Topic:

Healthcare-related *Candida* infections:

A medical challenge requiring increased surveillance and diagnostic efforts.

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Introduction:

New diagnostics to address the difficult challenges in invasive fungal disease have been called for by the medical profession. Physicians are acutely aware of the high morbidity and mortality associated with these diseases. Fungitell®, an FDA-cleared and CE-Marked *in vitro* diagnostic kit for the detection of (1→3)-β-D-glucan, addresses this need. The utility of Fungitell has been demonstrated with *Candida, Aspergillus, Pneumocystis, Fusarium,* and other major fungal pathogens.

Data demonstrating the incidence of invasive fungal infections (IFI) typically indicate that there are two age-related peaks. The high prevalence of invasive candidiasis occurring in neonatal intensive care units (NICU) is the basis of the peak among the very young[1]. The peak at the other end of the age spectrum is due to the high incidence of immunosuppression-associated and metabolism deranging underlying conditions that are risk factors for IFI. These include cancer, gastrointestinal surgery, transplant, diabetes, ICU stays, etc.[2,3] Hospital-acquired (or nosocomial) candidal infections and community onset (CO; observed within two days of admission) are associated with considerable morbidity, mortality, and cost[4]. Pfaller *et al*[5] (2011) recently described the observations made in a 79 medical center study over a two year period, 2008-2009. 1,354 episodes of *Candida* blood stream infection (BSI) were observed. 36.5% were CO and 63.5% were nosocomial. In the Pfaller *et al* study *C. albicans* comprised almost half the isolates (48.4%), with *C. glabrata, parapsilosis, tropicalis*, and *krusei* comprising most of the rest (47.9%). Considering the large number of CO candidal infections, it is hypothesized that the steep rise in the number of patients being treated for serious illnesses, as out-patients, may be creating more opportunity for community-acquired fungal infections.[5] In pulmonary care, this phenomenon has given rise to a new category, Health Care Associated Pneumonia (HCAP), to distinguish it from classical community acquired pneumonia (CAP)[6]. The combination of aggressive medical intervention and treatment in the outpatient setting has created diagnostic needs focused upon recognizing candidal infections early enough to allow efficacious intervention.

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Recent Publication:

Bellanger, AP. *et al.* Retrospective assessment of (1→3)-β-D-glucan for presumptive diagnosis of fungal infections. APMIS 2011; 119: 280-286. This study evaluated the timing of BG positivity relative to galactomannan in a cohort of 28 patients diagnosed with invasive fungal infection. For invasive aspergillosis (N=15), (1→3)-β-D-glucan was positive earlier than galactomannan in 5 cases, at the same time in 8 cases, and later in 2 cases. The remaining 13 cases were a mixture of *zygomycoses* (2), *fusariosis* (3), *cryptococcosis* (3), *candidemia* (3), and *pneumocystosis* (2). (1→3)-β-D-glucan was high in all but the *zygomycoses* and one of the *fusarioses*.

Damiani, C. *et al.* Serum (1→3)-β-D-glucan levels in primary infection and pulmonary colonization with *Pneumocystis jirovecii*. J. Clin. Micro. 2011; 23 March, [Epub ahead of print].
This study evaluated several classes of patients at risk for *Pneumocystis* pneumonia with a view to evaluating the issue of *Pneumocystis* presence in the lung at levels undetectable by conventional BAL staining and microscopy. The study evaluated BAL, PCR and (1→3)-β-D-glucan results in infants with primary *Pneumocystis* infection, colonized adults, and adults with PCP. 13 of 14 infants had positive results (>80 pg/mL; maximum 217 pg/mL), 6 of 8 colonized patients had negative results (two had 83 and 84 pg/mL, respectively), and all 6 patients with PCP were positive (184-2710 pg/mL; median, 1768 pg/mL). Accordingly, adult patients with PCP were observed to have much higher serum BG levels than colonized adult patients or infants with primary *Pneumocystis* infections. A control group of 14 infants, hospitalized for acute respiratory syndrome, but negative for Pneumocystis, were negative for serum (1→3)-β-D-glucan.

