| Table 3. Microbiologic Testing, Discharge Diagnoses, Outcomes | | | |
|---|---|---|---|
| Category | Post-Implementation Cases (n=1127) | Pre-Implementation Controls (n=1124) | P Value |
| **Overall Testing** | | | |
| Number of Singleplex PCR Tests per CSF Specimen | | | <0.0001 |
| 0 | 969 (90%) | 539 (50%) | |
| 1 | 97 (9%) | 289 (27%) | |
| >2 | 7 (1%) | 255 (24%) | |
| CSF Singleplex PCR Positive | 4 (0%) | 72 (6%) | |
| MEP Testing Performed | 805 (72%) | N/A | |
| MEP Positive | 102 (9%) | N/A | |
| Time to Positive CSF Test Result (hrs) | 4.8 (2.4, 4.8) | 9.6 (4.8, 16.8) | <0.0001 |
| **Bacterial Testing** | | | |
| Positive Gram Stain | 16 (1%) | 11 (1%) | 0.4243 |
| Positive CSF culture | 20 (2%) | 17 (2%) | 0.7109 |
| Positive MEP for bacteria | 19/805 (2%) | N/A | |
| **Viral Testing (positive/tested)** | | | |
| Enterovirus detected in CSF by singleplex PCR | 1/25 (4%) | 63/348 (18%) | |
| Enterovirus detected in CSF by MEP | 54/805 (7%) | N/A | |
| Enterovirus neurologic cases (any site) | 88 (8%) | 68 (6%) | 0.1189 |
| HSV detected in CSF by singleplex PCR | 3/80 (4%) | 3/442 (1%) | |
| HSV detected in CSF by MEP | 3/805 (0%) | N/A | |
| HSV neurologic cases (any site) | 15 (1%) | 13 (1%) | 0.8547 |
| Parechovirus detected in CSF by singleplex PCR | 0/4 (0%) | 5/72 (0%) | |
| Parechovirus detected in CSF by MEP | 11/805 (1%) | N/A | |
| Parechovirus neurologic cases (any site) | 12 (1%) | 5 (0%) | 0.1456 |
| HHV-6 detected in CSF by singleplex PCR | 0/3 (0%) | 1/8 (13%) | |
| HHV-6 detected in CSF by MEP | 13/805 (2%) | N/A | |
| VZV detected in CSF by singleplex PCR | 0/5 (0%) | 0/41 (0%) | |
| VZV detected in CSF by MEP | 2/805 (0%) | N/A | |
| CMV detected in CSF by singleplex PCR | 0/2 (0%) | 0/16 (0%) | |
| CMV detected in CSF by MEP | 0/805 (0%) | N/A | |
| **Fungal Testing (positives/tested)** | | | |
| Cryptococcus Ag detected in CSF | 0/2 (0%) | 0/2 (0%) | |
| Cryptococcus detected in CSF by MEP | 0/805 (0%) | N/A | |
| **Discharge Diagnosis** | | | |
| Neurologic Discharge Diagnosis | 499 (44%) | 430 (38%) | 0.0017 |
| Infectious Neurologic Disease Discharge Diagnosis | 167 (15%) | 115 (10%) | 0.0298 |
| Proportion due to Viral Cause | 124 (74%) | 86 (75%) | |
| Proportion due to Bacterial Cause | 35 (21%) | 27 (23%) | |
| Non-CNS Bacterial Infection | 178 (16%) | 175 (16%) | 0.9149 |
| Respiratory Viral Infection | 284 (25%) | 253 (23%) | 0.1347 |
| **Outcomes** | | | |
| Hospitalized | 1033 (92%) | 1024 (91%) | 0.6929 |
| Length of Inpatient Stay (median days) | 4 (3,9) | 4 (3,9) | 0.9635 |
| Death During Hospitalization | 13 (1%) | 21 (2%) | 0.2264 |
| Death Due to CNS Infection | 7 (1%) | 6 (1%) | 1 |
| Started on Antibacterials | 768 (68%) | 799 (71%) | 0.1685 |
| Number of IV Antibacterials Received | 2 (2,3) | 2 (2,3) | 0.5326 |
| IV Antimicrobial Duration (hrs) | 24 (0, 50.4) | 36 (0, 60) | 0.0037 |
| IV Antimicrobial Hours (hrs) | 38 (0, 98) | 60 (0, 118) | 0.0007 |
| Received IV Acyclovir | 284 (25%) | 301 (27%) | 0.42 |
| Duration of IV Acyclovir Amongst Those Started | 17 (8, 40) | 24 (8, 40) | 0.206 |
| Time to Effective Antimicrobials for Cases with Treatable Etiology (hrs) | 0.75 (0.43, 1.02) | 0.68 (0.48, 0.93) | 0.471 |
| Time to Effective Antimicrobials for Cases with Treatable Organism in CSF | 0.65 (0, 1.58) | 0.43 (0, 1.7) | 0.5817 |
| Time to Optimal Antimicrobial Regimen Initiation (hrs) | 18 (13, 21) | 28 (25, 32) | <0.0001 |

