8001

LONGITUDINAL RESPONSES IN THE TISSUES AND BLOOD OF NON-HUMAN PRIMATES DURING IMMUNIZATION WITH WHOLE *PLASMODIUM* SPOROZOITES

Gregory Boggy[1], Rowland Osii[1], Melanie Shears[2], David Morrow[1], Maya Aleshnick[1], Payton Kirtley[1], Derek Haumpy[1], Julie Mitchell[1], Jack Schell[1], Roxanne Beebe[1], Miranda Fischer[1], Sean Murphy[2], Jeremy Smedley[1], Scott Hansen[1], Benjamin Bimber[1], **Brandon Wilder**[1]

[1]Oregon Health and Science University, Beaverton, OR, United States, [2]University of Washington, Seattle, WA, United States

A hallmark feature of malaria is that an individual can be repeatedly infected with the same *Plasmodium* species, and even the same parasite clone, with induction of little functional immunity. With years of exposures, the likelihood of symptomatic infection decreases and malaria becomes an often chronic, asymptomatic infection. The exact mechanisms underlying this complex immunology are incompletely understood, but involve a myriad of innate and adaptive immune responses from the host with numerous compensatory immune evasion tactics by the parasite. The impact of this broad immune regulation on vaccine responses is unclear, but the efficacy of live-attenuated whole sporozoite vaccines is clearly lower in malaria endemic areas. Studying this interaction between previous infection and vaccine responses in humans is difficult, owing to heterogeneity in exposure to parasites and inaccessibility of the tissues where much of the parasite infection and immunology occur. To address this, we have used a non-human primate model of malaria, *P. knowlesi* infection of macaques. We vaccinated with live sporozoites under chemoprophylaxis ("CVac") with or without previous infection as a means to study the interaction between infection and complex, tissue-resident immunity following vaccination. Using minimally-invasive tissue sampling, we studied the longitudinal immune response to infection and vaccination in n=16 animals. At multiple time points we sampled the liver, bone marrow, lymph nodes and spleen and analyzed these at the single cell level. Data collection is complete and analysis is ongoing. Our early analysis has demonstrated that the tissues hold unique immunological signatures as compared to the blood, and our strategy has allowed us to see the *in situ* cellular response to parasite infection/immunization in the liver by sampling early after sporozoite inoculation. We will present the latest findings with a focus on innate and innate-like cells as well as classic adaptive immune subsets and how these responses relate to previous exposure and protection from sporozoite challenge.

8002

TREATING CEREBRAL MALARIA IN AFRICAN CHILDREN, TRANSLATING MECHANISTIC INSIGHTS TO BEDSIDE RESULTS

Brittany A. Riggle[1], Dorian B. McGavern[2], Douglas G. Postels[3], Louis H. Miller[1], Susan K. Pierce[1]

[1]National Institutes of Health-NIAID, Rockville, MD, United States, [2]National Institutes of Health-NINDS, Bethesda, MD, United States, [3]Children's National Hospital, Washington, DC, United States

Mosquito-transmitted *Plasmodium falciparum* infections cause malaria, an infectious disease that is disproportionately fatal in young children in Africa. Malaria-associated fatalities are overwhelmingly caused by the most severe form of malaria, cerebral malaria (CM). CM does not adequately respond to intravenous antimalarial therapy and at present we have no adjunctive therapies to treat CM. The abundance of infected red blood cells observed accumulated in the cerebral vasculature of children that die of CM led to the dogma that brain-sequestered infected red blood cells were the lead cause of CM. A widely used mouse model of CM provided evidence that $CD8^+$ T cells play a critical role in pathogenesis but because few studies reported lymphocytes in human cerebral vasculature in CM, the findings in mice were largely ignored, stymying efforts to identify therapies that target human T cells in CM. Using the mouse model, we sought to identify drugs that rescued mice from CM even after disease onset including blood brain barrier breakdown and brain swelling. We also looked for clues that disease pathogenesis in mice closely mirrored human disease and discovered remarkable similarities between mice and humans in both the frequency and distribution of $CD8^+$ T cells in brains, and in brain pathology by MRI. Based on our findings we identified a strong candidate for CM therapy, DON, and initiated a Phase I/IIa clinical trial of DON as an adjunctive therapy for CM in African children in Malawi involving healthy adults, adults with uncomplicated malaria and children with CM. Thus far DON has proven to be safe in adults and we are poised to begin DON studies in children. We are also continuing studies to determine the cellular and molecular mechanisms underlying disease pathology and the role of immunologic responses along the CNS borders in the mouse using intravital imaging and multiparameter immune histochemistry with a view towards the development of future CM therapies.

8003

THE PUTATIVE RECEPTOR BINDING REGION IS THE IMMUNODOMINANT REGION OF PLASMODIUM MALARIAE RETICULOCYTE BINDING PROTEIN 1A

Harry Danwonno[1], Daniel Dosoo[1], Richmond Boateng[1], Peter Okutu[1], Nelson Edu[1], Kwadwo Kusi[2], Gordon Awandare[1], Yaw Aniweh[1]

[1]West African Centre for Cell Biology of Infectious Pathogens, Legon, Ghana, [2]The Noguchi Memorial Institute for Medical Research, Legon, Ghana

The adoption of highly sensitive molecular diagnostic techniques has highlighted the underreporting of *Plasmodium malariae* infections. *P. malariae* has been linked to severe complications, including nephrotic syndrome, cholecystitis, and fatal anemia. The mechanisms behind these complications remain poorly understood. Moreover, the oversight of *P. malariae* in malaria elimination programs may contribute to the continued prevalence and spread of this parasite. Among the P. malariae reticulocyte binding proteins (*Pm*RBPs), *Pm*RBP1a is notably distinct, suggesting its potential role as a critical factor in host specificity and a key mediator in erythrocyte invasion. To explore this, the large antigen was segmented into five fragments, carefully preserving functional domains. These fragments were then expressed, purified, and assessed for the presence of acquired antibodies using indirect ELISA in human plasma samples collected from four localities in Ghana: Akwakrom, Kintampo, Navrongo, and Suhum. Seropositivity was high across the fragments, indicating significant exposure: 70% for fragment one, 62% for fragment two, 65% for fragment three, 57% for fragment four, and 58% for fragment five, compared to 85% for *Pf*DBL-2 and 61% for *Pf*Rh5. Notably, fragment one, which contains the putative receptor-binding domain, showed the highest antibody levels, underscoring its importance in host-pathogen interactions. Additionally, antibody responses correlated positively but marginally with age and exposure, particularly for fragment one again. This data not only reveals a higher exposure to *P. malariae* than previously reported but also emphasizes the need for further research into the receptor-binding domain. Future studies should also investigate the cross-reactivity of these antibodies with homologous antigens in other Plasmodium species.

8004

CHARACTERIZATION OF COINFECTION WITH SOIL TRANSMITTED HELMINTHS CAUSED BY *PLASMODIUM VIVAX* BASED ON CITOKINE BALANCE IN A CHILD POPULATION FROM AN ENDEMIC AREA OF COLOMBIA

Mayra Raciny[1], María Fernanda Yasnot Acosta[1], Ana Rodriguez Fernandez[2]

[1]Cordoba University, Monteria, Colombia, [2]New York University, New York, NY, United States

Characterizaction of *Plasmodium vivax* geohelminth coinfection from the cytokine balance in a child population in a Colombian endemic area.The balance of the immune response mediated by the plasma balance of pro/anti-inflammatory cytokines in the infantile population

of an endemic area for geohelminths - *P. vivax* coinfection allows to know its behavior in front of the coinfection, which through antagonistic answers consent the homeostasis of the immune system. The effect of geohelminths - *P. vivax* coinfection on the balance of pro/anti-inflammatory cytokines in children population of Colombian endemic area was measured. An analytical observational study was carried out, fifty-eight (58) children were selected and studied in two groups (coinfected and control). Stool samples were processed by Kato Katz for identification and quantification of geohelminths and blood plasma was used for flow cytometry quantification of cytokines and chemokines. The prevalence of confection was 46% (33.1-58.8). When comparing cytokines and chemokines between groups, those of the proinflammatory profile IL-6 (19.4(14.7-83.9)P<0.0001), IFN-γ (98.8 (6.8-20.4)P<0.0001) and IP-10 (1036 (159. 4 - 2611)P<0.0001) showed higher concentrations in coinfected than in controls; as did the anti-inflammatory cytokines IL-10 (121.4 (49.7 - 1654)P<0.0001) and TGF-β (162.4 (13.5 - 412.1)P= 0.0007). The results of IL4 (4.3 (3.7 - 5.4) P= 0.0354) did not show biologically important elevation in plasma concentrations in the coinfected children; which supports the idea that the concentrations of this cytokine depend on the levels of host parasitemia, in this study it was found that both geohelminths and *P. vivax* in the coinfected group had mild to moderate intensities of infection. In conclusion, cytokine and chemokine variations of proinflammatory and anti-inflammatory profiles in coinfected individuals exhibit marked increases in IL10 concentration when individuals are infected with *P. vivax*, acting as a regulator of the expression of these molecules; geohelminths do the same with increased plasma concentration of TGF-β1.

8005

PLASMODIUM INFECTION AND ANTIBIOTIC USE DURING SEVERE MALARIA INDUCE GUT BACTERIA DYSBIOSIS THAT INCREASES THE RISK OF MORTALITY IN CHILDREN

Olivia J. Bednarski[1], Ruth Namazzi[2], Robert O. Opoka[3], Chandy C. John[1], Andrea L. Conroy[1], Nathan W. Schmidt[1]

[1]IUSM, Indianapolis, IN, United States, [2]Makerere University College of Health Sciences, Kampala, Uganda, [3]Aga Khan University East Africa Medical College, Nairobi, Kenya

The gut microbiome has been implicated in malaria pathogenesis in murine models and limited cross-sectional human studies. However, it remains unknown if severe malaria impacts the gut microbiome in humans or if the gut microbiome contributes to the pathogenesis of severe malaria in African children. To investigate how the gut microbiome contributes to severe malaria, we analyzed gut bacteria populations in stool samples from children under 5 years old collected during hospital admission for severe malaria in 449 children and 71 healthy age-matched community children in Uganda. Differential bacterial abundance analysis revealed that the Enterobacteriaceae family was elevated in children with severe malaria as well as Bacteroides, Enterococcus, and Parabacteroides genera. Expansion of Enterobacteriaceae was associated with death in children with severe malaria and was found to mediate death through multiple comorbidities like lactic acidosis and intestinal damage. The Enterobacteriaceae family contains potential pathogens including Shigella, Escherichia, Klebsiella, Enterobacter, and Salmonella that can cause serious complications if they enter the bloodstream. Of the children with positive blood cultures, over half of the bacteria were members of the Enterobacteriaceae family. Factors associated with the expansion of these bacteria include prior antibiotic use, increased time since eating, neutrophil abundance, and hemeoxygenase-1. Increased inflammation and changes in the nutrient niche through the removal of commensals and enhanced oxygen and nitrogen respiration may support the expansion of Enterobacteriaceae. Consistently, metagenome sequencing confirmed the potential for aerobic respiration of alternative carbon sources in Enterobacteriaceae in children with severe malaria. Collectively, severe malaria is associated with gut bacteria dysbiosis, including the expansion of Enterobacteriaceae that may contribute to severe malaria-related deaths. Treatments that prevent the expansion of or target Enterobacteriaceae may help reduce mortality in children with severe malaria.

8006

VAR2CSA EXPRESSION IN CEREBRAL MALARIA IN MALIAN AND MALAWIAN CHILDREN

Emily M. Stucke[1], Drissa Coulibaly[2], Rafal Sobota[1], Jonathan G. Lawton[1], Savy M. Sebastian[1], Jean-Paul Courneya[1], Matthew Adams[1], Noah T. Ventimiglia[1], James B. Munro[1], Ankit Dwivedi[1], Antoine Dara[2], Abdoulaye K. Koné[2], Karim Traoré[2], Bouréima Guindo[2], Bourama Tangara[2], Amadou Niangaly[2], Modibo Daou[1], Issa Diarra[2], Youssouf Tolo[2], Mody Sissoko[2], Bryan Cummings[1], Albert E. Zhou[1], Matthew B. Laurens[1], Amed Ouattara[1], Bourema Kouriba[2], Ogobara K. Doumbo[2], Shannon Takala-Harrison[1], Christopher V. Plowe[1], Joana C. Silva[1], Don P. Mathanga[3], Terrie E. Taylor[4], Mahamadou A. Thera[2], Karl B. Seydel[4], Mark A. Travassos[1]

[1]University of Maryland School of Medicine, Baltimore, MD, United States, [2]University of Sciences, Techniques, and Technologies, Bamako, Mali, [3]Kamuzu University of Health Sciences, Blantyre, Malawi, [4]Michigan State University, East Lansing, MI, United States

VAR2CSA is the most conserved *Plasmodium falciparum* erythrocyte membrane protein-1 (PfEMP1) antigen and mediates binding to chondroitin sulfate A in placental malaria. Recent studies have found that *var2csa* transcription may also reflect *var* switching and regulation. To identify PfEMP1 variants expressed in severe malaria, we conducted a case-control study in children in Mali, West Africa from 2014-2018. We enrolled cases of cerebral malaria (CM), severe malarial anemia (SMA), concurrent CM+SMA, and matched uncomplicated malaria controls with or without a history of CM. Using RNA-seq and *de novo* assembled transcripts, we identified PfEMP1 transcripts expressed in clinical infections and quantified expression by calculating the metric transcripts per million. *var2csa* transcripts were present in more than half (62%) of infections. Across all severe malaria cases, we found significantly greater expression of *var2csa* compared to controls without a history of CM (Wilcoxon signed-rank test, N=34 pairs, P=0.0096) and controls with a history of CM (N=18 pairs, P=0.016). Unique *var* transcript count within each infection was significantly higher in severe malaria cases compared to both control groups (without history of CM: P=0.0075; with history of CM: P=0.0038). In the CM subset, there was significantly greater expression of *var2csa* compared to controls without a history of CM (N=14 pairs, P=0.00061) but not compared to controls with a history of CM (N=8 pairs, P=0.27). Unique *var* transcript count was significantly greater in CM compared only to controls without a CM history (P=0.049). Interestingly, we did not observe any significant differences in *var2csa* expression in SMA or CM+SMA cases compared to matched controls. We detected levels of *var2csa* expression in Malawian children with CM (9/10 cases) that were similar to that in Malian CM cases. Significant expression of *var2csa* in CM may reflect higher rates of *var* switching, which could allow infection to persist. Further investigation of *var2csa* in CM may provide insights into how patterns of *var* expression contribute to disease severity.

8007

CIRCULATING PLATELET-LEUKOCYTE AGGREGATES CORRELATE WITH THROMBOCYTOPENIA AND DEATH IN PEDIATRIC CEREBRAL MALARIA

Sushantti Rupesh[1], Visopo Harawa[2], Monica Soko[2], Priscilla Suleman[2], Patricia Mawindo[2], Terrie Taylor[3], Karl B. Seydel[3], Iset M. Vera[1], Kami Kim[1]

[1]University of South Florida, Department of Internal Medicine, Division of Infectious Diseases and International Medicine, Tampa, FL, United States, [2]Blantyre Malaria Project, Kamuzu University of Health Sciences, Blantyre, Malawi, [3]Michigan State University, Department of Osteopathic Medical Specialties, College of Osteopathic Medicine, Michigan State University, East Lansing, MI, United States

Cerebral malaria (CM) is a severe manifestation of malaria that is characterized by coma and seizures. Parasite load, virulence factors, host-derived molecules and cellular interactions contribute to pro-inflammatory mechanisms leading to pathophysiological exacerbation. Monocytes and platelets are independently implicated in the pathogenesis of CM and

found at sites of parasite sequestration in the brain microvasculature. Platelet-Monocyte Aggregates (PMA) in the periphery serve as a marker of platelet activation and inflammation. Increased levels of PMA are associated with severity in cardiovascular disease, autoimmune disease, and other infections (Dengue, HIV, tuberculosis, sepsis and COVID-19). Using flow cytometry, we analyzed circulating PMA and circulating activated platelets (aPLT) in the blood of children with CM (N=45) relative to children with uncomplicated malaria (UM, N=45). Levels of both PMA (%CD41+ monocytes/total monocytes) and aPLT (%CD62p+/total platelets) were lower in the blood of CM patients relative to UM patients (PMA: 23% vs. 51.1%, p=0.001; aPLT: 7% vs. 12%, p=0.01). In CM cases, PMA levels correlated positively with aPLT levels (R_s=0.53, p=0.001), with platelet count (R_s= 0.67, p<0.001), and with soluble CD62p, an acute phase marker of platelet activation (R_s=0.51, p<0.001). PMA and aPLT levels were inversely related to levels of TNFα, a marker of inflammation (R_s=-0.45, p=04), and host cell-free DNA levels (R_s=-0.47, p=0.04), a marker of NETosis which we have previously shown to be associated with death, and with parasitemia (R_s=-0.47, p=01). Logistic regression analysis associated decreased levels of PMA (LR=3.97, AUROC=0.731, p=0.046) and aPLT (LR=5.39, AUROC=0.791, p=0.02) with death in CM patients. Collectively, these data suggest platelet activation and coagulation processes occur early in acute malaria with platelet consumption as inflammation progresses during severe disease. The inverse relationship between platelet activation and disease severity, different from that seen in other pathologies, emphasizes the unique role of consumptive coagulopathy in the pathogenesis of CM.

