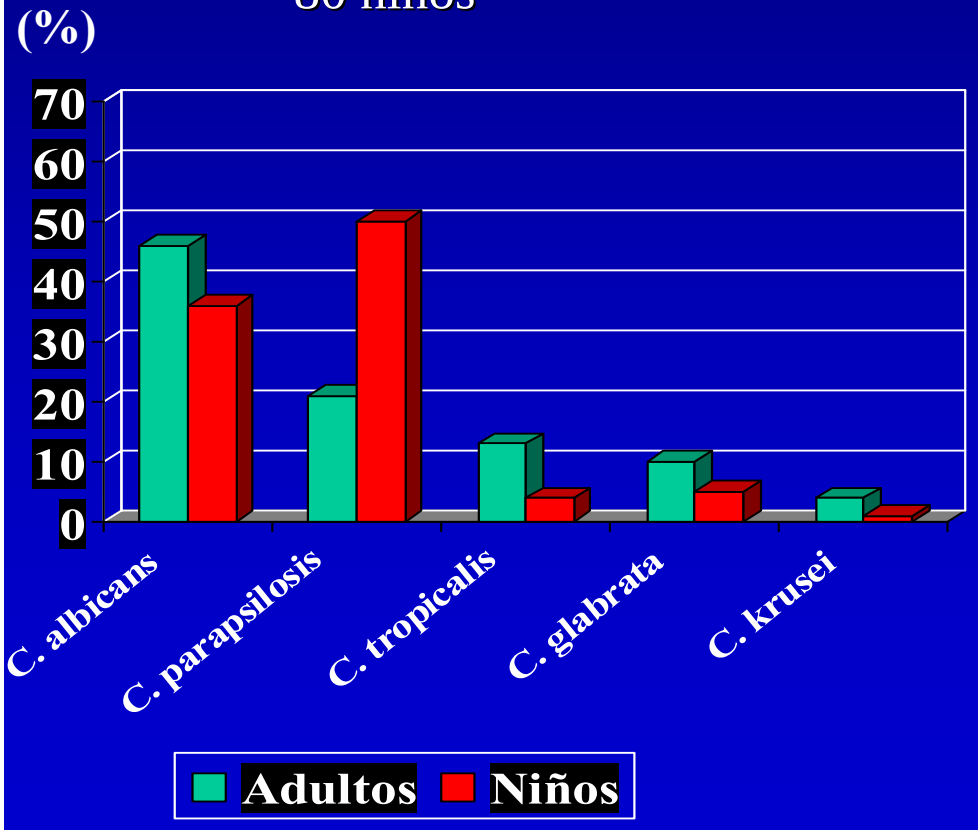
CANDIDEMIA ASOCIADA A CATÉTER

Jesús Fortún. Servicio de Enfermedades Infecciosas
Hospital Ramón y Cajal. Madrid

CANDIDEMIA EN ESPAÑA

Pemán et al. Rev Iberoam Micol 2002

- 290 episodios: 19 hospitales (8 CCAA): 1997-1999
  - 210 adultos
  - 80 niños



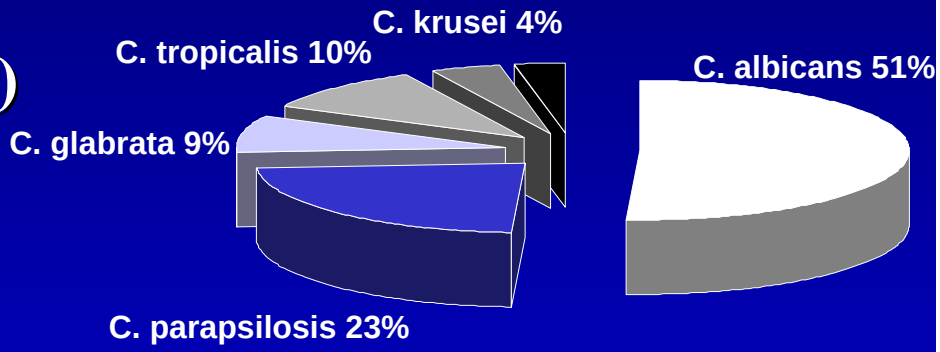
	Adultos	Niños
Factor de riesgo:		
Catéter IV:	77,6	96
Central	82,2	92,0
Periférico	17,1	6,2
Antibioterapia previa	73,3	87,5
Estancia en UCI:	40,5	60
Habitación individual	8,2	47,9
Habitación múltiple	86,0	52,1
Corticoterapia	20,5	17,5
Cirugía	31,9	27,5
Trasplante	7,6	5
Quemados	1,4	-
Inmadurez fetal	-	38,8
Enfermedad de base:		
Tumor sólido	17,6	8,7
Hematológica	11,9	18,8
Infección VIH	5,2	1,3

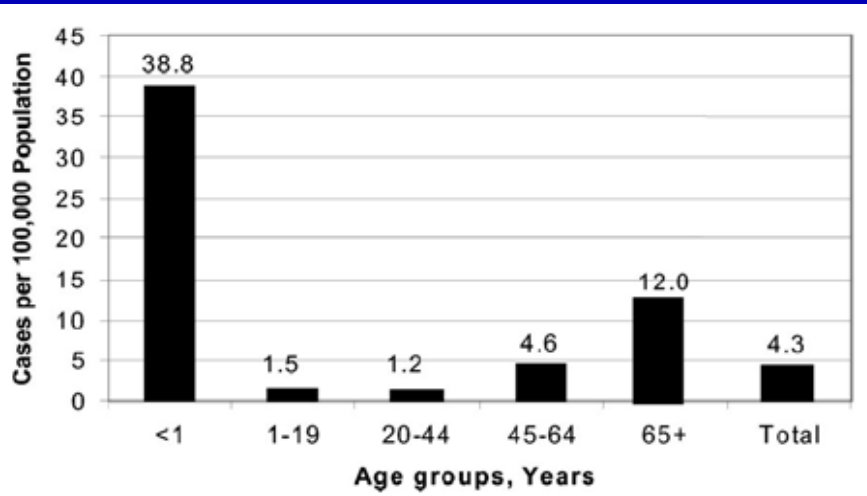
JOURNAL OF CLINICAL MICROBIOLOGY, Apr. 2005, p. 1829–1835 Vol. 43, No. 4
0095-1137/05/$08.00+0 doi:10.1128/JCM.43.4.1829–1835.2005

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†

- **354 episodios de candidemia (2 a)**
  - **4,3 casos x 100.000 habitantes**
    - ✓ **38 x 100.000 en <1 año**
    - ✓ **12 x 100.000 en >65 años**
  - **0,53 casos x 1.000 altas hospitalarias;**
  - **0,73 casos x 10.000 pacientes-día**
- **11% episodios origen comunitario**
- **33% episodios en UCI**
- **Mortalidad 44%**





JOURNAL OF CLINICAL MICROBIOLOGY, May 2006, p. 1681–1685 Vol. 44, No. 5
0095-1137/06/$08.00+0 doi:10.1128/JCM.44.5.1681–1685.2006
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Epidemiology, Risk Factors, and Prognosis of *Candida parapsilosis* Bloodstream Infections: Case-Control Population-Based Surveillance Study of Patients in Barcelona, Spain, from 2002 to 2003

Benito Almirante,[1]* Dolors Rodríguez,[1] Manuel Cuenca-Estrella,[2] Manel Almela,[3] Ferran Sanchez,[4] Josefina Ayats,[5] Carles Alonso-Tarres,[6] Juan L. Rodriguez-Tudela,[2] Albert Pahissa,[1] and the Barcelona Candidemia Project Study Group

78 candidemias por *C. parapsilosis*
175 candidemias por *C. albicans*

Factores de riesgo Candidemia por *C. parapsilosis*:

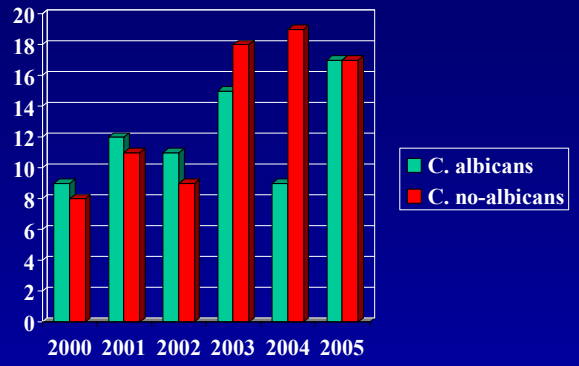
- Neonatos (OR: 7,5 IC95%: 2,1-26,8)
- Trasplante (OR: 9,2 IC95%: 1,9-43,3)
- Antifúngico previo (OR: 5,4 IC95%: 1,8-15,9)
- Nutrición parenteral (OR: 2,2 IC95%: 1,09-4,6)

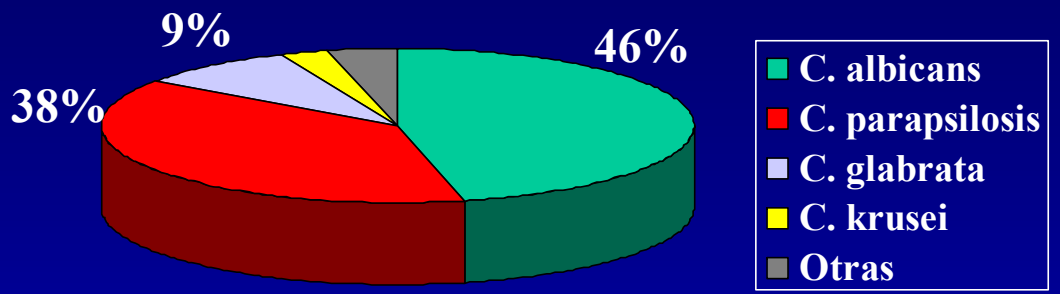
Mortalidad menor: 23% vs 43% ($p<0,01$)

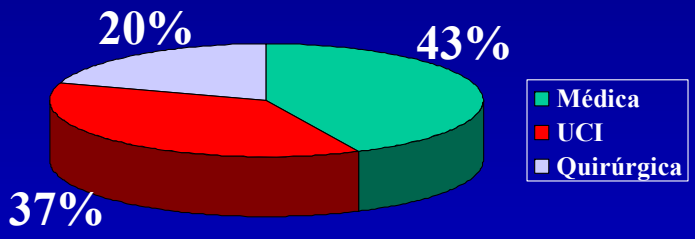
CANDIDEMIA: Hospital Ramón y Cajal

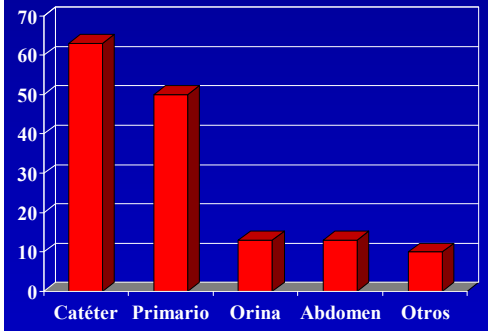
Martín-Dávila et al. ECCMID 2008

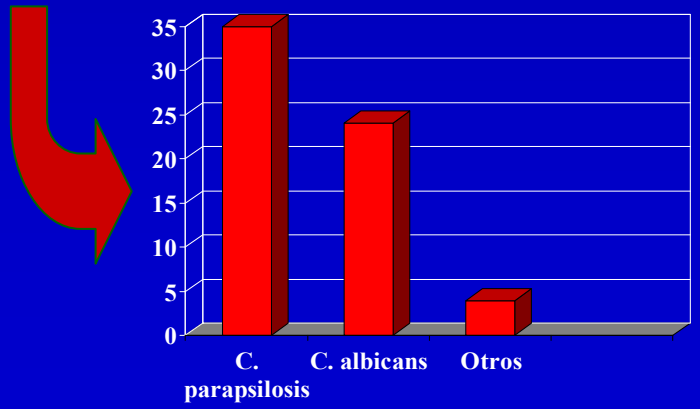
Periodo: 2000-2005: 157 episodios



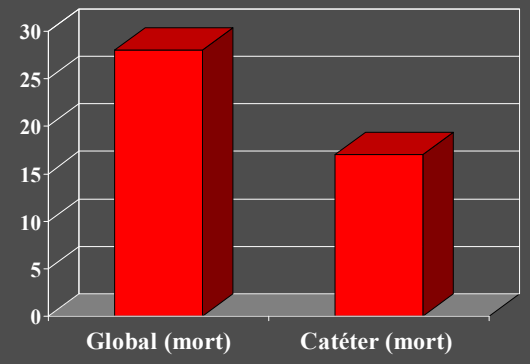








Mortalidad (A. multiv)



