Background. Previous studies suggest that RSV increases NP bacterial colonization and may facilitate infection. However, the role of NP colonization with potentially pathogenic bacteria (PPB) in the pathogenesis of RSV bronchiolitis is not well understood. We sought to determine the frequency, type, and density of NP PPB detection in infants with RSV infection compared with healthy controls (HC), and its association with clinical outcomes.

Methods. Single-center, prospective study of previously healthy infants with RSV infection and age-matched HC. Inpatients (IP) were enrolled within 24 hours of hospitalization, outpatients (OP) at the ED or primary clinics and HC at well-child visits. RSV infection and the following PPB: [*S. pneumoniae*, *M. catarrhalis*, *H. influenzae*, and *S. aureus*] were detected and quantified by PCR. We compared demographic, clinical characteristics, and outcomes of care according to NP PPB detection.

Results. From 2010 to 2018, we enrolled 815 infants: 664 with RSV infection [IP, 560; OP, 104] and 151 HC. RSV+ OP (6.1 [3.7–10.7] months) and HC (6.9 [3.8–10.8] months) were older than IP (2.5 [1.4–5.4] months; $P < 0.001$). Identification of ≥1 PPB was 89% in RSV+ infants [IP, 88%; OP, 90%] versus 63% of HC ($P < 0.0001$). While *H. influenzae* or >1 PPB detection was higher in RSV infection ($P < 0.001$), *S. aureus* detection predominated in HC ($P < 0.05$; Figure 1). Frequency of *S. pneumoniae* detection was comparable between groups; however, *S. pneumoniae* loads were one log higher in RSV+ infants versus HC ($P = 0.001$) adjusted for antibiotic use. Differences in colonization rates remained different in RSV+ infants versus HC across age ranges (<3, 3–6, >6–12, and >12–24 months; Figure 2). Last, RSV patients (both IP and OP) with *S. pneumoniae* or *H. influenzae* detection had fever more frequently (70%–74% vs. 25%–47%; $P < 0.0001$), higher clinical disease severity scores ($P = 0.01$), and higher blood neutrophil counts (34%–36% vs. 16%–19%; $P < 0.001$), versus those with *M. catarrhalis*, *S. aureus* detection or PCR negative. In addition, NP detection of *H. influenzae* in RSV children was associated with higher frequency of atelectasis/consolidation by chest X-ray ($P < 0.005$).

Conclusion. These data suggest that NP colonization with PPB is high in infants with RSV infection independent of age, and that specific bacteria, namely *S. pneumoniae* and *H. influenzae*, are associated with enhanced clinical disease severity.

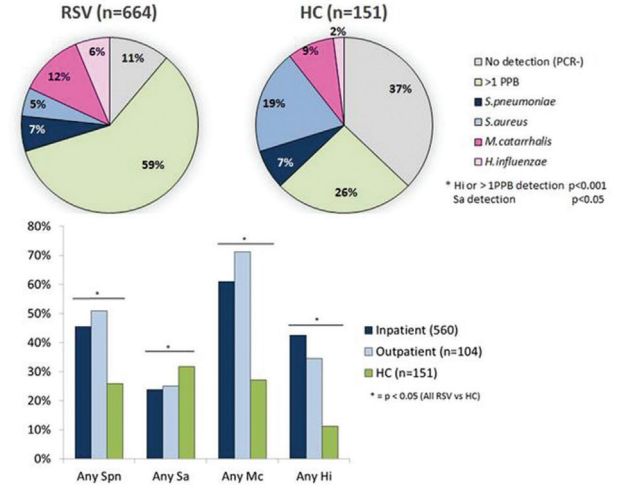


Figure 1. Frequency of NP bacterial detection of potentially pathogenic bacteria (PPB) in infants with RSV (inpatient and outpatient) and healthy controls (HC)

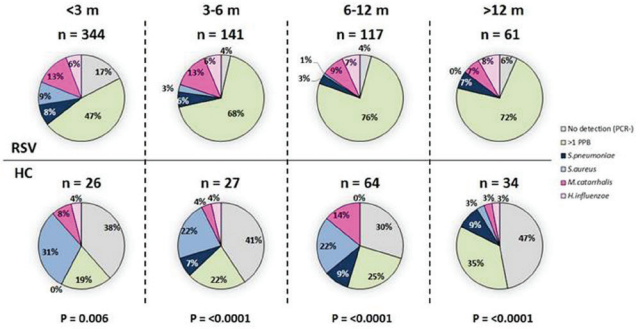


Figure 2. Frequency of NP bacterial detection in infants with RSV and healthy controls stratified by age. HC: Healthy control; PPB: Potentially pathogenic bacteria. Statistical comparisons by Chi-square test.

