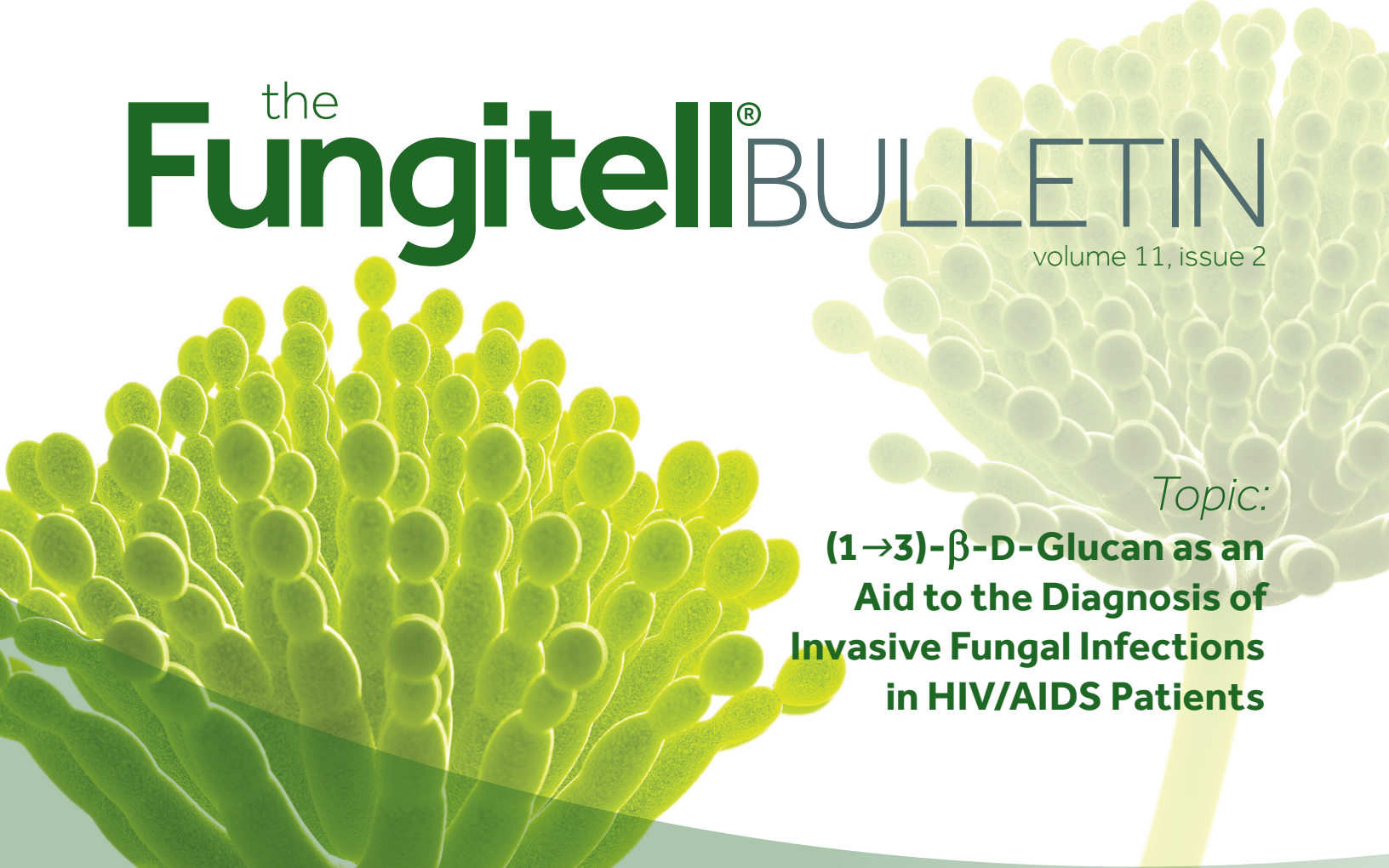
the Fungitell® BULLETIN
volume 11, issue 2



*Topic:*

# (1→3)-β-D-Glucan as an Aid to the Diagnosis of Invasive Fungal Infections in HIV/AIDS Patients

## Discussion:

HIV/AIDS significantly weakens the immune system, leaving patients highly susceptible to opportunistic infections, including invasive fungal infections (IFIs). Diagnosing IFIs in these patients is challenging due to non-specific symptoms and the need for invasive sampling methods. Traditional diagnostic techniques such as culture and histopathology are slow and can be insensitive. The biomarker (1→3)-β-D-Glucan (BDG), a major fungal cell wall component released during the fungal life cycle, has been used for over two decades to aid in IFI diagnosis. As BDG is absent in mammalian cells, its detection usually indicates fungal presence*.

The Fungitell® and Fungitell STAT® assays offer results within 1 hour from a serum sample, providing a safer alternative to diagnostics which require invasive procedures such as biopsy or bronchoalveolar lavage to obtain a sample. Rapid results are critical for early antifungal therapy, improving outcomes. BDG testing detects a broad range of fungal pathogens affecting HIV patients, including *Pneumocystis, Candida, Histoplasma,* and *Aspergillus* species. HIV/AIDS patients, particularly those with very low CD4+ T cell numbers, are highly vulnerable to IFIs. BDG detection strongly indicates the presence of an IFI, making it an invaluable diagnostic tool in these cases.

