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La diagnosi delle infezioni micotiche invasive nel paziente immunocompromesso: attualità e prospettive

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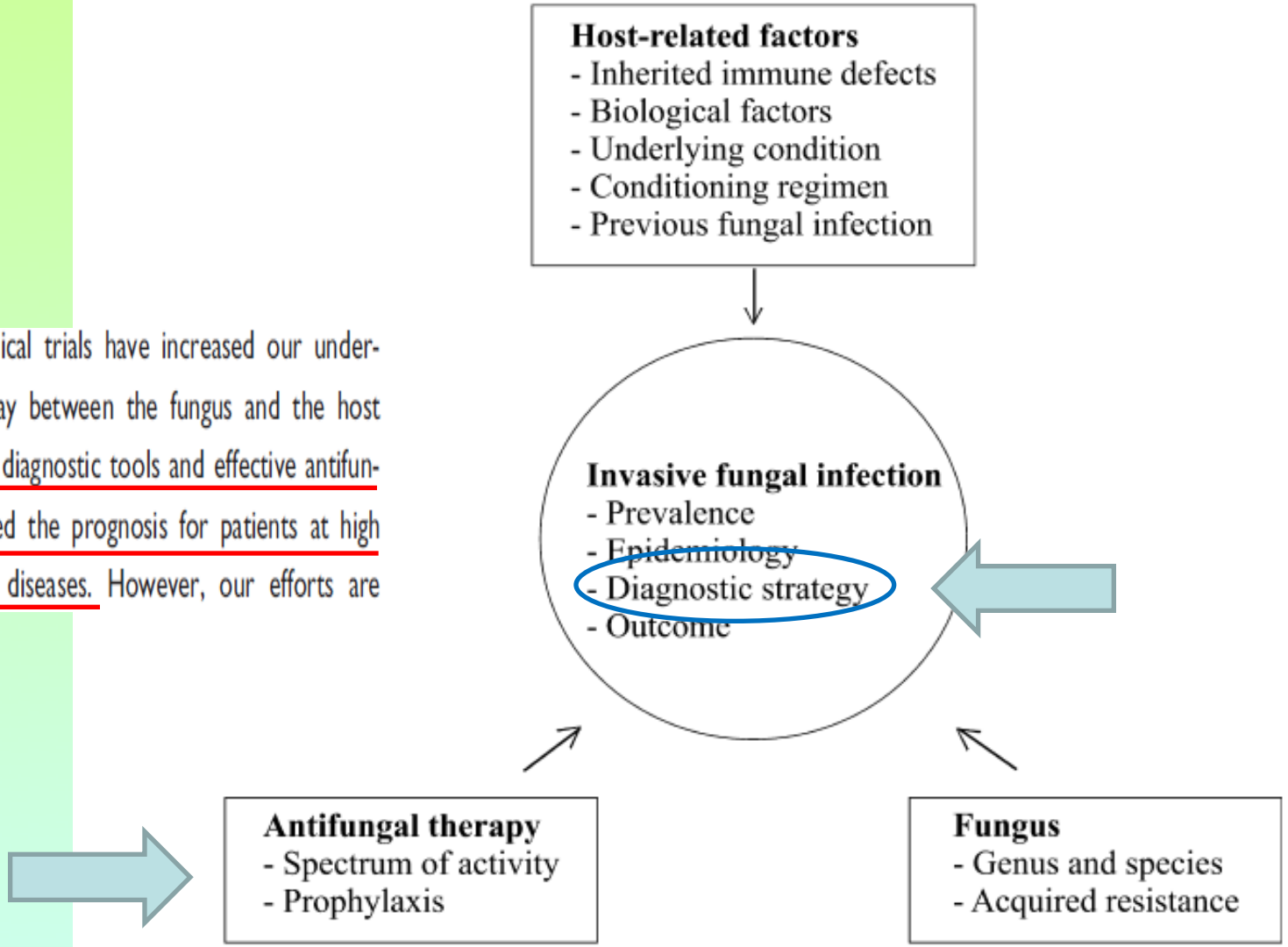
Basic research and clinical trials have increased our understanding of the interplay between the fungus and the host (Fig. 1). More accurate diagnostic tools and effective antifungal drugs have improved the prognosis for patients at high risk of invasive fungal diseases. However, our efforts are



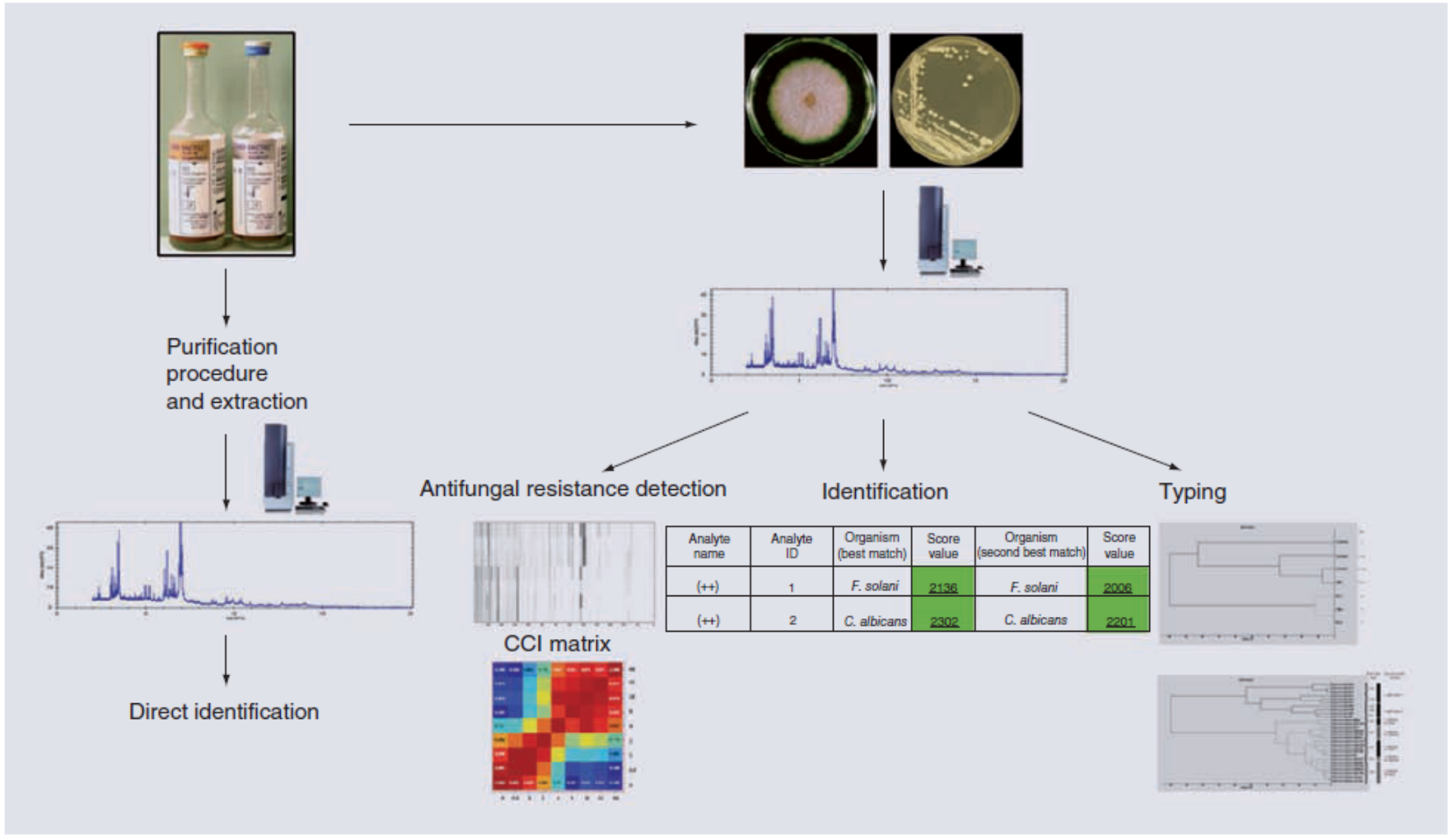


Figure 1. The role of MALDI-TOF mass spectrometry in clinical mycology diagnostics. Principal applications such as identification, typing and antifungal susceptibility testing of yeasts and molds starting from colonies, and direct identification of positive blood cultures are shown.
CCI: Composite correlation index.

From: Posteraro *et al.*, Expert Rev. Proteomics, 2013

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Early Release / Vol. 65
November 4, 2016

Investigation of the First Seven Reported Cases of *Candida auris*, a Globally Emerging Invasive, Multidrug-Resistant Fungus — United States, May 2013–August 2016

TABLE. Characteristics of the first seven cases of *Candida auris* identified in the United States—May 2013–August 2016

Patient	Isolation month/ year	State	Site of *C. auris* isolation	Underlying medical condition(s)	Outcome*
1	May 2013	New York	Blood	Respiratory failure requiring high-dose corticosteroids	Died
2	July 2015	New Jersey	Blood	Brain tumor and recent villous adenoma resection	Died
3	April 2016	Maryland	Blood	Hematologic malignancy and bone marrow transplant	Died
4	April 2016	New York	Blood	Hematologic malignancy	Died
5	May 2016	Illinois	Blood	Short gut syndrome requiring total parenteral nutrition and high-dose corticosteroid use	Survived
6	July 2016	Illinois	Urine	Paraplegia with long-term, indwelling Foley catheter	Survived
7	August 2016	New York	Ear	Severe peripheral vascular disease and skull base osteomyelitis	Survived

* Mortality was not necessarily attributable to *C. auris* infection.

Schelenz *et al. Antimicrobial Resistance and Infection Control* (2016) 5:35
DOI 10.1186/s13756-016-0132-5

Antimicrobial Resistance and Infection Control

RESEARCH Open Access

First hospital outbreak of the globally emerging *Candida auris* in a European hospital

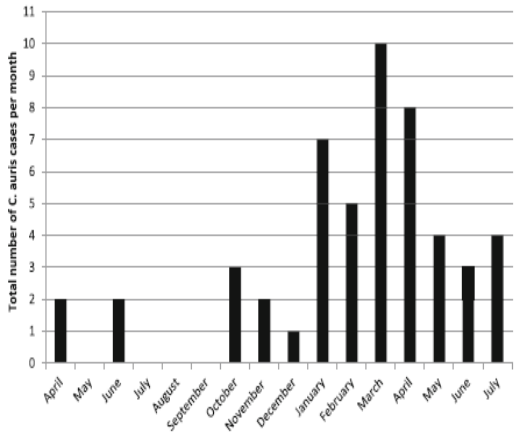


Fig. 1 New cases of *C. auris* per month. Total number of monthly new cases of *C. auris* are listed from the 1 April 2015 to the end of July 2016

AMERICAN SOCIETY FOR MICROBIOLOGY | Journal of Clinical Microbiology

Optimized Use of the MALDI BioTyper System and the FilmArray BCID Panel for Direct Identification of Microbial Pathogens from Positive Blood Cultures

B. Fiori,[a] T. D'Inzeo,[a] A. Giaquinto,[a] G. Menchinelli,[a] F. M. Liotti,[a] F. de Maio,[a] G. De Angelis,[a] G. Quaranta,[a] D. Nagel,[a] M. Tumbarello,[b] B. Posteraro,[c] M. Sanguinetti,[a] T. Spanu[a]

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March 2016 Volume 54 Number 3