8008

INVESTIGATING THE ROLE OF HOST C1QBP IN *PLASMODIUM FALCIPARUM* INFECTED ERYTHROCYTE BINDING TO HUMAN BRAIN MICROVASCULAR ENDOTHELIAL CELLS

Nouhoum Diallo, Alexandra Rowe
University of Edinburgh, Edinburgh, United Kingdom

Sequestration of *P. falciparum* infected erythrocytes in human brain microvasculature is the hallmark of cerebral malaria. Sequestration is mediated by the interaction between *P. falciparum* erythrocyte membrane protein one (PfEMP1) family members and receptors expressed on human endothelial cells. Severe and cerebral malaria are associated with the expression of specific PfEMP1 subtypes, while the identity of the key host receptors involved in brain sequestration remains controversial but may include endothelial protein C receptor (EPCR) and intercellular adhesion molecule one. Previous work suggests that C1q Binding Protein (C1QBP) may also play a role in sequestration in the brain, but this has rarely been studied. In this study, we used a) immunofluorescence assays to examine the cellular localization of C1QBP and b) adhesion experiments to determine the role of C1QBP in *P. falciparum* infected erythrocyte (IT4VAR19 and HB3VAR03) adhesion to the human brain microvascular endothelial cell (hCMEC/D3). Resting and TNFα-activated hCMEC/D3 showed intracellular staining for C1QBP but cell surface staining was not observed. However, incubation with soluble C1QBP or human plasma (which contains soluble C1QBP), hCMEC/D3 did exhibit positive surface membrane expression of C1QBP. In static binding assays to purified receptors, IT4VAR19 showed low-level but consistent binding to C1QBP and high-level binding to EPCR. Adhesion inhibition assays showed that a monoclonal antibody (mAb) to EPCR blocked the interaction between IT4VAR19 and hCMEC/D3, whereas a mAb to C1QBP did not. HB3VAR03 did not bind to C1QBP, nor to any other known endothelial receptors in the static assays, despite showing good binding to hCMEC/D3 cells. C1QBP is not constitutively expressed on the surface of human brain endothelial cells but can become membrane-associated after exposure to human plasma. However, the *P. falciparum* lines tested here did not show high level binding to C1QBP and their adhesion to human brain endothelial cells was not substantially inhibited by a mAb to C1QBP. Overall, the results do not support C1QBP being a key host receptor in cerebral malaria.

8009

CHILDREN WITH CEREBRAL MALARIA LACK IMMUNITY TO SPECIFIC RIFIN AND STEVOR ANTIGENS

Jonathan G. Lawton[1], Albert E. Zhou[1], Drissa Coulibaly[2], Aarti Jain[3], Rie Nakajima[3], Algis Jasinskas[3], Emily K. Silzel[3], Biraj Shrestha[1], Emily M. Stucke[1], Abdoulaye K. Kone[2], Amadou Niangaly[2], J. Alexandra Rowe[4], Matthew B. Laurens[1], Amed Ouattara[1], Bourema Kouriba[2], Shannon Takala-Harrison[1], Kirsten E. Lyke[1], Christopher V. Plowe[1], Ogobara K. Doumbo[2], Philip L. Felgner[3], Mahamadou Thera[2], Mark A. Travassos[1]
[1]University of Maryland School of Medicine, Baltimore, MD, United States, [2]University of Sciences, Techniques and Technologies, Bamako, Mali, [3]University of California, Irvine, Irvine, CA, United States, [4]University of Edinburgh, Edinburgh, United Kingdom

In severe malaria, *Plasmodium falciparum* parasites sequester in the microvasculature and adhere to erythrocytes, processes mediated by variant surface antigens. Protection against severe malaria is associated with antibodies targeting parasite antigens and host traits like blood type O. The roles of the RIFIN and STEVOR antigen families in severe malaria and their interactions with host ABO blood antigens remain poorly understood. We hypothesized that severe malaria cases exhibit lower antibody responses to virulence-associated RIFIN-A and STEVOR variants than uncomplicated malaria controls during acute infection, indicating immune deficits that may predispose children to severe outcomes. These "gaps" may vary by disease phenotype and ABO blood type. We analyzed sera from 236 Malian children aged 0-14 years enrolled in a 1999-2003 severe malaria case-control study, including 67 age-matched pairs. Severe cases had cerebral malaria (CM; 37 pairs), severe malarial anemia (SMA; 20 pairs), or a syndrome featuring both CM and SMA (CM+SMA; 10 pairs). We used protein microarrays to measure serological responses to 116 RIFIN-As, 51 RIFIN-Bs, and 35 STEVOR variants, including 189 3D7 and 13 non-3D7 sequences. Antibody gaps were defined as statistically significant seroreactivity deficits in cases vs. controls (p-value < 0.05), assessed using paired Wilcoxon tests or unpaired, age-adjusted linear regressions. Sera of CM cases had antibody gaps against 16 RIFIN-As, including two variants that inhibit B cells via LILRB1 binding, and two RIFIN-Bs. CM+SMA cases had gaps against two RIFIN-As, four RIFIN-Bs, and eight STEVORs. SMA cases had no significant gaps to RIFINs or STEVORs. CM cases with blood type O (n=7) had gaps against 37 RIFINs and two STEVORs vs. unmatched type O controls, including two LILRB1-binding RIFIN-As and one RIFIN-A involved in rosetting. CM cases with non-O blood (n=25) had no gaps to RIFINs or STEVORs. Antibody gaps to RIFIN and STEVOR antigens varied significantly by malaria syndrome and host ABO blood type. Our future serologic and transcriptomic studies will continue to decipher these complex host-pathogen interactions.

8010

DECIPHERING THE HOST RESPONSE TO *PLASMODIUM FALCIPARUM* BY PLASMA PROTEOMICS

Pinkus Tober-Lau, Clemens Dierks, Michael Mülleder, Markus Ralser, Florian Kurth
Charité - Universitätsmedizin Berlin, Berlin, Germany

Plasmodium falciparum malaria may present with a wide range of disease severity, depending, among other factors, on genetic background and previous exposure to the parasite. Here, we applied high-throughput LC-MS/MS plasma proteomics to identify signatures of disease severity and varying immunity in 263 malaria patients from an endemic region and returning travellers, including 25 asymptomatic (APF), 180 uncomplicated (UPF), and 58 severe (SPF) cases with varying degrees of semi-immunity (i.e., childhood and residency in an endemic region, previous malaria episodes), as well as healthy controls (HC). Patients were enrolled in two prospective cohort studies at Centre de Recherches Médicales de Lambaréné (CERMEL), Gabon, and Charité - Universitätsmedizin Berlin, Germany. Clinical data and samples were collected at d0, d3, d7, and d14. Of 330 detected proteins, 209 were differentially regulated depending

on disease severity, mainly reflecting the acute phase response (e.g. SAA1, AHSG), immune reaction (e.g. C1, immunoglobulins), and tissue reconstitution (e.g. GSN, EFEMP1). The degree of dysregulation generally correlated with severity, reflecting a continuous increase in the host response. Notably, many protein levels were similar in APF and HC. In UPF, proteome alterations were more pronounced in patients in Germany: numerous markers associated with inflammation (e.g. LBP, SAA1) were significantly lower in patients in Gabon than in Germany, regardless of descent, and proteins associated with milder disease (e.g. GSN) were higher, indicating a modulated immune response in frequently exposed patients. Applying an SVM-based machine learning (ML) classifier, we were able to accurately distinguish between disease severities and immunity. Combining plasma proteomics and routine clinical data with ML techniques allows for better understanding of the specific host response to P.f. malaria in different populations with varying degrees of immunity. This is especially important in light of increasingly effective management of malaria and consequently less exposure and waning semi-immunity in formerly endemic regions.

8011

HYPERPARASITAEMIA: A CONSISTENT PRESENTATION IN *PLAMODIUM FALCIPARUM* MALARIA IN THE UK SINCE COVID

Debbie Nolder[1], Lindsay B. Stewart[1], Helen Liddy[1], Claire Rogers[1], Kieran Killington[1], Anna Checkley[2], Peter L. Chiodini[2], Colin J. Sutherland[1]

[1]London School of Hygiene & Tropical Medicine, London, United Kingdom, [2]Hospital for Tropical Diseases, London, United Kingdom

Malaria caused around 240 million cases and over 600,000 deaths in 2020, a marked increase on 2018-19, largely attributable to the COVID-19 pandemic.. Although most malaria deaths occur in endemic countries, imported malaria in the UK continues to cause avoidable deaths.
The UK Health Security Agency (UKHSA) Malaria Reference Laboratory (MRL) runs a passive case detection system. All notified malaria cases are initially diagniosed by blood film microscopy or rapid diagnostic tests at the referring hospital. For subsequent confirmation and/or diagnosis by the MRL, thick and thin blood films for microscopy and an aliquot of EDTA blood for molecular analyses and archiving are requested from the referring hospital. The MRL carries out retrospective qPCR molecular surveillance on all received blood samples to confirm species and drug resistance genotypes in relation to geographical origin. For each notified case, demographic, clinical and epidemiological data supplied are entered onto a database by MRL staff. From mid-2020 onwards we noticed increased numbers of cases with high parasitaemia (>2%) and hyperparasiatemia (>5%) presenting, a post-pandemic trend which has continued. To investigate, we analysed all *available P. falciparum*-positive blood samples received by the MRL from Jan 2019 to Dec 2022. We used an in-house probe-based qPCR protocol targeting the 18S rRNA gene, normalised to the WHO International Standard for P. falciparum DNA, to estimate *P. falciparum* parasitaemia in all samples. Results were compared with estimated parasite densities from microscopy, available for only a subset of blood samples. For data analyses, samples were separated into pre- (n=1332) and post-pandemic (n=2022) using 1st March 2020 as pivotal date. We present data from 3,354 successfully quantified UKHSA MRL samples collected during this period. Our results suggest an increase in the prevalence of P. falciparum hyperparasitaemia among notified UK malaria cases from the coronavirus pandemic onset until the present time. Risk factor analysis for hyperparasitaemia in this patient group will also be presented.

8012

PLASMODIUM FALCIPARUM ESTABLISHES CHRONIC INFECTIONS THROUGH HIGH *VAR* GENE EXPRESSION SWITCHING RATE

Mathieu Quenu[1], Prince Nyarko[1], Thomas Lavstsen[2], Antoine Claessens[1]

[1]Université de Montpellier, Montpellier, France, [2]University of copenhagen, Copenhagen, Denmark

How can *Plasmodium falciparum* parasites evade the immune system for months to establish long chronic asymptomatic infections? The prevailing hypothesis, mainly based on *in vitro* data from cultured parasites, is the antigenic variation of *var* genes, a family encoding PfEMP1 antigens located at the surface of the erythrocyte. The parasite would regularly switch between the expression of one of its ~60 *var* genes, therefore escaping the immune response built from pre-existing host antibodies. Here, in a study conducted in The Gambia where malaria is seasonal, we investigated the pattern of *var* gene expression in 26 *P. falciparum*-infected individuals during the wet season and in 16 chronically-infected individuals with 6 monthly blood samples. *Var* transcription was determined by amplicon sequencing of the semi-conserved *var* DBLa domain. In parallel, full length *var* gene sequences were retrieved from DNA long-read sequencing (PacBio). The Shannon entropy index, which measures the breadth of *var* gene expression within an isolate, was significantly lower in the dry season compared to the wet season, suggesting of immune selection pressure. Thanks to the longitudinal monthly timepoints, we observed distinct *var* gene transcription patterns from one month to the next, indicating a high *var* turnover rate. Against expectations, our investigation of monoclonal infections revealed the widespread presence of *var* genes that were recurrent, i.e. expressed at multiple timepoints within the same infection. These results suggest that a pattern of low *var* gene immunogenicity could contribute to the establishment of long chronic asymptomatic malaria infections, with parasites populations capable of re-utilizing a subset of their *var* genes throughout the infection.

8013

TRANSCRIPTIONAL ANALYSIS OF DIFFERENTIALLY EXPRESSED GENES AND PATHWAYS IN THE DEVELOPMENT OF SEVERE MALARIA

Linda Onyeka Anagu[1], Samuel Wassmer[2], Ikenna Anagboso[3], Jacinta Elo-ilo[4], Dorothy Ezeagwuna[4], Alfred Amambua-Ngwa[5]

[1]Nnamdi Azikiwe University, Agulu, Nigeria, [2]London School of Hygiene and Tropical Medicine, London, United Kingdom, [3]Nnamdi Azikiwe University, Nnewi, Nigeria, [4]Nnamdi Azikiwe University, Awka, Nigeria, [5]Medical Research Council Unit The Gambia at LSHTM, Banjul, Gambia

The occurrence of malaria in immune-naïve individuals or individuals with low immunity can be severe and lethal. The severity of malaria is partly due to an excessive pro-inflammatory immune response and the virulence of *Plasmodium*. *Plasmodium falciparum* parasites that cause severe malaria are mainly a subpopulation expressing specific *P. falciparum* erythrocyte membrane protein 1 (PfEMP1) which binds endothelial protein C receptor (EPCR) on endothelial cells. Peripheral blood mononuclear cells (PBMCs) are comprised of lymphocytes and monocytes that are differentiated and activated by inflammatory and pathophysiological conditions including febrile temperature, pipecolic acid (PA) & depleted lysophosphatidylcholine (LPC) and they equally affect the expression of PfEMP1. Can *P. falciparum* sense if there is immune pressure & alter its virulence phenotype? We will assess the differential transcriptional responses that occur in an *in vitro* system that mirrors blood-stage infection in malaria. Using a co-culture model, we will evaluate the transcriptome of pooled PBMCs from malaria-naive individuals or semi-immune individuals and parasites isolated from children with severe malaria. The PBMCs and parasites will be grown on a layer of human dermal endothelial cells expressing EPCR. Co-culture will be repeated in the presence of PA and depleted LPC. RNA sequencing of the PBMCs and parasites, and bioinformatics analysis of the resulting immunological and parasite responses will identify genes and pathways

involved in the regulation of anti-disease immunity and parasite adaptation to immune pressure. Our findings will help in the identification of modifiable host and parasite factors involved in the development of severe malaria. Our preliminary findings show that in the presence of endothelial cells majorly expressing EPCR, heat shock can increase the expression of PfEMP1 EPCR-binding domain, CIDR α1.5a, in the parasite. We did not see the impact of the immune cells used in the co-culture because we were only able to use immortalized monocytes/macrophages. Further studies of this parasite-host immune interaction are ongoing.

