Conclusion. In a Phase I trial of RBX2660 for rCDI, participant BA compositions signifi-
cantly changed from before to after treatment, remained so for at least two years, and correlated with treatment outcome. The resulting predominance of secondary BAs coincided with microbiome compositional changes. Because secondary BA are thought to repres C. difficile colonization, these changes may partly explain how RBX2660 reduced CDI recurrence. Continued evaluation of RBX2660 for rCDI is underway.

Disclosures. Romeo Papayan, PhD. Ferring Pharmaceuticals (Employee) Dana Walsh, PhD. Rebiotix Inc. (Employee) Steve Qi, PhD. Ferring Pharmaceuticals (Employee) Ken Blount, PhD. Rebiotix Inc. (Employee) Karthik Srinivasan, PhD. Ferring Pharmaceuticals (Employee) Bryan Fuchs, PhD. Ferring Pharmaceuticals (Employee)

30. Antimicrobial Resistance Genes Are Reduced Following Administration of Investigational Microbiota-based Therapeutic RBX7455 to Individuals with Recurrent clostridoides Difficile Infection

Dana Walsh, PhD; Carlos Gonzalez, MS; Bill Shannon, PhD MBA; Ken Blount, PhD; Rebiotix, Inc., Roseville, Minnesota; BioRankings, LLC, St. Louis, Missouri

Session: O-6. Antimicrobial insights

Background. Antimicrobial resistance (AMR) is a challenge in individuals at risk for recurrent C. difficile infection (rCDI). Recognizing that AMR bacteria colonize the intestinal microbiota, therapeutic approaches that decolonize the gut of AMR bacteria would be valuable. Herein, we assessed the microbial resistome before and after treatment with RBX7455—a room temperature-stable, orally-administered investigational microbiota-based therapeutic—in a Phase 1 trial for reducing CDI recurrence.

Methods. This investigator-sponsored trial enrolled 30 rCDI patients in 3 open-label treatment groups (n=10 per group): 1) Four RBX7455 capsules BID for 4 days, 2) Four RBX7455 capsules BID for 2 days, 3) Two RBX7455 capsules BID for 2 days. RBX7455 administration began 48 hours after finishing CDI antibiotics. Participants were asked to submit stool samples at baseline, 1, 7, 28 and 56 days after treatment. These were extracted and sequenced using a shallow shotgun method. Relative taxonomic abundances at the class level and the presence of AMR genes were determined. This study aimed to determine if there is a difference among the groups with respect to clinical response or changes in microbiome compositions after treatment with RBX7455—a room temperature-stable, orally-administered investigational microbiota-based therapeutic—in a Phase 1 trial for reducing CDI recurrence.

Results. Ninety percent of participants met the primary endpoint of no CDI recurrence through 8 weeks after treatment, and participant microbiome compositions became more similar to RBX7455 after treatment. The total AMR counts per participant decreased from before to after treatment (p<.05, mixed effects model), with the pattern of AMRs identified (resistome) becoming more like the RBX7455 resistome (Figure 1). Most notably, AMRs associated with multi-drug, tetracyclolone, and betalactam resistance decreased from before to after treatment. There was no significant difference among the groups with respect to clinical response or changes in microbiome compositions and AMR content.

Figure 1: Average total and per-class AMR gene counts in participant samples before and after RBX7455 treatment.

Conclusion. In a Phase 1 trial of RBX7455 for rCDI, AMR gene content decreased after treatment. This underscores the potential of microbiota-based therapies for decolonizing AMR bacteria from the gut microbiota. Continued clinical evaluation of RBX7455 is underway.