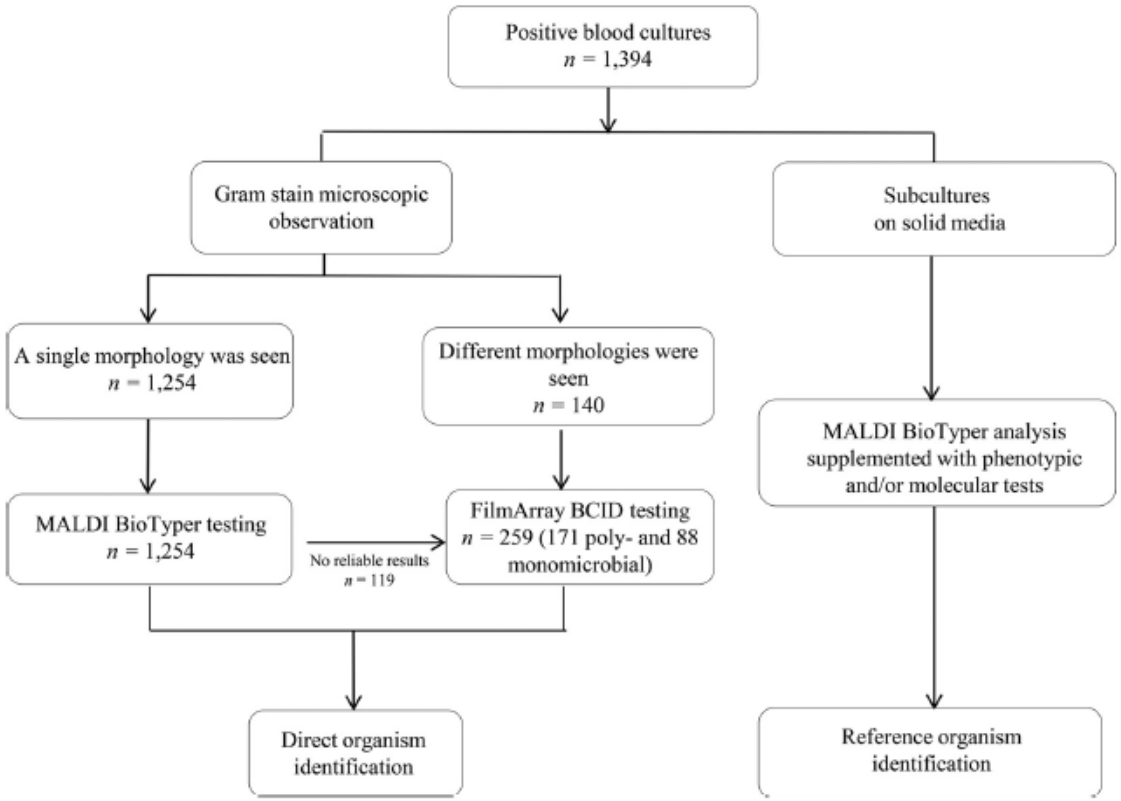


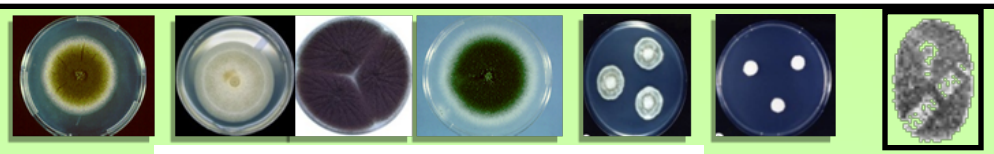
FIG 1 Bloodstream infection diagnostic workflow using direct (MALDI-TOF MS [MALDI BioTyper system] and/or FilmArray BCID panel) or culture-based (reference) microbial identification methods on positive blood culture (BC) broths. According to the developed algorithm, the FilmArray BCID panel assays were performed on BC broths that revealed multiple morphologies by Gram staining and in all cases for which MALDI BioTyper analysis failed to provide reliable results (i.e., identifications with scores of <1.8, multiple hits in the top 10 matches list with scores ranging from >1.7 to <1.8 that were suggestive of the presence of >1 microbial species, and identifications of organisms, such as *S. pneumoniae*). MALDI-TOF MS, matrix-assisted laser desorption ionization–time of flight mass spectrometry; BCID, blood culture identification.

Variabili correlate alla lunghezza dell'ospedalizzazione nei pazienti con sepsi – UCSC – Analisi multivariata

	HR	IC 95%	*P*
Number of comorbidities	-2.29	-4.18; -0.41	0.017
Medicine ward	5.71	1.87; 9.54	0.004
MALDI+call	-4.61	-4.18; -0.41	0.023

Courtesy R. Cauda, R. Murri

Work-flow for mould identification by MALDI-TOF MS



Unknown mould

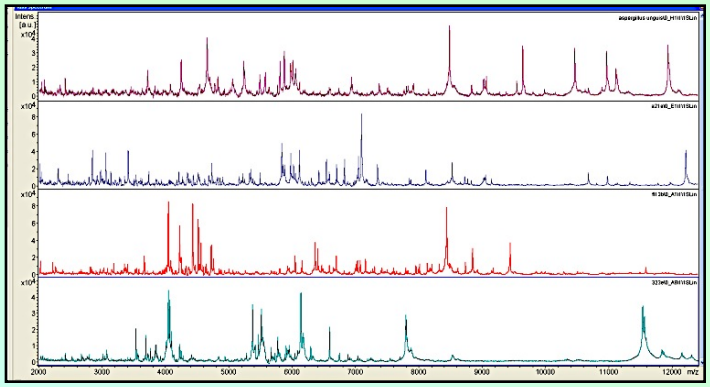
MALDI-TOF MS processing

H_2O

Absolute ethanol

HCCA matrix

MALDI-TOF spectrum profile acqusition



Match to fungi database

Log(score)≥2.0?

YES

Species identification

NO

Molecular identification

Data entry in fungi database

Journal of Clinical Microbiology®
MINIREVIEW

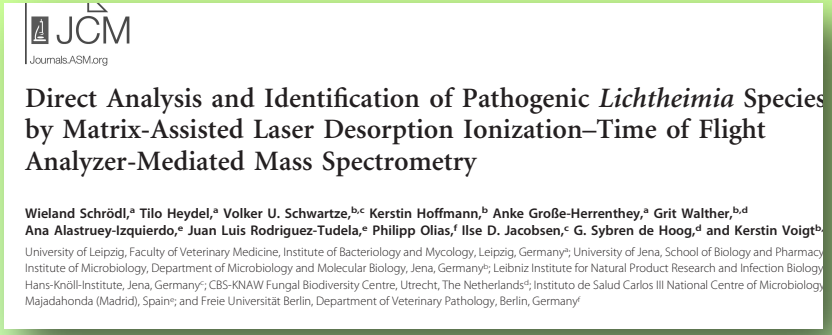
Identification of Molds by Matrix-Assisted Laser Desorption Ionization–Time of Flight Mass Spectrometry

Maurizio Sanguinetti,[a] Brunella Posteraro[b]
Institute of Microbiology, Università Cattolica del Sacro Cuore, Rome, Italy[a]; Institute of Public Health (Section of Hygiene), Università Cattolica del Sacro Cuore, Rome, Italy[b]

February 2017 Volume 55 Issue 2

TABLE 1 Studies evaluating the performance of MALDI-TOF MS for species identification of clinically relevant molds[a]

MALDI system[b]	Genus or group	Species studied (no. of species)	Acceptance criterion for ID[c]	No. of isolates with ID result/total no. of isolates identifiable in DB[d]	DB used for identification of isolates	Accuracy (%)	Comparator method(s)[e]	Reference
Vitek MS	*Aspergillus*	*A. flavus*	≥60%	3/9	Vitek MS IVD	33.0	MB, MO	23
				6/9	SARAMIS	66.0		
		A. nomius	≥60%	0/3	Vitek MS IVD	0.0	MB, MO	
				0/3	SARAMIS	0.0		
		A. tamarii	≥60%	0/2	Vitek MS IVD	0.0	MB, MO	
				0/2	SARAMIS	0.0		
Bruker Daltonics	*Aspergillus*	*Aspergillus* spp. (23)[f]	≥2.0	20/21	Biotyper	95.2	MB, MO	24
				24/24	In-house	100		
Bruker Daltonics	*Fusarium*	*Fusarium* spp. (19)[g]	≥2.0	222/268	In-house	82.8	MB, MO	25
Bruker Daltonics	*Rhizopus*	*R. arrhizus*	NR	25/25	In-house	100	MB	27
		R. microsporus	NR	13/13	In-house	100	MB	
Bruker Daltonics	*Talaromyces*	*T. marneffei*	≥2.0	39/39	In-house	100	MB	28
Bruker Daltonics	*Talaromyces*	*T. marneffei*	≥2.0	23/28	In-house (NTUH-3370)	82.1	MB, MO	29
	Paecilomyces	*Paecilomyces* spp. (3)	≥2.0	0/12	Biotyper (general library and Filamentous Fungi Library 1.0)	0.0	MB, MO	
	Fusarium	*Fusarium solani*	≥2.0	1/6	Biotyper (general library and Filamentous Fungi Library 1.0)	16.6	MB, MO	
	Rhizopus	*Rhizopus* spp. (3)	≥2.0	0/3	Biotyper (general library and Filamentous Fungi Library 1.0)	0.0	MB, MO	
Bruker Daltonics	*Paecilomyces*	*Paecilomyces* spp. (4)	≥2.0, ≥1.8	67/71	Original Biotyper library, supplemented	94.3	MB, MO	30
Vitek MS	Dermatophytes	*Trichophyton* spp. (7), *Arthroderma benhamiae*, *Microsporum* spp. (4), *Epidermophyton floccosum*	≥60%	125/131	In-house Vitek MS knowledge base	95.4	MB, MO	31
Bruker Daltonics	Dermatophytes	*Trichophyton* spp. (6), *Microsporum* spp. (4), *Epidermophyton floccosum*	>2.0, 1.7–2.0	64/64	In-house	100	MB, MO	32
Bruker Daltonics	Dermatophytes	*Trichophyton* spp. (7), *Microsporum* spp. (3), *Epidermophyton floccosum*	≥2.0	17/126	Original Biotyper library	13.5	MO	33
			<2.0	113/126	Original Biotyper library, supplemented	89.7		



JCM
Journals.ASM.org

Direct Analysis and Identification of Pathogenic *Lichtheimia* Species by Matrix-Assisted Laser Desorption Ionization–Time of Flight Analyzer-Mediated Mass Spectrometry

Wieland Schrödl,[a] Tilo Heydel,[a] Volker U. Schwartze,[b,c] Kerstin Hoffmann,[b] Anke Große-Herrenthey,[a] Grit Walther,[b,d] Ana Alastruey-Izquierdo,[e] Juan Luis Rodriguez-Tudela,[e] Philipp Olias,[f] Ilse D. Jacobsen,[c] G. Sybren de Hoog,[d] and Kerstin Voigt[b,c]

University of Leipzig, Faculty of Veterinary Medicine, Institute of Bacteriology and Mycology, Leipzig, Germany[a]; University of Jena, School of Biology and Pharmacy, Institute of Microbiology, Department of Microbiology and Molecular Biology, Jena, Germany[b]; Leibniz Institute for Natural Product Research and Infection Biology, Hans-Knöll-Institute, Jena, Germany[c]; CBS-KNAW Fungal Biodiversity Centre, Utrecht, The Netherlands[d]; Instituto de Salud Carlos III National Centre of Microbiology, Majadahonda (Madrid), Spain[e]; and Freie Universität Berlin, Department of Veterinary Pathology, Berlin, Germany[f]

- MALDI-TOF MS can be used to clearly discriminate *Lichtheimia* species from other pathogenic species of the Mucorales.
- The reliability and robustness of the MALDI-TOF-based identification are evidenced by the ability to discriminate between clinically relevant (*Lichtheimia corymbifera*, *L. ramosa*, and *L. ornata*) and irrelevant (*L. hyalospora* and *L. sphaerocystis*) species.
- In total, all 34 strains were unequivocally identified by MALDI-TOF MS to the generic level, 32 out of 34 of the *Lichtheimia* isolates were identified accurately with score values of >2 (probable species identification), and 25 of 34 isolates were identified to the species level with score values of >2.3 (highly probable species identification).
- The MALDI-TOF MS-based method reported here was found to be reproducible and accurate, with low consumable costs and minimal preparation time.

