women, and compare this to the prevalence among infants tested for CMV following clinical suspicion of a congenital infection.

Methods. In November 2013, the "Programme québécois de dépistage de la surdité chez les nouveau-nés" (PQDSN), a provincially mandated hearing screening program, was implemented at Centre Hospitalier Universitaire Sainte-Justine, a tertiary maternal-child health center in Montreal, Quebec, along with CMV screening for all infants who failed their hearing test (excluding patients in the neonatal intensive care unit). Concurrently, beginning in April 2013, all infants of HIV-infected women were screened for cCMV infection within 48 hours of birth. The birth prevalence of cCMV infection in these targeted populations was compared with the prevalence among newborns tested for a clinical suspicion of cCMV.

Results. Out of 11 734 newborns screened for hearing through the PQDSN program between April 2014 and March 2018, 536 failed their initial hearing screen and 4 of these newborns tested positive for cCMV infection (0.75%). Out of a total of 130 HIV-exposed newborns born during this period, 116 were screened for cCMV and 3 (2.6%) confirmed positive. An additional 455 newborns were identified by the attending pediatrician as having a risk factor for any congenital infection; of these, 22 (5.3%) tested positive for cCMV. Using these combined methods, a total of 0.24% of newborns enrolled in the PQDSN program tested positive for cCMV infection.

Conclusion. The overall birth prevalence of cCMV was 0.75% among infants who failed their hearing screen, 2.6% among HIV exposed newborns, and 5.3% among infants with a clinical suspicion of a congenital infection. In the absence of a universal screening program for newborns, these results reinforce the importance of maintaining a high index of clinical suspicion for cCMV infection.

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

116. Role of Maternal Antibodies in Protection Against Postnatal Cytomegalovirus Acquisition

Frances Saccoccio, MD, PhD[1]; Hannah Itell, BS[2]; Skukhang Li, BS[2]; Jennifer Jenks, BS[2]; Guan Xie, PhD[2]; Justin Pollara, PhD[2]; Soren Gantt, MD, PhD[3] and Sallie Permar, MD, PhD[2], [1]Pediatrics Infectious Diseases, Duke University Hospital, Durham, North Carolina, [2]Duke Human Vaccine Institute, Duke University, Durham, North Carolina, [3]University of British Columbia, Vancouver, British Columbia, Canada

Session: 31. Infant Viral Infections
Thursday, October 4, 2018: 8:45 AM

Background. Congenital cytomegalovirus (CMV) is the leading infectious cause of birth defects in the United States. Development of an effective CMV vaccine is a public health priority. However, CMV vaccine development is limited by a poor understanding of the immune correlates of protection, including the role of CMV-specific IgG. Defining the role of passively acquired maternal IgG in the protection of half of the CMV-exposed, breastfeeding infants against postnatal CMV acquisition may inform CMV vaccine design

Methods. We analyzed CMV-specific humoral responses in 29 CMV-seropositive Ugandan mother–infant pairs. Seventeen mothers were HIV co-infected. Infants were followed weekly for postnatal CMV acquisition using saliva PCR. Twelve infants acquired CMV and 17 infants did not acquire CMV in the first 6 months of life. We compared CMV-specific IgG responses at delivery of mothers whose infants acquired CMV to mothers whose infants did not acquire CMV by 6 months of life and in the infants at 6 weeks of life. We also compared CMV-specific responses in mothers at delivery and infants at 6 weeks of life based on maternal HIV status.

Results. We found similar CMV-specific total IgG and IgG3 binding, avidity index, neutralization, antibody-dependent cellular phagocytosis, and antibody-dependent cellular cytotoxicity responses in mothers whose infants did or did not acquire CMV by 6 months of life. Moreover, similar CMV-specific IgG binding and neutralization responses were also found between infants who did or did not acquire CMV by 6 months of life. Finally, CMV-specific IgG responses were similar in HIV-infected and uninfected mothers at delivery and in infants at 6 weeks of life regardless of perinatal HIV exposure.

Conclusion. CMV-binding and functional IgG responses do not appear to impact infant susceptibility to postnatal CMV acquisition in the first 6 months of life, and therefore other viral or immunologic factors contribute to the inefficiency of this mode of CMV transmission. Thus, to provide sterilizing protection against mucosal CMV acquisition, an antibody-based CMV vaccine would likely have to induce higher magnitude or qualitatively different responses than that of natural infection.