Disclosures. Dana Walsh, PhD. Rebiotix Inc. (Employee) Carlos Gonzalez, MS. BioRankings, LLC (Employee) Bill Shannon, PhD MBA. BioRankings, LLC (Employee) Ken Blount, PhD. Rebiotix Inc. (Employee)

31. Post-ebola Syndrome Presents with Multiple Overlapping Symptom Clusters: Evidence from an Ongoing Cohort Study in Eastern Sierra Leone

Sarah Talia Himmellfarb, MD; Nell Bond, PhD; Adora Okoli, MD, MPH; John Schieffelin, MD, MSPh; Jeffrey Shaffer, PhD; Robert J. Samuels, M.B.Ch.B.; Emily J. Engel, MPH&TM; Tidiane, Université New Orleans, Louisiane; Tidiane University School of Medicine, New Orleans, Louisiane; Tidiane University School of medicine, New Orleans, Louisiane; Vanderbilt School of Medicine, Visiting Scholar, Nashville, Tennessee

Session: O-7. Around the World - Understanding Infectious Disease and Health Interventions

Background. Since the outbreak of Ebola Virus Disease (EVD) in West Africa from 2013–2016, a large cohort of survivors with persistent health complaints has emerged. This constellation of issues is termed post-ebola syndrome. Here we characterize the symptoms and physical exam findings of this syndrome in a cohort of survivors from Sierra Leone 2.6 years after resolution of disease. Ebola survivors present with clusters of symptoms that represent sub phenotypes of post-ebola syndrome.

Methods. Potential survivor participants in Eastern Sierra Leone were identified and recruited through the Sierra Leone Association of Ebola Survivors. Household contacts of survivors were identified by enrolled survivors. Both groups were administered a questionnaire assessing self-reported symptoms. A physical exam was performed by a limited number of trained providers. Symptoms were then compared using hierarchical clustering. Statistical analysis of the correlations between clusters was conducted using conditional logistic regression. Both SPICE and principal component (PCA) analyses were performed to explore the relationships between symptom clusters.

Results. Between March 2016 and January 2019, 375 Ebola survivors and 1040 contacts were enrolled. At enrollment, Ebola survivors of all age groups reported significantly more symptoms than their contacts in all categories. Six symptom clusters were identified representing distinct organ systems. SPICE revealed 2 general phenotypes: with or without rheumatologic symptoms. Clusters including rheumatologic symptoms were correlated with one another (r = 0.63) but not with other clusters (r < 0.35). Ophthalmologic/auditory symptoms were moderately correlated with the non-rheumatologic clusters (r > 0.5). Interestingly, psychologic/neurologic, cardiac/GI and constitutional clusters correlated with one another (r > 0.6) p < 0.0001 in all cases. The symptom clusters were then mapped onto a PCA. Each symptom cluster separated from the remainder along PC1, particularly the phenotypes with rheumatologic symptoms.

Conclusion. This study presents an in-depth characterization of post-Ebola syndrome in Sierra Leonean survivors. The interrelationship between symptom clusters indicates that post-Ebola syndrome is a heterogeneous disease. The phenotypes identified may have unique mechanisms of pathogenesis, and require distinct therapies.

Disclosures. John Schieffelin, MD, MSPh, Wolters-Kluwer (Independent Contractor)

32. Risk Factors for Vertical Transmission of t. Cruzi Infection in an Endemic Setting

Melissa D. Klein, BS; Freddy Tinajeros, PhD; Edith Malaga, BS; Manuela Verástegui, PhD; Beth J. Condori, BS; Federico Urquizu, MD; Robert Gilman, MD; Natalie M. Bowman, MD, MPH; University of North Carolina at Chapel Hill, Chapel Hill, North Carolina; 4 Association Beneficcia PRISMA, Santa Cruz de la Sierra, Santa Cruz, Bolivia; Universidad Peruana Cayetano Heredia, Lima, Lima, Peru; 5 Percy Boland Women’s Hospital, Santa Cruz de la Sierra, Santa Cruz, Bolivia; 7 Johns Hopkins University, Baltimore, Maryland; 8 University of North Carolina, Chapel Hill, North Carolina

Session: O-7. Around the World - Understanding Infectious Disease and Health Interventions

Members of the Chagas Disease Working Group participating in Peru and Bolivia include: Edith Hinojosa, Clariza Chavez, Jean Karla Velarde, Carla Chavarria, Victoria Serrudo, Roberto Araya, Alcides Buitron, Rita Mendieta, Holger Mayta, Marilza Calderon, Holger Mayta and Yagahira Castro.

