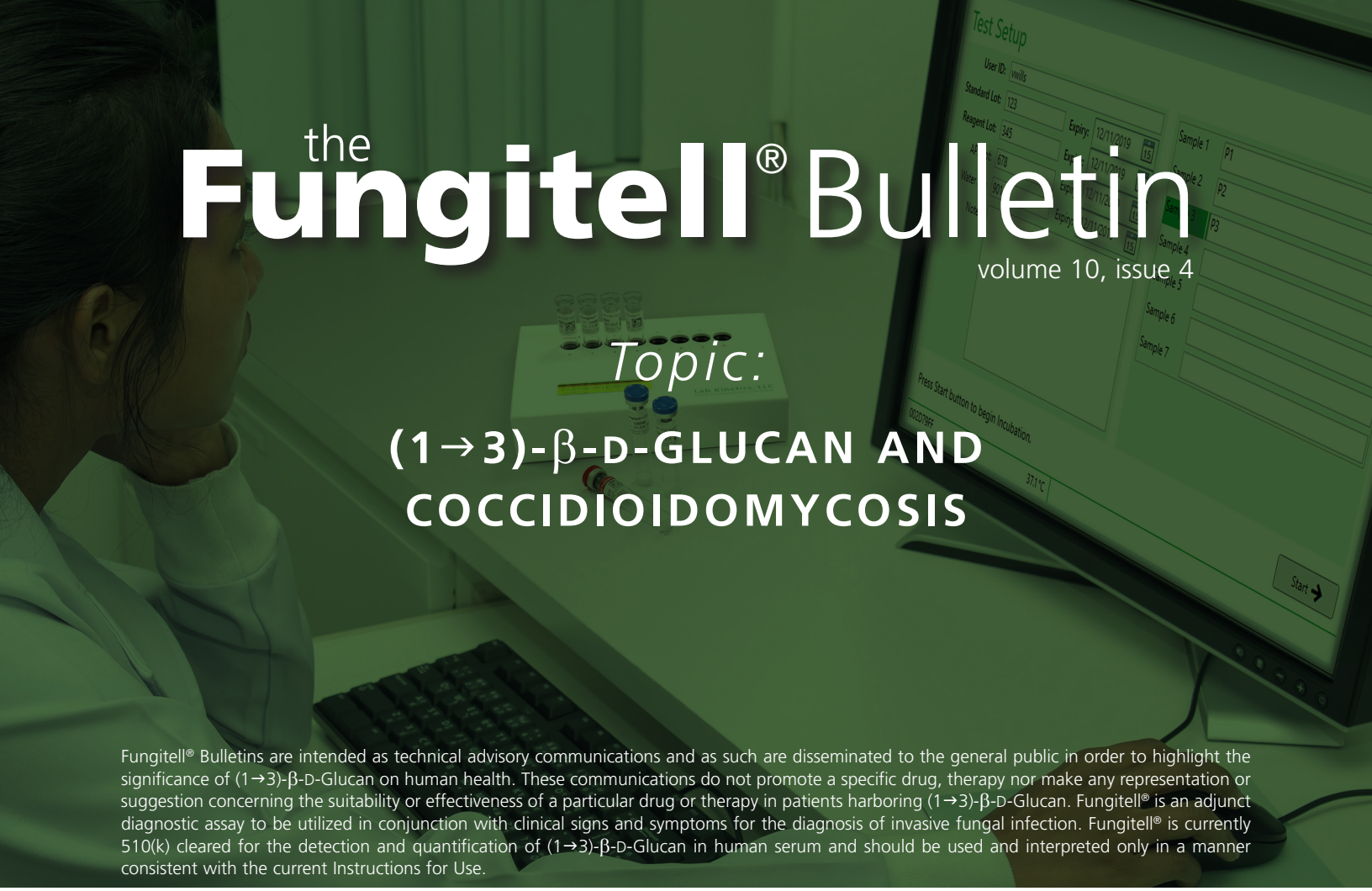

the Fungitell® Bulletin

volume 10, issue 4

Topic:

(1→3)-β-D-GLUCAN AND COCCIDIOIDOMYCOSIS

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:

Coccidioidomycosis, commonly known as Valley Fever, presents a significant challenge to clinicians in endemic regions due to its varied and often non-specific symptoms, which can be easily misdiagnosed as other infectious and non-infectious lung diseases[1]. Coccidioidomycosis is contracted through the inhalation of arthroconidia from the soil-dwelling fungi *Coccidioides immitis* and *Coccidioides posadasii*, affecting both immunocompromised and immunocompetent individuals in endemic areas such as the southwestern United States (California, Arizona), Central America, and South America. Recent Centers for Disease Control & Prevention (CDC) data show annual increases in coccidioidomycosis cases and expanding areas of endemicity[2]. A pan-fungal biomarker such as (1→3)-β-D-glucan, may help clinicians determine whether a fungal infection is present in patients with symptoms of community-acquired pneumonia[1].

