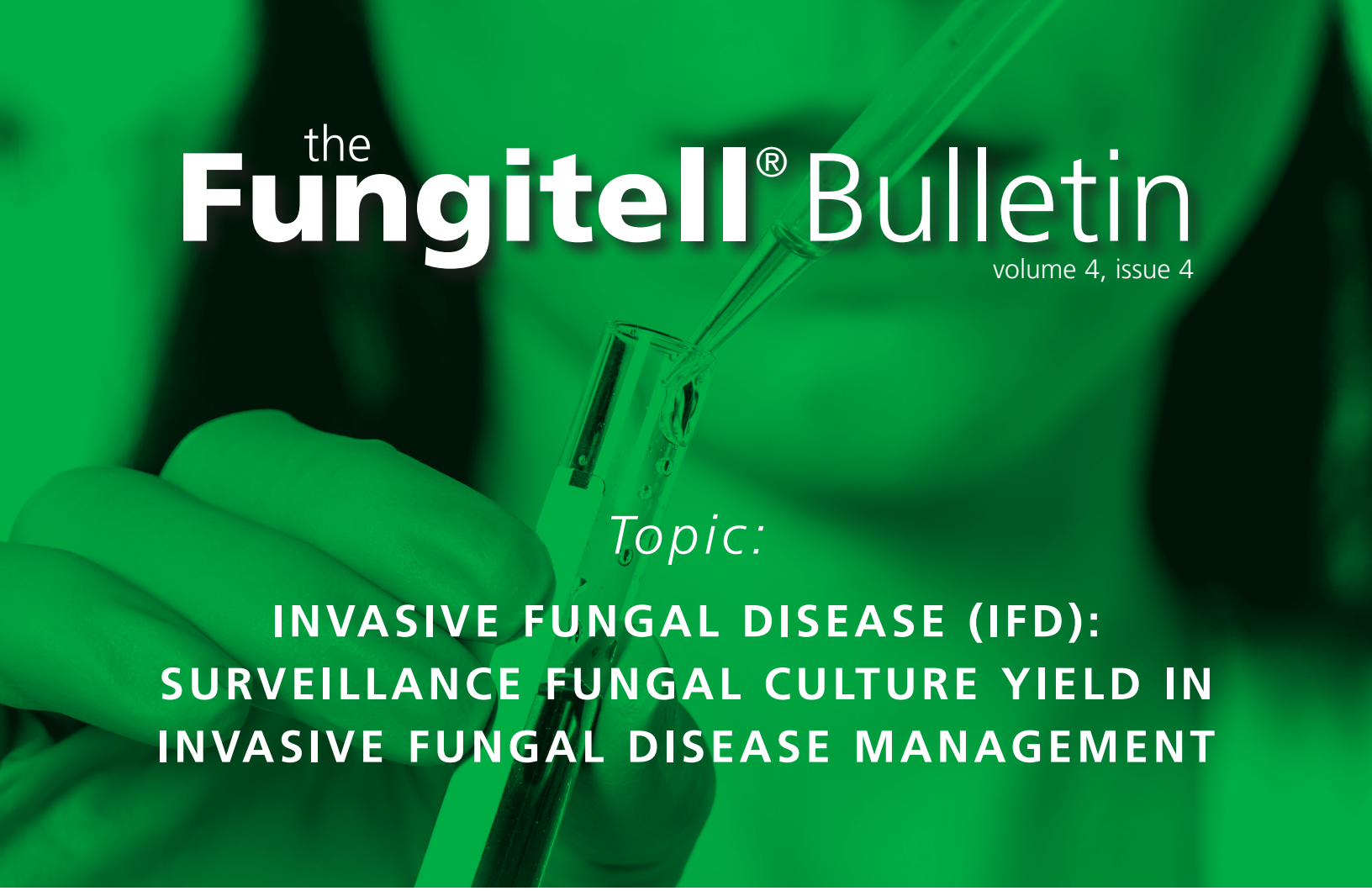
the Fungitell® Bulletin
volume 4, issue 4



Topic:

INVASIVE FUNGAL DISEASE (IFD): SURVEILLANCE FUNGAL CULTURE YIELD IN INVASIVE FUNGAL DISEASE MANAGEMENT

Discussion:

Invasive Fungal Disease is difficult to diagnose, especially in its early stages, and new serological tests have been developed to overcome some of the deficiencies of existing tests.[1] The utilization of "Gold Standard" diagnostic reference data is required in the evaluation of the clinical performance of new diagnostic tests. As a "Gold Standard" for the diagnosis of Invasive Fungal disease (IFD), fungal culture has suffered much criticism as being relatively insensitive.[2, 3, 4] With an insensitive "Gold Standard," new, higher sensitivity tests are at risk of excess apparent false positives relative to the standard.