Key reasons underlying the demand for noninvasive and reliable fungal diagnostic tools

- Early diagnosis and identification of fungal infection (to improve the survival of affected patients)
- Accurate estimates of fungal disease burden (to sustain long-term surveillance programs for fungal diseases)

The Screening Performance of Serum 1,3-Beta-D-Glucan in Patients with Invasive Fungal Diseases: A Meta-Analysis of Prospective Cohort Studies

Tie-Ying Hou[1], Shou-Hong Wang[2], Sui-Xin Liang[3], Wen-Xin Jiang[4], Dan-Dong Luo[5], De-Hong Huang[6]*

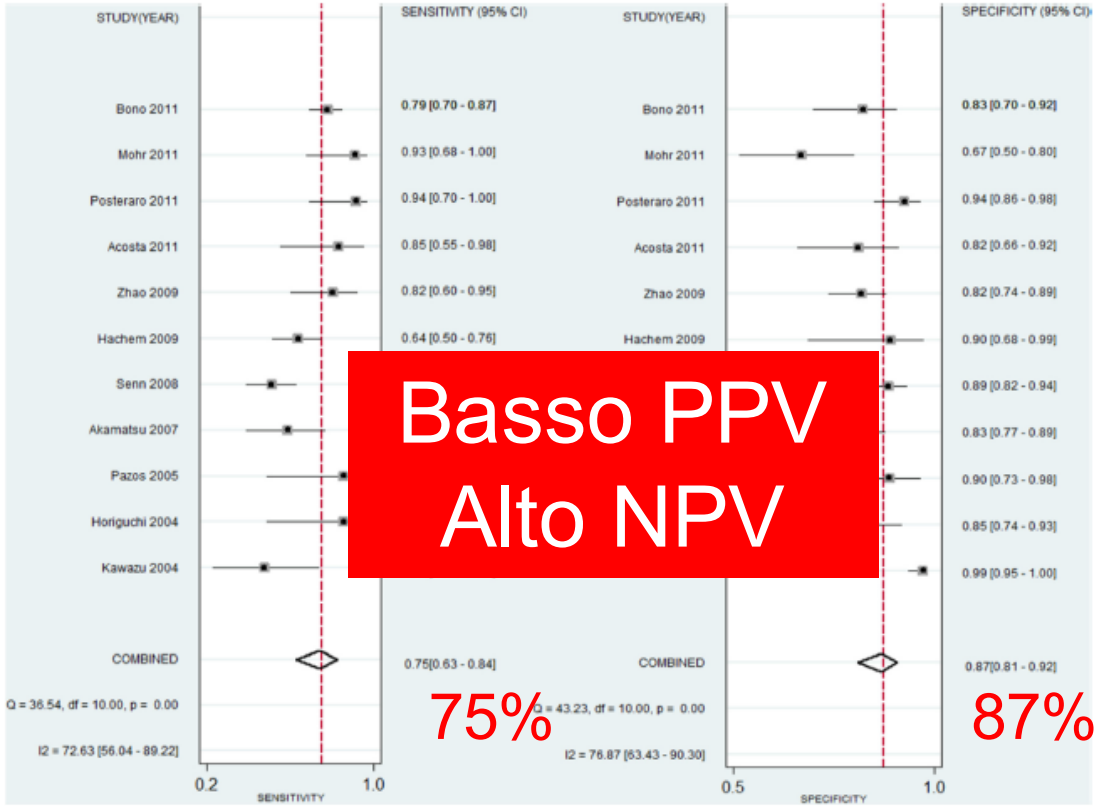


Fig 3. Forest plot of the pooled sensitivity and specificity of the BG assays for the diagnosis of IFDs.

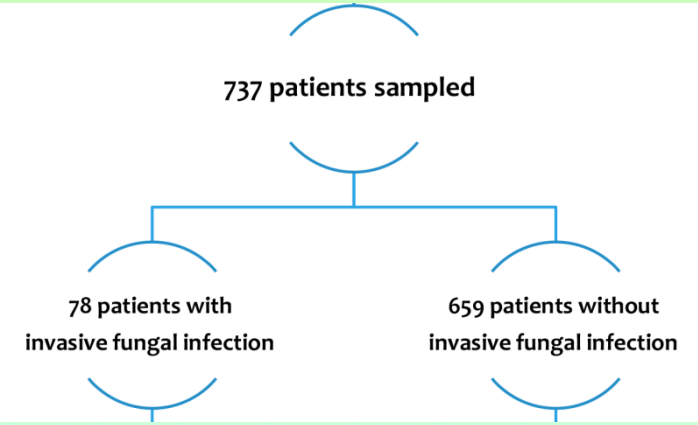
www.impactjournals.com/oncotarget/ Oncotarget, Advance Publications 2016

Oncotarget, Vol. 7, No. 16

February 18, 2016

(1, 3)-β-D-glucan assay for diagnosing invasive fungal infections in critically ill patients with hematological malignancies

ELie Azoulay[1], Nicolas Guigue[1], Michael Darmon[2], Djamel Mokart[3], Virginie Lemiale[1], Achille Kouatchet[4], Julien Mayaux[5], François Vincent[6], Martine Nyunga[1], Fabrice Bruneel[1], Antoine Rabbat[7], Stéphane Bretagne[1], Christine Lebert[8], Anne-Pascale Meert[9], Dominique Benoit[10], Frédéric Pene[7]



Cut-Off	Sensitivity	Specificity	Youden's index
60 pg/mL	0.82	0.52	0.34
80 pg/mL	0.72	0.65	0.37
100 pg/mL	0.62	0.70	0.32

10% IFI prevalence
PPV 21%
NPV 94%

bacterial infection. In conclusion, in unselected critically ill hematology patients with factors known to affect serum BG, this biomarker showed only moderate diagnostic performance and rarely detected IFI. However, the negative predictive value was high.

Posteraro et al. Critical Care 2011, 15:R249
http://ccforum.com/content/15/5/R249

CRITICAL CARE

RESEARCH Open Access

Early diagnosis of candidemia in intensive care unit patients with sepsis: a prospective comparison of (1→3)-β-D-glucan assay, *Candida* score, and colonization index

Brunella Posteraro[1], Gennaro De Pascale[2], Mario Tumbarello[3*], Riccardo Torelli[1], Mariano Alberto Pennisi[2], Giuseppe Bello[2], Riccardo Maviglia[2], Giovanni Fadda[1], Maurizio Sanguinetti[1] and Massimo Antonelli[2]

Table 3 Performances of (1→3)-β-D-glucan assay (BG), *Candida* score (CS), and colonization index for detection of invasive candidiasis in 95 patients

	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	PPV (%) (95% CI)	NPV (%) (95% CI)	PLR (%) (95% CI)	NLR (%) (95% CI)
BG cut-off value, 80 pg/mL	92.9 (66.1 to 99.8)	93.7 (85.8 to 97.9)	72.2 (46.5 to 90.3)	98.7 (92.8 to 99.9)	14.74 (4.65 to 47.52)	0.07 (0.02 to 0.39)
CS ≥3	85.7 (57.2 to 98.2)	88.6 (79.5 to 94.7)	57.1 (34.0 to 78.2)	97.2 (90.3 to 99.7)	7.51 (2.79 to 18.29)	0.16 (0.02 to 0.54)
Colonization index ≥0.5	64.3 (35.1 to 87.2)	69.6 (58.2 to 79.5)	27.3 (13.3 to 45.5)	91.7 (81.6 to 97.2)	2.12 (0.84 to 4.25)	0.51 (0.16 to 1.11)

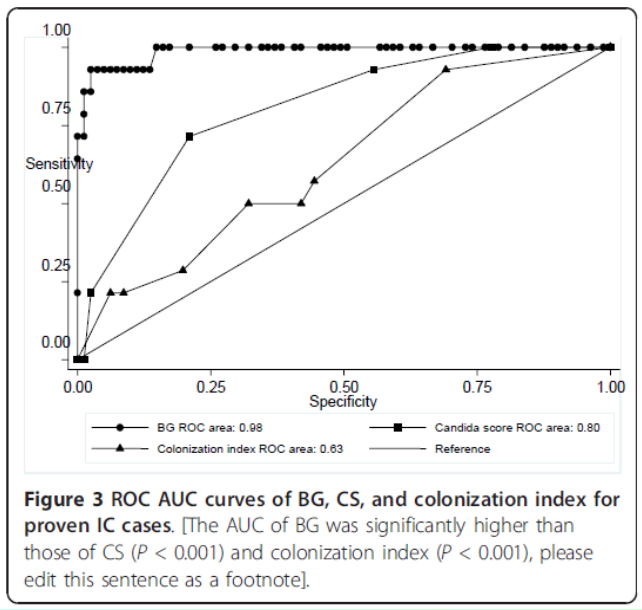
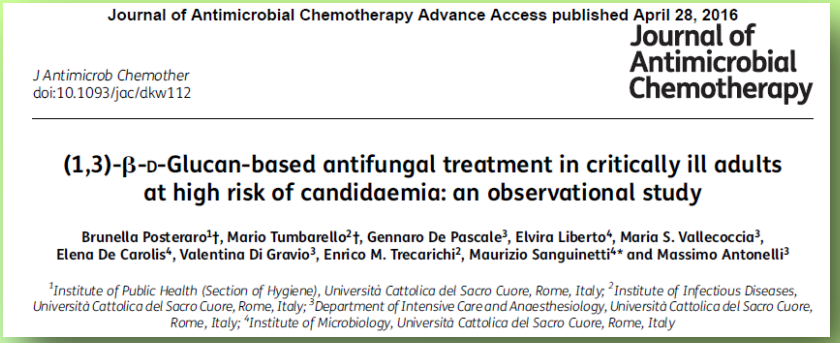


Figure 3 ROC AUC curves of BG, CS, and colonization index for proven IC cases. [The AUC of BG was significantly higher than those of CS ($P < 0.001$) and colonization index ($P < 0.001$), please edit this sentence as a footnote].

16% IFI prevalence
PPV 72,2%
NPV 98,7%

Posteraro *et al. Critical Care* 2011



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doi:10.1093/jac/dkw112

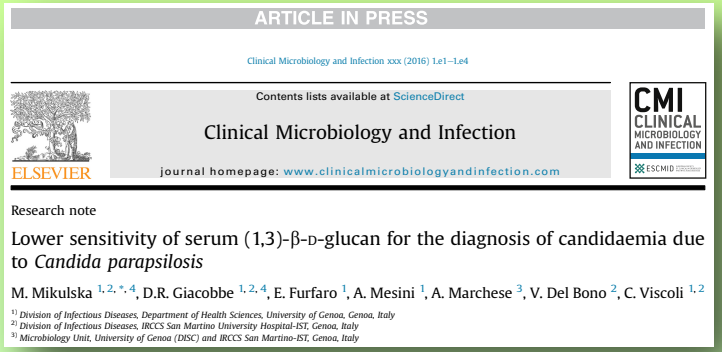
Journal of Antimicrobial Chemotherapy

(1,3)-β-D-Glucan-based antifungal treatment in critically ill adults at high risk of candidaemia: an observational study

Brunella Posteraro[1]†, Mario Tumbarello[2]†, Gennaro De Pascale[3], Elvira Liberto[4], Maria S. Vallecoccia[3], Elena De Carolis[4], Valentina Di Gravio[3], Enrico M. Trecarichi[2], Maurizio Sanguinetti[4]* and Massimo Antonelli[3]

[1]Institute of Public Health (Section of Hygiene), Università Cattolica del Sacro Cuore, Rome, Italy; [2]Institute of Infectious Diseases, Università Cattolica del Sacro Cuore, Rome, Italy; [3]Department of Intensive Care and Anaesthesiology, Università Cattolica del Sacro Cuore, Rome, Italy; [4]Institute of Microbiology, Università Cattolica del Sacro Cuore, Rome, Italy

- **Objectives:**
  - To determine the effects of a strategy that uses (1,3)-β-D-glucan (BDG) results for antifungal treatment of ICU patients at high risk of invasive candidiasis.
- **Methods:**
  - Patients were included in the analysis if they exhibited sepsis at the time of BDG testing, and they met *Candida*-score components (i.e., severe sepsis, total parenteral nutrition, surgery, or multifocal *Candida* colonization) to reach a ≥3 value.
- **Results:**
  - 198 patients were studied
  - Of 63 BDG-positive patients, 47 with candidemia and 16 with probable *Candida* infection, all received antifungal therapy
  - Of 135 BDG-negative patients, 110 (55.5%) did not receive antifungal therapy, whereas 25 (12.6%) were initially treated. In 14 of these 25 patients antifungals were discontinued as negative BDG results were notified. Candidemia was subsequently diagnosed only in one patient who did not receive prior antifungal therapy
  - The median antifungal therapy duration in candidemic patients differed from that in non-candidemic patients (14 days [IQR, 6–18 d] vs 4 days [IQR, 3–7 d]; p <0.001)
  - **Thus, unnecessary antifungal therapy was avoided in ~73% of potentially treatable patients and it was shortened in another ~20%**



