Nuevas técnicas de diagnóstico y estudios de sensibilidad

Dr Javier Afeltra

SALÓN ATLÁNTICO A

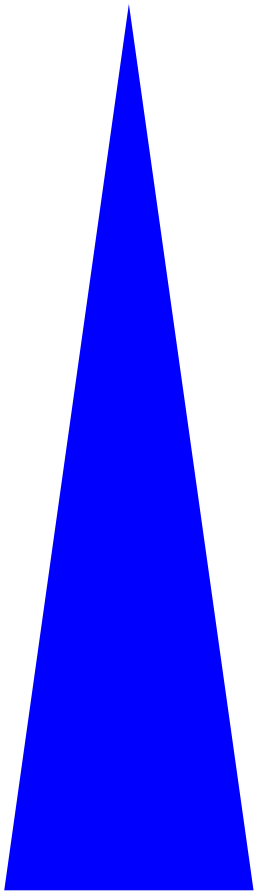
Mesa redonda. Infecciones fúngicas: nuevos desafíos

Conflictos de interés

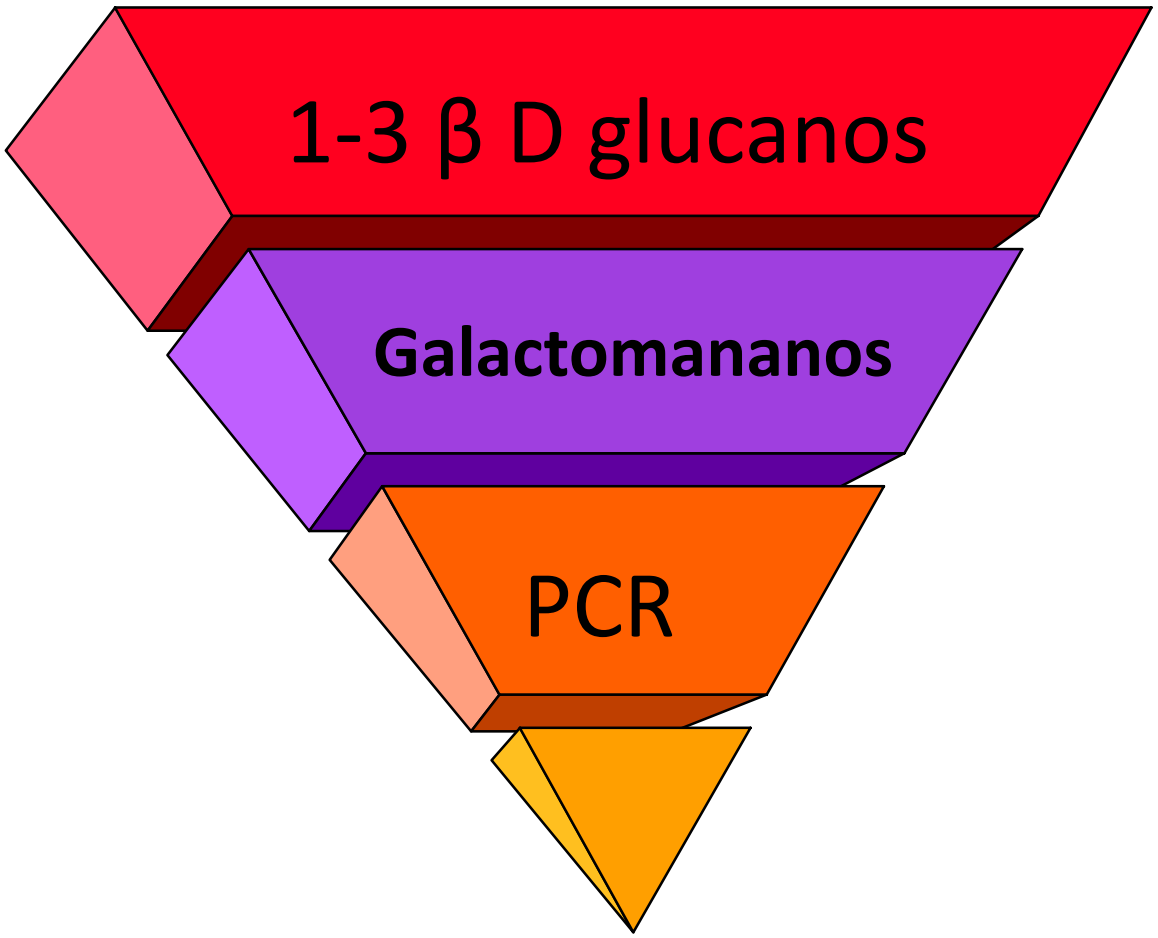
- Merck
- Pfizer
- Gador
- Raffo
- Ivax
- Biodiagnóstico

Nuevas herramientas diagnósticas

- Mananos/Antimananos.
- 1-3 β D glucanos
- T2 candida
- Galactomananos
  - ELISA
  - Lateral flow
- Polisacárido capsular.
  - Lateral flow



Especificidad



Histopatología
Directos y Cultivos
MADI-TOF

MAJOR ARTICLE

T2 Magnetic Resonance Assay for the Rapid Diagnosis of Candidemia in Whole Blood: A Clinical Trial