-Edad >50:
-Shock séptico
-Foco metastásico
-Antifúngico < 5días
-No asociada catéter

CANDIDEMIA
-Mortalidad en adultos y niños con cáncer-

Adultos (99) y niños (130) con cáncer y candidemia

Mortalidad:

C. albicans:	**16,7 %**	
C. no-albicans:	**22,1 %**	**p: ns**

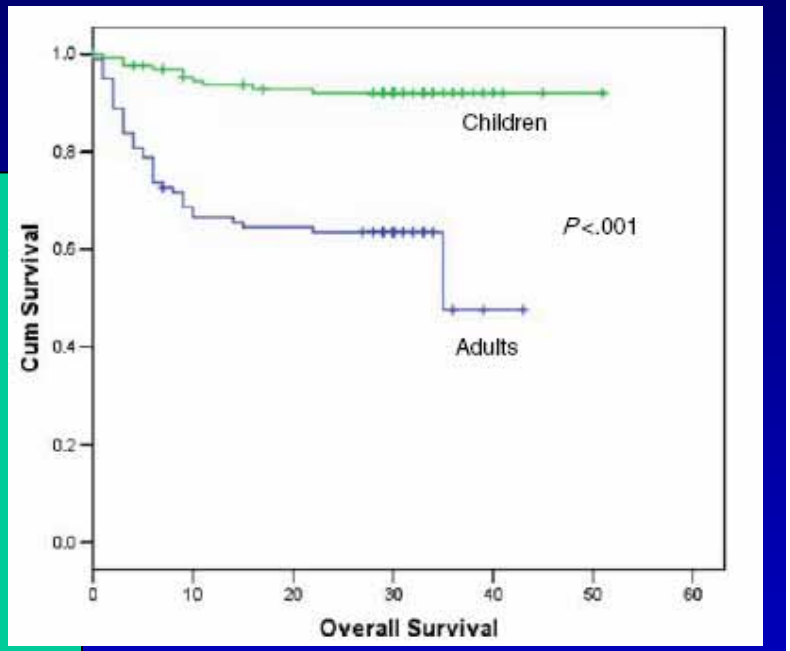
C. glabrata:	**57,1 %**	
C. krusei:	**50,0 %**	
C. tropicalis:	**38,5 %**	
C. parapsilosis:	**7,1 %**	**p<0,01**

Mortalidad adultos:

Comorbilidad:	**OR: 2,6 (IC95%: 14-4,6)**
Neutropenia:	**OR: 10,2 (IC95%:1,5-58)**

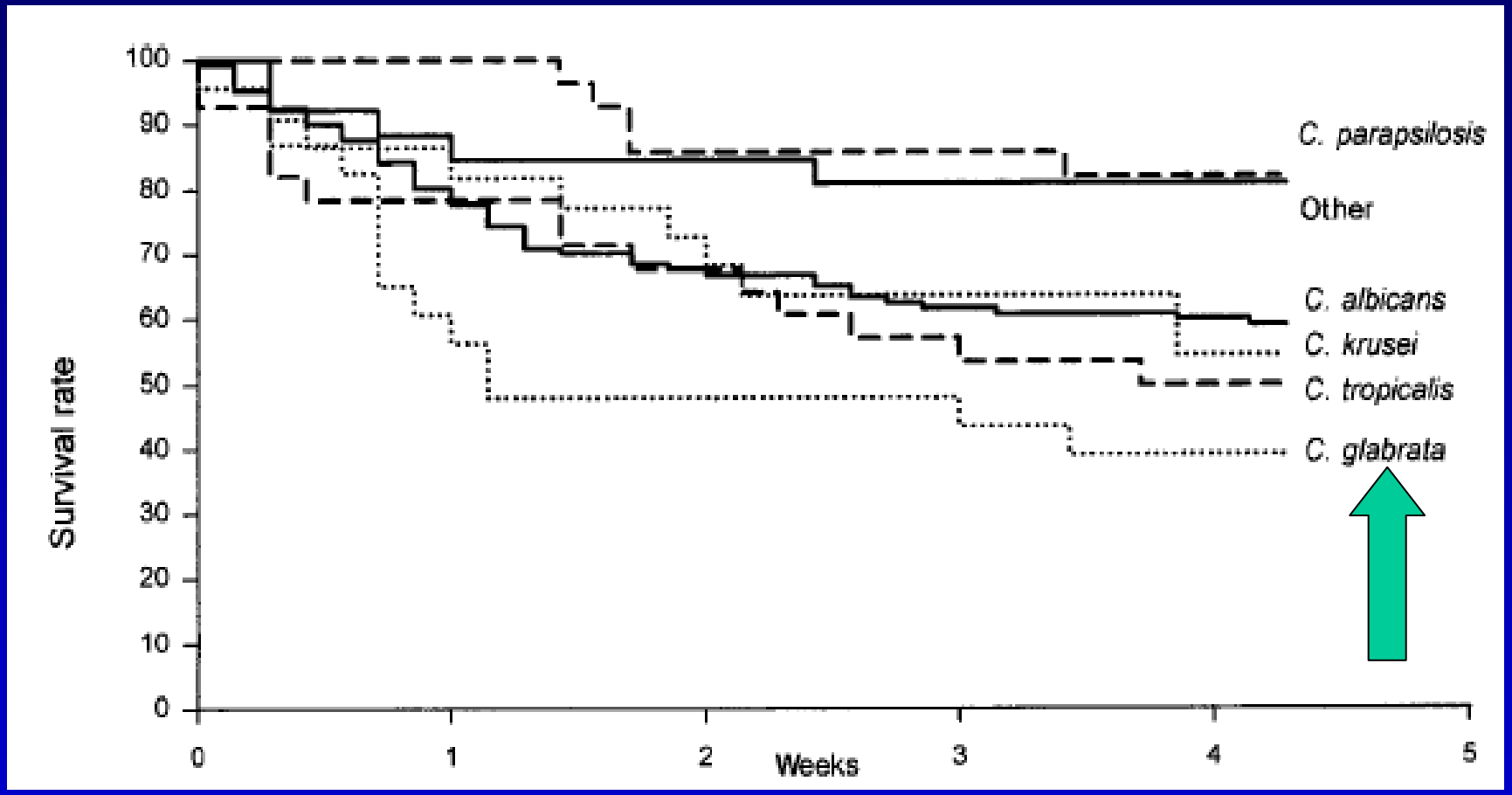
Mortalidad niños:

Comorbilidad:	**OR: 2,2 (IC95%: 1,2-4,0)**



Velasco et al.
Eur J Clin Microbiol 2008

Mortalidad de las diferentes especies de *Candida* en pacientes con cancer (EORTC)



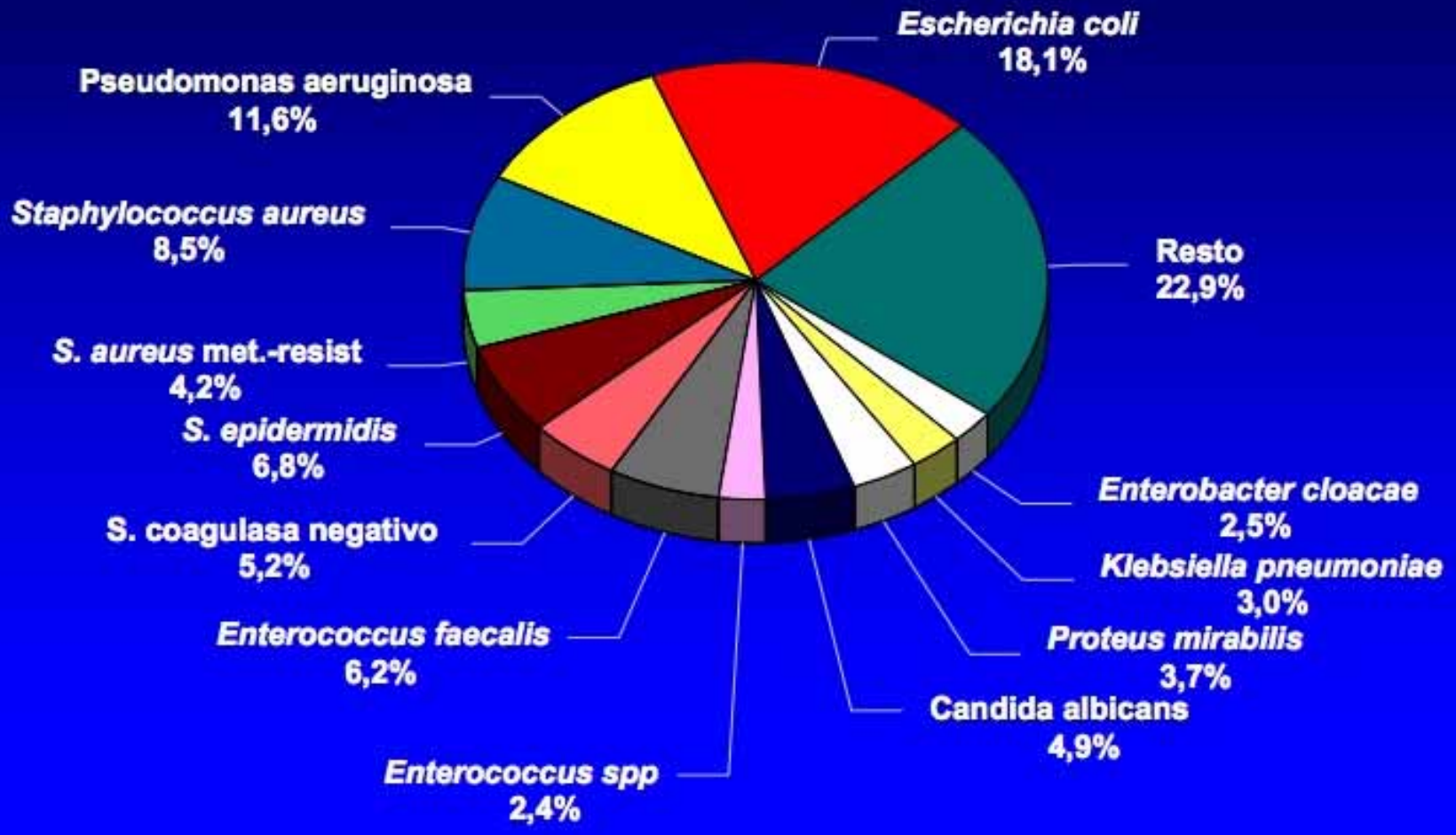
Viscoli C. Clin Infect Dis 1998

Candidiasis en pacientes oncológicos: Anderson Center, USA *Hachem et al, Cancer 2008*

