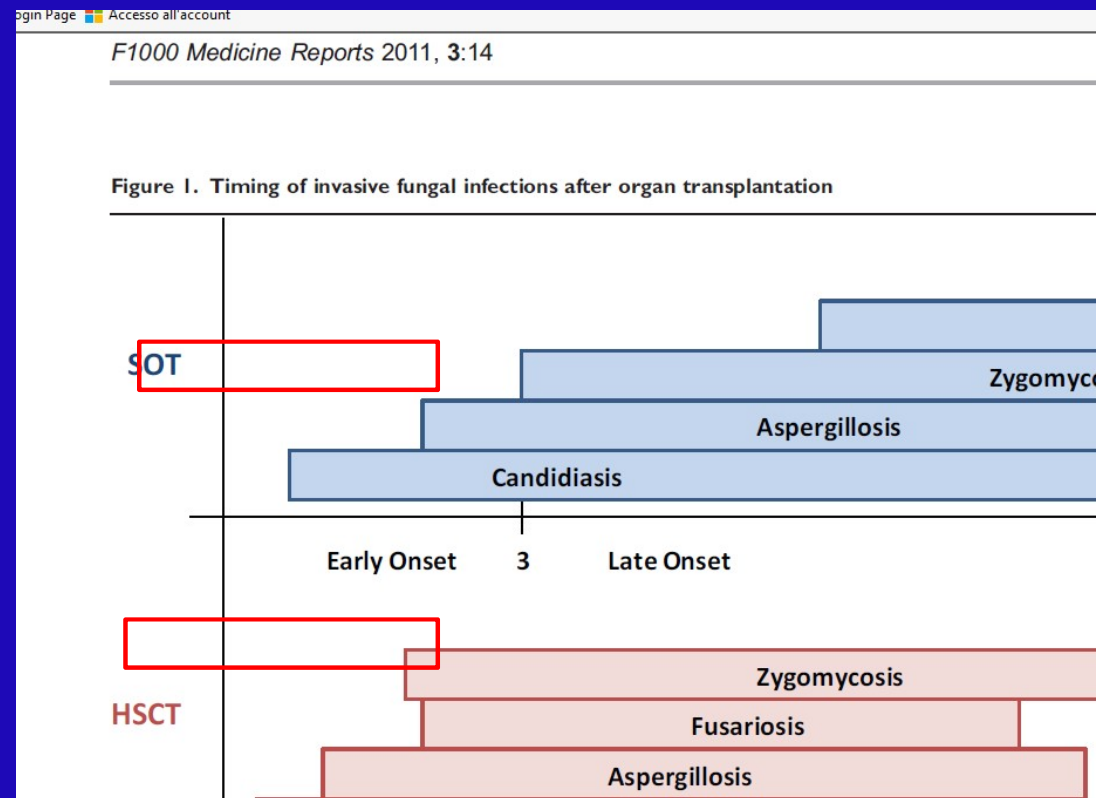
Dopamine is found in CNS where function as neurotransmitter

Areas rich in these molecules, such as the basal ganglia, are often involved in infection with *C. neoformans*

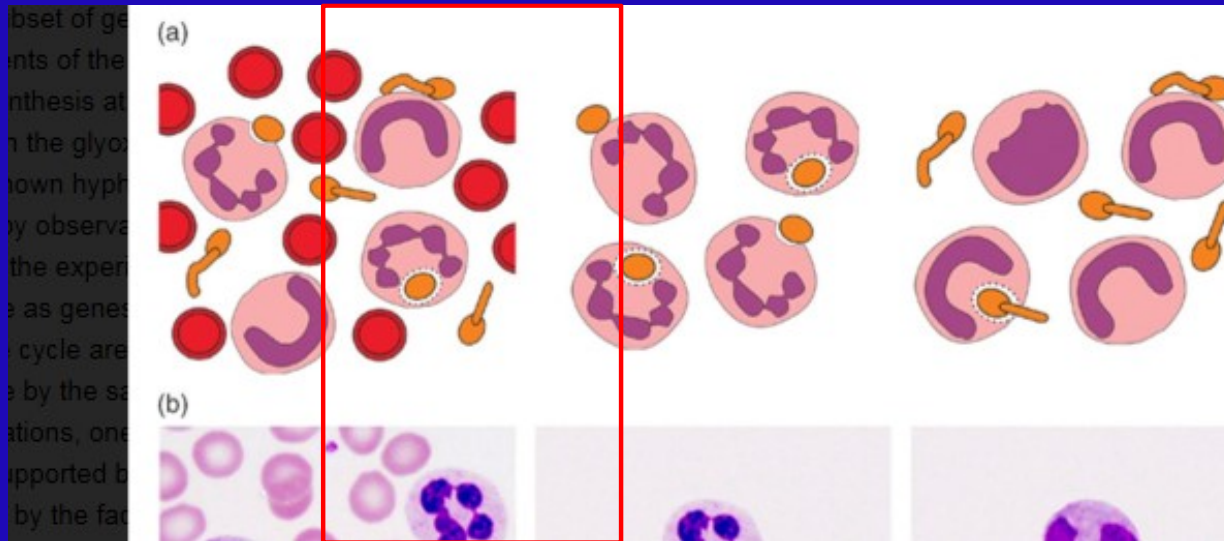
Distribution of fungal infections transplant type