Eleftherios Mylonakis,[1] Cornelius J. Clancy,[2] Luis Ostrosky-Zeichner,[3] Kevin W. Garey,[4] George J. Alangaden,[5] Jose A. Vazquez,[6] Jeffrey S. Groeger,[7] Marc A. Judson,[8] Yuka-Marie Vinagre,[9] Stephen O. Heard,[10] Fainareti N. Zervou,[1] Ioannis M. Zacharioudakis,[1] Dimitrios P. Kontoyiannis,[11] and Peter G. Pappas[12]

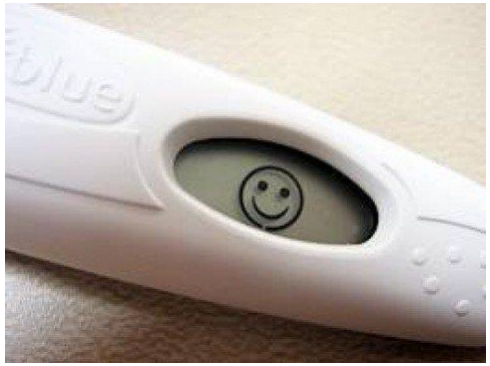
- Nanotecnologia: Extracción. Aglutinación de partículas supermagnéticas.
- Detección automatizada.
- Estudio multicéntrico
- 1800 pacientes.

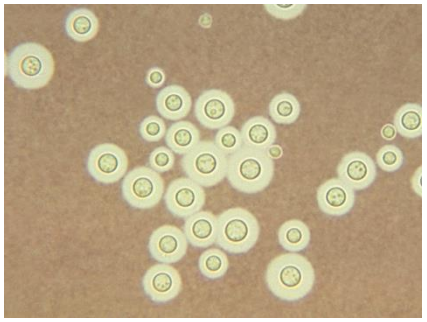
- Sensibilidad: 91.1% (95% CI, 86.9%-94.2%)
  - *C. albicans/tropicalis :92.3%*
  - *C. parapsilosis:94.2%*
  - *C. krusei/glabrata:99.9%*
- Especificidad:99.4% (95% CI, 99.1%-99.6%)
  - *C. albicans/tropicalis :98.9%*
  - *C. parapsilosis:99.3%*
  - *C. krusei/glabrata:99.9%*
- Tiempo de detección e identificación: 4.4 ± 1.0 hs vs129.9 ± 26.3 hs para los HC (5 días ± 1) .

VPP Y VPN

Table 3. Positive and Negative Predictive Values of T2 Magnetic Resonance Method for a Range of Prevalence of Candidemia

Prevalence of Disease	91.0% Sensitivity/98.1% Specificity	
	PPV	NPV
1%	32.6%	99.9%
2%	49.4%	99.8%
5%	71.6%	99.5%
10%	84.2%	99.0%
20%	92.3%	97.8%
35%	96.3%	95.3%
50%	98.0%	91.6%





Lateral flow

- PROs
  - Fácil de usar.
  - No requiere equipamiento especial.
  - No requiere personal altamente entrenado.
  - Test rápidos (15-60 minutos).
  - Fácil de interpretar vs (NO interpretar).
  - Múltiples muestras
  - Semicuantitativo
- CONTRAs
  - Cualitativo
  - Lectura subjetiva

RESEARCH ARTICLE

Evaluation of a New Cryptococcal Antigen Lateral Flow Immunoassay in Serum, Cerebrospinal Fluid and Urine for the Diagnosis of Cryptococcosis: A Meta-Analysis and Systematic Review

Hua-Rong Huang, Li-Chao Fan, Bhavana Rajbanshi, Jin-Fu Xu*

Department of Respiratory Medicine, Shanghai Pulmonary Hospital, Tongji University School of Medicine, Shanghai, China

* jfxucn@gmail.com

- Meta-analisis: 12 estudios ; muestras:4622.
- Solo se incorporaron pacientes con cripto en SNC.

Table 2. The diagnostic accuracy of LFA for cryptococcal infection in serum, CSF and urine.

Sample types	Parameter	Estimates	95%CI
Serum	Sensitivity	0.98	0.96–0.99
	Specificity	0.98	0.97–0.99
	Positive LR	43.79	22.60–84.81
	NegativeLR	0.03	0.01–0.09
	DOR	2180.30	868.92–5471.00
CSF	Sensitivity	0.99	0.98–1.00
	Specificity	0.99	0.98–1.00
	Positive LR	48.83	21.59–110.40
	NegativeLR	0.02	0.01–0.04
	DOR	2931.10	1149.20–7475.90
Urine	Sensitivity	0.85	0.79–0.90

- Sensibilidad del test en LCR es «superior» al del plasma.

