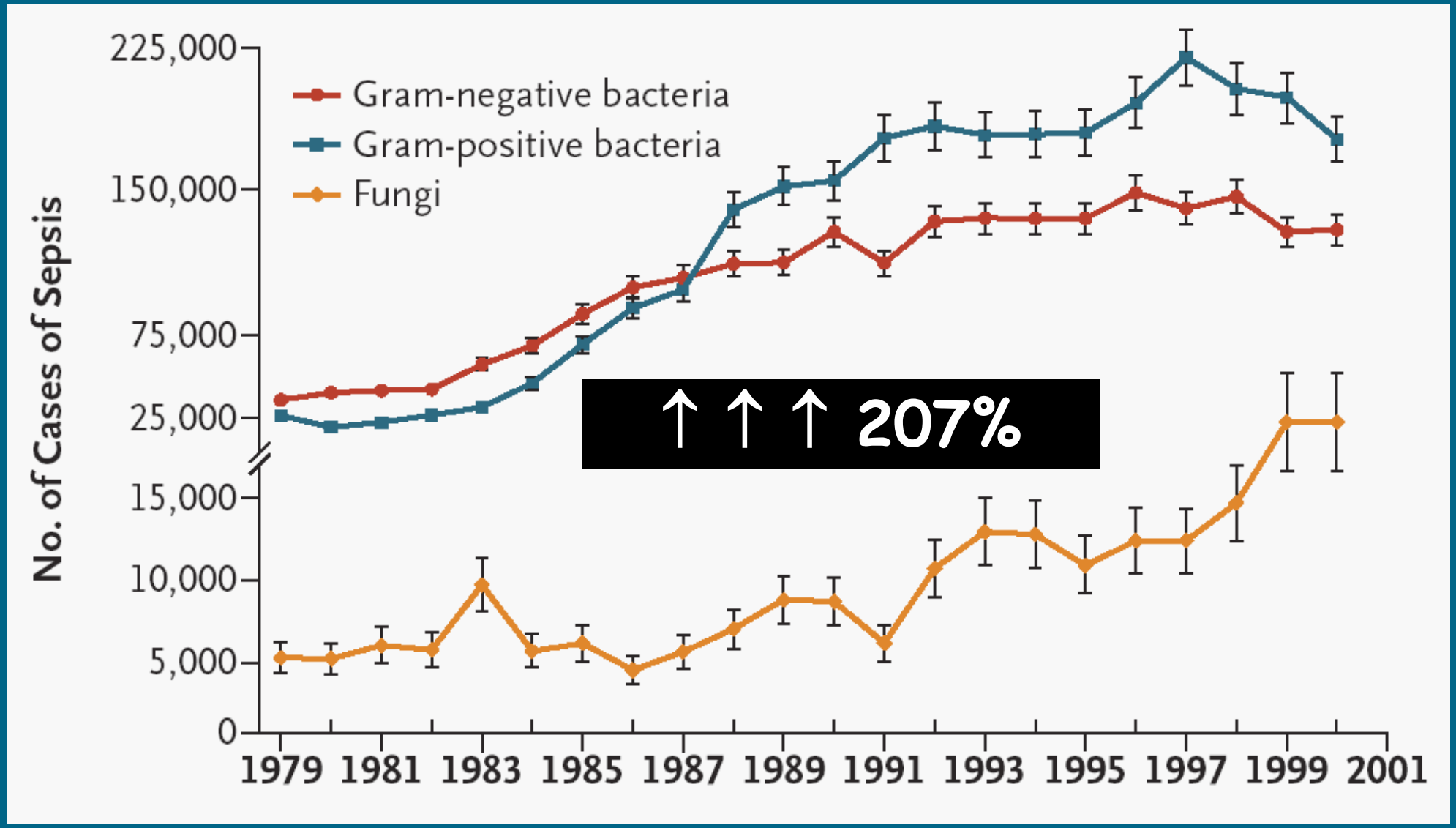
Instituto de Salud Carlos III

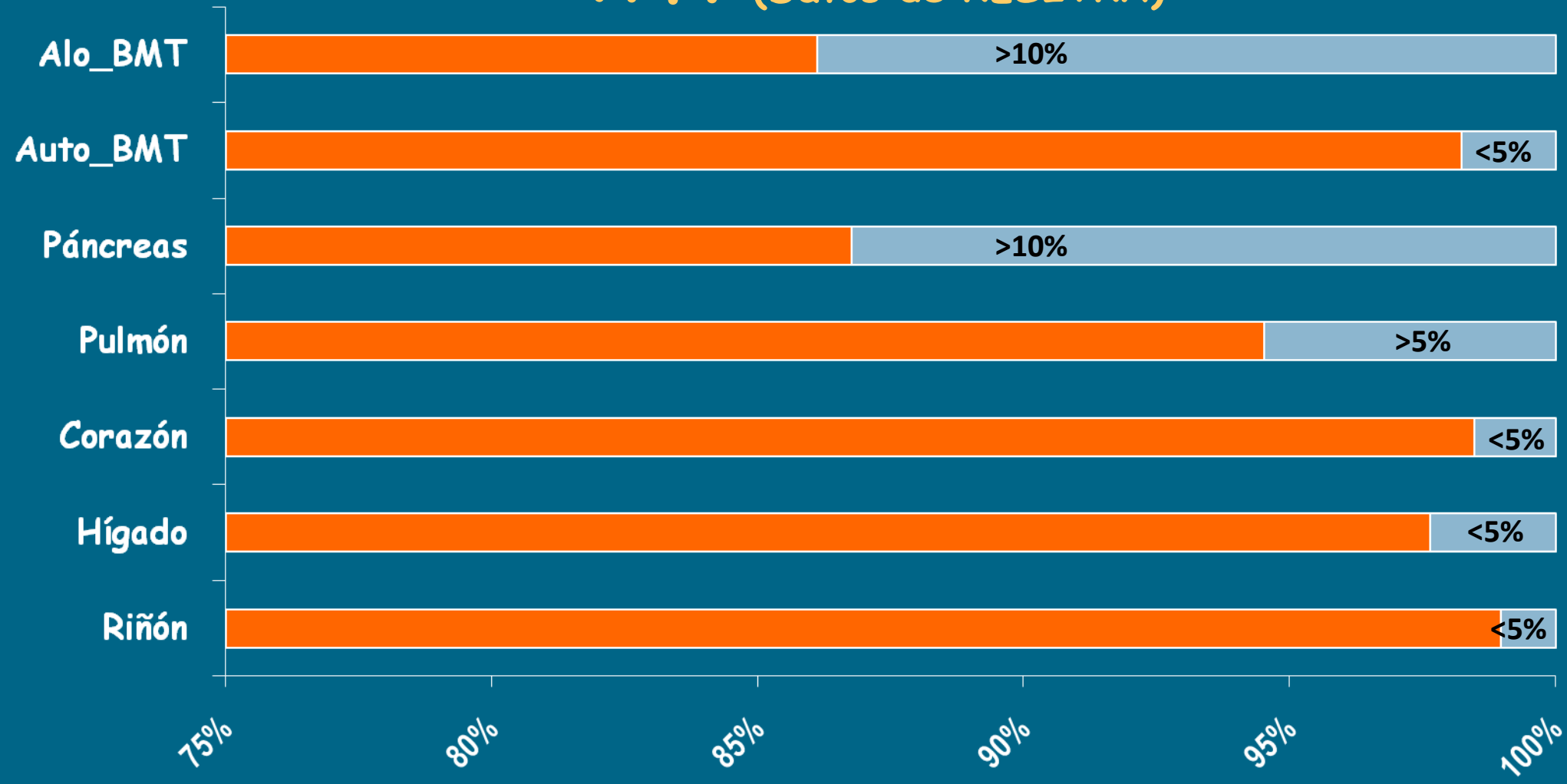
Epidemiología de las infecciones fúngicas en el ámbito hospitalario: hongos emergentes

Juan Luis Rodríguez Tudela
Servicio de Micología
Centro Nacional de Microbiología

Epidemiology of sepsis in USA (Martin NEJM, 2003)



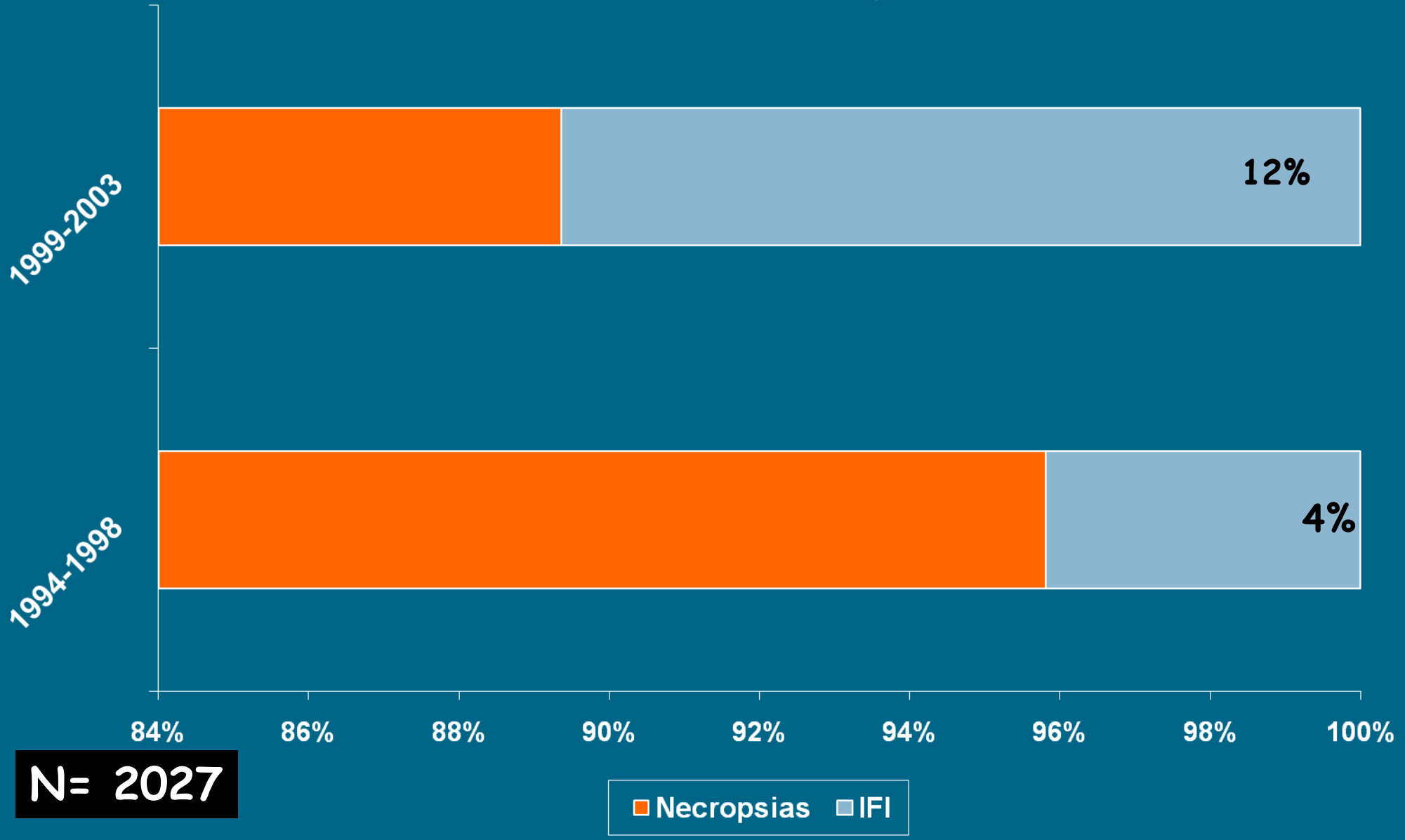
Epidemiología de la IFI en TOS y TPH (Datos de RESITRA)



N= 3487

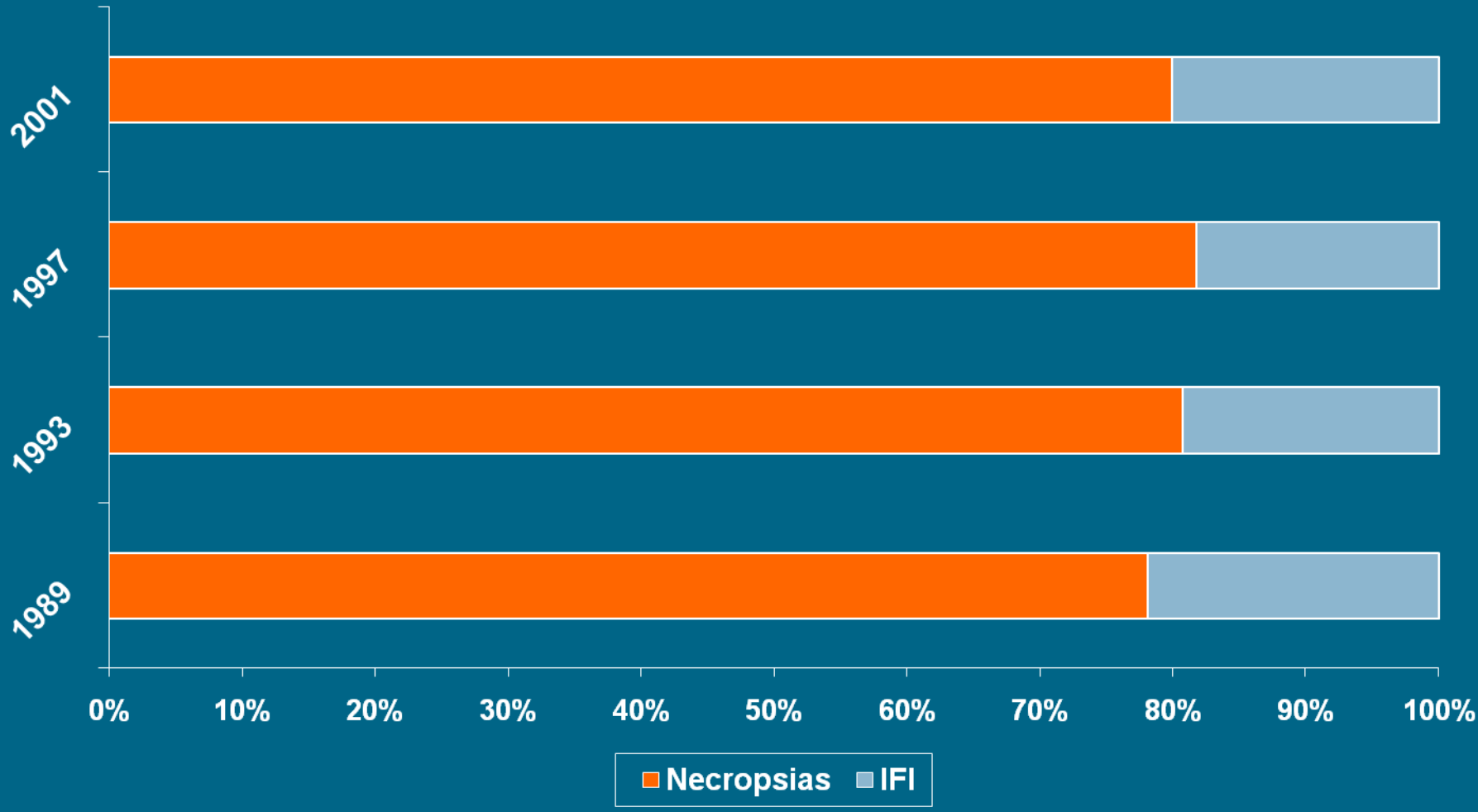
Epidemiología de la IFI en necropsias

(Schwesinger et al. Mycoses´05)

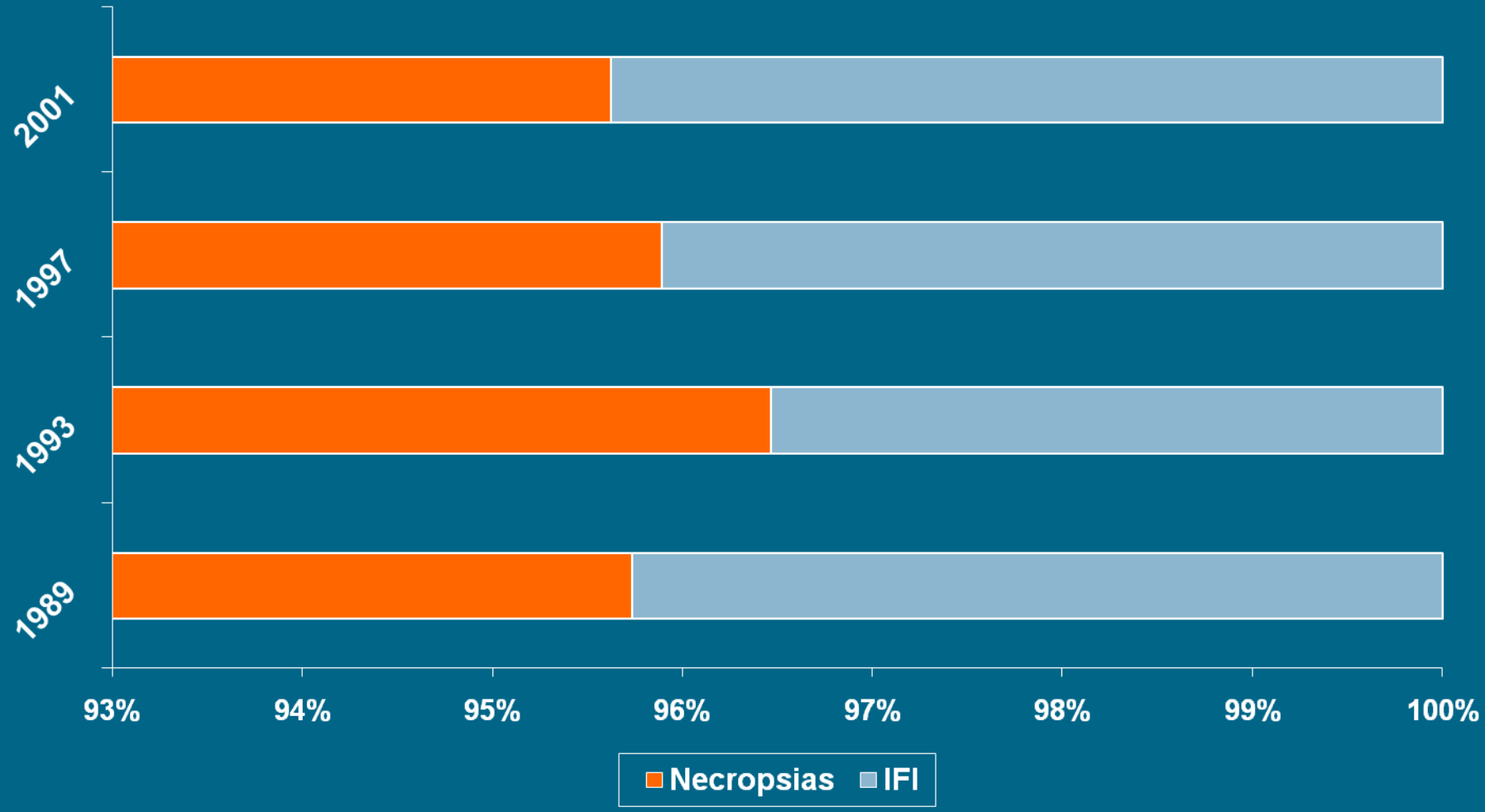


N= 2027

Kume H et al. Epidemiology of visceral mycoses in patients with leukemia and MDS – Analysis of the data in annual of pathological autopsy cases in Japan in 1989, 1993, 1997 and 2001



Kume H et al. Analysis of the data in annual of pathological autopsy cases in Japan in 1989, 1993, 1997 and 2001



JOURNAL OF CLINICAL MICROBIOLOGY, Apr. 2005, p. 1829–1835
0095-1137/05/$08.00+0 doi:10.1128/JCM.43.4.1829–1835.2005
Vol. 43, No. 4

Epidemiology and Predictors of Mortality in Cases of *Candida* Bloodstream Infection: Results from Population-Based Surveillance, Barcelona, Spain, from 2002 to 2003

Benito Almirante,[1]* Dolors Rodríguez,[1] Benjamin J. Park,[2] Manuel Cuenca-Estrella,[3] Ana M. Planes,[4] Manuel Almela,[5] Jose Mensa,[6] Ferran Sanchez,[7] Josefina Ayats,[8] Montserrat Gimenez,[9] Pere Saballs,[10] Scott K. Fridkin,[2] Juliette Morgan,[2] Juan L. Rodriguez-Tudela,[3] David W. Warnock,[2] Albert Pahissa,[1] and the Barcelona Candidemia Project Study Group†

