

Non-albicans Candida

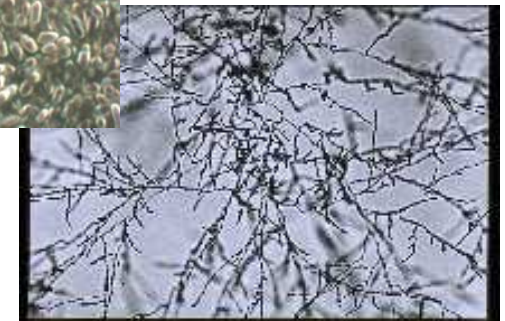
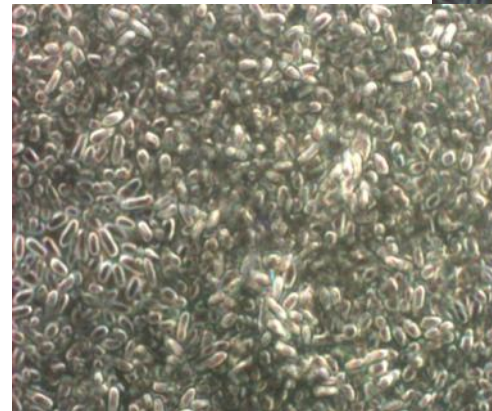
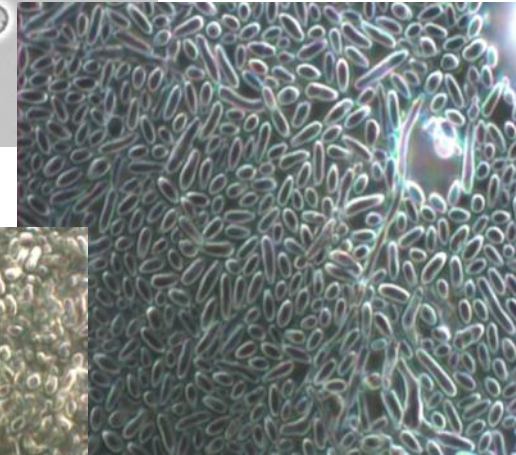
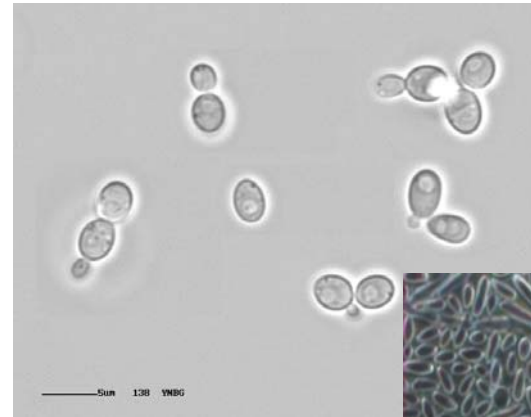
Elisabeth Presterl

Medizinische Universität Wien
Univ. Klinik für Innere Medizin I –
Klinische Abt. f. Infektionen und
Tropenmedizin

PEG-SAC 4.4.2008

Non-albicans Candida

- *C. glabrata*
- *C. tropicalis*
- *C. parapsilosis*
- *C. krusei*
- ...
- CBS - 209 Candida
Arten



Klinik

– Candida albicans vs. Non-albicans

Candida

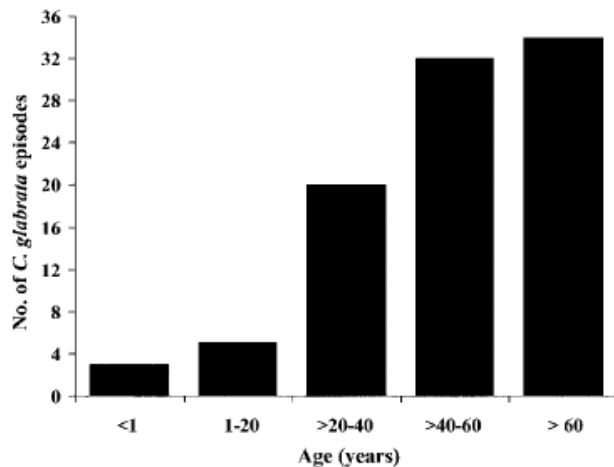
- ICU – Candidaemie (5 Jahre): n=56
 - 36 C. albicans
 - 20 Non-albicans Candida (C.g. 8, C.t. 3, C.p.1, C.l. 1, C.k. 1, C.d. 1)
- Letalität:
 - C.a. 18/36 (52.8%) – vs. N.a.C 9/20 (90 %) *
- Therapieansprechen
 - C.a. 29/39 (80.6%)* vs. N.a.C. 9/20 (52.8%)