Low *Cryptococcus* antigen titers by a lateral flow assay should be interpreted cautiously in patients without a prior diagnosis of cryptococcal infection

Marie Dubbels, Dane Granger, Elitza S. Theel#

Division of Clinical Microbiology, Department of Laboratory Medicine and Pathology, Mayo Clinic, Rochester, MN, USA

- Junio 2014 Diciembre 2016
- 3969 pacientes testeados.
- 55 pacientes positivos.
- 11 pacientes con CrAgLF 1:2 o 1:5 (falsos positivos)
- 34% de Falsos positivos

JCM Accepted Manuscript Posted Online 31 May 2017
J. Clin. Microbiol. doi:10.1128/JCM.00751-17

JCM
Journals.ASM.org

Rapid Diagnosis of Cryptococcal Meningitis by Use of Lateral Flow Assay on Cerebrospinal Fluid Samples: Influence of the High-Dose "Hook" Effect

Adré Lourens,[a] Joseph N. Jarvis,[b,c,d] Graeme Meintjes,[e] Catherine M. Samuel[a]

Division of Medical Microbiology, Stellenbosch University, National Health Laboratory Services, Tygerberg Hospital, Cape Town, South Africa[a]; Department of Clinical Research, Faculty of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, London, United Kingdom[b]; Botswana-University of Pennsylvania Partnership, Gaborone, Botswana[c]; University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, USA[d]; Institute of Infectious Disease and Molecular Medicine and the Division of Infectious Diseases and HIV Medicine, Department of Medicine, University of Cape Town, Cape Town, South Africa[e]

- 465 LCR
- Sin diluir
  - Sensibilidad 91%
- Con dilución
  - Sensibilidad 100%

TABLE 2 Performance of the lateral flow assay and conventional cryptococcal latex agglutination test on 465 CSF samples before and after CSF dilution

Comparator	Total no. of CSF samples in study	Sensitivity (%)	Specificity (%)	PPV[b] (%)	NPV[c] (%)	Kappa
LFA[a] predilution						
CLAT[d]	465	91	99.8[e]	96.8	92.9	0.9329
Culture	465	88.4	98.1	74.1	99.3	0.7945
LFA postdilution[f]						
CLAT	465	100	99.8[e]	97	100	0.9839
Culture	465	100	98.1	76.4	100	0.8576

[a] LFA, lateral flow assay

JCM 2014 (52) 12:4172

Aspergillus lateral flow

- Pocos estudios clínicos.
- Suero:
  - **Sensibilidad: 20-68%**
  - **Especificidad: 72-98%**
- LBA:
  - **Sensibilidad: 80-100%**
  - **Especificidad: 81-95%**

- Similares a los obtenidos por galactomananos
- Influencia de uso de antifungicos sistémicos contra hongos filamentosos

Miceli et al Sem Resp and Crit Care Med 2015 (36) 650

Utilidad de combinación de GM, qPCR y LFD en pacientes con IA

Test	Sensibilidad	Especificidad	VPP	VPN
GM (PC0.8)	87.50	66.6	58.3	90.9
GM (PC 1)	75	66.6	54	83
qPCR	100	86,67	80	100
LFD	100	80	72.7	100

Utilidad para confirmar o descartar AI por LBA en GM >0.5 y <1

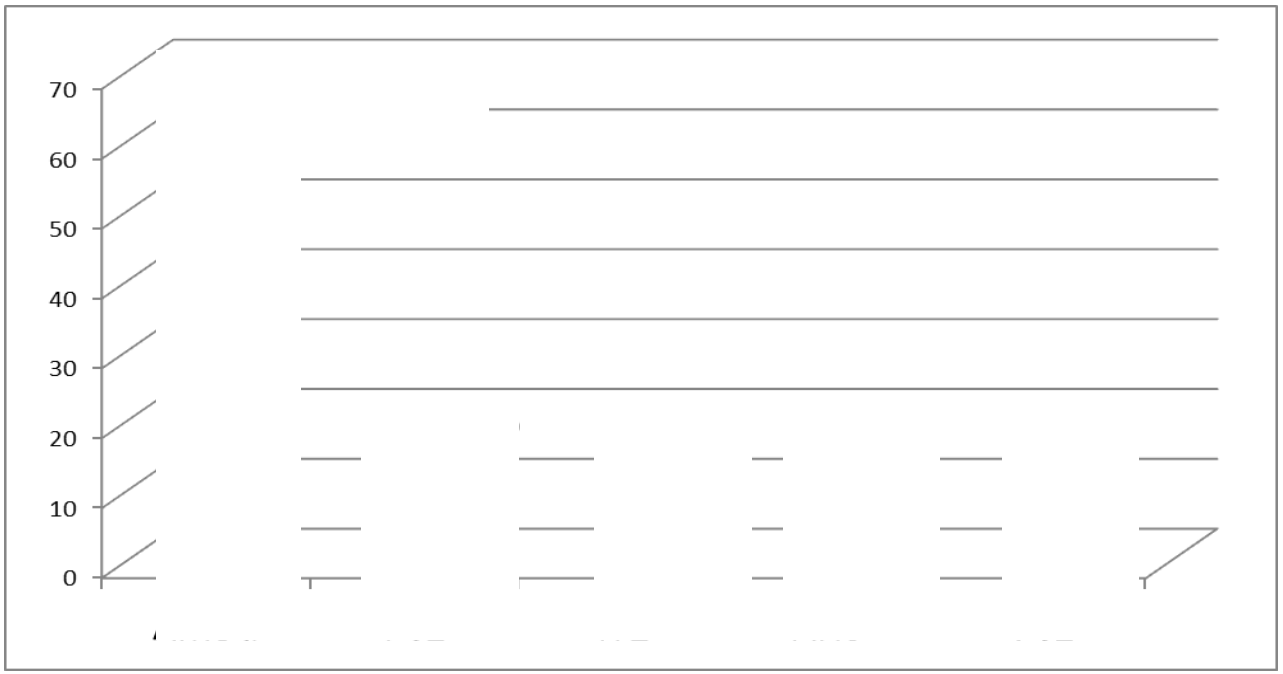
- Johnson et al JCM 2015 53 (7) pp2103

Estudio multicéntrico para el diagnóstico de aspergilosis invasora mediante detección de galactomananos en pacientes neutropénicos febriles