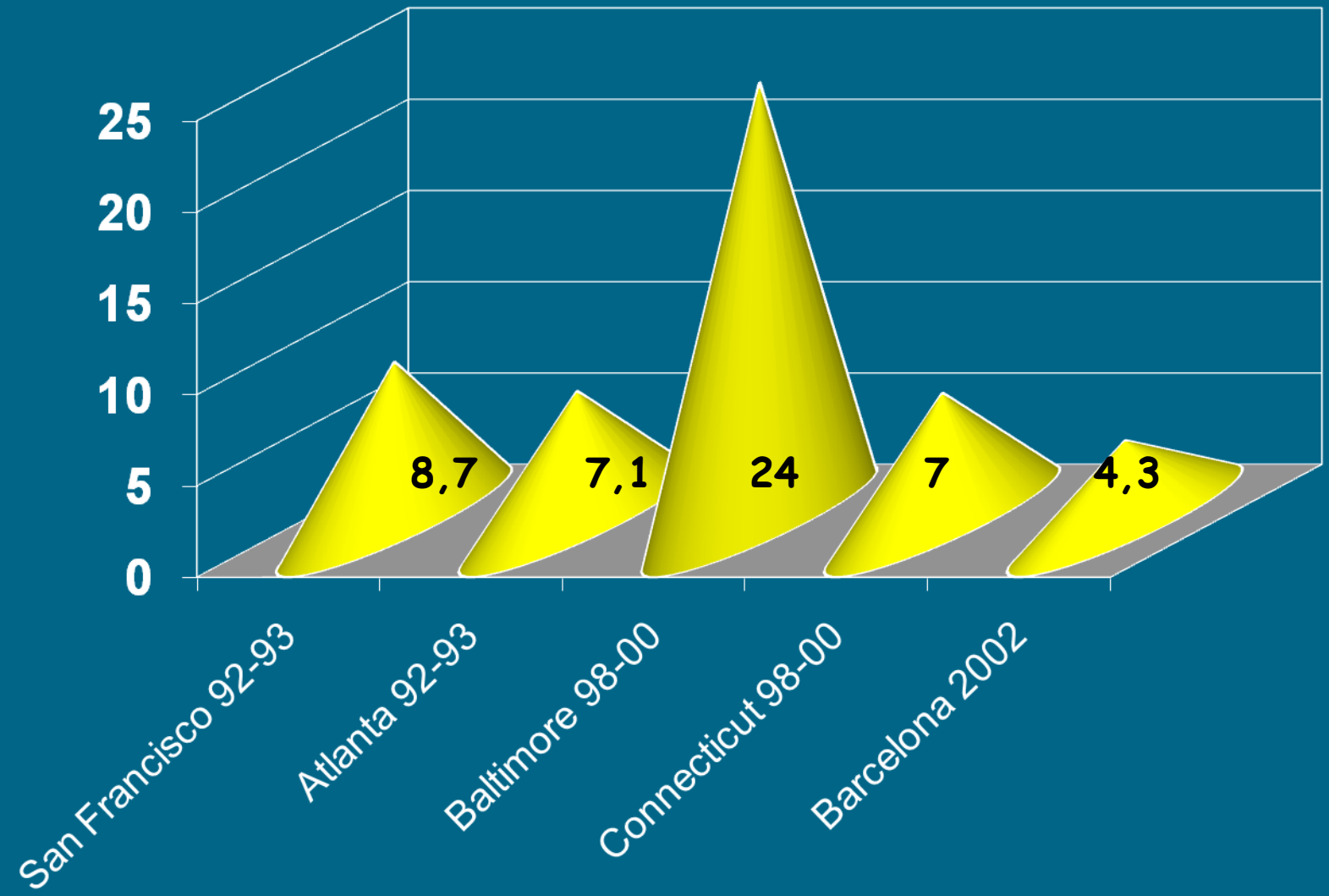
Journal of Antimicrobial Chemotherapy (2005) **55**, 194–199
doi:10.1093/jac/dkh548
Advance Access publication 23 December 2004
JAC

In vitro susceptibilities of bloodstream isolates of *Candida* species to six antifungal agents: results from a population-based active surveillance programme, Barcelona, Spain, 2002–2003

Manuel Cuenca-Estrella[1]*†, Dolores Rodriguez[2]†, Benito Almirante[2], Juliette Morgan[3], Ana Maria Planes[4], Manel Almela[5], José Mensa[6], Ferran Sanchez[7], Josefina Ayats[8], Montserrat Gimenez[9], Margarita Salvado[10], David W. Warnock[3], Albert Pahissa[2] and Juan L. Rodriguez-Tudela[1] on behalf of the Barcelona Candidemia Project Study Group

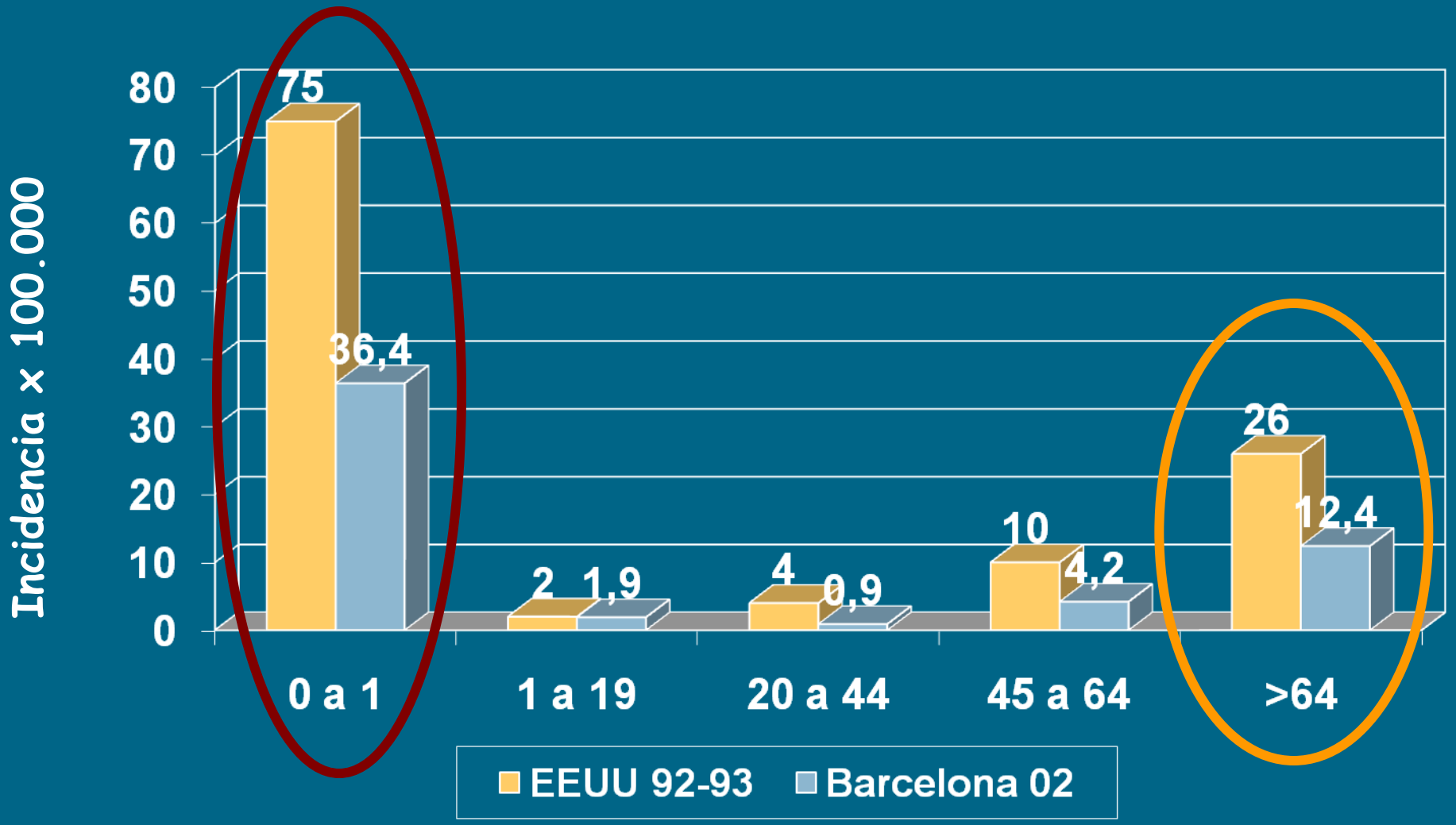
Candidemia

Incidencia x 100.000 habitantes



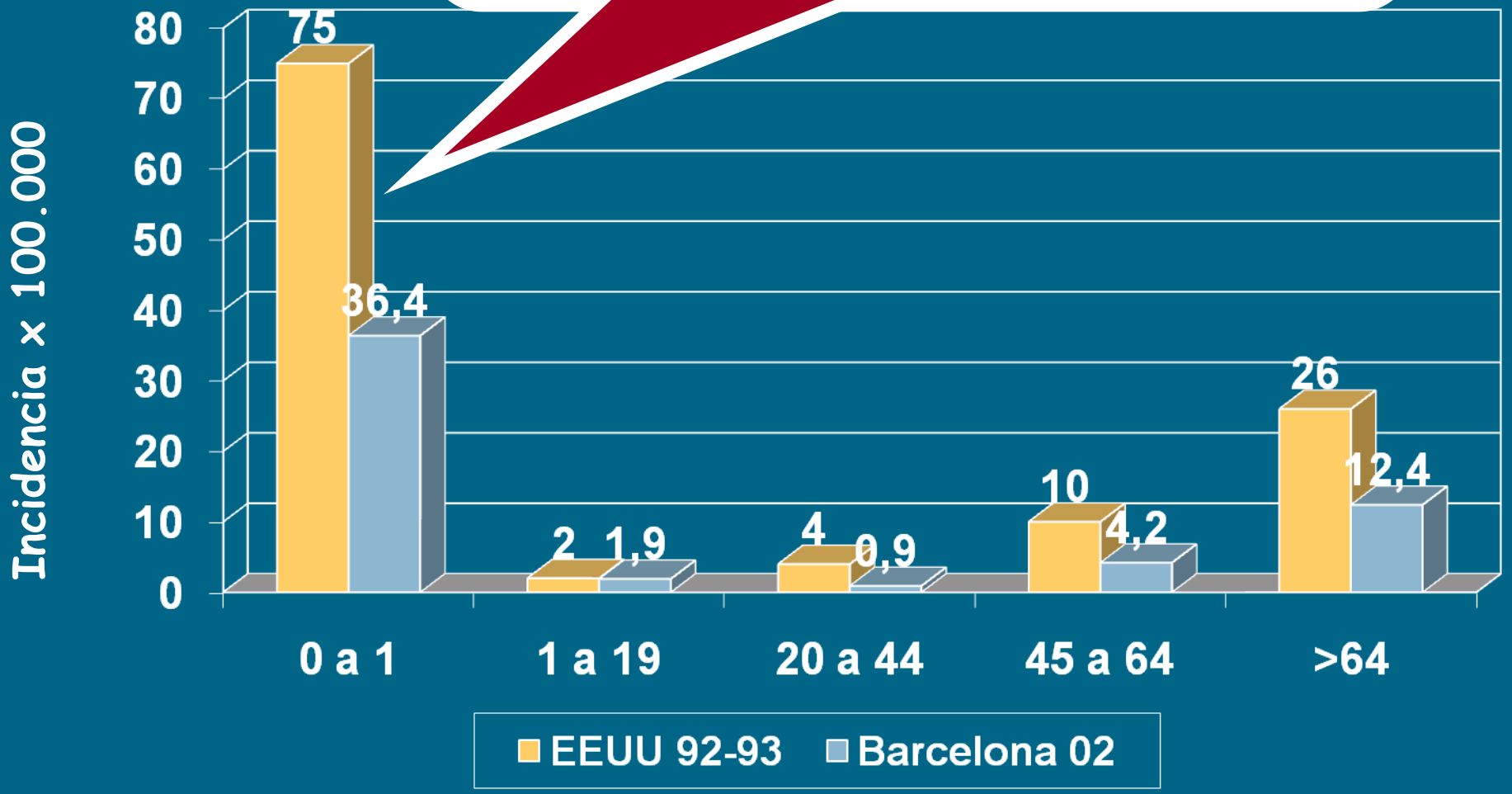
Candidemia

Incidencia por edades x 100.000



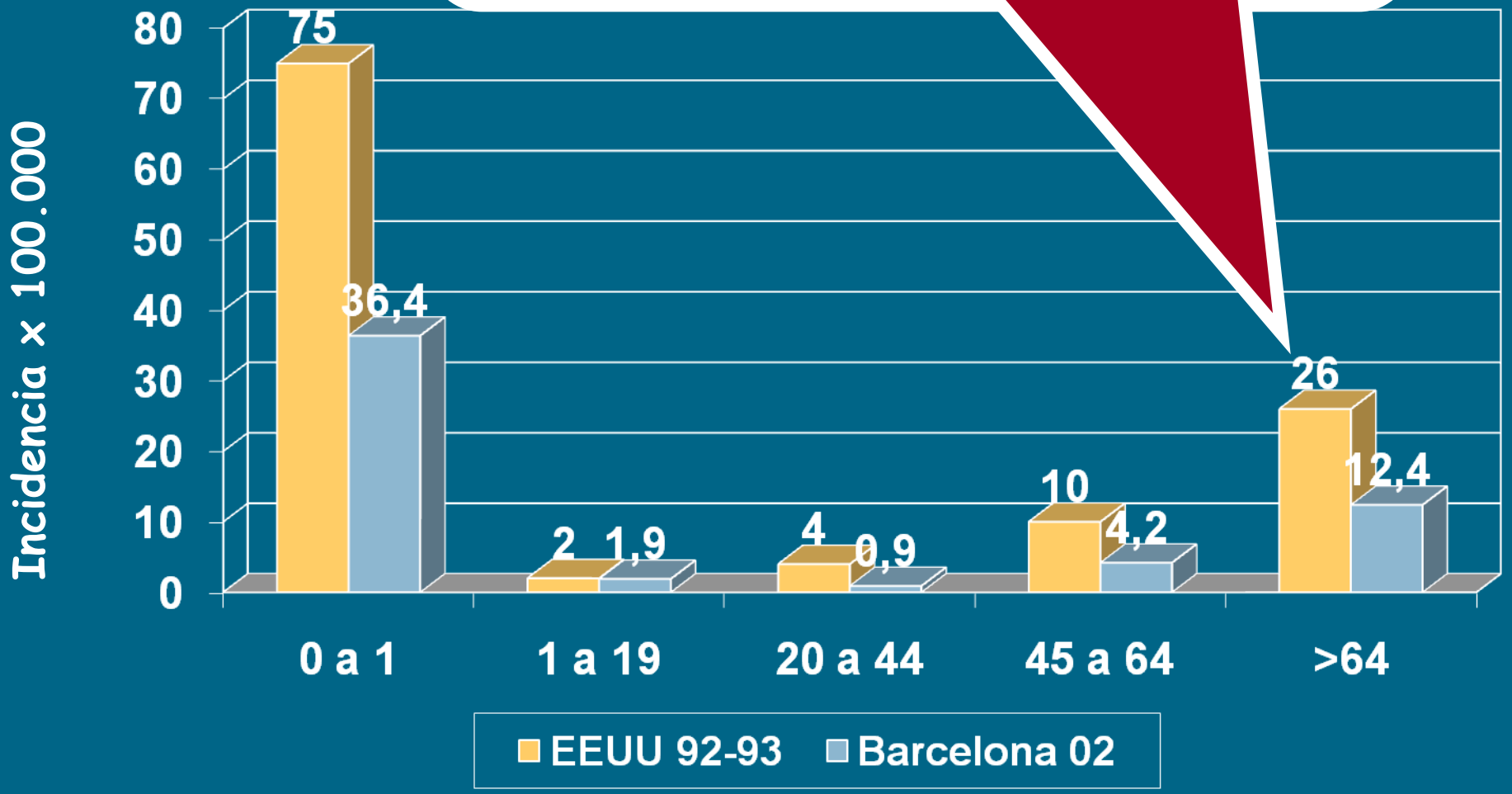
Inc

C. albicans
&
C. parapsilosis



Inc

C. glabrata



Otros estudios recientes

Country	Year	*albicans*	*glabrata*	*krusei*	*parapsilosis*	*tropicalis*	Polyfungal infections
Australia	01-04	47.3	15.4	4.3	19.9	5.1	2.2
Canada	99-04	51.1	21.5	4.7	6.2	5.7	
Denmark	04-08	59.8	20.5	4.1	4.0	4.6	4.0
Finland	95-99	70.0	9.0	8.0	5.0	3.0	
Germany	04-05	58.4	18.7	1.6	9.3	6.3	
Iceland	80-99	64.4	12.4	0.56	9.6	5.6	
Israel	1994	53.6	6.5	0.7	11.9	10.9	
Italy	00-03	40.0	12.8	3.2	22.3	16.0	9.3
Japan	01-02	40.7	17.9	2.4	23.0	11.6	
Mexico	04-07	31.9	8	2.7	37.9	14.8	
Norway	91-03	69.8	13.2	1.6	5.8	6.7	1.5
Scotland	05-06	52.0	22.7	1.0	11.7	6.0	
Sweden	98-99	67.0	15.7	1.0	7.3	2.1	2.7
USA	92-93	52.0	12.0	4.0	21.0	10.0	
USA	98-0000	45.0	24.0	2.0	13.0	12.0	

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Anfotericina B y 5FC

Candida en hemocultivos

	% Resistencias		
	n	Anfo (≥2)	5-FC (≥8)
C. albicans	953	0	0.5
C. parap.	766	1.6	0.3
C. tropicalis	284	0.7	3.5
C. glabrata	312	0.3	6.8
C. krusei	111	3.6	18.9

Datos del Servicio de Micología. CNM. ISCIII.2009

Azoles

Puntos de corte de FZ en Europa-EUCAST

Sensible	Intermedio	Resistente
≤ 2 mg/L	4 mg/L	≥ 8 mg/L

Para *C. albicans*. *C. parapsilosis* y *C. tropicalis*

No recomendamos Fz para el tratamiento de las infecciones causadas por *C. glabrata* o *C. krusei*

Puntos de corte de VOR en Europa-EUCAST

Sensible	Intermedio	Resistente
≤ 0,12 mg/L	---	≥ 0,25 mg/L

Para *C. albicans*. *C. parapsilosis* y *C. tropicalis*

No recomendamos VOR para el tratamiento de las infecciones causadas por *C. glabrata* o *C. krusei*

Candida en hemocultivos

	% Resistencias			
	n	Fluco (≥8)	Vori (≥0,25)	Posa (≥0,25)
C. albicans	953	1.0	0.8	0.9
C. parap.	766	1.6	1.2	0.4
C. tropicalis	284	4.7	9.0	6.1
C. glabrata	312	42.9	39.2	58.4
C. krusei	111	100	80.7	12.1

Datos del Servicio de Micología. CNM. ISCIII.2009

¿Es *C. glabrata* sensible al fluconazol?

