Background. β-D-Glucan assay (BDG) has been recently introduced in India and is recommended for the early diagnosis of invasive candidiasis (IC), but there are a number of factors (eg β-lactam antibiotics, immunoglobulin and albumin infusions, bacteremia and surgical mesh) which may falsely elevate BDG levels.

Methods. This was a retrospective, observational study done in the 23 bedded multi disciplinary ICU of a tertiary care hospital in South India. Case records of adult (> 18 years) non-neutropenic patients with severe sepsis or shock with ≥ 1 risk factor for IC were analyzed. As a standard practice, BDG assay was sent and effective antifungals were started on the day of suspicion of IC. All neutropenic, immunocompromised patients, those already on antifungal and those who were diagnosed with other invasive fungal infections were excluded from the study. FDA approved Fungitell assay was used to measure serum BDG levels (pg/mL).

Results. Patients were divided into 3 groups, Group A (n = 16) comprised of patients in whom diagnosis of IC was confirmed (blood culture or another sterile site grew candida). Group B (n = 30) comprised of patients in whom alternative diagnosis of severe sepsis or septic shock was found or they did not improve after administration of antifungals. Group C (n = 31) comprised of those patients in whom neither diagnosis of IC was confirmed nor an alternative explanation was found but they improved clinically on giving antifungal therapy. Mean BDG levels was significantly higher in Group A as compared with Group B and Group C (448.75 ± 88.30 vs 144.46 ± 82.49 vs 292.90 ± 137.0 pg/mL; P < 0.001). The mean value of the BDG was higher than the accepted cutoff of 80 pg/mL in all three groups (Figure 1). The use of agents which cause false elevation of BDG was significantly higher in Group B as compared with Group A (P = 0.02).

Conclusion. A BDG assay cutoff of 80 pg/mL leads to a higher number of false positive results in ICU patients, where false positive factors are unavoidable. The results of this study suggest that a higher cutoff of at least 144 pg/mL will be more specific for IC, although this may need further validation with larger trials.

Figure 1: Mean BDG values in various groups

Disclosures. All authors: No reported disclosures.

2079. PCR-based Diagnosis of Mucormycosis Targeting Mucorales-specific Genes
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Background. Mucormycosis is a life-threatening infection caused by fungi in the order Mucorales. Rhizopus spp are the most common causes of Mucormycosis in ICU patients, where false positive factors are unavoidable. The rapid progression of the disease and the current lack of early and reliable diagnostic assay contribute to the high mortality rates of 50%-100%.

Methods. We propose a PCR-based approach targeting the sorne coaing protein homolog encoding ColtH genes. ColtH genes are universally and uniquely present among Mucorales and they encode cell surface proteins that are required for mucormycosis pathogenesis. Bioinformatic analyses were used to identify short consensus sequences present in ColtH genes from different Mucorales to be used as PCR primers. Candidates were tested for the amplification of PCR-products from gDNA of different Mucorales. The specificity of selected primers was tested using biological samples spiked with different spores concentrations. Finally, the best candidate primers were used to detect the presence of pathogen DNA from biological samples taken from mice infected intra-currently with different Mucorales.

Results. Our best candidate primers could amplify the specific sequence from Rhizopus, R. oryzae, M. circinelloides, L. corymbifera and Cunninghamella bertholletiae. These primers had a sensitivity of detecting 10 spores into a spiked sample. The specificity for the unique ColtH target enabled us to differentiate between Mucorales and closely related filamentous fungi, e.g., Aspergillus fumigatus. Genomic DNA extraction was successful from all considered biological samples; remarkably, infection was successfully detected from biological samples taken from mice infected with different Mucorales as early as 24 hours post infection.

Conclusion. We have successfully developed a simple PCR-based approach which is fast, reliable and sensitive enough to detect Mucorales gDNA in murine biological samples as early as 1 day post infection. Our target will allow a better differentiation between Mucorales species and other closely related filamentous fungi.