	Onco-hematología (281)	Tumores sólidos (354)	p
Edad	53,0	53,3	ns
APACHE II	15,3	13,4	<,001
Requerimiento UCI	46%	32%	,001
Uso corticoides	42%	21%	<,001
Candidemia-catéter	12%	36%	<,001
Profilaxis Fluconazol	54%	16%	<,001
Neutropenia coincidente	75%	20%	<,001
Respuesta a antifúngicos	49%	73%	<,001

LOS DIEZ PATÓGENOS MÁS FRECUENTES ASOCIADOS A LAS INFECCIONES NOSOCOMIALES

Resultados agregados 1990-2008. Distribución porcentual %



PREVALENCIA DE INFECCIÓN NOSOCOMIAL POR PATÓGENOS SELECCIONADOS
EPINE 1990-2008

	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
Acinetobacter baumannii	1,4	1,5	2,2	2,0	1,5	2,1	2,0	3,1	2,6	2,8	3,1	2,8	2,6	2,5	2,7	3,5	2,6	4,1	2,8
S. aureus meticilina-resist.	0,4	1,4	2,3	2,1	1,7	1,3	1,8	2,0	2,5	3,4	3,1	3,5	4,8	4,0	4,0	4,6	4,7	5,1	4,8
Candida albicans	2,4	3,0	2,7	2,5	2,3	3,0	2,9	3,1	3,8	3,2	3,3	2,9	3,1	3,6	3,5	5,4	5,8	5,1	5,7

AGENTES CAUSALES

Hampton et al. Surg Clin Noth Am 1988;68:57

Microorganismos	**%**
Staphylococcus coagulasa negativa	27
Staphylococcus aureus	26
Levaduras	17
Enterobacter spp.	7
Serratia spp.	5
Enterococcus spp.	5
Klebsiella spp.	4
Streptococcus grupo *viridans*	3
Pseudomonas spp.	3
Proteus spp.	2
Otros	1

Etiología y lugar de cateterización

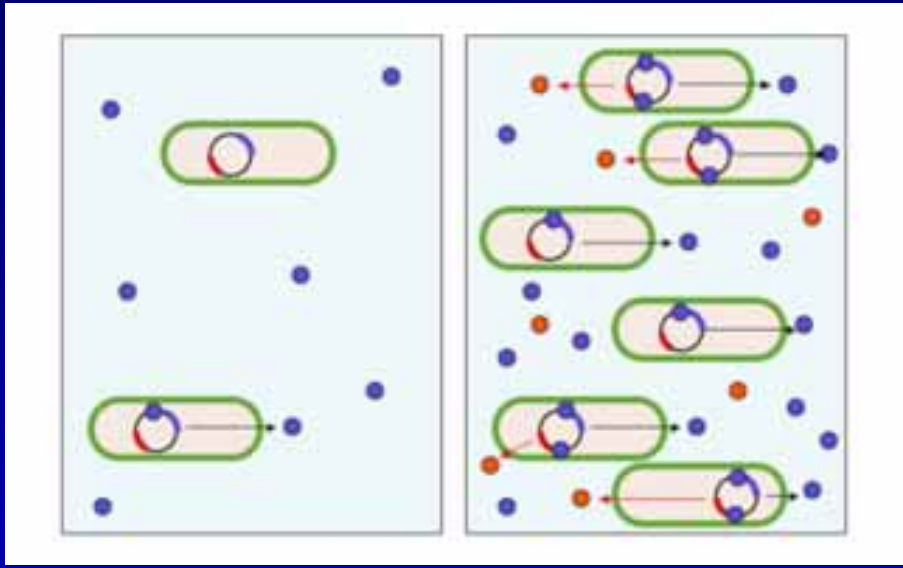
- UCI polivalente
- 88 BAC
  - 36 catéter femoral
  - 52 catéter yugular o subclavia
- Ajuste por APACHE, días ingreso, pat. Base

	Femoral	Yugular/subclavia	p
BGN	14/36 (39%)	4/52 (8%)	0,001
Levaduras	6/36 (17%)	1/52 (2%)	0,035

