Neues zu den Biomarkern

Prof. Dr. med. Peter-Michael Rath
Institut für Medizinische Mikrobiologie
Universitätsklinikum Essen

pm.rath@uni-due.de

Interessenkonflikte keine

Universitätsklinikum Essen

Positive (1,3)-ß-D-Glucan (BDG) ELISA Reaktionen

Praktisch alle Pilze inklusive *Pneumocystis* (Zysten)
aber nicht *Cryptococcus,* Zygomyzeten

Hämodialyse mit Cellulose-Membranen
Blutprodukte, Immunglobuline, Albumin
OP-Gaze, Gaze bei Verbrennungspatienten
ß-Lactam-Antibiotika, Colistin
Bakteriämien
Nocardia (Liquor)

Leistung des ß-Glucan-Testes (Serum)

Meta-Analysen zu invasive Pilzinfektionen

bei hämato-onkologischen Patienten

- **Sensitivität: 60 – 80 %**
- **Spezifität: 82 – 87 % (98 %: 2 Proben innerhalb einer Woche)**
- **Positiver prädiktiver Wert: 46 %**
- **Negativer prädiktiver Wert: 97 %**
- **Probleme: unterschiedliche Erkrankungen, Pilzspezies, Assays mit unterschiedlichen Grenzwerten**

Karageorgopoulos DE et al. Clin Infect Dis. 2011;52(6):750-70.
Lamoth F et al. Clin Infect Dis. 2012;54(5):633-43.
Onishi A et al. J Clin Microbiol. 2012;50(1):7-15.

Use and Limits of (1-3)-β-D-Glucan Assay (Fungitell), Compared to Galactomannan Determination (Platelia *Aspergillus*), for Diagnosis of Invasive Aspergillosis

Annie Sulahian,[a] Raphael Porcher,[b] Anne Bergeron,[c] Sophie Touratier,[d] Emmanuel Raffoux,[e] Jean Menotti,[a] Francis Derouin,[a] Patricia Ribaud[f]

105 hämatoonkologische Patienten (14 proven, 97 probable aspergillosis)

97 patients at risk, 50 Blutspender, 60 Patienten mit Bakteriämien

	GM	BDG
Sensitivität	49 %	81 %
Spezifität	97 %	82 %
Bakteriämien	2 %	37 %
ß-Laktame (in vitro)	29 %	33 %

Journal of Clinical Microbiology p. 2328–2333 July 2014 Volume 52 Number 7

Reactivity of (1→3)-β-*d*-glucan assay in bacterial bloodstream infections

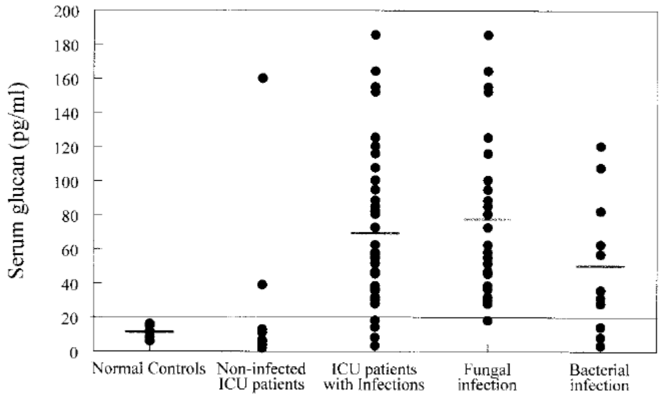
O. Albert • D. Toubas • C. Strady • J. Cousson •

Patient group	No. of patients with BG test		
	Positive	Indeterminate	Negative
Group A (n=19)	0	0	19 (100%)
Patients with BSI (n=39)	16 (41%)	4 (10%)	19 (49%)
Group B (n=22)	13 (59%)	3 (14%)	6 (27%)
E. coli subgroup (n=13)	8 (61%)	1 (8%)	4 (31%)
P. aeruginosa subgroup (n=7)	4 (57%)	2 (29%)	1 (14%)
Group C (n=17)	3 (18%)	1 (6%)	13 (76%)
S. aureus subgroup (n=8)	3 (38%)	1 (12%)	4 (50%)
S. pneumoniae subgroup (n=8)	0	0	8 (100%)