Gonzales, B. E. *et al.* Elevated serum beta-D-glucan levels in immunocompromised children with clinical suspicion for *Pneumocystis jirovecii* pneumonia. Clin. Vacc. Immunol. 2011; May 4 [Epub ahead of print].
This pediatric case series report describes the utility of serum (1→3)-β-D-glucan levels in the diagnosis of *Pneumocystis* pneumonia. In two of the three patients, BAL was either negative for *Pneumocystis jirovecii* or unavailable. In all three patients, the serum (1→3)-β-D-glucan levels exceeded 500 pg/mL. In one patient, negative BAL microscopy resulted in discontinued anti-*Pneumocystis* therapy followed by clinical deterioration. Anti-*Pneumocystis* therapy was re-established. All three patients received appropriate anti-*Pneumocystis* therapy and survived.

Montagna, M.T. *et al.* Invasive fungal infections (IFI) in neonatal intensive care units of southern Italy: A multicentre regional active surveillance (AURORA Project). J. Prev. Med. Hyg. 2010; 51: 125-130. This report describes the invasive fungal infection epidemiology in neonatal intensive care units (NICU) in southern Italy. The average IFI prevalence was 1.3%, with a crude mortality of 23.8%. IFI incidence was much higher in very low birth weight neonates relative to higher birth weights 4.7%, ≤1000 gm; 4%, ≤1500 gm; 0.2%, ≤2500 gm). (1→3)-β-D-glucan data was available for 7 infants with a 100% sensitivity reported. Interestingly, all 7 infants were undergoing prophylaxis with fluconazole.

Ostrosky-Zeichner, L. *et al.* Early treatment of candidemia in adults; A review. Medical Mycology 2011; 49: 113-120. This article provides a review of the negative consequences of the failure to diagnose, and appropriately treat, candidemia early in its presentation. In addition, the authors review predictive approaches to candidemia & invasive candidiasis, as well as new laboratory tests such as serum (1→3)-β-D-glucan. The paper includes a discussion of the economic impact of *Candida* colonization and infection. Data are presented showing that both ICU and hospital stays were increased substantially, producing a significant increase in costs. An analysis of pre-emptive therapy economics suggests that this could be very cost effective with appropriate criteria for patient selection.

Recent Fungal Diagnostic Method Reviews

Cuenca-Estrella, M. *et al.* Detection and investigation of invasive mould disease. J. Antimicrob. Therapy 2011; 66 Suppl 1: i15-24.

Oz, Y & Kiraz, N. Diagnostic methods for fungal infections in pediatric patients: Microbiological, serological, and molecular methods. Expert Rev. Anti Infect. Ther. 2011; 9: 289-298.

Matsumura, Y. *et al.* Clinical characteristics of *Pneumocystis* pneumonia in non-HIV patients and prognostic factors including microbiological genotypes. BMC Infect. Dis. 2011; 11 [Epub ahead of print]

References

1. Romeo, M.G. *et al.* Role of probiotics in the prevention of the enteric colonization by Candida in preterm newborns: incidence of late-onset sepsis and neurological outcome. J. Perinatatol. 2011; 31: 63-69.
2. Person AK, Kontoyiannis DP, Alexander BD Fungal infections in transplant and oncology patients. Infect Dis Clin North Am. 2010;24:439-59.
3. Ostrosky-Zeichner, L. *et al.* Multi-center evaluation of the (1→3)-β-D-glucan assay as an aid to diagnosis of fungal infections in humans. Clin. Inf. Dis. 41: 654-659.
4. Mikulska, M. *et al.* Invasive candidiasis in non-hematological patients. Mediterr J Hematol Infect Dis. 2011; 3(1): e2011007. Epub 2011 Jan 25.
5. Pfaller. M.A., *et al.* Candida bloodstream infections: Comparison of species distributions and antifungal resistance patterns in community-onset and nosocomial isolates in the SENTRY antimicrobial surveillance program, 2008-2009. Antimocrob. Agents Chemo. 2011; 55:561-566.
6. Falcone, M. *et al.* Healthcare-associate pneumonia; Diagnostic criteria and distinction from community-acquired pneumonia. Int. J. Infect. Dis. 2011; May 25, [Epub ahead of print]

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