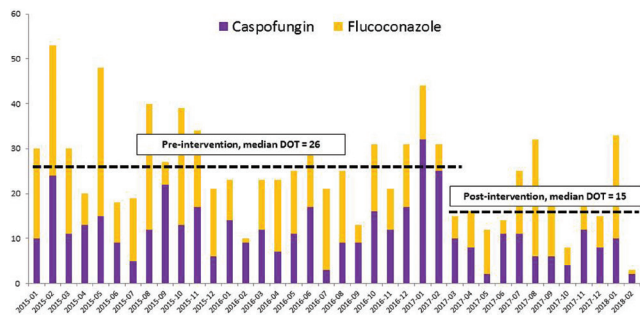


Figure. Antifungal days of therapy (DOT) per month in the MICU



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

Nuria Trevijano Contador, PhD Biology¹ and Liise-Anne Pirofski, MD, FIDSA²; ¹Medicine Infectious Diseases, Albert Einstein College of Medicine, Bronx, New York and ²Department of Medicine, Division of Infectious Diseases, Albert Einstein College of Medicine and Montefiore Medical Center, Bronx, New York

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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 30°C. 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 μ M sodium azide) at 37°C with CO₂ 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 (μ m) 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

Dane Granger, BSc¹; ¹Division of Clinical Microbiology, Mayo Clinic, Rochester, Minnesota

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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 Diagnostics [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.

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

Martin Hoening, MD¹; Scott Letendre, MD²; Malcolm Finkelman, MD³ and Sara Gianella, MD¹; ¹University of California San Diego, San Diego, California, ²Medicine, University of California San Diego, La Jolla, California, ³Associates of Cape Cod, Inc., Falmouth, Massachusetts

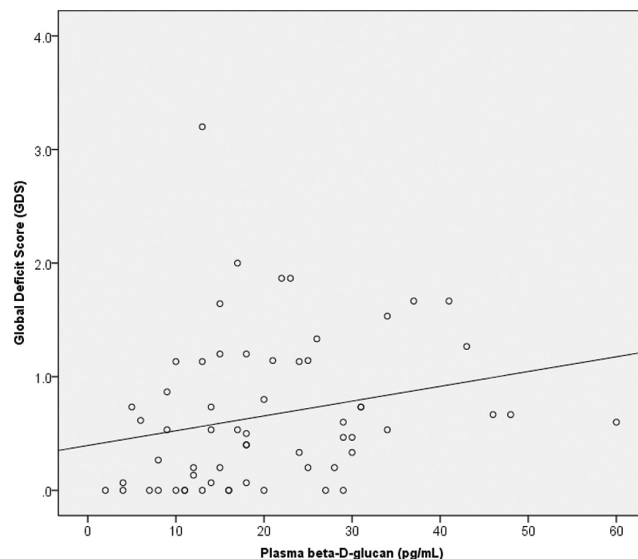
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Background. Although antiretroviral therapy (ART) has improved survival and morbidity, HIV-infected adults still have higher rates of non-AIDS disorders, such as neurocognitive impairment, than HIV-uninfected adults. (1–3)- β -D-Glucan (BDG) is a fungal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



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2037. Utilization of the T2 Magnetic Resonance in the Early Detection of Invasive Candidiasis

Sonal Patel, PharmD, BCPS¹; David Behrman, MD (2021)²; Andrew Chao, MD^{3,4}; Allison McMullen, PhD⁵; Jose Vazquez, MD, FACP, FIDSA¹ and Arni Sr Srinivasa Rao, PhD⁶; ¹Pharmacy, Augusta University Medical Center, Augusta, Georgia, ²Augusta University at the Medical College of Georgia, Augusta, Georgia, ³Infectious Diseases, Baylor College of Medicine, Houston, Texas, ⁴Infectious Diseases, Augusta University Medical Center, Augusta, Georgia, ⁵Augusta University Medical Center, Augusta, Georgia, ⁶Population Health Sciences, Medical College of Georgia/Augusta University, Augusta, Georgia

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Background. The current gold standard for diagnosing invasive *Candida* infections is by blood culture, which has low specificity and take up to 2–5 days to grow. T2 magnetic resonance (T2MR) rapidly detects *Candida* species with high sensitivity/specificity. T2MR identifies five *Candida* species and reports it in three groups: *C. albicans*/*C. tropicalis*, *C. parapsilosis*, and *C. glabrata*/*C. krusei*.