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

117. Effect of Nasopharyngeal Pneumococcal Carriage on RSV and hMPV Illness Severity in Infants in Nepal

Alastair Murray, BA[1]; Janet Englund, MD, FIDSA[2]; Jane Kuypers, PhD[3]; James Tielsch, PhD, MA[4]; Joanne Katz, ScD[5]; Laxman Shrestha, MBBS, MD[6]; Subarna Khatry, MBBS, DOMS[7]; Steven C Leclerq, MPH[8]; Mark C. Steinhoff, MD, FIDSA[9] and Helen Y. Chu, MD MPH[10], [1]George Washington University School of Medicine, Washington, DC, [2]Vaccine and Infectious Disease Division, Fred Hutchinson Cancer Research Center, Seattle, Washington, DC, [3]Department of Laboratory Medicine, University of Washington, Seattle, Washington, DC, [4]George Washington University, Washington, DC, [5]Johns Hopkins University, Baltimore, Maryland, [6]Pediatrics and Child Health, Institute of Medicine, Tribhuvan University, Kathmandu, Nepal, [7]NNIPS, Kathmandu, Nepal, [8]NNIPS, Baltimore, Maryland, [9]Division of Infectious Diseases, Global Health Center, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio and [10]Allergy and Infectious Diseases, University of Washington, Seattle, Washington, DC

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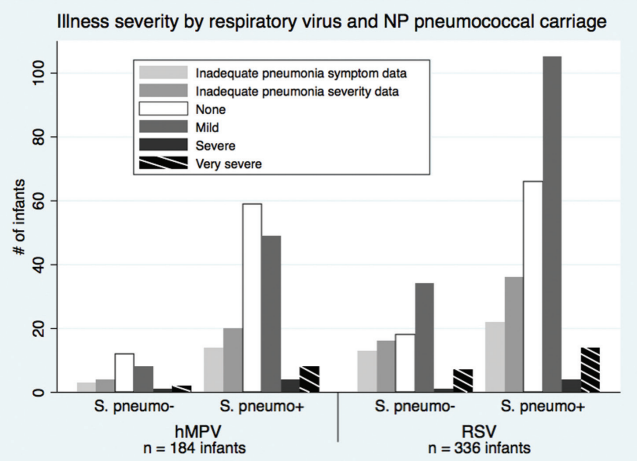
Background. Pneumococcal pneumonia after a preceding respiratory viral illness is associated with morbidity and mortality in infants. Our study sought to determine how pneumococcal carriage impacted illness severity due to respiratory syncytial virus (RSV) or human metapneumovirus (hMPV) in infants 0–6 months in a low resource setting in South Asia without pneumococcal vaccination. Previous studies in this population found an overall 79.4% prevalence of pneumococcal carriage in ages 1–36 months with higher rates of carriage among healthy controls when compared with those with respiratory illness.

Methods. Infants were enrolled at the time of birth in a maternal influenza immunization trial conducted in rural Nepal from 2011 to 2014. Weekly household-based active surveillance was performed from birth to 6 months to assess for infant respiratory illness, defined as fever, cough, difficulty breathing, wheeze, or otorrhea. Midnasal swabs were collected and tested by PCR for RSV, hMPV, and streptococcus pneumoniae with inclusion of first illness episode in the surveillance period. Disease severity was defined using the World Health Organization Integrated Management of Childhood Illness criteria.

Results. Altogether, 247 (73.5%) of 336 infants with RSV and 154 (83.7%) of 184 infants with hMPV had *S. pneumoniae* detected. Mean age at RSV illness with concurrent pneumococcal carriage was 97.0 days (91.3–102.6) versus 72.8 days (63.3–82.4) for infants without carriage ($P < 0.001$). Mean age at hMPV illness with concurrent pneumococcal carriage was 101.3 days (93.9–108.7) versus 77.2 days (56.5–98.0) for infants without carriage ($P = 0.01$). Frequency of reported lower respiratory tract infection did not differ with or without carriage (RSV: 64.4% vs. 65.2% respectively; $P = 0.89$, hMPV: 52.6% vs. 50.0% $P = 0.79$). *S. pneumoniae* PCR cycle threshold value did not differ by duration or severity of RSV or hMPV illness episode.

Conclusion. High rates of pneumococcal carriage were observed with RSV and hMPV illness episodes in a birth cohort of infants in rural Nepal. The majority of infants with RSV or hMPV illness had pneumococcus detected at the time of first observed illness. However, no increase in RSV or hMPV illness severity or duration was seen with pneumococcal carriage.