Sensibilidad comparada de *C. glabrata* según EUCAST y CLSI

	S	I/S-DD	R
EUCAST	≤ 2 mg/L	4 mg/L	≥ 8 mg/L
CLSI	≤ 8 mg/L	16-32 mg/L	≥ 64 mg/L

	S	I /S-DD	R
EUCAST	18.9	38.1	42.9
CLSI	79.2	12.2	8.6

Datos del Servicio de Micología. CNM. ISCIII.2009

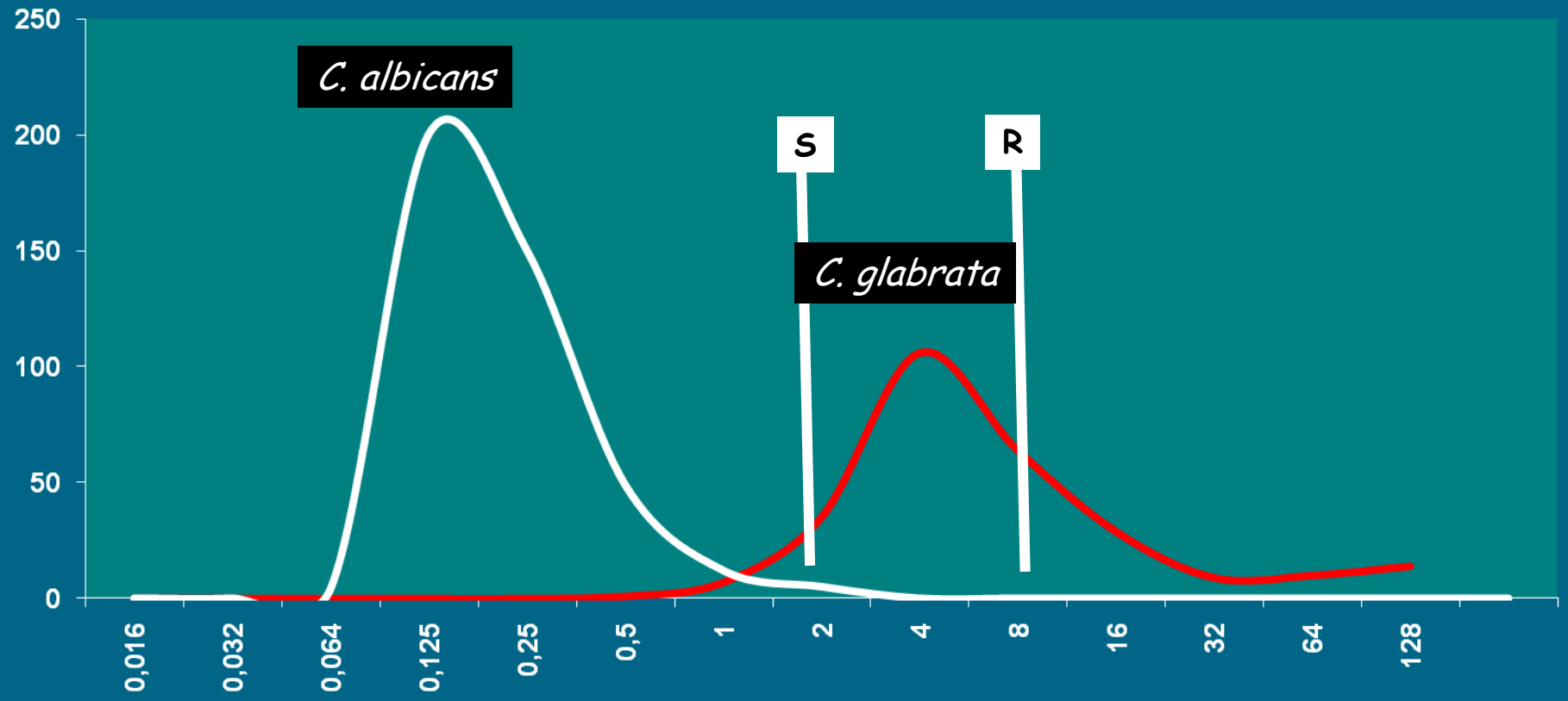
Evaluation by Data Mining techniques of Fluconazole Breakpoints established by the Clinical and Laboratory Standards Institute (CLSI), and its comparison with those of the European Committee on Antimicrobial Susceptibility Testing (EUCAST)

Cuesta I, Bielza C, Cuenca-Estrella M, Larrañaga P, Rodríguez-Tudela JL.

Antimicrob Agents Chemother. 2010 Feb 1. [Epub ahead of print]

Sensible	Intermedio	Resistente
≤ 2 mg/L	4 mg/L	≥ 8 mg/L

Fluconazole



ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Apr. 2009, p. 1628–1629 Vol. 53, No. 4
0066-4804/09/$08.00+0 doi:10.1128/AAC.01624-08
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Breakpoints for Susceptibility Testing Should Not Divide Wild-Type Distributions of Important Target Species[▽]

Maiken Cavling Arendrup,[1]* Gunnar Kahlmeter,[2]
Juan Luis Rodriguez-Tudela,[3] and J. Peter Donnelly[4]

- One *C. glabrata* susceptible (MIC = 2 mg/L) to fluconazole according EUCAST BPs

S	I	R
≤ 2	4	>4

- 51 repetitions in different days

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Apr. 2009, p. 1628–1629 Vol. 53, No. 4
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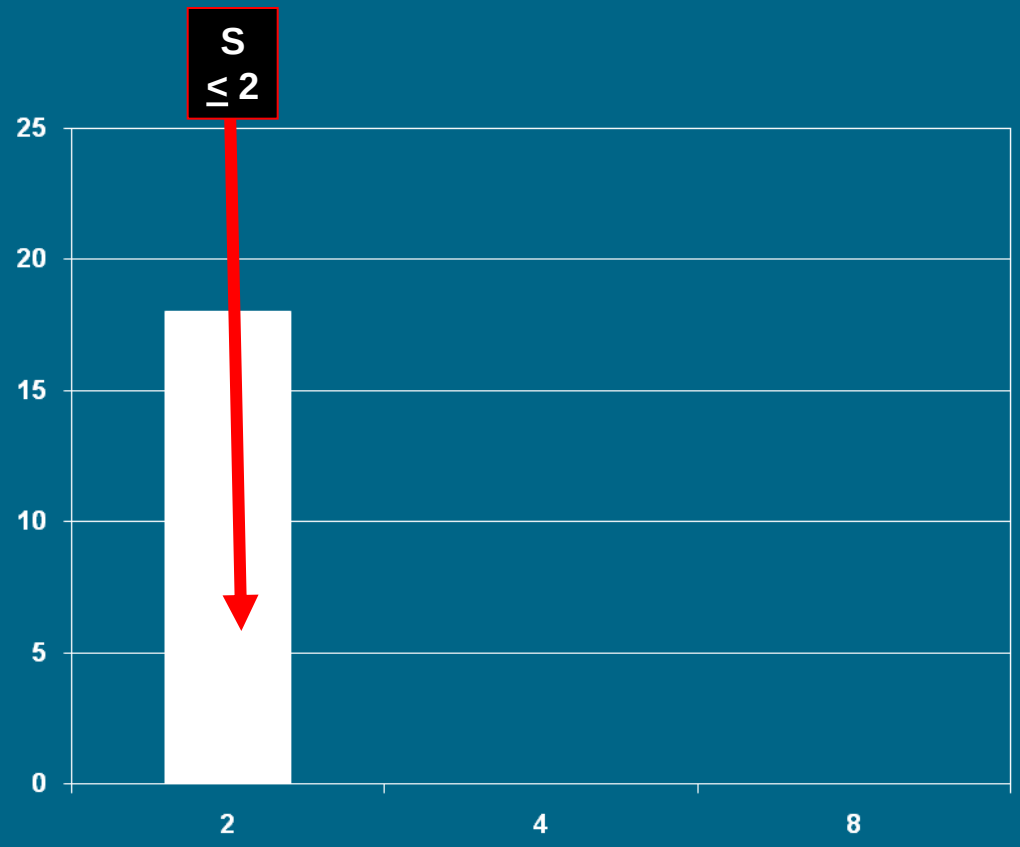

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Apr. 2009, p. 1628–1629 Vol. 53, No. 4
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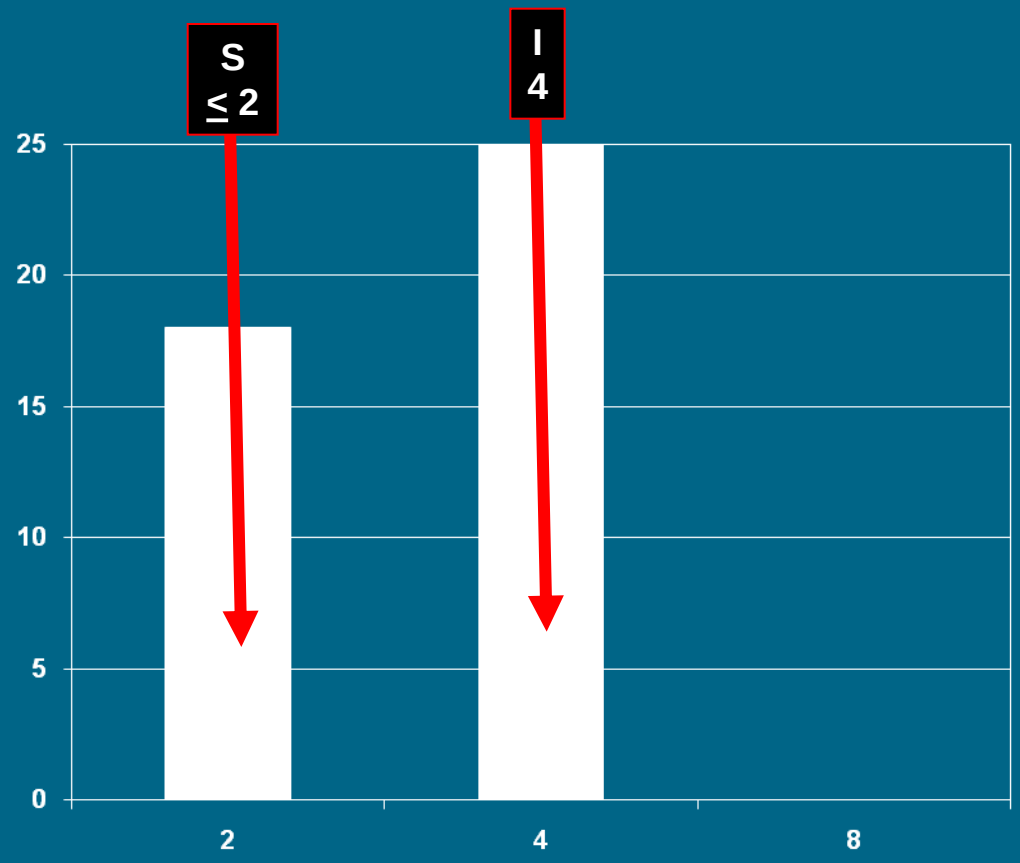

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Apr. 2009, p. 1628–1629 Vol. 53, No. 4
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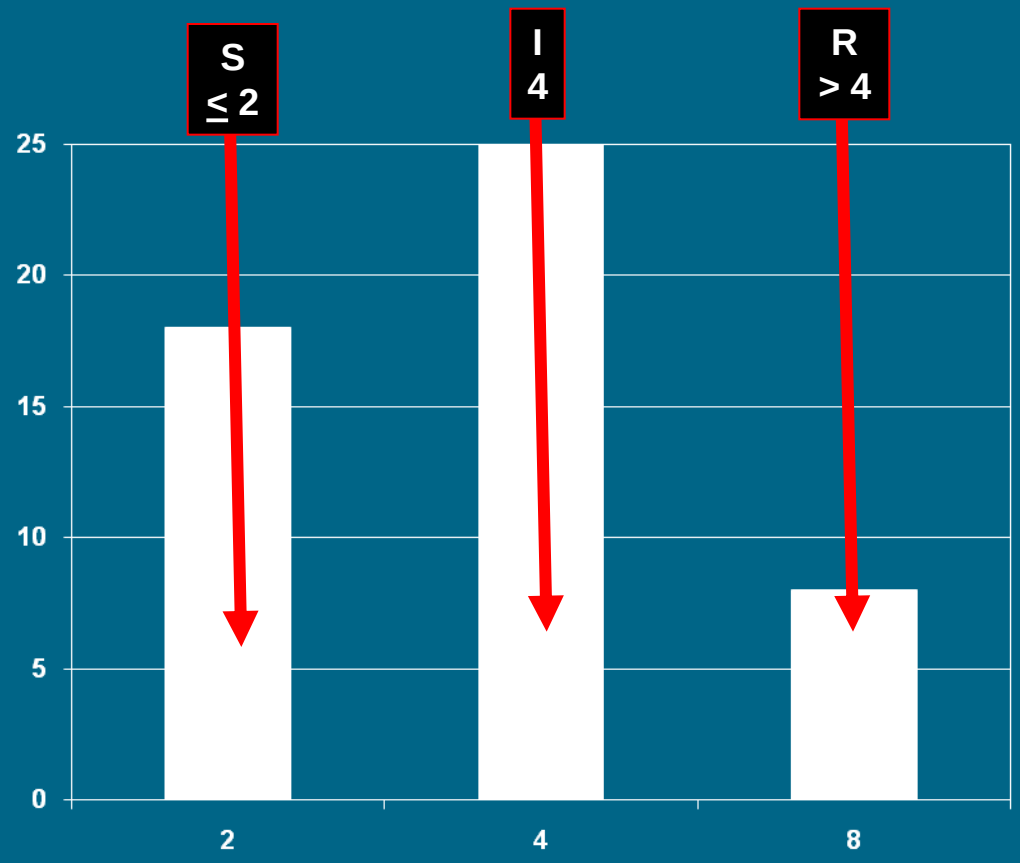

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- Splitting the wild-type distribution will result in a random susceptible, intermediate (or susceptible-dose-dependent), and resistant categorization of isolates with identical susceptibilities.
- This is futile and confusing and will undermine the credibility of the susceptibility testing.

Fluconazole & *C. glabrata*

Candida Pathogen	Successful Microbiologic Response			Successful Global Response†		
	Anidulafungin Group	Fluconazole Group	P Value	Anidulafungin Group	Fluconazole Group	P Value
	no. of isolates/total no. (%)			*no. of patients/total no. (%)*		
Candida albicans	77/81 (95)	57/70 (81)	0.01	60/74 (81)	38/61 (62)	0.02
C. glabrata	15/20 (75)	18/30 (60)	0.37	9/16 (56)	11/22 (50)	0.75
C. parapsilosis	9/13 (69)	14/16 (88)	0.36	7/11 (64)	10/12 (83)	0.37
C. tropicalis	13/15 (87)	7/11 (64)	0.35	13/14 (93)	4/8 (50)	0.04
Other candida species	5/6 (83)	3/3 (100)	1.00	3/4 (75)	2/3 (67)	1.00
All candida species	119/135 (88)	99/130 (76)	0.02	92/119 (77)	65/106 (61)	0.01

Reboli, NEJM 2007; 356:2472-82

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Transplant Infectious Disease. ISSN 1398-2273

Outcomes of antifungal prophylaxis in high-risk liver transplant recipients

The aim of this study was to evaluate the safety and efficacy of antifungal therapy (liposomal amphotericin B [L-amB] and fluconazole) in patients undergoing OLT who are at high risk for IFI.

En el brazo de fluconazol las 3 infecciones de brecha fueron causadas por *C. glabrata*

¿Se puede usar voriconazol para tratar las infecciones causadas por *C. glabrata?*

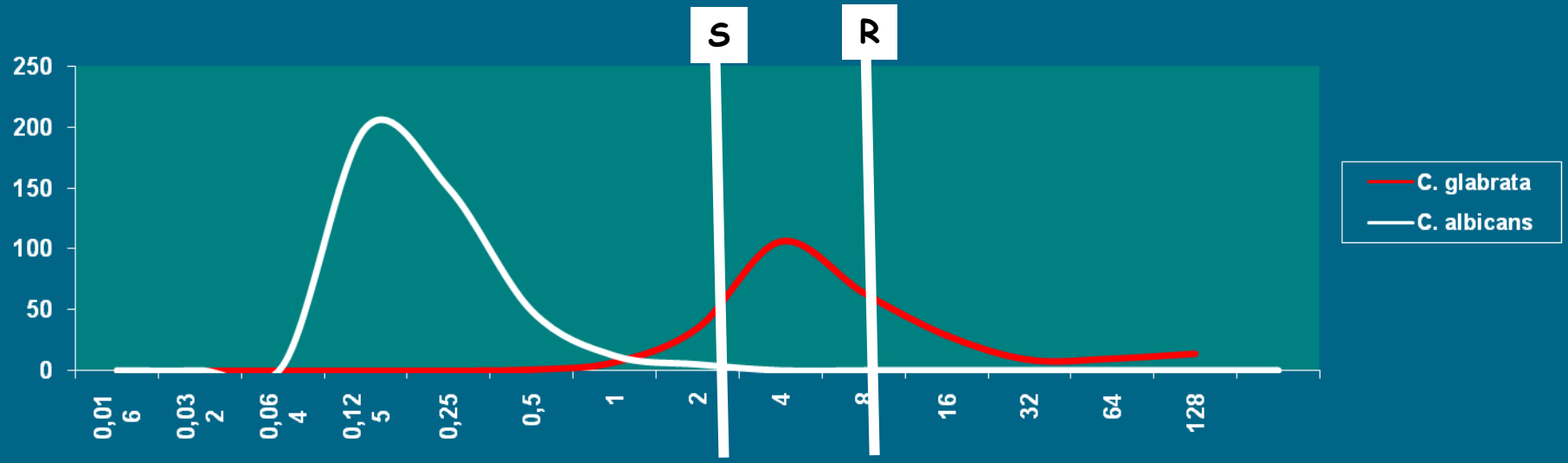
Puntos de corte de VOR en Europa-EUCAST

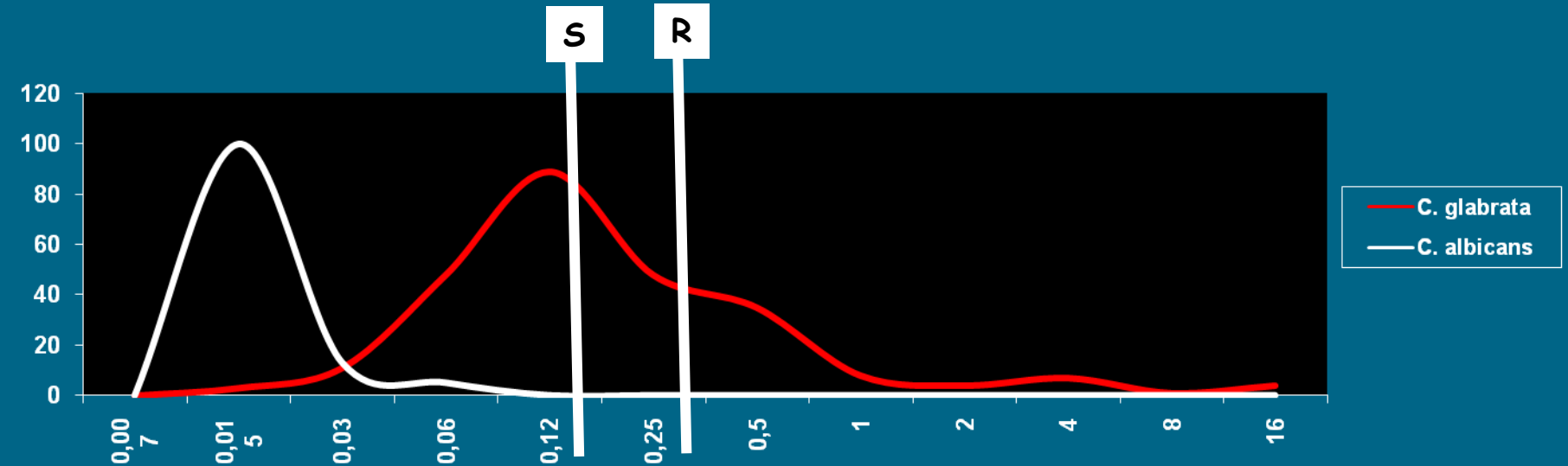
Sensible	Intermedio	Resistente
≤ 0,12 mg/L	---	≥ 0,25 mg/L

Para *C. albicans*. *C. parapsilosis* y *C. tropicalis*

No recomendamos VOR para el tratamiento de las infecciones causadas por *C. glabrata* o *C. krusei*

Fluconazole





Voriconazole

JOURNAL OF CLINICAL MICROBIOLOGY, Mar. 2006, p. 819–826 Vol. 44, No. 3
0095-1137/06/$08.00+0 doi:10.1128/JCM.44.3.819–826.2006
Copyright © 2006, American Society for Microbiology. All Rights Reserved.

Correlation of MIC with Outcome for *Candida* Species Tested against Voriconazole: Analysis and Proposal for Interpretive Breakpoints

M. A. Pfaller,[1]* D. J. Diekema,[1] J. H. Rex,[2] A. Espinel-Ingroff,[3] E. M. Johnson,[4] D. Andes,[5] V. Chaturvedi,[6] M. A Ghannoum,[7] F. C. Odds,[8] M. G. Rinaldi,[9] D. J. Sheehan,[10] P. Troke,[11] T. J. Walsh,[12] and D. W. Warnock[13]

TABLE 3. *Candida* species, geometric mean MICs, and investigator-assessed response to voriconazole therapy[a]

Species	No. of isolates tested	Geometric mean MIC (μg/ml)	% Success
C. albicans	96	0.0164	72
C. parapsilosis	34	0.0266	85
Candida spp.	12	0.0712	92
C. tropicalis	51	0.1283	73
C. krusei	9	0.3650	78
C. glabrata	47	0.7937	55

[a] Broth microdilution MICs were determined in accordance with CLSI M27-A2. Baseline isolates from studies 603, 608, 309/604, and 301/606 were used.