ICU – *C.albicans* v.s *C. glabrata*

- ICU – Candidaemie (7 Jahre): n=56
 - 41 *C. albicans*
 - 15 *C. glabrata*
- Alter * *C.a.* 50 Jahre - *C.g.* 61 Jahre
AP II *C.a.* 22.8 – *C.g.* 26.9
- Letalität:
 - *C.a.* 41.5 % – vs. *C.g.* 60 % ns
- Therapie/-ansprechen ? Nicht signifikant unterschiedlich

C. glabrata Candidämie

- 8 Jahre, Zentralkrankenanstalt
- 103/609 Candidämien
- Grundkrankheiten: die üblichen



Outcome	No. (%) of episodes, by antifungal therapy				
	Flu (n = 26)	AmB (n = 21)	AmB + Flu (n = 33)	Caspo + (n = 3)	None (n = 11)
Fungemia cleared by end of treatment	22 (85)	18 (86)	31 (94)	2 (67)	3 (27)
Death at 30 days					
All causes	6 (23)	6 (29)	7 (21)	1 (33)	7 (64)
Candidemia ^a	2/6 (33)	2/6 (33)	1/7 (14)	0/1 (0)	7/7 (100)
Other causes ^b	4/6 (67)	4/6 (67)	6/7 (86)	1/1 (100)	0/7 (0)

Candidämie durch *C. tropicalis*

- Brasilien, 2003 -2005 (ins. 21 Mon.)- 12 Zentral/Schwerpunktkrankenanstalten
- 188 von 924 Candidämien
- *C.t.* Candidämie 15.7 – 25.8% abh. von KH
- Letalität: C.a. 59% - *C.t.* 62%
- Grundkrankheiten:
 - Neoplasien *C.t.* 30%, C.a. 24%, D.m., schwere Herz, Lungen, Leber und Nierenerkrankungen (ns) Nucci & Colombo 2007; 58: 77-82

Candida parapsilosis Candidämie

- Nosokomial
 - Neugeborene: Frühgeburtlichkeit, kontaminierte Transducer etc., Umgebung, HCW
 - Assoziiert mit zentralen Gefäßkathetern, parenterale Ernährung, horizontale Übertragung, Infusionslösungen, Umgebung
 - CAPD, Prothesenklappen-EC
- Letalität: 6/17 Neugeborenen, 1/7 Dialysepatienten, 3/4 Herzklappenpatienten

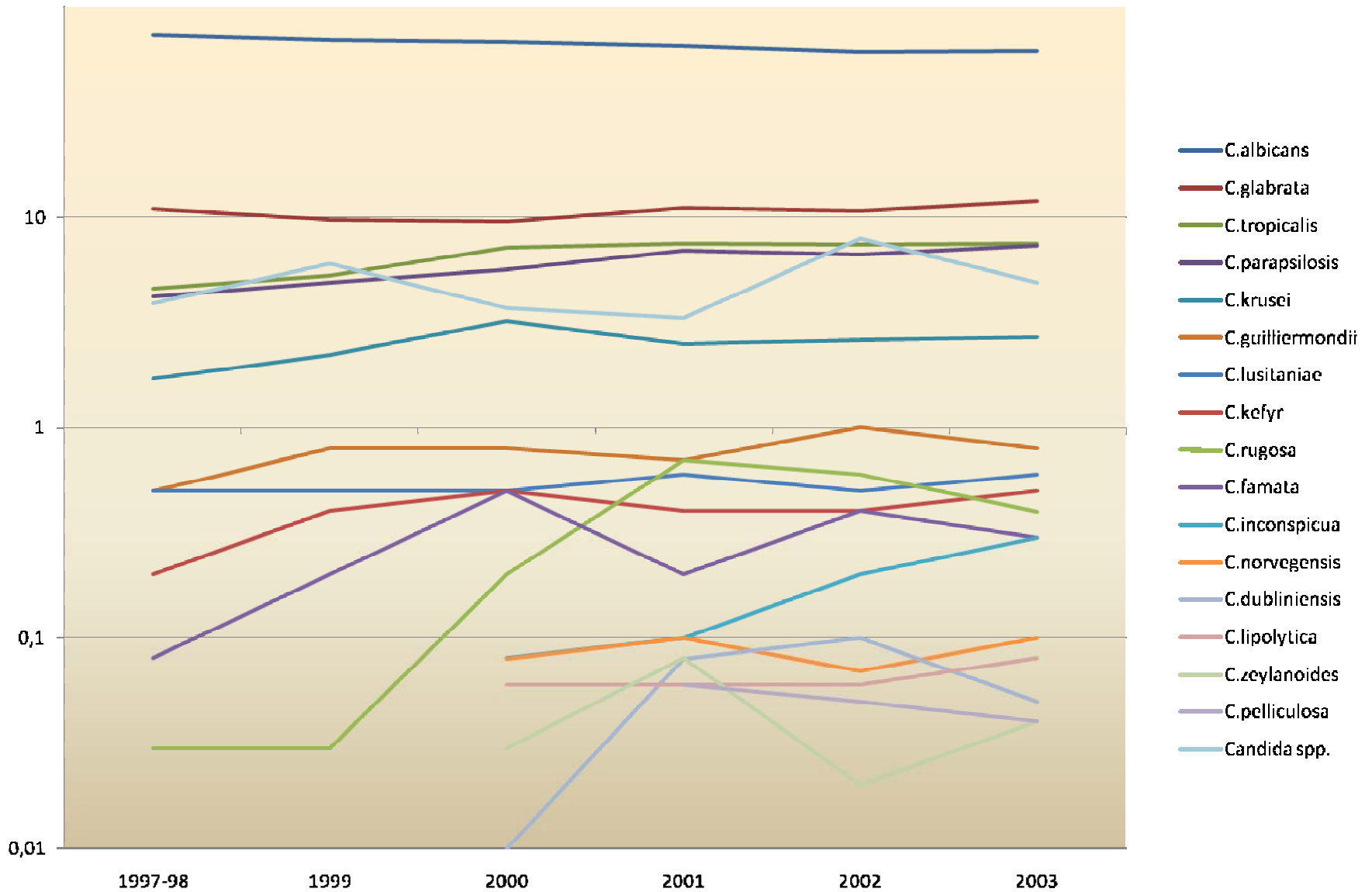
Diekema et al., Diagn Microbiol Infect Dis 1997; 29: 147
Pfaller, Clin Infect Dis 1996; 22: S89
Weems, Clin Infect Dis 1992; 14: 756
Huang YC et al., Infection 1998; 27: 23
Safdar et al., Diagn Microbiol Infect Dis 2002; 44:11