***Conclusion.*** Implementation of MEP with a rapid CNS diagnostic stewardship program improved antimicrobial use with faster results shortening empiric therapy. Routine MEP testing in high-yield cases rapidly detects common viral causes and rules out bacterial targets to enable antimicrobial optimization

***Disclosures.*** **Samuel R. Dominguez, MD, PhD**, **BioFire Diagnostics** (Consultant, Research Grant or Support)**DiaSorin Molecular** (Consultant)**Pfizer** (Grant/Research Support) **Samuel R. Dominguez, MD, PhD**, BioFire (Individual(s) Involved: Self): Consultant, Research Grant or Support; DiaSorin Molecular (Individual(s) Involved: Self): Consultant; Pfizer (Individual(s) Involved: Self): Grant/Research Support

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### 1020. BioFiring on all Cylinders: Validation of BioFire FilmArray Pneumonia Panel and Determination of Optimal Utility

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**Session:** P-58. New Approaches to Diagnostics

***Background.*** Respiratory cultures can take up to five days to grow, time that can be crucial in treating patients with serious infections. Newer rapid microbiological identification tests are designed to shorten this delay between specimen collection and test result. The BioFire® FilmArray® Pneumonia Panel is a multiplex PCR panel that can identify 8 viral, 18 bacterial, and 7 resistance gene targets in one hour. In this study, we aimed to calculate the predictive value of this test and its utility in the clinical setting.

***Methods.*** This retrospective study compared BioFire® FilmArray® Pneumonia Panel results to respiratory cultures run at our center from 3/1/2020 to 2/28/2021. For every BioFire sample, a respiratory culture was run concurrently. We examined correlations between these two tests using data collected from the microbiology laboratory and the electronic medical record.

***Results.*** 190 BioFire samples from 124 patients were submitted for processing. Of these, 148 samples had a concomitant respiratory culture result that grew organisms that BioFire could detect. BioFire and culture results were compared, and sensitivity and specificity were calculated on a per-sample basis. Sensitivity was calculated at 91%, specificity at 67%, positive predictive value at 46%, and negative predictive value at 96%.

BioFire detected 30 resistance genes total, including *mec*A/C and MREJ, CTX-M, and KPC. The sensitivity and negative predictive value for BioFire resistance gene detection was 100%. However, specificity was 94-98%, and the positive predictive value ranged between 25-41% when compared to culture.

***Conclusion.*** Despite the promise of faster results and better screening, our data suggests that further study is needed to determine the utility of the BioFire pneumonia panel. The strength of the panel appears to lie in its negative predictive value and sensitivity, but as a positive predictive tool, it is suboptimal.