Subcomisión de Micología Clínica (SADEBAC) y Asociación Argentina de Microbiología (AAM)
Dr Gustavo Giusiano Dr Guillermo Garcia Effron

- Instituciones de las provincias.
- 297pacientes
- 35 con valores positivos
- Promedio de las muestras: 3 (1-10)
- En LBA: 4

Drogas utilizadas para el Tratamiento



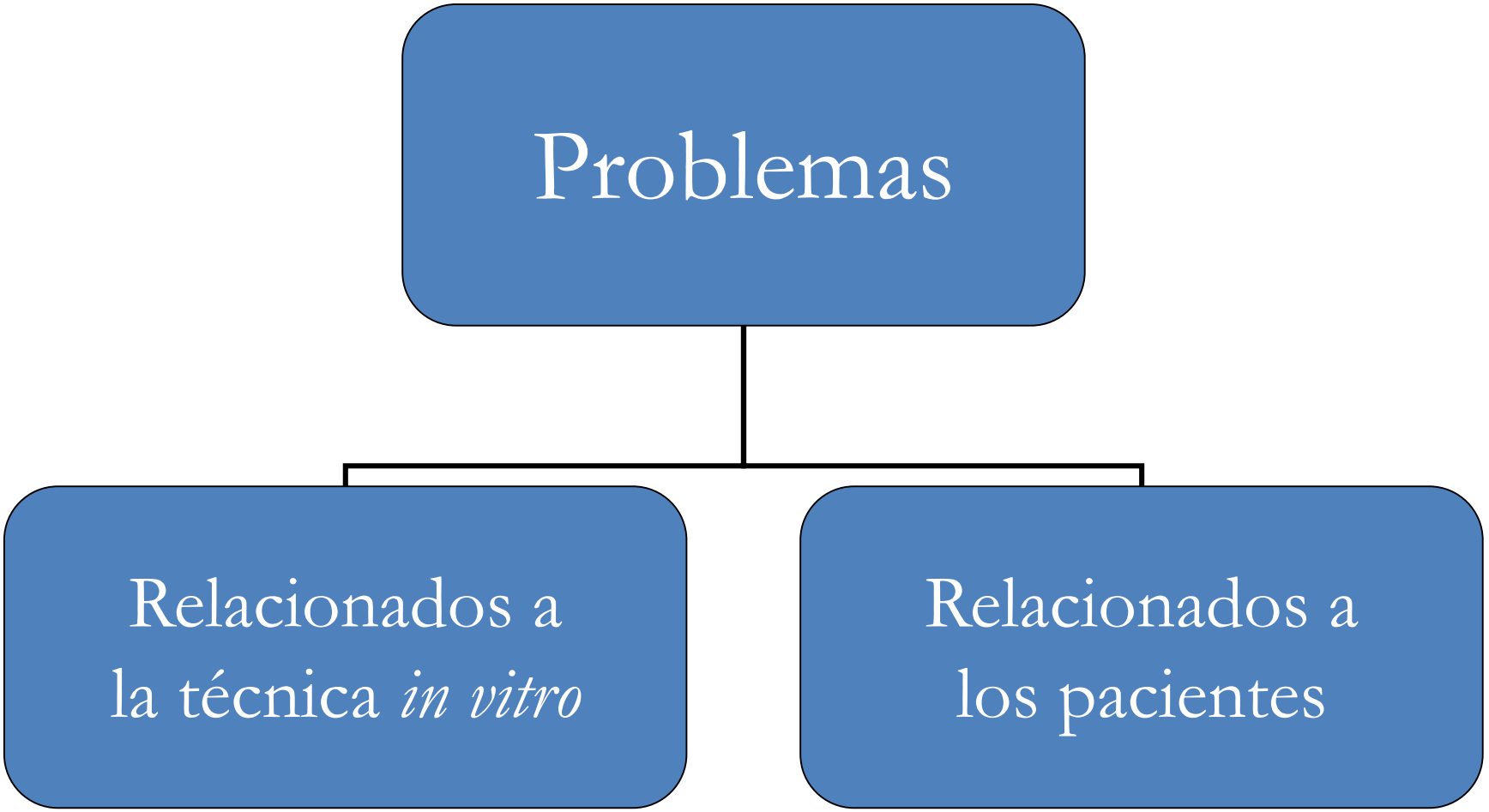
Utilidad de los métodos diagnósticos

- «Cambiar una conducta»
- Jerarquizar el riesgo individualizado vs no jerarquizar.
- Utilizar el diagnóstico por TC de alta resolución vs no usarlo
- Solicitar biomarcadores vs No cambiar conducta.

