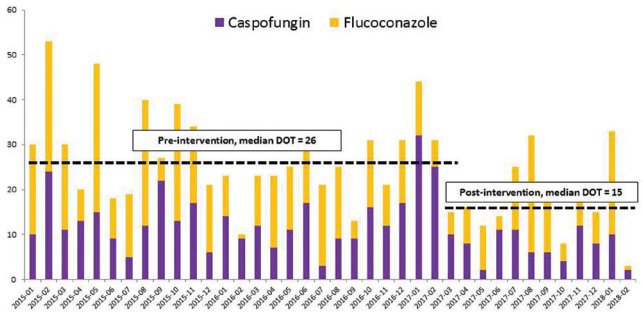
Figure. Antifungal days of therapy (DOT) per month in the MICU



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

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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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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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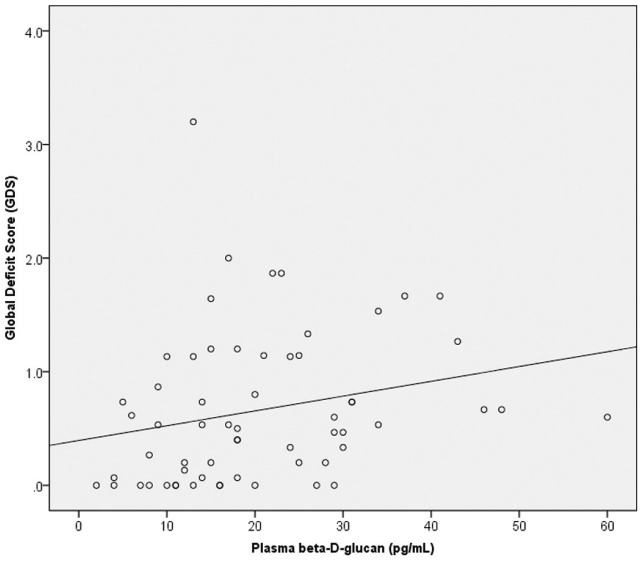
Background. Although antiretroviral therapy (ART) has improved survival and morbidity, HIV-infected adults still have higher rates of non-AIDS disorders, such as neurocognitive impairment, than HIV-uninfected adults. (1–3)-b-D-Glucan (BDG) is a fungal cell wall component which serves as a plasma biomarker 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.