Eur J Clin Microbiol Infect Dis (2011) 30:1453–1460

Serum Glucan Levels Are Not Specific for Presence of Fungal Infections in Intensive Care Unit Patients

Justin Digby, John Kalbfleisch, Andy Glenn, Angie Larsen, William Browder, and David Williams*



G-Test

Clinical and Diagnostic Laboratory Immunology, Sept. 2003, p. 882–885

Comparison of (1→3)-β-D-Glucan, Mannan/Anti-Mannan Antibodies, and Cand-Tec *Candida* Antigen as Serum Biomarkers for Candidemia

Jürgen Held,[a] Isabelle Kohlberger,[a] Elfriede Rappold,[a] Andrea Busse Grawitz,[b] Georg Häcker[a]

56 Patienten mit Candidämie, 100 Patienten Bakteriämie, 100 Patienten neg.-Kontrolle
Ausschluß: Immunglobulin- bzw. Albumingabe

	BDG	Mannan-Ag*	Mannan-AK	CA	BDG+M-Ag
Sensitvität	87 %	58 %	62 %	13 %	89 %
Spezifität	85 %	23 %	65 %	94 %	85 %

* Mannan-Ag erfasst nicht C. parapsilosis und C. guilliermondii

Cutoffs optimieren !

BDG (Sen: 89,3 %, Spez: 84 %)

oder

Mannan-Ag (Sen: 69,6 %, Spez: 93,5 %)

Journal of Clinical Microbiology p. 1158–1164 April 2013 Volume 51 Number 4

Contribution of (1,3)-Beta-D-Glucan to Diagnosis of Invasive Candidiasis after Liver Transplantation

E. Levesque,[a] S. El Anbassi,[b] E. Sitterle,[b] F. Foulet,[b] J. C. Merle,[a] F. Botterel[b]

52 % der Patienten unter Prophylaxe (Caspofungin oder Fluconazol)

3 Patienten (5 Episoden) gesicherte Candida-IFI

TABLE 3 Performance of (1,3)-beta-D-glucan measurements and colonization index in diagnosis of invasive candidiasis in 52 liver transplant patients

Criterion used[a]	Sensitivity (95% CI) (%)	Specificity (95% CI) (%)	PPV (95% CI) (%)	NPV (95% CI) (%)
One BG-positive specimen	100 (61-100)	61 (45-75)	25 (10-47)	100 (90-100)
Colonization index of ≥0.5	100 (61-100)	58 (43-73)	24 (10-45)	100 (90-100)
Two sequential BG-positive specimens	83 (36-99)	87 (73-95)	45 (11-77)	97.6 (87-100)
Two sequential BG-positive specimens plus colonization index of ≥0.5	83 (36-99)	89 (76-96)	50 (18-81)	97.6 (87-100)

[a] The positive BG cutoff value was 146 pg/ml. BG, (1,3)-beta-D-glucan; PPV, positive predictive value; NPV, negative predictive value.

2 positive Seren: Sensitivität 83%, Spezifität 87%

Kolonisationsindex: wenig zusätzliche Erkenntnisse

March 2015 Volume 53 Number 3 Journal of Clinical Microbiology

Performance of Galactomannan, Beta-D-Glucan, *Aspergillus* Lateral-Flow Device, Conventional Culture, and PCR Tests with Bronchoalveolar Lavage Fluid for Diagnosis of Invasive Pulmonary Aspergillosis

M. Hoenigl,[a,g] J. Prattes,[a] B. Spiess,[b] J. Wagner,[a] F. Prueller,[c] R. B. Raggam,[d] V. Posch,[a] W. Duettmann,[d] K. Hoenigl,[a] A. Wölfler,[d] C. Koidl,[e] W. Buzina,[e] M. Reinwald,[b] C. R. Thornton,[f] R. Krause,[a] D. Buchheidt[b]