Background. Vertical transmission of Trypanosoma cruzi infection accounts for a growing proportion of new cases of Chagas disease. Congenital infection is curable if
treated promptly, but the majority of infected infants do not receive timely diagnosis or treatment. Better risk stratification is needed to predict which women are more likely to transmit the infection.

Methods. This study enrolled women who presented for delivery and their infants at the Percy Boland Women’s Hospital in Santa Cruz, Bolivia. Pregnant women were screened for Chagas disease by rapid test. The infants of seropositive mothers underwent diagnostic testing with microscopy (“micromethod”) and quantitative polymerase chain reaction (qPCR) as newborns and at one- and nine-month follow-up. Mothers completed surveys about demographics and medical history.

Results. Among 5,826 enrolled women, 1,271 (21.8%) screened positive for Chagas disease. Of the 1,325 infants of seropositive mothers, 113 (8.5%) were diagnosed with congenital Chagas disease by microscopy or qPCR. Cesarean delivery was significantly associated with lower odds of vertical transmission (adjusted OR: 0.63, 95% CI: 0.41–0.98, p=0.040). Congenital infection was more common in twins (adjusted OR: 3.30, 95% CI: 1.97–5.54, p<0.001) and male infants (adjusted OR: 1.50, 95% CI: 1.01–2.22, p=0.045).

Conclusion. Our findings suggest that Cesarean delivery may be protective against vertical transmission of T. cruzi, while twins and male infants may have an increased risk. A better understanding of risk stratification for congenital Chagas disease may help improve regional initiatives to reduce disease burden.

Disclosures. All Authors: No reported disclosures

33. Concerning Trends of Pediatric Leprosy in Minas Gerais, Brazil and Associations with Number of Municipality Medical Facilities

Taylor Land,2,3 TP,; Jane A. Gionfriddo, PhD4; José A. Ferreira, PhD5; Lucila A. Fraga, PhD5; Maria Aparecida E Grossi, MD, PhD4; Jessica K. Fairley, MD MPH1; Emory University Rollins School of Public Health, Atlanta, Atlanta, GA; 1Emory University College of Arts and Sciences, Atlanta, Georgia; 2Faculdade da Saúde e Ecologia Humana, Vespasiano, Minas Gerais, Brazil; 3Universidade Federal de Juiz de Fora - Campus GV, Governador Valadares, Minas Gerais, Brazil; 4Emory University, Division of Infectious Diseases, Atlanta, Georgia

Session: O-7. Around the World - Understanding Infectious Disease and Health Interventions

Background. Leprosy in children under 15 years of age, and in particular, the presence of leprosy grade 2 disability (G2D) in children, signifies ongoing transmission and the need for improved surveillance. Our objective was to describe the epidemiology of pediatric leprosy in Minas Gerais, Brazil and to explore associations with access to medical facilities. Methods. A cross-sectional study was conducted using data from the Brazilian Notifiable Diseases Surveillance System (SINAN) from 2002–2017. Incident cases were included if they resided in a municipality with both adult and pediatric cases. Municipalities were divided by the number of medical facilities per municipality: < 5, 5–17, and 18 or higher. Analyses compared pediatric cases across two time periods (2002–2009 and 2010–2017) and number of medical facilities / municipality using chi-square, t-tests, and logistic regression.

Results. A total of 27,725 cases were reported with 1,611 under 15 years of age. Overall incidence declined from 34.8 per 100,000 to 13.6 per 100,000 during the study period with pediatric incidence declining from 2.6 per 100,000 to 0.8 per 100,000. Incidence increased with lower number of medical facilities: 2.7 cases per 100,000 children residing in municipalities with < 5 medical facilities (aOR 1.88; 95% CI: 1.37–2.59), at 1.4 per 100,000 children was younger in TP2 then in TP1 (10.06 vs 10.43, p=0.02). In 2017, the pediatric incidence and the need for improved surveillance. Our objective was to describe the epidemiology of pediatric leprosy in Minas Gerais, Brazil and to explore associations with access to medical facilities. Methods. A cross-sectional study was conducted using data from the Brazilian Notifiable Diseases Surveillance System (SINAN) from 2002–2017. Incident cases were included if they resided in a municipality with both adult and pediatric cases. Municipalities were divided by the number of medical facilities per municipality: < 5, 5–17, and 18 or higher. Analyses compared pediatric cases across two time periods (2002–2009 and 2010–2017) and number of medical facilities / municipality using chi-square, t-tests, and logistic regression.