Investigator response to voriconazole therapy versus MIC

MIC	% response (success/total)
≤ 0,125	78 (131/167)
0,25-0,5	54 (24/44)
1	80 (8/10)
>2	57 (16/28)

Candida glabrata Fungemia in Transplant Patients Receiving Voriconazole after Fluconazole

Barbara D. Alexander,[1,3] Wiley A. Schell,[1] Jackie L. Miller,[1] Gwynn D. Long,[2] and John R. Perfect[1]

(*Transplantation* 2005;80: 868–871)

Clinical characteristics of stem cell transplant recipients with *C. glabrata* fungemia while receiving VZ

	1	2	3	4	5
Duration FZ	90	117	60	37	33
Duration VZ	84	48	21	92	4
VZ Dose	200 q 12	200 q 12	200 q 12	400 q 12	280 q 12
neutropenic	no	no	yes	no	yes
GVHD	severe	mild	no	severe	No
Steroids	yes	yes	no	yes	No
Monoclonal Ab	Alemtuz.	Gemtuzu.	Alemtuz.	Infliximab	Alemtuz.
CMV	yes	yes	no	yes	no
CMI	4	2	2	2	2
Outcome	Cure (CP+FC)	Cure (CP)	Cure (ABLC then CP)	Cure (CP)	Cure (ABLC then CP)

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GVHD	severe	mild	no	severe	No
Steroids	yes	yes	no	yes	No
Monoclonal Ab	Alemtuz.	Gemtuzu.	Alemtuz.	Infliximab	Alemtuz.
CMV	yes	yes	no	yes	no
CMI	4	2	2	2	2
Outcome	Cure (CP+FC)	Cure (CP)	Cure (ABLC then CP)	Cure (CP)	Cure (ABLC then CP)

Clinical characteristics of stem cell transplant recipients with *C. glabrata* fungemia while receiving VZ

	1	2	3	4	5
Duration FZ	90	117	60	37	33
Duration VZ	84	48	21	92	4
VZ Dose	200 q 12	200 q 12	200 q 12	400 q 12	280 q 12
neutropenic	no	no	yes	no	yes
GVHD	severe	mild	no	severe	No
Steroids	yes	yes	no	yes	No
Monoclonal Ab	Alemtuz.	Gemtuzu.	Alemtuz.	Infliximab	Alemtuz.
CMV	yes	yes	no	yes	no
CMI	**4**	**2**	**2**	**2**	**2**
Outcome	Cure (CP+FC)	Cure (CP)	Cure (ABLC then CP)	Cure (CP)	Cure (ABLC then CP)

Breakthrough Fungal Infections in Stem Cell Transplant Recipients Receiving Voriconazole

Alexander Imhof,[1] S. Arunmozhi Balajee,[1] David N. Fredricks,[1,2] Janet A. Englund,[1,3] and Kieren A. Marr[1,2]

Table 1. Clinical and demographic characteristics of stem cell transplant recipients receiving voriconazole (VOR) who developed invasive fungal infection.

Patient	Age, years	Sex	Type of malignancy	Transplant donor type	Indication for voriconazole	Organism[a]	Site of infection[b]	Day of breakthrough infection[c]	Duration of VOR exposure, days[d]	MIC of VOR, μg/mL	GVHD classification (grade)[e]	Steroid dose, mg/kg[f]	Outcome[g]
1	55	F	CML	MR	IA	*Candida glabrata*	Disseminated	272	7	2	Chronic	44	Death
2	39	F	AML	MM-UR	Prevention	Zygomycetes, NOS	Lung	275	94	NA	Chronic	…	Death
3	41	M	MM	MM-UR	IA	*C. glabrata*	Blood	75	37	2	Acute (g3)	29	Death
4	23	M	CML	MR	IA	*Aspergillus terreus*	Lung	184	39	1	Chronic	30	Death
5	51	M	AML	MR	IA	Zygomycetes, NOS	Lung	11	110	NA	None	0[h]	Death
6	56	M	Renal cell	MR	Prevention	*Rhizopus microsporus*	GI tract	183	89	8	Chronic	60	Death (relapse)
						Scedosporium prolificans	GI tract	183	89	32	…	…	…
7	41	M	Lymphoma	MM-UR	IA	*Acremonium* species	Sinus	44	11	1	Acute (g3)	0[h]	Death (relapse)
8	34	M	MDS	MM-UR	IA	*S. prolificans*	Lung	180	61	8	Chronic	43	Death
9	7	M	ALL	MM-UR	Prevention	*C. glabrata*	Blood	949	47	NA	Chronic	49	NA
						Acremonium species	Sinus	950	49	2	…	…	…
						Alternaria species	Sinus	950	49	2	…	…	…
10	60	M	ALL	MM-UR	IA	*Cunninghamella* species	Lung	19	6	8	None	…	Alive
11	49	F	AML	MM-UR	Prevention	*Aspergillus ustus*	Disseminated	69	4	2	Acute (g3)	59	Death
12	12	F	AA	MM-UR	IA	*C. glabrata*	Blood	82	76	NA	Acute (g3)	129	
						C. glabrata	Blood	119	13	NA	Acute (g3)	135	
						Rhizopus arrhizus	Lung	319	99	8	Chronic	49	Alive
13	64	M	AML	MM-UR	Invasive fusariosis	Zygomycetes, NOS	Lung	20	91	NA	None	…	Death

Bone Marrow Transplantation (2007) 40, 451–456
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ORIGINAL ARTICLE

Breakthrough fungal infections after allogeneic hematopoietic stem cell transplantation in patients on prophylactic voriconazole

S Trifilio[1], S Singhal[2], S Williams[2], O Frankfurt[2], L Gordon[2], A Evens[2], J Winter[2], M Tallman[2], J Pi[1] and J Mehta[2]

Table 2 Breakthrough fungal infections

Patient	*Disease and status*	*Transplant*	*Fungus*	*Site*	*Diagnostic material*	*Days post-transplant*	*GVHD*	*Cumulative methyl prednisolone or prednisone dose in the preceding 2 weeks (mg)*	*Neutropenia ($<0.5 \times 10^9$/l)*	*Voriconazole exposure (days)*	*Voriconazole level (weeks before infection)*	*Voriconazole dose in mg; total and mg/kg*	*Outcome at 2 months after fungus isolation*	*Contribution of fungus to death*
1	ALL, CR	MSD, myeloablative	C. Krusei	Lungs	BAL	183	Yes	40	No	157	0.53 (12)	400; 5.3	Dead	Yes
2	NHL, active	MSD, submyeloablative	C. glabrata	Lungs	BAL	145	Yes	160	Yes	136	0.63 (2)	400; 8	Alive	No
3	HD, CR	MUD, submyeloablative	C. glabrata	Lungs	BAL	837	Yes	280	No	832	0.2 (1)	500; 6.2	Dead	No
4	MDS, active	MUD, submyeloablative	C. glabrata	Lungs, blood	BAL, blood	179	Yes	600	Yes	159	1.78 (5)	400; 4.4	Dead	Yes
5	AML, active	MSD, submyeloablative	C. glabrata	Lungs	BAL	178	Yes	360	Yes	56	0.33 (1)	600; 4.6	Dead	No
6	MDS, active	MSD, myeloablative	C. glabrata	Lungs	BAL	9	Yes	0	Yes	7	0.33 (4)	400; 7.4	Alive	No
7	ALL, active	MUD, submyeloablative	Rhizopus	Lungs	Tissue	135	Yes	330	No	128	4.1 (12)	400; 5.1	Dead	Yes
8	ALL, active	MUD, submyeloablative	Rhizopus	Sinuses	Tissue	135	No	0	Yes	7	5.9 (1)	400; 4	Alive	No
9	NHL, CR	MUD, myeloablative	Mucor	Lungs	Tissue	78	Yes	0	No	78	3.5 (1)	400; 5	Alive	No
10	AML, active	MSD, myeloablative	Cunninghamella	Lungs	Endotracheal tube aspirate	80	Yes	400	Yes	17	1.1 (2)	800; 7.3	Dead	Yes

Bone Marrow Transplantation (2007) 40, 451–456
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www.nature.com/bmt

ORIGINAL ARTICLE

Breakthrough fungal infections after allogeneic hematopoietic stem cell transplantation in patients on prophylactic voriconazole

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Table 2 Breakthrough fungal infections

Patient	*Disease and status*	*Transplant*	*Fungus*	*Voriconazole level (weeks before infection)*	*Voriconazole dose in mg; total and mg/kg*	*Outcome at 2 months after fungus isolation*	*Contribution of fungus to death*
1	ALL, CR	MSD, myeloablative	C. Krusei	0.53 (12)	400; 5.3	Dead	Yes
2	NHL, active	MSD, submyeloablative	C. glabrata	0.63 (2)	400; 8	Alive	No
3	HD, CR	MUD, submyeloablative	C. glabrata	0.2 (1)	500; 6.2	Dead	No
4	MDS, active	MUD, submyeloablative	C. glabrata	1.78 (5)	400; 4.4	Dead	Yes
5	AML, active	MSD, submyeloablative	C. glabrata	0.33 (1)	600; 4.6	Dead	No
6	MDS, active	MSD, myeloablative	C. glabrata	0.33 (4)	400; 7.4	Alive	No

Does have any clinical importance the accurate id of……?

- *C. albicans* vs *C. dubliniensis*

JOURNAL OF CLINICAL MICROBIOLOGY, Feb. 1998, p. 329–334 Vol. 36, No. 2
0095-1137/98/$04.00+0
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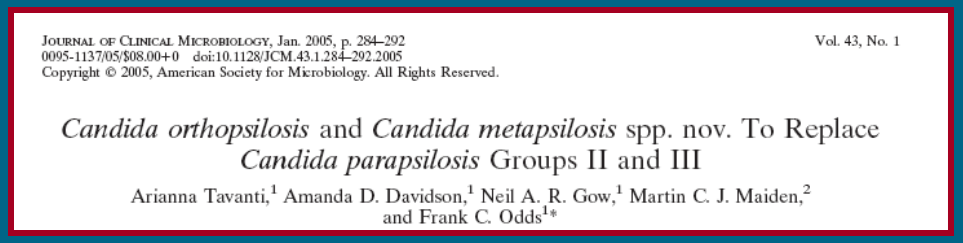
MINIREVIEW

Candida dubliniensis: Characteristics and Identification

DEREK SULLIVAN AND DAVID COLEMAN*

- *C. parapsilosis* vs *C. orthopsilosis & C. metapsilosis*



JOURNAL OF CLINICAL MICROBIOLOGY, Jan. 2005, p. 284–292 Vol. 43, No. 1
0095-1137/05/$08.00+0 doi:10.1128/JCM.43.1.284–292.2005
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Candida orthopsilosis and *Candida metapsilosis* spp. nov. To Replace *Candida parapsilosis* Groups II and III

Arianna Tavanti,[1] Amanda D. Davidson,[1] Neil A. R. Gow,[1] Martin C. J. Maiden,[2] and Frank C. Odds[1]*

- *C. glabrata vs C. nivariensis & C. bracarensis*

International Journal of Systematic and Evolutionary Microbiology (2006), 56, 313–317 DOI 10.1099/ijs.0.64076-0

Candida bracarensis sp. nov., a novel anamorphic yeast species phenotypically similar to *Candida glabrata*

Alexandra Correia,[1] Paula Sampaio,[1] Steve James[2] and Célia Pais[1]

JOURNAL OF CLINICAL MICROBIOLOGY, Aug. 2005, p. 4107–4111 Vol. 43, No. 8
0095-1137/05/$08.00+0 doi:10.1128/JCM.43.8.4107–4111.2005
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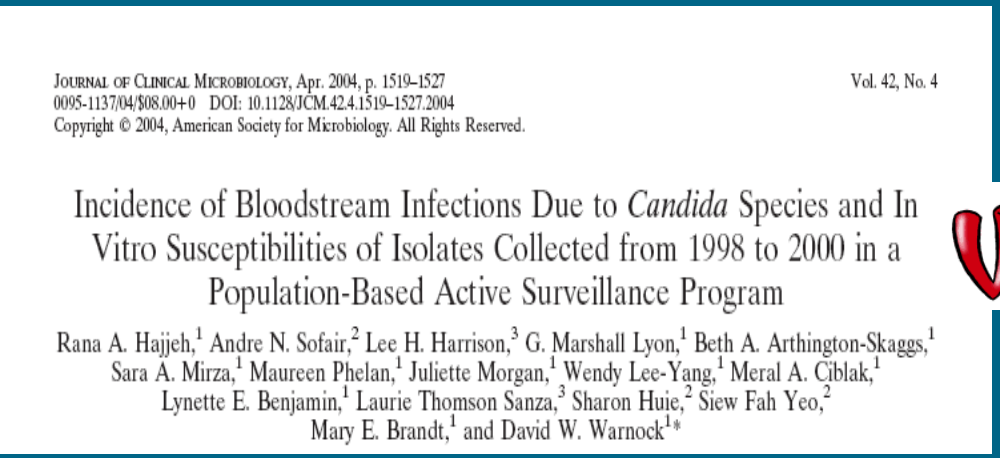
Phenotypic and Molecular Characterization of *Candida nivariensis* sp. nov., a Possible New Opportunistic Fungus

Julia Alcoba-Flórez,[1,2] Sebastián Méndez-Álvarez,[2,3,6] Josep Cano,[4] Josep Guarro,[4] Eduardo Pérez-Roth,[2] and María del Pilar Arévalo[5]*



JOURNAL OF CLINICAL MICROBIOLOGY, Apr. 2004, p. 1519–1527 Vol. 42, No. 4
0095-1137/04/$08.00+0 DOI: 10.1128/JCM.42.4.1519–1527.2004
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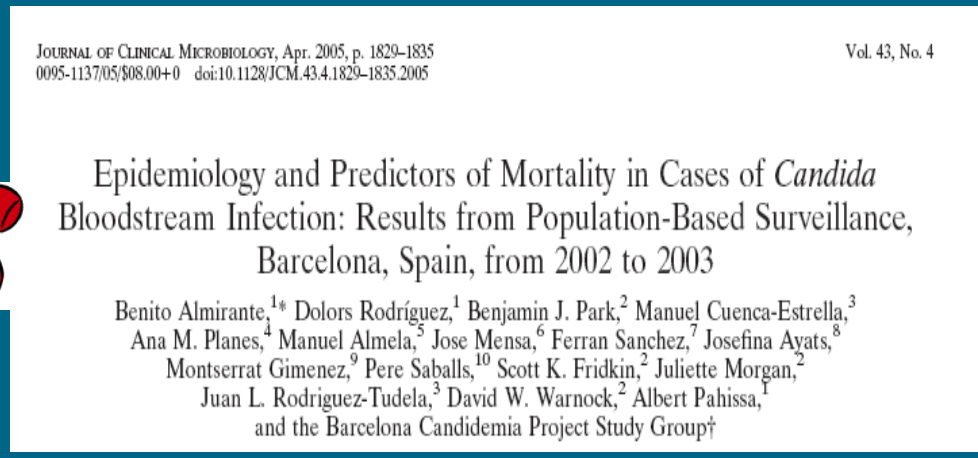
Incidence of Bloodstream Infections Due to *Candida* Species and In Vitro Susceptibilities of Isolates Collected from 1998 to 2000 in a Population-Based Active Surveillance Program

Rana A. Hajjeh,[1] Andre N. Sofair,[2] Lee H. Harrison,[3] G. Marshall Lyon,[1] Beth A. Arthington-Skaggs,[1] Sara A. Mirza,[1] Maureen Phelan,[1] Juliette Morgan,[1] Wendy Lee-Yang,[1] Meral A. Ciblak,[1] Lynette E. Benjamin,[1] Laurie Thomson Sanza,[3] Sharon Huie,[2] Siew Fah Yeo,[2] Mary E. Brandt,[1] and David W. Warnock[1]*

VS



JOURNAL OF CLINICAL MICROBIOLOGY, Apr. 2005, p. 1829–1835 Vol. 43, No. 4
0095-1137/05/$08.00+0 doi:10.1128/JCM.43.4.1829–1835.2005

Epidemiology and Predictors of Mortality in Cases of *Candida* Bloodstream Infection: Results from Population-Based Surveillance, Barcelona, Spain, from 2002 to 2003

Benito Almirante,[1]* Dolors Rodríguez,[1] Benjamin J. Park,[2] Manuel Cuenca-Estrella,[3] Ana M. Planes,[4] Manuel Almela,[5] Jose Mensa,[6] Ferran Sanchez,[7] Josefina Ayats,[8] Montserrat Gimenez,[9] Pere Saballs,[10] Scott K. Fridkin,[2] Juliette Morgan,[2] Juan L. Rodriguez-Tudela,[3] David W. Warnock,[2] Albert Pahissa,[1] and the Barcelona Candidemia Project Study Group†

	N	%		N	%
C. albicans	423	45.2%	*C. albicans*	178	51
C. dubliniensis	8	0.85%	*C. dubliniensis*	1	0.28

C. dubliniensis susceptible to Ampho B and azole drugs

Susceptibility profile of *C. albicans & C. dubliniensis*

	N	CMI_{50}	CMI_{90}	Range
AmB	1856	0.25	1	**0.03-2**
	17			**0.03-0.5**
FZ	2145	0.25	16	**0.06-128**
	17			**0.12-0.5**
VZ	1315	0.015	0.03	**0.015-16**
	15			**0.015-0.015**
CP	506	0.06	0.25	**0.015-32**
	12			**0.03-16**

Data from Mycology Reference Laboratory of Spain

JOURNAL OF CLINICAL MICROBIOLOGY, Aug. 2008, p. 2659–2664 Vol. 46, No. 8
0095-1137/08/$08.00+0 doi:10.1128/JCM.00803-08
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Geographic Distribution and Antifungal Susceptibility of the Newly Described Species *Candida orthopsilosis* and *Candida metapsilosis* in Comparison to the Closely Related Species *Candida parapsilosis*▽

Shawn R. Lockhart,[1]* Shawn A. Messer,[1] Michael A. Pfaller,[1] and Daniel J. Diekema[1,2]

- 1,929 invasive isolates
  - 117 *C. orthopsilosis* 6.1%
  - 34 *C. metapsilosis* 1.8%

TABLE 2. MIC_{50}/MIC_{90} and mean MIC of *C. parapsilosis*, *C. orthopsilosis*, and *C. metapsilosis* isolates

Drug	*C. parapsilosis*		*C. orthopsilosis*[a]		*C. metapsilosis*[a]	
	MIC_{50}/MIC_{90}	Mean MIC	MIC_{50}/MIC_{90}	Mean MIC	MIC_{50}/MIC_{90}	Mean MIC
Fluconazole	0.5/2	2.3	1/4	2.1	1/2	1.4
Amphotericin B	1/4	1.5	1/2	1.1	0.5/1	0.7
Caspofungin	0.5/1	0.4	0.12/0.25	0.2	0.12/0.25	0.2
Anidulafungin	2/2	1.9	1/2	1.0	0.5/1	0.6
Micafungin	1/2	1.1	0.25/0.5	0.4	0.25/0.5	0.4

[a] $P < 0.001$ for the difference in MIC distribution compared with *C. parapsilosis* for all drugs tested. For fluconazole, *C. orthopsilsosis* and *C. metapsilosis* MIC distributions were higher than those of *C. parapsilosis*, while for amphotericin B and all the echinocandins, *C. orthopsilosis* and *C. metapsilosis* MIC distributions were lower than those of *C. parapsilosis*.