Methods. This was a retrospective quasi-experimental study at the Augusta University Medical Center. Patients with a positive sterile site culture for *Candida* species and/or T2MR result were reviewed between April 2014 and March 2016 (pre-T2MR group) and April 2016–May 2017 (T2MR group).

Results. The pre-T2MR group consisted of 84 patients who had a *Candida* species isolated from a sterile site culture. The T2MR group consisted of 396 unique patients for whom there were a total of 549 T2MR tests ordered. Of these, 34 were positive, 466 were negative result, and 49 were invalid result (due to malfunctioning of T2MR). Of the 35 tests that were T2MR negative but sterile site culture positive, 27 (77%) of the cultures isolated a *Candida* sp. that should be detected by the T2MR but did not. The most common site of isolation for these cultures was intraabdominal (41%), followed by blood (33%). For 23% of these results, sterile site cultures grew a *Candida* that the T2MR does not detect.

Table 1: Performance of T2MR Results in Comparison to Sterile Site Cultures

	T2 + (n = 549)	T2 - (n = 466)
Sterile site culture +	16	35
Sterile site culture -	18	431

Table 2: Comparison Between Invasive Candidiasis as Detected by Standard Blood Cultures (Pre-T2MR) and T2MR

	Pre-T2MR	T2MR	P-value
Time to identification of <i>Candida</i> ±SD (hours)	± 210.1	± 14.4	0.00
All-cause 30-day mortality, n (%)	19 (23%)	7 (23%)	0.56

Conclusion. Unfortunately, *Candida* that grew in sterile site cultures was not always detected by the T2MR, particularly for intraabdominal Candidiasis. T2MR is thought to have high sensitivity and specificity for detecting Candidemia, but in our limited experience, it was found that up to one-third of Candidemias (as diagnosed by blood cultures) were missed by the T2MR. The most common *Candida* isolate in the T2MR group was *C. parapsilosis*, which is not typically thought of as a leading cause of invasive candidiasis.

Disclosures. All authors: No reported disclosures.

2038. Invasive Mucormycosis Management: Mucorales PCR Provides Important, Novel Diagnostic Information

Kyle Wilgers, BS¹; Joel Waddell, DO²; Aaron Tyler, BS¹; Michelle Altrich, PhD¹; Allyson Hays, MD³; Steve Kleiboeker, PhD¹; Dwight Yin, MD, MPH⁴ and Mark Wissel, PhD¹; ¹Viracor Eurofins Clinical Diagnostics, Lees Summit, Missouri, ²Children's Mercy Hospitals and Clinics, Kansas City, Missouri, ³Hematology/Oncology, Children's Mercy Hospital - Kansas City, Kansas City, Missouri, ⁴Pediatrics, University of Missouri-Kansas City School of Medicine, Kansas City, Missouri

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Background. In immunocompromised patients, high mortality and morbidity of invasive mucormycosis (IM) remain significant healthcare issues due in part to confusion of IM with invasive aspergillosis (IA) and failure to initiate appropriate therapy. A validated *Mucorales* (MUC) PCR detects the causative agents of IM with good sensitivity and specificity, as reported previously (M-227, ICAAC 2013). Published studies have not definitively determined the frequency of patients for whom pulmonary IA is suspected but IM is present. We aimed to (1) estimate the frequency of MUC PCR positivity in bronchoalveolar lavage (BAL) samples submitted for *Aspergillus* (ASP) PCR panel testing.

Methods. We identified 1,067 clinical BAL specimens originally submitted to a reference laboratory for ASP PCR panel testing. Eluates from DNA extraction were tested by MUC PCR, which detects known pathogens from seven *Mucorales* genera (*Apophysomyces*, *Cunninghamella*, *Lichtheimia* [previously *Absidia*], *Mucor*, *Rhizomucor*, *Rhizopus* and *Saksenaia*).

