Background. Sepsis is an orthopedic emergency requiring immediate surgical intervention. Joint aspirations detect inflammatory cells within hours but often cannot distinguish between infections (e.g., bacterial) or other causes (e.g., gout). Cultures take about an hour. The BCID2 Panel builds upon the existing BCID Panel with several additions: 11 bacterial resistance genes plus resistance for antibiotics (e.g., penicillin, cephalosporin, carbapenem, and ESBL). Here, we summarize studies conducted to establish clinical performance using an Investigational Use Only version of the BCID2 Panel.

Results. Of 270 patients tested, 111/270 (41.1%) were PP bacteria negative/culture no growth or normal flora (Group 1), 59/270 (21.9%) were PP positive/culture positive (Group 2), and 100/270 (37.0%) were PP positive without growth (Group 3) for at least 1 concordant bacterial potential pathogen. Hospital length of stay (LOS), P = 0.0274, ANOVA; ICU LOS P = 0.0007 and BAL % Polys P < 0.0001 were significantly longer/higher in Group 3 than in Groups 1 and 2 (Table 1). Max daily temp on the day of culture in PP-positive groups 2 and 3 was significantly higher than the PP-negative group 1, P = 0.0260, ANOVA, (Table 1). Age, daily WBC, lowest paO2, max FiO2, % on antibiotics (>280% for all groups), and % with viruses in the PP were not significantly different across groups. While all PP pathogens were grouped by copy #/mL, ICU LOS was significantly longer for 107 copies/mL (P = 0.0088), as was BAL % polys (P = 0.0006). Max daily temp was almost significantly higher for PP-positive groups 10(5), 10(6), and 10(7) combined compared with the PP-negative group (Table 2, P = 0.0608).

Conclusion. Hospital LOS was significantly longer and BAL % Polys higher in the PP-positive group culture positive/PP positive group vs. negative groups. ICU LOS and BAL % Polys were significantly higher for the PP-positive groups vs. PP-negative regardless of culture results. PP results (copy #/mL) independently correlated with outcome and clinical measures.

Disclosures. All authors: no reported disclosures.

651. Multi-Center Evaluation of the BioFire FilmArray Blood Culture Identification 2 Panel for the Detection of Microorganisms and Resistance Markers in Positive Blood Cultures

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Background. The BioFire FilmArray Blood Culture Identification 2 (BCID2) Panel is a diagnostic test that provides results for 26 bacterial, 7 fungal pathogens and 10 antimicrobial resistance (AMR) genes from positive blood culture (PBC) specimens in about an hour. The BCID2 Panel builds upon the existing BCID Panel with several additional assays that include Candida auris and an expanded AMR gene menu that provides methicillin-resistant Staphylococcus aureus (MRSA) results plus detection for vancomycin-resistant Enterococcus and ESBL. Here, we summarize studies conducted to establish clinical performance using an Investigational Use Only version of the BCID2 Panel.

Methods. Three studies were performed. The first involves prospective collection and testing of an expected 1,000 residual PBCs at 7 US and 2 EU sites, which began in

648. Baloxavir Resistance: qPCR Detection of Antiviral Resistance Markers in Influenza A Virus

Background. Influenza (flu) infections affect a large subset of the population every year and have significant impacts on the health of patients, especially those with weak or compromised immune systems such as the elderly, children, cancer patients, and transplant recipients. Baloxavir marbidol was approved in October 2018 as a novel antiviral therapeuetic for treating flu. During clinical trials, mutations were identified at the I28 codon of the polymerase acidic (PA) protein that greatly increased the resistance of a flu strain to this novel drug. In this study, a qPCR was developed and validated to identify these resistance mutations, allowing for guided therapeutic approaches based on the resistance profile of the strain.

Methods. Flu A sequences (6,175) of the PA gene from the NCBI Influenza Virus Database collected over the last 5 years were compiled and aligned. Primers and probes were designed to target the I28 codon of the PA gene, and specific probes for each codon yielding a resistant amino acid mutation (I28T, -M, and -F) were designed. Locked nucleic acid (LNA) bases were used to increase the specificity of the probes. A combination of clinical flu specimens, laboratory strains, and synthetic constructs of each potential resistance mutation were used to validate the precision, sensitivity, and accuracy of the assay in nasopharyngeal swabs.

