was developed and posted online on August 2, 2017. Featuring three faculties with therapeutic expertise, the activity addressed: Distinguishing characteristics of various diagnostic methods; considerations when interpreting test results; and applying findings to patient care decisions Educational effectiveness was assessed with a repeated-pairs pre-/post-assessment study design, in which each individual served as his/her own control. Responses to three multiple-choice, knowledge/competence questions and 1 self-efficacy confidence question were analyzed. A chi-squared test assessed changes pre- to post-assessment. *P* value of <0.05 is statistically significant. Effect sizes were evaluated using Cramer's V (<0.05 modest; 0.06–0.15 noticeable effect; 0.16–0.26 considerable effect; >0.26 extensive effect). Data were collected through September 7, 2017.

Results. A total of 4,712 healthcare providers, including 3,317 physicians have participated in the activity. Data from ID specialists (n = 266) who answered all pre-/post-assessment questions during the study period were analyzed. Significant improvements were observed overall (P = 0.0002; V = 0.156) and in several specific areas of assessment (figure). Following activity participation, 29% of ID specialists indicated increased confidence in diagnosing meningitis and encephalitis using rapid molecular tests and 89% of ID specialists indicated a commitment to incorporate one or more changes into practice. Finally, the findings also uncovered educational needs that are the focus of ongoing interventions.

Conclusion. Participation in this online education significantly improved ID specialists' knowledge and competence with regard to using rapid molecular tests to diagnose meningitis and encephalitis. These findings highlight the positive impact of well-designed online education.

Assessment of Educational Effectiveness			
Area of Assessment	% relative improvement (% of ID specialists selecting the correct response at pre- vs post-assessment)	*P*-value for change	Cramer's V for the magnitude of the change
Evaluate the clinical implications of findings from single- vs multiple-pathogen tests	8% improvement (86% vs 93%)	*P*=NS	V=0.103 (Noticeable)
Interpret diagnostic findings and recognize the need for follow-up testing to distinguish between latent and active infections	25% improvement (59% vs 74%)	*P*=.0205	V=.169 (Considerable)
Identify key characteristics that differentiate rapid molecular tests from traditional diagnostic methods for meningitis and encephalitis	29% improvement (62% vs 80%)	*P*=.0064	V=.169 (Considerable)

Disclosures. **S. Hurst**, BioFire Diagnostics: Independent Medical Education, Educational grant. **S. Smith**, BioFire Diagnostics: Independent Medical Education, Educational grant.

2018. Host Gene Expression Classifiers Distinguish Bacterial and Viral Infections in Sri Lankan Patients with Acute Febrile Respiratory Illness

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Session: 229. Diagnostics: Biomarkers and Novel Approaches
Saturday, October 6, 2018: 12:30 PM

Background. Acute febrile illness is a frequent cause of hospitalization in the tropics and often presents with respiratory symptoms, even when caused by non-respiratory pathogens. Previously, host-based gene expression signatures accurately identified acute respiratory infections as being bacterial or viral in a U.S. cohort. We determined signature performance in a Sri Lankan cohort with acute febrile respiratory illness (AFRI).

Methods. We enrolled patients with AFRI in Sri Lanka from July 2012 to May 2013 and collected nasopharygeal swabs, acute/ convalescent sera, and blood in PAXgene RNA tubes. Bacterial (*Orientia tsutsugamushi*, *Leptospira* spp.) and viral (influenza A/B, dengue) infections were confirmed using polymerase chain reaction, virus isolation, enzyme immunoassay, and/or microscopic agglutination testing. We extracted total RNA and performed host RNA sequencing (Illumina). We aligned reads to hg38 reference genome using Bowtie2, quantified at isoform level using Express version 1.5.1, and normalized using trimmed-mean normalization. The original model estimated three classes and separate signatures predicted bacterial infections, viral infections, and non-infectious illnesses. Regularized regression was used to predict bacterial and viral infections based on prior signatures. Accuracy was estimated using leave-one-out cross-validation.