Results. The proportions of MUC PCR and ASP PCR positive BAL specimens were 1.5% (16) and 6.9% (74), respectively. 87.5% (14/16) of the MUC positive (POS) were ASP negative (NEG). One patient had two MUC PCR POS BAL samples within the testing period. The MUC quantification averaged 20,000 copies per mL BAL (range 24–266,000), which is >1,000-fold above the assay the 20 copies/mL limit of detection (LOD). Two of the ASP POS's were MUC POS (~400 and 20-fold above LOD). For patients with MUC POS BALs, physicians requested on average 6.3 pneumonia-related tests (e.g., ASP PCR, Galactomannan, Legionella PCR, etc.) within 2 weeks of the tested BAL. In total 94.0% (85/91) of these orders yielded NEG results. The MUC PCR was physician-ordered in only one (6.25%) of the MUC POS BALs.

Conclusion. In BAL samples submitted for IA testing, 16 cases (1.5%) had POS MUC PCR. The observed 5:1 (ASP:MUC) ratio approximates published literature on invasive mould incidence. MUC POS concurrent with NEG results for other pathogens suggest potential missed opportunities for MUC early diagnosis and treatment in cases of suspected invasive mould.

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2039. New York State 2016–2018: Progression from *Candida auris* Colonization to Bloodstream Infection

Karen Southwick, MD, MSc¹; Eleanor H. Adams, MD, MPH¹; Jane Greenko, RN, MPH, CIC²; Belinda Ostrowsky, MD, MPH³; Rafael Fernandez, MPH⁴; Rutvik Patel, MSW¹; Monica Quinn, RN, MS, CIC⁵; Snigdha Vallabhaneni, MD, MPH⁶; Ronald Jean Denis, BS⁷; Richard Erazo, BS⁸; Sudha Chaturvedi, PhD⁹; Valerie B. Haley, PhD⁵; Lynn Leach, MS²; Yan Chun Zhu, MS²; Rosalie Giardina, BS²; Emily C. Lutterloh, MD, MPH² and Debra S. Blog, MD, MPH¹; ¹Healthcare Epidemiology and Infection Control, New York State Department of Health, New Rochelle, New York, ²Healthcare Epidemiology and Infection Control, New York State Department of Health, Central Islip, New York, ³Dhqp, Centers for Disease Control and Prevention, New York, New York, ⁴Healthcare Epidemiology and Infection Control, New York State Department of Health, New York, New York, ⁵Bureau of Healthcare-Associated Infections, New York State Department of Health, Albany, New York, ⁶Mycotic Diseases Branch, Centers for Disease Control and Prevention, Atlanta, Georgia, ⁷Wadsworth Center, New York State Department of Health, Albany, New York, ⁸New York State Department of Health, Albany, New York, ⁹Division of Epidemiology, New York State Department of Health, Albany, New York

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Background. New York State (NYS) is experiencing a continuing outbreak of *Candida auris*, first identified in 2016. Patients who are colonized asymptotically with *C. auris* can progress to bloodstream infection (BSI).

Methods. Colonized patients with positive nares or axilla/groin *C. auris* cultures were followed prospectively. Laboratories, hospitals and skilled nursing facilities reported *C. auris* clinical infections to the NYS Department of Health. Patient demographics, clinical history, hospital admission, procedures, and outcomes data were obtained using a standardized case report form. Patient-days were determined from date of first positive colonization to date of first positive clinical isolate, death, or March 30, 2018, whichever was first.

Results. Between September 28, 2016 and March 30, 2018, 187 *C. auris* colonized patients were identified. Of these, seven progressed to BSI during at least 24,781 patient days of follow-up (median: 98 patient-days, range 0–548 days.) The median time from date of first colonization to date of BSI was 86 days (range 3–310 days). The median patient age at time of colonization was 71 years (range 57–89 years). Between colonization and BSI, patients had a median of five admissions in healthcare facilities (range 1–12). All patients had central neurologic disease, gastrostomy tubes, chronic wounds, and vascular lines at time of BSI. All patients had a positive culture for one or more other multi-drug resistant organisms within 90 days of a positive *C. auris* culture, and all received antibiotics in the 30 days before BSI. Six (86%) patients received mechanical ventilation and had tracheostomies. Five (71%) patients had diabetes. Four (57%) had vascular lines replaced in the 30 days before BSI onset. Two (29%) cases had gastrostomy tube replacement between colonization and BSI. One patient died a week after *C. auris* BSI; a second died 4 months later.

Conclusion. In NYS, 4% of *C. auris* colonized patients developed BSI, a rate of 0.3 BSI per 1,000 patient-days. BSI patients have portals of entry such as indwelling medical devices and wounds. Neurologic disease and diabetes may be risk factors for