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Contents lists available at ScienceDirect

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journal homepage: www.clinicalmicrobiologyandinfection.com

Research note

Lower sensitivity of serum (1,3)-β-D-glucan for the diagnosis of candidaemia due to *Candida parapsilosis*

M. Mikulska [1, 2, *, 4], D.R. Giacobbe [1, 2, 4], E. Furfaro [1], A. Mesini [1], A. Marchese [3], V. Del Bono [2], C. Viscoli [1, 2]

[1] Division of Infectious Diseases, Department of Health Sciences, University of Genoa, Genoa, Italy
[2] Division of Infectious Diseases, IRCCS San Martino University Hospital-IST, Genoa, Italy
[3] Microbiology Unit, University of Genoa (DISC) and IRCCS San Martino-IST, Genoa, Italy

- The aim of this study was to evaluate the sensitivity and the levels of 1,3-beta-D-glucan (BDG) among patients with candidaemia due to different *Candida* species
- Retrospective study of all (107) patients who had a single-species candidaemia and BDG testing performed within 48 h from the onset of candidaemia during 2009-2015 was performed.
- Factors influencing the sensitivity of BDG (presence of a central venous catheter, antifungal therapy and *Candida* species) were analysed in univariate and multivariate models.
- BDG sensitivity and levels were the highest in *C. albicans* candidaemia and lowest for *C. parapsilosis*
- In multivariate analysis, *Candida* species (*parapsilosis* versus others) was the only factor influencing the sensitivity of BDG (OR 0.3, 95% CI 0.1-0.7, p 0.006).
- The sensitivity of BDG in candidaemia seems highly dependent on the fungal species, with the lowest being for *C. parapsilosis.*

Open Forum Infectious Diseases

MAJOR ARTICLE

Prospective Evaluation of Serum β-Glucan Testing in Patients With Probable or Proven Fungal Diseases

Cécile Angebault,[1,7] Fanny Lanternier,[2,7,8] Frédéric Dalle,[9] Cécile Schrimpf,[2] Anne-Laure Roupie,[2] Aurélie Dupuis,[1] Aurélie Agathine,[1] Anne Scemla,[3,7,11] Etienne Paubelle,[4,7] Denis Caillot,[10] Bénédicte Neven,[5] Pierre Frange,[5,6] Felipe Suarez,[4,7] Christophe d'Enfert,[12,13] Olivier Lortholary,[2,7,8] and Marie-Elisabeth Bougnoux[1,7,12,13]

Table 1. Demographics, Clinical Characteristics, and Mycological Data of the Patients With Invasive Candidiasis at the Time of Diagnosis

								BG at TOD	
Patient ID	Age	Gender	Category of Patient	Sample Providing Diagnosis	*Candida* Species/ Diagnostic Element	Location of Candidiasis	Duration of Candidemia (Days)	Time Interval Between Sample Providing Diagnosis and BG Sample (Days)	BG Value (pg/mL)
1	23	M	Hematology	Blood culture	*Candida lusitaniae*	Blood	3	2	267
2	72	M	Hematology	Blood culture	*Candida krusei*	Blood	1	−1	>523
3	41	F	Hematology	Blood culture	*Candida glabrata*	Blood	3	3	<80
4	46	M	Hematology	Blood culture	*Candida tropicalis*	Blood	1	2	>523
5	59	M	Hematology	Blood culture	*C. glabrata*	Blood	4	3	<80
6	61	M	Hematology	Blood culture	*Candida guilliermondii*	Blood	5	−1	<80
7	76	M	Hematology	Blood culture	*C. glabrata*	Blood	2	0	471
8	64	F	Hematology	Blood culture	*Candida albicans*	Blood	1	0	156
9	62	F	Hematology	Blood culture	*C. guilliermondii*	Blood	1	−1	<80
10	51	F	Hematology	Blood culture	*C. krusei*	Blood	6	3	116
11	46	M	Hematology	Blood culture	*C. guilliermondii*	Blood	2	2	<80
12	68	M	Hematology	Blood culture	*Candida norvegensis*	Blood	5	−1	<80
13	74	M	Hematology	Blood culture	*C. albicans*	Blood	4	1	278
14	61	F	Hematology	Blood culture	*C. norvegensis*	Blood	3	2	<80
15	75	M	Hematology	Blood culture	*C. albicans*	Blood	1	3	<80
16	77	M	Hematology	Blood culture	*C. albicans*	Blood	1	2	233
17	30	M	Hematology	Blood culture	*C. albicans*	Blood	4	1	>523
18	56	M	SOT	Blood culture	*Candida parapsilosis*	Blood	1	2	131
19	65	M	SOT	Blood culture	*C. parapsilosis*	Blood	4	3	>523
20	70	F	SOT	Blood culture	*C. parapsilosis*	Blood	1	5	87
21	44	F	SOT	Blood culture	*C. tropicalis*	Blood	1	0	260
22	14	F	Pediatric ICU	Blood culture	*Kodamaea ohmeri*	Blood	3	6	<80
23	0	M	Pediatric ICU	Blood culture	*C. albicans*	Blood	1	2	372
24	17	F	Pediatric ICU	Blood culture	*C. albicans*	Blood	1	4	100
25	2	M	Pediatric ICU	Blood culture	*C. albicans*	Blood	2	5	>523
26	2	M	Pediatric ICU	Blood culture	*C. parapsilosis*	Blood	1	3	<80
27	6	F	Pediatric ICU	Blood culture	*Hyphopichia burtonii*	Blood	2	2	<80
28	1	F	Pediatric ICU	Blood culture	*C. lusitaniae*	Blood	2	7	<80
29	1	F	Pediatric ICU	Blood culture	*C. tropicalis*	Blood	1	3	216
30	2	M	Pediatric ICU	Blood culture	*C. guilliermondii*	Blood	1	2	<80
31	75	M	Hematology	Blood culture	*C. albicans*	Blood, Urine	1	2	428
32	12	M	Pediatric ICU	Blood culture	*C. lusitaniae*	Blood, Urine	1	3	<80

Patients with *C. albicans* candidemia were significantly more likely to have a positive BG result at the TOD (15 of 16) than did patients with candidemia due to another *Candida* species (9 of 25; multivariate odds ratio = 25.4; 95% confidence interval, 3.6–560.3; P <.01)

The most difficult *Candida* species to be detected were *C. guilliermondii*, *C. norvegensis* and *C. parapsilosis*

J Antimicrob Chemother 2016; **71**: 2386–2396
doi:10.1093/jac/dkw156 Advance Access publication 12 May 2016

Journal of Antimicrobial Chemotherapy

ECIL guidelines for the diagnosis of *Pneumocystis jirovecii* pneumonia in patients with haematological malignancies and stem cell transplant recipients

Alexandre Alanio[1], Philippe M. Hauser[2], Katrien Lagrou[3], Willem J. G. Melchers[4], Jannik Helweg-Larsen[5], Olga Matos[6], Simone Cesaro[7], Georg Maschmeyer[8], Hermann Einsele[9], J. Peter Donnelly[10], Catherine Cordonnier[11]*, Johan Maertens[12] and Stéphane Bretagne[1] on behalf of the 5th European Conference on Infections in Leukemia (ECIL-5†), a joint venture of The European Group for Blood and Marrow Transplantation (EBMT), The European Organization for Research and Treatment of Cancer (EORTC), the Immunocompromised Host Society (ICHS) and The European LeukemiaNet (ELN)

Table 1. Recommended diagnosis of PCP in adult patients with haematological malignancies and stem cell transplant recipients (it is not recommended that PCP diagnosis should rely only on clinical criteria or imaging)

Specimen/technique	Recommended usage	Strength of recommendation	Quality of evidence
Diagnostic specimen			
BAL fluid	allows detection of multiple aetiologies	A	II
other (non-invasive specimens[a])	alternative specimen to BAL	B	II
Diagnostic technique			
Respiratory samples			
immunofluorescence assays	most sensitive microscopic diagnostic method	A	II
real-time quantitative PCR	routine diagnosis allowing quantification	A	III
	exclusion of PCP by negative result in BAL only	A	II
Serum			
β-D-glucan	detection in serum as a contributive diagnostic tool	A	II
	exclusion of PCP by negative result	A	II
genotyping using multilocus sequence markers	investigation of suspected outbreaks	A	II
detection of dihydropteroate synthase mutations	not recommended in case of treatment failure	B	II

[a]Includes induced sputa, sputa and upper respiratory samples (nasopharyngeal aspirates, nasal or oral washes).

J Antimicrob Chemother 2016; **71**: 2386–2396
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Journal of Antimicrobial Chemotherapy

ECIL guidelines for the diagnosis of *Pneumocystis jirovecii* pneumonia in patients with haematological malignancies and stem cell transplant recipients

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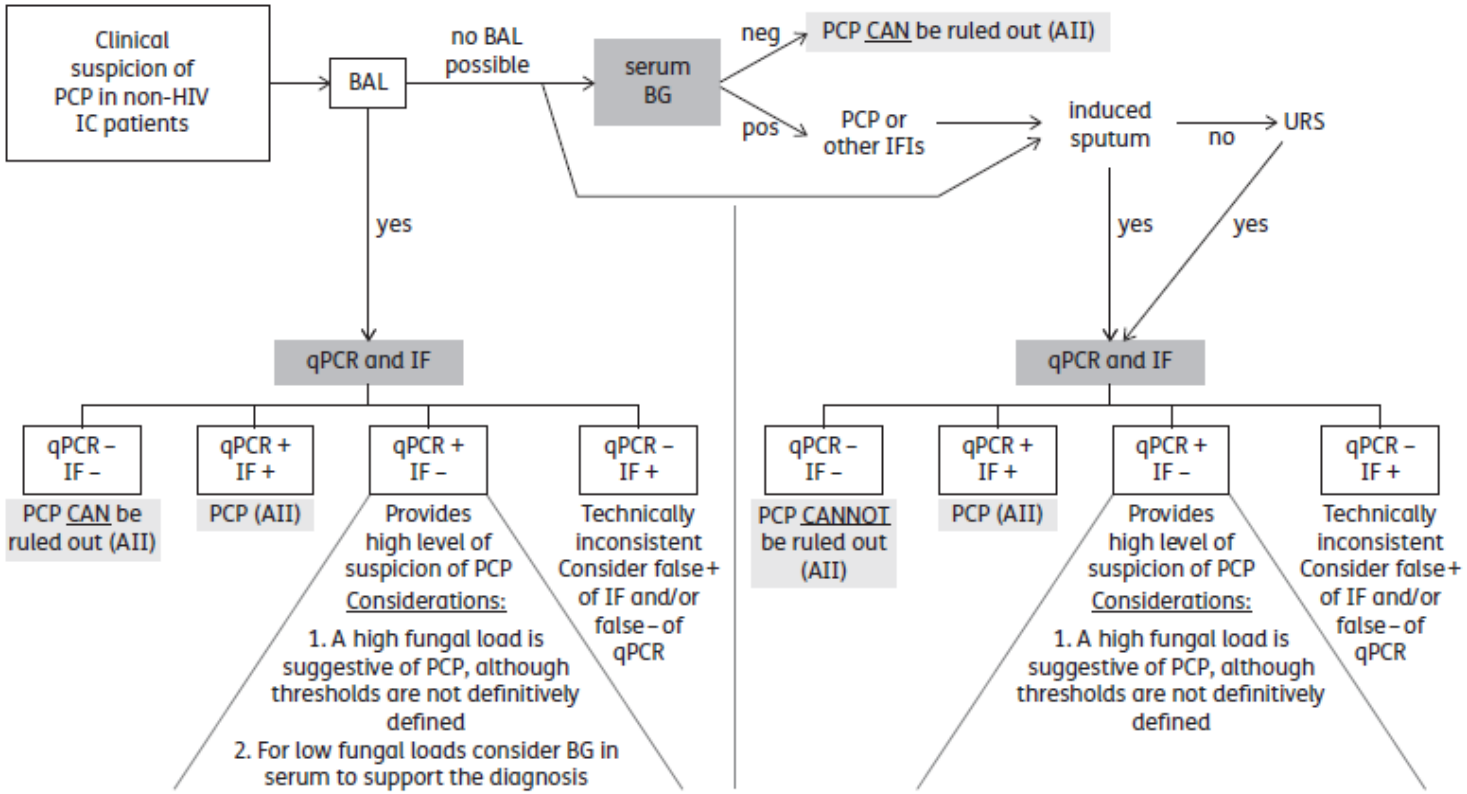

Figure 1. Flow chart for the diagnosis of *Pneumocystis* pneumonia in non-HIV immunocompromised (IC) patients. Biological tests are highlighted in dark grey and recommendations in light grey. BG, β-D-glucan; A-II, level of recommendation; IFI, invasive fungal infection.