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

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### 1021. Utility of Cell-Free DNA Sequencing in Diagnosing *Murine typhus* in Children

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**Session:** P-58. New Approaches to Diagnostics

***Background.*** Murine typhus is a zoonotic infection caused by Rickettsia typhi and transmitted through infected fleas. Geographic distribution within the United States is limited primarily to South Texas and Southern California. Infection is typically associated with a triad of fever, headache, and rash, although is only present in one-third of cases. Immunofluorescence assay (IFA) is currently the gold standard for diagnosis, but it has its limitations as it is dependent on the time to seroconversion and has low specificity due to cross-reactivity among other rickettsial species. Cell-free DNA (cfDNA) sequencing for broad-range pathogen detection may offer higher sensitivity at the early stages of the disease.

***Methods.*** We performed a retrospective electronic medical record search of children with cfDNA sequencing detection of Murine typhus at Driscoll Children's Hospital, Corpus Christi, Texas, between June 2020 and May 2021.

***Results.*** We found 4 children (range 9-15 year-old) positive for R. typhi by cfDNA sequencing. All patients presented with fever of unknown origin and rash. Also, 2 patients were diagnosed with pneumonia. One patient exhibited severe illness with acute kidney injury, elevation of transaminases and encephalitis that warranted admission to the pediatric intensive care unit. All patients defervesced and improved within 48 hours of doxycycline initiation; average length of stay 6 days (range 3-12 days). In one patient, M. typhus was detected by Karius® test only, in the other three was concordant with serology.

***Conclusion.*** We highlight next-generation cfDNA sequencing as a useful tool in identifying the etiologic agent of patients with fever of known origin, where murine typhus is one of the possible etiologies. Preventing extensive laboratory workup and subsequent delay of assessment and management. The rapid turnaround time of cfDNA test allows for de-escalation of therapy and initiation of appropriate treatment.

***Disclosures.*** **Jaime Fergie, MD**, **AstraZeneca** (Scientific Research Study Investigator)**Explify** (Speaker's Bureau)**Karius** (Speaker's Bureau)**Pfizer, Merck, AstraZeneca, and Sanofi** (Speaker's Bureau)**Pfizer, Merck, Sanofi, and Moderna** (Consultant, Advisor or Review Panel member)

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### 1022. Evaluating the Impact of GenMark Dx ePlex® Blood Culture Identification (BCID) on Gram-negative Bloodstream Infections

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**Session:** P-58. New Approaches to Diagnostics

***Background.*** The GenMark Dx ePlex BCID Gram-Negative (GN) panel utilizes electrowetting technology to detect the most common causes of GN bacteremia (21 targets) and 6 antimicrobial resistance (AMR) genes from positive blood culture (BC) bottles. Rapid detection of extended spectrum β-lactamases (ESBL: CTX-M & carbapenemases: KPC, NDM, IMP, VIM, OXA 23/48), and highly resistant bacteria such as *S. maltophilia* should enable early optimization of antimicrobial therapy.

***Methods.*** In this prospective study, aliquots of positive BC bottles with GN bacteria detected on Gram stain (GS) (n=108) received standard of care (SOC) culture and antimicrobial susceptibility testing (AST). Additionally, samples were evaluated with the BCID-GN panel but only SOC results were reported in the EMR and available to inform clinical decisions. Chart reviews were performed to evaluate the impact of the BCID-GN panel on the time to organism identification, AST results, and optimization of antimicrobial therapy.