67 Proben, 3 proven, 7 probable, 16 possible, 41 no IPA

TABLE 2 Diagnostic performance of BAL fluid GM test, culture, BDG test, LFD test, and PCR for probable and proven IPA patients with all test results available[a]

Test method and/or conditions[b]	Performance characteristic (%)[c] Sensitivity ($n = 10$)	Specificity ($n = 41$)	PPV	NPV
GM ODI of >1.0	70	98	88	93
GM ODI of >0.5	80	98	89	95
Mycological culture	50	95	71	89
BDG > 80 pg/ml	80	76	44	94
BDG > 200 pg/ml	60	88	55	90
LFD test	80	95	80	95
PCR	70	100	100	93
PCR and/or BDG > 80 pg/ml	90	76	47	97
PCR and/or LFD test	90	95	82	98
GM ODI of >1.0 and/or PCR	100	98	91	100
GM ODI of >1.0 and/or LFD test	90	93	75	97

GM > 1.0 +/- LFD bzw. PCR: Sensitivität und Spezifität ≥ 90%

June 2014 Volume 52 Number 6 Journal of Clinical Microbiology p. 2039–2045

Bronchoalveolar Lavage Fluid (1,3)β-D-Glucan for the Diagnosis of Invasive Fungal Infections in Solid Organ Transplantation: A Prospective Multicenter Study

Wolfgang Mutschlechner,[1] Brigitte Risslegger,[1] Birgit Willinger,[2] Martin Hoenigl,[3] Brigitte Bucher,[4] Stephan Eschertzhuber,[5] and Cornelia Lass-Flörl[1]

233 BAL, 109 Sera von 135 Patienten 85 % TX (Niere, Leber, Herz)
4.4 % proven, 16.3 % probable aspergillosis
31.9 % der Patienten ohne IFI hatten eine Candida-Kolonisation der Lunge
Cutoff 100 pg/ml

BAL: Sensitivität 79.2 %, Spezifität 38.5 %, PPV 27.6 %, NPV 86.3 %

Serum: Sensitivität 79.2 %, Spezifität 81.8 %, PPV 69.2 %, NPV 83.1 %

to now, we do not recommend the Fungitell test as an independent screening test for early detection of IFI using BAL in SOT patients.

Hoher NPV in BAL und Serum mag beim Ausschluß einer pulmonalen Infektion hilfreich sein.

Transplantation ■ Month 2015 ■ Volume 00 ■ Number 00 DOI: 10.1097/TP.0000000000000635

(1,3)-β-D-Glucan in Cerebrospinal Fluid for Diagnosis of Fungal Meningitis Associated with Contaminated Methylprednisolone Injections

Anurag N. Malani,[a] Bonita Singal,[b] L. Joseph Wheat,[c] Ola Al Sous,[d] Theresa A. Summons,[c] Michelle M. Durkin,[c] April C. Pettit[e]

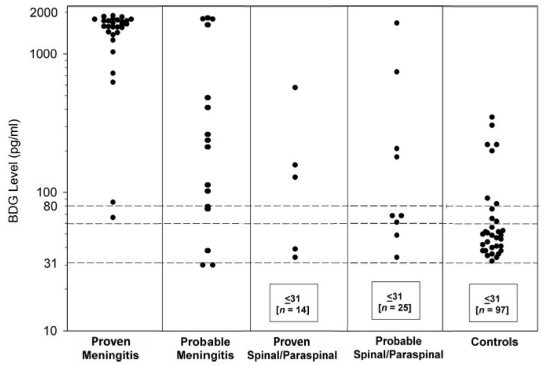


FIG 2 Cerebrospinal (1,3)-β-D-glucan (BDG) levels in proven fungal meningitis cases, probable meningitis cases, proven spinal or paraspinal infection cases, probable spinal or paraspinal infection cases, and controls. Manufacturer recommendations for serum BDG specimens are indicated by the dashed lines (values of <60 are interpreted as negative, and values of 80 or higher are interpreted as positive).