ß-D-glucan assay in diagnosing invasive aspergillosis

(ESCMID & ECMM joint recommendations for the laboratory diagnosis of invasive aspergillosis)

Population	Intention	Intervention	SoR	QoE	Comment
Mixed population: adult ICU, haematological disorders, SOT	To diagnose IFD	Diagnostic assay	C	II	5 different assays. Fungitell FDA approved and available in US and Europe, others only available in Japan Overall sensitivity of 77% and specificity of 85% Specificity limits its value in this setting
		Screening assays	C	II	Two or more consecutive samples: sensitivity: 65% Specificity: 93% Studies included once to twice weekly
Adult haematological malignancy and HSCT	To diagnose IFD	Diagnostic assay	C	II	Overall sensitivity: 50-70%, specificity : 91-99%
ICU – mixed adult immunocompromised patients (haematology, SOT, cancer, immunosuppressive therapy, HIV)	To diagnose IA	Diagnostic assay	C	II	Overall sensitivity: 78 -85%, specificity: 36-75%, NPV: 85-92% Specificity increased at higher cut-off values
ICU – mixed adult population: SOT, liver failure, immunosuppressed		Screening assays	C	III	Sensitivity: 91%, specificity: 58%, PPV: 25%, NPV: 98%. Positive mean of 5.6 days before positive mould culture High false positive rate in early ICU admission
Adult haematological malignancy and HSCT	To diagnose IA	Diagnostic assay	C	II	Overall sensitivity: 57-76%, specificity: 95-97%
		Screening assays	C	II	Overall sensitivity: 46%, specificity: 97% Confirmation with GM increases specificity

ICU, intensive care unit; SOT solid organ transplantation; IFD, invasive fungal disease; IA, invasive aspergillosis; PPV, positive predictive value; NPV, negative predictive value; GM, galactomannan; BDG, beta-D-glucan test.

From: Lagrou *et al*, in preparation

Blood GM testing in diagnosing invasive aspergillosis

(ESCMID & ECMM joint recommendations for the laboratory diagnosis of invasive aspergillosis)

Population	Intention	Intervention	SoR	QoE	Comment
Prolonged neutropenic patients and allogeneic stem cell transplantation recipients not on mold-active prophylaxis	Prospective screening for IA	GM in blood	A	I	Highest test accuracy requiring 2 consecutive samples with an OD index ≥ 0.5 or retesting the same sample Prospective monitoring should be combined with HRCT and clinical evaluation
		Draw samples every 3-4 days	C	III	
Prolonged neutropenic patients and allogeneic stem cell transplantation recipients on posaconazole prophylaxis	Prospective screening for iIA	GM in blood	D	II	Low prevalence of invasive aspergillosis in this setting with consequently low PPV of blood GM test Prophylaxis may have a negative impact on sensitivity of the test
Patients with a haematological malignancy	To diagnose IA	GM in blood			
•Neutropenic patients			A	II	
•Non-neutropenic patients			B	II	Significant lower sensitivity in non-neutropenic patients
ICU patients	To diagnose IA	GM in blood	C	II	Better performance in neutropenic than in non-neutropenic patients
Solid organ recipients	To diagnose IA	GM in blood	C	II	Low sensitivity, good specificity. Most data for lung TX (few other SOT patients with IA included)
Cancer patients	To monitor treatment	GM in blood	A	II	

From: Lagrou *et al*, in preparation

MAJOR ARTICLE

Serum Galactomannan–Based Early Detection of Invasive Aspergillosis in Hematology Patients Receiving Effective Antimold Prophylaxis

Rafael F. Duarte,[1] Isabel Sánchez-Ortega,[1] Isabel Cuesta,[2] Montserrat Arnan,[1] Beatriz Patiño,[1] Alberto Fernández de Sevilla,[1] Carlota Gudiol,[1] Josefina Ayats,[3] and Manuel Cuenca-Estrella[2]

[1]Department of Hematology, Catalan Institute of Oncology, Hospital Duran i Reynals, Barcelona, [2]Centro Nacional de Microbiología, Instituto de Salud Carlos III, Madrid, and [3]Department of Microbiology, Hospital Universitario de Bellvitge, Barcelona, Spain

Table 5. Performance of the Serum Galactomannan Assay in High-Risk Patients Receiving Effective Antimold Prophylaxis

Evaluable episodes[a], No.	217	
GM test results[b]		
True positive, No. (%)	5 (2.3)	
True negative, No. (%)	182 (83.9)	
False positive, No. (%)	30 (13.8)	
False negative	. . .	
Sensitivity, %	100[c]	70[d]
Specificity, %	85.5[c]	90[d]
Scenario 1: GM screening of all cases[e]		
Negative predictive value, %	100[c]	99.4[d]
Positive predictive value, %	11.8[c]	11.9[d]
Scenario 2: Diagnosis of IFD suspicion only[f]		
Negative predictive value, %	100[c]	70.6[d]
Positive predictive value, %	89.6[c]	89.7[d]

CLINICAL AND VACCINE IMMUNOLOGY, May 2007, p. 638–640 Vol. 14, No. 5
1556-6811/07/$08.00+0 doi:10.1128/CVI.00479-06

Histoplasmosis-Associated Cross-Reactivity in the BioRad Platelia *Aspergillus* Enzyme Immunoassay▽

L. Joseph Wheat,[1]* Emily Hackett,[1] Michelle Durkin,[1] Patricia Connolly,[1] Ruta Petraitiene,[2,3] Thomas J. Walsh,[2] Kenneth Knox,[4] and Chadi Hage[4]

MiraVista Diagnostics, Indianapolis, Indiana[1]; National Cancer Institute, Pediatric Oncology Branch, Immunocompromised Host Section, CRC, Rm. 1W-5750, 10 Center Drive, Bethesda, Maryland 20892-1100[2]; Laboratory Animal Sciences Program, SAIC-Frederick, Inc., Frederick, Maryland 21702[3]; and Indiana University School of Medicine, Department of Pulmonary Medicine, Roudebush Veterans' Administration Hospital, 1481 West Tenth Street, Indianapolis, Indiana 46202[4]

Received 19 December 2006/Returned for modification 24 January 2007/Accepted 8 February 2007

We observed false-positive results in the Platelia *Aspergillus* enzyme-linked immunoassay (EIA) for specimens from patients with histoplasmosis and mice with experimental infection. Platelia *Aspergillus* EIA-positive specimens were negative in the second-generation *Histoplasma* antigen EIA. Care must be taken to exclude histoplasmosis for patients with positive Platelia *Aspergillus* EIA results.

TABLE 1. Clinical specimens identified to have positive results in second-generation *Histoplasma* EIA and Platelia *Aspergillus* EIA

Case no.	Second-generation *Histoplasma* EIA result (U)[a]		Platelia *Aspergillus* EIA result for serum (GMI)	Type of histoplasmosis[b]
	Serum	Urine		
1	42.6	31.4	6.2	Pulmonary
2	QNS	20.4	5.5	Disseminated
3	4.2	12.5	5.5	Cavitary
4	33.9	32.0	1.5	Disseminated
5	24.2	ND	4.7	Disseminated
6	98.7	66.8	7.8	Disseminated

[a] QNS, quantity not sufficient to test; ND, not done.
[b] None of these patients showed evidence of aspergillosis.

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DIAGNOSTIC MICROBIOLOGY AND INFECTIOUS DISEASE
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Notes

Galactomannan testing might be useful for early diagnosis of fusariosis☆

Małgorzata Mikulska[a,*], Elisa Furfaro[a], Valerio Del Bono[a], Francesca Gualandi[b], Anna Maria Raiola[b], Maria Pia Molinari[c], Paola Gritti[c], Maurizio Sanguinetti[d], Brunella Posteraro[d], Andrea Bacigalupo[b], Claudio Viscoli[a]

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Received 13 November 2011; accepted 13 December 2011

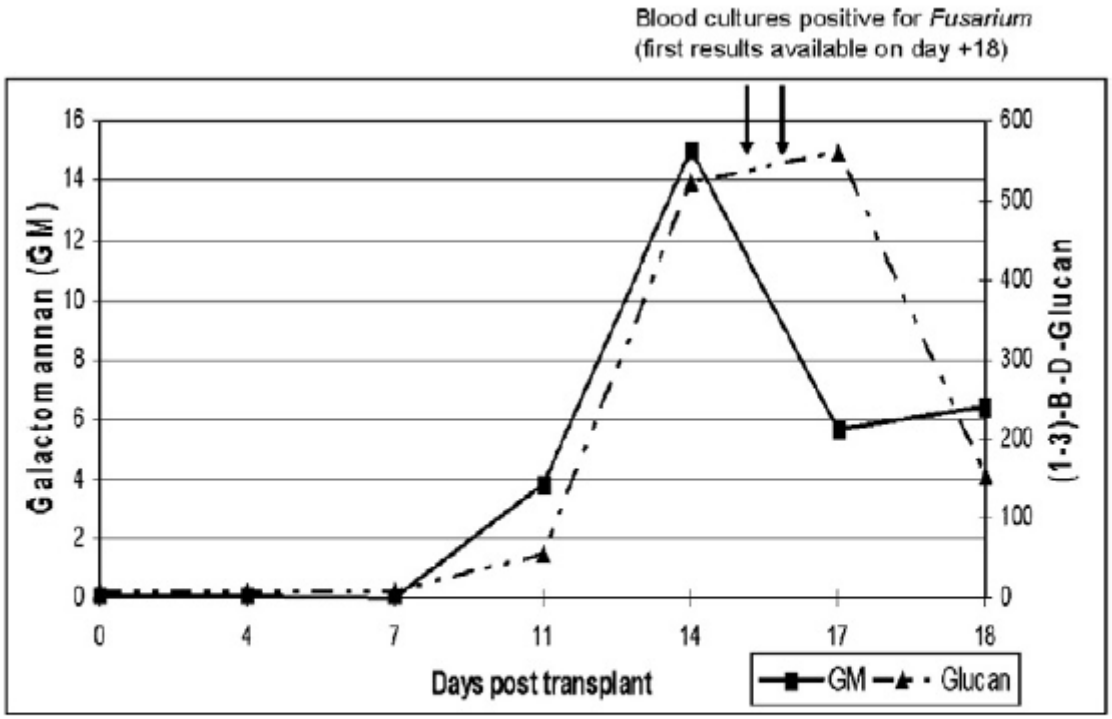

Fig. 1. Galactomannan (GM) and (1,3)-beta-glucan serum levels in a patient with fusariosis.

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Cross-Reactivity of *Fusarium* spp. in the *Aspergillus* Galactomannan Enzyme-Linked Immunosorbent Assay

Anna Maria Tortorano,[a] Maria Carmela Esposto,[a] Anna Prigitano,[a] Anna Grancini,[b] Cristina Ossi,[c] Caterina Cavanna,[d] and Giuliana Lo Cascio[e]

TABLE 1 Serum GM index results for patients with disseminated/deep-seated *Fusarium* infection[a]

Patient	Sex	Age (yr)	Predisposing factor(s)	*Fusarium* infecting isolate	Positive biological sample(s)	Serum GM index range
1	M	29	Allo-HSCT	*F. oxysporum*	Pleural fluid	0.69–0.90
2	M	63	Leukemia	*F. oxysporum*	Bronchial secretions	1.40–2.30
3	M	55	AML	*F. proliferatum*	Blood	0.89–0.86
4	F	61	Allo-HSCT	*F. proliferatum*	Blood	1.37–2.33
5	F	56	AML, allo-HSCT	*F. proliferatum*	Blood	0.7–2.15
6	M	8	Non-Hodgkin's lymphoma	*F. proliferatum*	Blood	0.53–7.7
7	M	19	ALL, auto-HSCT	*F. proliferatum*	Blood	0.54–1.45
8	F	57	Postchemotherapy aplasia, RAEB	FSSC	Purulent nasal discharge	0.50–0.60
9	M	41	Non-Hodgkin's lymphoma, allo-HSCT	*F. verticillioides*	Skin biopsy	Negative
10	M	5	ALL	*F. verticillioides*	Blood	Negative
11	F	9	ALL, auto-HSCT	*F. verticillioides*	Blood	0.70–4.16

[a] M, male; F, female; allo-HSCT, allogeneic hematopoietic stem cell transplantation; AML, acute myeloid leukemia; ALL, acute lymphoblastic leukemia; RAEB, refractory anemia with excess blasts; auto-HSCT, autologous hematopoietic stem cell transplantation; FSSC, *Fusarium solani* species complex.

