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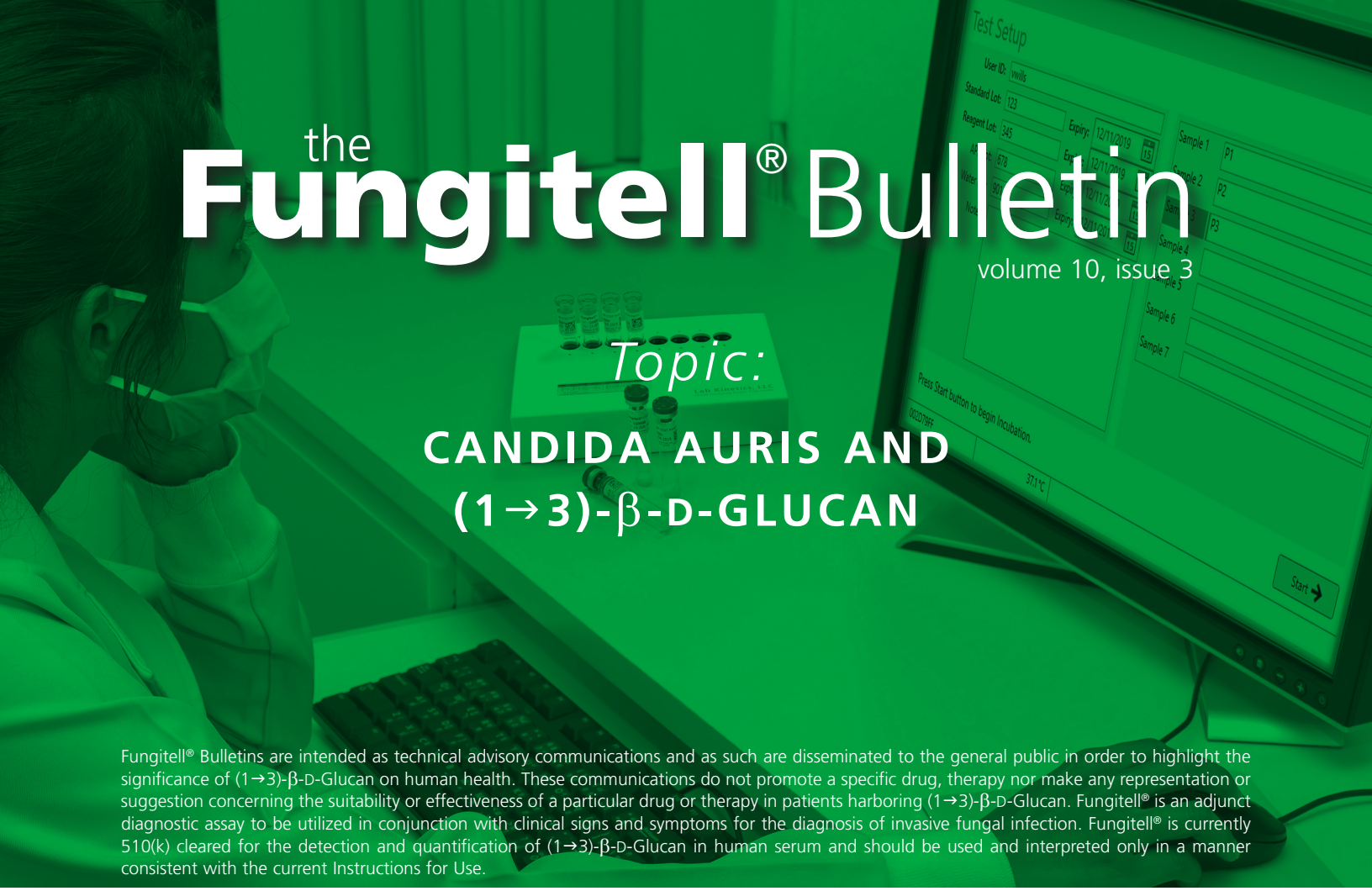

Topic:

CANDIDA AURIS AND (1→3)-β-D-GLUCAN

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.

Discussion:

The (1→3)-β-D-glucan (BDG) assay is widely recognized for its high negative predictive value (NPV)[1,2]. When used in conjunction with additional evidence, the BDG assay allows for the exclusion of infections caused by various fungal organisms, including *Candida, Aspergillus, Pneumocystis*, and most endemic fungi. A negative BDG test in high-risk patients with suspected invasive fungal disease provides clinicians with confidence to modify empiric antifungal therapy, leading to improved patient outcomes[3]. However, when positive BDG results are reported, it becomes important to understand the varying sensitivity of the assay, especially in cases where certain species of microorganisms are highly prevalent. This may be relevant in the context of the significant increase in global cases of *Candida auris*.

Candida auris is a multidrug-resistant yeast that can cause severe invasive infections, particularly in hospitalized patients with underlying health conditions. Classified as a 'critical priority'[4] and an 'urgent threat'[5], *Candida auris* has garnered increased attention due to a 61% rise in clinical cases in the US from 1,474 (2021) to 2,377 (2022)[6]. First isolated almost 15 years ago[7], cases of *Candida auris* have now been reported in thirty-nine countries[8]. The mortality rate for *Candida auris* infections is high, ranging from 30-72%, with the most severe invasive infections occurring in critically ill patients[9]. Although several meta-analyses have investigated the use of Fungitell for the detection of invasive fungal disease in a critical care setting[10], there are limited publications specifically examining the utility of Fungitell in relation to *Candida auris* infection.

Timely identification of patients is crucial for effective *Candida auris* infection prevention and control[11]. Parak *et al.*[12] demonstrated that all cases of *Candida auris* infection in their study were healthcare-acquired (positive culture obtained >48 hours after admission). Chibabhai *et al.*[13] showed that a positive BDG (≥80pg/mL) was observed approximately 2.5 days **prior** to blood culture collection, showing utility of timely serial BDG measurements in monitoring high-risk patients for candidemia. This finding is supported by Tissot

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et al.[14] which showed early BDG positivity in relation to other *Candida* species.

Levels of serum BDG in confirmed cases of *Candida auris* were found to be lower (129pg/mL) compared to *Candida albicans* (410pg/mL)[15,16]. The reduced BDG burden in *Candida auris* candidemia leads to decreased BDG sensitivity (from ~80% to 71-43%) compared to candidemia caused by other *Candida* species[12,13,16]. Affinity for biofilm formation, cell wall composition among *Candida* species, and prior antifungal therapy, are believed to influence BDG sensitivity. Furthermore, detectable BDG levels may vary among different clades of *Candida auris*[16], illustrated by the variability in reported serum BDG levels in studies from South Africa[13], Pakistan[17], and Italy[16].

In summary, lower BDG values may be observed when screening patients in intensive care with a high prevalence of *Candida auris* infection. In cases of suspected candidemia, measuring BDG levels at enrolment and subsequently every 48-72 hours for 14 days is recommended to increase sensitivity. The high negative predictive value of Fungitell can guide antimicrobial therapy, leading to a reduction in the duration of empirical antifungal treatment for critically ill septic/candidemic patients[18]. Despite the decreased sensitivity observed in some patients, elevated BDG levels may still serve as a useful marker for *Candida auris* candidemia.

Discussion References

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