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Session: 229. Diagnostics: Biomarkers and Novel Approaches
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Background. Intravenous immunoglobulin (IVIG) is used to treat an increasing number of conditions including hematologic, rheumatologic and immunodeficiency diseases. The immunomodulatory effects can be life-saving, however recent administration can complicate diagnostics when patients later present with symptoms necessitating serologic testing. We evaluated the serologic profile of IVIG for commonly ordered infectious diseases serologies.

Methods. Patients were enrolled if they received and were naïve to IVIG therapy. Blood was drawn prior to IVIG and 72–96 hours post-infusion. All samples were tested for: *Bartonella*, *Coccidioides*, *Brucella*, *Histoplasma*, *Coxiella*, West Nile, St. Louis, California, Eastern, and Western Encephalitis, Lyme, Dengue, HSV 1 and 2, *Chikungunya*, cytomegalovirus, varicella zoster, Epstein-Barr and *Toxoplasma* by standard methodologies (ARUP, Salt Lake City, UT). Pre- and post-infusion antibody concentrations were evaluated to determine the potential false-positive rate of serologic testing.

Results. Seven patients received IVIG (renal transplant rejection, two patients; Guillain–Barre syndrome, three patients; bone marrow transplant, two patients). Six of seven patients receiving IVIG had at least one evaluated serology become positive 72 hours after IVIG infusion. Antibodies for CMV, HSV-2, and EBV early antigen D turned positive in three patients. Antibodies for WNV, *Coccidioides* IgG, and *Histoplasma* yeast IgG became positive in two patients.Finally, antibodies for HSV-1 and -2, and EBV nuclear antigen each turned positive in one patient. Patients received between 20 and 112.5 g. Of the three patients who received more than 100 g of IVIG, two had at least four serologies turn positive. Of the patients who received <100 g (20–50 g), none had >3 turn positive ($P < 0.05$). One patient had three serologies turn negative (*Coccidioides*, HSV 2, and EBV Early D) after infusion of 36.5 g of IVIG, with none turning positive.

Conclusion. Use of IVIG has increased significantly over the past decade; however, the potential pitfalls in serologic diagnostics associated with receipt of IVIG have not been studied systematically and is likely a confounder in serologic diagnostics causing both false-positive and false-negative results. We found a number of screening and diagnostic serologies can be artificially altered after infusion of IVIG.

Disclosures. **All authors:** No reported disclosures.

2032. Predictors of 6-Week Mortality in Patients with Positive Bronchoalveolar Lavage (BAL) Galactomannan (GM)

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Session: 230. Diagnostics: Mycology
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Background. BAL-GM is a mycologic criterion for diagnosis of probable invasive aspergillosis (IA). However, in a contemporary cohort of consecutive patients with BAL-GM measured as part of their workup for potential IA, we previously showed that 42% of positive (≥0.5) BAL-GM values can be falsely positive; positive predictive value was increased by using higher cutoffs and in patient groups with high pre-test probability for IA. In this study from the same cohort, we analyze the prognostic value of BAL-GM and identify predictors of 6-week mortality, the main outcome in most studies of mold-active antifungal drugs.

Methods. We reviewed clinical and microbiologic data of patients who had ≥1 positive BAL-GM (≥0.5), at Brigham and Women's Hospital (November 2009–March 2016). We applied EORTC/MSG invasive mold infection (IMI) definitions to classify cases as possible, probable or proven IMI, excluding BAL-GM result as mycologic criterion, and used Cox regression to identify factors associated with 6-week all-cause mortality.

Results. We studied 134 patients (median age 58 years, 49% women, 55% with hematologic malignancy, 10% solid-organ and 34% hematopoetic stem-cell transplant recipients). APACHE II score, liver disease, acute kidney injury, and shock were independently associated with higher 6-week mortality. ICU stay, mechanical ventilation, corticosteroids, hypertension, EORTC/MSG category, serum-GM and antifungal treatment were associated with higher mortality in univariate, but not multivariate analyses. BAL-GM value was independently associated with 6-week mortality (adjusted HR 1.24(continuous variable), 95% CI 1.1–1.39, $P < 0.001$). The association of BAL GM strata with 6-week crude mortality was significant in patients with possible, probable or proven IMI, but not in those without IMI (Figure 1).

Conclusion. Higher BAL-GM values were an independent predictor of 6-week mortality, having prognostic value in patients with possible, probable or proven IMI, but not in patients who did not meet other criteria for IMI. We propose critical reassessment of BAL-GM cutoff values in different patient populations.

