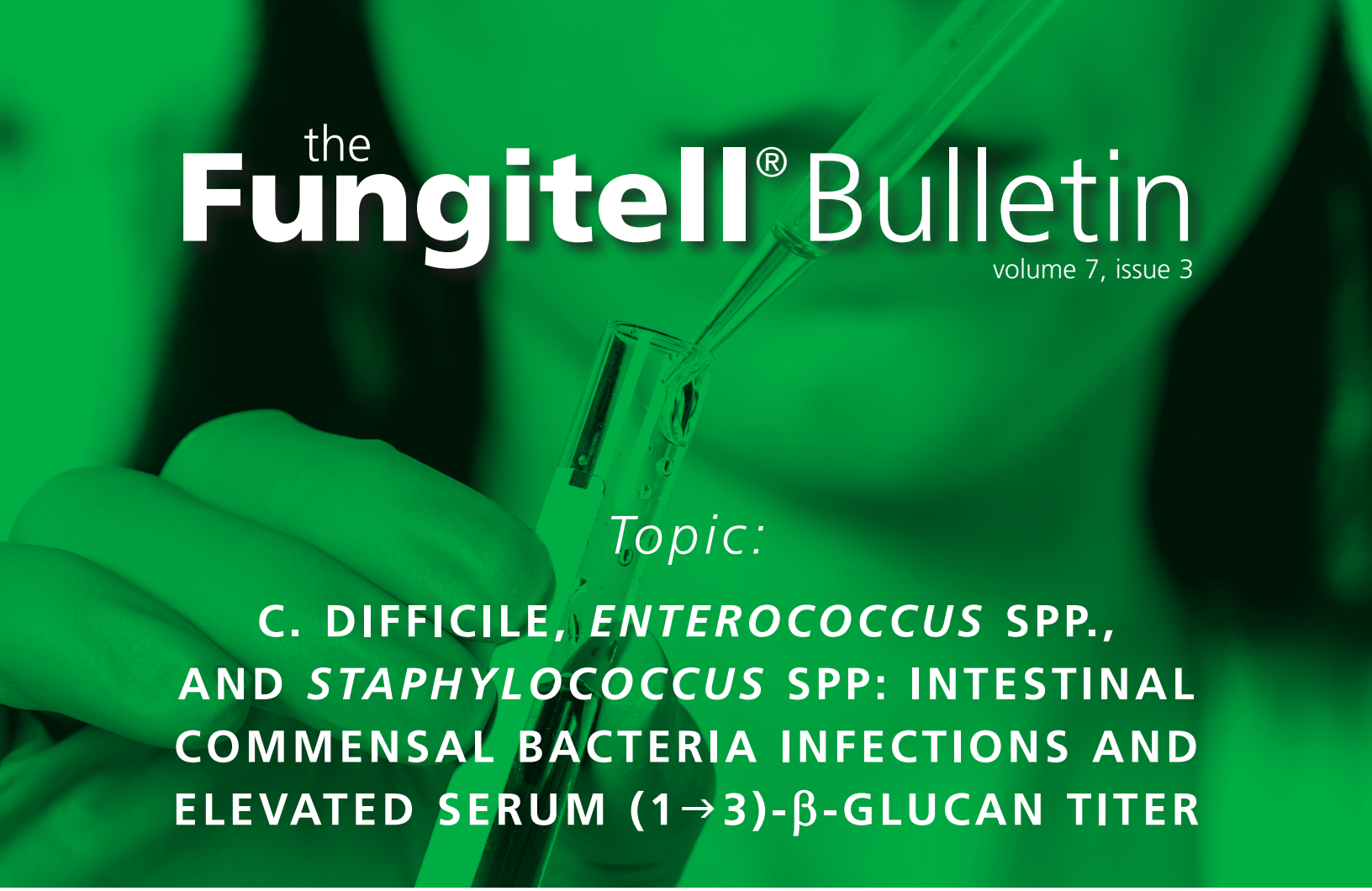
the Fungitell® Bulletin
volume 7, issue 3



Topic:

C. DIFFICILE, *ENTEROCOCCUS* SPP., AND *STAPHYLOCOCCUS* SPP: INTESTINAL COMMENSAL BACTERIA INFECTIONS AND ELEVATED SERUM (1→3)-β-GLUCAN TITER

Discussion:

Bacteremia is variably associated with elevated serum (1→3)-β-glucan[1,2,3]. The role of gut permeability in bacteremia with elevated BG is of special interest given the need to differentiate invasive fungal disease from bacterial disease or bacterial-fungal coinfection. Recently, Giacobbe et al demonstrated the excellent discriminatory ability of combining BG and procalcitonin titers to distinguish candidemia from bacteremia. A positive BG titer with a procalcitonin level less than 2 nanograms/ml had a positive predictive value for candidemia of 96%[4]. It is of interest, however, to understand whether particular factors such as bacterial genus and specific virulence factors can influence whether serum BG titers may become elevated, potentially due to translocation. Elevated serum (1→3)-β-glucan has been described in the case of *Enterococcus* bacteremia[5] and, in an experimental murine model, in which *Clostridium* gut infection was associated with elevated serum BG[6]. Infections with these microbes are known to arise from overgrowth in the gut, causing epithelial inflammation and permeability barrier disruption.

A clue to the differential capacity of bacteria to generate elevated BG may be found in the work of Held *et al* who studied a population of bacteremic patients and observed that those infected with *Enterococcus* generated a mean serum BG level of 135 pg/ml, while the non-*Enteroccocus* species mean was 15 pg/ml[5]. As *Enteroccoci* produce gelatinase protease and secreted proteinase (GeE and SprE gene products, respectively), which degrade the intestinal lining, as virulence factors, bacterially-induced barrier damage may be a mechanism through which BG translocation can occur[7]. Similarly, the toxins of *Clostridium difficile* likely represent the permeability barrier-weakening activity of that infection[8].

Fungitell®
(1→3)-β-D-Glucan Assay

Bulletin Volume 7, issue 3
Publish Date: November 2018

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In analyses of coinfections involving *Candida* spp. and bacteria, *Staphylococcus* is highly over-represented. *Staphylococcus* is commonly observed in the intestinal microbiota[9,10].

In addition to the above-mentioned bacteria, the fine structure of the intestinal luminal epithelium has been shown to be susceptible to a spectrum of injury from other bacterial species. In a murine model, Bucker *et al*, demonstrated that alpha-hemolysin-producing *E. coli* produced epithelial damage that included focal lesions of up to 50,000 square microns in area and which penetrated through to the underlying tissue[11]. Additional bacterial species demonstrated to affect the gut include *Aeromonas hydrophila* (aerolysin production) and *Arcobacter butzleri*[12,13]. Both degrade the intestinal epithelium and degrade the permeability barrier function.

As antibiotic-generated dysbiosis can potentiate overgrowth of pathogens, including the above-mentioned species, the question of whether elevated serum BG shows an elevated risk for *Candida* translocation and candidemia is of central interest. Recently, Jensen and colleagues described increased *Candida* fungal infection in patients receiving "high exposure" ciprofloxacin (HR, 2.1)[14]. This follows from data produced by Mavromanolakis *et al* who described gut *Candida* elevation by multiple different quinolones, in patients[15].

Based upon multiple observations of concomitant elevation of serum BG and inflammatory cytokines/chemokines, markers of microbial translocation, bacteremia with certain organisms, increased risk of death[16,17], and antibiotic-mediated gut *Candida* overgrowth, physicians need to carefully consider the interpretation of elevated serum BG results and patient status.

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