Timing of invasive fungal infection after organ transplantation



Interaction of *Candida albicans* with blood



MINIREVIEW

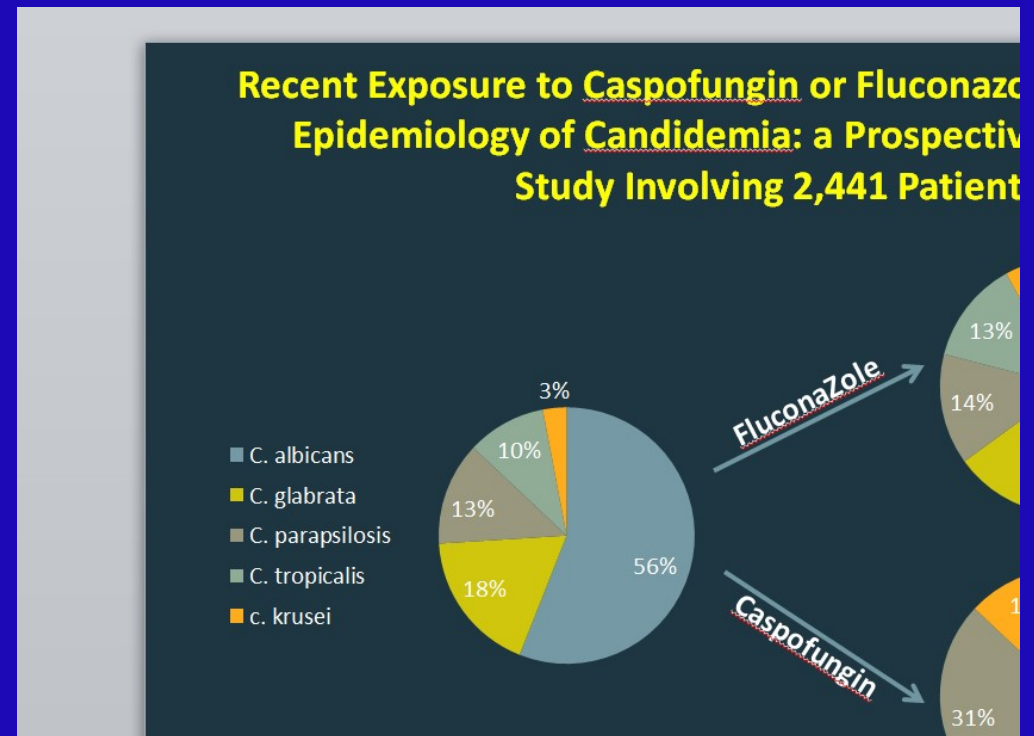
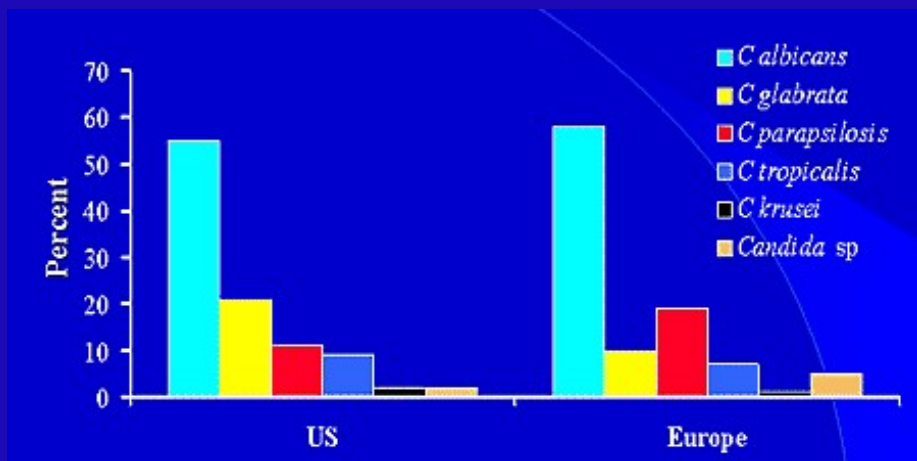
Identifying infection-associated genes of *Candida albicans* in the postgenomic era