Figure 1.
RSV and hMPV disease severity, as defined by World Health Organization Integrated Management of Childhood Illness pneumonia criteria, by nasopharyngeal pneumococcal carriage status in a population of infants 0-6 months, Nepal 2011-2014. Inadequate pneumonia symptom data refers to lack of clinical data to determine if symptoms met WHO criteria, while inadequate pneumonia severity data refers to infants meeting WHO criteria with lack of clinical data to determine severity.



Disclosures. **H. Y. Chu**, sanofi pasteur: Grant Investigator, Grant recipient. Novavax: Grant Investigator, Grant to co-investigator's institution.

118. Nasopharyngeal (NP) Bacterial Detection in Infants With Respiratory Syncytial Virus (RSV) Infection: Impact on Clinical Outcomes

Alejandro Diaz, MD[1]; Eleonora Bunsow, MD PhD[2]; Cristina Garcia-Maurino, MD[2]; Jeffrey Naples, MD[3]; Alexis Juergensen, BA[3]; Sara Mertz, BS[2]; Huanyu Wang, PhD[3]; Douglas Salamon, BS[3]; Amy Leber, PhD[4]; Octavio Ramilo, MD, FPIDS[5] and Asuncion Mejias, MD, PhD, MsCS[6], [1]Infectious Diseases, Nationwide Children's Hospital, Columbus, Ohio, [2]Center for Vaccines and Immunity, The Research Institute at Nationwide Children's Hospital, Columbus, Ohio, [3]Nationwide Children's Hospital, Columbus, Ohio, [4]Department of Laboratory Medicine, Nationwide Children's Hospital, Columbus, Ohio, [5]Pediatrics, Nationwide Children's Hospital, Columbus, Ohio, [6]The Research Institute at Nationwide Children's Hospital, Columbus, Ohio

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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.

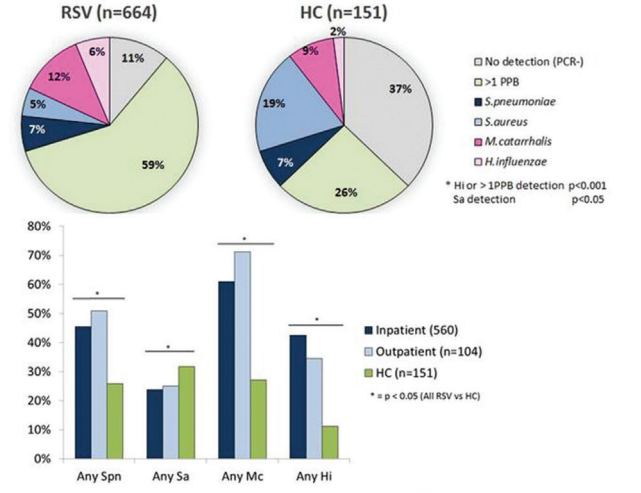

Figure 1. Frequency of NP bacterial detection of potentially pathogenic bacteria (PPB) in infants with RSV (inpatient and outpatient) and healthy controls (HC)

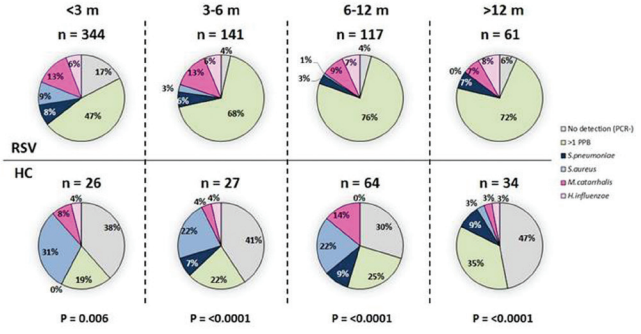

Figure 2. Frequency of NP bacterial detection in infants with RSV and healthy controls stratified by age. HC: Healthy control; PPB: Potentially pathogenic bacteria. Statistical comparisons by Chi-square test.

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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
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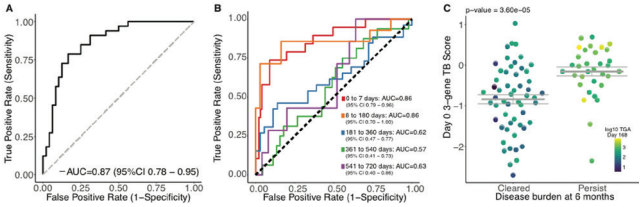
Background. The World Health Organization (WHO) has identified the need for a nonsputum-based triage test for tuberculosis (TB) that can be used to identify those who need further testing to identify active disease. We investigated whether our previously described 3-gene TB score could identify individuals 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