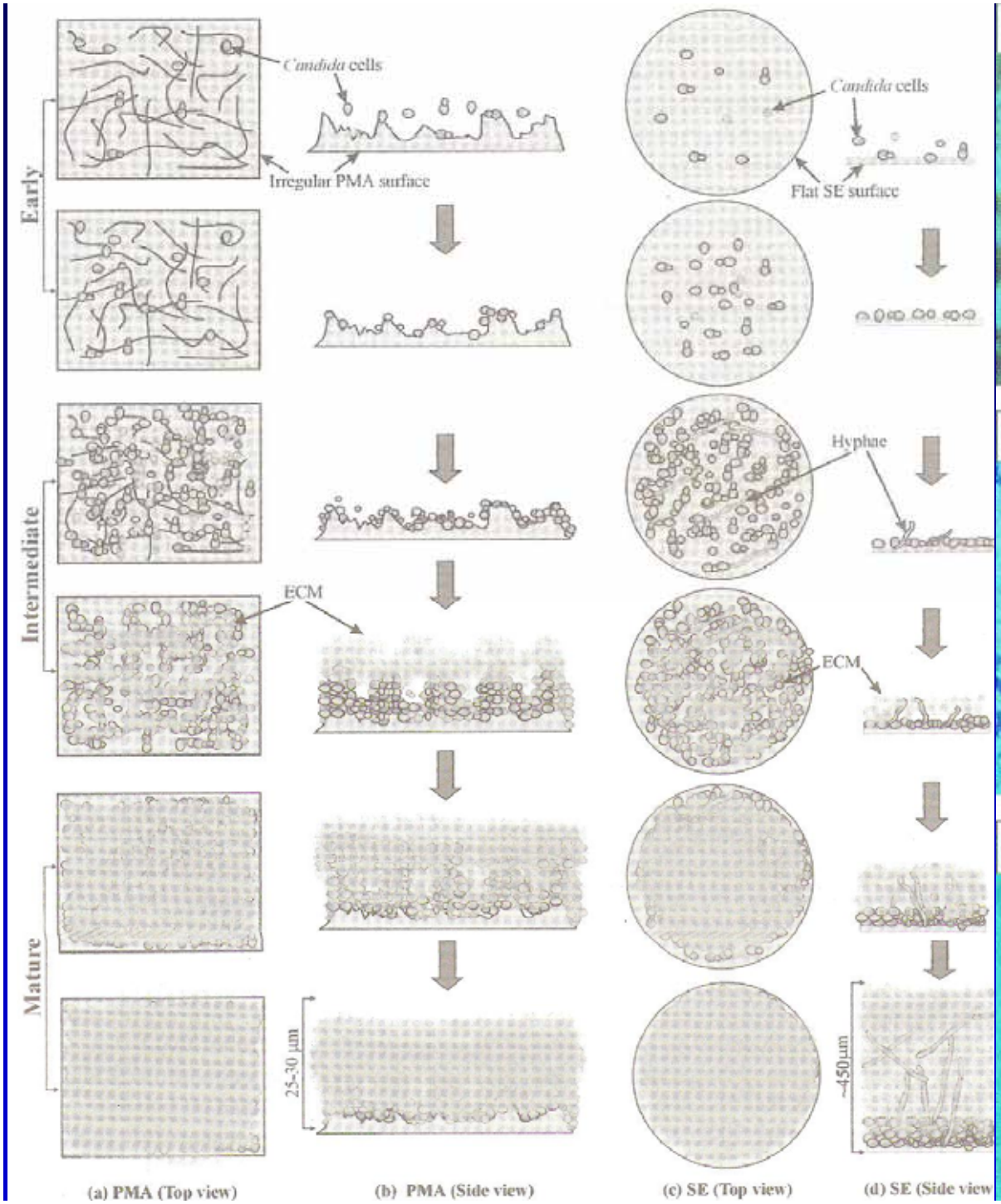
Lorente et al. Crit Care Med 2007

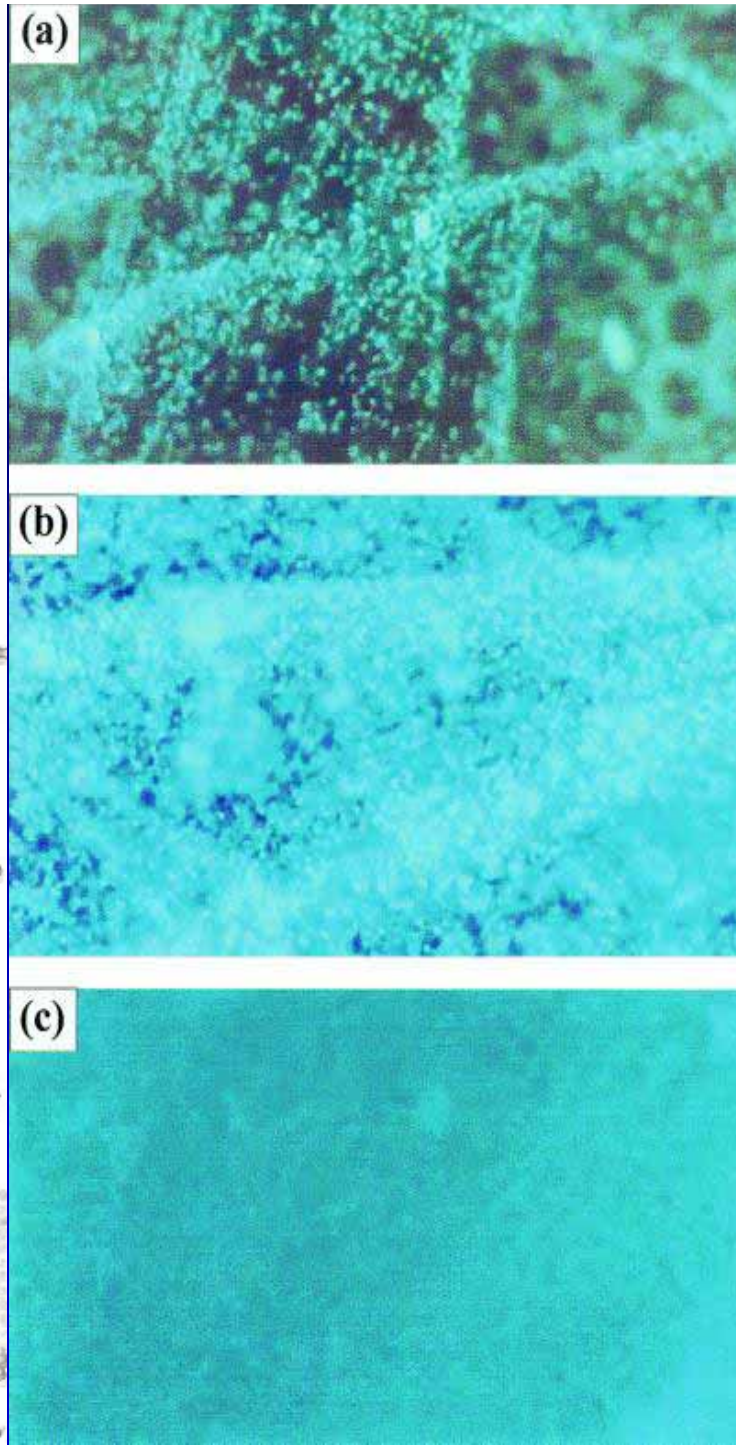
CANDIDA Y BIOFILMS

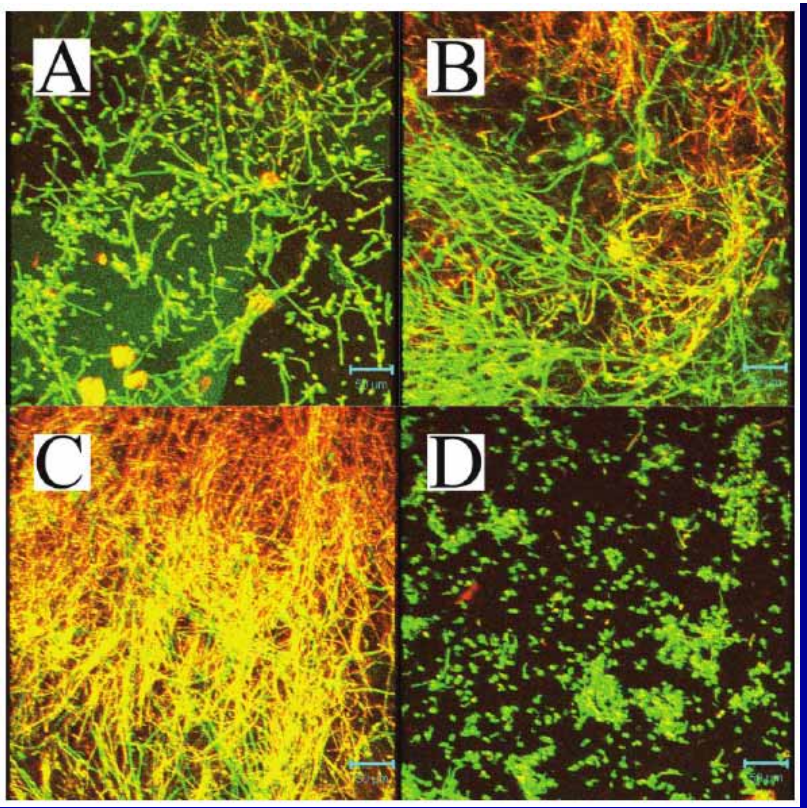
- Quorum-sensing :
  - En *P. aeruginosa, B. cepacia*:
    - ✓Acil-homoserina-lactona
  - En S. *aureus, E. faecalis*.
    - ✓ Oligopéptidos
  - en *Candida albicans*
    - ✓Tirosol: favorece filamantación y biofilm
      - – Farnesol: bloquea filamantación y biofilm
    - ✓Ác. Grasos: favorece filamentación
      - – Cerulenina: bloquea filamantación



Alem MA et al. Eukaryotic Cell 2006

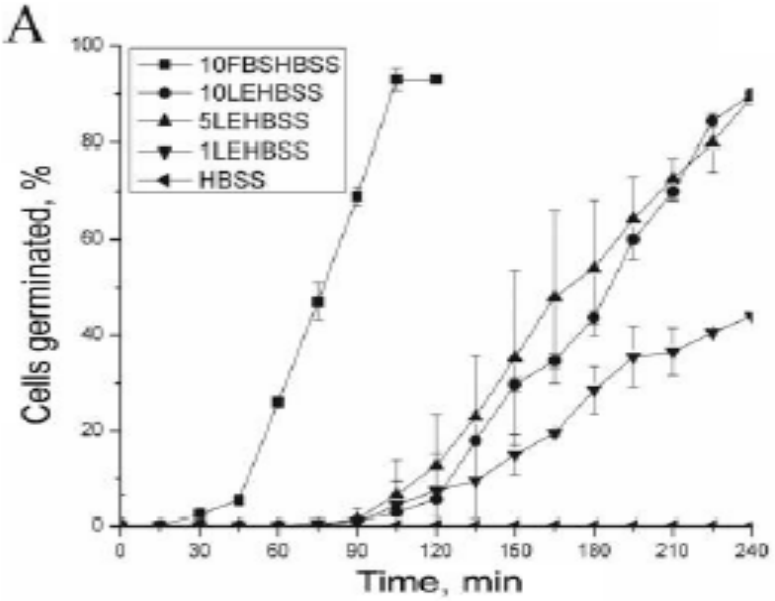

Early
Intermediate
Mature
Candida cells
Irregular PMA surface
ECM
25-30 μm
Candida cells
Flat SE surface
Hyphae
ECM
~450μm
(a) PMA (Top view)
(b) PMA (Side view)
(c) SE (Top view)
(d) SE (Side view


(a)
(b)
(c)



Candida albicans y Biofilms con EL

- sin emulsión lipídica (EL)(A), 5% EL (B), 10% LE (C), 10% LE sin dextrosa (D)
- Confocal scanning laser + IF (concanavalina A)



Candida albicans y germinación con EL

- 10% suero fetal bovino
- 10% EL, 5% EL, 1% EL
- Solución salina

Swindell et al. JID 2009

"Replace tubing used to administer blood, blood products, or lipid emulsions (those combined with amino acids and glucose in a 3-in-1 admixture or infused separately) within 24 hours of initiating the infusion (*158*,*226*–*229*). **Category IB**."

"If the solution contains only dextrose and amino acids, the administration set does not need to be replaced more frequently than every 72 hours (*226*). **Category II**"

O´Grady et al. Guidelines for the Prevention of ICRI. MMWR 2002

Mortalidad y producción de biofilm

Tumbarello et al. J Clin Microbiol 2007

- 294 candidemias: 60 (20%) CAC
- Producción biofilm (espectofotometría)
  - C. tropicalis: 20/28 (71%)
  - C. glabrata: 6/26 (23%)
  - C. albicans: 38/168 (23%)
  - C. parapsilosis: 14/64 (22%)
- Mortalidad (an. Multiv.)
  - Antifúngico inadecuado; OR: 2,3 (IC95%:1,1-5,1)
  - Biofilm; OR: 2,3 (IC95%:1,26-4,30)
  - APACHE III; OR: 1,03 (IC95%: 1,01-1,15)

TABLE 3. Crude OR and 95% CI for mortality according to biofilm production by isolates of *Candida* species

Candida species	Patients infected by biofilm-positive isolate		Patients infected by biofilm-negative isolate		OR (95% CI)	P^a
	Total no.	No. (%) who died	Total no.	No. (%) who died		
C. albicans	38	32 (84.2)	130	65 (50)	3.90 (1.72–8.83)	<0.001
C. parapsilosis	14	10 (71.4)	50	14 (28)	4.16 (1.46–11.82)	0.003
C. tropicalis	20	8 (40)	8	4 (50)	0.88 (0.54–1.45)	0.62
C. glabrata	6	4 (66.6)	20	11 (55)	1.46 (0.32–6.62)	0.61
Other[b]	2	2 (100)	6	4 (66.6)		0.34
Total	80	56 (70)	214	98 (45.7)	2.76 (1.55–5.00)	<0.001

Candida parapsilosis

- Menos virulencia que *Candida albicans* en modelos animales

Weems et al. CID 1992

- Mayor adherencia a biomateriales

Critchley et al. FEMS Microbiol Lett 1985

- Proliferación en soluciones ricas en glucosa

Wemms et al, J Clin Microbiol 1987

Candida parapsilosis

- Distribución universal. Habitat: suelo, agua, plantas

- Reservorio hospitalario: desconocido.
  Frecuente aislamiento en manos personal sanitario

  Diekema, Diag Microbiol Infect Dis 1997
  Lewin, Diag Microbiol Infect Dis 1998
  Rangel-Frausto, CID 1999,
  Huang J Hosp Inf 1998)

- Mayores tasas de infección en:
  - Neonatos, con nutrición parenteral, transductores de presión, otros dispositivos intravasculares
  - Brotes epidémicos en UCIs de neonatos

    Welbel et al. Pediatr. Infect. Dis. J.1996

JOURNAL OF CLINICAL MICROBIOLOGY, July 2002, p. 2363–2369 Vol. 40, No. 7
0095-1137/02/$04.00+0 DOI: 10.1128/JCM.40.7.2363–2369.2002
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Horizontal Transmission of *Candida parapsilosis* Candidemia in a Neonatal Intensive Care Unit

Antonella Lupetti,[1] Arianna Tavanti,[1] Paola Davini,[1] Emilia Ghelardi,[1] Valerio Corsini,[1] Ilaria Merusi,[2] Antonio Boldrini,[2] Mario Campa,[1] and Sonia Senesi[1]*