Prophylactic Empiric Driven Premptive Antifungal Therapy

Pruebas de sensibilidad

NECESITAMOS EL HONGO



ARTÍCULO ORIGINAL

ISSN 0325-7541
Revista Argentina de Microbiología (2011) 43: 176-185

Species distribution and susceptibility profile of yeasts isolated from blood cultures: results of a multicenter active laboratory-based surveillance study in Argentina

SUSANA CÓRDOBA[1*], WALTER VIVOT[1], MARIA E BOSCO-BORGEAT[1], CONSTANZA TAVERNA[1], WANDA SZUSZ[1], OMAR MURISENGO[1], GUILLERMINA ISLA[1], GRACIELA DAVEL[1] AND THE RED NACIONAL DE LABORATORIOS DE MICOLOGIA[2], ARGENTINA

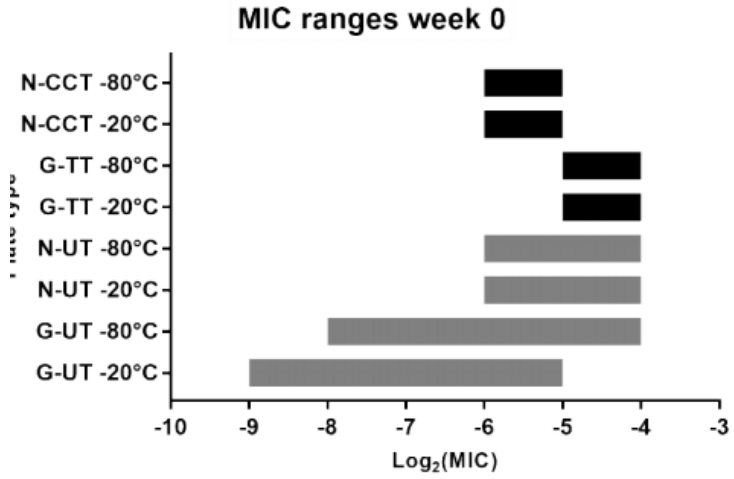
[1]*Departamento Micología, Instituto Nacional de Enfermedades Infecciosas "Dr. C. Malbrán". Av. Vélez Sarsfield 563 (1281) Ciudad Autónoma de Buenos Aires, Argentina*
** Correspondence: E-mail: scordoba@anlis.gov.ar*

- 461 levaduras (*Candida* y *Criptococcus*)
- *C. albicans* 38.4%
- *C.parapsilosis* 26%
- *C.tropicalis* 14%
- *C.glabrata* 4.3%

Candida	Droga	Rango	%Resistencia
Todas (420)	AMB	0.06-2	0.2
	FCZ	0.06-64	1.6
	ITZ	<0.015-0.5	0
	VCZ	<0.015-2	1.6
	AND	<0.015-4	6.2
	CAS	<0.015-2	0
C. albicans			
	FCZ	0.06-4	0
	ITZ	<0.015-0.13	0
	VCZ	<0.015-1	0.5
	AND	<0.015-0.13	0
	CAS	<0.015-0.13	0
C. glabrata	AMB	0.13-1	0
	FCZ	0.06-16	20
	ITZ	<0.015-0.13	0
	VCZ	<0.015-1	0.5
	AND	<0.015-0.06	0
	CAS	<0.015-0.13	0

Problemas relacionados a la técnica in vitro

- Composición de la placa del plástico modifica las CIM



- Tiempo desde el descongelado – preparación del inóculo – incubación de la placa.

Jorgensen ECCMID 2017 poster 1759

European Committee on Antimicrobial Susceptibility Testing

Antifungal Agents

Breakpoint tables for interpretation of MICs

Antifungal agent	MIC breakpoint (mg/L)													
	C. albicans		*C. glabrata*		*C. krusei*		*C. parapsilosis*		*C. tropicalis*		*C. guilliermondii*		Non-species related breakpoints[1]	
	S ≤	R >	S ≤	R >	S ≤	R >	S ≤	R >	S ≤	R >	S ≤	R >	S ≤	R >
Amphotericin B	1	1	1	1	1	1	1	1	1	1	IE	IE	IE	IE
Anidulafungin	0.032	0.032	0.064	0.064	0.064	0.064	0.002	4	0.064	0.064	IE[2]	IE[2]	IE	IE
Caspofungin	Note[3]	Note[3]	Note[3]	Note[3]	Note[3]	Note[3]	Note[3]	Note[3]	Note[3]	Note[3]	IE[2]	IE[2]	IE	IE
Fluconazole	2	4	0.002	32	-	-	2	4	2	4	IE[2]	IE[2]	2	4
Isavuconazole	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE
Itraconazole	0.064	0.064	IE[2]	IE[2]	IE[2]	IE[2]	0.125	0.125	0.125	0.125	IE[2]	IE[2]	IE	IE
Micafungin	0.016	0.016	0.032	0.032	IE[4]	IE[4]	0.002	2	IE[4]	IE[4]	IE[4]	IE[4]	IE	IE
Posaconazole	0.064	0.064	IE[2]	IE[2]	IE[2]	IE[2]	0.064	0.064	0.064	0.064	IE[2]	IE[2]	IE	IE
Voriconazole	0.125[5]	0.125[5]	IE	IE	IE	IE	0.125[5]	0.125[5]	0.125[5]	0.125[5]	IE[2]	IE[2]	IE	IE