Results. The cycle threshold (Ct) values for each detector was determined to have a standard deviation of less than 3 for inter-assay and less than 2 for intra-assay replicates. Sensitivity was determined to be 800 copies/mL in nasopharyngeal swabs. Accuracy was found to be 92.3%. A single laboratory strain from the H1N1 2009 wild type strain was cross-reacting with both wild-type and resistant probes, but no circulating clinical H1N1 samples tested showed this response.

Conclusion. The precision, sensitivity, and accuracy of a qPCR for resistance mutations to baloxavir marbidol support this assay’s utility as an aid in the treatment of flu in at-risk patient groups. This assay allows for rapid detection (~24 hours) of resistance markers to aid clinicians in improving flu case outcomes.

Disclosures. All authors: no reported disclosures.

649. Prospective Validation of an 11-mRNA Host Immune Signature as a Novel Blood Test for Acute Septic Arthritis

Background. Septic arthritis is an orthopedic emergency requiring immediate surgical intervention. Joint aspirations detect inflammatory cells within hours but often cannot distinguish between infections (e.g., bacterial) or other causes (e.g., gout). Cultures take about an hour. The BCID2 Panel builds upon the existing BCID Panel with several additions: 11 bacterial resistance genes plus resistance for antibiotics (e.g., penicillin, cephalosporin, carbapenem, and ESBL). Here, we summarize studies conducted to establish clinical performance using an Investigational Use Only version of the BCID2 Panel.

Results. Of 270 patients tested, 111/270 (41.1%) were PP bacteria negative/culture no growth or normal flora (Group 1), 59/270 (21.9%) were PP positive/culture positive (Group 2), and 100/270 (37.0%) were PP positive without growth (Group 3) for at least 1 concordant bacterial potential pathogen. Hospital length of stay (LOS), P = 0.0274, ANOVA; ICU LOS P = 0.0007 and BAL % Polys P < 0.0001 were significantly longer/higher in Group 3 than in Groups 1 and 2 (Table 1). Max daily temp on the day of culture in PP-positive groups 2 and 3 was significantly higher than the PP-negative group 1, P = 0.0260, ANOVA, (Table 1). Age, daily WBC, lowest paO2, max FiO2, % on antibiotics (>280% for all groups), and % with viruses in the PP were not significantly different across groups. While all PP pathogens were grouped by copy #/mL, ICU LOS was significantly longer for 107 copies/mL (P = 0.0088), as was BAL % polys (P = 0.0006). Max daily temp was almost significantly higher for PP-positive groups 10(5), 10(6), and 10(7) combined compared with the PP-negative group (Table 2, P = 0.0608).

Conclusion. Hospital LOS was significantly longer and BAL % Polys higher in the PP-positive group culture positive/PP positive group vs. negative groups. ICU LOS and BAL % Polys were significantly higher for the PP-positive groups vs. PP-negative regardless of culture results. PP results (copy #/mL) independently correlated with outcome and clinical measures.

Disclosures. All authors: no reported disclosures.

650. Relationship of a Multiplex Molecular Pneumonia Panel (PP) Results with Hospital Outcomes and Clinical Variables

Background. The Pneumonia Panel (PP) (BioFire Diagnostics, Salt Lake City, UT) detects 15 potentially pathogenic bacteria semiquantitatively (copy #/mL), 8 viruses and 7 resistance genes from the lower respiratory tract in ~1 hour in the laboratory. Since identification and susceptibility test take ~2 days, this rapid result time is very attractive; however, the clinical significance of the PP copy #/mL as well as a predictable group of PP positive but culture negative patients is unknown. We retrospectively studied the relationship of 270 PP results to culture results, clinical data and outcomes.

Methods. Bronchoalveolar lavage fluid (N = 197) and endotracheal aspirates (N = 73) submitted to the UF Health Shands Hospital microbiology laboratory from June-September 2018 were frozen at -70°C, until tested on the PP. Patient data were extracted from the inpatient electronic medical record (Epic).