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Apr. 2008, p. 1506–1509 Vol. 52, No. 4
0066-4804/08/$08.00+0 doi:10.1128/AAC.01595-07
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Prevalence and Susceptibility Profile of *Candida metapsilosis* and *Candida orthopsilosis*: Results from Population-Based Surveillance of Candidemia in Spain[▽]

A. Gomez-Lopez,[1] A. Alastruey-Izquierdo,[1] D. Rodriguez,[2] B. Almirante,[2] A. Pahissa,[2] J. L. Rodriguez-Tudela,[1] M. Cuenca-Estrella,[1]* and the Barcelona Candidemia Project Study Group

- Prevalence
  - *C. metapsilosis* 1.7%
  - *C. orthopsilosis* 1.4%

JOURNAL OF CLINICAL MICROBIOLOGY, Apr. 2009, p. 1216–1217 Vol. 47, No. 4
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Identification of *Candida nivariensis* and *Candida bracarensis* in a Large Global Collection of *Candida glabrata* Isolates: Comparison to the Literature▽

Shawn R. Lockhart,[1]* Shawn A. Messer,[1] Michael Gherna,[2] Justin A. Bishop,[2] William G. Merz,[2] Michael A. Pfaller,[1] and Daniel J. Diekema[1]

- 1598 isolates
  - 0.2% prevalence in this study

TABLE 2. MICs for the non-*C. glabrata* isolates from global surveillance

Species	MIC (μg/ml)				
	Fluconazole	Amphotericin B	Caspofungin	Anidulafungin	Micafungin
C. nivariensis	2	1	0.06	0.06	0.015
C. bracarensis no. 1	16	8	0.03	0.06	0.015
C. bracarensis no. 2	2	1	0.03	0.06	0.015

ORIGINAL ARTICLE

Clin Microbiol Infect 2009; 15: 662–669

10.1111/j.1469-0691.2009.02821.x

Candidaemia with uncommon *Candida* species: predisposing factors, outcome, antifungal susceptibility, and implications for management

S. C. A. Chen[1,*], D. Marriott[2,*], E. G. Playford[3], Q. Nguyen[2], D. Ellis[4], W. Meyer[1,5], T. C. Sorrell[1], M. Slavin[6] and the Australian Candidaemia Study

TABLE 1. Uncommon *Candida* spp. causing candidaemia, Australia 2002–2004

Candida spp.	No. (%)
Candida dubliniensis[a]	22 (39)
Candida guilliermondii	11 (19)
Candida lusitaniae	7 (12)
Candida kefyr	5 (9)
Candida rugosa	3 (5)
Candida pelliculosa	3 (5)
Candida famata	2 (4)
Candida colliculosa	1 (2)
Candida lambica	1 (2)
Candida lipolytica	1 (2)
Candida sake	1 (2)
All species	57 (100)

[a]Two episodes of *C. dubliniensis* candidaemia involved >1 *Candida* sp. (one episode of *C. dubliniensis*/*C. glabrata* and on e of *C. dubliniensis*/*C. albicans*).

ORIGINAL ARTICLE | *Clin Microbiol Infect* 2009; 15: 662–669 | 10.1111/j.1469-0691.2009.02821.x

Candidaemia with uncommon *Candida* species: predisposing factors, outcome, antifungal susceptibility, and implications for management

S. C. A. Chen[1,*], D. Marriott[2,*], E. G. Playford[3], Q. Nguyen[2], D. Ellis[4], W. Meyer[1,5], T. C. Sorrell[1], M. Slavin[6] and the Australian Candidaemia Study

TABLE 2. Comparison of characteristics of bloodstream infection due to uncommon *Candida* spp. with *Candida albicans* candidaemia[a]

Variable (total no.)[b]	*Candida dubliniensis* (*n* = 22 episodes)	p[c]	Uncommon *Candida* spp. other than *C. dubliniensis* (*n* = 35 episodes)	p[c]	*C. albicans* (*n* = 517 episodes)
Acquisition of candidaemia					
OHCA (9)	1/20 (5)	1.0	8/31 (26)	0.01	42/441 (9.5)
CA (6)	2/20 (10)	0.30	4/31 (13)	0.08	23/441 (5.2)
IHCA (36)	17/20 (85)	1.0	19/31 (61)	0.002	376/441 (85.3)

- OHCA: outpatient health care associated
- CA: Community acquired
- IHCA: inpatient health care associated

ORIGINAL ARTICLE

Clin Microbiol Infect 2009; 15: 662–669

10.1111/j.1469-0691.2009.02821.x

Candidaemia with uncommon *Candida* species: predisposing factors, outcome, antifungal susceptibility, and implications for management

S. C. A. Chen[1,*], D. Marriott[2,*], E. G. Playford[3], Q. Nguyen[2], D. Ellis[4], W. Meyer[1,5], T. C. Sorrell[1], M. Slavin[6] and the Australian Candidaemia Study

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Variable (total no.)[b]	*Candida dubliniensis* (*n* = 22 episodes)	p[c]	Uncommon *Candida* spp. other than *C. dubliniensis* (*n* = 35 episodes)	p[c]	*C. albicans* (*n* = 517 episodes)
Multivariate analysis	Adjusted OR (95% CI)	p	Adjusted OR (95% CI)	p	
Age ≤65 years	–	NS	11.1 (1.4–86)	0.02	
Male sex	–	NS	3.0 (1.1–8.3)	0.03	
Intravenous drug use	7.3 (1.5–34)	0.01	–	NS	
Liver disease	2.4 (0.6–8.8)	0.03	–	NS	
HIV infection	–	NS	9.0 (1.0–83)	0.05	

CA, community-acquired; HIV, human immunodeficiency virus; HSCT, haematopoeitic stem cell transplantation; ICU, intensive-care unit; IHCA, inpatient healthcare-associated; NS, not significant; OHCA, outpatient healthcare-associated; TPN, total parenteral nutrition.

[a]No./total no. (%) for each category where the data were available, unless otherwise indicated.

[b]Refers to the total no. present in all episodes of bloodstream infection with uncommon *Candida* spp.

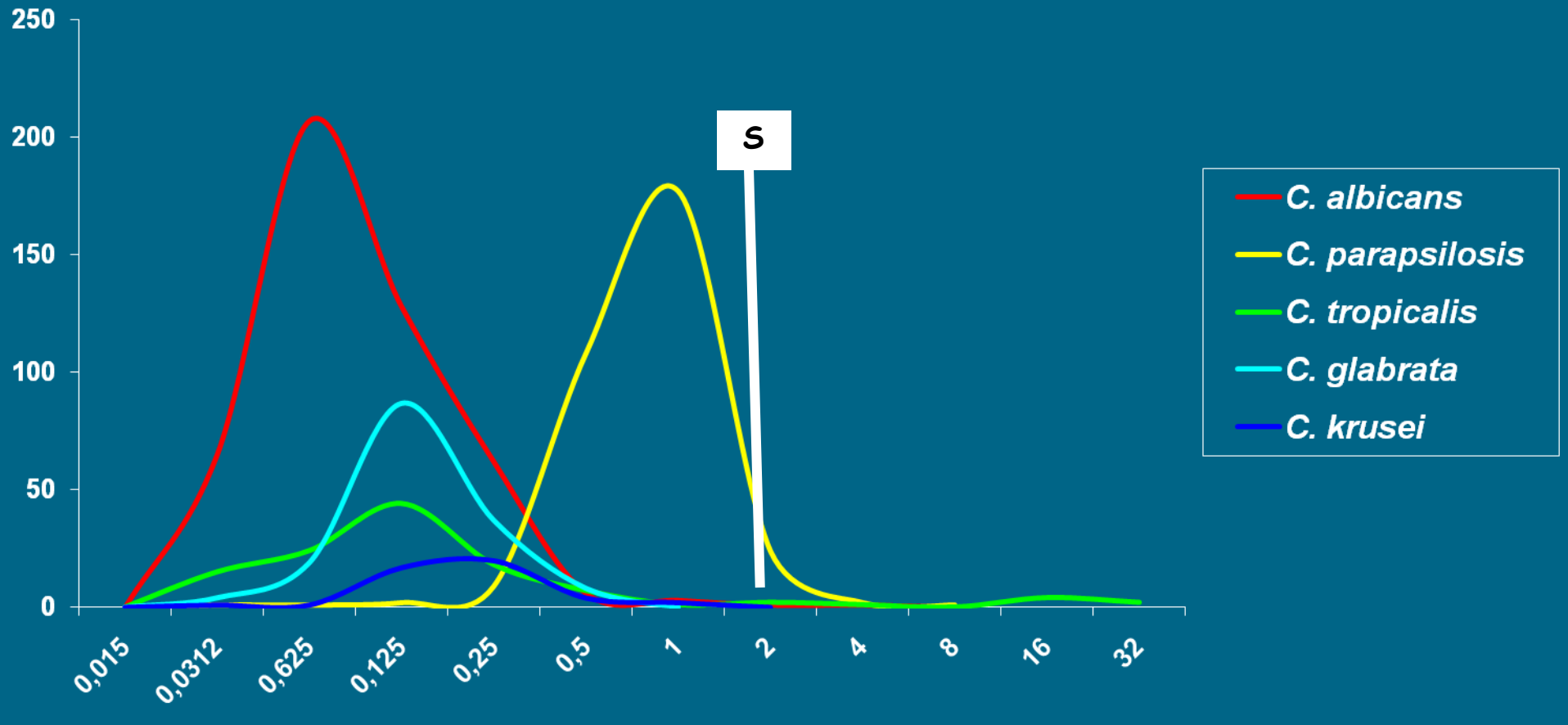
[c]Comparisons using *C. albicans* candidaemia as reference category.

Puntos de corte del CLSI para equinocandinas

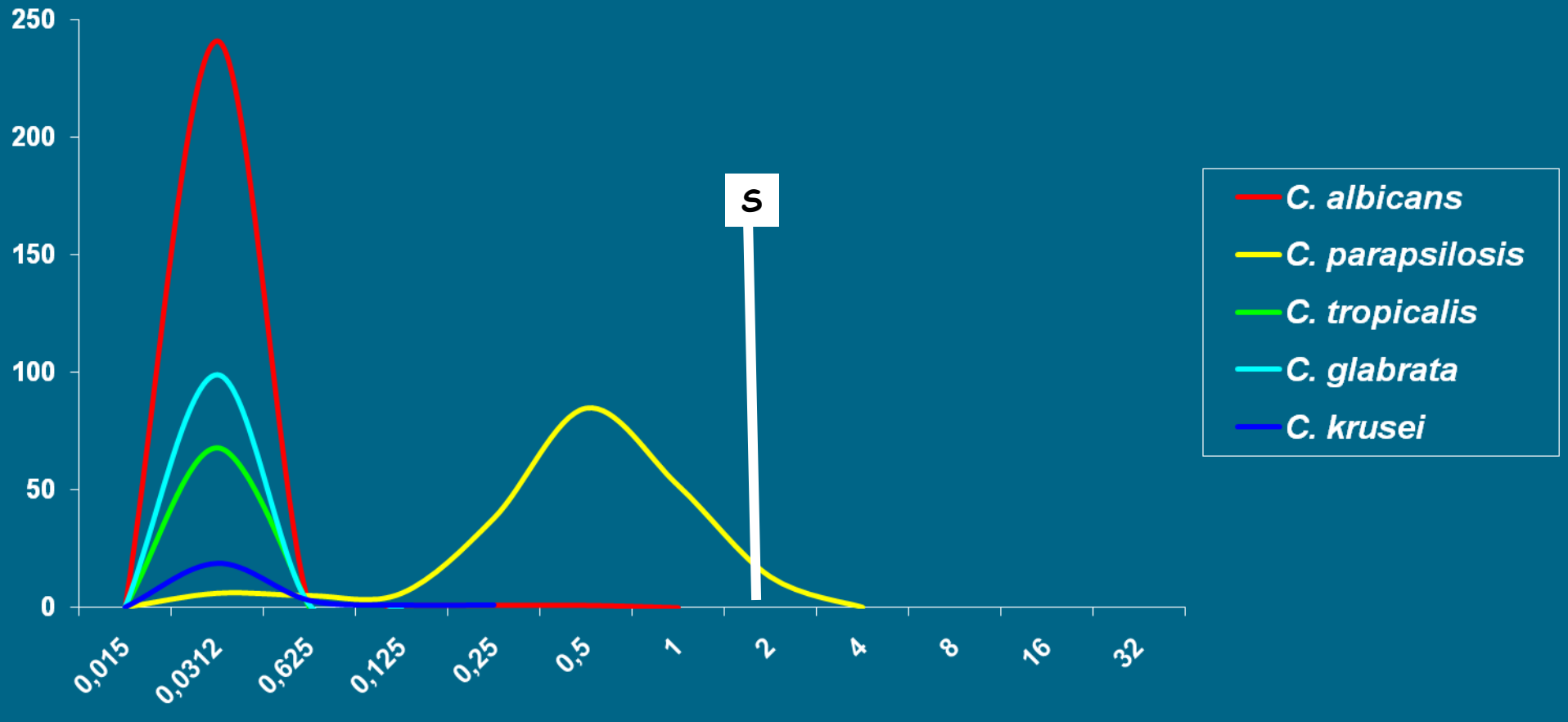
Sensible	No sensibles
≤ 2 mg/L	>2 mg/L

Pfaller et al JCM 2008

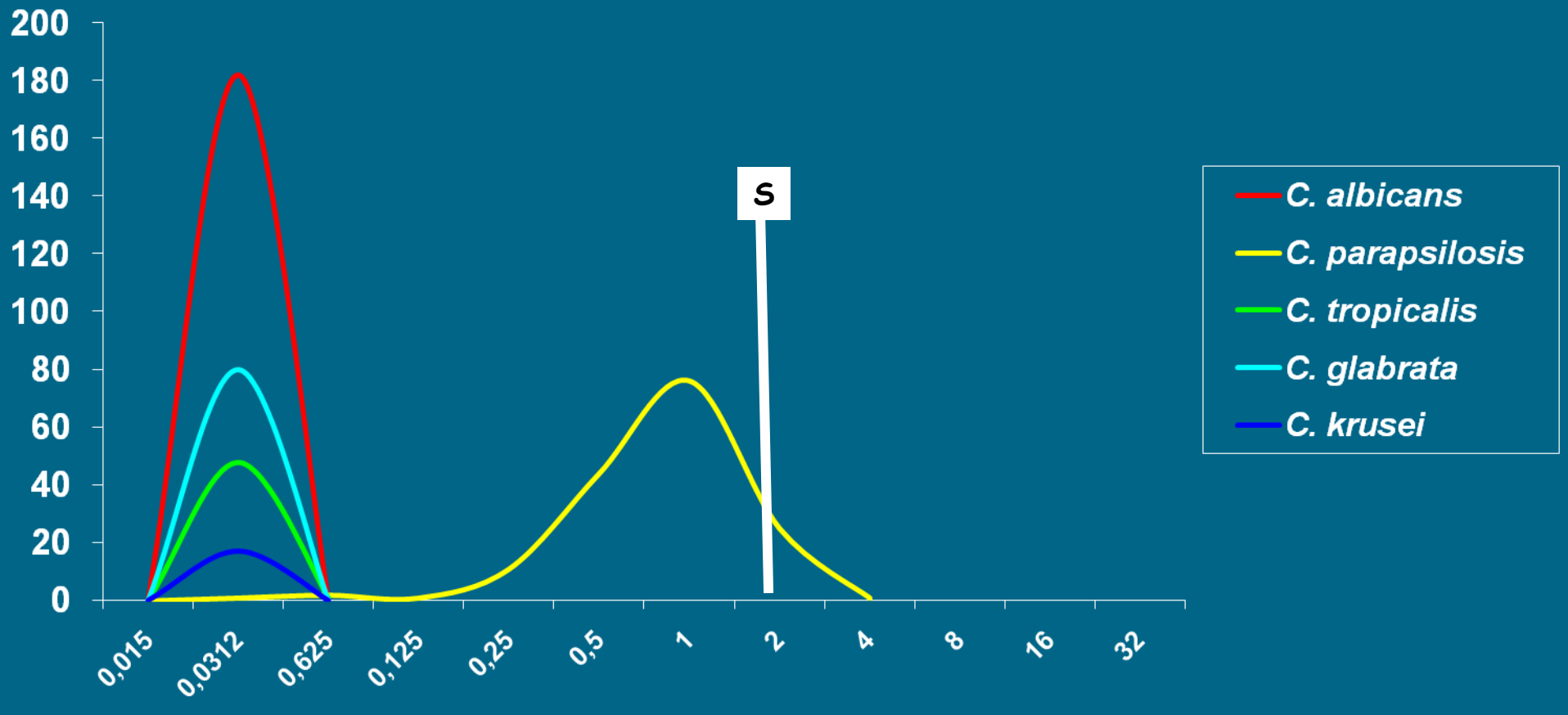
Distribución de CMIs para caspofungina



Distribución de CMIs para micafungina



Distribución de CMIs para anidulafungina



ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, July 2008, p. 2305–2312 Vol. 52, No. 7
0066-4804/08/$08.00+0 doi:10.1128/AAC.00262-08
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A Naturally Occurring Proline-to-Alanine Amino Acid Change in Fks1p in *Candida parapsilosis*, *Candida orthopsilosis*, and *Candida metapsilosis* Accounts for Reduced Echinocandin Susceptibility[▽]

Guillermo Garcia-Effron,[1] Santosh K. Katiyar,[2] Steven Park,[1]
Thomas D. Edlind,[2] and David S. Perlin[1]*

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Jan. 2010, p. 426–439 Vol. 54, No. 1
0066-4804/10/$12.00 doi:10.1128/AAC.01256-09
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Echinocandin Susceptibility Testing of *Candida* Species: Comparison of EUCAST EDef 7.1, CLSI M27-A3, Etest, Disk Diffusion, and Agar Dilution Methods with RPMI and IsoSensitest Media▽

Maiken Cavling Arendrup,[1]* Guillermo Garcia-Effron,[2] Cornelia Lass-Flörl,[3] Alicia Gomez Lopez,[4] Juan-Luis Rodriguez-Tudela,[4] Manuel Cuenca-Estrella,[4] and David S. Perlin[2]

Applying the CLSI breakpoint (S ≤ 2 μg/ml) for CLSI results, 89.2% *fks* hot spot mutants were classified as anidulafungin susceptible, 60.7% as caspofungin susceptible, and 92.9% as micafungin susceptible. In conclusion, no test was perfect, but anidulafungin susceptibility testing using the WT-UL to define susceptibility reliably identified *fks* hot spot mutants.

% of FSK mutants classified as susceptible according CLSI BP ≤ 2 mg/L	
Anidulafungin	89.2%
Caspofungin	60.7%
Micafungin	92.9%

¿Se pueden usar las equinocandinas para tratar las infecciones causadas por *C. parapsilosis?*

JOURNAL OF CLINICAL MICROBIOLOGY, Apr. 2005, p. 1829–1835 Vol. 43, No. 4
0095-1137/05/$08.00+0 doi:10.1128/JCM.43.4.1829–1835.2005

Epidemiology and Predictors of Mortality in Cases of *Candida* Bloodstream Infection: Results from Population-Based Surveillance, Barcelona, Spain, from 2002 to 2003

TABLE 2. Demographics, clinical characteristics, and outcomes of candidemia cases by select species, Barcelona, Spain, 2002 to 2003

Characteristic	All cases[a]	*C. albicans*	*C. glabrata*	*C. tropicalis*	*C. krusei*	*C. parapsilosis*
Death by day 3–7	74 (22)	42 (24)	9 (31)	11 (33)	2 (17)	5 (6)
Overall mortality	150 (44)	83 (47)	14 (50)	19 (59)	5 (46)	22 (28)
Total cases	345 (100)	176 (51)	29 (8)	34 (10)	12 (4)	78 (23)

[a] All data are given as no. (%), except where a range is indicated.
[b] Outpatient, cases with positive blood culture either prior to or at ≤2 days of hospitalization.
[c] Absolute neutrophil count less than 0.5 × 109/liter.

The New England Journal of Medicine

COMPARISON OF CASPOFUNGIN AND AMPHOTERICIN B FOR INVASIVE CANDIDIASIS

JORGE MORA-DUARTE, M.D., ROBERT BETTS, M.D., COLEMAN ROTSTEIN, M.D., ARNALDO LOPES COLOMBO, M.D., LUIS THOMPSON-MOYA, M.D., JUANITA SMIETANA, B.S., ROBERT LUPINACCI, M.S., CAROLE SABLE, M.D., NICHOLAS KARTSONIS, M.D., AND JOHN PERFECT, M.D., FOR THE CASPOFUNGIN INVASIVE CANDIDIASIS STUDY GROUP*

TABLE 5. TREATMENT FAILURES AND RELAPSES (MODIFIED INTENTION-TO-TREAT ANALYSIS).

FAILURE OR RELAPSE	CASPOFUNGIN (N=109)	AMPHOTERICIN B (N=115)
	no. (%)	
Failure at end of therapy	29 (26.6)	44 (38.3)
Persistently positive cultures	9 (8.3)	10 (8.7)*
Candida albicans	3	8
C. glabrata	1	0
C. krusei	0	1
C. parapsilosis	5†	0
C. albicans and *C. lusitaniae*	0	1

Micafungin versus liposomal amphotericin B for candidaemia and invasive candidosis: a phase III randomised double-blind trial

	Micafungin		Liposomal amphotericin B	
	Number of patients*	Number of patients with mycological persistence (%)	Number of patients*	Number of patients with mycological persistence (%)
Any *Candida* spp	194	18 (9%)	174	16 (9%)
Candida albicans	85	9 (11%)	73	8 (11%)
Non-albicans *Candida* spp	120	11 (9%)	107	9 (8%)
C tropicalis	49	1 (2%)	45	2 (4%)
C parapsilosis	35	5 (14%)	29	3 (10%)
C glabrata	22	3 (14%)	15	3 (20%)
C krusei	6	1 (17%)	5	1 (20%)
C guilliermondii	7	0	4	0
C lusitaniae	1	0	6	0
C rugosa	1	1	4	0
C kefyr	1	0	1	0
C famata	0	..	1	0
C dubliniensis	1	0	1	0
More than one *Candida* spp	15	2 (13%)	11	1 (9%)

*Number of patients with the respective *Candida* spp at baseline. *Candida* spp were identified by a central laboratory. Incidental non-*Candida* spp present at baseline are not included in the summary table.