European Committee on Antimicrobial Susceptibility Testing

Antifungal Agents

Breakpoint tables for interpretation of MICs

Antifungal agent	MIC breakpoint (mg/L)											
	A. flavus		*A. fumigatus*		*A. nidulans*		*A. niger*		*A. terreus*		Non-species related breakpoints[1]	
	S ≤	R >	S ≤	R >	S ≤	R >	S ≤	R >	S ≤	R >	S ≤	R >
Amphotericin B	IE[2]	IE[2]	1	2	Note[3]	Note[3]	1	2	-	-	IE	IE
Anidulafungin	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE
Caspofungin	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE
Fluconazole	-	-	-	-	-	-	-	-	-	-	-	-
Isavuconazole	IE[2]	IE[2]	1	1	0.25	0.25	IE[2]	IE[2]	1	1	IE	IE
Itraconazole[4]	1	2	1	2	1	2	IE[2,5]	IE[2,5]	1	2	IE[5]	IE[5]
Micafungin	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE
Posaconazole[4]	IE[2]	IE[2]	0.125[6]	0.25[6]	IE[2]	IE[2]	IE[2]	IE[2]	0.125[6]	0.25[6]	IE	IE
Voriconazole[4]	IE[2]	IE[2]	1	2	IE	IE	IE[2]	IE[2]	IE[2]	IE[2]	IE	IE