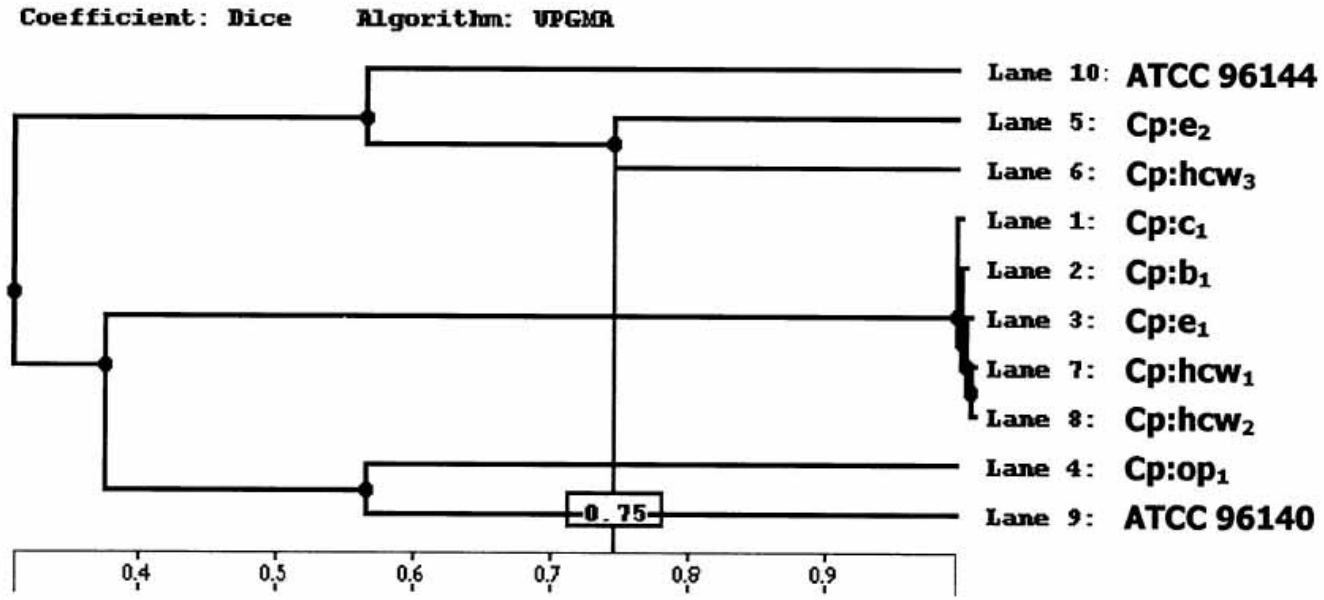
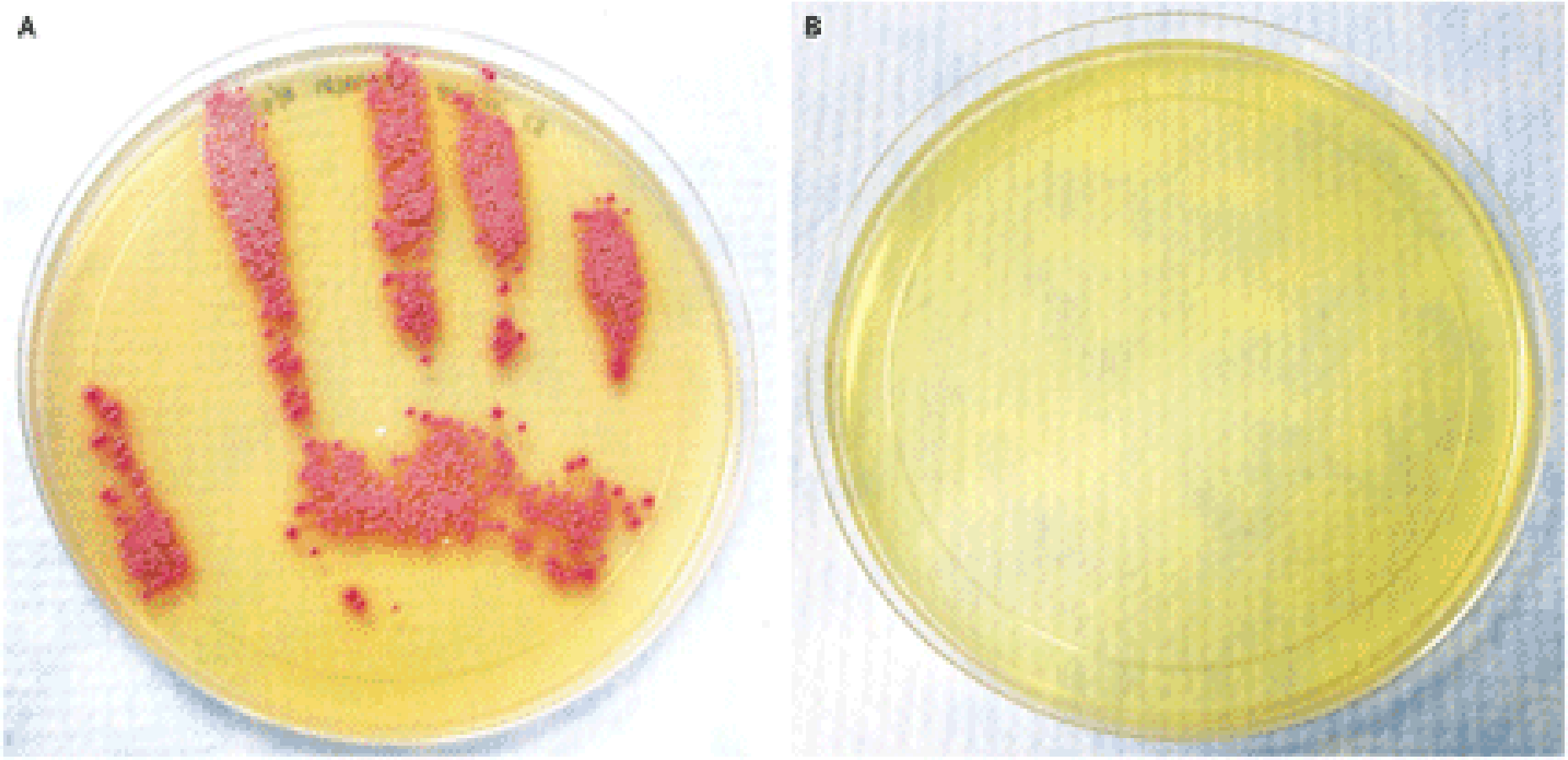
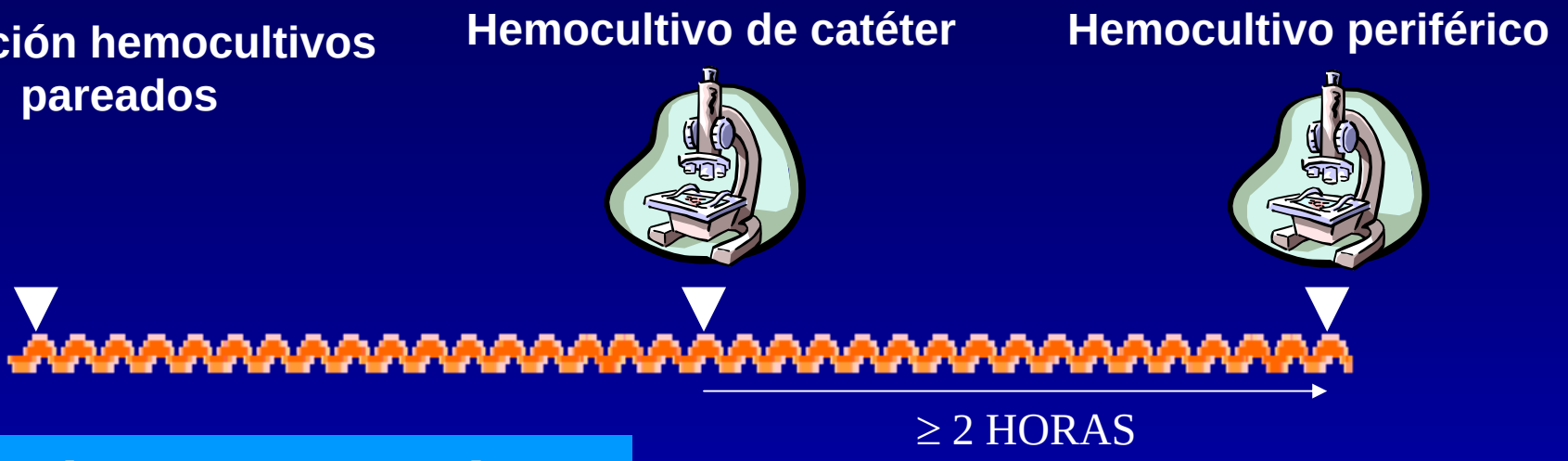


FIG. 3. Electrophoretic separation of DNA products obtained by RAPD-PCR from *C. parapsilosis* strains with RPO2 as a primer. (A) Lanes: M, λ DNA-*Eco*RI/*Hin*dIII used as a marker; 1, 2, 3, 7, and 8, *C. parapsilosis* isolates recovered, respectively, from the conjunctiva (Cp:c1) and blood (Cp:b1) of the newborn with progeria, from the sink area of the NICU (Cp:e1), and from two health care workers of the NICU (Cp:hcw1 and Cp:hcw2); 4, 5, and 6, genetically unrelated strains of *C. parapsilosis* isolated, respectively, from an outpatient (Cp:op1), from the environment of a different ward (Cp:e2), and from one health care worker of the NICU (Cp:hcw3); 9 and 10, reference strains ATCC 96140 and ATCC 96144, respectively. Molecular sizes (in kilobases) are shown to the left of the gel. (B) Dendrogram showing the genetic similarity of the strain collection.



…manos limpias salvan vidas…

Tiempo de Positivización de Hemocultivos



Raad et al. Ann Intern Med 2004

	DTP	BRC Si(n)	BRC No(n)	Sensib.	Especif.	Pos LR	Neg LR
Tipo catéter							
-corta dur.	>120 min	29	3	81 (68-93)	92 (84-100)	10,5 (3,5-31,4)	0,22 (0,1-0,4)
	<120 min	7	36				
-larga dur.	>120 min	67	11	93 (87-99)	75 (62-88)	3,7 (2,2-6,2)	0,09 (0,04-2)
	<120 min	5	33				
Antibioter.							
-no	>120 min	86	9	89 (82-95)	88 (81-95)	7,49 (4,0-13,8)	0,13 (0,07-0,2)
	<120 min	11	67				
-si	>120 min	10	5	91 (74-100)	29 (0-62)	1,27 (0,7-2,1)	0,32 (0,04-2,9)
	<120 min	1	2				

JOURNAL OF CLINICAL MICROBIOLOGY, July 2008, p. 2222–2226 Vol. 46, No. 7
0095-1137/08/$08.00+0 doi:10.1128/JCM.00214-08
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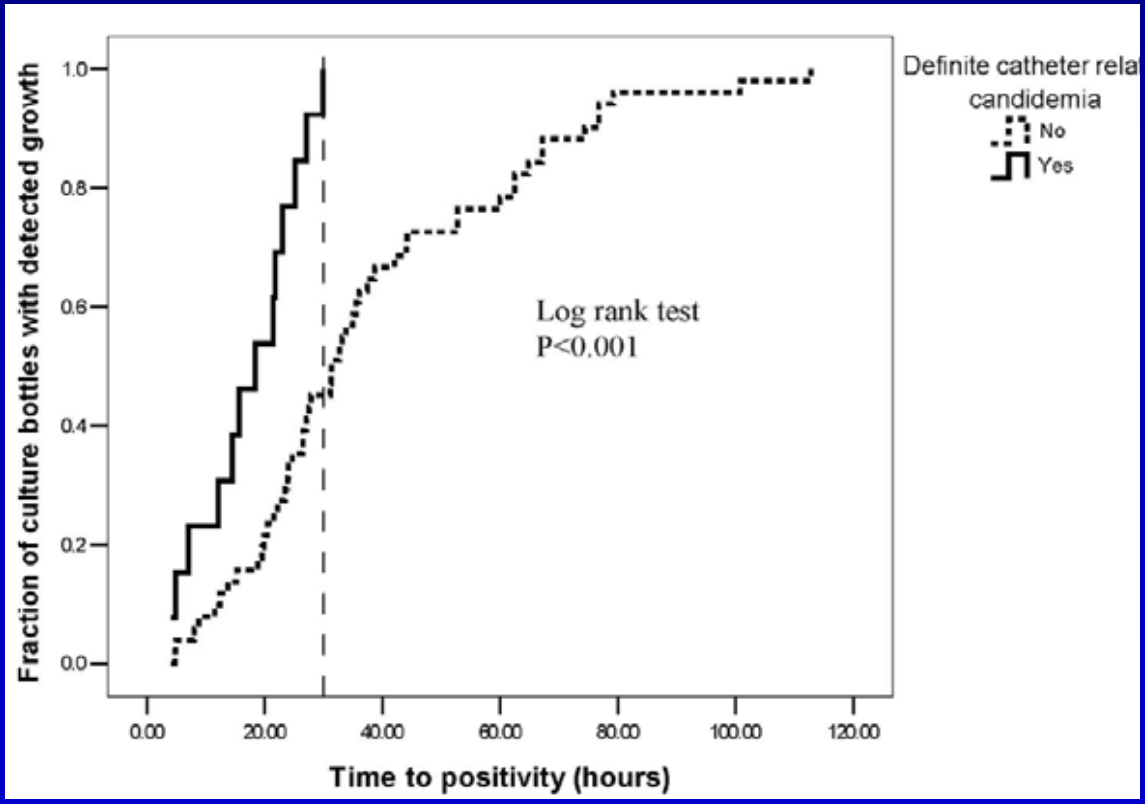
Time to Blood Culture Positivity as a Marker for Catheter-Related Candidemia▽

Ronen Ben-Ami,[1,5]* Miriam Weinberger,[3,5] Ruth Orni-Wasserlauff,[1,2,5] David Schwartz,[2] Avraham Itzhaki,[3] Tzipora Lazarovitch,[4] Edna Bash,[2] Yuval Aharoni,[2] Irina Moroz,[1] and Michael Giladi[1,2,5]



64 episodios de candidemia
- 20%: CRC

TTP:
- CRC: 17,3 ± 2h
- noCRC: 38,2 ± 2h p<0,001

- >30 h, para CRC:
  S: 100%
  E: 51,4%
  VPP: 41,9%
  VPN: 100% ROC: 0,76

- *C. glabrata*: 61,3 vs 25,6 (p<0,001
(8 episodios: todos en noCRC)

IDSA GUIDELINES

Clinical Infectious Diseases 2009; 48:503–35

Clinical Practice Guidelines for the Management of Candidiasis: 2009 Update by the Infectious Diseases Society of America

Peter G. Pappas,[1] Carol A. Kauffman,[2] David Andes,[4] Daniel K. Benjamin, Jr.,[5] Thierry F. Calandra,[11] John E. Edwards, Jr.,[6] Scott G. Filler,[6] John F. Fisher,[7] Bart-Jan Kullberg,[12] Luis Ostrosky-Zeichner,[8] Annette C. Reboli,[9] John H. Rex,[13] Thomas J. Walsh,[10] and Jack D. Sobel[3]

[1]University of Alabama at Birmingham, Birmingham; [2]University of Michigan and Ann Arbor Veterans Administration Health Care System, Ann Arbor, and [3]Wayne State University, Detroit, Michigan; [4]University of Wisconsin, Madison; [5]Duke University Medical Center, Durham, North Carolina; [6]Harbor–University of California at Los Angeles Medical Center, Torrance; [7]Medical College of Georgia, Augusta; [8]University of Texas at Houston, Houston; [9]Cooper Hospital, Camden, New Jersey; [10]National Cancer Institute, Bethesda, Maryland; [11]Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland; [12]Nijmegen University Centre for Infectious Diseases, Nijmegen, The Netherlands; and [13]Astra Zeneca Pharmaceuticals, Manchester, United Kingdom

Central venous catheters should be removed when candidemia is documented, if at all possible [82–84]. The data supporting this are strongest among nonneutropenic patients and show that catheter removal is associated with shorter duration of candidemia [82, 83] and reduced mortality in adults [82, 84] and neonates [85]. Recently completed trials in adults suggest better outcomes and shorter duration of candidemia among patients in whom central venous catheters were removed or replaced [28, 54]. Among neutropenic patients, the role of the gastrointestinal tract as a source for disseminated candidiasis is evident from autopsy studies, but in an individual patient, it is difficult to determine the relative contributions of the gastrointestinal tract versus catheter as primary sources of candidemia [82, 86]. An exception is made for candidemia due to *C. parapsilosis*, which is very frequently associated with catheters [87]. There are no randomized studies on this topic, but the Expert Panel strongly favors catheter removal when feasible. The role for antifungal lock solutions is not well defined.