8014

UNDERSTANDING HOW VARIABILITY IN CULTURE TECHNIQUE IMPACTS THE LEVEL OF OXYGEN TENSION IN *PLASMODIUM FALCIPARUM* IN VITRO STUDIES

Dinah Nahid[1], Cameron Sherlock[1], Amy K. Bei[2], Regina Joice Cordy[3]

[1]Wake Forest University, Winston-Salem, NC, United States, [2]Yale School of Public Health, New Haven, CT, United States, [3]Wake Forest University, Winston Salem, NC, United States

Plasmodium falciparum is exposed to variations in environmental oxygen during its development within different organ systems having different oxygen concentrations, in humans. The effect of this oxygen tension variation within-host on the parasite is not well understood. Foundational work done for making in vitro study of the parasite possible established that the parasite thrives best in lower oxygenated environments, making it a microaerophilic organism. This allowed researchers to be able to study the parasite in the lab and to date, the technical execution of in vitro parasite studies varies considerably by research groups. The range of culture containment devices and oxygen administration methods used are grounded in feasibility in maintaining long-term culture. What is not often considered is the effect of these devices on the dissolved oxygen concentration reaching the parasite cultures and the impact that variable oxygen tension has on parasite multiplication rate. We tested different containment devices and assessed the dissolved oxygen concentration of the parasite cultures for those contained in plugged flasks, in petri dishes within modular chambers, and for cultures contained within a tri-gas incubator with 1% O2 and 13% O2 administered to the parasite cultures. We also quantified the amount of oxygen binding to hemoglobin within erythrocytes of these parasite cultures via a colorimetric plate reader assay measuring the amount of oxyhemoglobin, deoxyhemoglobin, and methemoglobin. Furthermore, we measured parasite multiplication rate (PMR) in each condition to determine how oxygen conditions in culture impacted growth rate. Gaining a better understanding of oxygen diffusion within parasite culture will contribute to an enhanced understanding of how oxygen variation impacts the parasite's biology.

8015

IMPACTS OF CONCURRENT SEVERE MALARIA AND ENTERIC INFECTION ON CHILD HEALTH OUTCOMES

Nuzrath Jahan[1], Ruth Namazzi[2], Robert Opoka[3], Chandy John[4], Drew Capone[1]

[1]Indiana University, Bloomington, IN, United States, [2]Makerere University, Kampala, Uganda, [3]Aga Khan University East Africa, Nairobi, Kenya, [4]Indiana University School of Medicine, Indianapolis, IN, United States

Malaria and enteric infection - which may cause diarrheal disease - are major global health challenges and leading causes of childhood mortality and morbidity. There is a critical need to advance our understanding of the role that concurrent enteric infection and severe malaria has on child mortality and morbidity. These co-infections present a complex challenge in the management of severe malaria, as they may exacerbate the severity of the disease. Limited studies, which have typically focused on helminths, have shown that concurrent infections may modulate the host's immune response to *Plasmodium falciparum*, potentially contributing to deleterious long term health effects among children. We tested stool samples from children diagnosed with severe Malaria in Uganda to advance our understanding of these co-infections on health outcomes. From 2014 to 2017 we enrolled 598 children with severe malaria and 120 matched community controls ages 6 months to 4 years. Enrollment was conducted at Mulago National Referral Hospital in Kampala and Jinja Regional Referral Hospital in Uganda. At enrollment we collected stool and whole blood and characterized severe malaria by type. We followed up with children 12-months later and collected anthropometry data and assessed neurodevelopment via standardized tests. We analyzed a subset (n = 213) of the collected samples for 30 common enteric pathogens using real-time quantitative PCR. Among the 213 fecal samples analyzed, including children with severe malaria (n=188) and community controls (n=25), nearly all were positive for ≥1 bacterial pathogen (96%), followed by ≥1 protozoan pathogen (75%), and ≥1 viral pathogen (26%). Common enteric infections included Enteroaggregative *E. coli* (60%), *Giardia* (54%), *Cryptosporidium* (27%), *Campylobacter jejuni/coli* (24%), and *Shigella* (15%). We also detected *Plasmodium* spp. DNA in 28% of stools. Our planned analysis includes regression modelling to assess the impacts of co-infection by *Plasmodium falciparum* and enteric pathogens on long-term health outcomes (cognition, growth, and weight).

8016

THE IMPACT OF FALCIPARUM MALARIA INFECTION ON THE BRAIN: NEW FINDINGS FROM AN INDIAN COHORT

Sanjib Mohanty[1], Praveen K. Sahu[1], Angelika Hoffmann[2], **Samuel Wassmer**[3]

[1]Community Welfare Society Hospital, Rourkela, India, [2]Inselspital, University Hospital of Bern, Bern, Switzerland, [3]London School of Hygiene & Tropical Medicine, London, United Kingdom

Cerebral malaria (CM) is an acute nontraumatic encephalopathy and the most severe neurological complication of *Plasmodium falciparum* infection. Mortality is high, long-term neurocognitive deficits are frequently reported in pediatric survivors, and the pathogenetic mechanisms leading to CM are still debated. However, the recent application of advanced neuroimaging techniques to patients with CM has revolutionized our understanding of the disease. Over the past 8 years, our team has recruited severe and uncomplicated falciparum malaria patients at Ispat General Hospital in Rourkela, India. We combined serial brain magnetic resonance imaging (MRI) with cutting-edge clinical and laboratory investigations to better understand the factors influencing the development and outcome of CM. We demonstrated distinct pathogenic mechanisms in pediatric and adult CM and evidenced for the first time a frequent brain involvement in uncomplicated malaria and severe, non-CM patients. In the latter group, ~20% had MRI signatures associated with CM despite the absence of coma; this feature was strongly associated with the occurrence of acute kidney injury. Brain involvement in these patients was confirmed by elevated circulating levels of S100B and UCHL-1, two markers of brain damage and neuronal injury, respectively. Overall, our findings suggest that brain involvement is common in *P. falciparum* infection, which warrants closer neurocognitive follow-up, especially in adults.

8017

ROLE OF *PLASMODIUM FALCIPARUM* HEMOZOIN-ASSOCIATED PROTEINS IN THE PATHOGENESIS OF CEREBRAL MALARIA

Kelly Crotty, Ioana Clotea, Beatrix Ueberheide, Ana Rodriguez

NYU School of Medicine, New York, NY, United States

One of the hallmarks of cerebral malaria, a severe complication of *Plasmodium falciparum* infection, is the adhesion of *P. falciparum*-infected red blood cells (iRBCs) to the microvasculature of the brain, which is frequently accompanied by the weakening of the junctions between endothelial cells lining the blood-brain barrier (BBB), resulting in vasogenic edema. We have observed that incubation of human brain microvascular endothelial cells (HBMECs) with iRBCs *in vitro* results in the disruption of endothelial intercellular junctions and loss of barrier integrity. We have also observed that the rupture of iRBCs and release of its contents is necessary for the endothelial barrier disruption. Removing hemozoin, a heme crystal

that is formed during the blood stage of the parasite's life cycle, eliminates the iRBC lysate's ability to disrupt intercellular junctions in HBMECs. Furthermore, natural hemozoin purified from *P. falciparum*-iRBCs disrupts intercellular junctions in HBMECs, indicating that hemozoin carries the ability to induce the loss of barrier function in the brain endothelium. We also observed that, while natural hemozoin actively induces endothelial barrier disruption, commercially-available synthetic hemozoin does not have this effect. Since a variety of biomolecules including proteins, lipids, and nucleic acids from *P. falciparum*-iRBCs are bound to natural hemozoin, but not to synthetic hemozoin, we hypothesize that the biomolecules associated with natural hemozoin are required for endothelial barrier disruption. Further, treatment of the natural hemozoin with proteases inhibits endothelial barrier disruption, indicating that a protein bound to the hemozoin is contributing to this effect. To identify the protein(s) responsible for endothelial barrier disruption, fractionation of the hemozoin-bound proteins followed by quantitative mass spectrometry will be conducted. Further elucidating the mechanism behind brain endothelial barrier disruption in cerebral malaria may lead to the development of targeted therapeutics which could drive down the high morbidity and mortality rates of this complication.

8018

PHARMACOKINETIC AND PHARMACODYNAMIC MODELING OF MONTHLY TAFENOQUINE IN HEALTHY VIETNAMESE VOLUNTEERS FOR MALARIA PROPHYLAXIS AND ELIMINATION

Song H. Le[1], The T. Nguyen[1], Thu M. Nguyen[2], Long K. Tran[2], Huy C. Nguyen[3], Andrew G. Letizia[3], John S. Brooks[3], Michael J. Gregory[3], Geoffrey W. Birrell[4], Karin Van Breda[4], Dennis Shanks[4], Michael D. Edstein[4], **Joel Tarning**[5]

[1]108 Military Central Hospital, Hanoi, Vietnam, [2]Vysnova Partners (A Culmen International Company), Alexandria, VA, United States, [3]U.S. Naval Medical Research Unit INDO PACIFIC, Singapore, Singapore, [4]Australian Defence Force Malaria and Infectious Disease Institute, Brisbane, Australia, [5]Mahidol Oxford Tropical Medicine Research Unit, Bangkok, Thailand

Tafenoquine (TQ) is used for the radical cure of *Plasmodium vivax* infections and prevention of malaria. Because of TQ's favourable pharmacokinetics (e.g., elimination half-life ~15 days) the drug possesses attributes for monthly dosing to enhance drug adherence. We report on blood TQ concentrations to generate a pharmacokinetic (PK)/pharmacodynamic (PD) model of TQ in healthy Vietnamese volunteers participating in a TQ dose-escalating study. Participants received consecutively three TQ regimens: Regimen 1 (loading dose of 200 mg x 3 days, then two weekly 200 mg doses), Regimen 2 (two monthly 600 mg doses) and Regimen 3 (two monthly 800 mg doses). Adverse events (AEs) were recorded. Participants were randomized to two cohorts (A and B). Cohort A had sparse PK sampling during 1st weekly and 1st monthly dosing and cohort B had PK sampling during 2nd weekly and 2nd monthly dosing. A total of 193 participants were enrolled (97 (50.3 %) males, mean age 26.8 years and mean body weight 58 kg). Of these, 165 participants completed Regimen 1, 132 completed Regimen 2, and 107 completed either the 1st or 2nd monthly dose of Regimen 3. Blood TQ and 5,6 orthoquinine TQ concentrations were measured by liquid chromatography mass spectrometry (LCMS). Of the 107 participants that received Regimen 3, steady-state mean (±SD) maximum and minimum blood TQ concentrations, respectively, were 626 ± 120 ng/mL and 416 ± 71 ng/mL after the 1st weekly 200 mg dose, 953 ± 182 ng/mL and 269 ± 58 ng/mL after the 1st monthly 600 mg dose, and 970 ± 241 ng/mL and 286 ± 62 ng/mL after the 1st monthly 800 mg dose for cohort A participants (n=53). Corresponding values for cohort B participants (n=54) were 628 ± 140 ng/mL and 421 ± 98 ng/mL after the 2nd weekly 200 mg dose, 821 ± 217 ng/mL and 221 ± 81 ng/mL after the 2nd monthly 600 mg dose, and 1,025 ± 179 ng/mL and 291 ± 61 ng/mL after the 2nd monthly 800 mg dose. Metabolism of TQ to 5,6 orthoquinine TQ was low (1.1 ± 0.3%). AEs were few, mild and transient, with an incidence of vomiting: 0.9% for Regimen 1, 1.9% for Regimen 2 and 4.7% for Regimen 3. LCMS and AE analysis is ongoing for all participants. PK/PD modeling will be reported for AEs, TQ dose and regimen optimization.

8019

THE EFFECT OF ADDITIONAL DOSES OF SULFADOXINE-PYRIMETHAMINE ADMINISTERED AS PERENNIAL MALARIA CHEMOPREVENTION (PMC) ON HEMOGLOBIN LEVELS AMONG CHILDREN IN A MALARIA ENDEMIC AREA OF CAMEROON

Michaela Gross[1], Jonna M. Mosoff[2], Albertine Lele[3], Mercy Tah-Monunde[3], James Sinsai[3], Alba McGirr[2], Carine Nfor[3], Sham Lal[2], Roland Gosling[2], Wilfred F. Mbacham[4], Akindeh M. Nji[3], R Matthew Chico[2], Gillian Stresman[1]

[1]University of South Florida, Tampa, FL, United States, [2]London School of Hygiene and Tropical Medicine, London, United Kingdom, [3]Fobang Institutes for Innovations in Science and Technology, Yaounde, Cameroon, [4]Fobang Institutes for Innovations in Science and Technology, Tampa, FL, United States

The World Health Organization recommends the provision of perennial malaria chemoprevention (PMC) with sulfadoxine-pyrimethamine (SP) to children who are resident in areas of high malaria transmission. While SP can reduce malaria in children, thereby indirectly increasing hemoglobin levels, this effect isn't always consistent, especially in areas with high drug resistance or varying SP dosing regimens. Thus, the evidence base remains unclear regarding the impact of PMC with SP on hemoglobin. We began an open-cohort study of children aged 6-9 months in two Cameroon sites, Soa and Mbankomo, July 2023. Children receive SP at health facilities as part of their normal expanded program on immunization (EPI) schedule with eight total SP in Soa (intervention) and up to five doses in Mbankomo (control) according to Cameroon's National Malaria Programme (NMP). Children are followed up every 3-months for up to 7 visits; all doses of SP received through the PMC program at the facility were recorded. At each household visit, parents of all consenting children completed a questionnaire and children had their hemoglobin levels measured by Hemocue. Linear mixed effects models were utilized for analysis to account for within-subject variation and for missing visits. Preliminary results, based on 748 of 2080 targeted children over three follow-up visits, revealed a dose-dependent effect of SP on hemoglobin levels over time. After adjusting for child age, each additional dose of SP resulted in an average increase of hemoglobin levels of 0.06 g/dL (95% CI: 0.01-0.11; p=0.016). Currently, PMC planning focuses primarily on known antimalarial effects. This study will provide valuable insight for policymakers and NMPs regarding potential further health effects on hemoglobin from receiving additional doses of SP as PMC.

8020

COMMUNITY ACCEPTANCE OF A NOVEL MALARIA INTERVENTION, ATTRACTIVE TARGETED SUGAR BAIT (ATSB) STATIONS, IN THE CONTEXT OF THE ATSB ZAMBIA PHASE III TRIAL

Erica Orange[1], Annie Arnzen[1], Chuma Muluma[2], Situmbeko Akalalambili[2], Titus Tobolo[2], Frank Ndalama[2], Chama Chishya[2], Kochelani Saili[3], Ruth A. Ashton[4], Thomas P. Eisele[4], Joshua Yukich[4], Irene Kyomuhangi[5], John Miller[2], Kafula Silumbe[2], Javan Chanda[2], Busiku Hamainza[6], Joseph Wagman[7], Laurence Slutsker[8], Thomas R. Burkot[9], Megan Littrell[7]

[1]PATH, Seattle, WA, United States, [2]PATH, Lusaka, Zambia, [3]Macha Research Trust,, Choma, Zambia, [4]Centre for Applied Malaria Research and Evaluation, Tulane School of Public Health and Tropical Medicine, New Orleans, LA, United States, [5]Centre for Health Informatics Computing and Statistics, Lancaster University, Lancaster, United Kingdom, [6]National Malaria Elimination Centre, Lusaka, Zambia, [7]PATH, Washington, DC, United States, [8]Independent Consultant, Atlanta, GA, United States, [9]Australian Institute of Tropical Health and Medicine, James Cook University, Cairns, Australia

Community acceptance is acknowledged as an important criterion to assess in community trials, particularly for new tools that require uptake by a target population. Acceptability is also an important indicator of the feasibility of scaling-up a new tool and the level of community engagement required for the tool to be successful. Installed on exterior walls of

household structures, the attractive targeted sugar bait (ATSB) is a new tool for malaria vector control designed to attract and kill mosquitos. ATSBs were evaluated in Western Zambia during a two-year phase III cluster randomized controlled trial to assess the efficacy of ATSBs in reducing malaria transmission. Community acceptance of ATSBs was critical for successful trial implementation. A community engagement strategy was developed to outline routine and response activities to deliver key messages to promote acceptance. Annual cross-sectional surveys assessed households for presence of ATSBs and measured perceived benefits, concerns, and willingness to use ATSBs. Results suggest that community acceptance and acceptability of ATSBs was high with ATSB coverage >90%, >70% of households reported perceived benefits, and <10% reported safety concerns. Focus group discussions (FGDs) and in-depth interviews (IDIs) were conducted at the end of each ATSB deployment period to obtain a range of experiences with ATSBs. Common facilitators identified in FGDs/IDIs included the desire for protection against malaria and reduction of mosquitos, trust, and understanding of the product. Common barriers identified in FGDs/IDIs included misconceptions of product impact on mosquitos, continued cases of malaria, association with satanism, perception of "attracting" mosquitos, and damage to household structures. Future introduction and scale-up of ATSBs will likely require supporting interventions aimed at fostering community acceptance and acceptability. This presentation will describe ATSB acceptance and acceptability in the trial context, household survey and qualitative results, the community engagement strategy for ATSB acceptance, and implications on future ATSB scale-up.