Epidemiologie

(12000-33000 Isolate/Jahr)

TABLE 7. Species distribution of *Candida* from cases of invasive candidiasis^a

Species	% of total no. of cases ^b					
	1997–1998	1999	2000	2001	2002	2003
<i>C. albicans</i>	73.3	69.8	68.1	65.4	61.4	62.3
<i>C. glabrata</i>	11.0	9.7	9.5	11.1	10.7	12.0
<i>C. tropicalis</i>	4.6	5.3	7.2	7.5	7.4	7.5
<i>C. parapsilosis</i>	4.2	4.9	5.6	6.9	6.6	7.3
<i>C. krusei</i>	1.7	2.2	3.2	2.5	2.6	2.7
<i>C. guilliermondii</i>	0.5	0.8	0.8	0.7	1.0	0.8
<i>C. lusitaniae</i>	0.5	0.5	0.5	0.6	0.5	0.6
<i>C. kefyr</i>	0.2	0.4	0.5	0.4	0.4	0.5
<i>C. rugosa</i>	0.03	0.03	0.2	0.7	0.6	0.4
<i>C. famata</i>	0.08	0.2	0.5	0.2	0.4	0.3
<i>C. inconspicua</i>			0.08	0.1	0.2	0.3
<i>C. norvegensis</i>			0.08	0.1	0.07	0.1
<i>C. dubliniensis</i>			0.01	0.08	0.1	0.05
<i>C. lipolytica</i>			0.06	0.06	0.06	0.08
<i>C. zeylanoides</i>			0.03	0.08	0.02	0.04
<i>C. pelliculosa</i>				0.06	0.05	0.04
<i>Candida</i> spp. ^c	3.9	6.0	3.7	3.3	7.9	4.9
Total no. of cases	22,533	20,998	11,698	21,804	24,680	33,002