CID, 1 Mar 2009

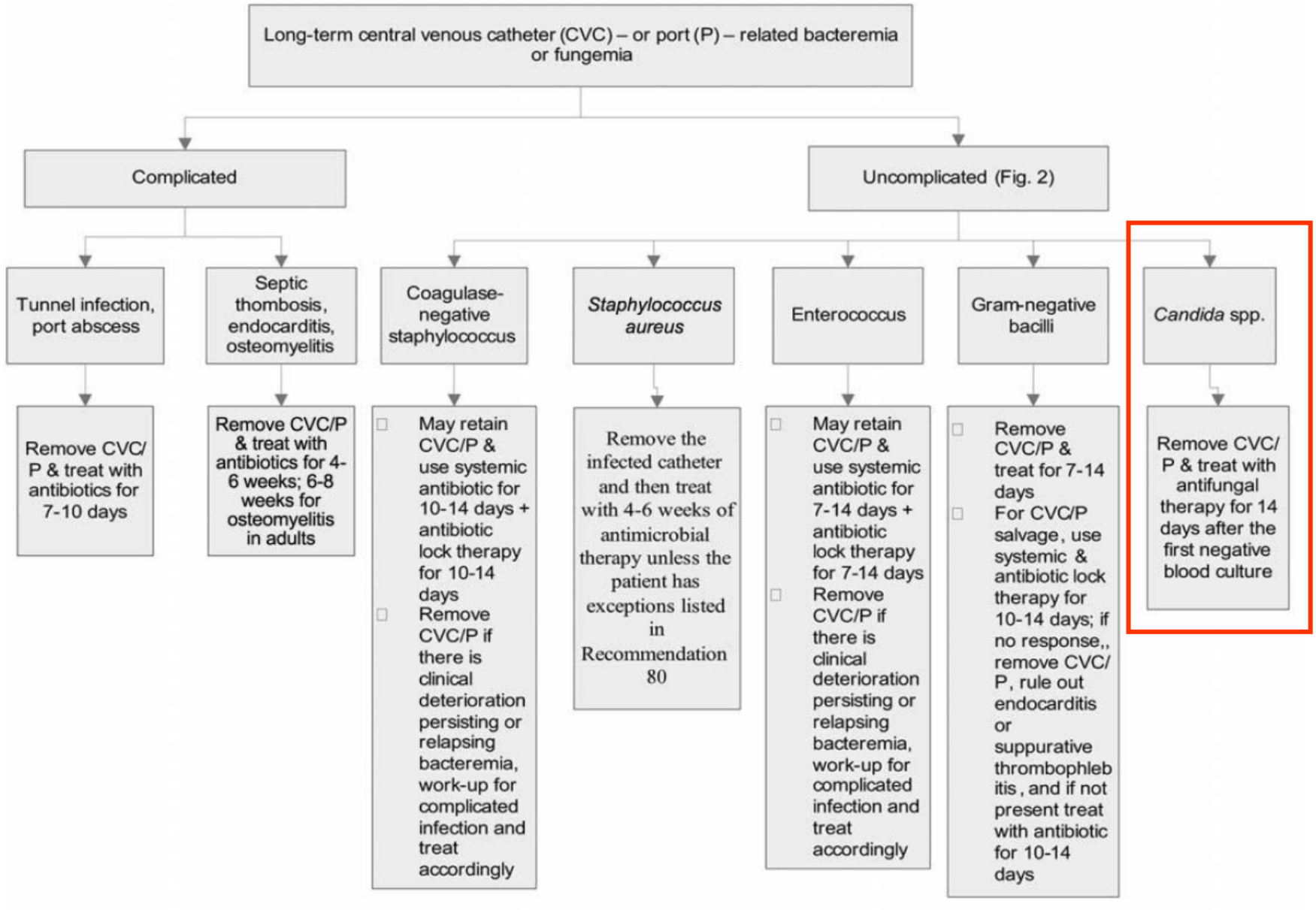
IDSA GUIDELINES

Clinical Infectious Diseases 2009; 49:1–45

Clinical Practice Guidelines for the Diagnosis and Management of Intravascular Catheter-Related Infection: 2009 Update by the Infectious Diseases Society of America

Leonard A. Mermel,[1] Michael Allon,[2] Emilio Bouza,[9] Donald E. Craven,[3] Patricia Flynn,[4] Naomi P. O'Grady,[5] Issam I. Raad,[6] Bart J. A. Rijnders,[10] Robert J. Sherertz,[7] and David K. Warren[8]

[1]Division of Infectious Diseases, Warren Alpert Medical School of Brown University, Providence, Rhode Island; [2]University of Alabama-Birmingham Hospital, Birmingham, Alabama; [3]Tufts University School of Medicine, Lahey Clinic Medical Center, Burlington, Massachusetts; [4]St. Jude Children's Research Hospital, Children's Infection Defense Center, Memphis, Tennessee; [5]National Institutes of Health, Critical Care Medicine Department, Bethesda, Maryland; [6]Section of Infectious Diseases, University of Texas-Cancer Center, Houston; [7]Section of Infectious Diseases, Wake Forest University School of Medicine, Winston-Salem, North Carolina; [8]Division of Infectious Diseases, Washington University School of Medicine, St Louis, Missouri; [9]Servicio de Microbiología Cliínica y E. Infecciosas Hospital General "Gregorio Marañón," Madrid, Spain; and [10]Internal Medicine and Infectious Diseases, Erasmus University Medical Center, Rotterdam, the Netherlands


Long-term central venous catheter (CVC) – or port (P) – related bacteremia or fungemia
Complicated
Uncomplicated (Fig. 2)
Tunnel infection, port abscess
Septic thombosis, endocarditis, osteomyelitis
Coagulase-negative staphylococcus
Staphylococcus aureus
Enterococcus
Gram-negative bacilli
Candida spp.
Remove CVC/P & treat with antibiotics for 7-10 days
Remove CVC/P & treat with antibiotics for 4-6 weeks; 6-8 weeks for osteomyelitis in adults
May retain CVC/P & use systemic antibiotic for 10-14 days + antibiotic lock therapy for 10-14 days
Remove CVC/P if there is clinical deterioration persisting or relapsing bacteremia, work-up for complicated infection and treat accordingly
Remove the infected catheter and then treat with 4-6 weeks of antimicrobial therapy unless the patient has exceptions listed in Recommendation 80
May retain CVC/P & use systemic antibiotic for 7-14 days + antibiotic lock therapy for 7-14 days
Remove CVC/P if there is clinical deterioration persisting or relapsing bacteremia, work-up for complicated infection and treat accordingly
Remove CVC/P & treat for 7-14 days
For CVC/P salvage, use systemic & antibiotic lock therapy for 10-14 days; if no response,, remove CVC/P, rule out endocarditis or suppurative thrombophlebitis, and if not present treat with antibiotic for 10-14 days
Remove CVC/P & treat with antifungal therapy for 14 days after the first negative blood culture

CANDIDEMIA	Evidencia
Candidemia asociada a catéter: retirar y enviar a cultivo	 A-II
Candidemia origen incierto y CVC corta duración: retirar y enviar a cultivo	 A-II
Candidemia origen incierto y accesos venosos limitados: cambio mediante guía retirar si cultivo catéter +	 B-II A-II
Candidemia resuelta tras retirada de catéter: tratamiento antifúngico:	 A-II

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CANDIDEMIA ASOCIADA A CATÉTER
-retirada: reducción de mortalidad -

Nguyen, 1995 prospect	Retención catéter: mayor mortalidad (427 adultos) (p<0,001)
Nucci, 1998 prospect	Retención catéter: mayor mortalidad (145 adultos) [OR: 4,2; 95% IC (2,1-11,6)]
Karkowicz, 2000 prospect	Retención catéter: mayor mortalidad (104 neonatos)
Anaissie, 1998 retrospect	Retención catéter: mayor mortalidad (416 adultos) (p=0,002)
Luzzati, 2000	Retención catéter: mayor mortalidad (189 adultos)