8021

SEASONAL MALARIA CHEMOPREVENTION (SMC) ELIGIBILITY ANALYSIS AND IMPACT EVALUATION USING MATHEMATICAL MODELING TO GUIDE DECISIONS ON THE IMPLEMENTATION OF SMC IN GUINEA

Abdourahamane Diallo[1], Ousmane Diallo[2], Yaya Barry[1], Claude Irandouno[1], Irene Kolou Pivi[1], Fatoumata Battouly[3], Souleymane Bereté[4], Timothé Guilavogui[5], Fode Bangaly Sako[6], Galatas Beatriz[7], Jaline Gerardin[2], Alioune Camara[1]

[1]National Program for Malaria Control, Conakry, Guinea, [2]Northwestern University, Chicago, IL, United States, [3]Catholic Relief Services, Conakry, Guinea, [4]Research Triangle Institute, Conakry, Guinea, [5]Program Management and Coordination Support Unit, Ministry of Health, Conakry, Guinea, [6]National Directorate of Epidemiology and Disease Control, Ministry of Health, Conakry, Guinea, [7]Global Malaria Program, Geneva, Switzerland

In areas where malaria transmission is seasonal, as in Guinea, WHO recommends SMC in children under 5 (CU5). In 2015, Guinea introduced SMC in 6 districts, followed by a gradual expansion to 17 districts by 2020. In Guinea, SMC is organized into 4 monthly cycles between July and October in 16 districts, and 5 monthly cycles in just one district (Dabola). . The National Malaria Control Program (NMCP) has recently considered extending SMC geographically to identify new eligible districts, as well as others districts that could benefit from a 5th cycle of SMC. A seasonality analysis based on rainfall data and malaria cases reported by routine surveillance was carried out using an algorithm to answer this question. A mathematical model was used to predict the impact of SMC extension and the number of preventable malaria cases by introducing an additional cycle in either June or November. Three new districts - Telimélé, Kissidougou and Kérouané - were identified as eligible for SMC extension due to their high incidence in children and favorable seasonal patterns. Mathematical modelling estimated that the potential impact of the extension, with a projected coverage of 80% in the new districts, would prevent more than 450,000 cases of malaria and nearly 700 deaths in CU5 between 2023 and 2027. Cross-analysis of meteorological and case data showed that a 5th cycle in November rather than June would be more beneficial. In all districts, the proportion of cases occurring in November was higher than in June, suggesting that a fifth cycle in November would prevent more cases. The NMC used these results to lobby its partners to mobilize resources to finance this extension.

8022

ASSESSMENT OF THE MALARIA SCORECARD'S IMPACT ON HEALTH OUTCOME THROUGH HOME-BASED MANAGEMENT IN RWANDA

Epaphrodite Habanabakize

Rwanda Biomedical Centre, Kigali, Rwanda

Today malaria continues to represent a real public health concern in Rwandan and continue to implement integrated different malaria control interventions including LLIN distribution through mass campaigns and routine channels, IRS, behavior change communication, and improved access to diagnostics and treatment and those combined interventions resulted in significant malaria infection reduction. The Malaria Scorecard(MS), introduced as a monitoring tool, and home-based management is pivotal in Rwanda's successful efforts to combat malaria and to bolster community-driven approaches to malaria control. This study delves into the assessment of the Malaria Scorecard's impact on health outcome through home-based management, offering vital insights to optimize strategies and empower communities in their ongoing endeavors to combat malaria. This is a retrospective study, to assess the impact of the Malaria Scorecard on community-driven home-based management. Furthermore, we assessed the change in malaria incidence, severe cases and deaths before (FY2020/21) and after the implementation of the scorecard FY 2022/23. Paired t-test analysis was employed to determine the significance difference level for Malaria Scorecard impact on HBM. The findings indicate a positive change in the implementation of the Malaria Scorecard, resulting in an increase in HBM from 54.7%; 95% CI (55.1-55.3) in FY 2020/21 to 58%; 95% CI (57.9-58) in FY 2022/23. The scorecard introduction significantly reduces malaria incidence rate from 114/1,000 population to 47/1,000 population after implementation of the SC.3, severe malaria cases from 2,592 to 1316, and deaths from 94 to 51. This study supports the positive impact of the Malaria Scorecard on community-driven home-based management in Rwanda, highlighting its potential to enhance community practices. To optimize effectiveness, recommendations include targeted activities, improved resource accessibility, and community engagement. Findings contribute to the broader discourse on innovative malaria control strategies, continued integration and refinement of tools like the Malaria Scorecard.

8023

IMPACT OF THE DISCONTINUATION OF UNIVERSAL INDOOR RESIDUAL SPRAYING (IRS) IN MAPUTO PROVINCE DURING THE 2020-2021 SEASON

Sheila Nhate[1], Helena Martí-Soler[2], Júlia Montañà[2], Pedro Aide[3], Luis Fortunato[4], Fabiao Luis[3], Baltazar Candrinho[5], Samira Sibindy[5], Francisco Saúte[3], Caterina Guinovart[2]

[1]Maputo Provincial Health Service, Ministry of Health, Matola, Mozambique, [2]ISGlobal, Barcelona, Spain, [3]Centro de Investigaçao em Saúde de Manhiça (CISM), Manhiça, Mozambique, [4]Tchau Tchau Malária, Maputo, Mozambique, [5]National Malaria Control Program, Ministry of Health, Maputo, Mozambique

In Maputo Province, Mozambique, where malaria transmission is very low, the indoor residual spraying (IRS) strategy switched from a universal to a focal approach in 2020. Focal IRS consists of targeting only the neighborhoods (bairros) with the highest incidences within each district, which resulted in different thresholds being used by district. To evaluate the impact of IRS discontinuation on malaria incidence, we used a difference-in-difference approach. Malaria case data by bairro were extracted from health facility registers for the peak transmission season of Dec 2019-Mar 2020 (baseline) and Dec 2020-Mar 2021 (endline, first year of focal IRS). Bairros were stratified by baseline incidence quartiles (Q1: 0.2-3.1; Q2: 3.1-6; Q3: 6-14; Q4> 14-561 cases/1000) and within each stratum, the change in incidence between baseline and endline was compared in bairros that received vs barrios that did not receive IRS in 2020-21. Negative binomial regression was used to estimate the interaction between baseline/endline incidence and IRS/no IRS by strata and overall. The maximization of the

area under the ROC curve was used to find the "best threshold" above which incidence starts increasing when IRS is withdrawn. Overall, there was a significant 27% larger increase in the average number of malaria cases in bairros without IRS compared to bairros with IRS (IRR=0.73, 95% CI 0.58-0.91). When stratified by quartiles, a significant impact was only found for quartile 4. The incidence threshold that maximized the area under the curve was 6.2/1000. When stratifying by this threshold, there was a significant 47% greater increase in the average number of malaria cases in areas without IRS compared to areas with IRS (IRR= 0.53, 95% CI 0.33-0.84) only in areas with an incidence ≥6.2/1000. In conclusion, during the first four months of follow up, the discontinuation of IRS resulted in an increase in the malaria incidence only in bairros with higher transmission. Bairros with a baseline incidence of ≥6.2 cases/1000 should continue to receive IRS to avoid this resurgence. Additional follow up time would be needed to understand if the long-term impact remains the same.

8024

EVALUATION OF A PILOT IMPLEMENTATION OF INTERMITTENT PREVENTIVE TREATMENT WITH DIHYDROARTEMISININ-PIPERAQUINE TO PREVENT ADVERSE BIRTH OUTCOMES IN PAPUA, INDONESIA

Firdaus Hafidz[1], Freis Candrawati[2], Jenna Hoyt[1], Enny Kenangalem[2], Eve Worrall[1], James Dodd[1], Feiko ter Kuile[1], Jeanne Rini Poespoprodjo[3], Jenny Hill[1]

[1]Liverpool School of Tropical Medicine, Liverpool, United Kingdom, [2]Yayasan Pengembangan Kesehatan dan Masyarakat Papua, Mimika, Indonesia, [3]Yayasan Pengembangan Kesehatan dan Masyarakat Papua, Miimika, Indonesia

Malaria in pregnancy is a major cause of maternal and neonatal death in Papua. Our previous trial in Papua showed that monthly intermittent preventive treatment with dihydroartemisinin-piperaquine (IPTp-DP) among pregnant women from the second trimester was safe, tolerable and more efficacious than standard of care with single screening and treatment (SST). We conducted a mixed method evaluation of a Ministry of Health pilot of IPTp-DP in 10 health facilities in Mimika district. The effectiveness of antenatal clinics (ANCs) to deliver IPTp-DP alongside continuous quality improvement (CQI) was assessed through ANC exit interviews (N=1136), and women's adherence to the full regimen in a 'real life' setting through home visits (N=484). We used routine health information to assess the impact on maternal and infant outcomes. We explored health provider perceptions on drivers of successful integration to inform scale-up, and pregnant women's acceptability of IPTp-DP to refine strategies to improve uptake. Delivery effectiveness of IPTp-DP, defined as the administration of 9 tablets, the first dose by DOT, and reminders on days 2-3, was 40.7% (range). Among women who received IPTp-DP effectively, full adherence was 90.3%. The likelihood of women receiving effective IPTp-DP were lower educational status (aOR 2.1, 95% CI 1.3-3.4, p 0.004), lower socioeconomic status (aOR 1.9, 1.2-2.8, p 0.004), resident in semi-urban areas (aOR 2.3, 1.7-3.1, p <0.001) and second trimester visit (aOR 1.9, 1.5-2.6, p<0.001). Being married (aOR 3.1, 1.1-8.6, p 0.03) and having more than three ANC visits (aOR 2.6, 1.1-6.3, p 0.03) were significant predictors of high adherence. Themes associated with effective delivery were DP availability, trust in providers and active CQI. Themes linked to high adherence were history of malaria in pregnancy, support from midwives, husbands, and health education. Compared to SST, IPTp-DP≥3 was associated with significant reductions in confirmed malaria (aOR 0.5, 0.36-0.74, p <0.001) and moderate anaemia (aOR 0.64, 0.31-2.7x, p 0.003).

8025

FACTORS ASSOCIATED WITH LOW INTERMITTENT PREVENTIVE TREATMENT OF MALARIA IN PREGNANCY (IPTP) COVERAGES IN LOW PERFORMING HEALTH FACILITIES IN GHANA 2023

Paul Boateng[1], Ihsan Abubakari[1], Dora Dadzie[1], Alexander Asamoah[1], Mildred N. Komey[1], Grace Adza[1], Kingsley E. Amegah[2], Wahjib Mohammed[1], Benjamin Oteng[1], Ferguson Duvor[1], Joel J. Idun-Acquah[1], Nana Yaw Peprah[1], Keziah L. Malm[1]

[1]National Malaria Elimination Program, Ghana Health Service, Accra, Ghana, [2]St. Martins De Porres Hospital, Eikwe, Westerm Region, Ghana

Malaria in pregnancy (MiP) poses significant risks to both mother and baby. Prevention of MiP include Intermittent Preventive Treatment of Malaria in Pregnancy (IPTp). Between 2020 and 2022, IPTp 3 coverage increased from 44% to 60%, coinciding with a decrease in MiP cases from 145,472 to 125,757. However, in early 2023, IPTp 3 coverage decreased prompting a targeted supervision to low performing facilities. We report findings from the supervision and factors that might have contributed to the low IPTp 3 coverage. Fifty-two health facilities across 6 regions were visited, all providing Antenatal Care (ANC) and IPTp services. We conducted health staff interviews (one per facility), observations and review of ANC registers. Results are summarized as frequencies and proportions. Most (71.2%) of assessed facilities were government-owned and provided Glucose-6-Phosphate Dehydrogenase (G6PD) testing services. However, there were notable gaps in staff knowledge and practices; 32.7% (17/52) of interviewed staff knew 0.4ug Folic Acid should be administered daily from registration and 73.1% (38/52) knew to avoid administering 5mg Folic Acid concurrently with Sulphadoxine Pyrimethamine (SP). Stockouts of SP were reported in 27.5% of facilities within the last three months, while discrepancies in SP stock balance were noted in 28.8% (15/52). Client education on IPTp was also lacking, with averagely 65% of the staff providing adequate information on its benefits, safety, and proper usage. Less than 45% of facilities had protocols, charts, or job aids for IPTp. Concerning data practices, 23.1% (12/52) had evidence of data validation meetings, 87.8% (43/52) had data capture in line with guidelines and 75.5% (37/52) achieved 100% data completeness. SP availability and sub-optimal client education are barriers to achieving optimal IPTp coverage. Addressing these issues, along with improving the supply of protocols and enhancing data validation practices, are crucial for improving IPTp 3 coverage and reducing MiP in Ghana.

8026

HEALTH PROVIDERS ON-SITE TRAINING APPROACH IN IMPROVING THE QUALITY OF MALARIA SERVICES DELIVERY IN COTE D'IVOIRE, 2023

Yoffoua Jacques Agnon[1], Melly Aissatou Traore[2], Jean Louis Assa[2], Mamadou Silue[2], Eric Akkatia[2], Mea Antoine Tanoh[1], Collette Yah Epse Kokrasset[1], Patricia L. Yepassis-Zembrou[3], Christie Billingsley[4], Blaise Kouadio[4]

[1]Côte d'Ivoire National Malaria Control Program, Abidjan, Côte D'Ivoire, [2]Population Services International Côte d'Ivoire, Abidjan, Côte D'Ivoire, [3]U.S. President's Malaria Initiative, Centers for Disease Control and Prevention, Abidjan, Côte D'Ivoire, [4]U.S. President's Malaria Initiative, U.S. Agency for International Development, Abidjan, Côte D'Ivoire

In 2019 and 2022, the Cote d'Ivoire National Malaria Control Program revised its guidelines for malaria case management and prevention and organized training workshops to upgrade health providers skills on the revised guidelines. Post-training follow-up through Outreach Training and Supportive Supervision Plus (OTSS+) revealed shortcomings in applying what was learned during the training. Two training strategies were developed in 2020 and 2023 to refresh provider skills in: 1) performing malaria rapid diagnostic tests (RDT); 2) managing uncomplicated malaria; and 3) providing insecticide treated nets (ITN) to children under five years of age. Strategy one, implemented in 2020, involved theoretical workshop trainings held at district level and facilitated by central-level trainers. Strategy two, implemented in 2023, involved theoretical workshop and

practical on-site trainings held in health centers and facilitated by district-level trainers. The OTSS+ was used to assess the skills of 550 providers within three month post each training strategy in the 34 health districts. Individual performances were scored according to skills: good for a score of 90% and above; medium between 80% and 89%, and low at less than 80%. This assessment compares the results of the two strategies. For RDT performance, 47.0% demonstrated good skills with strategy one and 79.5% with strategy two. For uncomplicated malaria case management, 27.5% demonstrated good skills with strategy one compared to 52.8% with strategy two. Regarding ITNs 30% demonstrated good skills for strategy one and 43.3% for strategy two. Number of providers trained with strategy two was higher than with strategy one, 6893 versus 2060, and the average overall per diem-related training cost was substantially lower for strategy two (16 USD) compared to strategy one (83 USD). On-site training strategy appears to be more effective than workshop trainings alone in improving provider performance. In addition, this strategy allowed for training a larger number of health providers due to its lower per diem cost. Continuing to follow up will enable understanding the longer-term impact on skills.