IOs y Android

Home

Search

FAQ

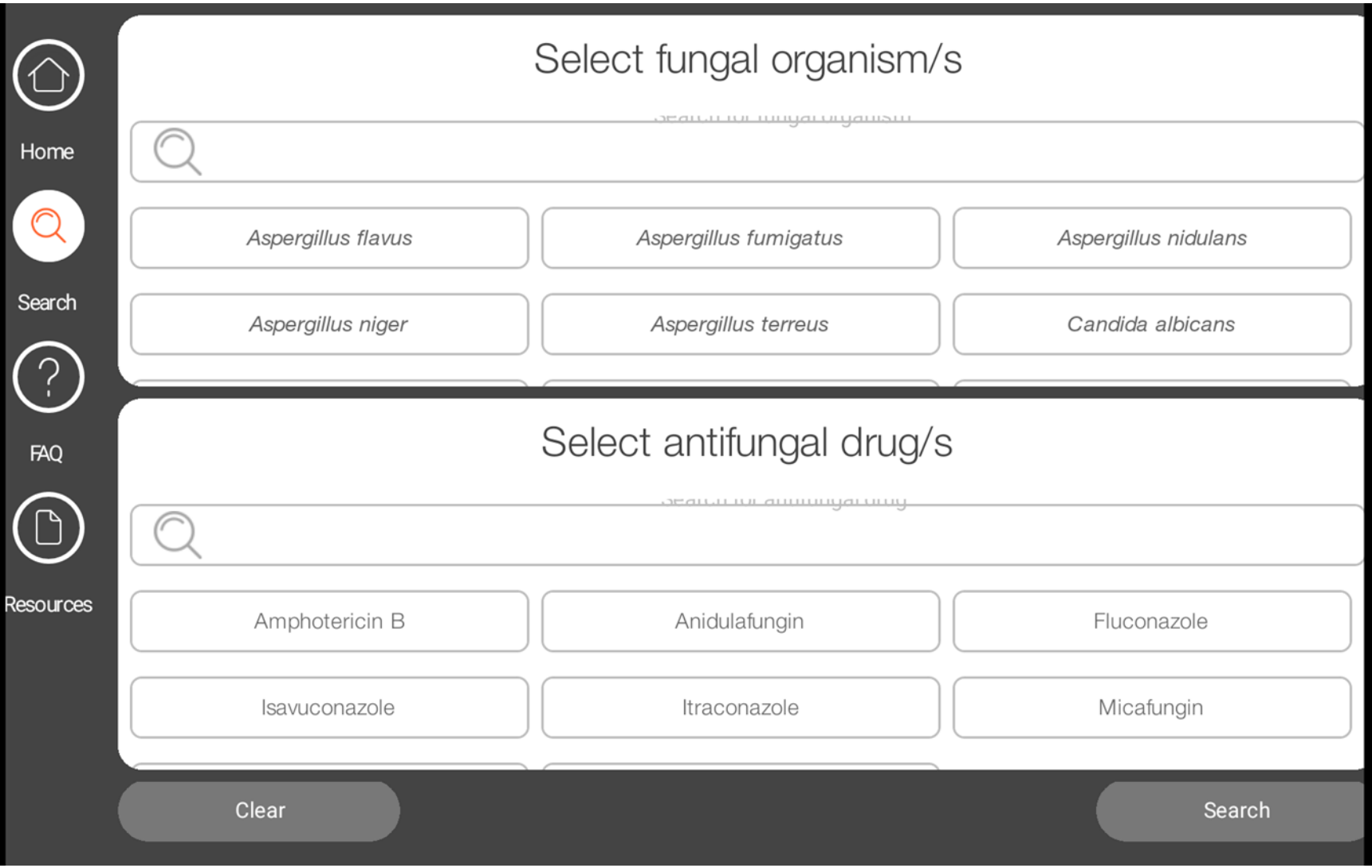
Resources

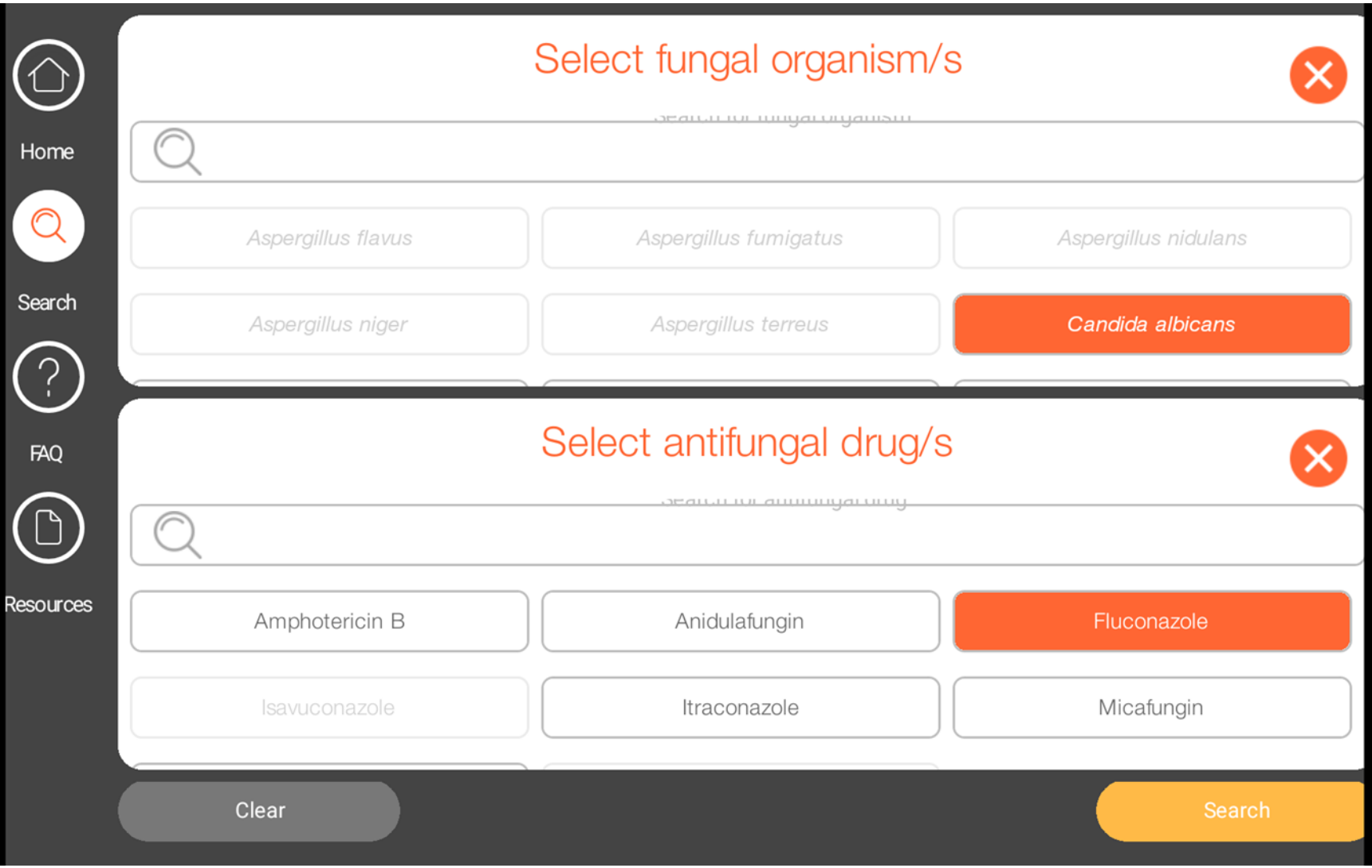
FungiMICs

FungiMICs is intended as an easy-to-use information source for physicians working in the field of fungal infections. The app aims to provide MIC data and associated clinical breakpoints and epidemiological cut-off (ECOFF) values for different organism–drug interactions, in an intuitive and practical format.

Tap the search icon to select a fungal organism and/or antifungal drug to reveal the associated data.