Results. A total of 27,725 cases were reported with 1,611 under 15 years of age. Overall incidence declined from 34.8 per 100,000 to 13.6 per 100,000 during the study period with pediatric incidence declining from 2.6 per 100,000 to 0.8 per 100,000. Incidence increased with lower number of medical facilities: 2.7 cases per 100,000 children residing in municipalities with < 5 medical facilities (aOR 1.88; 95% CI: 1.37–2.59), adjusted for age and sex. See map (Fig. 1).

Figure 1. Cases of Pediatric Leprosy By Number of Municipality Medical Facilities from 2002–2017 (White areas without reported pediatric leprosy)

Conclusion. The increasing proportion of G2D in children in the second half of the study period despite declining incidence suggest occult infections among children and adults alike in Minas Gerais. Furthermore, the average age of diagnosis in children should increase, not decrease, if M. leprae transmission was truly declining. Lastly, the association between fewer municipality health facilities and increased disability suggests barriers to timely diagnosis and a critical area of focus for research into access to healthcare and leprosy risk.

Disclosures. All Authors: No reported disclosures

34. Impact of Universal Mass Vaccination Programs of Children Against Hepatitis a with 2-dose and 1-dose Schedules: A Systematic Literature Review

Anar Andani, BSc1; Pierre van Damme, MD, PhD2; Eveline M. Bunge, PhD3; Fernanda Salgado, MD, MSc4; Rosa C. van Hoorn, MSc5; Bernard Hoet, MD, FFPMP6; GSK, Wavre, Belgium, Wavre, Brabant Wallon, Belgium; 7University of Antwerp, Campus Drie Eiken, wilrijk, Antwerpen, Belgium; 8Pallas Health Research and Consultancy, Rotterdam, the Netherlands, Rotterdam, Zuid-Holland, Netherlands

Session: O-7. Around the World - Understanding Infectious Disease and Health Interventions

Background. With more than 100 million new hepatitis A (HepA) virus (HAV) infections estimated each year, HepA is a serious health concern worldwide. Several countries implemented 2- or 1-dose universal mass vaccination (UMV) programs of children with HAV vaccines. Here we present the first systematic review describing the impact of 2- and 1-dose UMV programs on HepA incidence and related health outcomes.

Methods. We systematically searched several databases for data published between Jan 2000–Jul 2019 (Figure 1). We assessed available evidence for 2- and 1-dose UMV programs with inactivated HAV vaccine in children worldwide, in terms of impact on HepA incidence, disease severity and mortality, vaccine efficacy, vaccine effectiveness and antibody persistence.

Figure 1. PRISMA flowchart

Results. 3739 articles were screened and 34 studies were included in our analysis (Figure 1). 18 real-world studies in 9 countries showed that HepA incidence declined in all ages following introduction of 2-dose and 1-dose UMV programs and persisted for at least 14 years (2-dose) and at least 6 years (1-dose) (Figure 2). Evidence for 1-dose schedule was limited to only 3 studies. HAV related outcomes (disease severity, mortality) decreased after UMV with either 2-dose or 1-dose schedules. Vaccine effectiveness for the 2-dose schedule was ≥ 95% over 3–5 years. Vaccine efficacy for the 1-dose schedule was > 98% over 0.1–7.5 years. Anti-HAV antibody persistence rates for the 1-dose schedule were ≥ 90% up to 10 years with 2-dose and 1-dose schedules. Vaccine efficacy and antibody persistence rates for the 1-dose schedule. Anti-HAV antibody GMC data is presented in Table 1.

Figure 2. Impact of vaccination on hepatitis A incidence in countries implementing 2-dose or 1-dose schedules (data from studies presenting all ages’ incidence data)