8027

EQUITY AND COVERAGE ANALYSIS OF POPULATION-BASED HEALTH PROGRAMS: A COMPARATIVE STUDY OF SEASONAL MALARIA CHEMOPREVENTION, INSECTICIDE-TREATED NET DISTRIBUTION STRATEGIES, AND THE ESSENTIAL PROGRAM ON IMMUNIZATION IN AFRICAN COUNTRIES

Maria Suau Sans, Chuks Nnaji, Katherine Theiss-Nyland
Malaria Consortium, London, United Kingdom

Seasonal malaria chemoprevention (SMC) consists of administrating monthly doses of antimalarials to children aged 3-59 months old during the malaria transmission season. SMC has been identified as a potential platform for the integration of other interventions such as mass drug administration, and nutrition supplementation. Similarly, the essential programme on immunization (EPI) and insecticide-treated net (ITN) distribution campaigns have been identified as useful integration platforms for many maternal and child health programmes. Integration can help to deliver services at the same time and through fewer personnel which can lead to operational efficiencies and ultimately improves health outcomes. Achieving equity in these programmes is not only socially responsible, but it is an important disease prevention strategy. The comparison of routine population-based programme styles, and the equity achieved as a result, can be used to inform the integration of other interventions. This study aims to measure and compare the coverage of SMC and EPI programmes, and ITNs distribution strategies, and how equitable they are. In this study we are conducting a secondary analysis using data from Demographic and Health Surveys and Malaria Consortium's SMC end-of-round surveys to assess intervention coverage across 27 African countries. The analysis focuses on measuring the equity and coverage of ITNs, EPI, and SMC, comparing outcomes between and within countries. Coverage of each intervention will be assessed using binary indicators, with equity measured through concentration indices (Erreygers index). The study will provide insights into the distribution of ITNs, routine immunisation services, and SMC across wealth quintiles and their relationship to program coverage. We will present graphical comparisons and pooled concentration indices that elucidate the equity of intervention delivery within and between 27 countries. The findings will contribute to evidence-based decision-making for maximizing equitable access to preventive interventions across diverse socio-economic contexts.

8028

PREVENTING MALARIA AMONGST CONFLICT-AFFECTED COMMUNITIES IN CAMEROON SOUTH-WEST AND LITTORAL REGIONS

Margaret Ebob Besem.E.O[1], Brenda M. Yankum[2], Elizabeth G. Chestnutt[2], Annesophie Stratil[2], Laura Donovan[2], Claude Nkfusai[2], Helen Hawkings[2], Elizabeth R. Berryman[2], Helen Counihan[2], Blanka Homolova[2], Kevin Baker[2], Yakouba Zoungrana[3], Maxwell Kolawole[3], Elvis A. Tanue[1], Glennis A. Tabe-Ebob[1], Bibiche M. Noukeme[4], Alain Metuge[4], Isabelle Nganmou[5], Dorothy Achu[6], Samuel Wanji[1], LundiAnne Omam[7]
[1]Buea University, Buea, Cameroon, [2]Malaria Consortium, London, United Kingdom, [3]Malaria Consortium, Abuja, Nigeria, [4]Reach Out Cameroon (REO), Buea, Cameroon, [5]Konmofamba Actions Sans Frontieres (KASAFRO), Penja, Cameroon, [6]Ministry of Public Health, Yaounde, Cameroon, [7]University of Cambridge, Cambridge, United Kingdom

Conflict in Southwest and Littoral regions of Cameroon led to reduced healthcare, internal displacement limiting access to malaria prevention and treatment services. Breaking Barriers is a 4-year implementation study researching community solutions in 80 high malaria-burden conflict-affected communities. Formative research in May 2021 resulted in introduction of a community dialogue approach (CDA), community health workers (CHW) supportive supervision, and vouchers for subsidized care from May 2022. A mid-term review (MTR) was conducted in November 2023, endline planned for June 2024, adopting qualitative and quantitative observational designs. The qualitative formative research studied barriers to care, CHW utilization, and community engagement preferences, 29 focus group discussions (FGDs), 11 in-depth interviews (IDIs). Data were analyzed thematically; open, descriptive coding combined with exploration of pre-determined investigative areas. The MTR evaluated process, 15 FGDs, 21 IDIs. Data were analyzed thematically using rapid summary analysis. Quantitative studies were cross-sectional knowledge, attitude, and practice surveys, 2,386 baseline participants, MTR, 2,523. malariometric prevalence studies, baseline 1,752 children, MTR, 2,042. Data entry was completed with Epi-Info 7.2.4.0, analysis with SPSS 25.0 and R 4.2.1. Qualitative formative research found poor prevention and treatment knowledge, health-seeking and CHW utilization. MTR results found communities value their CDA role and requested sustained capacity strengthening for community stakeholders. Voucher importance depends on health service confidence. Quantitative studies found improvements in knowledge of transmission and prevention practices; early diagnosis from CHWs, perceiving malaria a concern, prevention practices and prompt treatment for sick children. Malaria positive cases reduced from 54.5% to 33%. CDA is effective providing strengthened investment. Conflict affects CHW resourcing, supervision, and supplies. Effective cash assistance requires a continuum of care. To be concluded at endline survey and presented.

8029

ZAMBIA 2023 ITN DISTRIBUTION CAMPAIGN DIGITALIZATION EXPERIENCES: LESSONS LEARNED AND BEST PRACTICES

Japhet Chiwaula[1], Mercy Mwanza[1], Ketty Ndhlovu[1], Busiku Hamainza[1], Reuben Kaponde[2], Edwin Kaponde[2], **Dingani Chinula**[2], Isaac Mwase[3]
[1]National Malaria Elimination Centre, lusaka, Zambia, [2]USAID Evidence For Health, lusaka, Zambia, [3]U.S. President's Malaria Initiative, Zambia., lusaka, Zambia

In 2023, the Zambian Ministry of Health (MoH) and partners, including the Global Fund (GF), Against Malaria Foundation (AMF), and the U.S. President's Malaria Initiative (PMI) undertook a nationwide mass distribution of insecticide-treated bed nets (ITNs). ITN campaigns are conducted every three years and the 2023 campaign was the country's largest ever, targeting 18 million people with over 11.5 million ITNs and was the first to be digitized. Digitalization was a condition for accepting AMF funding for a set of provinces. However, the MoH embraced this innovation as a best

practice for adoption in all ten provinces. The digitization process involved customizing paper-based ITN registers into electronic formats; configuring them onto smartphones and training community-based volunteers (CBVs) to use these tools to capture data in real time during household registration and distribution exercises. CBVs moved in pairs, one using a traditional paper register for backup and the other using the digital tools, which auto calculated the quantity of ITNs needed for each household, captured location coordinates, and generated household identifiers. The data was transmitted to a central server and readily visualized, informing MoH's management decisions at health facility, district, and provincial levels. Observed benefits have included improved data quality, transparency, and accountability. Technological and administrative challenges ranged from the extra cost resulting from procurement of devices, training, conducting the pilot; to incomplete datasets due to poor connectivity in rural areas and inadequate supply of devices and accessories. Completion of the campaign was delayed by months in part due to these bottlenecks. Among the important recommendations for future campaigns is to ensure a comprehensive workplan with a realistic timeline supported by a detailed budget that accounts for all costs. It is also critical to conduct a pilot prior to the main campaign for viability testing. Finally, staff at all levels should be trained to be able to troubleshoot and resolve issues locally.

8030

COST AND COST-EFFECTIVENESS OF ATTRACTIVE TARGETED SUGAR BAITS (ATSB): CLUSTER RANDOMIZED CONTROL TRIALS (CRCT) IN ZAMBIA, KENYA, AND MALI

Brooke E. Mancuso

Tulane University School of Public Health, New Orleans, LA, United States

Malaria remains a serious public health problem in sub-Saharan Africa, accounting for 580,000 deaths in 2022. Current vector control methods, Insecticide-Treated Nets (ITN) and Indoor Residual Spraying (IRS) are two of the most effective methods for reducing malaria. Insecticide resistance and evolving mosquito biting behaviours remain persisting challenges in reducing malaria transmission. Attractive Targeted Sugar Baits (ATSB) are a potential new tool for malaria vector control to address these challenges. ATSB stations containing sugar laced with toxicant are placed on housing structures, aiming to attract and kill mosquitoes after feeding from them. Three cluster randomized control trials (cRCT) were concluded in Zambia (June 2023), Kenya (March 2024), and Mali (January 2024) to assess the efficacy of ATSB. Main trial results from Zambia indicated a 9% reduction in malaria case incidence and results from Kenya and Mali are forthcoming. To assess the costs and cost-effectiveness of ATSB, costs of procurement, distribution, maintenance, and disposal were collected in the context of each cRCT. Economic and financial costs were estimated using an ingredients approach. In Zambia, from October 2021 to June 2023, the total costs were USD 1.1 Million, with cost-effectiveness of ATSB at USD 37 per clinical malaria case averted, and USD 366 per DALY averted. Data from Kenya indicate a total cost over 12 months of intervention of USD 1.7 Million. Results from the three trials indicate variation in the cost-effectiveness of ATSB, depending on site-characteristics. This variation may help to determine where and when ATSB may be utilized most efficiently to complement existing vector control.

8031

MALARIA, ANEMIA, MALNUTRITION IN PREGNANCY: PREVALENCE AND ASSOCIATED FACTORS, HIGH MALARIA TRANSMISSION AREA MALI

Aissata Koné[1], Mady Cissoko[1], Fady Touré[1], Daouda S. Samaké[1], Mahamadou Magassa[1], Halidou Sidibé[1], Vincent Sanogo[1], Assitan Dembélé[1], Akory Ag Iknane[2], Hamadoun Sangho[2], Kassoum Kayentao[3]

[1]Programme National de Lutte contre le Paludisme, Bamako, Mali, [2]Faculté de Médecine et Odontostomatologie, Bamako, Mali, [3]Malaria Research and Training center, Bamako, Mali

Malaria and anaemia are diseases responsible for a large number of healthcare visits and deaths among pregnant women in areas of high malaria transmission, especially during the rainy season. This winter period corresponds to the hunger gap and field work, which can expose pregnant women to infections. The aim of this study is to assess the prevalence of malaria, anaemia and malnutrition among pregnant women in a high malaria transmission zone, and the associated factors. The study involved the 27 community health areas in the Dioila Health District, Koulikoro region, Mali. Data were collected from June 2022 to May 2023 in the health facilities during antenatal consultations. They included socio-demographic and economic data, malaria and haemoglobin tests, physical examination (including branchial perimeter). Descriptive analysis focused on the prevalence of malaria, anemia and acute malnutrition, with confidence intervals. We performed univariate and multivariate logistic regression analysis with prevalences (malaria and anemia), malnutrition, dietary habits and household income. A total of 829 women were included in the study, with a mean age of 25.7 (sd 6.22). The prevalence of malaria was 23.7% [95%: 0.21; 0.27], malnutrition 25% [95%: 0.22; 0.28]. The prevalence of anemia was 59% [95%: 0.55; 0.63]. Factors such as multiparity and low daily household spending were significantly associated with malnutrition, malaria and anemia in pregancy. The results show a need to integrate screening for malnutrition and anemia and their management during prenatal consultations in Mali to further reduce the burden of malaria. In addition, there is a need to develop income-generating activities for women.

8032

AN OBSERVATIONAL STUDY EVALUATING THE EPIDEMIOLOGICAL AND ENTOMOLOGICAL IMPACTS OF PIPERONYL BUTOXIDE INSECTICIDE-TREATED NETS COMPARED TO A COMBINATION OF INDOOR RESIDUAL SPRAYING PLUS STANDARD PYRETHROID-ONLY ITNS IN AMHARA REGION, ETHIOPIA, 2019-2022

Kelly M. Davis[1], Amha Worku[2], Meshesha Balkew[2], Peter Mumba[3], Sheleme Chibsa[4], Jon Eric Tongren[4], Gudissa Assefa[5], Achamyelesh Sisay[5], Dawit Teshome[2], Banchamlak Tegegne[6], Mastewal Worku[7], Mulat Yimer[8], Delenasaw Yewhalaw[9], Isabel Swamidoss[10], Carla Mapp[10], Melissa Yoshimizu[11], Sarah Zohdy[12], Jimee Hwang[13], Wendy Inouye[14], Aklilu Seyoum[15], Cecilia Flatley[15], Emily R. Hilton[14], Dereje Dengela[2], Sarah M. Burnett[16]

[1]PMI Evolve Project, PATH, Washington, DC, United States, [2]PMI Evolve Project, Abt Associates, Addis Ababa, Ethiopia, [3]U.S. President's Malaria Initiative,, Addis Ababa, Ethiopia, [4]U.S. President's Malaria Initiative, Addis Ababa, Ethiopia, [5]Malaria and Other Vector-Borne Diseases Prevention and Control Desk, Federal Ministry of Health, Addis Ababa, Ethiopia, [6]Amhara Public Health Institute, Bahir Dar, Ethiopia, [7]Amhara Public Health Institute,, Bahir Dar, Ethiopia, [8]Bahir Dar University, Bahir Dar, Ethiopia, [9]Tropical and Infectious Disease Research Center, Jimma University, Jimma, Ethiopia, [10]U.S. President's Malaria Initiative, Entomology Branch, Division of Parasitic Diseases and Malaria, Center for Global Health, Centers for Disease Control and Prevention, Atlanta, GA, United States, [11]U.S. President's Malaria Initiative, U.S. Agency for International Development, Washington, DC, United States, [12]U.S. President's Malaria Initiative, Entomology Branch, Division of Parasitic Diseases and Malaria, Center for Global Health, Centers for Disease Control and Prevention, Atlanta, Georgia, [13]U.S. President's Malaria Initiative, Malaria Branch, US Centers for Disease Control and Prevention, Atlanta, GA, United States, [14]PMI Evolve Project, PATH, Seattle,

WA, United States, [15]PMI Evolve Project, Abt Associates, Rockville, MD, United States, [16]U.S. President's Malaria Initiative (PMI) Evolve Project, PATH, Washington, DC, United States

National malaria programs must weigh the relative benefits of different vector and elimination tools to prioritize resource allocation with greatest impact. An open-label, stratified block-cluster randomized trial was designed to assess the epidemiological and entomological impacts of piperonyl butoxide insecticide-treated nets (PBO ITN arm) compared to the combination of pirimiphos-methyl-based indoor residual spraying (IRS) and standard pyrethroid ITNs (IRS + Standard Pyrethroid ITN arm) in the Amhara Region of Ethiopia. Confirmed malaria cases reported during the high transmission season (September to December) were compared two years before (2019 and 2020) versus two years after (2021 and 2022) the ITN distribution and the first IRS campaign, using a multilevel mixed-effects negative binomial model. Generalized linear mixed models were used to assess the difference in *Anopheles gambiae* s.l. density per trap and indoor resting density (IRD) between the two arms during the 2021 and 2022 seasons. Estimated malaria cases decreased significantly by 53.6% in the IRS + standard pyrethroid ITN arm (mean: -53.6%; 95% CI: -72.9%, -29.8%), and by 55.9% in the PBO ITN arm (mean: - 55.9%; 95% CI: -73.0%, -32.5%). There was no significant difference in the overall epidemiological impact between these two arms (mean: -2.2%; 95% CI: -30.9%, 24.0%). However, while cases decreased non-significantly in the IRS + standard pyrethroid ITN arm from the first to second post-interventions season, there was a significant increase in the PBO ITN arm. Vector density per trap and IRD were not found to be significantly different between intervention arms in either post-intervention year (2021 Vector density per trap: IRR=0.78; 95% CI 0.47-1.31; p=0.348; IRD: IRR=0.80; 95% CI 0.37-1.75; p=0.580 or 2022 Vector density per trap: IRR=1.27; 95% CI 0.75-2.12; p=0.372; IRD: IRR=1.02; 95% CI 0.45-2.28; p=0.971). These findings indicate that while there was an overall impact observed in both intervention arms, the deployment of annual IRS alongside standard pyrethroids ITNs may provide a greater, sustained vector control impact over time compared to PBO ITNs only.

8033

INTRODUCING HAMMOCK NETS AND BEDNETS IN INDIGENOUS AND VULNERABLE COMMUNITIES OF PANAMÁ

Tania Blanco[1], Carmen Perez[1], Santiago Chérigo[1], Lucía Fernández Montoya[2], Bernardo García Espinosa[2], Nicholas Presley[2], Alexia Rivera[2], Mariela Mosquera[2]

[1]Departamento de Control de Vectores, Ministry of Health Panama, Panama City, Panama, [2]Clinton Health Access Initiative, Panama City, Panama

In 2009, Panama conducted their first Long Lasting Insecticide treated bednets (LLIN) mass campaign using long-lasting insecticide-treated bednets. However, it became apparent that a significant portion of individuals in the most malaria-affected and indigenous regions slept in hammocks, a fact that may have undercut the impact of the bednet distribution. With a renewed commitment to malaria elimination in 2018, Panama aimed to achieve comprehensive coverage with either LLINs or indoor residual spraying (IRS) in all active transmission areas. To test whether LLINs (bednets and hammock nets) were an adequate intervention for the locally affected populations, Panama devised a pilot initiative, spanning from 2019 to 2022, to evaluate the feasibility, acceptability, and use of both bednets and hammock nets among indigenous and latin communities. During this session, we will present the outcomes of the distribution phase and two subsequent rounds of monitoring, which highlight that, despite the high initial coverage and local communities expressing satisfaction with the color, fabric and size of the bednets and hammock nets, the percentage of sleeping spaces that were visibly covered with a net rapidly decreased in 6 months to 46.8% for hammock nets and 73.6% for bednets and the percentage of people using a net 6 months after distribution was merely 57%, with great heterogeneities across localities. This underscores the importance of strengthening SBCC campaigns after distribution and conducting post-distribution monitoring to capture the heterogeneity between localities and take appropriate focal actions to increase use. We will show how the findings from this pilot endeavor informed the national LLIN distribution campaign conducted in 2023. By sharing the lessons learned and best practices derived from this initiative, we aim to provide valuable guidance for other countries using LLINs and grappling with malaria elimination among indigenous and other vulnerable populations in the region.