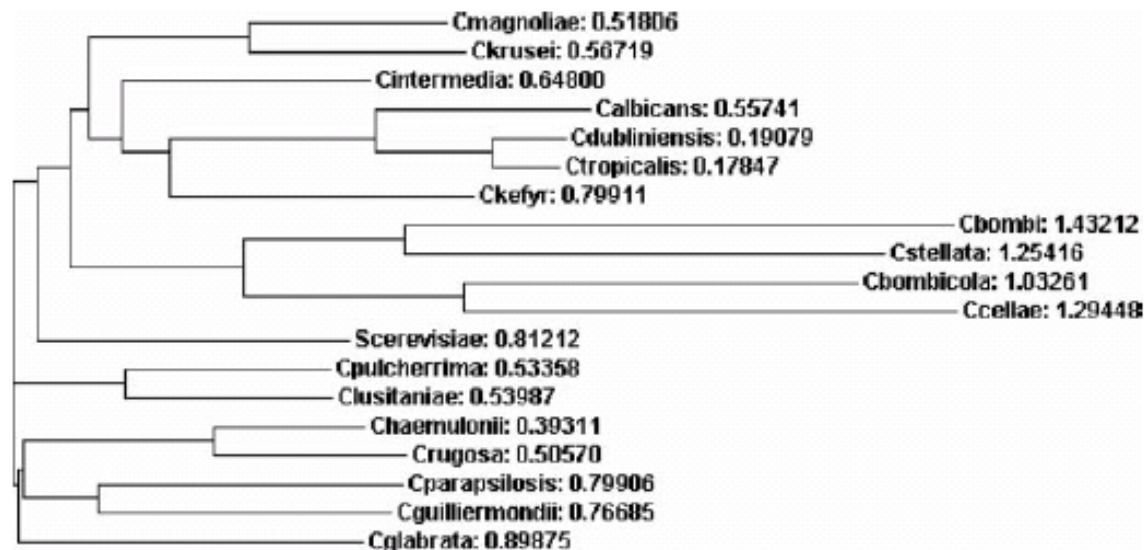
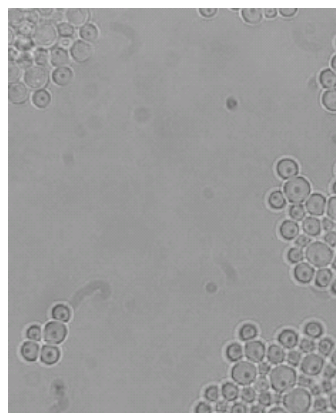
First Case of Bloodstream Infection Due to *Candida magnoliae* in a Chinese Oncological Patient[∇]

G. Lo Cascio,^{1*} L. Dalle Carbonare,³ L. Maccacaro,² F. Caliarì,³ M. Ligozzi,²
V. Lo Cascio,² and R. Fontana²

Servizio di Microbiologia, Ospedale G.B., Rossi, Verona, Italy¹; Dipartimento di Patologia, Sezione di Microbiologia, Università di Verona, Verona, Italy²; and Dipartimento di Scienze Biomediche e Chirurgiche, Università di Verona, Verona, Italy³

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We report a case of fungemia caused by *Candida magnoliae*, a yeast never associated with human disease. The infection occurred in a 42-year-old Chinese patient with gastric cancer complicated by peritoneal carcinosis. Multiple blood cultures were positive for yeast; the species was well identified with biochemical and molecular methods. The phylogenetic analysis showed a close relationship of *C. magnoliae* to *Candida krusei*.



Epidemiologie

(12000-33000 Isolate/Jahr)

TABLE 8. Geographic variation in species distribution among BSI isolates of *Candida*

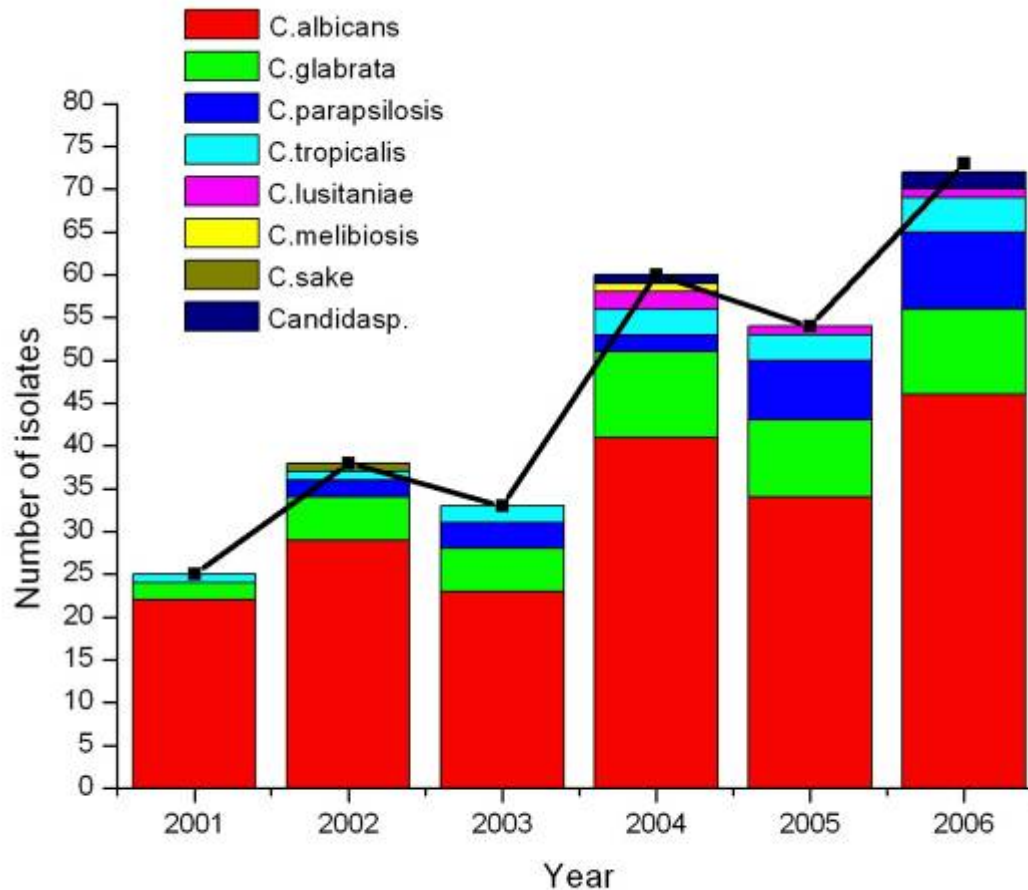
Location	Study period	Reference ^a	No. of isolates	% of total by species						
				<i>C. albicans</i>	<i>C. glabrata</i>	<i>C. parapsilosis</i>	<i>C. tropicalis</i>	<i>C. krusei</i>	<i>C. guilliermondii</i>	<i>C. lusitanae</i>
United States	1992–1993	113	837	52	12	21	10	4		
United States	1993–1995	205	79	56	15	15	10			
United States	1995–1997	188	1,593	46	20	14	12	2	<1	1
United States	1995–1998	205	934	53	20	10	12	3		
United States	1998–2000	92	935	45	24	13	12	2		
North America	2001–2004	224	2,773	51	22	14	7	2	<1	<1
Canada	1992–1994	322	415	69	8	10	7	1	<1	1
Europe	1992–1994	299	249	49	10	11	11	9		
Latin America	1995–1996	39	145	37	4	25	24	1	2	
Europe	1997–1999	291	2,089	56	14	13	7	2	1	1
Norway	1991–2003	259	1,415	70	13	6	7	2	<1	<1
Taiwan	1994–2000	33	1,095	50	12	14	21	<1		
Spain	2002–2003	5	351	51	9	23	10	4		
Europe	2001–2004	224	2,515	60	10	12	9	5	1	<1
Asia-Pacific	2001–2004	224	1,344	56	10	16	14	2	<1	<1
Latin America	2001–2004	224	1,565	50	7	16	20	2	4	<1
Denmark	2003–2004	10	307	63	20	4	4	3	<1	<1
Spain	2001–2006	49	1,997	47	12	19	10	5	3	1