Duncan Wilson¹, Sascha Thewissen², Katherine Zakikhany³, Chantal Eradin⁴, Antio

The effect of blood or blood fractions on *C. albicans* morphology:

- heterogenous morphology of fungal cells in whole blood,
- repression of hyphal formation in the PMN (neutrophil) fraction: **neutrophils arrested cell growth**
- hyphal development in the MNC (monocyte/lymphocyte) and red blood cells (RBC) (erythrocyte) fractions

Which Candida species?



Centers for Disease Control and Prevention

MMWR

Morbidity and Mortality

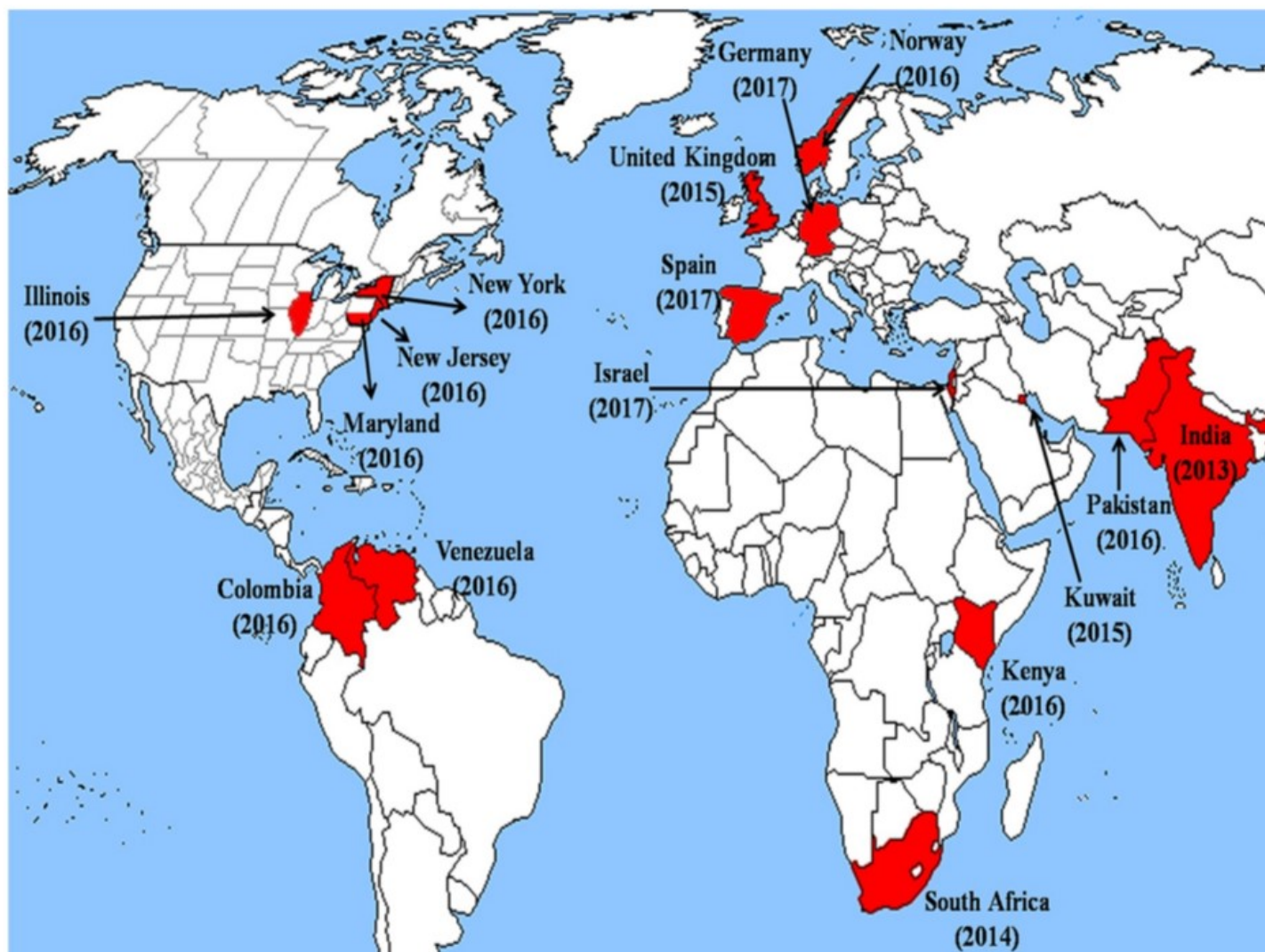
Early Release / Vol. 65

Investigation of the First Seven Reported Cases of *Candida auris*

Early Release

TABLE. Characteristics of the first seven cases of *Candida auris* identified in the United States—May 2013–August 2015

Patient	Isolation		Site of <i>C. auris</i>	
	month/ year	State	isolation	Underlying medical condition(s)
1	May 2013	New York	Blood	Respiratory failure requiring high-dose corticosteroids
2	July 2015	New Jersey	Blood	Brain tumor and recent villous adenoma resection



elevated minimum inhibitory concentration (MIC) for an antifungal drug should not necessarily preclude its use if the patient's clinical response to the drug has been effective.