8034

THE IMPACT OF ROUTINE DISTRIBUTION AND USE OF ITN TO REDUCE MALARIA IN PREGNANCY AND FOR CHILDREN UNDER 5 YEARS

Mangara Jean Louis Ndikumana

Rwanda Biomedical Center, Kigali, Rwanda

This abstract presents a comprehensive overview of ITN coverage and utilization in Rwanda, with data reflecting national level statistics, offering insights into the effectiveness of ITN distribution and usage strategies. We conducted a comparative analysis on annually indicators from national HMIS including pregnant women confirmed and treated malaria for pregnant and lactating (42 days) women between 15 to 49 years of age and Children under five years who was confirmed and treated malaria from 2020 to 2023. We analyzed also the indicators of ownership of ITN and use collected by RDHS and RMIS.After ownership of ITNs increasing from 81% in the 2014-15 RDHS, 84% in the 2017 RMIS, dropped to 66% in 2019-20 RDHS was again increased to 80.2% RMIS 2023. The use of ITN for pregnant women was 73% 2014-15 RDHS decreased to 69% RMIS 2017, and 56% in 2019-20 RDHS with a slight rise to 56.5% RMIS 2023 while the use of ITN for children under 5 years was 68 % 2014-15 RDHS, 68 % RMIS 2017, was decreased to 56% 2019-20 RDHS was again increased to 56.8% RMIS 2023The malaria in children under five years dropped in last four years from 300,405 in 2020, 230,137 in 2021, 145,890 in 2022 and 100,049 in 2023. This represent respective cumulative decrease of 23% in 2021, 51% in 2022 and 67% in 2023. While malaria in pregnancy was also decreased from 17,126 in 2020; 10,221 in 2021, 5,460 in 2022 to 3,106 cases in 2023, with a cumulative decrease of 40% in 2021, 68% in 2022 and 82% in 2023Overall, the data underscores the importance of continuous monitoring and evaluation of ITN distribution and utilization programs to address disparities and optimize malaria control efforts. Targeted interventions may be necessary to improve coverage and ensure equitable access to ITNs, particularly in the lower rates of utilization area. By prioritizing access and promoting consistent ITN usage among vulnerable populations, Rwanda can further strengthen its malaria prevention strategies and contribute to reducing the burden of the disease nationwide.

8035

USING NATIONAL SURVEY DATA TO LEARN IMPACT OF INTERMITTENT PREVENTIVE TREATMENT OF MALARIA IN PREGNANCY ON BIRTH WEIGHT IN NIGERIA

Bright C. Orji[1], Charity I. Anoke[2], **William Robert Brieger**[3]

[1]Health Promotion and Education Alumni Association, Faculty of Public Health, College of Medicine, University of Ibadan, Ibadan, Nigeria, [2]Ebonyi State University, Abakaliki, Nigeria, [3]The Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, United States

Intermittent preventive treatment of malaria in pregnant women (IPTp) promotes health of the mother and unborn child. One noteworthy benefit is reduction of low birth weight (LBW, less than 2.5kg). Large survey data sets aid learning about such benefits on a national scale. We analyzed data from the 2018 Nigeria Demographic and Health Survey (DHS) to document the impact of IPTp on birth weight. Key variables included IPTp which based on national guidelines is given monthly at antenatal clinics from the 13th week, aiming to provide a minimum of 3 doses. DHS obtained this information from women giving birth in the previous two years. Birth weight included women giving birth in the previous five years. A quarter had a record of newborn weight reported from a health facility Since many did not, women were also asked to estimate the size of the baby at birth:

very small, smaller than average, average, larger than average, and very large. We combined the latter three categories into "average or larger". Of those giving birth in the past 2 years, 23% took only one dose, 24% took 2 doses, while 17% had 3 or more doses. In the broader sample of those giving birth in the previous 5 years 2.8% estimated that their baby was very small. Among those women with a record of birth weight, 7% were LBW. Preliminary analysis comparing perceived size and IPTp doses found 3% receiving only one dose thought their baby was "very small" at birth, as did 3% of those taking 2 doses and 4% receiving 3 or more. Among the subset with a recorded birth weight, 9% who took only one dose of IPTp had LBW baby, as did 7% who received 2 doses, and 6% who got 3 or more doses. It appears possible to compare outcomes (LBW) with interventions (IPTp), but data type and availability may limit conclusions. Even though a smaller subset of women had access to a recorded birth weight (most women delivered outside a health facility), birth weight appears to provide a better indication of IPTp effectiveness than subjective perceptions of child's size at birth. The findings even with limitations show the value of national surveys to justify policies protecting pregnant women from malaria.

8036

DECENTRALIZING MALARIA CASE MANAGEMENT SERVICES IN EQUATORIAL GUINEA: A CAPACITY BUILDING APPROACH AT THE DISTRICT LEVEL

Sandra Djalle Incardona[1], Julie Buekens[1], Maria Consuelo Oki Eburi[2], Wonder P. Phiri[3], Carlos A. Guerra[1], Matilde Riloha Rivas[4], Guillermo A. García[1]

[1]MCD Global Health, Silver Spring, MD, United States, [2]MCD Global Health, National Malaria Control Program, Ministry of Health and Social Welfare of Equatorial Guinea, Malabo, Equatorial Guinea, [3]MCD Global Health, Malabo, Equatorial Guinea, [4]National Malaria Control Program, Ministry of Health and Social Welfare of Equatorial Guinea, Malabo, Equatorial Guinea

Historically centralized, the health system of Equatorial Guinea is transitioning to decentralization to improve local responsiveness for health programs, particularly for those related to malaria service delivery. This shift, led by the Ministry of Health (MOH) with support from the National Malaria Control Program (NMCP) and the Bioko Island Malaria Elimination Project (BIMEP), aims to improve malaria case management services by empowering district-level entities. A strategic decentralization initiative was launched in 2023 to train clinicians and lab technicians to become trainers and supervisors for malaria case management, in three phases: 1) Initial training utilizing updated clinical and lab manuals together with competency assessments, 2) Monitoring and coaching of in-service practices through OTSS (Outreach Training and Supportive Supervision) visits, and 3) Advanced training focusing on skills needed to lead impactful training sessions and supervisory visits. Participants were selected based on their proficiency identified in previous training or OTSS visits. This effort has resulted in developing a comprehensive toolkit that includes clinical and diagnostics training manuals, digitized malaria case management supportive supervision tools, and manuals focusing on trainer's and supervisor's skills, all being integrated into the NMCP. Initial training results from December 2023 show high competency scores among participants, demonstrating effective learning transfer. The complete implementation of all phases is projected for the end of Q3 2024. The aim for this initiative is that it will not only help increase the quality of malaria services and tackle challenges with the overutilization of medicines and inaccurate malaria diagnoses, but it will also strengthen local leadership and ownership for a decentralized and more effective health system. The malaria program hereby establishes a framework and precedent for a more comprehensive health system reform in line with global malaria elimination goals and with Equatorial Guinea's decentralization agenda across the different disease programs.

8037

EFFECT OF INTERMITTENT PREVENTIVE TREATMENT OF MALARIA IN SCHOOLCHILDREN ON ANEMIA THROUGH REDUCTION OF MALARIA INFECTIONS AND CLINICAL MALARIA EPISODES: MEDIATION ANALYSIS

Alick Sixpence[1], Wangisani Kumalakwaanthu[2], Alfred Matengeni[2], Laurence S. Magder[3], Karl B. Seydel[4], Miriam K. Laufer[5], Don P. Mathanga[2], Lauren M. Cohee[6], Clarissa Valim[7], Judith J. Lok[8]

[1]Department of Epidemiology, Boston University School of Public Health, Boston, MA, United States, [2]Malaria Alert Centre (MAC), Kamuzu University of Health Sciences (KUHeS), Blantyre, Malawi, [3]Department of Epidemiology and Public Health, University of Maryland School of Medicine, Baltimore, MD, USA, Baltimore, MD, United States, [4]Department of Osteopathic Medical Specialties, College of Osteopathic Medicine, Michigan State University, East Lansing, MI, United States, [5]Center for Vaccine Development and Global Health, University of Maryland School of Medicine, Baltimore, MD, United States, [6]Department of Clinical Sciences, Liverpool School of Tropical Medicine, Pembroke Place, Liverpool, United Kingdom, [7]Department of Global Health, Boston University School of Public Health, Boston, MA, United States, [8]Department of Mathematics and Statistics, Boston University, Boston, MA, United States

Anemia undermines the health and education of children. Its causes are multi-factorial, and the relative contribution of its etiologies are heterogeneous in terms of age and geography. Malaria is a significant cause of anemia in school-age children (SAC), but effects may be mediated by both episodes of clinical malaria and chronic *Plasmodium falciparum* (*Pf*) infection. Understanding the contribution of these two helps anticipate the impact of malaria control interventions on anemia. A recent school-based open label randomized, controlled trial of malaria intermittent preventive treatment (IPT), found that the risk of anemia in children in IPT arm was lower than those in control arm. In the IPT arm, three rounds of dihydroartemisinin-piperaquine (DP) or chloroquine were delivered at 6-week intervals for parasite clearance and prophylaxis. The control arm did not receive any medication. In the current analysis, we aimed to evaluate whether the reduction in the rate of anemia was mediated by parasite clearance, and/or frequency of clinical malaria episodes. We used mediation analysis to decompose total effect (TE) of IPT on anemia into unmediated and mediated effects. At the end of the study, prevalence of anemia was 8% (20/239) in IPT arm vs 15% (35/238) in control arm yielding a TE of 0.55 [OR=0.55 (0.28, 0.90)]. Prevalence of *Pf* infection was 17% (40/239) in the IPT arm vs 53% (127/238) in the control arm [OR=0.18 (0.12, 0.27)]. Clinical malaria risk was 0.14 (40/239) in IPT arm vs 0.32 (77/238) in control arm over 6 months [RR=0.44 (0.31, 0.63)]. The odds of anemia were reduced by 26% [OR=0.74 (0.54, 0.93)] in IPT compared to control, due to a reduction in the odds of *Pf* infection, representing 45% proportion of anemia reduction mediated by reduction of *Pf* infection. There was no significant mediated effect of IPT treatment on anemia through clinical malaria (OR=1.07 (0.94, 1.18)). While IPT reduces the risk of clinical malaria among SAC, this reduction alone does not translate into a decrease in anemia prevalence. Our findings suggest that *Pf* infection clearance during IPT intervention is the primary mechanism contributing to the reduction in anemia.

8038

CHANGES IN IPTP UTILIZATION MEASURED AN ANNUAL CROSS-SECTIONAL HOUSEHOLD SURVEY WITHIN PROGRAM AREAS OF THE ISDELL: FLOWERS CROSS BORDER MALARIA INITIATIVE IN ZAMBIA

Alysse Maglior[1], Jesse Heitner[2], Rebecca J. Vander Meulen[1], Constance Njovu[3], Busiku Hamainza[4]

[1]J.C. Flowers Foundation, New York, NY, United States, [2]Mass General Brigham, Boston, MA, United States, [3]Anglican Diocese of Lusaka, Lusaka, Zambia, [4]National Malaria Elimination Centre, Lusaka, Zambia

Pregnant women are at increased risk of severe illness and death from malaria. Taking three or more doses of intermittent preventive treatment of malaria in pregnancy (IPTp 3+) is a key strategy to protect women and

their babies from malaria complications. The 2022-2026 Zambia National Malaria Strategic Plan aims to increase IPTp 3+ to at least 88% from its national baseline of 68% in 2021. This study assessed utilization of IPTp 3+ among women who gave birth in the prior 12 months in Southern and Western Province within 24 health facility catchment areas (HFCAs) that are program areas of the Isdell:Flowers Cross Border Malaria Initiative (IFCBMI), an implementing partner of Zambia's National Malaria Elimination Centre. Data were collected through cross-sectional surveys conducted from April-May 2022 (n=1982) and April-June 2023 (n=2553). Within program areas, the average proportion of women who took IPTp 3+ was already near the Strategic Plan goal in 2022 at 86.5% (83.6% - 89.0%). However, the proportion slipped by a statistically significant -4.9% (-10.2% - -0.5%, p=.025) in 2023 to 81.6% (78.5% - 84.4%). This change was concentrated most strongly in Mongu District program areas, which recorded a statistically significant (p=.011) drop of -37.9% (-72.8% - -5.5%) from 90.7% to 52.8%. More modest, non-significant losses were measured in IFCBMI HFCAs in Livingstone, Mulobezi, and Sesheke (-6.5%, -10.2%, -8.3%, respectively), while modest, non-significant gains were seen in HFCAs in Kalabo, Kazungula Shangombo, and Sikongo (+7.5%, +2.4%, +1.6%, +6.0%, respectively). In 2023, IFCBMI HFCAs in Mongu and Sikongo Districts had by far the lowest IPTp3+ levels at 52.8% (36.6% - 68.7%) and 54.3% (42.2% - 65.8%), respectively, with all other district program estimates exceeding 80%. Only the Senanga program area was measured to achieve 100% in either year, at which it was measured for both years. Strategic planning for increasing IPTp3+ utilization within Mongu and Sikongo Districts will be undertaken by IFCBMI and partners to achieve national goals. Data to be collected in 2024 will again measure IPTp3+ in these areas and assess relative changes.

8039

LEVERAGING HOUSEHOLD VISITS DURING INDOOR RESIDUAL SPRAYING TO IDENTIFY PREGNANT WOMEN AND INCREASE AWARENESS OF ANTENATAL CARE AND IPTP ADHERENCE ON BIOKO ISLAND, EQUATORIAL GUINEA

David S. Galick[1], Jeremias Nzamio Mba Eyono[1], Cristina Ngui Otogui[1], Matilde Riloha Rivas[2], Monica Idelviina[1], Wonder P. Phiri[1], Carlos A. Guerra[3], **Guillermo Alberto Garcia**[3]

[1]MCD Global Health, Malabo, Equatorial Guinea, [2]National Malaria Control Program, Ministry of Health and Social Welfare of Equatorial Guinea, Malabo, Equatorial Guinea, [3]MCD Global Health, Silver Spring, MD, United States

Pregnant women are particularly vulnerable to malaria, and the Bioko Island Malaria Elimination Project (BIMEP) prioritizes reinforcing knowledge, attitudes, and practices (KAP) around malaria in pregnancy to increase antenatal care attendance, adherence to intermittent preventive treatment in pregnancy with sulfadoxine-pyrimethamine (IPTp-SP), and long-lasting insecticidal net use. This study aims to evaluate the effectiveness of leveraging household visits during indoor residual spraying (IRS) activities to identify pregnant women and increase awareness of ANC and IPTp adherence on Bioko Island, Equatorial Guinea. During the annual IRS round on Bioko Island in 2023, pregnant women in sprayed households were identified and enrolled in a follow-up study after obtaining informed consent. Community outreach was conducted through household visits, during which communicators educated pregnant women on malaria prevention and health-seeking behaviors. Data on age, pregnancy age, education, phone contact, malaria knowledge, and prevention practices, such as ANC attendance and IPTp-SP, were collected. Consenting women were enrolled in a registry to receive text messages, home education, and invitations to community talks on malaria. A total of 589 pregnant women were visited in their homes and educated on malaria prevention and treatment-seeking behaviors. More than 95% of the women consented to receive text messages, home education, and invitations to community talks on malaria. The project aims to build a registry to reinforce the strategy for malaria prevention in pregnancy through targeted interventions. Leveraging household visits during IRS activities is an effective approach to identify pregnant women and increase awareness of ANC and IPTp adherence. The high consent rate for receiving educational interventions demonstrates the potential for targeted strategies to improve malaria prevention and treatment-seeking behaviors among pregnant women on Bioko Island.