Disclosures. **A. Leber**, Nationwide Children's Hospital: Research Contractor, Research support. **O. Ramilo**, Janssen Scientific Affairs, LLC: Consultant, Consulting fee. **A. Mejias**, Janssen: Grant Investigator and Scientific Advisor, Consulting fee and Research grant. Abbvie: CME talks, Speaker honorarium.

119. Prospective Validation of a 3-Gene Signature for Tuberculosis Diagnosis, Predicting Progression and Evaluating Treatment Response

Hayley Warsinske, PhD[1]; Aditya Rao, BA[2]; Flora Martinez Figueira Moreira, BS[3]; Paulo Cesar Pereira Dos Santos, BS[3]; Andrew Liu, MS[2]; Madeleine Scott, BA[2]; Stephanus Malherbe, MD, PhD[4]; Katharina Ronacher, PhD[5]; Gerhard Walzl, PhD[4]; Jill Winter, PhD[6]; Timothy E. Sweeney, MD, PhD[7]; Julio Croda, MD PhD[8]; Jason R. Andrews, MD[9] and Purvesh Khatri, PhD[10], [1]Immunology, BMI, Stanford University, Stanford, California, [2]Stanford University, Stanford, California, [3]Federal University of Grande Dourados, Dourados, Brazil, [4]Stellenbosch University, Stellenbosch, South Africa, [5]The University of Queensland, Brisband, Australia, [6]Catalysis Foundation for Health, Emeryville, California, [7]Institute for Immunity, Transplantation, and Infections and Division of Biomedical Informatics, Department of Medicine, Stanford University, Stanford, California, [8]Faculty of Medicine, Federal University of Grande Dourados Oswaldo Cruz Foundation, Dourados, Brazil, [9]Division of Infectious Diseases and Geographic Medicine, Stanford University School of Medicine, Stanford, California, [10]2-Institute for Immunity, Transplantion and Infections, 3- and Biomedical Informatics Research, Dept. of Medicine, Stanford University, Palo Alto, California

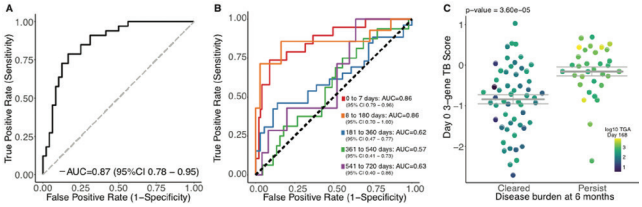
Session: 32. Tuberculosis and other Mycobacterial Infections
Thursday, October 4, 2018: 8:45 AM

Background. The World Health Organization (WHO) has identified the need for a nonsputum-based triage test for tuberculosis (TB) that can be used to identify those who need further testing to identify active disease. We investigated whether our previously described 3-gene TB score could identify individuals with active tuberculosis (ATB) prior to seeking care ("active case detection") and how the 3-gene TB score correlated with the timing of disease onset, disease severity, and response to treatment.

Methods. This study consisted of a prospective nested case–control trial, Brazil Active Screening Study (BASS; 2016), and re-analysis of data from 2 prospective cohort studies, the Adolescent Cohort Study (ACS; 2005–2007), and the Catalysis Treatment Response Cohort (CTRC; 2010–2013). The BASS case–control subcohort contained 81 adults (ages 20–72 years, 33 ATB, 48 controls). The ACS contained 153 adolescents (ages 12–18 years, 46 ATB, 107 LTBI). The CTRC-contained 138 adults (ages 17–67 years, 100 ATB, 17 other lung disease patients, 21 healthy controls).