Surveillance culture has been suggested as a useful tool to assess risk of IFD. Recently, Youngster *et al.*, published the results of a large single center study of the diagnostic performance of fungal surveillance culture (FSC) in pediatric hematopoietic stem cell transplant (HSCT) patients.[5] As a reference standard, proven and probable cases of IFD were determined using the revised guidelines of the European Organization for Research and Treatment of Cancer-Mycosis Study Group.[6] A total of 5,618 FSCs from 360 individual HSCT patients were analyzed. A single positive FSC was observed with 232 patients (64.4%); 30.3% of stool samples were positive; and 30 patients (8.3%) met the definition for IFD. Of the 232 patients with a positive FSC 17, (7.9% [sic]) developed an IFD. Interestingly, of the 128 patients with a negative FSC, 13 (10.1%) developed an IFD. The rate of IFD was 0.127 (95% CI, 0.041 – 0.121) and 0.089 (95% CI, 0.052 – 0.13) per 1,000 days in the FSC-positive and FSC-negative populations, respectively. Among patients with a positive FSC, there was no significant difference between those who received a change in antifungals relative to those who did not. The authors noted that nares and throat cultures added little data of clinical value and there was a low concordance between the fungal species detected by FSC and the organisms responsible for the IFD cases. The cost of a FSC at their institution was $80 and the total FSC expenditure during the study period was $449,000. They analyzed survey data from 40 HSCT transplant centers, which revealed that 40% practiced weekly post-transplant FSC and that the respondents felt the FSC results were of little value. The study conclusions include a call for wider evaluation of newer strategies for assessing the likelihood of IFD, including routine use serum fungal markers.

Fungitell®
(1→3)-β-D-Glucan Assay

Bulletin Volume 4, issue 4
Publish Date: March, 2014

Corporate Headquarters
Associates of Cape Cod, Inc.
124 Bernard E. Saint Jean Drive
East Falmouth, MA 02536 USA
Tel: (508) 540–3444
www.acciusa.com

United Kingdom
Associates of Cape Cod Int'l., Inc.
Deacon Park, Moorgate Road
Knowsley, Liverpool L33 7RX
United Kingdom
Tel: (44) 151–547–7444
www.acciuk.co.uk

European Office
Associates of Cape Cod Europe GmbH
Opelstrasse 14
D-64546 Mörfelden-Walldorf, Germany
Tel: (49) 61 05–96 10 0
www.acciusa.de

INVASIVE FUNGAL DISEASE (IFD): SURVEILLANCE FUNGAL CULTURE YIELD IN INVASIVE FUNGAL DISEASE MANAGEMENT

Recent Publications on Serum BG and Related Matters:

Chen, M. *et. al.* Pulmonary fungus ball caused by *Penicillium capsulatum* in a patient with type 2 diabetes: a case report. BMC Infectious Diseases 2013, 13:496-500. This case report describes the clinical investigation and therapy of a diabetic Chinese garden worker who was determined to have an upper left lobe pulmonary fungus ball. The organism was determined to be *Penicillium capsulatum* based upon culture from a biopsy specimen. A serum beta-glucan test revealed a BG burden of 459 pg/mL. The patient was cured by a combination of surgery (lobectomy) and sequential fluconazole (400 mg/day, 90 days) and caspofungin (70 mg/day, 14 days) treatment.