Results. Of 270 patients tested, 111/270 (41.1%) were PP bacteria negative/culture no growth or normal flora (Group 1), 59/270 (21.9%) were PP positive/culture positive (Group 2), and 100/270 (37.0%) were PP positive without growth (Group 3) for at least 1 concordant bacterial potential pathogen. Hospital length of stay (LOS), P = 0.0274, ANOVA; ICU LOS P = 0.0007 and BAL % Polys P < 0.0001 were significantly longer/higher in Group 3 than in Groups 1 and 2 (Table 1). Max daily temp on the day of culture in PP-positive groups 2 and 3 was significantly higher than the PP-negative group 1, P = 0.0260, ANOVA, (Table 1). Age, daily WBC, lowest paO2, max FiO2, % on antibiotics (>280% for all groups), and % with viruses in the PP were not significantly different across groups. While all PP pathogens were grouped by copy #/mL, ICU LOS was significantly longer for 107 copies/mL (P = 0.0088), as was BAL % polys (P = 0.0006). Max daily temp was almost significantly higher for PP-positive groups 10(5), 10(6), and 10(7) combined compared with the PP-negative group (Table 2, P = 0.0608).

Conclusion. Hospital LOS was significantly longer and BAL % Polys higher in the PP-positive group culture positive/PP positive group vs. PP-negative groups. ICU LOS and BAL % Polys were significantly higher for the PP-positive groups vs. PP-negative regardless of culture results. PP results (copy #/mL) independently correlated with outcome and clinical measures.

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October 2018 and will conclude in June 2019. BCID2 Panel performance is compared with reference methods of microbial culture as well as PCR/sequencing for AMR genes. In addition, BCID2 Panel MRSA results are compared with the FDA-cleared Xpert MRSA/SA BC system (Cepheid, Inc.). Relevant bacterial isolates recovered from PBCs are also evaluated by various phenotypic antimicrobial susceptibility testing (AST) methods. The prospective evaluation is implemented with a second study that involves testing of >500 pre-selected, archived PBCs containing rare organisms. The third study includes over 500 seeded blood cultures containing very rare organisms with an evaluation of co-spiked samples.

Results. With over 1,200 samples tested to date (out of an anticipated 1,800 total), the BCID2 Panel has demonstrated an overall sensitivity of >98% and specificity of >99% for identification of microorganisms compared with culture. Concordance between the BCID2 Panel and the Xpert MRSA/SA BC test is >99% for identification of MRSA. Evaluation of BCID2 Panel AMR gene detection relative to AST and PCR is ongoing.

Conclusion. The FilmArray Meningitis Encephalitis Panel (MEP) rapidly detects 14 pathogens in <1 hour. In the first year of implementation at BCH, a positive MEP was conducted by MEP in 96% of cases and HSV PCR in 8% of cases. In both eras, a significant proportion of children underwent HSV testing (MEP or HSV PCR) doubled from 25% in the pre-MEP to 54% in the MEP era (P = 0.05). Overall, however, a similar proportion of children with suspected CNS infection undergoing HSV testing without affecting the rate of HSV positivity (0.5% vs. 0%) was maintained. The proportion of CSF specimens from children with suspected CNS infection undergoing HSV testing (MEP or HSV PCR) doubled from 25% in the pre-MEP era to 54% in the MEP era (P < 0.01; Figure 1). In the MEP era, HSV testing was conducted by MEP in >96% of cases and HSV PCR in >8% of cases. In both eras, a majority of CSF specimens undergoing HSV testing had no pleocytosis (63% vs. 59%, P = 0.27). Children with negative HSV testing by MEP were less likely to be started on acyclovir than those with negative HSV testing by singleplex PCR (18% vs. 50%, P < 0.01) and, amongst those started, acyclovir was discontinued sooner, after a median 3 vs 5 doses (P = 0.05). Overall, however, a similar proportion of children with suspected CNS infection received acyclovir in the MEP and pre-MEP eras (13% vs. 12%), despite a low rate of HSV positivity (0.5% vs. 0%).

Conclusion. Implementation of MEP for syndromic CSF testing in children >60 days with suspected CNS infection doubled HSV testing without affecting the rate of empiric acyclovir initiation. Patients with negative HSV testing on MEP were less likely to be started on acyclovir, and if started, received fewer doses than those who tested negative on HSV singleplex PCR, likely due to more rapid turnaround time. However, increased MEP testing offset this, suggesting increased use of newer rapid syndromic tests will not cure creeping empiricism. Diagnostic stewardship targeting MEP use toward children with pleocytosis to decrease unnecessary test utilization are warranted.