^a All studies cited were multicenter surveys.

Erreger-Spektrum

- Candidämie
 - 1995-8, Australien
 - 366 Isolate/361 Pat.
 - Mortality 25 %
 - Chirurgie: 126 Isolate
 - C. albicans 69%
 - C. glabrata 12%
 - C. parapsilosis 10%
 - „Schimmel“
 - N=43, keine epidem. Abgaben, Neutropenie
- „Interne“: 185 Isolate
 - C. albicans 52 %
 - C. glabrata 14%
 - C. parapsilosis 16 %
 - C. tropicalis 4%
- Haematol. 53 Isolate
 - C. albicans 43 %
 - C. krusei 27 %
 - C. parapsilosis 9 %
 - C. glabrata 7%
 - C. guilliermondii 5 %

Candidämie im Universitätsspital AKH Wien 2001-2006



Empfindlichkeit von Blutkulturisolaten

Table 3. MIC ranges and MIC₅₀ and MIC₉₀ values (mg/L) for 1025 fungal isolates

	Amphotericin B			Caspofungin			Fluconazole			Itraconazole			Voriconazole ^a		
	Range	MIC ₅₀	MIC ₉₀	Range	MIC ₅₀	MIC ₉₀	Range	MIC ₅₀	MIC ₉₀	Range	MIC ₅₀	MIC ₉₀	Range	MIC ₅₀	MIC ₉₀
<i>Candida albicans</i>	≤0.06–1	0.25	0.5	≤0.06–1	0.25	0.5	≤0.125–>16	0.25	0.5	≤0.03–0.25	≤0.03	0.06	≤0.03–0.125	≤0.03	≤0.03
<i>Candida dubliniensis</i>	≤0.06–0.25	≤0.06	0.125	≤0.06–1	0.5	1	≤0.125–1	0.25	1	≤0.03–0.06	≤0.03	0.03	≤0.03	≤0.03	≤0.03
<i>Candida glabrata</i>	≤0.06–2	0.25	0.5	0 ≤ 0.06–2	0.5	1	0.5–>16	8	>16	≤0.03–>4	1	2	≤0.03–>4	0.25	1
<i>Candida krusei</i>	0.25–2	1	1	0.25–2	0.5	2	1–>16	>16	>16	≤0.03–0.5	0.25	0.5	0.06–1	0.25	1
<i>Candida parapsilosis</i>	≤0.06–1	0.5	1	0.25–>8	2	2	0.125–>16	1	4	≤0.03–0.125	0.06	0.125	≤0.03–0.25	≤0.03	0.06
<i>Candida tropicalis</i>	0.125–1	0.5	1	≤0.06–2	0.5	1	0.125–>16	1	2	≤0.03–1	0.03	0.25	≤0.03–2	≤0.03	0.25
<i>Candida</i> spp.	≤0.06–1	0.25	1	0.125–4	1	2	≤0.125–>16	1	>16	≤0.03–>4	0.125	1	≤0.03–2	≤0.03	0.25
Other fungi	≤0.06–2	0.5	2	0.5–>8	4	>8	1–>16	8	>16	≤0.03–>4	0.5	>4	≤0.03–4	0.5	4