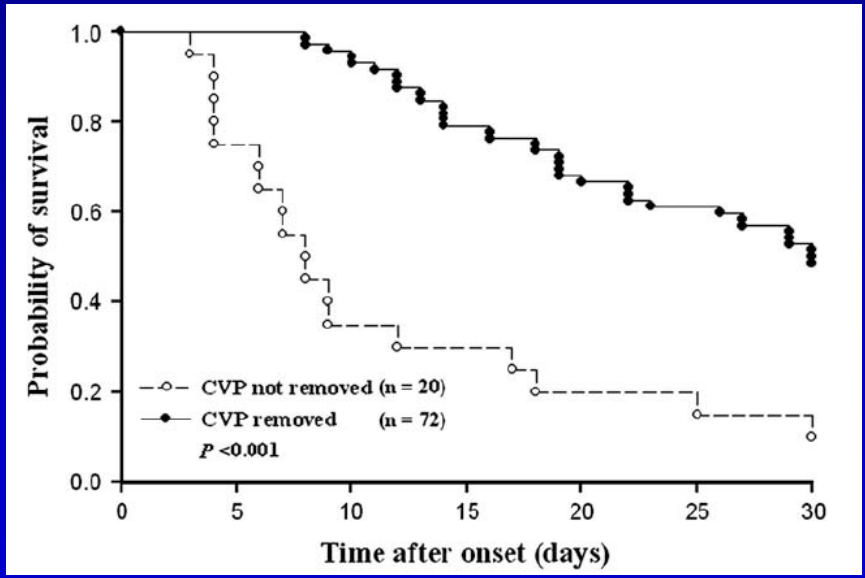
Estudios prospectivos

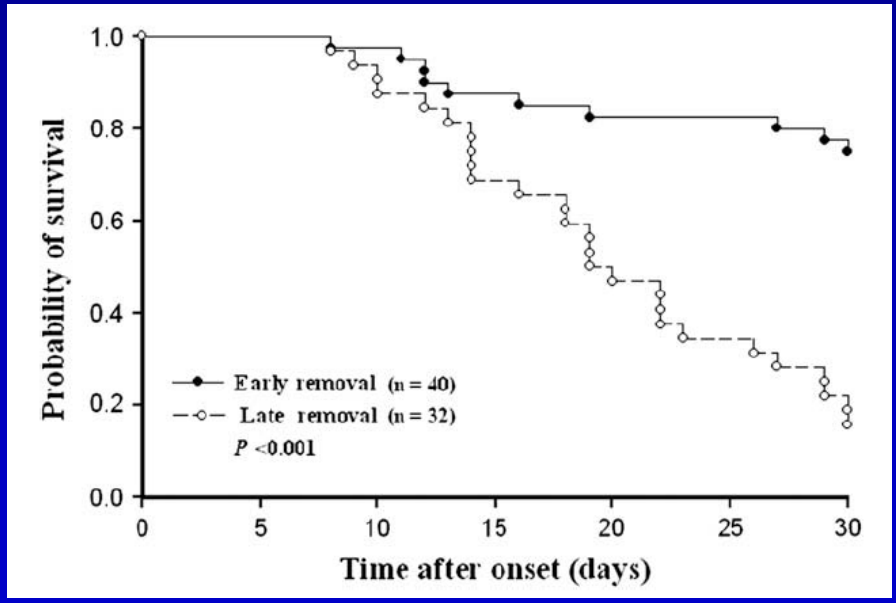
Estudios retrospectivos

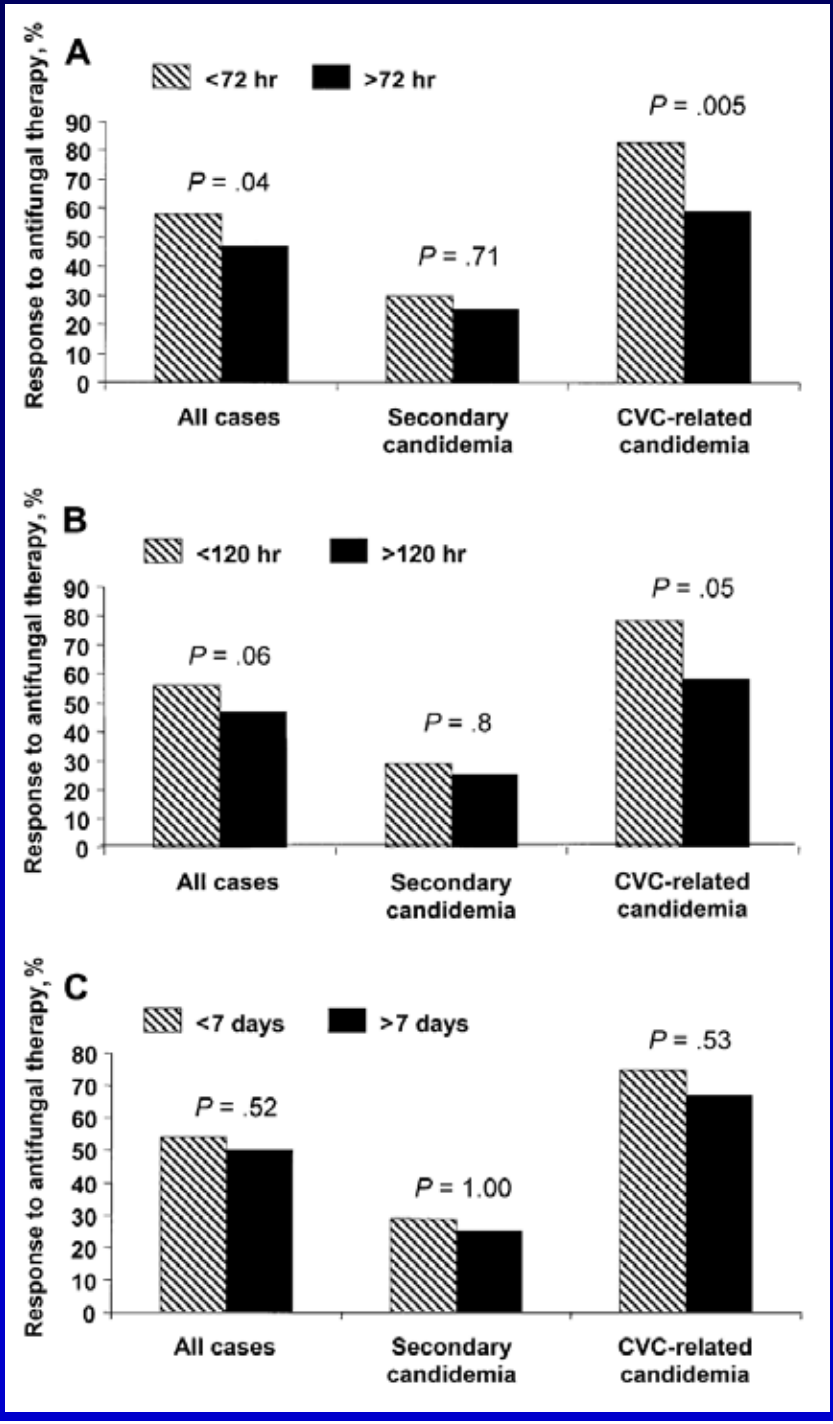
Candidemia in cancer patients: Impact of early removal of non-tunneled central venous catheters on outcome

J. Infection 2009

C.Y. Liu [a,d], L.J. Huang [b,d], W.S. Wang [d,e], T.L. Chen [b,d], C.C. Yen [a,d], M.H. Yang [a,d], L.T. Hsiao [a,d], C.Y. Liu [b,d], P.M. Chen [a,d], T.J. Chiou [c,d,*]







Beneficio de la retirada precoz del catéter en candidemias

Raad et al. Clin Infect Dis 2004

CANDIDEMIA EN NIÑOS
-factores de riesgo de mortalidad-

- Brasil, 1995-2003:
  - 61 niños con candidemia y catéter central
  - Patología base
    - ✓ Malf. Congénitas: 46%
    - ✓ Tumores sólidos: 10%
    - ✓ Tumores hematológicos: 13%
    - ✓ Neonatos: 23%
    - ✓ Neutropenia (<500): 21%
  - Origen candidemia
    - ✓ Primaria: 37%
    - ✓ Catéter: 33%
    - ✓ Secundaria: 30%
  - Especies Candida
    - ✓ C. albicans: 20%
    - ✓ C. no-albicans: 80%

Mortalidad (Análisis multivariante):

Precoz (<7 días)
No retirada catéter

Tardía (8-30 días)
Severidad infección (PRISM III)

Pasqualotto et al. Inf Control Hosp Epidemiol 2007

Should Vascular Catheters Be Removed from All Patients with Candidemia?

Nucci, Anaissie. CID 2002

1966-2000: 203 estudios: 4 evaluables

a) beneficio en 21 neutropénicos
b) no beneficio
c) y d) beneficio marginal

Significativo mayor escore gravedad y neutropenia en pacientes sin retirada

Reference, year	Population	Patients with neutropenia, %	Assessment of severity of illness	OR and 95% CI provided	Effect of CVC removal or retention and comments
Nguyen 1995	427 Patients; cancer in 46%	DNP	4-Point grading system	No	Prognostic factor for death on univariate and multivariate analyses. Other prognostic factors on multivariate analysis: critical illness, older age, recent administration of corticosteroids, lung involvement.
Hung 19965	118 Adult patients; cancer in 58%	15	4-Point grading system	No	Prognostic factor for death on univariate and multivariate analyses. Other prognostic factors: persistent candidemia, higher severity 4 of illness score, no antifungal treatment.
Goodrich 1996	102 BMT recipients	DNP	None	Yes	Longer duration of fungemia but no influence on mortality. Prognostic factors for death: female sex (RR, 1.8), acute lymphoid leukemia (RR, 3.6), conditioning regimen (RR, 2.0), no. of days of candidemia (RR, 1.1), engraftment (RR, 0.6).[a]
Annaissie 1998	476 Patients with cancer	45	SAPS and APACHE III	Yes	Modest improvement in mortality rates in a subgroup of patients whose CVCs were changed over a guidewire; OR was 2.2 for catheter retention (95% CI, 1.6–3.2). Other prognostic factors: higher APACHE III score (OR, 1.05; 95% CI, 1.04–1.07), visceral dissemination (OR, 6.2; 95% CI, 3.5–11), remained or became neutropenic (OR, 13; 95% CI, 5.9–28), antifungal treatment (OR, 0.21; 95% CI, 0.09–0.50).
Nucci 1998	54 Patients with cancer	48	Karnofsky scale	Yes	Prognostic factor for death on univariate but not on multivariate analysis. Prognostic factors: poor performance status score (OR, 46.6; 95% CI, 6.33–861), persistent neutropenia (OR, 33.1; 95% CI, 2.2–498), older age (OR, 1.06; 95% CI, 1.01–1.11)
Nucci 1998	145 Patients; cancer in 34%	24	Karnofsky scale	Yes	Prognostic factor for death. OR for catheter retention was 4.81 (95% CI, 2.0–11.6). Other prognostic factors: *Candida parapsilosis* (OR, 0.27; 95% CI, 0.09–0.79), older age (OR, 1.02; 95% CI, 1.00–1.03).
Luzzati 2000	189 Adult patients; cancer in 21%	0	McCabe scale	Yes	Modest improvement in mortality; OR for catheter removal was 0.62 (95% CI. 0.38–0.99, P = .047). Other prognostic factors: duration of positive blood cultures (OR, 1.08; 95% CI, 1.01–1.12), being in an ICU (OR, 2.06; 95% CI, 1.21–3.51), adequate antifungal treatment (OR, 0.52; 95% CI, 0.32–0.84).

CANDIDEMIA
-factores predictores asociados a catéter-

- Hemocultivos cuantitativos > 3:1
- Hemocultivos diferenciales >2 horas
- No quimioterapia en último mes
- No corticoterapia en último mes
- No diseminación
- Nutrición parenteral
- Candidemia brecha
- *C. parapsilosis*

Raad et al. Clin Infect Dis 2004
Mermel et al. Clin Infect Dis 2009

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, May 2004, p. 1727–1732 Vol. 48, No. 5
0066-4804/04/$08.00+0 DOI: 10.1128/AAC.48.5.1727–1732.2004
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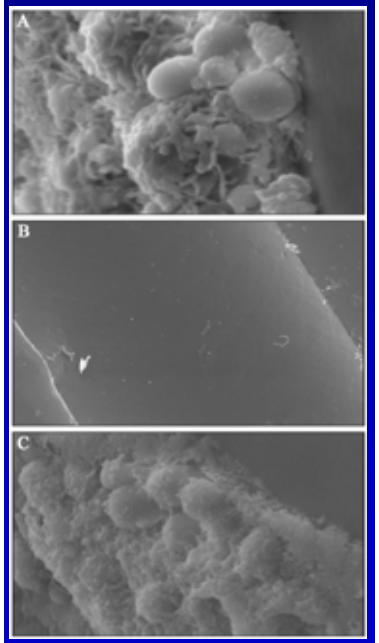
Rabbit Model of *Candida albicans* Biofilm Infection: Liposomal Amphotericin B Antifungal Lock Therapy

Matthew K. Schinabeck,[1,2] Lisa A. Long,[1] Mohammad A. Hossain,[1] Jyotsna Chandra,[1] Pranab K. Mukherjee,[1] Sotohy Mohamed,[1] and Mahmoud A. Ghannoum[1]*