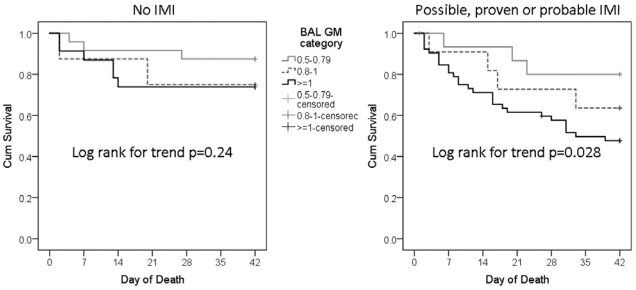

Figure 1. Kaplan–Meier (KM) curves for different cutoffs of BAL GM.

Disclosures. **All authors:** No reported disclosures.

2033. Incorporating T2Candida Testing into Rational Antifungal (AF) Management: A Successful Pilot Study of Diagnostic Stewardship (DS) Directed Toward Specific Intensive Care Unit (ICU) Patients At-Risk for Sepsis due to Invasive Candidiasis (IC)

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Session: 230. Diagnostics: Mycology
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Background. Blood cultures (BC) are ~50% sensitive for diagnosing IC. T2Candida (T2) detects five leading Candida spp. directly in blood and was ≥90%/90% sensitive/specific (S/Sp) for candidemia in clinical trials. Optimal use of T2 in clinical practice is unclear. We targeted T2 to specific ICU patients at-risk for IC, and implemented AF management algorithms developed with ICU teams.

Methods. A DS team ordered concurrent T2 and BC, and used results to guide AF in patients fulfilling pre-specified criteria for septic shock (medical ICU (MICU)), sepsis after abdominal surgery (trauma ICU), or sepsis with mechanical circulatory support (cardiothoracic ICU). We focused on groups with anticipated pre-test IC probabilities of ~3–15%. Proven IC was defined if BC+ and possible IC if BC- but a compatible clinical picture was observed.

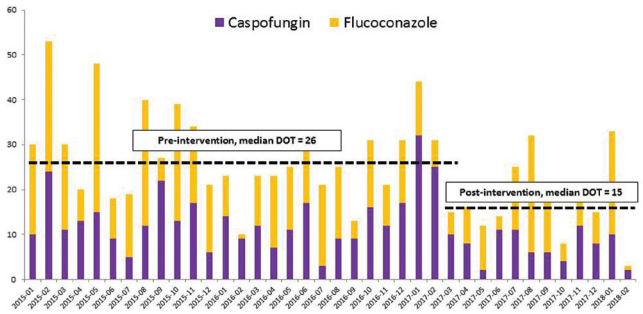
Results. Seven percent (6/88) of BC in ICU patients with sepsis were Candida +. T2 and BC results are shown in the table. Using BC as gold standard, T2 S/Sp and PPV/NPV were 50%/87% and 33%/96%, respectively. Including possible IC, T2 S/Sp increased to 69%/96%, and 67% (4/6) of T2+/BC– results were likely true positive; two false-positive results were for *C. parapsilosis*. We focused on MICU outcomes initially since 75% (66/88) of tests were performed here. Empiric AFs were discontinued in 12 patients following a T2- result; AFs were avoided in all others. Median combined days of therapy (DOT)/month for caspofungin and fluconazole as empiric or definitive treatment prior to and after introducing DS were 26 (range: 10–53) and 15 (3–32), respectively ($P = 0.0047$). AF consumption was decreased 47% (figure).

Conclusion. Targeted DS using T2 in select ICU patients with sepsis significantly reduced AF usage. 14% of patients with sepsis were diagnosed with IC using either T2+ or BC+, compared with 7% with BC+ alone, as would be expected if BC S was 50%. T2 S and T2–/BC+ results were lower and higher, respectively, than previously reported, indicating that treatment decisions should be based on results of both tests. Most T2+/BC– results were ascribed to possible IC.

Table. Rates of T2 and BC Positive Results and Corresponding *Candida* Species

	% (*n*) tests	Candida spp.
T2+	10% (9)	5 CP, 4 CA/CT
BC+	7% (6)	5 CA, 1 CP
T2+/BC+	3% (3)	2 CA, 1 CP
T2+/BC-	7% (6)	2 CA/CT, 4 CP
T2-/BC+	3% (3)	3 CA
T2-/BC-	86% (76)	

Figure. Antifungal days of therapy (DOT) per month in the MICU



Disclosures. **M. H. Nguyen**, Merck: Grant Investigator, Research grant. Astellas: Grant Investigator, Research grant.