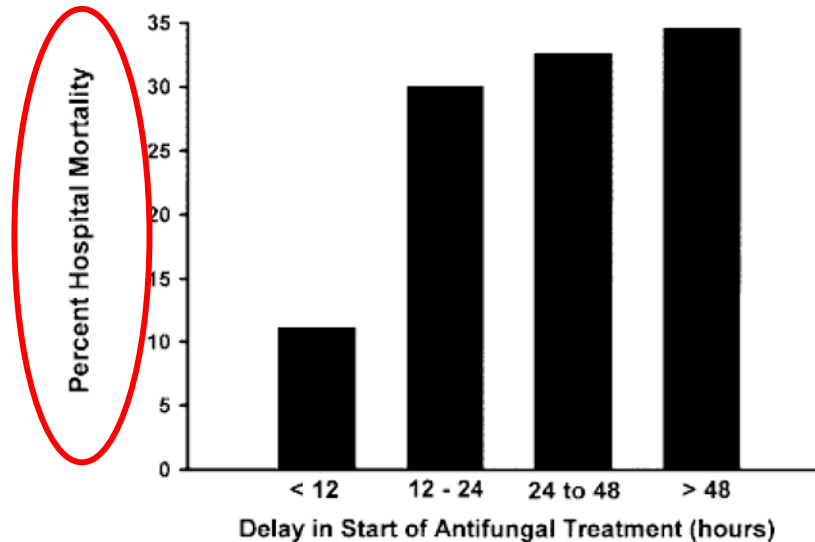
Arendrup et al., CMI 2008; Feb epubl.

Table 2. Antifungal susceptibilities of 561 clinical isolates of fungal species by the CLSI reference microdilution method

	MIC ₅₀	MIC ₉₀	Range of MICs	No. (%) of isolates	
				R	S-DD
Flucytosine	<0.125	2	<0.125 to >16	25 (4.5%)	10 (1.8%)
Fluconazole	0.5	16	<0.25 to >64	21 (3.7%)	33 (5.9%)
Itraconazole	0.125	1	0.0313 to 16	99 (17.6%)	107 (19.1%)
Voriconazole	0.0313	0.5	<0.0313 to 16	2 (0.4%)	3 (0.5%)
Amphotericin B	0.5	1	<0.0313 to 4	3 (0.5%)	
Caspofungin	0.0313	0.25	<0.0313 to 16	ND	ND

Borg-Von Zeppelin, JAC 2007; 60:424

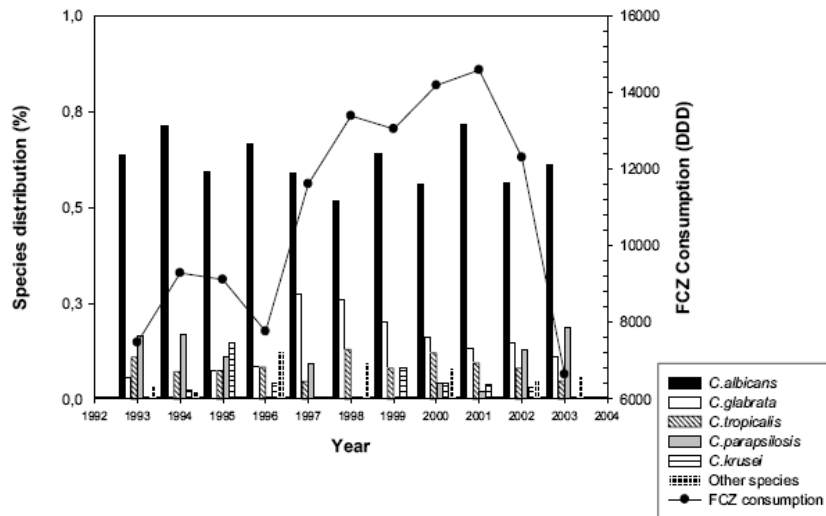
Stellenwert der rechtzeitigen und richtigen Therapie



- Morrell et al.: 157 Patienten mit Candidämie
- 9 patients received „appropriate antifungal therapy“ within 12 hours (vs. 148 patients after 12h)
- Hospital mortality 31.8% (n=50), attributed to Candida infection n=11

