

invasive

aiding the diagnosis of

funggal

disease

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Introduction:

Fungitell[®] is a (1→3)-β-D-Glucan (BG) detection kit with an indication as an adjunct test for the diagnosis of invasive fungal disease. As BG is released into the bloodstream due to infection by a wide variety of pathogenic fungi, the test has broad applicability. One type of fungal infection, pneumonia due to *Pneumocystis jirovecii* (PCP or PJP), is often seen in HIV-positive individuals, as well as other immunocompromised patients. There have been a number of publications in 2009 that have demonstrated the high sensitivity of BG detection for PCP in both the HIV-positive and HIV-negative populations.



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Posters From ICAAC 2009
(Interscience Conference on Antimicrobial Agents and Chemotherapy)
San Francisco, Sept. 11-15.

Sax, P.E. *et al.* (1→3)-β-D-Glucan is a promising non-invasive diagnostic test for HIV-related *Pneumocystis jirovecii* pneumonia. Poster H-1564a.

This study presented the results of the investigation of diagnostic performance of Fungitell® in a large group (N=273) of HIV-positive patients with opportunistic infection. The sensitivity of the test for *Pneumocystis* pneumonia was 92.5%. For patients with glucan levels above 500 pg/mL, 97% had either *Pneumocystis*, or another fungal, infection.

Bryar, J. *et al.* *Pneumocystis jirovecii* pneumonia (PCP) in patients with early stage (ES) breast cancer (BC). Poster K-950.

This study examined the incidence and characteristics of PCP occurrence in BC. Beta-glucan levels were available for 14/15 cases presented. All were positive and 7/14 were >500 pg/mL. Of particular interest is the observation that in all cases where BG was > 500 pg/mL, broncho-alveolar lavage fluid examination indicated few, rare, or absent *Pneumocystis* cysts. Glucan testing was concluded to be useful as a diagnostic tool for PCP.

Recent Literature On Diagnosis of *Pneumocystis* Pneumonia

Del Bono, V. *et al.* Clinical evaluation of (1→3)-β-D-Glucan assay in presumptive *Pneumocystis jirovecii* pneumonia in immunocompromised patients. Clin. Vacc. Immunol. In Press

The authors (from the University of Genoa) evaluated the use of Fungitell® in the diagnosis of *Pneumocystis* pneumonia (PCP or PJP). PCP is a serious lung infection, caused by *Pneumocystis jirovecii*, a fungus. PCP is typically observed in patients with either immunosuppressive therapy or diseases such as AIDS. The standard method for diagnosis of PCP is broncho-alveolar lavage (BAL), a technique that requires the instillation of 50, or more, mL of saline into a lung, its recovery, and subsequent microscopic examination of the contents of the material in the recovered fluid. This procedure is rather stressful and may be impossible in patients with severely impaired respiratory performance. Accordingly, the availability of a non-invasive procedure, such as a blood test, can be advantageous. They evaluated 31 consecutive immunosuppressed pneumonia patients including 16 with PJP (8 HIV+ and 8 HIV-), 15 with non-PJP pneumonia, and 11 healthy volunteers. The sensitivity and specificity was 100% and 88%, respectively. All of the healthy volunteers were negative. The two positive results among the non-PJP (by clinical criteria) were HIV positive and had presumptive bacterial pneumonia, one with *Streptococcus pneumoniae*.

Nakamura *et al.* (2009) Clinical utility of serum β-D-Glucan and KL-6 levels in *Pneumocystis jirovecii* pneumonia. Intern. Med. 48: 195-202. The paper describes the evaluation of two markers, (1→3)-β-D-Glucan (BG) and KL-6, a lung cell (pneumocyte) glycoprotein, as aids in diagnosis of *Pneumocystis* pneumonia. The authors used the SKB Fungitec® G kit for the detection of BG. 19 patients were HIV positive and 16 were otherwise immunosuppressed, for a total of 34 subjects. HIV-positive PCP patients were observed to have higher average BG values compared to HIV-negative PCP patients. Sensitivity and specificity for PCP was 100% and 88% for HIV-positive patients and 88% and 88% for HIV-negative patients.

Watanabe, T. *et al.* (2009) Serum (1→3)-β-D-Glucan as a non-invasive adjunct marker for the diagnosis of *Pneumocystis* pneumonia in patients with AIDS. Clin. Inf. Dis. In Press.

The study assessed the diagnostic performance for *Pneumocystis* pneumonia in a series of 111 HIV-positive patients, with confirmed PCP, and also looked at 425 control patients. The SKB Fungitec® G glucan test was used. The glucan test results were 96.4% and 87.8%, for sensitivity and specificity, respectively.

Desmet, S. *et al.* (2009) Serum (1→3)-β-D-Glucan as a tool for diagnosis of *Pneumocystis jirovecii* pneumonia in patients with human immunodeficiency virus infection or hematological malignancy. J. Clin. Micro. 47: 3781-3784. The study evaluated 28 patients with either HIV infection (N=16) or hematological malignancy (N=12). The diagnostic "sensitivity and specificity were reported as "100% and 96.4%, respectively, using a cutoff value of 100 pg/mL." The typically observed highly elevated serum BG concentration was also observed in this study, with median values of 1,496 pg/mL (range, 264-2,732) for HIV-infected patients and 3,779 pg/mL (range, 111-21,938) for patients with hematological disease.

Koo, S. *et al.* (2009) Diagnostic performance of the (1→3)-β-D-Glucan assay for invasive fungal disease. Clin. Inf. Dis. 49: 1650-1659. This study evaluated the diagnostic utility of the Fungitell assay in 871 patients, over a two year period, in a tertiary care setting. A total of 112 proven and probable fungal infections were observed at one week after the initial (1→3)-β-D-Glucan assay. A total of 14 P. jirovecii cases (PCP) were observed. Of these 71.4% had initial serum (1→3)-β-D-Glucan elevations greater than 500 pg/mL, "that often preceded microbiological diagnosis by several days." The authors observed that the "The BG assay appears to be more sensitive than the current standard for PCP in a fair number of cases, and the gold standard may need reevaluation." The observation of highly elevated serum BG values in a preponderance of PCP cases is consistent with observations made in a number of other studies.

Summary

The above-listed presentations and publications provide information concerning the utility of serum (1→3)-β-D-Glucan measurement in the setting of *Pneumocystis* infection. Invasive techniques such as the instillation and recovery of broncho-alveolar lavage fluids are difficult for many patients and impossible for some. Elevated serum beta-glucan levels were shown to be closely associated with pneumocystosis in multiple clinical situations, including pneumonia, HIV, and cancer.

Fungitell® & Guideline Links

- ACC Clinical: <http://www.acciusa.com/clinical/index.html>
- Beacon Diagnostics® Laboratory: <http://www.acciusa.com/clinical/beacon/index.html>
- Revised EORTC-MSG Definitions (2008): <http://www.journals.uchicago.edu/doi/pdf/10.1086/588660>
- Guidelines for Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents; Recommendations from CDC, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America: <http://www.cdc.gov/mmwr/pdf/rr/rr5804.pdf>
- Clinical Practice Guidelines for the Management of Candidiasis: 2009 Update by the Infectious Diseases Society of America Clin. Inf. Dis. 48:503-535 <http://www.journals.uchicago.edu/doi/pdf/10.1086/596757>



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