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2080. Invasive Candidiasis in Pediatric Patients at King Fahad Medical City in Riyadh, Saudi Arabia: A 5-year Retrospective Study
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Background. Invasive candidiasis in children is associated with high morbidity and mortality. We aim to identify predisposing factors, species distribution, antifungal susceptibility, and outcomes among patients with candidiasis.

Methods. A data collection form composed of seven sections including 51 questions was designed to gather demographic and clinical information. We collected data from all 129 patients with invasive candidiasis from January 2010 to January 2015.

Results. The 129 patients had the following risk factors: 30 (23.26%) were premature, 34 (26.38%) had low birth weight, 59 (45.74%) had a central venous catheter, 20 (15.51%) received immunosuppression, and 56 (43.41%) received ventilator support. A multivariate analysis revealed a more than two-fold mortality rate in patients who had vegetation in the heart (OR 2.9), and patients who had Candida isolated from their blood were more than twice as likely to die as patients with Candida isolated from other sites (OR 2.2). A total of 48.33% of patients on ventilator support died, and 26.09% of patients who were not on ventilator support died (P = 0.009); 43.75% of patients in the intensive care unit (ICU) died vs. only 24.49% of patients who were not in the ICU (P = 0.03). C. parapsilosis exhibited the highest mortality rate among all Candida species (56.2%).

Conclusion. The study revealed that C. albicans was the most common isolate among all Candida species. Mechanical ventilation and an ICU stay were significant risk factors for death in children with invasive candidiasis.

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Background. Candida species are the fourth leading cause of nosocomial bloodstream infections in the United States, however incidence is low and most patients who receive empiric treatment do not actually have candidemia. Unfortunately, detection, identification and susceptibility testing using standard instrumented blood culture systems and routine microbiological techniques takes 4–10 days. Astute clinicians may empirically treat patients with antifungal therapy (AFT) prior to having any results, often leading to unnecessary coverage for candida infection for up to 10 days. The T2 Candida panel is an FDA-approved assay that rapidly detects the presence of 5 Candida species directly from whole blood in 3–5 hours. We determined whether AFT decisions were altered based on negative (neg) results of a T2 assay.

Methods. We performed a retrospective chart review of the first 50 patients at our institution from March 1, 2016 to March 1, 2017 with a neg T2 Candida assay result (data collection is ongoing). If a patient had multiple valid T2 assays, only the first result was used for analysis. The patients' medical records were reviewed for use and duration of empiric AFT, results of blood cultures, treatment modification, underlying illness, risk factors for candida infection, length of stay, and 14-day mortality from the time of the T2 assay.

Results. Twenty-four patients were never started on AFT. Of the 26 who received AFT, it was stopped in 15 (57%) following T2 results (median time to stop empiric AFT = 2 days (1–16)). The reasons for continuing AFT in the cases of neg T2 assays included hematologic malignancy patients who were on long-term prophylaxis with antifungal agents (6 patients), empiric use in a case of severe sepsis (1 patient), and positive culture results despite neg T2 assay in 4 patients: 1 patient with C. lusitaniae in blood culture, 1 patient with C. parapsilosis from positive culture of medical device, 1 patient with neg T2 but positive blood cultures from 2 days prior for C. albicans (was on anti-fungal therapy at time of test), 1 patient with C. guilliermondii in blood culture.

Conclusion. We conclude that a neg T2 Candida assay affects empirical use of AFT in certain patient populations and may be useful in controlling the overuse of antifungal agents.