Table 4: **Mycological persistence at end of therapy by *Candida* spp at baseline in the per-protocol population**

Anidulafungin in candidemia & invasive candidosis

Candida Pathogen	Successful Microbiologic Response			Successful Global Response†		
	Anidulafungin Group	Fluconazole Group	P Value	Anidulafungin Group	Fluconazole Group	P Value
	no. of isolates/total no. (%)			*no. of patients/total no. (%)*		
Candida albicans	77/81 (95)	57/70 (81)	0.01	60/74 (81)	38/61 (62)	0.02
C. glabrata	15/20 (75)	18/30 (60)	0.37	9/16 (56)	11/22 (50)	0.75
C. parapsilosis	9/13 (69)	14/16 (88)	0.36	7/11 (64)	10/12 (83)	0.37
C. tropicalis	13/15 (87)	7/11 (64)	0.35	13/14 (93)	4/8 (50)	0.04
Other candida species	5/6 (83)	3/3 (100)	1.00	3/4 (75)	2/3 (67)	1.00
All candida species	119/135 (88)	99/130 (76)	0.02	92/119 (77)	65/106 (61)	0.01

Reboli, NEJM 2007; 356:2472-82

Resumen

- La epidemiología es local y su vigilancia debe ser permanente
- C. tropicalis comienza a tener tasas de resistencia secundaria elevadas
- *C. glabrata* es un patógeno emergente y resistente a los azoles
- Las equinocandinas no son muy activas frente a *C. parapsilosis.* La menor mortalidad que causa este patógeno es un factor a considerar
- Para conocer la importancia de las especies emergentes hay que hacer estudios multicéntricos y prolongados en el tiempo

Epidemiology of moulds is tough because……

- **To know the epidemiology only those cases with culture positive from sterile material are useful → Proven infection**
  - **Culture: high rate of false negative results**
  - **Blood culture: Reference for yeasts but not useful for moulds**
  - **Microscopy examination of sterile material → no ID to level species → No epidemiology**
- **Positive culture from non-sterile material when the infections is probable is also used for epidemiology purposes → Bias epidemiology?**

What's new about them?

- Changes in epidemiology?
- New clinical relevant species?
- Increasing rates of resistant isolates?
- Changes in associated mortality?

Epidemiology of moulds

	Hematological patients			SOT
	Neofytos CID'09	Pagano CID'07	Marr CID'02	Husain CID'03
Aspergillus	80%	94.5%	77.3%	69.8%
Zygomycetes	9.7%	1.1%	8.6%	5.6%
Fusarium	2.2%	3.2%	9.2%	3.7%
Scedosporium	---	1.1%	2.9%	5.6%
Other	9.2%	---	1.78%	15%

Most frequent mold pathogens are…

- *Aspergillus* spp is the most frequent mold
- Zygomycetes has got the silver medal and *Fusarium* spp the bronze one
- There are a miscellaneous of species including the most prevalent one: *Scedosporium* spp

Which *Aspergillus*?

	Hematological patients			SOT
	Neofytos CID'09	Pagano CID'07	Marr CID'02	Husain CID'03
fumigatus	37.2%	22.0%	66.5%	78.3%
flavus	3.4%	4.6%	3.46%	13.5%
terreus	0.6%	5.8%	1.92%	5.4%
niger	3.37%	5.8%	3.46%	2.7%
Other	2.7%	----	1.15%	---
Unknown	52.7%	61.6%	19.6%	---
Multiple	---	---	3.84%	---

Which *Aspergillus*?

	Hematological patients			SOT
	Neofytos CID'09	Pagano CID'07	Marr CID'02	Husain CID'03
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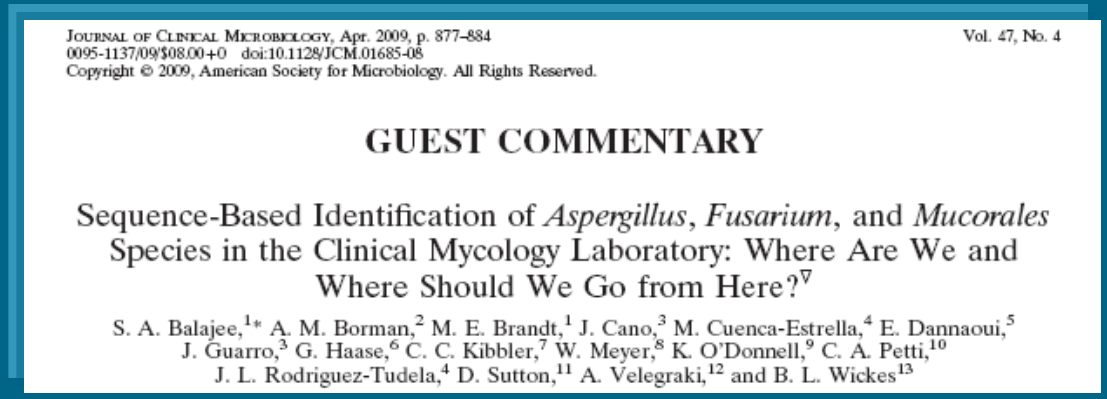
Other	2.7%	----	1.15%	---
Unknown	**52.7%**	**61.6%**	**19.6%**	**---**
Multiple	---	---	3.84%	---

Epidemiology and species complex

- Species complex group different species morphologically similar
- Only way to distinguish species complex is by means of sequencing specific targets
- Some species inside a species complex have different susceptibility what can have clinical implications



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0095-1137/09/$08.00+0 doi:10.1128/JCM.01685-08
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GUEST COMMENTARY

Sequence-Based Identification of *Aspergillus*, *Fusarium*, and *Mucorales* Species in the Clinical Mycology Laboratory: Where Are We and Where Should We Go from Here?[▽]

S. A. Balajee,[1]* A. M. Borman,[2] M. E. Brandt,[1] J. Cano,[3] M. Cuenca-Estrella,[4] E. Dannaoui,[5] J. Guarro,[3] G. Haase,[6] C. C. Kibbler,[7] W. Meyer,[8] K. O'Donnell,[9] C. A. Petti,[10] J. L. Rodriguez-Tudela,[4] D. Sutton,[11] A. Velegraki,[12] and B. L. Wickes[13]

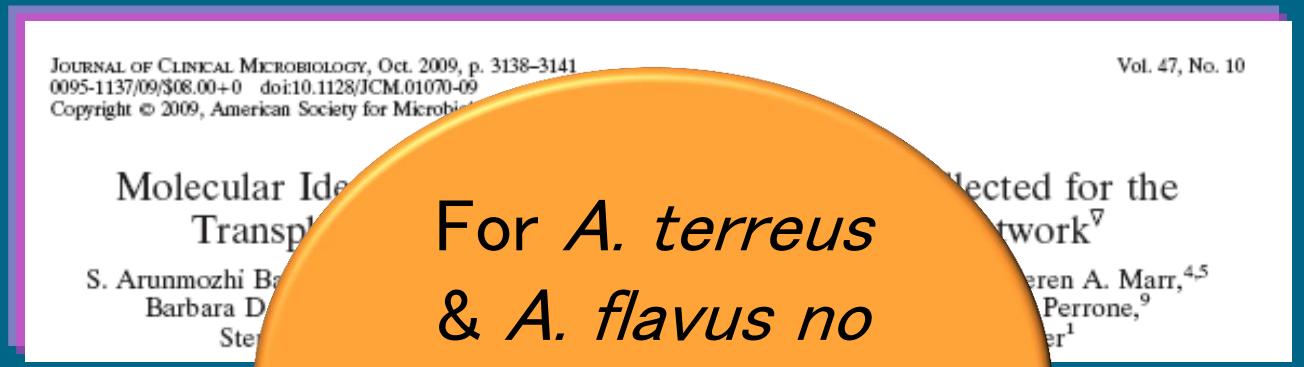
Aspergillus

Classic Risk Factors for *Aspergillosis*

- Hematological malignancies:
  - Leukemia
  - MDS
  - SCT
  - GVHD
  - Prolonged neutropenia
  - Induction chemo
- Critically ill?
- HIV/AIDS?

- Transplant patients:
  - Lung, liver, heart, renal
  - Liver transplant
  - Acute/ chronic rejection
  - Steroids
  - Tacrolimus
  - OKT3
  - Renal failure
  - CMV

Muhlemann K, *Leukemia* 2005;19:545–550.
Sole A, et al. *Clin Microbiol Infect.* 2005;11(5):359-65.
Singh N, et al. *Clin Microbiol Rev*. 2005;18(1):44-69.
Thursky K, et al. *Bone Marrow Transplant*. 2004;34(2):115-21.


JOURNAL OF CLINICAL MICROBIOLOGY, Oct. 2009, p. 3138–3141 Vol. 47, No. 10
0095-1137/09/$08.00+0 doi:10.1128/JCM.01070-09
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Molecular Ide lected for the
Transpl twork[▽]

S. Arunmozhi Ba eren A. Marr,[4,5]
Barbara D Perrone,[9]
Ste er[1]

For *A. terreus* & *A. flavus no more species were detected*

- 147 (67.4%) *A* x
- 29 (13.2%) *fla*
- 19 (8.7%) *A. niger* complex
- 11 (7.4%) *A. terreus* complex
- 6 (2.7%) *A. ustus* complex
- 5 (2.3%) *A. versicolor* complex
- 1 (0.45%) *A. nidulans* complex

bjh research paper

Epidemiology and outcome of infections due to *Aspergillus terreus*: 10-year single centre experience

Cornelia Lass-Flörl,[1] Katharina Griff,[1] Astrid Mayr,[1] Andreas Petzer,[2] Günter Gastl,[2] Hugo Bonatti,[3] Martin Freund,[4] Gabriele Kropshofer,[5] Manfred P. Dierich[1] and David Nachbaur[2]

Departments of [1]Hygiene, Microbiology and Social Medicine, [2]Haematology and Oncology, [3]Surgery, [4]Radiology I, and [5]Paediatrics, Medical University of Innsbruck, Innsbruck, Austria

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bjh research paper

Epidemiology and outcome of infections due to *Aspergillus terreus*: 10-year single centre experience

	A. terreus	Other species
Dissemination	**63%**	**32%**
CNS	31%	---
Skin	29%	---
AmB response	20%	47%

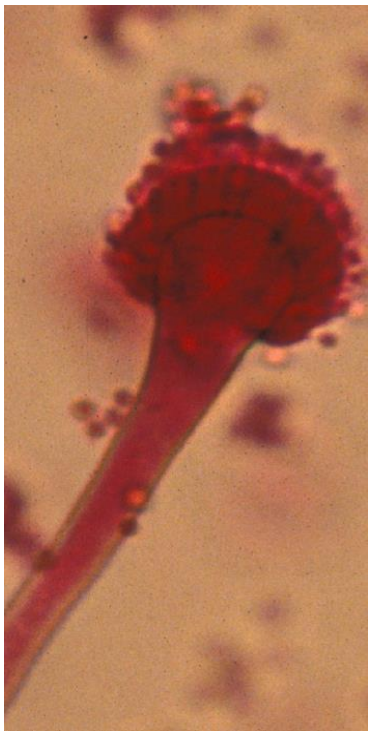
bjh research paper

Epidemiology and outcome of infections due to *Aspergillus terreus*: 10-year single centre experience

	A. terreus	Other species
Dissemination	63%	32%
CNS	31%	---
Skin	29%	---
AmB response	**20%**	**47%**

What about *Aspergillus fumigatus* species complex?

Molecular id by means of sequencing β – tubuline of moulds resembling *A. fumigatus* morphologically



Data obtained from Mycology Reference Laboratory. Spain

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0095-1137/09/$08.00+0 doi:10.1128/JCM.01070-09
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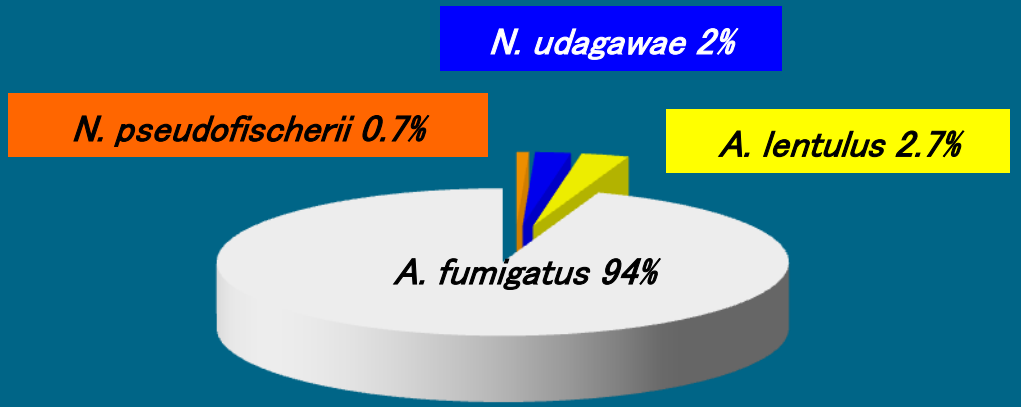
Molecular Identification of *Aspergillus* Species Collected for the Transplant-Associated Infection Surveillance Network[▽]

S. Arunmozhi Balajee,[1*] Rui Kano,[1] John W. Baddley,[2,11] Stephen A. Moser,[3] Kieren A. Marr,[4,5] Barbara D. Alexander,[6] David Andes,[7] Dimitrios P. Kontoyiannis,[8] Giancarlo Perrone,[9] Stephen Peterson,[10] Mary E. Brandt,[1] Peter G. Pappas,[2] and Tom Chiller[1]



	n	AmB	IZ	VZ	PZ	CP
A. lentulus	24	**4.4**	**2.3**	**4**	0.23	1.6
N. hiratsukae	9	0.8	0.22	0.8	0.09	0.11
N. pseudofischerii	6	0.25	**4**	**2.51**	0.22	0.86
A. fumigatiaffiinis	6	**9**	**8**	**5**	0.4	0.16
N. udagawae	4	1.7	0.5	**2**	0.25	0.8

Alcazar-Fuoli et al. AAC. 2008. 52: 1244–1251

OPEN ACCESS Freely available online PLOS MEDICINE

Emergence of Azole Resistance in *Aspergillus fumigatus* and Spread of a Single Resistance Mechanism

Eveline Snelders[1,2], Henrich A. L. van der Lee[1,2], Judith Kuijpers[1,2], Anthonius J. M. M. Rijs[1,2], János Varga[3,4], Robert A. Samson[3], Emilia Mellado[5], A. Rogier T. Donders[6], Willem J. G. Melchers[1,2], Paul E. Verweij[1,2*]

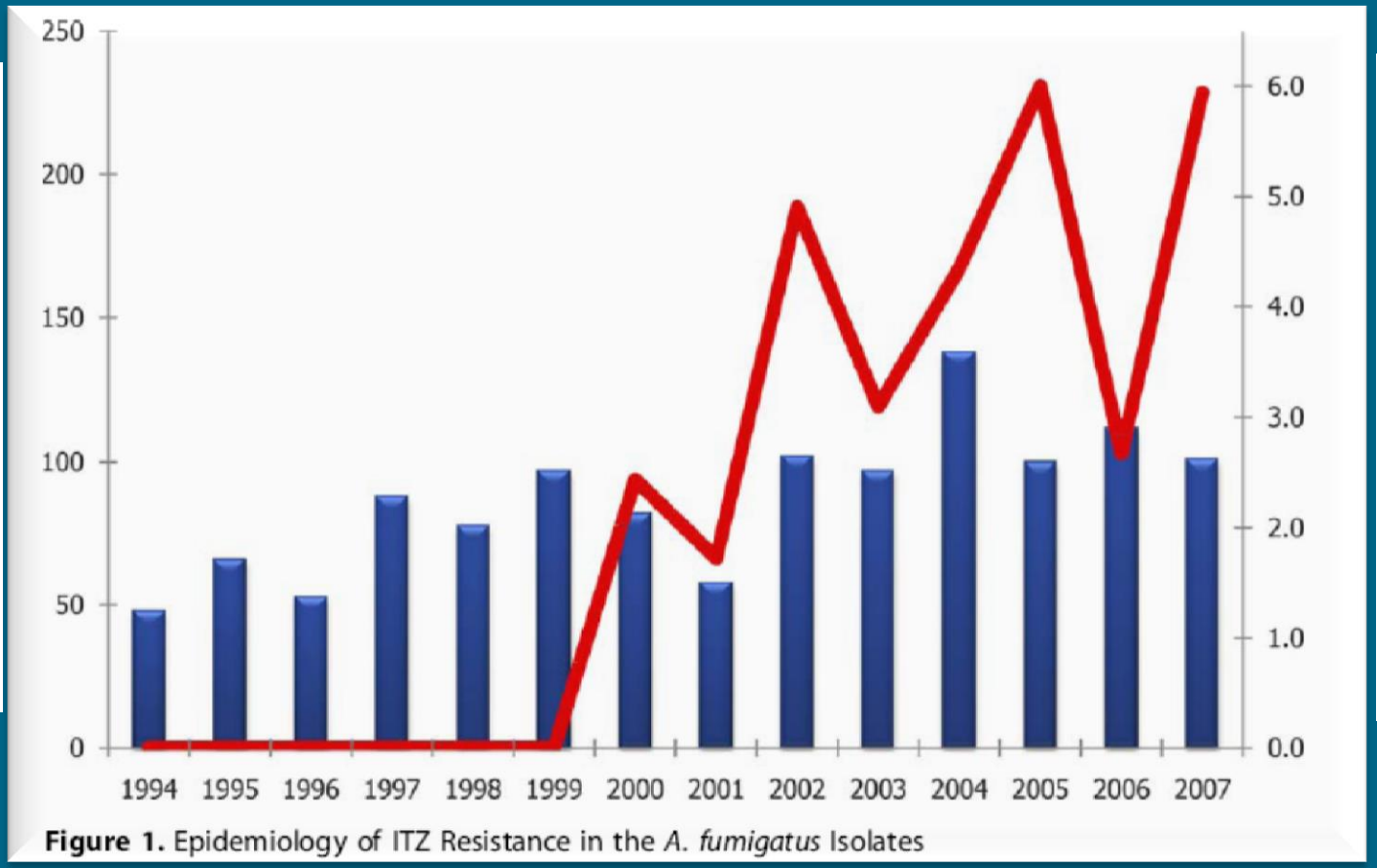


Figure 1. Epidemiology of ITZ Resistance in the *A. fumigatus* Isolates

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Azole resistance was found in 12.9% patients (13/101)