An effective approach to incorporating BDG testing into a comprehensive diagnostic strategy for HIV/AIDS patients is through risk stratification, using BDG as a screening tool for high-risk individuals, such as those with low CD4+ counts or respiratory symptoms. BDG testing becomes even more valuable when combined with other fungal biomarkers.

*Fungitell® Bulletins are intended as technical advisory communications and as such are disseminated to the general public in order to highlight the significance of (1→3)-β-D-Glucan on human health. These communications do not promote a specific drug, therapy nor make any representation or suggestion concerning the suitability or effectiveness of a particular drug or therapy in patients harboring (1→3)-β-D-Glucan. Fungitell® is an adjunct diagnostic assay to be utilized in conjunction with clinical signs and symptoms for the diagnosis of invasive fungal infection. Fungitell® is currently 510(k) cleared for the detection and quantification of (1→3)-β-D-Glucan in human serum and should be used and interpreted only in a manner consistent with the current Instructions for Use.*

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Publication Date: April 2025
CORP_0746

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### *Pneumocystis jirovecii*

*Pneumocystis jirovecii* pneumonia (PCP) is a common and severe IFI in HIV/AIDS patients, and numerous studies have evaluated the efficacy of the Fungitell® assay in diagnosing PCP in this cohort (Farhour *et al.,* 2018). A meta-analysis by Karageorgopoulos *et al.* (2013) reported very high sensitivity (94%) and high specificity (86%), demonstrating the diagnostic value of BDG.

### *Cryptococcus neoformans*

Cryptococcosis, usually caused by *Cryptococcus neoformans*, is another significant IFI in HIV/AIDS patients. BDG may aid in diagnosing cryptococcosis in specific circumstances. Abassi *et al.* (2015) highlighted BDG's potential as a prognostic marker for mortality, a tool for monitoring treatment response, and a means to distinguish between culture-positive relapse (characterised by elevated BDG levels) and paradoxical immune reconstitution inflammatory syndrome (IRIS), which is typically associated with negative BDG results.

### *Candida spp.*

In cases of invasive candidiasis, Nguyen *et al.* (2012) reported that BDG testing exhibits high sensitivity, ranging from 75% to 100%, and specificity between 80% and 90%, depending on the clinical setting and patient population. Testing for diagnosis of invasive candidiasis is moderately recommended according to the Global guideline for the diagnosis and management of candidiasis from ECMM, ISHAM and ASM (Cornely OA *et al*., 2025). For comprehensive care, it should be combined with clinical assessment and other diagnostic tools to ensure accurate diagnosis and appropriate treatment.Testing for serum BDG in non-invasive forms of candidiasis, such as mucosal infections common in HIV/AIDS patients, generally exhibit significantly low sensitivity (Mirchevska 2016).

### *Aspergillus spp.*

Although invasive aspergillosis is less common in HIV/AIDS patients than other opportunistic IFIs, it remains a concern (Holding *et al.,* 2000). BDG testing can complement other diagnostic methods, such as galactomannan assays and imaging, to improve diagnostic accuracy.

## Limitations

Elevated BDG levels have been responsible for false positive results from non-IFI sources such as hemodialysis, antibiotics (e.g., amoxicillin-clavulanate), and some bacterial infections. Finkelman (2020) reviewed factors affecting BDG specificity, which clinicians should be aware of to avoid misinterpretation. False negatives are also a concern, particularly with fungi like *Cryptococcus* that produce low BDG levels. These issues highlight the need for cautious interpretation and a multi-faceted diagnostic approach combining BDG with other tools for accurate detection (Esteves *et al.,* 2014; Del Corpo *et al.,* 2020).

There is also variability in BDG assay performance between manufacturers, with different assays showing varying sensitivity and specificity levels (Mercier *et al.,* 2019). However, it is important to note that Fungitell® and Fungitell STAT® are the only FDA-cleared and CE marked assays with clinically established cut-off values with over 20 years of supportive clinical data. Serial BDG measurements can be valuable for monitoring treatment response, with regular testing able to detect relapse or treatment failure, allowing timely therapy adjustments to improve outcomes (Onishi *et al.,* 2012).

In summary, BDG testing is a valuable addition to the clinician's toolbox of diagnostics for IFIs in HIV/AIDS patients. Its non-invasive nature, rapid turnaround time, and near pan-fungal fungal detection make it an attractive option for clinicians. However, careful interpretation of results, particularly regarding potential false positives and negatives, is critical. The best outcome for HIV/AIDS patients is likely integration of BDG testing with other diagnostics to improve outcomes when there is high suspicion of an IFI.

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** For further information on the specificity of Fungitell® and Fungitell STAT®, please refer to: Finkelman, M.A. (2020) Specificity Influences in (1→3)-β-D-Glucan-Supported Diagnosis of Invasive Fungal Disease. J Fungi (Basel). 2020;7(1):14. Published 2020 Dec 29. doi:10.3390/jof7010014*