Results. Among 43 patients with viral infections (14 dengue, 29 influenza) and 16 patients with bacterial infections (six *Leptospira* spp., 10 *O. tsutsumagushi*), median age was 37 years (IQR 23–51) and 49% were male. Of five respiratory symptoms (cough, sore throat, rhinitis/ congestion, shortness of breath, and pain with breathing), median (IQR) number of symptoms was 2 (1–2) for influenza, 2 (1–2) for dengue, 2 (2–3) for *Leptospira* spp., and 1.5 (1–2) for *O. tsutsumagushi*. We observed high predictive accuracy in discriminating bacterial and viral infections: AUROC 0.91 for the bacterial and AUROC 0.81 for the viral model. At enrollment, 65% of viral and 50% of bacterial AFRI patients received antibiotics.

Conclusion. Host gene expression classifiers performed well in a Sri Lankan population with AFRI, even with nonrespiratory pathogens that may not be readily identified. Host-based diagnostics may play a critical role in improving diagnostic ability and antibiotic use globally.

Disclosures. **E. L. Tsalik**, Host Response, Inc.: Founder, Equity. **G. S. Ginsburg**, Host Response Inc.: Board Member, Founder, Scientific Advisor and Shareholder, Stock (currently worth <$100). **C. W. Woods**, Host Response, Inc.: Founder, Equity.

2019. Host Gene Expression Signatures for Diagnosis of Acute Respiratory Infections in the Elderly

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Session: 229. Diagnostics: Biomarkers and Novel Approaches
Saturday, October 6, 2018: 12:30 PM

Background. Despite advances in molecular techniques the etiology of acute respiratory infections (ARIs) is often difficult to differentiate either at the point of care or with advanced microbiological techniques. There is growing interest in host biomarker assays, including those based on gene expression patterns in circulating cells, to aid in differentiation of viral and bacterial diseases. However, there are concerns about how such tests perform in vulnerable aging populations where host responses are often muted.

Methods. In order to assess performance of gene expression-based biomarkers, we enrolled patients presenting to the emergency department with clinical ARI and selected 184 individuals aged ≤25 and ≥60 years old with proven viral or bacterial ARI. Gene expression in peripheral blood was measured with Affymetrix microarrays. Published viral and bacterial signatures were applied to the data and Bayesian approaches were used to develop novel discriminative models.

Results. We noted a marked decline in signature performance between younger and older individuals in both viral (AUC 0.90 vs. 0.64) and bacterial (AUC 0.91 vs. 0.50) infections. Incorporation of age-related genomic changes was able to restore much of the signature performance in older individuals. When examining the genomic differences driving the drop in signature performance, we found marked perturbations in expression of immunoglobulin genes and pathways driving known immunoregulatory mechanisms that provide novel insights into an age-related decline in ARI-focused immunity.

Conclusion. Pathogen class-specific host-based gene expression signatures offer great promise as diagnostic tools. However, altered immune responses in vulnerable populations such as the elderly are also manifested at the genomic level and can affect diagnostic signature performance. Age-specific alterations in the components of a diagnostic signature can minimize much of this effect, however this work highlights the need for consideration of age during biomarker development for infectious diseases. Furthermore, studies of age-related differences in biomarker performance can lead to important breakthroughs in our understanding of age-associated alterations in immunity.

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

2020. Concordance of Direct vs. Indirect Pathogen Detection Using the BioFire® System

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Session: 229. Diagnostics: Biomarkers and Novel Approaches
Saturday, October 6, 2018: 12:30 PM

Background. Polymerase chain reaction (PCR) is a highly sensitive and specific method for pathogen detection. While direct methods enable rapid identification, they are limited by pathogen titer, available assays, or sample matrix. Transcriptomic analysis addresses these limitations by measuring systemic host gene expression changes to infections. The BioFire System uses sample-to-answer multiplex PCR that was adapted to detect 42 transcripts differentially expressed during viral and bacterial infections. Here we report concordance between indirect detection of viral respiratory pathogens and the FDA-cleared BioFire® Respiratory Panel 2 (RP2).

Methods. Paired nasal pharyngeal swabs and blood samples were obtained by informed consent from patients with suspected acute respiratory illness. Swabs (COPAN FLOQSwab™) were collected and stored in viral transport media (BD) for BioFire RP2 testing and peripheral blood samples were collected in PAXgene tubes (Qiagen) for testing with the research use only human response (HR) panel. A logistic regression model was developed to classify viral and nonviral positive samples using normalized quantification cycles for each assay. Probabilities of viral infection for each