Class/Drug	Tentative MIC Breakpoints (µg/mL)	Comment
Triazoles		
Fluconazole	≥32	Modal minimum inhibitory concentration (MIC) to fluconazole among isolates with MICs ≥32 were shown to have a resistance mutation to respond to fluconazole.
Voriconazole and other second generation triazoles	N/A	Consider using fluconazole susceptibility as a surrogate for second assessment. However, isolates that are resistant to fluconazole may not be resistant to voriconazole. The decision to treat with another triazole will need to be made on a case-by-case basis.
Polyenes		
Amphotericin B	≥2	Recent pharmacokinetic/pharmacodynamic analysis of <i>C. auris</i> in mice under standard dosing, the breakpoint for amphotericin B should be determined for other <i>Candida</i> species. Therefore, isolates with a MIC ≥2 are resistant . If using Etest for amphotericin B and an MIC of 1.5 is determined, the isolate is considered resistant.

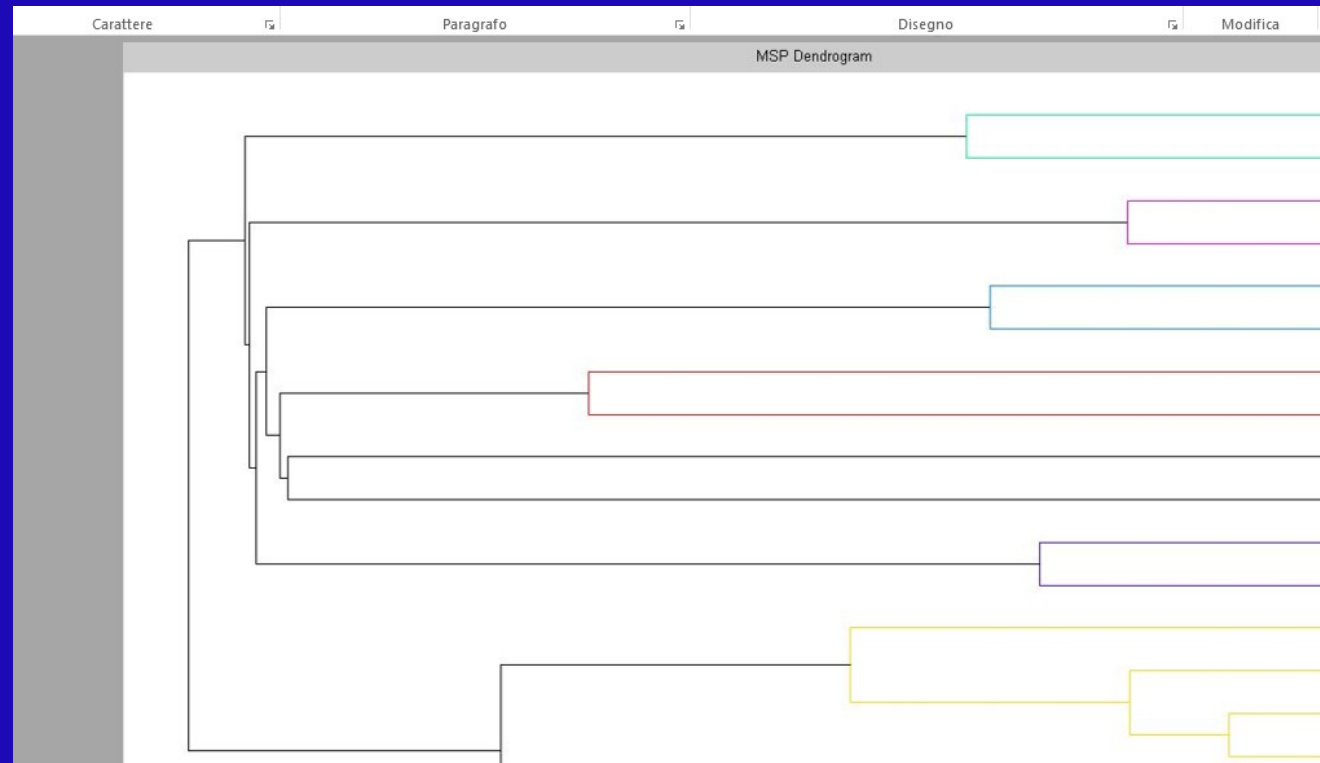
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Clin Infect Dis. 2017 Sep 15;65(6):1040-1042. doi: 10.1093/cid/cix460.