Exserohilum

March 2015 Volume 53 Number 3 Journal of Clinical Microbiology

Utility of Measuring (1,3)-β-D-Glucan in Cerebrospinal Fluid for Diagnosis of Fungal Central Nervous System Infection

Jennifer L. Lyons,[a] Kiran T. Thakur,[b] Rick Lee,[c] Tonya Watkins,[d] Carlos A. Pardo,[b] Kathryn A. Carson,[e] Barbara Markley,[f] Malcolm A. Finkelman,[f] Kieren A. Marr,[g] Karen L. Roos,[h] Sean X. Zhang[c,d]

ZNS-Pilzinfektionen

Disease category	No. of patients or case no.	BDG in paired serum and CSF samples: Level in serum (pg/ml)[a]	Level in CSF (pg/ml)[a]	P value[b]
CNS fungal infections				
Cryptococcus meningitis	No. 1 (<1:5[c])	30	<4	
	No. 2 (1:160[c])	16	37	0.43
	No. 3 (<1:5[c])	27	21	1.29
	No. 4 (1:80[c])	91	53	1.72
	No. 5 (1:40[c])	34	32	1.06
	No. 6 (1:10[c])	15	33	0.45
Probable cerebral histoplasmosis[f]	No. 7	14	110	0.13
Proven *Exserohilum* meningitis (outbreak patient)	No. 8	32	797	0.04
Probable *Exserohilum* meningitis (outbreak patient)	No. 9	33	1,524	0.02

Cryptococcus-Infektionen negativ
Exserohilum-Infektionen positiv im Liquor, nicht im Serum

January 2015 Volume 53 Number 1 Journal of Clinical Microbiology

Utility of Measuring (1,3)-β-D-Glucan in Cerebrospinal Fluid for Diagnosis of Fungal Central Nervous System Infection

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Pilzinfektionen ohne ZNS-Beteiligung

Disease category	No. of patients or case no.	BDG in paired serum and CSF samples: Level in serum (pg/ml)[a]	Level in CSF (pg/ml)[a]	P value[b]	
Non-CNS fungal infections					
Proven invasive candidiasis	No. 1	1,051	27		38.9
Probable invasive aspergillosis	No. 2	894	40		22.4
Proven fungal sinusitis/mastoiditis[d]	No. 3	201	57		3.5
Possible fungal sinusitis[e]	No. 4	11	$\boxed{685}$		0.02
Probable disseminated coccidioidomycosis	No. 5	14	$\boxed{139}$		0.10
Probable *Pneumocystis* pneumonia	No. 6	1179	$\boxed{158}$		7.5
Probable fungal pneumonia	No. 7	2,100	$\boxed{34}$		61.8
Probable invasive candidiasis	No. 8	260	64		4.1
Probable invasive candidiasis	No. 9	229	5		45.8
Probable invasive candidiasis	No. 10	685	7		97.9
Subtotal	10	472.5 (11–2,100)	48.5 (5–685)	0.03	14.9 (0.02–97.9)

BDG teilweise im Liquor erhöht

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Utility of Measuring (1,3)-β-D-Glucan in Cerebrospinal Fluid for Diagnosis of Fungal Central Nervous System Infection

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Non-fungale Erkrankungen

Disease category	No. of patients or case no.	BDG in paired serum and CSF samples: Level in serum (pg/ml)[a]	Level in CSF (pg/ml)[a]	P value[b]
Nonfungal infection				
Multiple sclerosis	9	20 (10–35)	9 (4–28)	0.02
Primary headaches	10	27.5 (12–64)	15.5 (<4–27)	<0.02
Pseudotumor cerebri	5	28 (18–58)	17 (13–43)	0.31
Other CNS abnormalities	24	28 (11–1334)	14 (<4–109)	0.10
Bacterial/viral CNS infection	18	25.5 (7–397)	13 (<4–71)	0.07
Subtotal	66	26.5 (7–1344)	13.5 (<4–109)	<0.001

Im Liquor weniger BDG als im Serum.