8040

POTENTIAL POPULATION IMPACT OF SCALING UP SEASONAL MALARIA CHEMOPREVENTION IN EAST AND SOUTHERN AFRICA: A MODELLING STUDY

Gina Maria Cuomo-Dannenburg[1], Matt Cairns[1], Andria Mousa[1], Ivan Alejandro Pulido Tarquino[2], Maria Suau Sans[3], Chuks Nnaji[3], John Baptist Bwanika[4], Craig Bonnington[3], Monica A. de Cola[1], Christian Rassi[3], Anthony Nuwa[4], Kevin Baker[3], Sam Gudoi[4], Patrick G T Walker[1], Lucy Okell[1]

[1]Imperial College London, London, United Kingdom, [2]Malaria Consortium, Maputo, Mozambique, [3]Malaria Consortium, London, United Kingdom, [4]Malaria Consortium, Kampala, Uganda

Seasonal malaria chemoprevention (SMC) aims to prevent malaria in young children in areas of seasonal malaria transmission. Historically, SMC was contraindicated in east and southern Africa, due to high-grade resistance to sulfadoxine-pyrimethamine, one of the drugs used for SMC. In 2022, geographic restrictions for SMC suitability were removed, prompting many countries to reconsider implementation. There is a need to understand the potential population-level impact of scaling up SMC in the region. Previously, the first clinical trials of SMC with SP + amodiaquine (SP+AQ) in Mozambique and Uganda showed good efficacy. We fit a model to the clinical data to characterise drug protection over time finding that SP+AQ reduces clinical malaria cases in the 30 days following drug administration by 87.4% (95% CrI: 78.0 - 92.4%). Here, we incorporate these estimates of SMC efficacy into an established *Plasmodium falciparum* transmission model developed at Imperial College, UK. We calibrate the model using data on entomology, rainfall, demography, historical intervention coverage, and malaria prevalence before validating against routine case data from seasonal regions in Mozambique, Uganda and other countries in East and Southern Africa. We estimate the potential impact of implementing SMC under various scenarios, including the number of cycles, their timing, targeted age groups and coverage achieved. Initial results suggest that even in areas of saturated *dhfr-dhps* quintuple SP resistance, SMC with SP+AQ could have a substantial population impact. Results from Uganda suggest that if SMC were delivered in seasonal areas, for 10,000 cycles of SMC administered, 536 clinical cases (range: 69 - 1412) and 19 severe cases (range 5 - 38) could be averted. We find that despite the high drug resistance present in East and Southern Africa, SMC has the potential to be highly effective and could avert a substantial burden of malaria in young children. It will be important to consider how SMC implementation may drive resistance to SP and AQ in areas with pre-existing resistance, and if higher grade resistance may negatively affect intervention effectiveness.

8041

WHAT HAPPENS WHEN CHEMOPREVENTION OF SEASONAL MALARIA IS STOPPED: EXPERIENCE IN THE SOUTHERN SENEGALESE REGION OF SÉDHIOU

Amadou Yéri Camara[1], Carlotta Carboni[2], Primo Buscemi[2], Maria Caldes[2], Mansour Faye[1], Mamadou Lamine Gueye[3], Alioune Badara Gueye[4], Adama Faye[5], Ibrahima Seck[6]

[1]region Medicale De Sedhiou, Sedhiou, Senegal, [2]centre De Sante Globale, Florence University, Italy, [3]region Medicale De Kolda, Kolda, Senegal, [4]usaid/Pmi, Sedhiou, Italy, [5]service Medecine Preventive, Universite Cheikh Anta Diop De Dakar, Senegal, [6]ised, Cheikh Anta Diop University Of Dakar, Senegal

In the Sédhiou region, we noted a drop in malaria incidence from 21‰ to 10.1‰ from 2015 to 2017. Thus no longer meeting the eligibility criteria for chemoprevention of seasonal malaria in children, the intervention was discontinued in Sédhiou in 2020. And in the absence of any other experience of stopping chemoprevention of seasonal malaria, we carried out a quasi-experimental study, with a mixed design taking the neighboring region of Kolda as a comparison zone, using case study

and linear regression modeling with the double-difference method. The discontinuation of chemoprevention of seasonal malaria is a source of concern for health workers and mothers/caregivers. The latter believe that this strategy reduces malaria cases, and fear a resurgence of cases when it is stopped. For the district medical officers, the cessation should be progressive, depending on the local incidence. Malaria incidence in children aged 3 to 120 months is 4.5 ‰ in 2017 and 17.47 ‰ in 2020. Correlations were sought between incidence and mortality and distance from the health center, existence of an ambulance, malaria training, structure, rainfall. No correlation was found between malaria incidence and rainfall or the implementation of mass distribution of mosquito nets. The number of malaria cases fell by 0.05% per month, with a difference of 31 cases between the Sédhiou region and the Kolda comparison ($p<0.01$). Mortality is correlated with the type of health facility, with a significant drop noted in health posts ($p<0.01$). There was no significant difference in malaria incidence between the Sédhiou region, where chemoprevention of seasonal malaria was stopped, and the Kolda region, where it was continued ($p=0.054$). No excess malaria mortality or morbidity among children or the general population was observed when chemoprevention of seasonal malaria was stopped. However, the mitigation plan, which reinforced early case management and larval nest control, may have contributed to such results.

8042

CONTRIBUTION TO THE IMPROVEMENT OF SEASONAL MALARIA CHEMOPREVENTION (SMC) SUPERVISION BASED ON REAL-TIME ANALYSIS OF DISAGGREGATED DATA FOR DECISION MAKING

Andre Kone[1], Moumouni Bonkoungou[1], Frederic Guigma[1], Ousmane Badolo[1], Francine Ouedraogo[1], Edward Kenyi[2], Gladys Tetteh[2], Lolade Oseni[2], Sidzabda Kompaore[3], Assetou Barry[3], Amsetou Ouiya[1], Arsène Traoré[1], Justin Tiendrebeogo[1], Sayouba Sebgo[1], Mame Diouf[4]

[1]U.S. President's Malaria Initiative, IHS Project, Ouagadougou, Burkina Faso, [2]Jhpiego, Baltimore, MD, United States, [3]SP/Palu, Ministry of Health, Ouagadougou, Burkina Faso, [4]US President's Malaria Initiative, USAID, Ouagadougou, Burkina Faso

Seasonal Malaria Chemoprevention (SMC) is one of the key interventions for reducing morbidity and mortality in children under 5 years of age in Burkina Faso. Despite reported SMC coverage in cycles 1 & 2 surpassing 100%, health facilities identified children not covered by the SMC campaign presenting with malaria between the two cycles. Further analysis was conducted to verify whether high SMC coverage at health facility level is associated with reduced malaria cases in three project regions. Secondary analysis of daily SMC monitoring data from 581 health facilities collected via a digitized version of the national SMC daily reporting tool was conducted. Confirmed malaria cases in children under 5 collected in health facility consultation registers were disaggregated by SMC-status. Quality control was carried out based on physical copies of the daily collection sheets, which were photocopied and attached to the registered data files to check for any coverage values that might be out of line. Descriptive and spatial analysis based on GIS was used to identify clusters with high SMC coverage and high proportion of malaria cases among children not covered by the SMC campaign. Descriptive analysis of these data will enable us to draw lessons to strengthen SMC implementation so it achieves its intended impact. 54.4% (n=4065) of malaria cases reported between cycle 1 and cycle 2 among children under 5 who were not covered by the SMC campaign came from health facilities with SMC coverage of over 100%. Validated SMC data revealed that SMC coverage was less than 100% (40-80%) in 52% of health facilities during the two cycles. Spatial analysis of SMC coverage disaggregated by health facility reveals three distinct clusters in the health districts of Garango (Centre-Est region), Nanoro (Centre-Ouest region) Diébougou (Sud-Ouest region). The results indicate that high coverage rates of over 100% do not mean that all children under 5 are fully covered during each campaign and will enable SP/Palu to strengthen the supervision system, which must focus on improving SMC coverage in areas where the number of malaria cases among children not covered by SMC is high.

8043

USE OF ALTERNATIVE LLIN DISTRIBUTION CHANNELS TO IMPROVE HOUSEHOLD OWNERSHIP AND USE OF LLINS

Nono Mvuama Mazangama[1], Eric Mafuta Musalu[1], Aimée Lulebo Mampasi[1], Marc Bosonkie[1], Jean-Bosco Kasonga[1], Branly Mbunga Kilola[1], Packy Mukanya Mbayo[2], Eric Mukomena Sompwe[2], Romain Jouffroy[3], Paul Samson Lusamba Dikassa[1]

[1]Kinshasa School of Public Health, Kinshasa, Congo, Democratic Republic of the, [2]National Malaria Control Program, Kinshasa, Congo, Democratic Republic of the, [3]Centre for Research in Epidemiology and Population Health (CESP), Villejuif, France

The Democratic Republic of Congo (DRC) has adopted the use of long-acting insecticide-impregnated mosquito nets (LLINs) as the principal means of preventing malaria infection. To promote LLIN ownership and use, the cyclical nationwide distribution of LLINs has become the primary concern of the national malaria control program. Despite these efforts, indicators of LLIN ownership and use in the country remain low and fluctuate according to whether the distribution is immediate. As a result, alternative distribution channels for LLINs have been devised to maintain their presence in households and improve their use. Based on data from the Vaccine Coverage Survey (VCS) 2022, coupled with malaria indicators, we set out to explore the contribution of alternative LLIN distribution channels to the rate of LLIN ownership and use in the country. The presence of at least one LLIN was reported in 72.8% of the 78,776 households nationwide that agreed to participate in the survey. A total of 114,185 LLINs were observed in households, of which 93.2% were insecticide-impregnated and 80.8% used to sleep under the night before the survey. For the country, 13.8% and 3.6% of these LLINs came from distribution to pregnant women at antenatal clinics (ANC) and to children under 5 at pre-school clinics (PSC) respectively. The rate of ownership of LLINs from these two sources seems proportional to the time spent post-campaign. In 9 of the country's 26 provinces, ANC-derived LLINs were in first place, with proportions ranging from 19% in Haut Katanga, 28% in Kinshasa, 30% in Haut Uele, 35% in Haut Lomami, 35% in Kongo Central, 37% in Tanganyika, 39% in Mai-Ndombe, 40% in Ituri, 41% in Sud Ubangi to 61% in Nord Ubangi. No influence of the school environment was found. Thus, ANC proves to be a reliable alternative for maintaining a stable rate of ownership and use in suitable proportions. Better monitoring of this activity will undoubtedly contribute to improving household ownership and use of LLINs and, indirectly, to reducing malaria morbidity and mortality.

8044

MALARIA IN PREGNANCY

Timah Tracy Mbayi

Centre de Rhumatologie Akwa Douala, Douala Cameroon, Cameroon

Malaria, a parasitic infection transmitted by mosquitoes, is one of the most devastating infectious disease killing more than one million people annually. Pregnant women, children, and immune-compromised individuals have the highest morbidity and mortality, and Africa bears the heaviest burden. Twenty-five million pregnant women are currently at risk for malaria, and, according to the World Health Organization (WHO), malaria accounts for 10,000 maternal and 200,000 neonatal deaths per year. The above statement leads the researcher to question the practices of health personnel regarding the management of malaria among pregnant women attending the Cite des Palmiers District Hospital, with the main aim to evaluate the practices of health personnel regarding the management of malaria in pregnancy.To achieve this, a quantitative, descriptive cross-sectional study was carried out and data was collected within 5 days at the ANC unit in the Cite des Palmiers District Hospital using questionnaires. During this study, 28 health personnel were identified by a simple random sampling technique, the analysis of data in word 2010, which allows us to express

our results on histogram, pie chart and tables.From our result, it appears that, most represented age range where 70% were between 21-25 years, 14% between 26-30 years, 7% between 31-35 years and 7% between 41-45 years while 0% was found between 36-49 years. For an overall practice of health personnel, 83% tell pregnant women to sleep under mosquito nets and to clean their environments while 17% do not. At the end of this study, it was concluded that 62% of health personnel had good practice towards the management of malaria among pregnant women while 38% were found to have challenges in the practice of management of malaria among pregnant women.

8045

THE SOCIO-DEMOGRAPHIC PREDICTORS OF INSECTICIDE-TREATED BED NET UTILIZATION FOR PROTECTION AGAINST MALARIA BY ASYMPTOMATIC INDIVIDUALS FROM RURAL COMMUNITIES ACROSS FIVE REGIONS IN MAINLAND TANZANIA

Gervas A. Chacha[1], Misago D. Seth[1], Rashid A. Madebe[1], Daniel A. Petro[2], Daniel P. Challe[3], Filbert Francis[3], Salehe S. Mandai[1], Angelina J. Kisambale[1], Rule Budodo[1], Ramadhan Moshi[1], Ruth B. Mbwambo[1], Dativa Pereus[1], Catherine Bakari[1], Sijenunu Aaron[4], Daniel Mbwambo[4], Samwel Lazaro[4], Ntuli Kapologwe[5], Celine I. Mandara[1], Deus S. Ishengoma[1]

[1]National Institute for Medical Research, Dar es Salaam, Tanzania, United Republic of, [2]University of Dar es Salaam, Dar es Salaam, Tanzania, United Republic of, [3]National Institute for Medical Research, Tanga Research Centre, Tanzania, United Republic of, [4]National Malaria Control Programme, Dodoma, Tanzania, United Republic of, [5]Directorate of Preventive Services, Ministry of Health, Dodoma, Tanzania, United Republic of

Insecticide-treated bed nets (ITNs) are the core vector control intervention used to prevent transmission and reduce malaria-related morbidity and mortality. Whereas ITNs are mainly targeting under-fives and pregnant women, there are potentially other vulnerable populations/groups which are yet to be identified and targeted. This community-based cross-sectional survey was conducted to evaluate predictors of ITNs usage among individuals of all age groups from five regions of Tanzania (Kagera, Kigoma, Njombe, Ruvuma and Tanga) with varying malaria endemicity. Logistic regression was used to determine the associations between ITNs usage and different predictors, and the results were presented as crude (cOR) and adjusted odds ratios (aOR) with 95% confidence interval (CI). The survey enrolled 10,228 individuals from 15 villages in five districts (one district/region). Of these, 77.62% owned and 77.23% used ITNs the night before the survey. The highest ITNs usage was in Nyasa (Ruvuma) (91.89%) while the lowest was in Kyerwa district (Kagera) (63.81%). All five villages from Kyerwa had lower usage of ITNs (<75%) while six villages; one village in Ludewa (Njombe), two in Muheza (Tanga) and three villages in Nyasa district had higher ITNs usage (>90%). ITNs usage were higher among females (aOR=1.21; 95% CI, 1.07-1.37) and under-fives (aOR = 2.28; 95% CI, 1.62 - 3.21). Four villages; one in Muheza and three in Nyasa had significantly higher odds of ITNs usage (>10 times) compared to a village in Kyerwa district (which had the lowest usage). Individuals with higher (aOR = 2.03; 95% CI, 1.72 - 2.40) and moderate socio-economic status (SES) (aOR = 1.59; 95% CI, 1.37 - 1.84) and living in houses whose walls had no holes (aOR = 1.29; 95% CI, 1.06 - 1.56) had significantly higher odds of ITNs usage. Thus, there was low usage of ITNs among males, school children, and individuals from households with low SES and poorly constructed houses. These findings should be considered by policymakers in ITNs distribution and targeting other vulnerable groups to close the socio-demographic gaps in ITNs usage and enhancing malaria control and elimination efforts in Tanzania.