2034. Natural Antibodies Affects the Formation of Titan Cells in *Cryptococcus neoformans In Vitro*

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Session: 230. Diagnostics: Mycology
Saturday, October 6, 2018: 12:30 PM

Background. An important feature of *Cryptococcus neoformans* (CN) is an ability to undergo morphological changes that enhance virulence and development of cryptococcal disease (CD). CN can change its size by capsule enlargement alone or capsule and cell body enlargement, resulting in "titan cells." Titan cells enable CN to evade host defense mechanisms. Human and mouse β-glucan antibodies bind and inhibit CN growth *in vitro*. Naturally occurring antibodies in human serum bind β-glucans. In this study, we determined the effect of human IgM and IgG on CN size and titan cell formation *in vitro*.

Methods. Experiments were performed with CN var. *grubii* H99 (serotype A) grown in liquid Sabouraud media at 30ºC. First, we established that human IgM (Sigma Aldrich) binds H99 and Laminarin (a polymer consisting primarily of β (1–3) glucan with occasional β (1–6) branching (Sigma Aldrich) by ELISA using Goat Anti-Human IgM-AP Then, we cultured CN in titan cell medium (TCM, 5% sabouraud and 5% fetal bovine serum diluted in MOPS 50 mM at pH 7.3 plus 15 µM sodium azide) at 37ºC with CO_2 for 18 hours with and without human IgM or IgG (Sigma Aldrich), after which cell size was evaluated using India Ink in a Zeiss microscope.

Results. We found that IgM-treated cells exhibited a significant reduction in CN capsule size and titan cell formation (total cell size) compared with controls without IgM or with IgG. Median total cell size (µm) were: IgM (15.04), IgG (20) and PBS (22.24), $P < 0.05$ using the Kolmogorov–Smirnow test to estimate normality and one-way ANOVA to compare between groups. There were no statistical differences in cell size after incubation with human IgG or PBS. To gain insight into how IgM may mediate its effect, we demonstrated that it bound mainly to the CN cell wall with some diffuse punctuate to the capsule by immunofluorescence.

Conclusion. Our results reveal that natural IgM has the ability to inhibit CN titan cell formation in cultured cells. Given the importance of titan cell formation in virulence, our results suggest that direct effects of natural antibody on CN biology may contribute to human resistance to CD. This hypothesis is under investigation in our laboratory.

Disclosures. **All authors:** No reported disclosures.

2035. Detection of *Blastomyces dermatitidis* Antigen in Urine Using a Novel Quantitative Enzyme-linked Immunosorbent Assay

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Session: 230. Diagnostics: Mycology
Saturday, October 6, 2018: 12:30 PM

Background. Detection of *Blastomyces dermatitidis* antigen (BdAg) in clinical specimens offers a rapid and non-invasive means to both diagnose blastomycosis and monitor patient response to therapy. There are currently no BdAg detection assays commercially available and the majority of BdAg testing is performed at a single reference laboratory (MiraVista Diagnositcs [MVDx], Indianapolis, IN). Here, we evaluated a novel, quantitative enzyme-linked immunosorbent assay (ELISA) based on a unique rabbit monoclonal antibody for detection of *B. dermatitidis* polysaccharide antigens in urine (Aliquot LLC, Gorham, Maine).

Methods. Clinical residual urine specimens collected from 86 unique patients with a previously negative (n = 63) or positive (n = 23) result by the MVDx *Blastomyces* Ag Quantitative EIA were evaluated by the Aliquot BdAg ELISA. Clinical information was available for five of these patients. In addition, analytical specificity was evaluated using 15 residual urine samples positive for *Streptococcus pneumoniae* (n = 5), *Legionella pneumophila* (n = 5) or *Histoplasma capsulatum* (n = 5) antigens.

Results. The Aliquot BdAg ELISA showed 95.7% (22/23), 96.8% (61/63) and 96.5% (83/86) positive, negative and overall agreement with the MVDx BdAg EIA, respectively. Seventeen of the 22 samples positive for BdAg by both assays resulted positive by a *H. capsulatum* antigen ELISA (IMMY, Norton, OK). Of the five well-characterized patients, one was diagnosed with blastomycosis based on a positive *B. dermatitidis* immunodiffusion result; this patient was positive by both BdAg assays. All urine samples positive for *S. pneumoniae* or *L. pneumophila* antigen were negative by the Aliquot BdAg ELISA, while all five samples positive by the IMMY *H. capsulatum* urine antigen ELISA were also positive by the Aliquot BdAg assay.