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2082. Rapid Detection of Pediatric Bacteriuria Using Narrow Angle Forward Laser Scattering Technology (NAFLST) with Bacterioscan

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Background. Pediatric urinary tract infections (UTI) are common, but culture-based diagnosis can take up to 48 hours. This time delay means patients are exposed to potentially unnecessary antibiotics. The sensitivity of screening urinalysis can vary with a rapid detection of UTI by another method would be beneficial. Narrow Angle Forward Laser Scattering Technology (NAFLST) with Bacterioscan can rapidly detect bacteriuria by shining a laser continuously through a liquid sample containing replicating bacteria, and graphing the degree of light refraction over time. Higher degrees of light refraction represent higher initial bacterial load and continued bacterial growth. After 3 hours, the optical scatter classifies a sample as either Likely Positive or Likely Negative. We compared Bacterioscan results to culture data in pediatric patients to assess the ability to diagnose UTI and avoid unnecessary urine culture.

Methods. This protocol was approved by the UNC Biomedical Institutional Review Board. Over one month, 169 pediatric (<18 yo) urine cultures were collected in Bacterioscan labeled assay tubes. Bacterioscan: Equipment necessary to perform this study

Results. Of the 169 urines, 96 were positive, but only 27 were positive for uropathogens. Bacterioscan was 100% sensitive and 58.4% specific in predicting clinically relevant/pathogenic bacterial growth in culture (PPV 31.3%, NPV 100%), and 74.1% sensitive and 75.3% specific in predicting any bacterial growth (PPV 79.0%, NPV 66.2%). If a “Likely Positive” Bacterioscan result had been used in our study population to screen urine samples for culture, then 58% (83/142) of negative urine cultures would have been eliminated with no UTIs missed.

Conclusion. By rapidly identifying urine cultures likely to be positive, NAFLST with Bacterioscan can safely obviate the plating of every urine sample and reduce empiric antibiotic use while waiting for culture results. Larger studies are required to confirm these results.

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2083. Direct Detection and Quantification of Bacterial Cell-free DNA in Patients with Bloodstream Infection (BSI) Using the Karius Plasma Next Generation Sequencing (NGS) Test

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Background. Blood cultures can have low sensitivity if a patient is pretreated with antibiotics. A molecular diagnostic for bloodstream infection (BSI) that can also quantify pathogen DNA could be a useful tool in detecting and managing culture-negative infections.

Methods. We prospectively enrolled 75 patients (50 with culture confirmed BSI due to Staphylococcus aureus [(n = 21)] or Gram-negative bacilli [(n = 29) at baseline, and 25 with negative blood cultures) to evaluate the Karius plasma next generation sequencing (NGS) test to detect BSI. Blood samples from patients with confirmed BSI were collected for the study within one day of positive blood culture and then every 2–3 days. Cell-free DNA (cfDNA) was extracted from plasma and underwent NGS in the Karius CLIA/CAP laboratory (Redwood City, CA). After removal of human sequences, remaining reads were aligned against a curated pathogen database. Organisms present at a significance-level above a predefined threshold were reported. Quantity of cfDNA for each reported pathogen was expressed as molecules per microliter (MPM).

Results. When compared with baseline blood culture, the plasma NGS test had a positive agreement of 80% (40/50) and negative agreement of 84% (21/25). Overall, serially collected samples were positive by plasma NGS testing significantly longer than baseline blood culture (mean 6.3 days vs. 2.4 days, respectively). Patients with BSI were positive longer by NGS testing than blood culture for both S. aureus (mean 6.9 days vs. 4.0 days, respectively; P < 0.005) and gram-negative bacilli (mean 5.4 days vs. 1.3 days, respectively; P < 0.001). Pathogen cfDNA in BSI patients, quantified as MPM, declined over time during treatment. S. aureus MPM declined more slowly than gram-negative MPM and was significantly higher than gram-negative MPM at day 6 (P < 0.001).

Conclusion. The Karius plasma NGS test can directly detect pathogens in patients with BSI. Pathogen cfDNA signal in plasma remains positive longer than blood culture and combined with quantification of pathogen cfDNA could be a useful biomarker to aid in diagnosis and monitoring of infections, particularly in those with sterile blood cultures.

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2084. Performance of the Karius Plasma Next Generation Sequencing Test in Determining the Etiologic Diagnosis of Febrile Neutropenia: Results from a Pilot Study

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