653. Diagnosis of Burn Sepsis Using the FcMBL ELISA: A Pilot Study in Critically Ill Burn Patients

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Background. Infection is the leading cause of death among burn survivors, with sepsis associated with more extensive burns. Conventional diagnostic criteria are insensitive in this population. We examined a novel diagnostic ELISA based on Mannose-Binding Lectin (MBL) linked to an immunoglobulin Fc domain, which measures the concentration of Pathogen-Associated Molecular Patterns (PAMPs) across a broad range of bacterial and fungal organisms, for diagnosis and antimicrobial management of sepsis in burn patients.

Methods. We prospectively enrolled burn patients with ≥15% Total Body Surface Area (TBSA) burns into groups of noninfected, sepsis, or incipient infection, and healthy volunteers. Sepsis was defined by clinical actions responsive to sepsis. The FcMBL ELISA was performed daily using fresh whole blood. Burn subjects were sampled daily until completing antimicrobials, for 14 days if noninfected, and once for healthy controls. Differences in median PAMP concentrations between groups were assessed with the Kruskal–Wallis test, including multiple comparisons between categories.

Results. 14 burn patients (3 noninfected, of whom 1 died prior to sampling, 4 sepsis, 7 Incipient) were enrolled. The median (25–75% CI) PAMP concentration was 0.53 (0.12–1.34) ng/mL in healthy controls, 3.725 (2.53–5.94) ng/mL in noninfected, 2.21 (1.11–4.07) ng/mL in sepsis, and 1.29 (0.83–2.29) ng/mL in sepsis groups. PAMP concentrations in sepsis were different (P = 0.0057) from noninfected, but infection did not differ from noninfected (P = 0.2025). The dynamic range was lower in healthy controls (2.69 ng/mL) than in sepsis (4.57 ng/mL), sepsis (4.76 ng/mL), or noninfected (5.90 ng/mL). PAMP elevations correlated with clinical deterioration from infection, and were not associated with OR visits for debridement and grafting. 7 of 11 infected patients had declining PAMP levels at completion of antimicrobial therapy. 2 subjects had PAMP elevations associated with Aspergillus molds in their burn wounds.

Conclusion. The FcMBL ELISA assay may be useful for diagnosis of infection in burn patients, and may facilitate earlier discontinuation of antimicrobials. This assay may also have a novel utility for early diagnosis of Invasive Fungal Infection.

Disclosures. All authors: No reported disclosures.

654. Evaluation of the FebriDx Host Response Point-of-Care Test to Differentiate Viral From Bacterial Etiology in Adults Hospitalized with Acute Respiratory Illness During Influenza Season

Kate Beard, MBBS; Cathleen Chan, MBBS; Samuel Mills, BM, BCh; Stephen Poole, MBBS; Nathan Brendish, MBBS; Tristan William. Clark, BM, MRCP; DTfMiH, MD; University of Southampton, Southampton, UK; University Hospital Southampton Foundation NHS Trust, Southampton, UK; NIHR Southampton Biomedical Research Centre, Southampton, UK

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Background. The FebriDx POC was associated with a failure rate of Seepis, 7 Incipient) were enrolled. The median (25–75% CI) PAMP concentration was 0.53 (0.12–1.34) ng/mL in healthy controls, 3.725 (2.53–5.94) ng/mL in noninfected, 2.21 (1.11–4.07) ng/mL in sepsis, and 1.29 (0.83–2.29) ng/mL in sepsis groups. PAMP concentrations in sepsis were different (P = 0.0057) from noninfected, but infection did not differ from noninfected (P = 0.2025). The dynamic range was lower in healthy controls (2.69 ng/mL) than in sepsis (4.57 ng/mL), sepsis (4.76 ng/mL), or noninfected (5.90 ng/mL). PAMP elevations correlated with clinical deterioration from infection, and were not associated with OR visits for debridement and grafting. 7 of 11 infected patients had declining PAMP levels at completion of antimicrobial therapy. 2 subjects had PAMP elevations associated with Aspergillus molds in their burn wounds.

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