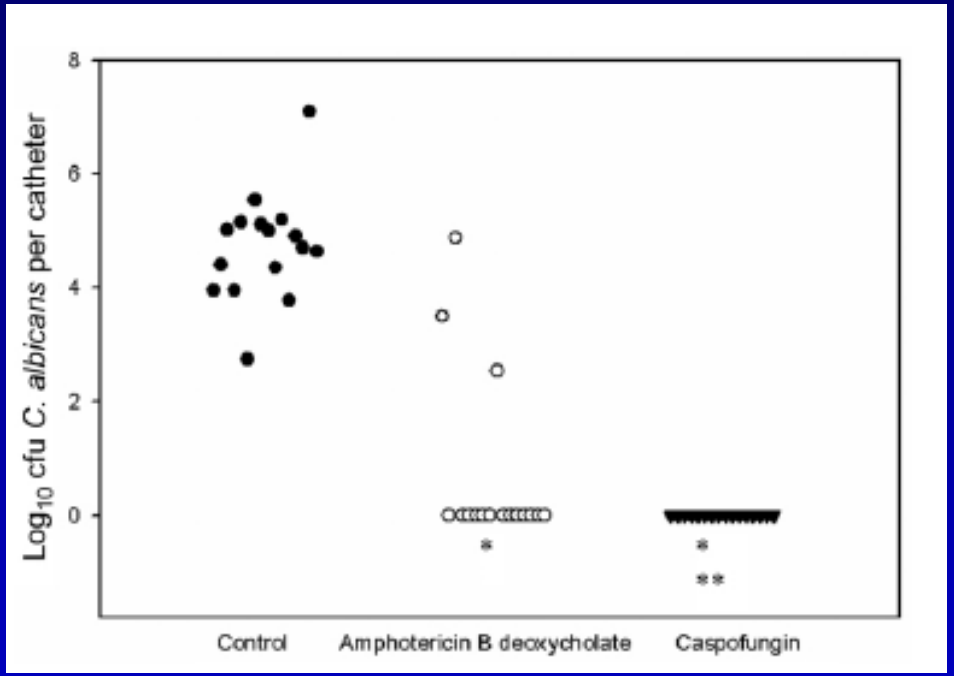
Animal	Treatment	Blood cultures			Quantitative catheter cultures (log_{10} CFU/cath segment ± SD)	
		Postinfection (day 3) cath	Posttreatment (day 10) cath	Posttreatment (day 10) cardiac puncture	Proximal	Distal
29709	Control	Pos	Pos	Pos	0.894 ± 1.189	0.426 ± 0.00
29711	Control	Clot	Pos	Neg	2.329 ± 0.119	2.872 ± 0.057
41365	Control	Pos	Clot	Neg	2.779 ± 0.111	2.891 ± 0.033
41367	Control	Pos	Clot	Neg	3.794 ± 0.154	3.312 ± 0.036
29797	Control	Clot	Pos	Neg	1.387 ± 0.234	1.466 ± 0.080
29049	Control	Pos	Clot	Pos	1.076 ± 0.357	0.125 ± 0.00
29044	Control	Clot	Clot	Neg	1.418 ± 0.166	1.000 ± 0.00
29710	L-AmB	Pos	Neg	Neg	0	0
29713	L-AmB	Pos	Pos	Neg	0	0
29708	L-AmB	Pos	Clot	Neg	0	0
41369	L-AmB	Clot	Neg	Neg	0	0
41371	L-AmB	Pos	Pos	Neg	0	0
29043	L-AmB	Pos	Neg	Neg	0	0
29045	L-AmB	Clot	Neg	Neg	0	0
29042	Fluc	Pos	Clot	Neg	1.529 ± 0.228	1.316 ± 0.133
29041	Fluc	Pos	Neg	Neg	0	0
29046	Fluc	Pos	Neg	Neg	0	1.023 ± 0.707
29050	Fluc	Clot	Pos	Neg	0	0.813 ± 0.410
41375	Fluc	Pos	Neg	Neg	0	0
41374	Fluc	Clot	Neg	Neg	2.463 ± 0.033	0
41364	Fluc	Pos	Neg	Neg	0.753 ± 0.00	0



AmBisome >>> FLUC (p<0,001) FLUC > control (p=0,29)
(3 mg+Hep 100 UI) (3 mg+Hep 100 UI)

BAC por Candida -caspofungina vs anfotericina B-

- **Modelo animal (conejos): 48**
- **Tratamiento sistémico y sellado, 7 días:**



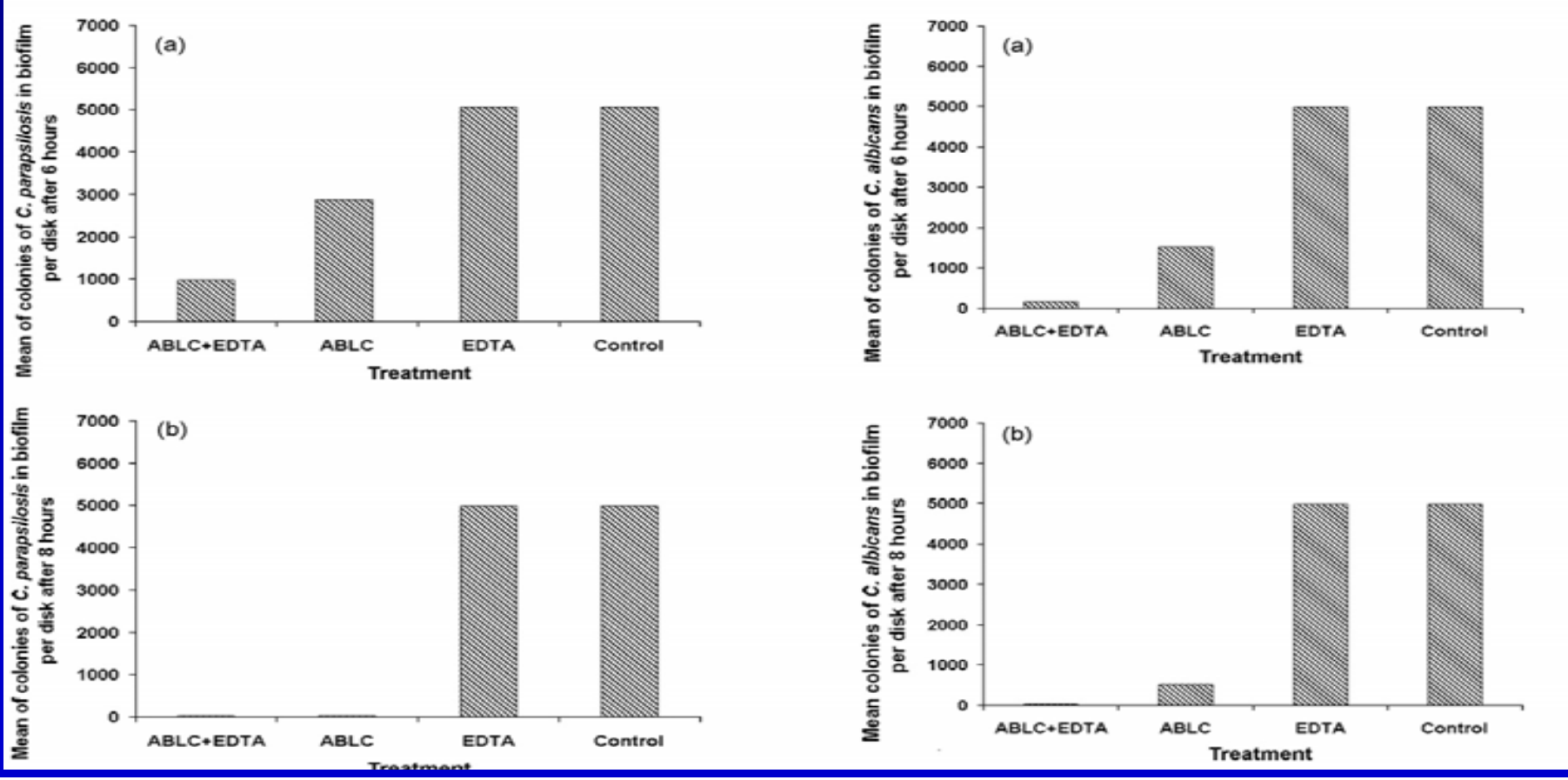
	Controles	Anfotericina B	Caspofungina
esterilización	0/16	13/16	16/16

Shuford et al. JID 2007

CANDIDEMIA ASOCIADA A CATÉTER -sellado: Anf-B + EDTA-

Raad et al. Int J Antimrob Agents 2008

- EDTA (Ácido Etilen-Diamino-Tetracético)
  - Quelante anticoagulante, Anti-fúngico, anti-biofilm



CANDIDIASIS EN NO-NEUTROPÉNICOS
-IDSA Guidelines 2009-

- Fluconazol (AI) ó Equinocandinas (AI)
  - Equinocandinas: si enfermedad grave o azoles previos (AIII)
  - Fluconazol: si estabilidad clínica y cepa probable sensible (AIII)
    - ✓ Anf-B ó L-Anf si intolerancia a otros o no disponibilidad (AI)

	1ª opción	Comentario
C. albicans (C. tropicalis)	FLU (AII)	EQ si gravedad Secuenciar a FLU
C. glabrata	EQ (BIII)	No secuenciar a FLU o VOR sin CMI
C. parapsilosis	FLU (BIII)	Si EQ inicial y estabilidad (BIII) Si gravedad: L-Anf ó Anf-B
C. krusei	EQ (BIII)	Posibilidad de secuenciar a VOR

CID, 1 Mar 2009

CANDIDIASIS EN NO-NEUTROPÉNICOS
-IDSA Guidelines 2009-

- Selección de antifúngico en virtud de:
  - ✓ Exposición a azoles
  - ✓ Intolerancia a antifúngicos
  - ✓ Epidemiología de especies de *Candida* spp y sensibilidad
  - ✓ Gravedad de enfermedad
  - ✓ Comorbilidad
  - ✓ Extensión de enfermedad (SNC, endovascular, afectación visceral)
- Fluconazol en primera línea si:
  - ✓ Hemodinamicamente estable
  - ✓ No azoles previos
  - ✓ No riesgo de infección por *C. glabrata*:
    - Azoles previos
    - Edad avanzada
    - Cáncer
    - Diabetes
  - ✓ No riesgo de infección por *C. krusei*:
    - Azoles previos
    - Pacientes oncohematológicos y TMO
- Antifúngico fungicida:
  - ✓ L-AmB ó Anf-B: endocarditis o SNC
  - ✓ EQ: endocarditis

CID, 1 Mar 2009

OMIGANAN

Fritsche et al. AAC 2008

- Péptido catiónico bactericida y fungicida
- Ensayo en fase III
- Europa y USA

Omiganan 1% (10.000 ug/ml): Eficaz decolonización cutánea de BGN y levaduras, incluidas formas R

CMI (ug/ml)d)	50%	90%	Range
S. aureus (110)	16	16	2-32
Coagulase-negative staphylococci (104)	4	4	1-8
Enterococcus spp. (111)	8	128	2-128
E. faecalis (44)	64	128	32-128
E. faecium (67)	4	8	2-16
β-haemolytic streptococci (30)	16	32	16-32
Viridans group streptococci (35)	32	128	8-128
E. coli (43)	32	32	8-64
Klebsiella spp. (41)	32	256	8-512
Enterobacter spp. (42)	64	512	8-1024
Pseudomonas aeruginosa (41)	128	256	32-256
All Enterobacteriaceae (126)	32	256	8-1024
All Gram-negative bacilli (167)	64	256	8-1024
All yeast (106)	64	256	16-256
C. albicans (52)	64	128	32-128
C. glabrata (22)	256	256	128-256
C. krusei (10)	64	128	32-128
C. parapsilosis (11)	128	256	32-256
C. tropicalis (11)	32	32	16-32
Moulds (20)	128	1024	1-1024
Aspergillus spp. (10)	64	1024	16-1024


Muchas gracias