GM testing in diagnosing invasive aspergillosis in other clinical samples

(ESCMID & ECMM joint recommendations for the laboratory diagnosis of invasive aspergillosis)

Population	Intention	Intervention	SoR	QoE	Comment
Any	To diagnose pulmonary aspergilosis	Galactommanan in BAL in haematological patients	A	II	Galactomannan in BAL is a good tool to diagnose Optimal cut-off-ranging from 0.5 to 1.0
Any	To diagnose cerebral aspergillosis	Galactomannan in CSF	B	II	No validated cut-off
Any	To detect galactomannan in tissue	To apply galactomannan test on lung biopsies	B	II	Cut-off 0.5; High sensitivity (90 %) and specificity (95%); Specimens need to be sliced, precondition for doing so is that sufficient material is available Dilution in isotonic saline

From: Lagrou *et al*, in preparation

Galactomannan and Polymerase Chain Reaction–Based Screening for Invasive Aspergillosis Among High-Risk Hematology Patients: A Diagnostic Meta-analysis

Marios Arvanitis,[1,2,3] Theodora Anagnostou,[1,2] and Eleftherios Mylonakis[1,2]

[1]Infectious Diseases Division, Rhode Island Hospital, and [2]Warren Alpert Medical School of Brown University, Providence, Rhode Island; and [3]Internal Medicine Department, Boston Medical Center, Massachusetts

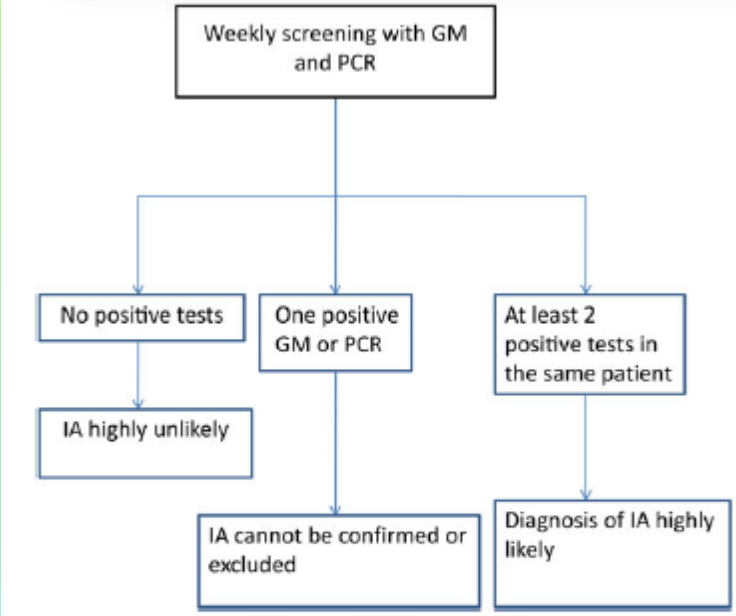

Figure 3. Algorithm for invasive aspergillosis (IA) screening for high-risk populations. When all test results are consistently negative, the negative predictive value for IA is 100%. When 2 tests are positive, the posttest probability is close to 88% and IA is highly likely. Abbreviations: GM, galactomannan; PCR, polymerase chain reaction.

The absence of any positive test can obviate the need for antifungal agents with a NPV of 100%, whereas the presence of at least 2 positive results is highly suggestive of an active infection with a PPV of 88%.

Practice Guidelines for the Diagnosis and Management of Aspergillosis: 2016 Update by the Infectious Diseases Society of America

Clinical Infectious Diseases® 2016;63(4):433–42

Thomas F. Patterson,[1,a] George R. Thompson III,[2] David W. Denning,[3] Jay A. Fishman,[4] Susan Hadley,[5,b] Raoul Herbrecht,[6] Dimitrios P. Kontoyiannis,[7] Kieren A. Marr,[8] Vicki A. Morrison,[9] M. Hong Nguyen,[10] Brahm H. Segal,[11] William J. Steinbach,[12] David A. Stevens,[13] Thomas J. Walsh,[14] John R. Wingard,[15] Jo-Anne H. Young,[16] and John E. Bennett[17,a]

- **If PCR assays are used, results should be considered with other diagnostic tests and the clinical context (strong recomm; moderate-quality evid.)**
- **Serum and BAL galattomannan (GM) is recommended as an accurate marker for the diagnosis of IA in adult and pediatric patients** when used in certain patient subpopulations (hematologic malignancy, HSCT) **(strong recomm; high-quality evid.)**
- **GM is not recommended for routine blood screening in patients receiving mold-active antifungal therapy or prophylaxis**, but can be applied to bronchoscopy specimens from those patients **(strong recomm; high-quality evid.)**
- •Serum assays for **(1->3)-β-D-glucan** are recommended for diagnosing IA in high-risk patients (hematologic malignancy, allogeneic HSCT), but are not specific for Aspergillus **(strong recomm; moderate-quality evid.)**
- **We recommend performing BAL** in patients with a suspicion of IPA **(strong recomm; moderate- quality evid.)**

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REVIEW

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Future MICROBIOLOGY

Laboratory diagnosis of mucormycosis: current status and future perspectives

Michaela Lackner[1], Rita Caramalho[1] & Cornelia Lass-Flörl*[,1]

Table 1. Immunological diagnostic tests for mucormycosis.

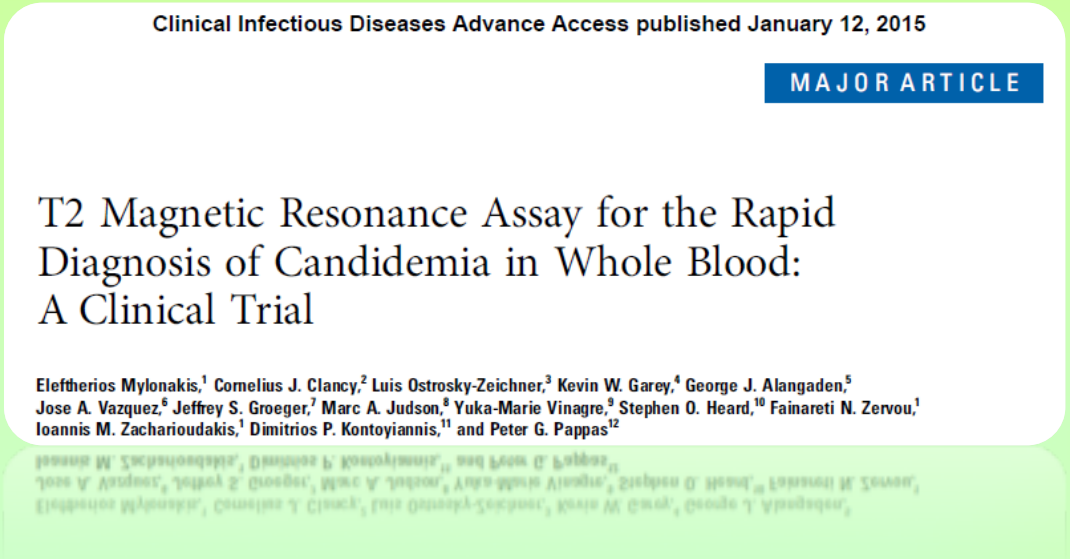
Method	Target structure	Clinical specimens	Clinical studies	Sensitivity/ specificity	Cross-reactivity	Comments	Ref.
ELISA	*Rhizopus arrhizus* and *Rhizopuspusillus* antibody	Sera from patients infected with *Mucorales* spp. (n = 43)	None	81%/94%	*Candida* spp., *Aspergillus* spp.	Minimal positivity titer dilutionof 1:400	[53]
Western immunoblotting	*R. arrhizus* antigen homogenates	Sera from patients infected with *R. arrhizus* (n = 5)	None	NA/NA	NA	NA	[50]
ELISA, Western blot, immunohistochemistry with anti-*R. arrhizus* monoclonal mouse antibody	Cytoplasm, hyphae, walls and septae, of *R. arrhizus* WSSAs	Tissue samples from patients with systemic mycoses (n = 40)	Limited data available	NA/NA	NA	14–110 kDa *R. arrhizus* 1–14 to 52 kDa *Lichtheimia corymbifera* 20–28 kDa *R. pusillus*	[54,55]
ELISA (ELISpot) or immunocytofluorimetric assays	Mucorales specific IFN-γ-producing T cells	Peripheral blood samples from patients with proven IM (n = 80)	None	*R. pusillis* (**6**/4) *R. arrhizus* (**5**/5) *L. corymbifera* (**5**/4)/NA	None	Positivity for 2–10 SFCs	[56]

Sensitivity/specificity: number of samples analyzed (in bold)/samples positive (not bold).
IM: Invasive mucormycosis; NA: Not available; SFC: Spot-forming cell; WSSA: Water-soluble somatic antigen.

T2Candida Panel powered by T2 Magnetic Resonance (T2MR)

Figure 1. T2Dx Instrument

- T2MR combines proven magnetic resonance with innovative nanotechnology to accurately identify *Candida* pathogens in whole blood faster and easier than blood culture-based diagnostics



Clinical Infectious Diseases Advance Access published January 12, 2015

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]

- T2MR demonstrated an overall specificity per assay of 99.4% with a mean time to negative result of 4.2 ± 0.9 hours. The overall sensitivity was found to be 91.1% (96.6% considering also other studies) with a mean time of 4.4 ± 1.0 hours for detection and species identification

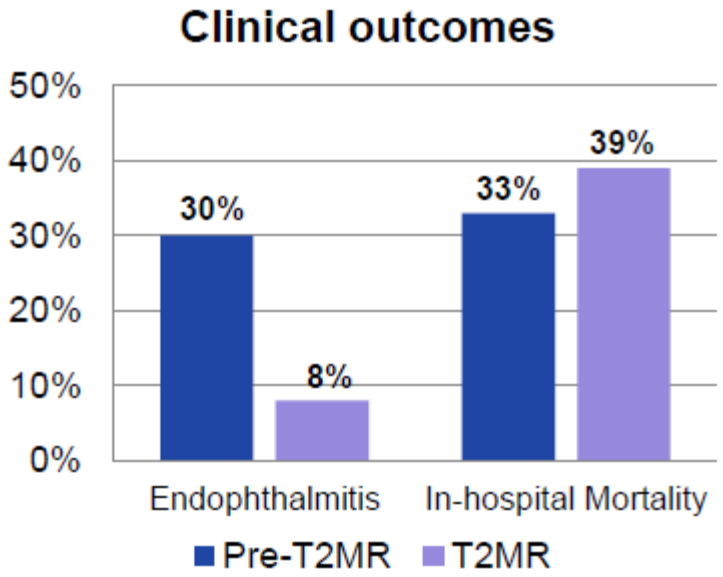
T2 Magnetic Resonance Improves the Timely Management of Candidemia

Nicole M Wilson[1], Rachel M. Kenney[1], Robert J. Tibbetts, George Alangaden[1], Susan L. Davis[1,2], Linoj P. Samuel[1]
[1]Henry Ford Hospital, Detroit, MI; [2]Wayne State University, Eugene Applebaum College of Pharmacy and Health Sciences

Time Endpoints and Patient Outcomes

Time Endpoints	Pre-T2MR	Post-T2MR	P value
Time to appropriate therapy, hrs	39.6 (12.9, 54.75)	26.6 (2.5, 47.1)	0.01
Time to detection of Candida species, hrs	41.75 (30.1, 65.9)	25.25 (6.3, 43)	0.01
Length of stay, days	13 (7-23)	9 (6-21	0.164
ICU length of stay, days	13 (6-21)	6 (4-13)	0.009

Data presented as median (IQR)



From: Wilson *et al*, ID Week 2016

Clinical Infectious Diseases

INVITED ARTICLE

HEALTHCARE EPIDEMIOLOGY: Robert A. Weinstein, Section Editor

Azole Resistance in *Aspergillus fumigatus*: Can We Retain the Clinical Use of Mold-Active Antifungal Azoles?