January 2015 Volume 53 Number 1 Journal of Clinical Microbiology

(1–3)-Beta-D-glucan in association with lactate dehydrogenase as biomarkers of *Pneumocystis* pneumonia (PcP) in HIV-infected patients

F. Esteves • C.-H. Lee • B. de Sousa • R. Badura • M. Seringa •
C. Fernandes • J. F. Gaspar • F. Antunes • O. Matos

Table 2 BG and LDH median levels of different patient groups

Patient group (*N*)	Median BG levels (pg/ml)	Median LDH levels (U/l)
PcP positive (69)	270	707
PcP negative (31)	45	420
Colonized (12)	67	474
Other pulmonary disease (19)	36	419
Blood donors (negative control) (50)	31	141

BG (1–3)-beta-d-glucan, *LDH* lactate dehydrogenase

Eur J Clin Microbiol Infect Dis (2014) 33:1173–1180

Serum and bal beta-D-glucan for the diagnosis of *Pneumocystis* pneumonia in HIV positive patients

D. Salerno [a,*], D. Mushatt [a], L. Myers [a], Y. Zhuang [a],
N. de la Rua [b], E.J. Calderon [c], D.A. Welsh [b]

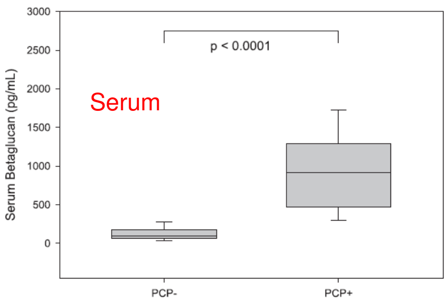


Figure 2 Whisker and Box plot comparing serum BG between PCP− and PCP+.

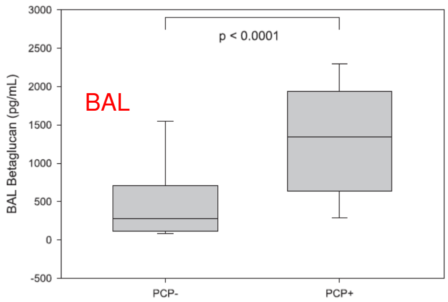


Figure 3 Whisker and Box plot comparing BAL BG between PCP− and PCP+.

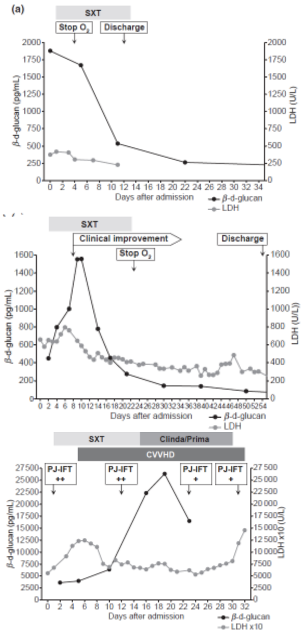
HIV + Pneumonie

Respiratory Medicine (2014) 108, 1688–1695

18 Patienten

β-D-Glucan kinetics for the assessment of treatment response in *Pneumocystis jirovecii* pneumonia

J. Held[1] and D. Wagner[2]



Abfallende BDG-Konzentration korrelieren mit klinischer Heilung.

Initial ansteigende BDG-Konzentrationen trotz klinischer Heilung.

Ansteigende BDG-Konzentrationen trotz reduzierter Zystenanzahl.

In 56% Therapieresponse trotz ansteigende BDG-Konzentrationen.

Clinical Microbiology and Infection, Volume 17 Number 7, July 2011

Zusammenfassung

(1-3)-ß-D-Glucan

Hohe Sensitivität (und damit NPV).

Niedrige Spezifität (und damit PPV) wegen Kreuzreaktionen.

Wenig geeignet für Intensivpatienten (viele Gründe für positive Reaktionen).

Screening: Unklare Datenlage bei Organtransplantierten.

Geeignet bei hämatologischen Patienten (ohne Prophylaxe).

In BAL möglich. Cave: Niedrige Spezifität !

In Liquor möglich. Cave: Wenig Daten.

Therapiekontrolle: Daten nur für PcP und im Serum: (wenig ?) geeignet.