The app contains MIC distributions from the EUCAST MIC distribution and


Home
Search
FAQ
Resources
Select fungal organism/s
Aspergillus flavus
Aspergillus fumigatus
Aspergillus nidulans
Aspergillus niger
Aspergillus terreus
Candida albicans
Select antifungal drug/s
Amphotericin B
Anidulafungin
Fluconazole
Isavuconazole
Itraconazole
Micafungin
Clear
Search


Home
Search
FAQ
Resources
Select fungal organism/s
Aspergillus flavus
Aspergillus fumigatus
Aspergillus nidulans
Aspergillus niger
Aspergillus terreus
Candida albicans
Select antifungal drug/s
Amphotericin B
Anidulafungin
Fluconazole
Isavuconazole
Itraconazole
Micafungin
Clear
Search

Home

Search

FAQ

Resources

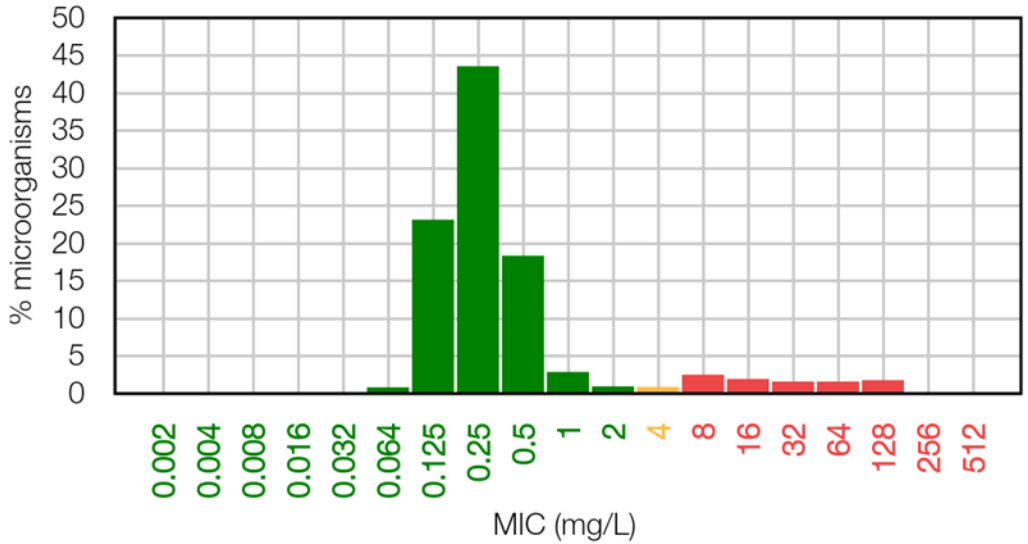
Candida albicans: Fluconazole

Source data

Clinical Breakpoint | ECOFF

Histogram | Box Plot

Description



MIC Breakpoint (mg/L)	
S≤	R>
2	4

Susceptible | Intermediate | Resistant

Home

Search

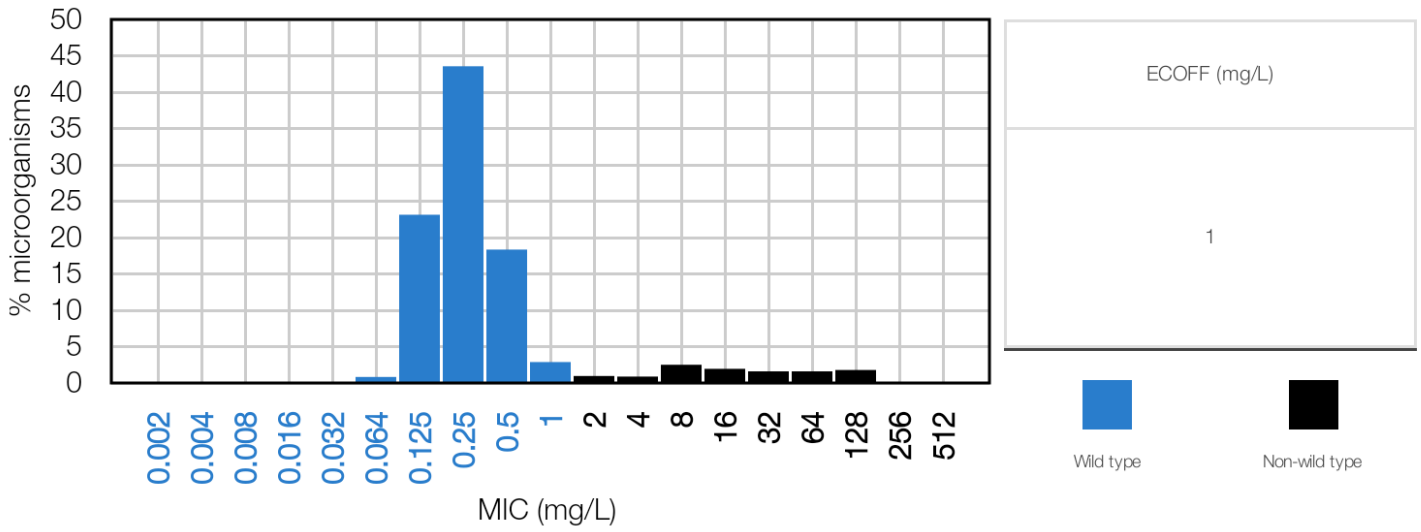
FAQ

Resources

Candida albicans: Fluconazole

Source data

Clinical Breakpoint | ECOFF | Histogram | Box Plot | Description



Conclusiones

- Nuevas técnicas diagnósticas son necesarias de implementar para el diagnóstico precoz, y poder realizar un adecuado seguimiento terapéutico.
- La utilidad del VPN permite excluir pacientes con IFI y reducir terapias innecesarias.
- El diagnóstico de tamizaje por «lateral flow» para *Cryptococcus* es de gran utilidad, pero debemos tener en cuenta falsos positivos y negativos.