Paul E. Verweij,[1] Anuradha Chowdhary,[2] Willem J. G. Melchers,[1] and Jacques F. Meis[1,3]

[1]Department of Medical Microbiology, Radboud University Medical Centre, Nijmegen, The Netherlands; [2]Department of Medical Mycology, Vallabhbhai Patel Chest Institute, University of Delhi, India; and [3]Department of Medical Microbiology and Infectious Diseases, Canisius Wilhelmina Hospital, Nijmegen, The Netherlands

Clinical Infectious Diseases® 2016;62(3):362–8

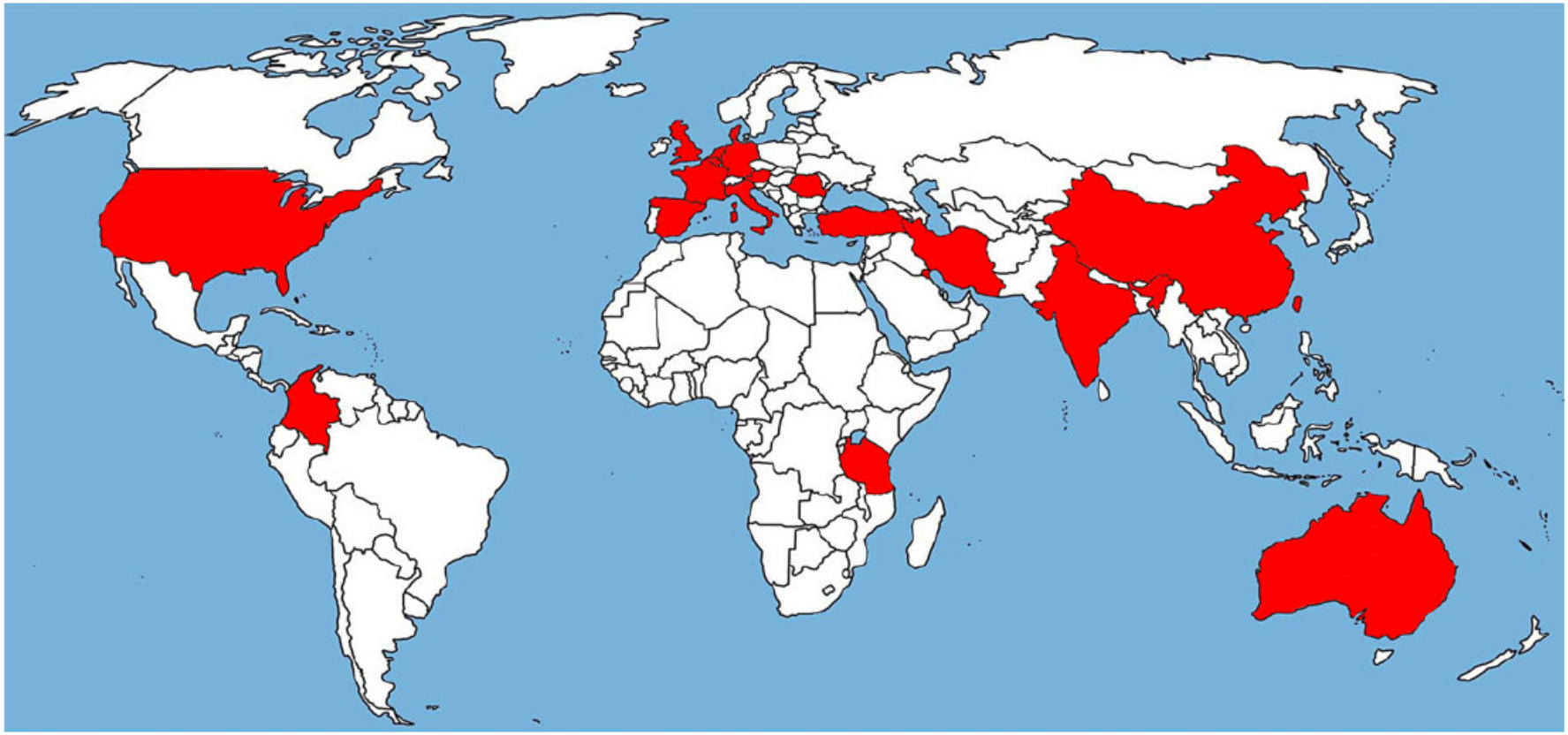


Figure 1. Shaded areas show countries that have reported the TR_{34}/L98H and TR_{46}/Y121F/T289A resistance mechanism in clinical or environmental *Aspergillus fumigatus* isolates.

Clinical Infectious Diseases

INVITED ARTICLE

HEALTHCARE EPIDEMIOLOGY: Robert A. Weinstein, Section Editor

Azole Resistance in *Aspergillus fumigatus*: Can We Retain the Clinical Use of Mold-Active Antifungal Azoles?

Paul E. Verweij,[1] Anuradha Chowdhary,[2] Willem J. G. Melchers,[1] and Jacques F. Meis[1,3]

[1]Department of Medical Microbiology, Radboud University Medical Centre, Nijmegen, The Netherlands; [2]Department of Medical Mycology, Vallabhbhai Patel Chest Institute, University of Delhi, India; and [3]Department of Medical Microbiology and Infectious Diseases, Canisius Wilhelmina Hospital, Nijmegen, The Netherlands

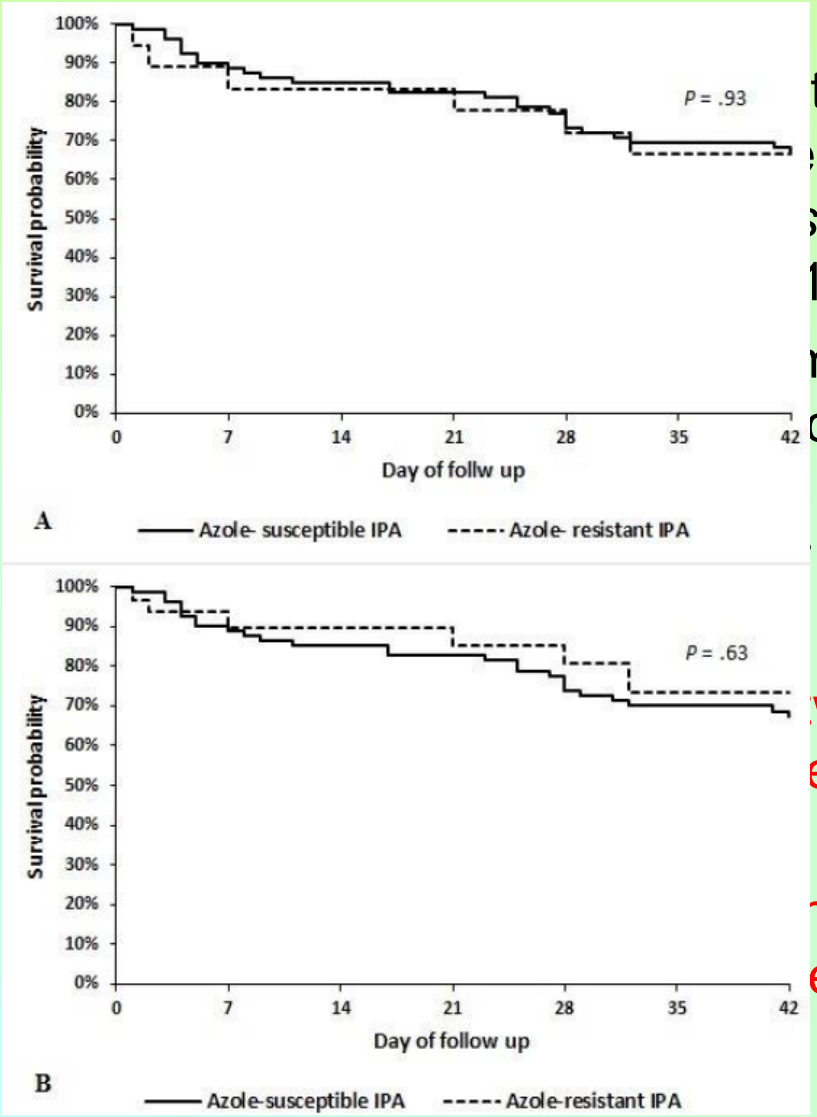
Clinical Infectious Diseases® 2016;62(3):362–8

Table 3. Reported Mortality Rates in Patients With Invasive Aspergillosis in Different Time Periods

	Aspergillus Disease			
Era	IA	Comment	CNS IA	Comment
c-AmB era	65% [2]	122 of 187 patients receiving c-AmB died.	95%–100% [3]	Literature review
	71.6% [55]	187 of 261 patients with IA died.	99% [56]	Review of 141 cases of CNS IA in immunocompromised patients, of whom 140 died.
Azole era	27.5% [57]	9-wk mortality: 39 of 142 patients receiving voriconazole monotherapy.	45.6% [7]	Retrospective analysis of 81 patients with CNS IA treated with voriconazole
	28.5% [58]	Population-based study analyzing 8563 aspergillosis cases in France.	35.4% [59]	Literature review: 4 of 11 patients with CNS IA who received voriconazole monotherapy.
Azole resistant	100% [44]	Culture-positive patients with proven and probable IPA treated with voriconazole (5/5)	86% [24, 44, 60]	7 cases of azole-resistant CNS IA have been reported, of which 6 were fatal.
	88% [45]	8 HSCT patients with culture-positive, azole-resistant IA, of whom 7 died.		
	100% [54]	ICU patients with culture-positive azole-resistant IA died (10/10), compared with 21 of 28 (75%) with azole-susceptible IA.		

Abbreviations: c-AmB, conventional amphotericin B; CNS, central nervous system; HSCT, hematopoietic stem cell transplant; IA, invasive aspergillosis; ICU, intensive care unit; IPA, invasive pulmonary aspergillosis.

Sang Taek Heo, Alexander M. Tatara, Cristina Jiménez-Ortigosa, Ying Jiang, Russell E Lewis, Jeffrey Tarrand, Frank Tverdek, Nathaniel D. Albert, Paul E. Verweij, Jacques F Meis, Antonios G. Mikos, David S. Perlin, Dimitrios P. Kontoyiannis; Changes in in vitro susceptibility patterns of *Aspergillus* to triazoles and correlation with aspergillosis outcome in a tertiary care cancer center (1999-2015). *Clin Infect Dis* 2017 cix297. doi: 10.1093/cid/cix297



time in triazole MICs of 290 sequential
d from respiratory sources from 1999-2002
spergillus-potent triazoles voriconazole and
15 at MD Anderson Cancer Center.
natologic cancer and/or HSCT with invasive
correlated *in vitro* susceptibility with 42 day
(13%) isolates and was only low level
ween *in vitro* MIC with 42 day mortality in
e of antifungal treatment.
CI = 2.5-173.5; *P* = .005) and azole
ns (OR = 9.6; 95% CI = 1.9-48.5; *P* = .006)
esistance.

Survival curves for patients who had either azole-wild type or azole non-wild type correlated *in vitro* susceptibility (IPA). A, Kaplan-Meier survival curves. B, Adjusted survival curves (adjusted for history of neutropenia, lymphopenia, intensive care unit admission, and time period of IPA diagnosis).