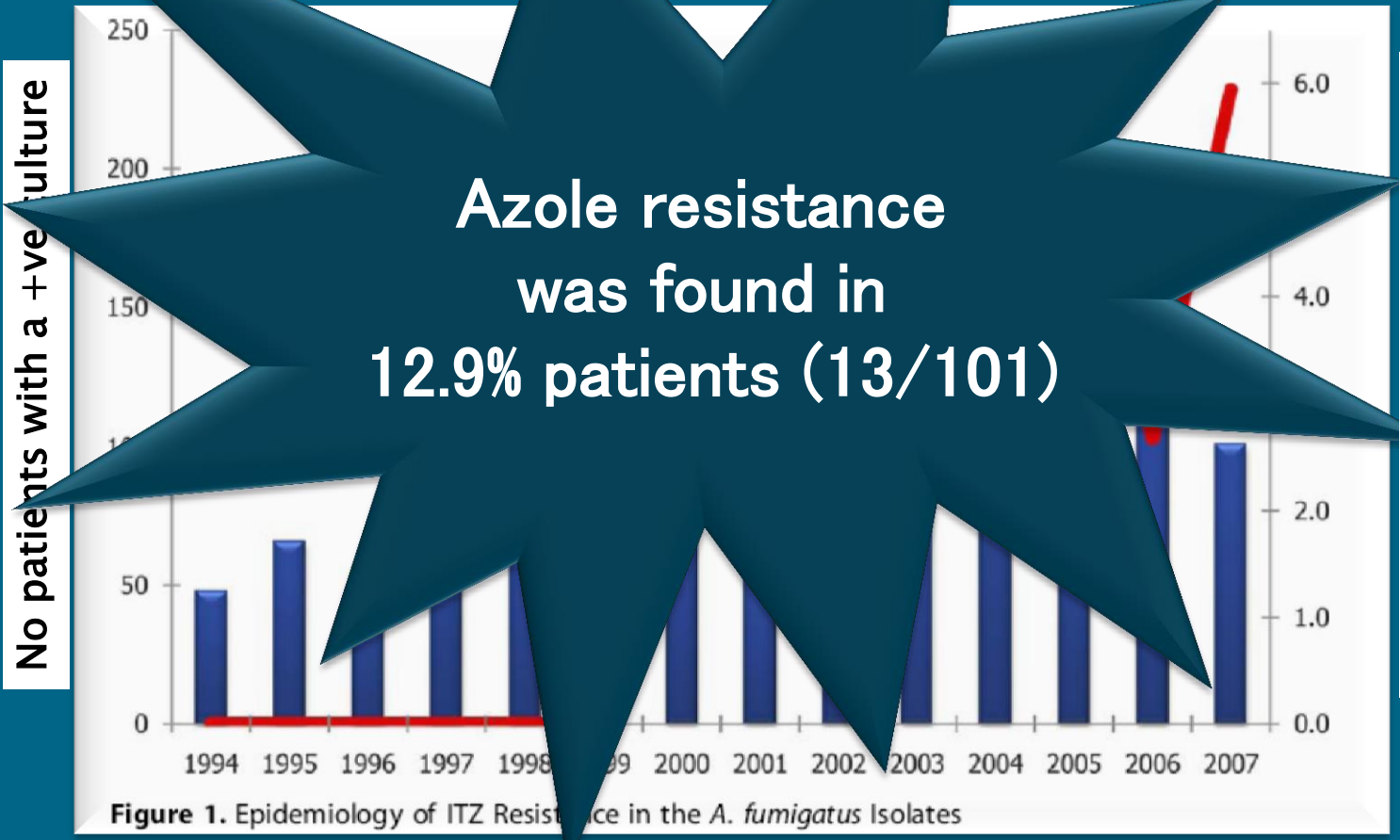

Figure 1. Epidemiology of ITZ Resist…ce in the *A. fumigatus* Isolates

Frequency and Evolution of Azole Resistance in *Aspergillus fumigatus* Associated with Treatment Failure[1]

Susan J. Howard, Dasa Cerar, Michael J. Anderson, Ahmed Albarrag, Matthew C. Fisher, Alessandro C. Pasqualotto, Michel Laverdiere, Maiken C. Arendrup, David S. Perlin, and David W. Denning

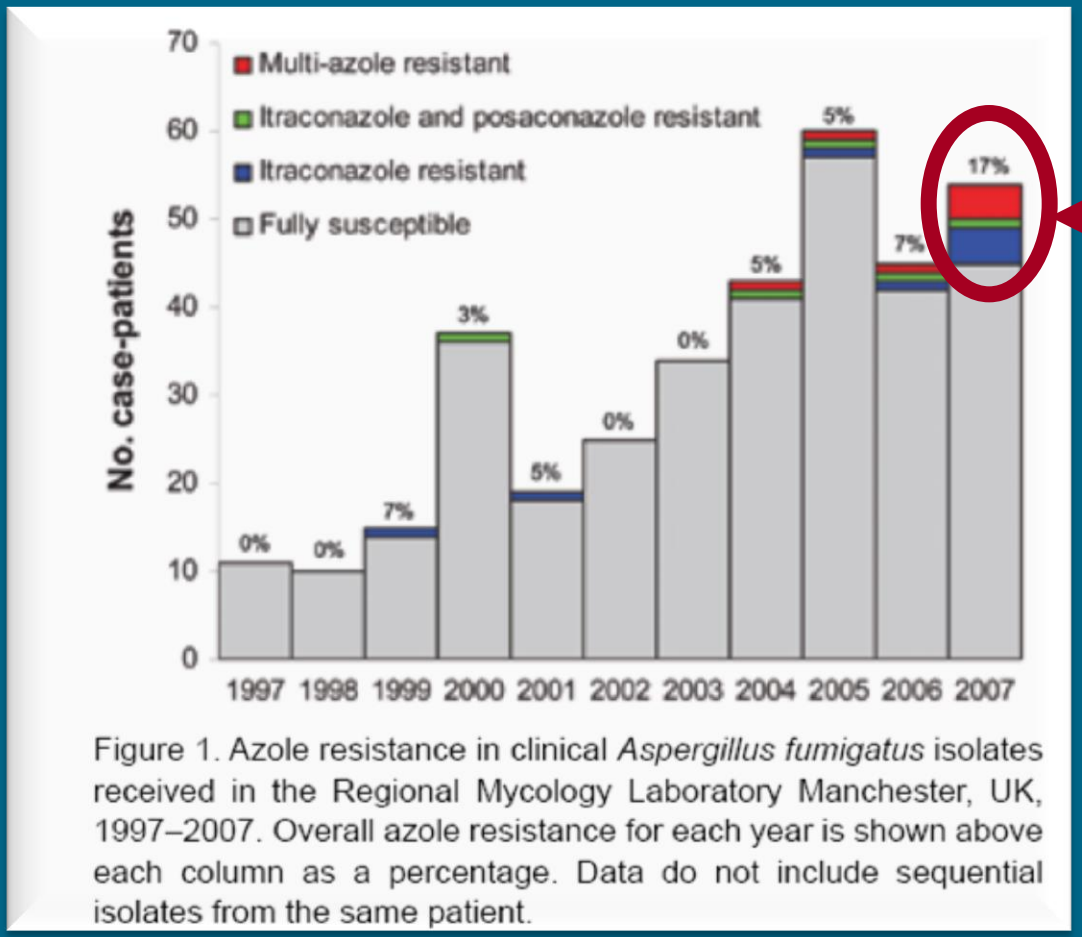

Figure 1. Azole resistance in clinical *Aspergillus fumigatus* isolates received in the Regional Mycology Laboratory Manchester, UK, 1997–2007. Overall azole resistance for each year is shown above each column as a percentage. Data do not include sequential isolates from the same patient.

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Molecular Identification of *Aspergillus* Species Collected for the Transplant-Associated Infection Surveillance Network[▽]

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19 *A. nigri* complex were identified as:

6 *A. tubingensis*

13 *A. niger*

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Oct. 2009, p. 4514–4517 Vol. 53, No. 10
0066-4804/09/$08.00+0 doi:10.1128/AAC.00585-09
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Species Identification and Antifungal Susceptibility Patterns of Species Belonging to *Aspergillus* Section *Nigri*[▽]

Laura Alcazar-Fuoli,* Emilia Mellado, Ana Alastruey-Izquierdo,
Manuel Cuenca-Estrella, and Juan L. Rodriguez-Tudela

TABLE 1. Source, molecular identification, MICs, and MECs for species of *Aspergillus* section *Nigri*[a]

Isolate	Source	Molecular identification (β-tubulin gene)	MIC (mg/liter)[b]						MEC (mg/liter)[c]	
			AMB	ITC	VCZ	RVC	POS	TRB	CAS	MICA
Isolates of *Aspergillus* section *Nigri* showing low ITC MICs										
CM-3236	Respiratory	*A. niger*	0.19	0.5	0.5	1.0	0.12	1.0	0.25	0.03
CM-3257	Respiratory	*A. niger*	0.25	1.0	1.0	1.0.	0.25	1.0	0.25	0.03
CM-3506	Respiratory	*A. niger*	0.19	0.5	0.75	1.0	0.12	0.31	0.15	0.03
CM-3507	Respiratory	*A. tubingensis*	0.19	0.5	1.0	1.5	0.15	0.62	0.06	0.03
CM-3585	Environmental	*A. tubingensis*	0.19	0.5	1.0	1.67	0.12	0.42	0.37	0.03
CM-3586	Catheter	*A. niger*	0.25	0.5	1.0	2.0	0.12	0.12	1.0	0.03
CM-3636	Respiratory	*A. niger*	0.25	0.5	0.5	1.0	0.19	1.0	0.25	0.03
CM-3641	Respiratory	*A. niger*	0.25	0.5	1.0	1.0	0.125	0.25	0.5	0.03
CM-3672	Cutaneous	*A. niger*	0.12	0.5	1.0	1.5	0.19	0.07	0.15	0.03
CM-4004	Unknown	*A. niger*	0.25	1.0	1.0	1.67	0.25	0.13	0.10	0.03
CM-4213	Respiratory	*A. niger*	0.33	0.14	0.33	0.58	0.03	0.22	0.39	0.03
CM-4264	Blood culture	*A. tubingensis*	0.12	0.5	1.0	1.5	0.12	0.50	0.03	0.03
CM-4296	Respiratory	*A. tubingensis*	0.12	0.75	1.0	1.5	0.19	0.62	0.25	0.03
CM-4316	Respiratory	*A. niger*	0.19	0.5	0.5	1.0	0.125	0.5	0.25	0.03
CM-5094	Respiratory	*A. tubingensis*	0.12	0.5	0.75	2.0	0.06	0.62	0.19	0.03
CM-5095	Respiratory	*A. niger*	0.19	0.5	0.75	1.5	0.12	0.62	0.25	0.03
GM for group			0.20	0.56	0.82	1.31	0.14	0.50	0.28	0.03

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Laura Alcazar-Fuoli,* Emilia Mellado, Ana Alastruey-Izquierdo, Manuel Cuenca-Estrella, and Juan L. Rodriguez-Tudela

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Isolate	Source	Molecular identification (β-tubulin gene)	MIC (mg/liter)[b]						MEC (mg/liter)[c]	
			AMB	ITC	VCZ	RVC	POS	TRB	CAS	MICA
Isolates of *Aspergillus* section *Nigri* showing much higher ITC MICs										
CM-3123	Respiratory	*A. tubingensis*	0.25	11	1.67	2.67	0.25	1.17	0.25	0.03
CM-3810	Respiratory	*A. tubingensis*	0.25	4.0	2.0	2.0	0.12	1.0	0.5	0.03
CM-4003	Unknown	*A. tubingensis*	0.12	16	2.0	4.0	0.25	1.0	0.25	0.03
CM-4005	Unknown	*A. tubingensis*	0.12	16	2.0	4.0	0.5	0.25	0.5	0.03
CM-4688	Respiratory	*A. tubingensis*	0.21	3.67	2.0	3.33	0.25	1.50	0.18	0.03
CM-5264	Respiratory	*A. foetidus*	0.12	16	2.0	8.0	0.5	0.5	0.06	0.03
GM for group			0.18	11.11	1.95	4.0	0.31	0.90	0.29	0.03

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			AMB	ITC	VCZ	RVC	POS	TRB	CAS	MICA
Isolates of *Aspergillus* section *Nigri* showing paradoxical effect against ITC										
CM-3125	Respiratory	*A. tubingensis*	0.12	0.5	1	1.67	0.12	0.5	0.05	0.03
CM-3177	Respiratory	*A. tubingensis*	0.16	1	2	3.33	0.25	0.67	0.05	0.03
CM-3551	Respiratory	*A. niger*	0.5	4.75	1	2	0.12	0.25	0.03	0.03
CM-3654	Blood culture	*A. tubingensis*	0.19	1	2	2.50	0.25	0.63	0.14	0.03
CM-4000	Unknown	*A. tubingensis*	0.16	1	2	2	0.25	0.33	0.10	0.03
CM-4001	Unknown	*A. tubingensis*	0.19	1	1.75	2.50	0.25	0.56	0.11	0.03
CM-4002	Unknown	*A. foetidus*	0.25	1	2	2.67	0.12	0.33	0.14	0.03
CM-4262	Ophthalmic	*A. niger*	0.25	1	2	2	0.25	0.29	0.13	0.03
CM-4352	Respiratory	*A. tubingensis*	0.28	1	0.88	2	0.25	0.31	0.15	0.03
CM-4897	Blood culture	*A. tubingensis*	0.16	1	2	2	0.25	0.42	0.10	0.03
CM-4899	Respiratory	*A. tubingensis*	0.16	1	2	2.67	0.25	0.33	0.10	0.05
CM-4995	Prosthesis	*A. foetidus*	0.21	1	2	2	0.16	0.33	0.14	0.03
GM for group			0.2	1.3	1.72	2.28	0.21	0.41	0.10	0.03

[a] GM, geometric means of MICs and MECs for the strains within each group.
[b] MIC geometric mean of amphotericin B (AMB), itraconazole (ITC), voriconazole (VCZ), ravuconazole (RVC), posaconazole (POS), and terbinafine (TRB).
[c] MEC geometric mean of caspofungin (CAS) and micafungin (MICA).

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Molecular Identification of *Aspergillus* Species Collected for the Transplant-Associated Infection Surveillance Network[▽]

S. Arunmozhi Balajee,[1]* Rui Kano,[1] John W. Baddley,[2,11] Stephen A. Moser,[3] Kieren A. Marr,[4,5] Barbara D. Alexander,[6] David Andes,[7] Dimitrios P. Kontoyiannis,[8] Giancarlo Perrone,[9] Stephen Peterson,[10] Mary E. Brandt,[1] Peter G. Pappas,[2] and Tom Chiller[1]

6 *A. ustus* complex were identified as *A. calidoustus*

Medical Mycology
2009, 1–7, iFirst article
informa healthcare

In vitro activity of nine antifungal agents against clinical isolates of *Aspergillus calidoustus*

ANA ALASTRUEY-IZQUIERDO*, ISABEL CUESTA*, JOS HOUBRAKEN†, MANUEL CUENCA-ESTRELLA*, ARACELI MONZÓN* & JUAN L. RODRIGUEZ-TUDELA*

- Our experience with 9 isolates of *A. calidoustus*

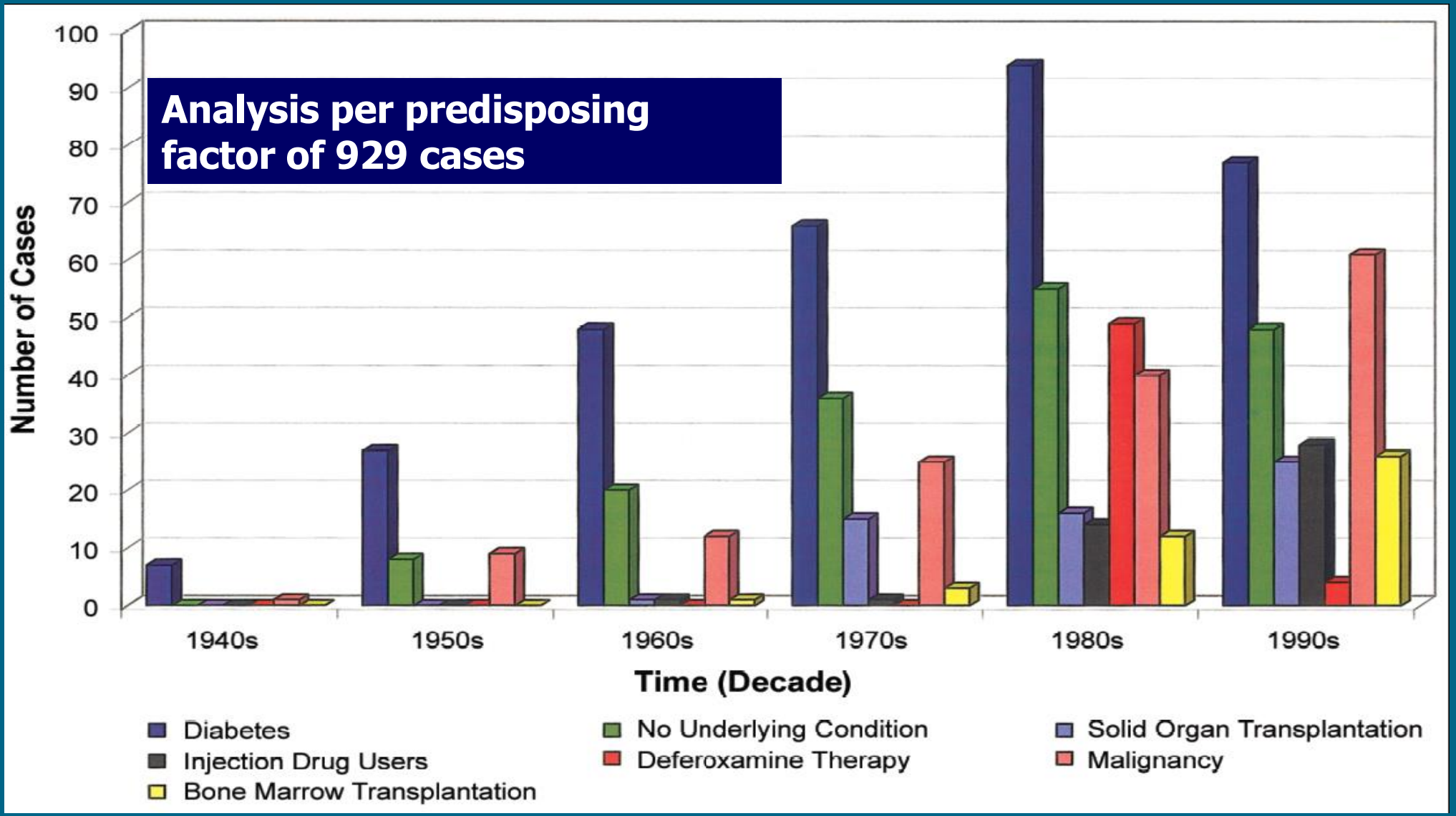
	Geo Mean
AmB	0.9
IZ	15.5
VZ	7.1
PZ	13.1
CP	3.1
MC	0.06
AN	0.02

Summary for *Aspergillus*

- Increasing rates of azole resistance in *A. fumigatus*
- *A. terreus* R AmB and dissemination
- Molecular identification of *Aspergillus* enlarges its epidemiology
  - More species causing IFI
  - Unpredictable AFST

Zygomycetes

Roden et al. Clinical Infectious Diseases 2005; 41:634–53



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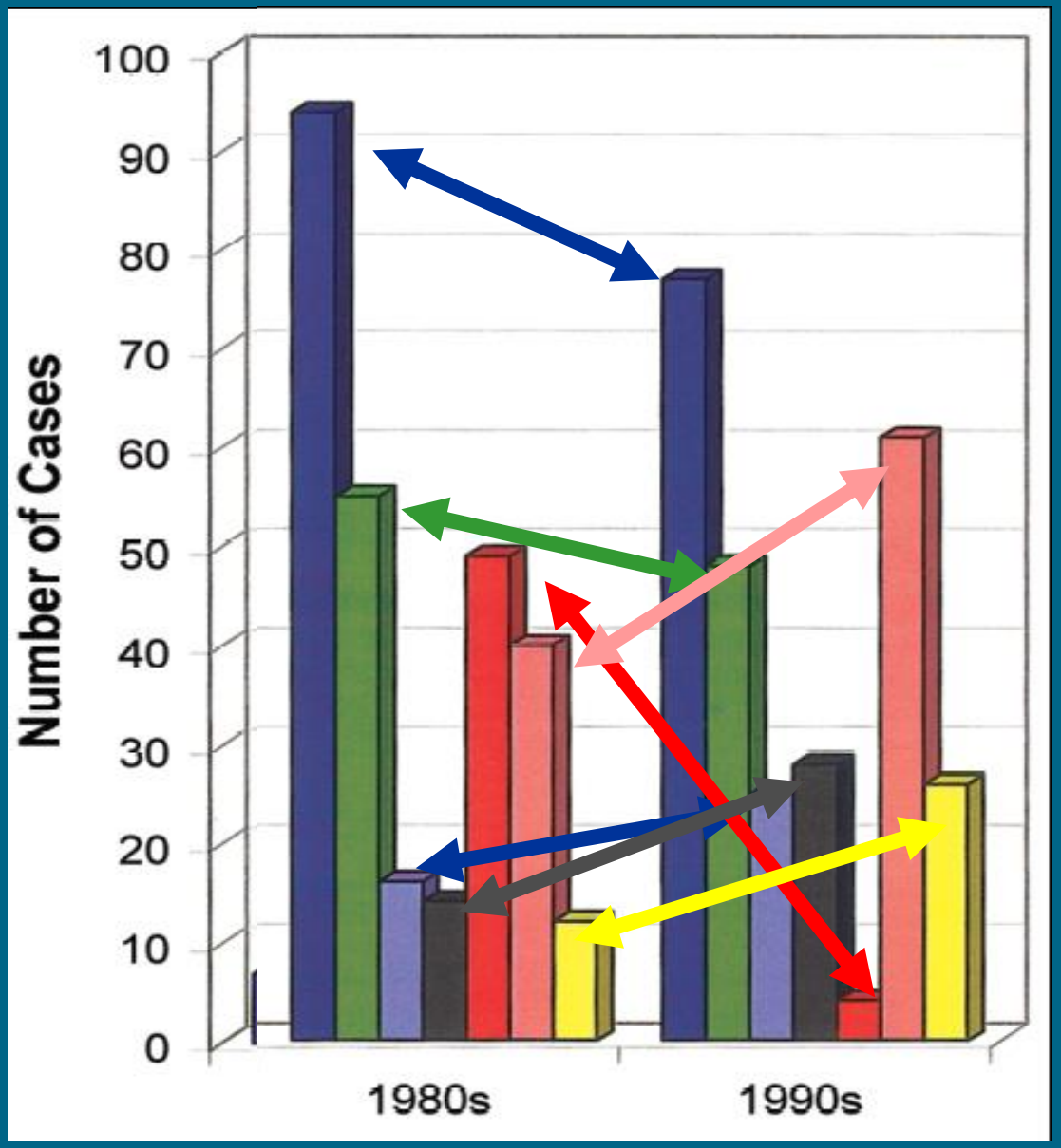

