Topic:

(1→3)-β-D-glucan and Treatment Guidelines for Invasive Fungal Disease (IFD)

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Discussion:

Since its 2004 clearance for marketing by the US Food and Drug Administration, (1→3)-β-D-glucan (BG) testing has been discussed in an increasing number of national and international guidelines. Typically, these guidelines contain diagnostic sections that describe the test categories and specific tests that are relevant to the invasive fungal disease (IFD). Some of these guidelines are generic to invasive fungal disease while others are specific to particular fungal genera such as *Aspergillus* or *Candida*. Some of these guidelines are listed below, along with references or links to them. Of additional interest is the inclusion of BG in the 2008 Definitions of IFD for clinical studies[1]. This represented the first adoption of serum BG positivity as a mycology criterion for the purposes of supporting the classification of "probable" IFD. Subsequent to the publication of the 2008 Definitions, multiple IFD guidelines have added a discussion of the use of BG results in the diagnosis of IFD.

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Invasive Fungal Disease Guidelines with (1→3)-β-D-Glucan Discussion

Title	URL or Reference
Revised Definitions of Invasive Fungal Disease from the European Organization for Research and Treatment of Cancer/Invasive Fungal Infections Cooperative Group and the National Institute of Allergy and Infectious Diseases Mycoses Study Group (EORTC/MSG) Consensus Group	1. De Pauw, B. et. al. Revised definitions of invasive fungal disease from the European Organization for Research and Treatment of Cancer/Invasive Fungal Infections Cooperative Group and the National Institute of Allergy and Infectious Diseases Mycoses Study Group (EORTC/MSG) Consensus Group. Clin Infect Dis. 2008; 46: 1813-21. http://cid.oxfordjournals.org/content/46/12/1813.full.pdf+html?sid=dd65b8f1-be4a-4554-94a5-214788d81a7d
HIV-Exposed and HIV-Infected Children: Recommendations from CDC, the National Institutes of Health, the HIV Medicine Association of the Infectious Diseases Society of America, the Pediatric Infectious Diseases Society, and the American Academy of Pediatrics	http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2821196/
Diagnosis and antimicrobial therapy of lung infiltrates in febrile neutropenic patients: Guidelines of the infectious diseases working party of the German Society of Haematology and Oncology	Eur J Cancer. 2009 Sep;45(14):2462-72. doi: 10.1016/j.ejca.2009.05.001. Epub 2009
Diagnosis of invasive fungal infections in hematology and oncology guidelines from the Infectious Diseases Working Party in Haematology and Oncology of the German Society for Haematology and Oncology (AGIHO)	Ann Oncol. 2012 Apr;23(4):823-33. doi: 10.1093/annonc/mdr407. Epub 2011 Sep 23.
β-Glucan antigenemia assay for the diagnosis of invasive fungal infections in patients with hematological malignancies: a systematic review and meta-analysis of cohort studies from the Third European Conference on Infections in Leukemia (ECIL-3)	Clin Infect Dis. 2012 Mar 1;54(5):633-43. doi:10.1093/cid/cir897. Epub 2011 Dec 23. http://cid.oxfordjournals.org/content/54/5/633.full.pdf+html
Clinical Practice Guideline for the Use of Antimicrobial Agents in Neutropenic Patients with Cancer: 2010 Update by the Infectious Diseases Society of America	Clin Infect Dis. 2011 Feb 15;52(4):e56-93. doi: 10.1093/cid/cir073 http://cid.oxfordjournals.org/content/52/4/e56.full.pdf+html
Clinical Practice Guidelines for the Management of Candidiasis: 2009 Update by the Infectious Diseases Society of America	Clinical Infectious Diseases 2009; 48:503–35 http://cid.oxfordjournals.org/content/48/5/503.1.full.pdf+html
ESCMID guideline for the diagnosis and management of Candida diseases 2012: diagnostic procedures	Clin Microbiol Infect 2012; 18 (Suppl. 7): 9–18

Recent Publications on Serum BG and Related Matters:

Steinbach, W.J. *et al.* Results from a prospective international epidemiological study of invasive candidiasis in children and neonates. Ped. Infect. Dis. J. 2012; 131: 1252 – 1257. This study, contributed by the Pediatric Fungal Diseases Network, described *Candida*-related infections as the third most common cause of pediatric nosocomial blood stream infections. The study enrolled a total of 196 pediatric and 25 neonatal invasive candidiasis patients. Non-*albicans* species predominated in both pediatric and neonatal patient populations, although 44% of the isolates were *C. albicans*. Treatment success was 76% for the pediatric cohort and 92% for the neonatal *C. glabrata* treatment outcomes were the poorest, with a 55% success rate.

Beirão, F & Araujo, R. State of the art diagnostic of mold diseases: a practical guide for clinicians. Eur J Clin Microbiol. Infect. Dis. DOI 10.1007/s10096-012-1722-7. The authors present a review of the clinical approaches to the diagnosis of mold infections. The overwhelming basis for the growth in mold diseases, world-wide, is presented as due to iatrogenic immunosuppression due to transplant and oncologic therapy, as well as HIV prevalence. Methods used to diagnose mold-based disease include traditional culture and histopathology as well as imaging. The newer, non-culture-based methods, including galactomannan and (1→3)-β-D-glucan are also described. A flow chart-based algorithm for mold infection diagnosis is presented as a practical guide to the physician.

Roilides, E. and Pana, Z.D. Application of diagnostic markers to invasive aspergillosis in children. Ann. N.Y. Acad. Sci. 2012; 1272: 1–8. In this review, the authors focus upon the diagnosis of invasive aspergillosis in pediatric patients. Invasive aspergillosis is noted as increasing and characterized by high attributable morbidity and mortality. Affected cohorts include those with immunodeficiency caused by medical therapy, HIV positivity, hematologic diseases, and immune function defects. Neonatal aspergillosis is described as associated with prematurity, antibiotic therapy, and prolonged steroid use. The authors describe the deficiencies of standard diagnostic methods including insensitivity and non-specificity. Novel diagnostic methods are described and include PCR, protein antigens, imaging, as well as galactomannan and (1→3)-β-D-glucan. The relative scarcity of data for (1→3)-β-D-glucan in pediatric cases was cited as a basis for an absence of recommendations in that population.

Sav. H. *et. al.* The importance of bronchoalveolar lavage (BAL) sample for galactomannan, 1,3-β-d-glucan and PCR tests. Mikrobiyol Bul. 2012; 46: 695-701. This case report describes observations in a 7 year old cystic fibrosis patient, with diffuse large cell B-cell lymphoma, in which bronchoalveolar lavage fluid and serum was investigated along with culture and imaging. Imaging, hyphal recovery and culture from BAL were consistent with invasive pulmonary aspergillosis. PCR, galactomannan, and (1→3)-β-D-glucan tests were negative in the serum but positive in the BAL. The authors noted the desirability of marker testing in BAL as well as serum in the establishment of invasive fungal infection diagnoses.

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