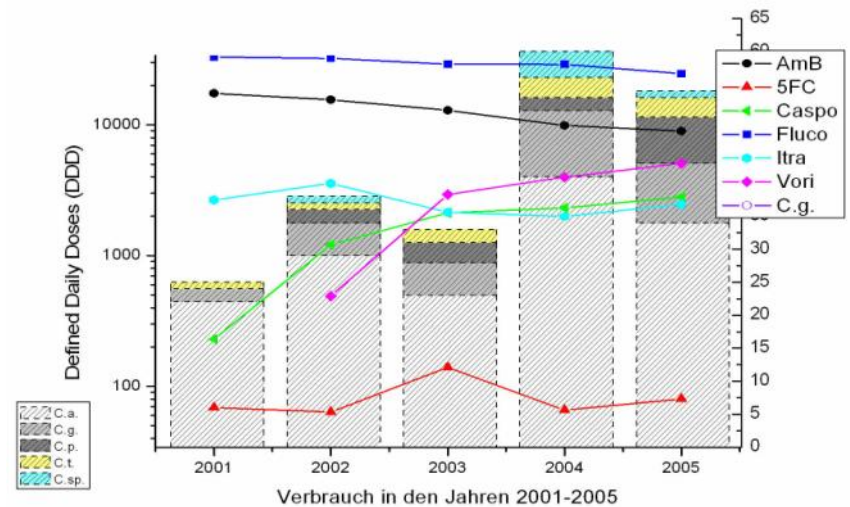
Non-albicans Candida und Fluconazol

Candidämie – Lille FR



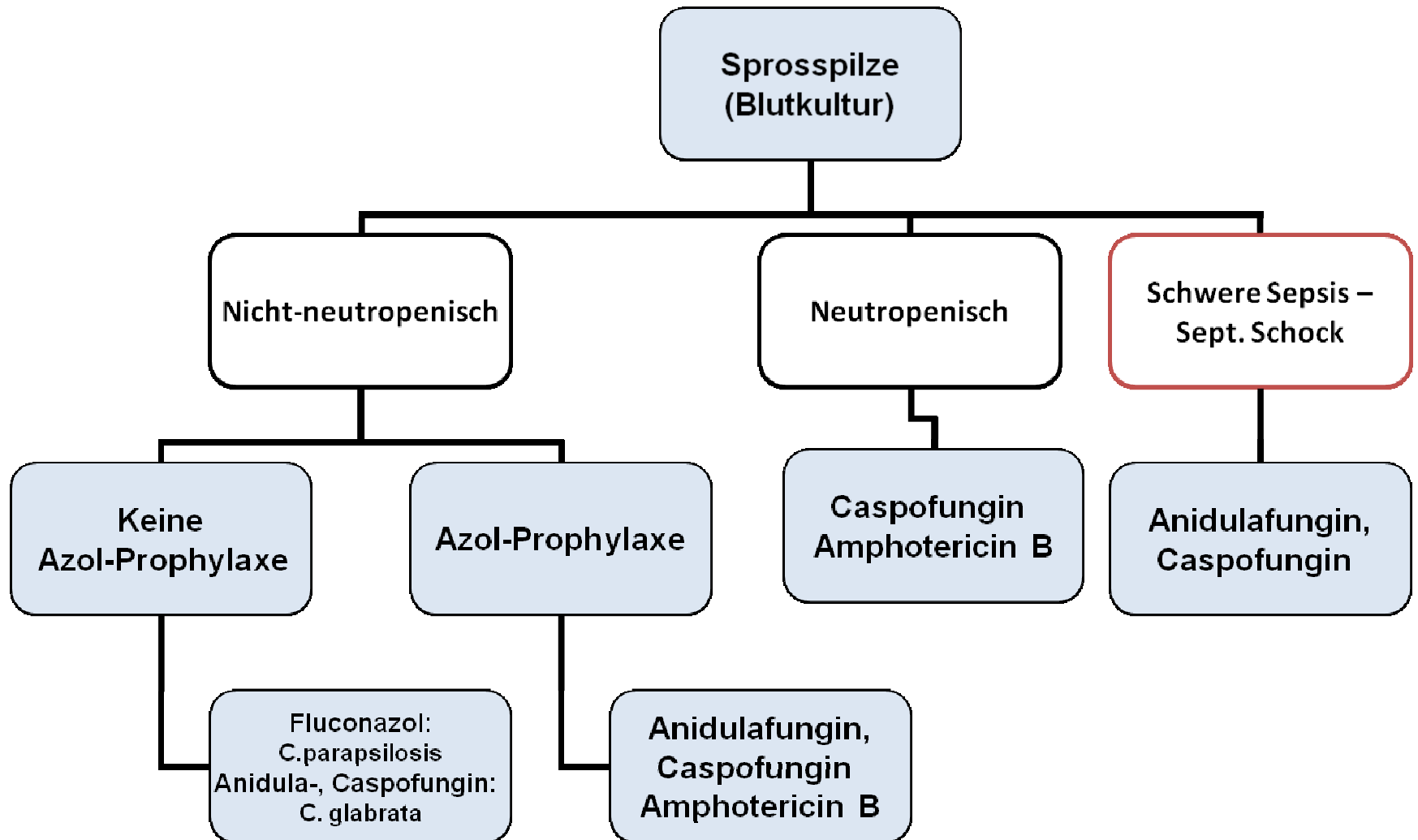
Sendid et al. BMC 2006

Candidämie AKH Wien

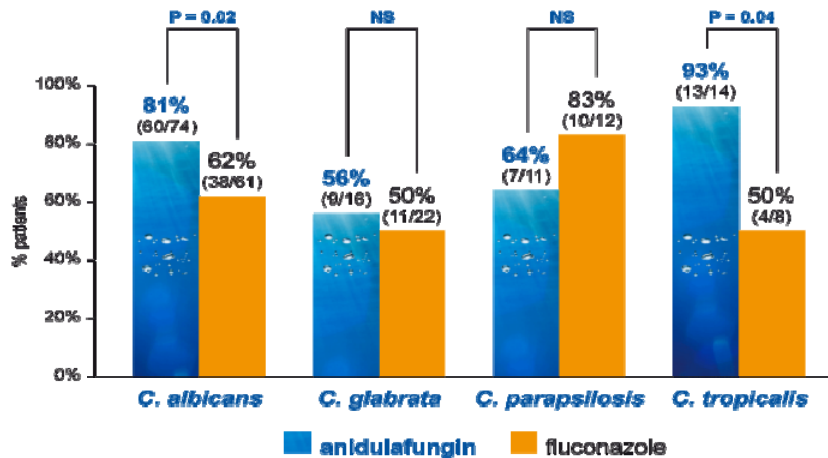


Presterl et al. CMI 2007

Therapie - Empfehlungen



Candine – die Rettung ?



Protocol 014: Efficacy by *Candida* pathogen

Pathogen	Caspofungin		Amphotericin B	
	n/m	(%)	n/m	(%)
<i>C. albicans</i>	23/36	(64)	34/59	(58)
<i>C. parapsilosis</i>	14/20	(70)	13/20	(66)
<i>C. tropicalis</i>	17/20	(85)	10/14	(71)
<i>C. glabrata</i>	10/13	(77)	8/10	(80)
<i>C. guilliermondii</i>	3/3	(100)	1/1	(100)
<i>C. krusei</i>	4/4	(100)	0/1	(0)
Mixed infection	3/3	(100)	2/4	(50)

Study	Species	Infection type	No. of isolates	Echinocandin MIC range ($\mu\text{g/ml}$) ^b
Moudgal et al. (167)	<i>C. parapsilosis</i>	Endocarditis	6	2–>16*
Dodgson et al. (63)	<i>C. glabrata</i>	Candidemia	15	0.12–>8*
Krogh-Madsen et al. (120)	<i>C. glabrata</i>	Candidemia	4	0.5–>8*
Hernandez et al. (102)	<i>C. albicans</i>	Esophagitis	3	0.25–>64*