***Results.*** A total of 108 patients are included in the analysis (Table 1). *Escherichia coli* was the most common bacteria identified followed by *Klebsiella pneumoniae, Pseudomonas aeruginosa,* and *Enterobacter* species (Table 2). There were 11 (10.2%) polymicrobial bacteremias. Repeat BCs were obtained in 68 (63%) patients of which 13 (19%) were persistently positive. Eight (7%) patients had evidence of additional gram-positive (GP) pathogens. Organism identification occurred 26.7 hours faster than culture. In conjunction with GS, negative pan-GP marker data could have helped providers make the decision to remove GP antibiotic coverage in 63 (58%) patients. Narrowing from empiric meropenem could have occurred in 5 patients. Of 10 individuals infected with resistant isolates (1 *S. maltophilia*, 1 OXA 23/48, and 8 CTX-M) empiric therapy was ineffective in 4 (40%) cases. Optimization of antimicrobial therapy for 9 (8.3%) patients could have occurred an average of 52.4 hours earlier than standard methods.

Table 1. Patient demographics and co-morbidities.

| Variable | Total (N=108) |
|---|---|
| Average Age (years) | 58.6 |
| Male – No. (%) | 64 (59.2) |
| Race/Ethnicity – No. (%) | |
| • White | 62 (57.4) |
| • Black | 44 (40.7) |
| • Asian | 2 (1.8) |
| Immunosuppression – No. (%) | |
| • Solid malignancy | 17 (15.7) |
| • Hematologic malignancy | 6 (5.6) |
| • SOT | 11 (10.2) |
| • HSCT | 3 (2.8) |
| • Other | 17 (15.7) |
| Diabetes – No. (%) | 34 (31.5) |
| Cardiovascular disease – No. (%) | 19 (17.6) |
| Chronic lung disease – No. (%) | 21 (19.4) |
| CKD – No. (%) | 19 (17.6) |
| ESRD – No. (%) | 8 (7.4) |
| Cirrhosis – No. (%) | 13 (12.0) |
| IVDU – No. (%) | 3 (2.8) |
| Mechanical ventilation – No. (%) | 19 (17.6) |
| Trauma at time of admission – No. (%) | 10 (9.3) |
| Burn at time of admission – No. (%) | 1 (0.9) |
| Pitt Bacteremia Score (Mean) | 2.8 |

Table 2. Gram-negative bacteria frequency.

| Gram-negative Bacteria | Total (%) |
|---|---|
| *E.coli* | 30 (27.8) |
| *Klebsiella pneumoniae* | 24 (22.2) |
| *Pseudomonas aeruginosa* | 11 (10.2) |
| Polymicrobial | 11 (10.2) |
| *Enterobacter* species | 9 (8.3) |
| Other | 7 (6.5) |
| Not detected | 6 (5.5) |
| *Klebsiella oxytoca* | 4 (3.7) |
| *Serratia marcescens* | 3 (2.8) |
| *Acinetobacter baumannii* | 3 (2.8) |

**Conclusion.** The BCID-GN panel enabled earlier time to optimal treatment of highly resistant bacteria as well as multiple opportunities for narrowing gram negative spectrum and a higher degree of certainty in cessation of broad-spectrum gram-positive antibiotics

**1023. Host Gene Expression Biomarkers to Distinguish Between Causes of Acute Respiratory Symptoms in Lung Transplant Recipients**

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**Session:** P-58. New Approaches to Diagnostics

*Background.* Long-term immunosuppression after lung transplantation increases susceptibility to a variety of respiratory infections that are often difficult to diagnose. Host gene expression patterns in circulating leukocytes may provide additional diagnostic information in these settings.

*Methods.* 107 lung transplant recipients (79% with cystic fibrosis) were enrolled at Duke University Medical Center over a 2-year period – 59% with acute respiratory symptoms, the remainder as healthy controls. Whole blood was collected by PAXGene for RNA sequencing. Prior to undergoing biomarker analysis, each case was adjudicated to the appropriate clinical phenotype: bacterial infection, viral infection, allograft rejection, and healthy. Logistic regression models were applied to gene expression data to identify classifiers capable of identifying each etiology.

*Results.* In lung transplant recipients, 117 genes were upregulated at least 2-fold in the presence of viral infection compared to healthy transplant controls. These genes clustered into expected antiviral pathways, including type I interferon signaling, interferon gamma mediated signaling, and defense response to virus, although the magnitude of gene expression was significantly less than that seen in non-transplant cohorts.