Bone Marrow Transplantation (2007) 40, 451–456
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www.nature.com/bmt

ORIGINAL ARTICLE

Breakthrough fungal infections after allogeneic hematopoietic stem cell transplantation in patients on prophylactic voriconazole

S Trifilio[1], S Singhal[2], S Williams[2], O Frankfurt[2], L Gordon[2], A Evens[2], J Winter[2], M Tallman[2], J Pi[1] and J Mehta[2]

Breakthrough Fungal Infections in Stem Cell Transplant Recipients Receiving Voriconazole

Alexander Imhof,[1] S. Arunmozhi Balajee,[1] David N. Fredricks,[1,2] Janet A. Englund,[1,3] and Kieren A. Marr[1,2]

Clinical Infectious Diseases 2004; 39:743–6

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Bone Marrow Transplantation (2007), 1–5
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www.nature.com/bmt

ORIGINAL ARTICLE

Breakthrough zygomycosis after voriconazole administration among patients with hematologic malignancies who receive hematopoietic stem-cell transplants or intensive chemotherapy

SM Trifilio[1], CL Bennett[2,3], PR Yarnold[4], JM McKoy[5], J Parada[6,7], J Mehta[3], G Chamilos[8], F Palella[9], L Kennedy[10], K Mullane[11], MS Tallman[3], A Evens[3], MH Scheetz[1], W Blum[12] and DP Kontoyiannis[13]

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Apr. 2009, p. 1686–1689 Vol. 53, No. 4
0066-4804/09/$08.00+0 doi:10.1128/AAC.01467-08
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Activity of Posaconazole and Other Antifungal Agents against *Mucorales* Strains Identified by Sequencing of Internal Transcribed Spacers▽

Ana Alastruey-Izquierdo, Maria Victoria Castelli, Isabel Cuesta, Araceli Monzon, Manuel Cuenca-Estrella, and Juan Luis Rodriguez-Tudela*

Servicio de Micología, Centro Nacional de Microbiología, Instituto de Salud Carlos III, Majadahonda, Spain

Species	No	AmB	Iz	Vz	Pz
Rhizopus oryzae	26	0.29	4	12.1	1.15
Mucor circinelloides	20	0.05	11.9	16	1.49
Lithcheimia corymbifera	7	0.08	0.68	14.5	0.41
Rhizopus microsporus	6	0.45	1.59	8	0.79
Rhizomucor pusillus	5	0.05	0.29	5.28	0.16
Rhizomucor variabilis	2	0.03	16	16	1.41
Cunninghamella spp	2	2.83	0.5	16	0.25
Actinomucor spp	2	1	2	16	0.06
Aphophysomyces spp	1	2	16	16	0.5

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Apr. 2009, p. 1686–1689 Vol. 53, No. 4
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Species	No			Vz	
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Mucor circinelloides	20			**16**	
Lithcheimia corymbifera	7			**14.5**	
Rhizopus microsporus	6			**8**	
Rhizomucor pusillus	5			**5.28**	
Rhizomucor variabilis	2			**16**	
Cunninghamella spp	2			**16**	
Actinomucor spp	2			**16**	
Aphophysomyces spp	1			**16**	

Zygomycosis in a Tertiary-Care Cancer Center in the Era of *Aspergillus*-Active Antifungal Therapy: A Case-Control Observational Study of 27 Recent Cases

Dimitrios P. Kontoyiannis,[1,4] Michail S. Lionakis,[1] Russell E. Lewis,[1,4] Georgios Chamilos,[1] Mimi Healy,[5] Cheryl Perego,[1] Amar Safdar,[1] Hagop Kantarjian,[3] Richard Champlin,[2] Thomas J. Walsh,[6] and Issam I. Raad[1]

- September'02 through March'04
  - Aspergillosis 70 cases (64%)
  - Zygomycosis 22 cases (20%)
  - Fusariosis 17 cases (16%)
- Logistic regression for
  - Zygomycosis vs Aspergillosis
  - Zygomycosis vs non-IMI (control)
  - Aspergillosis vs non-IMI (control)

Zygomycosis in a Tertiary-Care Cancer Center in the Era of *Aspergillus*-Active Antifungal Therapy: A Case-Control Observational Study of 27 Recent Cases

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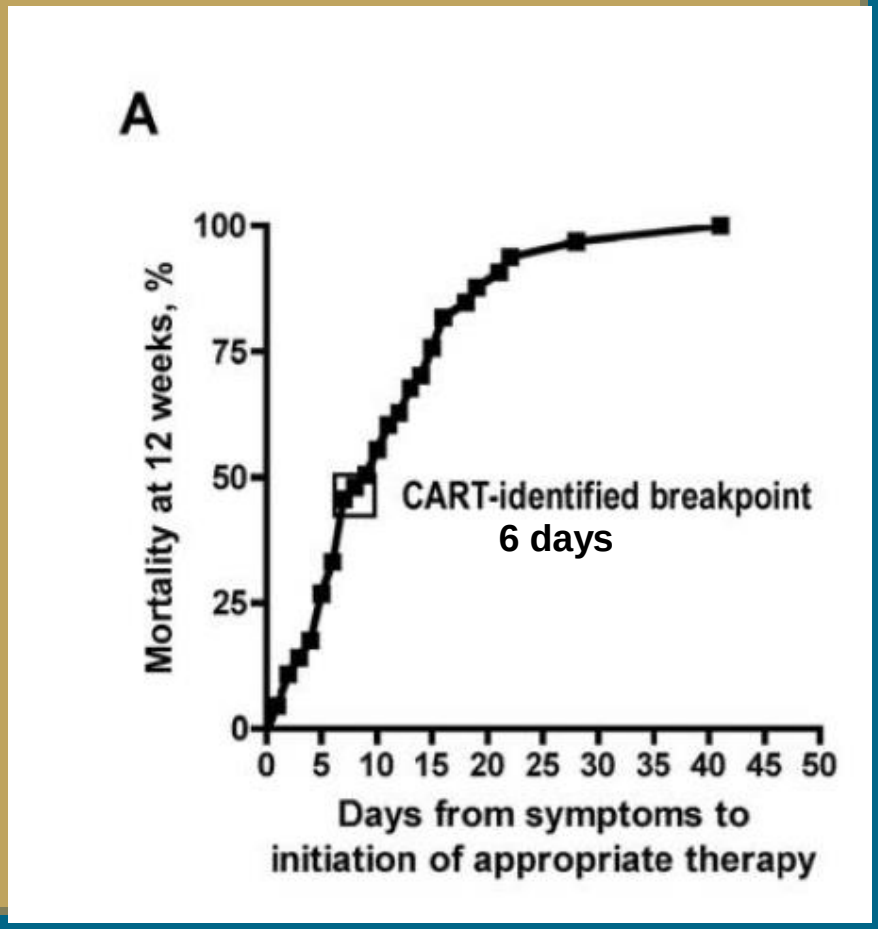
Risk Factor	OR	95% CI
Zygomycosis vs Aspergillosis		
VCZ prophylaxis	20.3	3.85-108.15
Sinus involvement	76.72	6.48-908.15
Zygomycosis vs control		
VCZ prophylaxis	10.37	2.76-38.97
Diabetes mellitus	8.39	2.04-34.5
Malnutrition	3.70	1.03-13.27
Aspergillosis vs control		
Grade III-IV GvHD	1.33	1.01-1.74
Corticosteroids	1.39	1.15-1.68

Delaying Amphotericin B–Based Frontline Therapy Significantly Increases Mortality among Patients with Hematologic Malignancy Who Have Zygomycosis

Georgios Chamilos,[1] Russell E. Lewis,[1,2] and Dimitrios P. Kontoyiannis[1,2]

70 patients with zygomycosis



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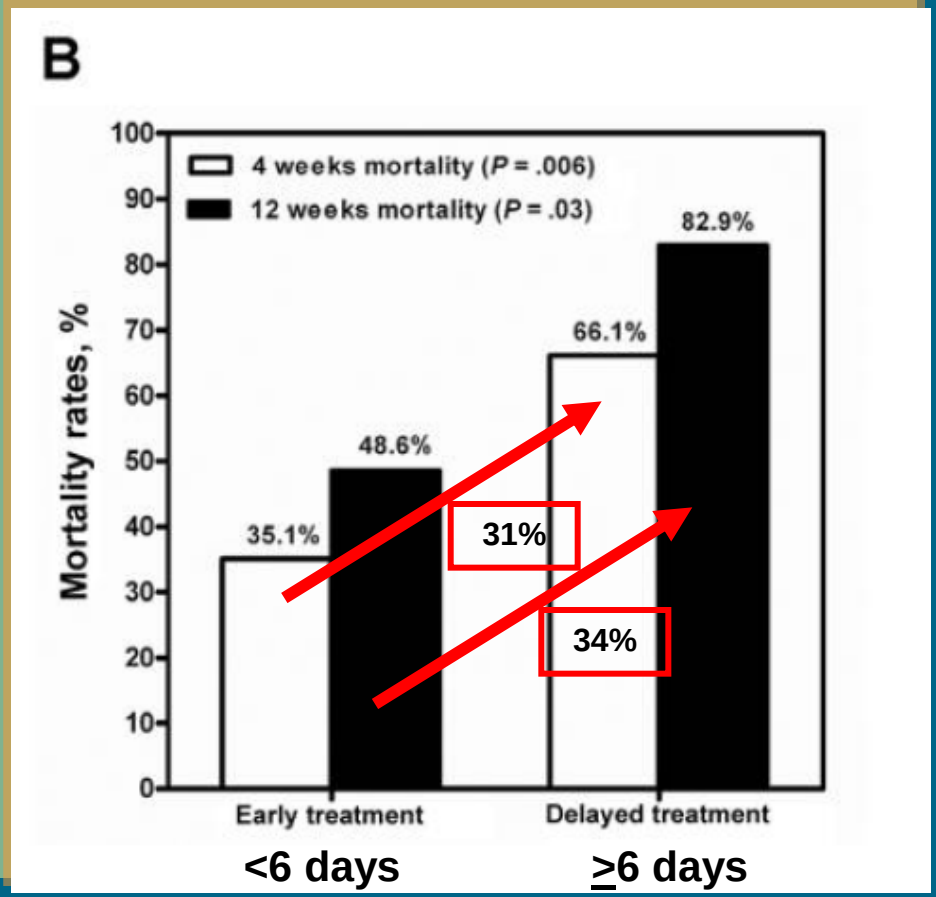

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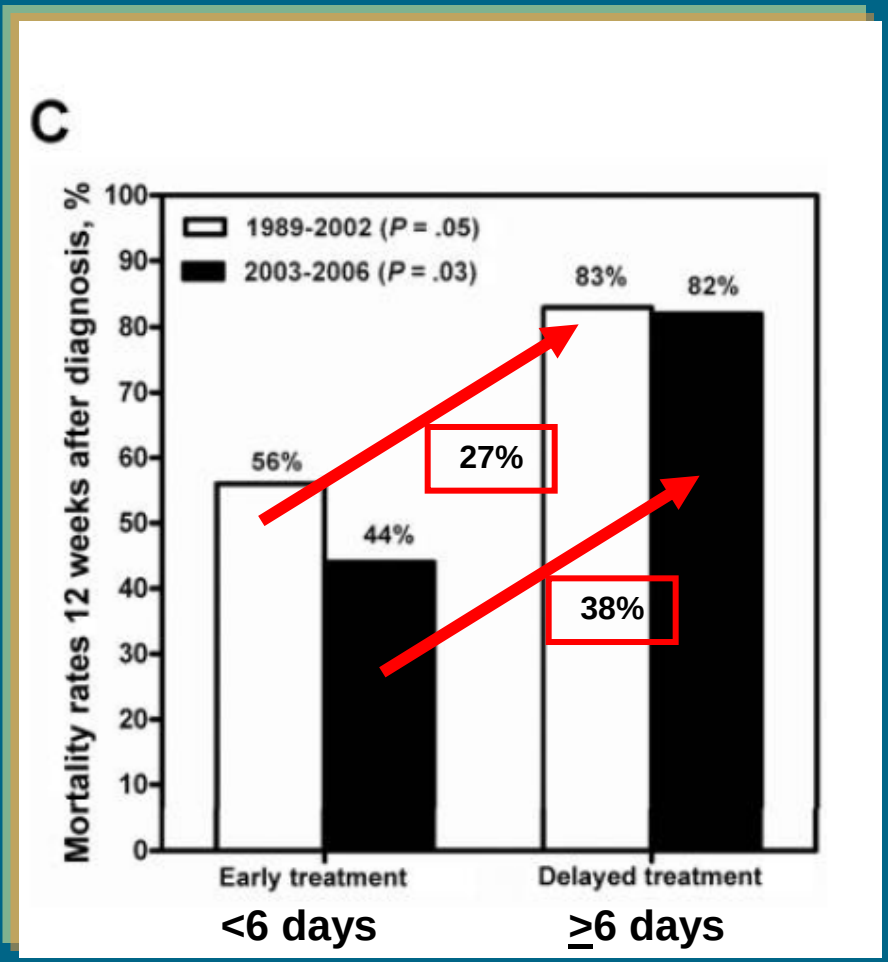

Fusarium

- *Fusarium solani* complex
  - Over 45 phylogenetically distinct species
  - At least 20 are associated with human infections
- *Fusarium oxysporum* complex
  - Many distinct species but the phylogeny is still unsolved

AFST of *Fusarium*

Species	No	AmB	Iz	Vz	Pz
F solani complex	47	1.3	11.1	12.8	13.2
F oxysporum complex	33	0.77	11.2	5.2	4.6
F verticilloides	17	1.8	7.1	6.8	2.47
F proliferatum	9	1.2	16	8	10.4

- Amphotericin B is the most active agent
- No activity of echinocandins
- No clear differences of susceptibility inside the species complex

Species of *Scedosporium* associated with human beings

- *Pseudallescheria boydii*
- *Pseudallescheria ellipsoidea*
- *Scedosporium apiospermum*
- *Scedosporium aurantiacum*
- *Scedosporium dehoogi*
- *Scedosporium prolificans*

Species of *Scedosporium* associated with human beings

- *S. prolificans* is multirresistant
- Limited data for the new species but no relevant differences in susceptibility among them
  - Usually resistant to amphotericin B (GM: 4.9 mg/L)
  - Good activity of voriconazole (GM: 0.92 mg/L) & posaconazole (GM: 1.18 mg/L)
  - Limited experience with echinocandins but good activity against some isolates

A high number of tissues with hyphae are culture negative
What are we missing?

Comparison of Histopathological Analysis, Culture, and Polymerase Chain Reaction Assays to Detect Invasive Mold Infections from Biopsy Specimens

Volker Rickerts,[1] Sabine Mousset,[1] Evelyn Lambrecht,[2] Kathrin Tintelnot,[4] Rainer Schwerdtfeger,[5] Elisabeth Presterl,[7] Volkmar Jacobi,[3] Gudrun Just-Nübling,[1] and Ralf Bialek[6]

- Patients with a suspected fungal infection
  - 27 histopathology +ve tissue samples
    - 17 positive cultures (63%)
  - 29 histopathology Ø tissue samples
    - 2 positive cultures (7%)

Rickerts et al. CID. 2007; 44:1078–83

Comparison of Histopathological Analysis, Culture, and Polymerase Chain Reaction Assays to Detect Invasive Mold Infections from Biopsy Specimens

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- Patients with a suspected fungal infection
  - 18 cases pathology was compatible with *Aspergillus*
    - 14 positive cultures (77%)
  - 6 cases pathology was compatible with Zygomycetes
    - 2 positive cultures (33%)
  - 3 cases unspecified hyphae at pathology
    - 1 positive culture (33%)

Our experience with 58 tissue samples and sequencing of ITS

- 38 *Aspergillus* spp (65.5%)
- 7 Zygomycetes (12%)
- 3 *Fusarium* (5.2%)
- 2 *S. apiospermum* (3.4%)
- 8 Other (14.8%)

Data from Mycology Reference Laboratory. Spain

Our experience with 58 tissue samples and sequencing of ITS

- What were the others?
  - 2 *Alternaria infectoria*
  - 1 *Arthrographis kalrae*
  - 1 *Phialemonium curvatum*
  - 1 *Metharrizium anisopliae*
  - 1 *Phomopsis longicolla*
  - 1 *Scopulariopsis* spp
  - 1 *Phoma* spp

Data from Mycology Reference Laboratory. Spain

Susceptibility of *Alternaria* spp

Antifungal	N	Geo mean	Range
AmB	25	0.3	0.015-32
ITZ	25	1	0.06-16
VZ	24	2.1	0.12-16
PZ	21	0.7	0.015-16
TB	25	3.6	0.03-32
CP	11	14.1	0.03-32
MC	10	11.3	0.06-32

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, July 2003, p. 2339–2341 Vol. 47, No. 7
0066-4804/03/$08.00+0 DOI: 10.1128/AAC.47.7.2339–2341.2003
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Scopulariopsis brevicaulis, a Fungal Pathogen Resistant to Broad-Spectrum Antifungal Agents

Manuel Cuenca-Estrella,* Alicia Gomez-Lopez, Emilia Mellado, Maria J. Buitrago, Araceli Monzón, and Juan L. Rodriguez-Tudela

TABLE 1. Modes, geometric means, and ranges for antifungal agents tested against 32 clinical isolates of *S. brevicaulis*

Antifungal agent	Geometric mean (μg/ml)	Mode (μg/ml)	Range (μg/ml)
Amphotericin B	13.0	16.0	4.0–16.0
Flucytosine	>64.0	>64.0	>64.0
Itraconazole	>8.0	>8.0	>8.0
Voriconazole	25.4	32.0	16.0–64.0
Terbinafine	14.4	>16.0	4.0–16.0

Case Reports

Infections due to *Phialemonium* species: case report and review

MARÍA RIVERO*, ANGEL HIDALGO†, ANA ALASTRUEY-IZQUIERDO‡, MAITE CÍA*, LUIS TORROBA§ & JUAN LUIS RODRÍGUEZ-TUDELA‡

Table 2 *In vitro* activity of antifungals against *Phialemonium* species

	P. curvatum		P. obovatum	
	Number of isolates	MIC (range, mg/l)	Number of isolates	MIC (range, mg/l)
AMB	14	0.125–2	6	0.5–36.94
FC	9	>64–256	5	>64–>322.75
MICO	6	0.5–10	2	0.5–1
KTC	6	0.25–>40	4	0.8–2
FLC	12	16–>40	6	16–80
ITC	14	0.06–>40	6	0.5–1.25
VOR	8	0.25–0.5	1	0.5
POS	9	0.03–1	1	1
CAS	7	8–>32	1	16

AMB, amphotericin B; CAS, caspofungin; FC, flucytosine; FLC, fluconazole; ITC, itraconazole; KTC, ketoconazole; MICO, miconazole; POS, posaconazole; VOR, voriconazole.

Summary to improve our epidemiology knowledge of IMIs

- Epidemiology of moulds is hard
  - Prospective studies are needed
  - Geographical changes are expected
  - A central database of proven cases with molecular species identification & AFST would be very helpful
- Urgent need of diagnostic techniques able to identify the pathogen to species level
  - Many pathogens with unpredictable AFST
  - Not a single antifungal is active against them
- There is no room for morphologically ID of moulds isolated from proven and probable IFIs
- PCR and sequencing must be done to all tissue samples from patients at risk