Conclusion. The Aliquot BdAg ELISA demonstrated excellent agreement with the MVDx BdAg EIA. Cross-reactivity between *B. dermatitidis* and *H. capsulatum* antigen detection assays has been previously established and is a notable limitation to the Aliquot BdAg assay. Further evaluation of this assay using specimens from well-characterized patients with and without blastomycosis is warranted.

Disclosures. **All authors:** No reported disclosures.

2036. Plasma (1→3)-β-D-Glucan Levels Correlate with Neurocognitive Functioning in HIV-Infected Adults

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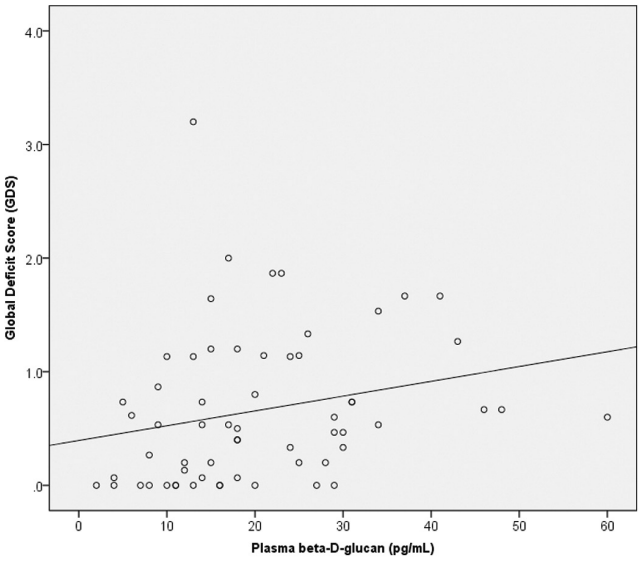
Session: 230. Diagnostics: Mycology
Saturday, October 6, 2018: 12:30 PM

Background. Although antiretroviral therapy (ART) has improved survival and morbidity, HIV-infected adults still have higher rates of non-AIDS disorders, such as neurocognitive impairment, than HIV-uninfected adults. (1–3)-b-D-Glucan (BDG) is a fungal cell wall component which serves as a plasma biomarker for fungal infection and—in the absence of fungal infections—for gut barrier integrity failure and microbial translocation. The objective of this study was to determine whether higher plasma and cerebrospinal fluid (CSF) levels of BDG are associated with neurocognitive impairment [evaluated by global deficit score (GDS)] in HIV-infected adults.

Methods. We measured levels of BDG in paired plasma and CSF samples, and compared levels with GDS, soluble urokinase plasminogen activator receptor (suPAR; a marker of monocyte activation and chronic inflammation that has previously been associated with non-AIDS disorders) and plasma CD4/CD8 ratio in a cohort of 61 HIV+ adults on suppressive ART. Study samples were collected as part of the prospective CHARTER study between 2005 and 2015 at the University of California San Diego and were stored at −80°C on the day of collection. BDG testing of blood plasma and CSF supernatant was performed at the Associates of Cape Cod, Inc., research laboratories using the Fungitell assay.

Results. Median plasma BDG level was 18 pg/mL (range: 2–60 pg/mL), median CSF BDG level was 20 pg/mL (range: 0–830 pg/mL). Higher levels of plasma BDG were associated with more severe cognitive impairment as measured by the GDS (Spearman r = 0.35; P = 0.006, Figure). Individuals with neurocognitive impairment (i.e., GDS > 0.5, n = 33) had higher plasma BDG levels compared with unimpaired individuals (P = 0.027). Plasma levels of BDG and suPAR correlated significantly (r = 0.31, P = 0.016), while all other correlations were nonsignificant (e.g., CSF BDG and GDS [r = 0.23], plasma suPAR and GDS [r = 0.19], CSF suPAR and GDS [r = −0.022], CD4/CD8 ratio and GDS [r = −0.028]).

Conclusion. Elevated plasma levels of BDG may be an indicator of gut barrier integrity failure and an independent biomarker associated with neurocognitive functioning in HIV+ adults on suppressive ART.



Disclosures. **M. Finkelman**, Associated of Cape Cod: Employee, Salary.