Similar results were seen during bacterial infection (defense response to bacterium, antibacterial humoral response) and rejection (upregulation in defensins DEFA3 and DEFA4). Interestingly, despite the presence of immunosuppression, a previously published gene expression signature of respiratory infection (derived from non-immunosuppressed subjects) was able to differentiate between bacterial and viral infection with 100% accuracy.

*Conclusion.* Even in the presence of systemic immunosuppression and regardless of presence/absence of cystic fibrosis, core canonical components of the host response to infection and rejection are seen. Gene expression signatures based on these conserved components offer the potential for diagnostic capability in the setting of nonspecific respiratory illness in these vulnerable hosts.

**1024. Using DOOR-MAT to Theoretically Compare Three Rapid Diagnostic Tests for Gram-Negative Bloodstream Infections in Immunocompromised Patients**

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**Session:** P-58. New Approaches to Diagnostics

*Background.* Molecular rapid diagnostic tests (RDTs) for bloodstream infections (BSI) utilize a variety of technologies and differ substantially in organisms and resistance mechanisms detected. RDT platforms decrease time to optimal antibiotics; however, data on RDTs in special populations, such as immunocompromised are extremely limited. This study aimed to compare theoretical changes in antibiotics based on differences in panel identification of organisms and resistance targets among three commercially available RDT panels.

*Methods.* Retrospective cohort of immunocompromised patients treated for gram-negative BSI at University of Maryland Medical Center from January 2018 to September 2020. Immunocompromised was defined as active hematologic or solid tumor malignancy at time of BSI diagnosis, history of hematopoietic stem cell transplantation (HSCT) or solid organ transplantation (SOT), or absolute neutrophil count (ANC) < 1000 cells/mm$^3$ at any time 30 days prior to BSI diagnosis. Verigene BC-GN was performed as standard of care. GenMark ePlex BCID and BioFire FilmArray BCID 2 results were assigned based on respective identifiable organism panels.

An infectious diseases clinician blinded to final antimicrobial susceptibility testing (AST) results used RDT results to assign antibiotic treatments for each platform. Decisions were referenced against *a priori* DOOR-MAT matrices. A partial credit scoring system (0 to 100) was applied to each decision based on final AST results. The mean and standard deviation (SD) were compared across panels using One-Way Repeated Measures ANOVA with modified Bonferroni for multiple comparisons.

*Results.* A total of 146 patients met inclusion. Baseline characteristics are summarized in Table 1. The mean (SD) DOOR-MAT scores for the three RDT panels were: 86.1 (24.4) Verigene BC-GN vs. 88.5 (22.2) GenMark BCID vs. 87.2 (24.4) BioFire BCID 2. There was no statistically significant difference between the panels for DOOR-MAT score (*P*=0.6).

Table 1. Baseline Patient Characteristics and Organism Identification

| | |
|---|---|
| **Age; mean (SD), years** | 57 (15) |
| **Male; n (%)** | 92 (63) |
| **Level of care; n (%)** | |
| Floor | 87 (59.6) |
| IMC | 39 (26.7) |
| ICU | 20 (13.7) |
| **Type of immunosuppression; n (%)** | |
| Hematologic malignancy only | 45 (30.8) |
| SOT only | 45 (30.8) |
| Any history of HSCT | 44 (30.1) |
| Hematologic malignancy and history of HSCT | 43 (29.5) |
| Solid tumor malignancy only | 12 (8.2) |
| Solid tumor malignancy and history of HSCT | 1 (0.7) |
| **Most common organisms isolated; n (%)** | |
| *Escherichia coli* | 48 (32.9) |
| *Pseudomonas aeruginosa* | 34 (23.3) |
| *Klebsiella pneumoniae* | 32 (21.9) |