Laverdiere et al. (126)	<i>C. albicans</i>	Esophagitis	4	0.03–2†

Oder Amphotericin B ?

Species	No. of isolates tested	MIC ($\mu\text{g/ml}$) ^b	
		50%	90%
<i>C. albicans</i>	4,195	0.5	1
<i>C. glabrata</i>	949	2	4
<i>C. krusei</i>	234	4	8
<i>C. lusitaniae</i>	103	0.25	1
<i>C. dubliniensis</i>	101	0.25	0.5
<i>C. guilliermondii</i>	102	0.25	1
<i>C. rugosa</i>	13	1	4

Virulenzfaktoren ? – Non-albicans Candida

- Biofilm-Bildung ?
 - 294 Patienten - Candidämie - Letalität
 - assoziiert mit inädaquater Therapie
 - Biofilm
 - C. albicans
 - C. parapsilosis
 - AP III
- C. parapsilosis
 - Biofilme, SAP – assoziiert mit Letalität
- ...

Tumbarello et al., J Clin Microbiol 2007; 45: 1843
Kuhn et al., Emerg ID 2004; 10:1074

Zusammenfassung

- Non-albicans Candida immer spezifizieren
- Lokale Epidemiologie
 - Krankenhaus – Hämatologie - IBS
- Identifikation von weiteren Risikofaktoren bzw. gefährdeten Patienten
 - Therapie – Prophylaxe ?
- Analyse der spezifischen Ökologie und Eigenschaften von Non-albicans Candida-Arten