Esteves, F. *et. al.* (1→3)-β-D-Glucan in association with lactate dehydrogenase as biomarkers of *Pneumocystis* pneumonia (PcP) in HIV-infected patients. Eur. J Clin. Microbiol. Infect Dis.. 2014 DOI 10.1007/s10096-014-2054-6. This study evaluated the relative contribution of serum levels of both (1→3)-β-D-Glucan (BG) and lactate dehydrogenase (LDH) in the diagnosis of *Pneumocystis* pneumonia (PcP). A cohort of PcP HIV-positive patients (N=100) and healthy controls (N=50) were compared. PcP was established by examination of pulmonary specimens with anti-*Pneumocystis* immunofluorescence microscopy and PCR. (PPV/NPV), and positive/negative likelihood ratios (PLR/NLR) were 91.3%, 61.3%, 85.1%, 79.2%, 2.359, and 0.142, respectively, for the BG kit assay, and 91.3%, 35.5%, 75.9%, 64.7%, 1.415 and 0.245, respectively, for the LDH test. Combining the test results using a BG cutoff of 400 pg/mL and a LDH cutoff of 350 U/L gave a 92.8% sensitivity, 83.9% specificity, 92.8% PPV, 83.9% NPV, 5.764 PLR and 0.086 NLR (P<0.001). The authors concluded that BG level is a reliable indicator of PcP and the its combination with LDH data is a promising alternative.

Hoarau, G. *et. al.* Detection of (1→3)-β-D-Glucan in situ in a *Candida* albicans brain granuloma. J Infect. 2013; 67: 622-4. This case report describes the contribution of (1→3)-β-D-Glucan (BG) to the diagnosis of a *Candida albicans* brain granuloma in a pediatric patient. A left frontal mass was observed in the 2 year old child. Biopsy and CSF culture were negative. Histopathological analysis of section stained with haematoxylin-eosin-safran and periodic acid Schiff showed fungal pseudomycelia and blastoconidia. BG analysis of serum and CSF were negative. A 3 mm^3 biopsy specimen homogenate (BG-free suspending solution) supernatant was tested for both BG and mannan. Both were positive at levels exceeding 500 pg/mL. With observations suggestive of a Candida infection, PCR was performed and *C. albicans* was identified.

Edathodou, J. *et. al.* Invasive fungal infection due to *Triadelphia pulvinata* in a patient with acute myeloid leukemia. J Clin Microbiol. 2013 Oct;51(10):3426-9. This case report describes a post-transplant fungal infection in a patient treated for acute myelogenous leukemia. After more than 4 months, the patient relapsed and was readmitted. Imaging and fungal growth from peripheral blood indicated a fungal infection. Results of serial testing for serum galactomannan and (1→3)-β-D-Glucan (BG) were negative for the former and initially negative and then positive for the latter. Laboratory investigation of the isolate revealed that it was *Triadelphia pulvinata*, a dematiaceous soil fungus. The supernatant of RPMI-culture was negative for galactomannan and strongly positive for BG (>500 pg/mL). The RPMI control was negative. The authors note that this is the first reported case of invasive fungal disease caused by this organism.

Discussion References:

1. Paramythiotou, E. *et. al.* Invasive Fungal Infections in the ICU: How to Approach, How to Treat. Molecules 2014; 19: 1085-1119.
2. Barton, R.C. Laboratory Diagnosis of Invasive Aspergillosis: From Diagnosis to Prediction of Outcome. Scientifica 2013;2013: 459405. doi: 10.1155/2013/459405. Epub 2013 Jan 14
3. Nguyen, M.H. *et. al.* Performance of Candida real-time polymerase chain reaction, b-D-glucan assay, and blood cultures in the diagnosis of invasive candidiasis. Clin. Infect. Dis. 2012; 54: 1240-8.
4. Avni, T. *et. al.* PCR diagnosis of invasive candidiasis: systematic review and meta-analysis. J. Clin. Microbiol. 2011; 49: 665-70.
5. Youngster, I. *et. al.* Yield of Fungal Surveillance Cultures in Pediatric Hematopoietic Stem Cell Transplant Patients: A Retrospective Analysis and Survey of Current Practice. Clin. Infect. Diseases. 2014; 58: 365 – 371.
6. 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.

Fungitell® (1→3)-β-D-Glucan Assay

Bulletin Volume 4, issue 4
Publish Date: March, 2014

Corporate Headquarters
Associates of Cape Cod, Inc.
124 Bernard E. Saint Jean Drive
East Falmouth, MA 02536 USA
Tel: (508) 540–3444
www.acciusa.com

United Kingdom
Associates of Cape Cod Int'l., Inc.
Deacon Park, Moorgate Road
Knowsley, Liverpool L33 7RX
United Kingdom
Tel: (44) 151–547–7444
www.acciuk.co.uk

European Office
Associates of Cape Cod Europe GmbH
Opelstrasse 14
D-64546 Mörfelden-Walldorf, Germany
Tel: (49) 61 05–96 10 0
www.acciusa.de