Results. The 3-gene TB score diagnosed ATB patients with high accuracy: BASS cohort AUC = 0.87 (95% CI = 0.82–0.91, Figure 1A), ACS cohort AUC = 0.86 (95% CI = 0.76–0.97, Figure 1B), and CTRC AUC = 0.93 (95% CI = 0.88–0.97). In the ACS, the 3-gene TB score predicted progression from LTBI to ATB 6 months prior to positive sputum test (AUC = 0.86; 95% CI = 0.79–0.92, Figure 1B). In the CTRC, the 3-gene TB score correlated with glycolytic activity ratio of PET-CT at baseline (correlation = 0.54, $P = 3.98 \times 10^{-8}$, Figure 1C) and at the end of treatment (correlation = −0.408, $P = 3.72 \times 10^{-5}$). In the CTRC, the 3-gene TB score at baseline predicted the likelihood of prolonged sputum positivity following treatment initiation and treatment response at 6 months ($P = 3.6 \times 10^{-5}$). Collectively, across all cohorts, the 3-gene TB score identified ATB patients with 90% sensitivity and 70% specificity, and had 99% negative predictive value (NPV) at 5% prevalence.

Conclusion. Across 3 independent prospective cohorts, the 3-gene TB score closely approaches the WHO target product profile benchmarks for non-sputum–based triage test at high NPV. These performance characteristics make it a potential test for ruling out ATB and for monitoring disease status.



Disclosures. **T. E. Sweeney**, Inflammatix, Inc.: Employee and Shareholder, Salary. **P. Khatri**, Inflammatix Inc.: Board Member, Equity

120. A Randomized Double-blind Trial Assessing the Efficacy of M72/AS01$_E$ Vaccine Against Pulmonary Tuberculosis Disease in Adults With Latent *Mycobacterium tuberculosis* Infection

Olivier Van Der Meeren, MD[1]; Mark Hatherill, MD[2]; Videlis Nduba, MBChB, MPH[3]; Robert J. Wilkinson, FMedSci[4]; Monde Muyoyeta, MBChB, PhD[5]; Elana Van Brakel, MBChB, MSc[6]; Helen M. Ayles, MBBS, PhD[7,8]; German Henostroza, MD[5,9]; Friedrich Thienemann, MD, MScIH, DTMPH[4]; Thomas J. Scriba, PhD[2]; Andreas Diacon, MD, PhD[6,10]; Gretta L. Blatner, MS, MPH[11,12]; Marie-Ange Demoitié, MSc[1]; Michele Tameris, MBChB[2]; Mookho Malahleha, MD, MPH[13]; James C. Innes, MBChB, MSc[14,15]; Elizabeth Hellstrom, MBChB[16]; Neil Martinson, MBChB, MD, MPH[17]; Tina Singh, MD[1]; Elaine J. Akite, MSc[1]; Aisha K. Azam, MBBS[1]; Anne Bollaerts, MSc[1]; Ann M. Ginsberg, MD, PhD[11]; Thomas G. Evans, MD[11,18]; Paul Gillard, MD[1] and Dereck R. Tait, FRCPath[19], [1]GSK, Wavre and Rixensart, Belgium, [2]South African Tuberculosis Vaccine Initiative (SATVI), Institute of Infectious Disease and Molecular Medicine and Division of Immunology, Department of Pathology, University of Cape Town, Cape Town, South Africa, [3]Kenya Medical Research Institute (KEMRI), Nairobi, Kenya, [4]Wellcome Centre for Infectious Diseases Research in Africa (CIDRI-Africa), Institute of Infectious Disease and Molecular Medicine, University of Cape Town, Cape Town, South Africa, [5]Centre for Infectious Diseases Research in Zambia (CIDRZ), Lusaka, Zambia, [6]Task Applied Science, Cape Town, South Africa, [7]Zambia AIDS Related Tuberculosis (ZAMBART), Lusaka, Zambia, [8]London School of Hygiene and Tropical Medicine, London, UK, [9]University of Alabama at Birmingham, Birmingham, Alabama, [10]University of Stellenbosch, Cape Town, South Africa, [11]AERAS, Rockville, Maryland, [12]Biomedical Advanced Research