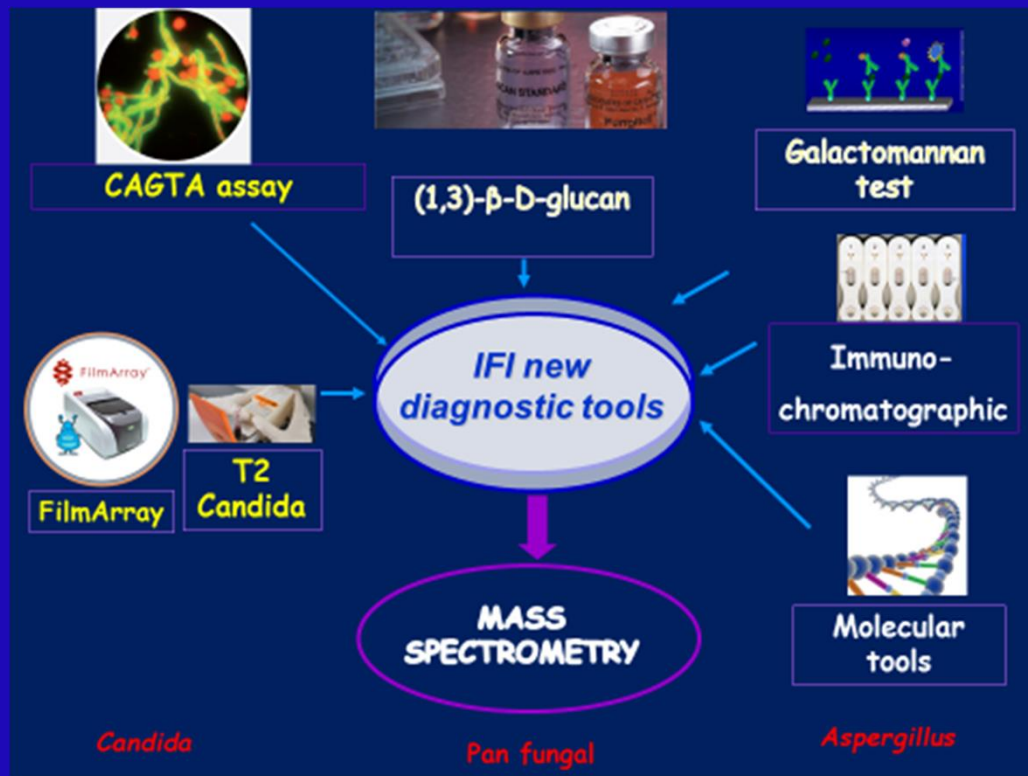
		species identity cannot be determined, further characterization using appropriate methodology	
	+		
		Identification Method	Organism <i>C. auris</i> can be misidentified as
ase	+	Vitek 2 YST	<i>Candida haemulonii</i> <i>Candida duobushaemulonii</i>
	+	API 20C	<i>Rhodotorula glutinis</i> (characteristic red color) <i>Candida sake</i>
		BD Phoenix yeast identification system	<i>Candida haemulonii</i> <i>Candida catenulata</i>

**MALDI-TOF
UPDATED
DATABASE**



JCM 2017

The management of invasive fungal infections begins with a high index of suspicion and prompt diagnosis



Thank you all