AsperGenius

- AsperGenius® is a multiplex real-time PCR assay developed by PathoNostics. It rapidly diagnoses *Aspergillus* infections and simultaneously identifies azole resistance.
- Species multiplex
  - *Aspergillus fumigatus*
  - *Aspergillus terreus*
  - *Aspergillus species*
- Resistance multiplex
  - L98H
  - Tandem repeat 34
  - T289A
  - Y121F

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PCR-based detection of *Aspergillus fumigatus Cyp51A* mutations on bronchoalveolar lavage: a multicentre validation of the AsperGenius assay® in 201 patients with haematological disease suspected for invasive aspergillosis

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Table 2. Diagnostic performance of the species probe of the AsperGenius® PCR according to different Ct cut-offs and positive/negative controls

Ct value cut-off of the AsperGenius® species PCR	Diagnostic performance	Positive control versus negative control BAL samples as defined in this study,[a] $n=201$	Proven, probable or non-classifiable IA versus no IA,[b] $n=169$	Proven or probable IA versus no IA, $n=126$
<36	sensitivity (%)	70.45	68.42	76.92
	specificity (%)	95.58	98.65	98.65
	PPV (%)	92.54	98.48	97.56
	NPV (%)	80.60	70.87	85.88
<37	sensitivity (%)	73.86	71.58	78.85
	specificity (%)	90.27	94.59	94.59
	PPV (%)	85.53	94.44	91.11
	NPV (%)	81.60	72.16	86.42
<38	sensitivity (%)	84.09	83.16	88.46
	specificity (%)	79.65	85.14	85.14
	PPV (%)	76.29	87.78	80.70
	NPV (%)	86.54	79.75	91.30
<39	sensitivity (%)	88.64	87.37	90.38
	specificity (%)	62.83	72.97	72.97
	PPV (%)	65.00	80.58	70.15
	NPV (%)	87.65	81.82	91.53

[a]BAL samples with a positive GM (≥1.0) and/or positive culture for *Aspergillus* of BAL, sputum or lung biopsy at most 5 days from date of the BAL were considered positive controls. BAL samples with a negative BAL GM in combination with a negative culture from BAL, sputum or lung biopsy were considered negative controls.

[b]Proven IA and probable IA were defined according to the revised EORTC/MSG consensus criteria. Non-classifiable was defined as a patient with EORTC/MSG host and microbiological criteria fulfilled and a pulmonary infiltrate without a halo or air-crescent or well-defined nodule. No IA was defined as no proven IA, no probable IA, no non-classifiable IA or no possible invasive fungal disease.

MAJOR ARTICLE

A Breath Fungal Secondary Metabolite Signature to Diagnose Invasive Aspergillosis

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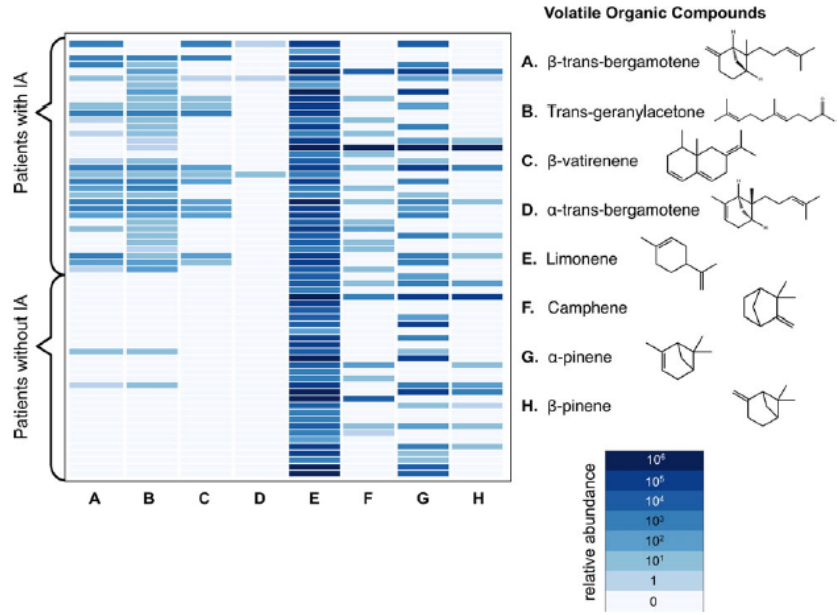

Figure 2. Relative abundance of *Aspergillus* terpene metabolites in breath samples. This heatmap shows the average integrated area of terpene metabolites (columns A–H) in the breath of 64 patients with and without invasive aspergillosis (IA).

Table 3. Breath Aspergillus Metabolite Signature by the Reference Standard and Test Parameters

Parameter	Invasive Aspergillosis[a]	Other Pneumonia	Total Patients
Aspergillus metabolite signature[b] +	32	2	34
Aspergillus metabolite signature –	2[c]	28	30
Total patients	34	30	64
Test parameters			
Sensitivity (95% CI)	0.94 (.81–.98)		
Specificity (95% CI)	0.93 (.79–.98)		
Positive likelihood ratio (95% CI)	14.1 (3.69–54.0)		
Negative likelihood ratio (95% CI)	0.063 (.02–.24)		

Abbreviation: CI, confidence interval.

[a] Proven or probable invasive aspergillosis, according to the revised European Organization for Research and Treatment of Cancer/Mycoses Study Group consensus criteria [28].

[b] Defined as the presence of any of the 4 elements of a metabolite volatile signature, comprised of β-trans-bergamotene, α-trans-bergamotene, trans-geranylacetone, and a β-vatirenene-like sesquiterpene, in the patient's breath.

[c] *Aspergillus niger* was identified as the etiology of invasive aspergillosis in 1 of these 2 patients.

ImmunoPET/MR imaging allows specific detection of *Aspergillus fumigatus* lung infection in vivo

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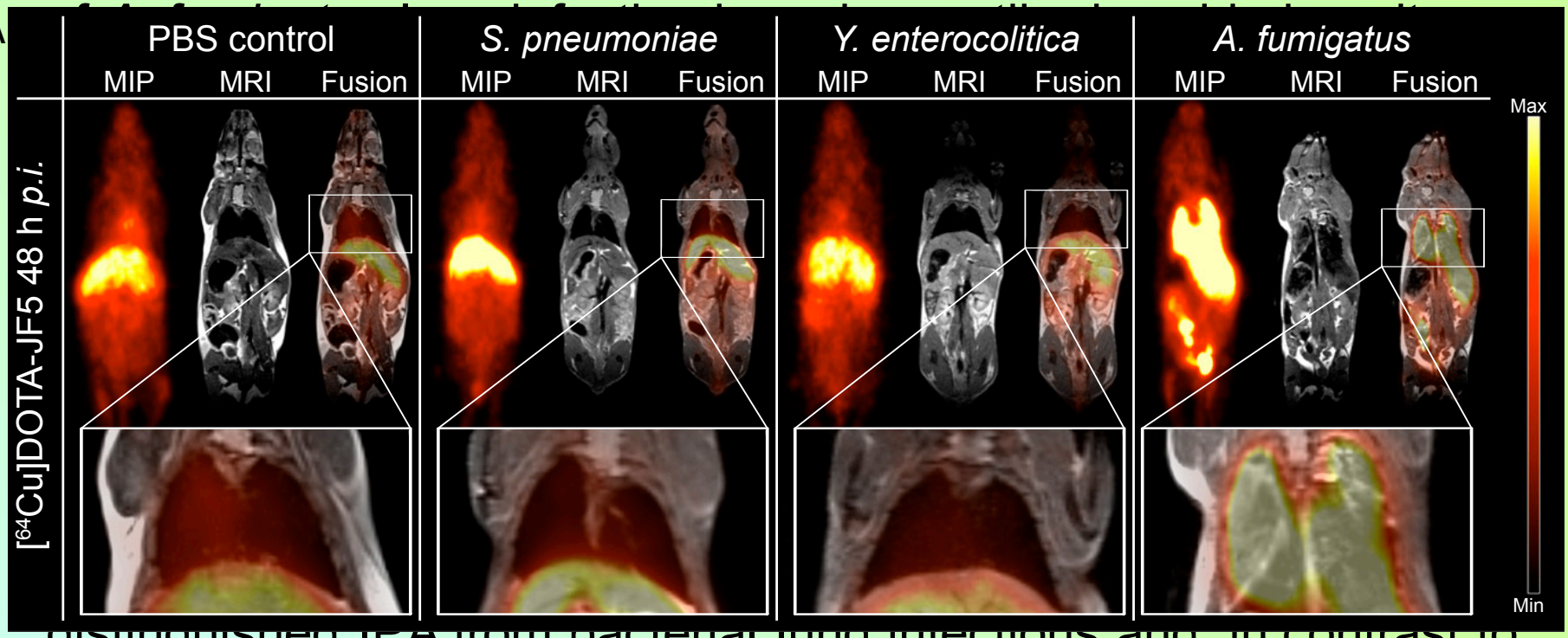
- In this paper was evaluated a novel probe for noninvasive detection
- distinguished IPA from bacterial lung infections and, in contrast to [18F]FDG-PET, discriminated IPA from a general increase in metabolic activity associated with lung inflammation.



mycoses
Diagnosis, Therapy and Prophylaxis of Fungal Diseases

Supplement article

Antifungal stewardship in daily practice and health economic implications

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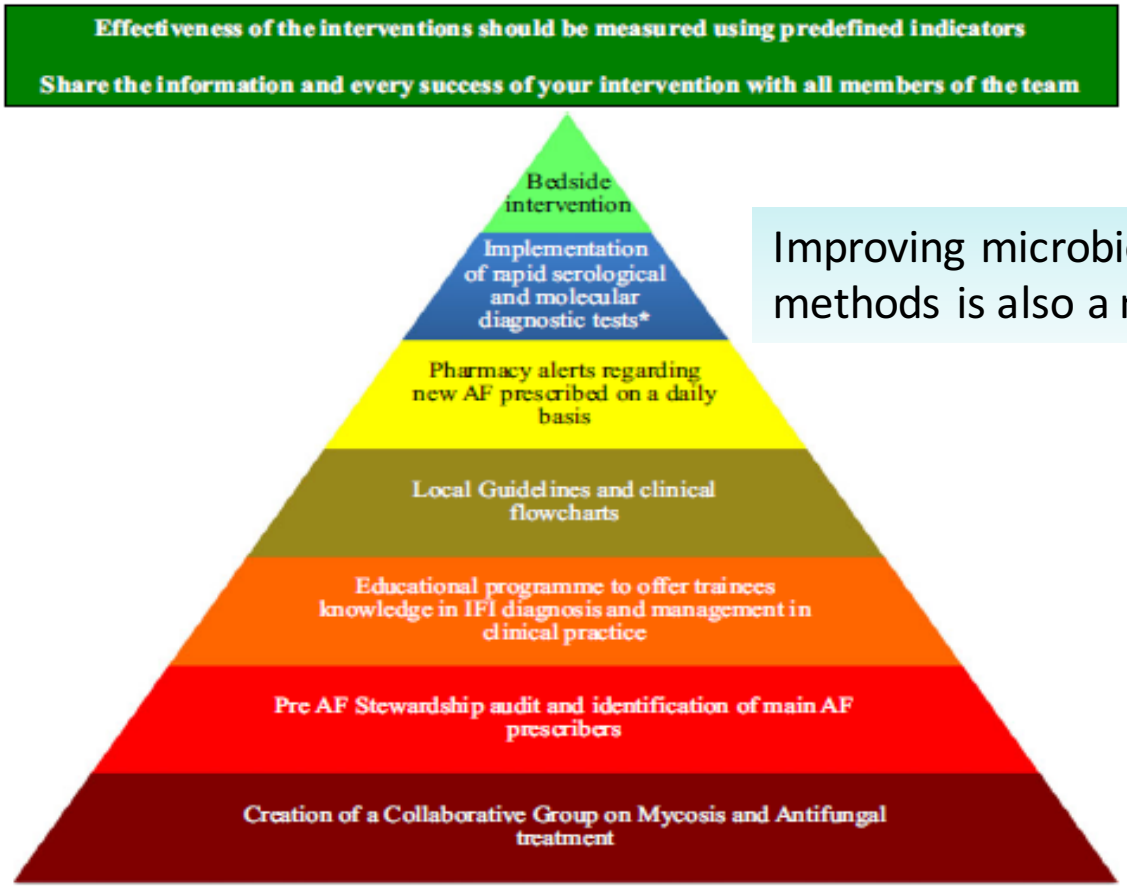

Improving microbiology diagnostic methods is also a means of AFS!!

Figure 1 AF stewardship step-by-step. *Use of molecular diagnostics and/or serological biomarkers like galactomannan and beta-D-glucan for early diagnosis. Implementation of TDM for AF plasma levels and susceptibility testing. IFI, invasive fungal infection; AF, antifungal.