Coccidioidomycosis encompasses a spectrum of disease. Most cases are asymptomatic or present as mild respiratory infections or flu-like symptoms. Approximately 1% of cases progress to life-threatening extrapulmonary disseminated disease, typically in immunocompromised individuals[3,4]. The gold standard for diagnosis includes culture and histopathology. Culture results typically take 4-5 days to yield positive results, but in some cases can take up to 2-3 weeks[5]. Serologic antibody testing is challenging because many assays are performed in reference laboratories, increasing turnaround time. Additionally, antibody-based assays have low sensitivity (21-56%) in patients who cannot mount a robust antibody response, leading to repeat testing or missed infections[6].

Recently, Fungitell® has emerged as a promising adjunct diagnostic, offering a rapid assay to aid in the evaluation of patients suspected of coccidioidomycosis while awaiting *Coccidioides* antigen/antibody testing results[7]. Al-Obaidi *et al.* showed that combined *Coccidioides* serology and (1→3)-β-D-glucan testing in immunocompromised patients can aid in the initial diagnostic workup where coccidioidomycosis is highly suspected, with 82% of patients showing a positive result in at least one of the assays[8].

Fungitell®
Bulletin Volume 10, issue 4
Publication Date: September 2024

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(1→3)-β-D-GLUCAN AND COCCIDIOIDOMYCOSIS

Thompson *et al.* demonstrated that (1→3)-β-D-glucan testing is most beneficial for patients with severe coccidioidomycosis requiring hospitalization. These findings were supported by a subsequent small-scale study by Zangeneh *et al.,* which showed (1→3)-β-D-glucan positivity in over 90% of patients who were highly positive for Coccidioides antigen[9]. Although Thompson *et al.* reported a modest sensitivity of 44% in hospitalized coccidioidomycosis patients, this improved with disease severity: (1→3)-β-D-glucan positivity was 53% in acute cases and 83% in disseminated and coccidioidal meningitis cases[7]. Stevens *et al.* (2016) specifically evaluated sensitivity and specificity of Fungitell® in cerebrospinal fluid (CSF) samples in patients with suspected coccidioidal meningitis. In this study, (1→3)-β-D-glucan testing outperformed CSF antibody testing for diagnosing coccidioidal meningitis[10].

While (1→3)-β-D-glucan values were higher in disseminated and coccidioidal meningitis cases than in acute infections, they did not correlate with serum or CSF coccidioidal IgG antibody titres[7,10]. Notably, (1→3)-β-D-glucan was elevated in some hyperacute infection cases before antibody responses were detectable. For example, Thompson *et al.* found elevated (1→3)-β-D-glucan in three patient samples before positive antibody testing[7], and Stevens *et al.* found elevated (1→3)-β-D-glucan in five CSF samples that were positive for coccidioidal antigen but had no detectable antibodies[10], suggesting utility in early-stage infections.

In a single case report, Fungitell® was evaluated by Wilmes *et al.* for its potential to guide the duration of antifungal therapy. Although (1→3)-β-D-glucan levels generally correlated with disease resolution, further work is needed to evaluate the utility of (1→3)-β-D-glucan for directing optimal treatment duration in this group of patients[11].

By identifying fungal infections early, (1→3)-β-D-glucan testing can facilitate timely intervention in patients hospitalized with coccidioidomycosis, coccidioidal meningitis, or hyperacute coccidioidomycosis, where the infection progresses rapidly[7,12]. The timing of (1→3)-β-D-glucan sampling in relation to the *Coccidioides* lifecycle may be important, as *Coccidioides* spherules contain roughly 60% (1→3)-β-D-glucan by dry weight, compared to arthroconidia, which contain only 20%. This lifecycle difference of (1→3)-β-D-glucan may explain the reduced sensitivity of Fungitell® with respect to coccidioidal infections compared to other invasive fungal infections[7,13].

In summary, in combination with traditional diagnostic methods for coccidioidomycosis, (1→3)-β-D-glucan testing with Fungitell® offers a rapid and useful adjunct, particularly in the context of severe disseminated and hyperacute cases where timely identification and treatment are critical.

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