8046

BENEFITS OF INCLUSIVE INNOVATION IN THE DEVELOPMENT OF A DECENTRALIZED ROUTINE DATA QUALITY AUDIT (RDQA) IMPLEMENTATION MODEL IN THE DEMOCRATIC REPUBLIC OF CONGO (DRC)

Jicko Bondole[1], Aline Nkulu[1], Jimmy Anzolo[1], Rova Ratsimandisa[1], Michael Hainsworth[2], Arantxa Roca Feltrer[3], Hyacinthe Kaseya[4], Alain Bokota[4], Ghislain Kikunda[4], Andre Kaseba[4], Eric Mukomena[4]

[1]PATH, Kinshasa, Congo, Democratic Republic of the, [2]PATH, Seattle, WA, United States, [3]PATH, Maputo, Mozambique, [4]National Malaria Control Program, Kinshasa, Congo, Democratic Republic of the

Problems with the quality of malaria data persist in the DRC, limiting the NMCP's ability to make informed decisions and launch a timely response to identified priorities. An effective surveillance and M&E system that produces high-quality data is essential for: i) monitoring malaria trends, ii) evaluating the impact of malaria control interventions, and iii) evidence-based decision-making. In 2023, the NMCP developed a decentralized RDQA approach targeting health zones and health facilities. This included a participatory approach involving stakeholders at all levels of the health system: national (NMCP, HMIS and technical partners), provincial (NMCP and HMIS), and health zone management teams through a series of consultative meetings. The following stages were crucial: i) landscape analysis of RDQA implementation at country level, ii) design of an RDQA model that would promote ownership and accountability of actors at provincial and peripheral levels, iii) development and updating of existing tools, and iv) adoption of a continuous learning approach during the RDQA pilot phase (June 2023 to March 2024). Integrating the perspectives of stakeholders across all heath administrative levels in the development of the RDQA approach has strengthened ownership and accountability of end-users in the implementation of RDQA and the monitoring of action outcomes. Actors are highly motivated to manage the feedback lifecycle from the national level to the province, from the provincial level to the health zone, and from the health zone to the health facilities, with increased responsibility and accountability of provincial and health zone level personnel in monitoring and supporting the implementation of corrective actions identified during the RDQA pilot phase. The proportion of recommended actions was 73% (106/145) from the first RDQA field visit, 70% (118/168) from the first formative supervision field visit, and 68% (115/167) from the second RDQA field visit.

8047

ASSESSING THE FEASIBILITY OF USING A MULTIPLEX SEROLOGICAL ASSAY TO CONDUCT SEROSURVEILLANCE FOR MALARIA EXPOSURE

Sidhartha Chaudhury[1], Jessica Bolton[2], Edwin Kamau[3], Elke S. Bergmann-Leitner[2]

[1]Walter Reed Army Institute of Research - Armed Forces Research Institute of Medical Sciences, Bangkok, Thailand, [2]Walter Reed Army Institute of Research, Silver Spring, MD, United States, [3]Tripler Army Medical Center, Honolulu, HI, United States

Measuring malaria exposure is critical for public health and malaria eradication efforts as well as in force health protection for military service members deployed to malaria endemic regions. Malaria disease surveillance is challenged by both natural immunity and chemoprophylaxis which can lead to under-estimate of malaria prevalence. In this effort, we test the feasibility of using a multiplex serological assay to measure malaria exposure based on antibody responses to 20 antigens including anopheline salivary antigens for vector exposure, pre-erythrocytic antigens for sporozoite exposure, and erythrocytic antigens for exposure to blood-stage parasitemia for both *P. falciparum* (Pf) and *P. vivax* (Pv) antigens. We validate this assay against samples from U.S. naïve subjects as well as subjects that underwent irradiated sporozoite treatment (IMRAS) or controlled human malaria infection (CHMI). We compare the serological profiles to those of samples collected from populations native to a region of Kenya with low

to moderate malaria endemicity and populations from Uganda with high malaria endemicity. We demonstrate that this multiplex serology assay can reliably detect exposure-induced antibody titers and we successfully applied this panel to 755 samples obtained from U.S. military service members returning from deployments to regions of Africa with significant malaria risk. Our findings reveal evidence of exposure: some individuals had anti-CSP antibody levels comparable to those found in endemic populations, suggesting exposure to sporozoites under chemoprophylaxis. We also observed isolated cases of anti-MSP1 levels that were as high as observed in endemic populations and CHMI studies, suggesting possible cases of clinical or subclinical parasitemia. The feasibility of implementation of this approach for serosurveillance in high-risk malaria settings is discussed.

8048

EVIDENCE OF *PLASMODIUM VIVAX* IN NORTHERN KENYA, AN EMERGING MALARIA CONTROL THREAT; AN INCIDENCE REPORT FROM THE OUTCOME OF THE MID-2023 EPIDEMIC RESPONSE AND FOLLOW UP SURVEY.

Francis T. Kimani, Kelvin Thiong,o
KEMRI, Nairobi, Kenya

Malaria mortality and morbidity in Kenya has all along been largely due to *Plasmodium falciparum* infections with no cases attributed to *P.vivax*. The northern Kenya counties are classified as zero to low-risk transmission zones. In mid-2023 an upsurge in febrile illnesses was reported in 3 such counties, requiring a pandemic response. In addition to possible viral infection that had featured in these areas previously, malaria disease was also investigated. A follow up sampling on the same spots was done six months after the initial outbreak. The presence of the diverse species present in this surveys is hereby reported. A total of 89 and later 64 blood samples were collected from patients suspected of malaria in the initial outbreak response and follow up survey. Positivity and speciation was performed using probes with species specific primers. From 3 health facilities in Marsabit, Mandera and Turkana counties a total of 24, 50, 15 and later 32 and 30 DBS samples were received respectively. There were 11, 40 and 15 in the first survey and 27 and 26, in the follow up, Plasmodium positive samples in the 3 facilities respectively. This translated to a total positivity of 74.8% in the select population. Speciation analysis recorded a total of 113 *P. falciparum* cases, 4 with a mixed infection of *P. malariae* and *P. falciparum*, 3 *P.vivax* mono infection, and 6 *P. vivax -P. falciparum* co-infected cases. No *P.ovale* was observed. A total of 4 patients in Mandera and 5 in Marsabit were found to be infected with *P.vivax* in the survey translating to an incidence rate of 7.1% and 6.3% respectively. The incidence of malaria from the response sites was quite high. Although the burden of *P. vivax* in these counties is undetermined, the presence of the observed proportions in such a small sample size is an indicator of an underlying or emerging problem of cases that are rarely diagnosed in a clinical setting and may often be asymptomatic. The presence of *Anopheles stephensi* that was recently identified in the same study region, presents a highly competent vector here, which could enhance the transmission of *P. vivax* and reverse all the malaria control gains made over the years.

8049

SOUTH-SOUTH EXCHANGE - USE OF A COLLABORATIVE CAPACITY STRENGTHENING MODEL FOR COUNTRIES APPROACHING MALARIA ELIMINATION

Elizabeth V. Burrough[1], Hannah M. Edwards[1], Lieven Vernaeve[2], Elizabeth Berryman[1], Médoune Ndiop[3], Wahjib Mohammed[4], Balthazar Candrinho[5], Arantxa Roca-Feltrer[6]
[1]Malaria Consortium, London, United Kingdom, [2]Malaria Consortium, Phnom Phen, Cambodia, [3]PNLP, Ministère de la Santé et de l'Action Sociale, Dakar, Senegal, [4]National Malaria Elimination Programme, Accra, Ghana, [5]Programa Nacional de Controlo da Malaria, Maputo, Mozambique, [6]PATH, Maputo, Mozambique

The Surveillance Practice and Data Quality Committee sits within the RBM Partnership to End Malaria's Surveillance, Monitoring and Evaluation Working Group. The committee aims to increase awareness of malaria surveillance guidelines among National Malaria Control Programmes (NMCP) and key stakeholders, and provides a platform to facilitate knowledge exchange in malaria surveillance and routine data management. Several NMPCs have requested support to adapt their surveillance systems for low transmission and pre-elimination settings. To respond to these requests an exchange programme was organised from 17 to 23 March 2024. The National Center for Parasitology, Entomology and Malaria Control (CNM), in Cambodia, was selected to host the exchange due to their achievement of reducing confirmed malaria cases by over 90% between 2010 and 2020. The exchange included participants from 11 African NMCPs and aimed to understand country priorities and support countries to build effective operational plans to transition from aggregate to case-based surveillance and develop models for cross-border surveillance. The programme started with CNM and partners discussing the malaria situation in Cambodia, national elimination strategy, and implementation experience, including challenges with drug resistance and cross-border surveillance. Field visits included meetings with provincial health department and health facility staff, and mobile and village malaria workers to understand the complexities of implementing a last mile operational plan and learn from the successful elimination of *Plasmodium falciparum*. Workshop discussions focused on understanding surveillance process, the importance of high-level ownership, collaboration, flexibility, and funding of country-driven technical capacity. We present key lessons from the exchange and short- and long-term priorities to be considered by Africa countries pursuing malaria elimination. The south-south exchange model provides a platform to facilitate knowledge exchange between countries, enabling those with first-hand experience to support others to achieve elimination goals.

8050

BENIN'S MALARIA SURVEILLANCE SYSTEM: INNOVATIONS TO PURSUE AND WEAKNESSES TO IMPROVE

Achille Couao-Zotti[1], Koffi Emmanuel YOVO[2], Julien Aïssan[1], William Houndjo[1], Macoumba Toure[3], Lundi-Anne Omam[2], Didier Agossadou[2], Rock Aikpon[1], Thibaud de Chevigny[3], Olajumoke Adekeye[2], Cyriaque Afoukou[1], Achille Batonon[1]
[1]National Malaria Control Program (NMCP), Ministry of Health (MoH), Benin, West Africa, Cotonou, Benin, [2]Clinton Health Access Initiative (CHAI), Cotonou, Benin, [3]Clinton Health Access Initiative (CHAI), Dakar, Senegal

In limited resources settings, the best way to optimize scarce resources in public health is to base decisions on evidence. For malaria control, countries have surveillance system, the aim of which is to guide decisions using data collected and analyzed on the epidemiological indicators of the disease. We used the Malaria Surveillance Assessment Toolkit under development with WHO in its latest pilot phase in Benin for a comprehensive assessment of the performance of the malaria surveillance system and the determinants of the level of performance. The toolkit was adapted to the Benin context for a comprehensive assessment. The assessment strategy combined; i) a desk review, ii) qualitative interviews with all the key players in malaria surveillance at central, intermediate, and peripheral levels of the health pyramid, and iii) quantitative data collection on a nationally representative sample of health facilities, including an assessment of data quality at health facility level. The low care seeking behavior in case of fever in under-5 children (53%), self-medication and the low contribution of the private sector in the routine malaria data collection system led to an estimated 17% representativeness of the cases captured by the surveillance system, according to the overall surveillance cascade figure. The monthly data reporting completeness rate is 81%, and the concordance of various indicators between the three sources: individual data registers at health facility level, monthly reporting forms and the entered data in the DHIS2 varies from 11% to 91% for the month of September 2021 which was evaluated. Routine data, campaign data, periodic survey data and routine supervision data are managed by different non-integrated parallel systems, which does not facilitate real-time data access for all stakeholders. A new strategy to improve data quality, based on the verification of used-RDT cassettes as proof of malaria confirmation, is a good practice to be pursued, and the implementation of interoperability between the different databases with DHIS2, the national repository, will be necessary to optimize the use of data for decision-making

8051

BED NET USE, MISUSE, AND MISCONCEPTION: A COMMUNITY-BASED CROSS-SECTIONAL STUDY IN FIVE REGIONS OF MAINLAND TANZANIA

Ruth Boniface Mbwambo[1], Filbert Francis[1], Daniel Challe[1], Misago D. Seth[1], Rashid A. Madebe[1], Rule Budodo[1], Angelina J. Kisambale[1], Gervas A. Chacha[1], Ramadhan Moshi[1], Salehe S. Mandai[1], Dativa Pereus[1], Catherine Bakari[1], Sijenunu Aaron[2], Daniel Mbwambo[2], Abdallah Lusasi[2], Stella Kajange[3], Samwel Lazaro[2], Ntuli Kapologwe[3], Celine I. Mandara[1], Deusdedith S. Ishengoma[1]

[1]National Institute for Medical Research-Tanzania, Dar es Salaam, Tanzania, United Republic of, [2]National Malaria Control Program, Dodoma, Tanzania, United Republic of, [3]President's Office, Regional Administration and Local Government, Dodoma, Tanzania, United Republic of

Bed nets are the most common vector control interventions in malaria endemic countries including Tanzania. Despite government efforts to distribute bed nets, studies have reported misconceptions and misuse of bed nets, leading to reduced effectiveness of bed nets in malaria control and elimination in Tanzania. This study aimed to upgrade the limited knowledge on the use, misuse, and misconceptions of bed nets in Tanzania. A community-based cross-sectional survey (CSS) was conducted in Kagera, Kigoma, Njombe, Ruvuma, and Tanga, regions from July to August 2023. In the CSS, anthropometric, demographic, clinical, parasitological, and socio-economic status data were collected through electronic devices using Open Data Kit software. Questionnaires with both open-ended and closed-ended questions were used to collect data on ownership, use, misuse, and misconceptions of bed nets. Descriptive statistics were used to summarize participants' responses to the questionnaires. Association between gender and bed net ownership was assessed using multivariate logistic regression analysis. A total of 10,228 individuals were recruited in the study. Most of the participants 5,005 (48.93%) were aged ≥15 years while under-fives and the school-aged children (5-15 years) were 1,538 (15.04%) and 3,685 (36.03%) respectively. The majority were females (60.25%) and 77.62% reported owning bed nets, with significant higher ownership among females (61.26%) than males (38.73%) ($p<0.001$). Of the participants, 7,899 (77.23%) reported using the nets the night before the survey. Only 659 (6.44%) participants were aware of other uses of bed nets and the most common misuse of bed nets was keeping chickens (4.81%, n=492) and making ropes (0.61%; n=63). Among the participants, 117 (1.14%) were aware of misconceptions related to bed nets and 85 (0.83%) reported heat stress as the most common misconceptions towards bed nets use. Misuse of bed nets is still a considerable challenge in Tanzania. This continues to reverse the government's efforts for malaria control and elimination. Educational programs are urgently needed to enhance use of bed and reduce misconceptions.

8052

QUANTIFY THE TREND IN MALARIA INCIDENCE AT HEALTH DISTRICT LEVEL AND IDENTIFY THE FACTORS ASSOCIATED WITH THIS INCIDENCE IN BURKINA FASO FROM 2016-2022 USING ROUTINE CASES DATA

Ousmane Oumou Diallo[1], Ambroise Ouédraogo[2], Sebastian Rodriguez[1], Oumar Billa[1], Jean Pascal Sandwidi[2], Jean Baptiste Ouedraougou[2], Aissata Barry[2], Beatriz Galatas[3], Noelle Samia[1], Jaline Gerardin[4], Sidzabda C. B. Kompaoré[2]

[1]Northwestern University, Evanston, IL, United States, [2]Secrétariat Permanent pour l'élimination du Paludisme, Ouagadougou, Burkina Faso, [3]Global Malaria Programme, World Health Organization, Geneva, Switzerland, [4]Northwestern University, Chicago, IL, United States

In recent years, Burkina Faso's national malaria control program has intensified malaria control interventions to reduce malaria morbidity and mortality. An analysis of routine malaria case data was undertaken to assess the impact of these interventions at health district (HD) level. Malaria incidence from routine surveillance was adjusted to account for incomplete testing, reporting, and care-seeking rates. We assessed the trend in malaria incidence in Burkina Faso between 2016 and 2022 by HD and identified predictors of malaria incidence. To analyze the trend, we used the seasonal trend decomposition (STL) using local regression smoothing, quantifying the significance of the trend with the Mann-Kendall test and direction and intensity of the trend with the Sen's slope coefficient. We used generalized additive mixed models with a smoothing spline function and district-level random effect to identify factors associated with malaria incidence at the district level.Between 2016 and 2022, the adjusted malaria incidence decreased by 15.2 % (from 864 to 733 cases per 1000 population) at national level. The STL method show that the trends decreased constantly for adjusted incidence in 39/70 HDs and the trend remained increasing in two HDs (N'dorola and Kampti). We found a significant positive relationship between number of days of IPTp stock-outs, bednets usage and health facility usage rate and adjusted incidence. We found a significant negative relationship between number of days of ACT stock-outs, number of years of seasonal malaria chemoprevention (SMC), number of SMC cycles and access to bednets and malaria incidence.The intensification of malaria control interventions has led to an overall reduction in the incidence of malaria. However, in some districts, a significant increase in incidence has been observed, hence the need to continue adapting strategies to meet these evolving challenges in order to reduce the incidence of malaria in these districts. In addition, the association between adjusted malaria incidence and some factors should be analyzed with caution and more in-depth analyses are needed to draw conclusions.

8053

FEASIBILITY OF USING GEOGRAPHIC INFORMATION SYSTEMS (GIS) TO FACILITATE POPULATION-PROPORTIONATE HOUSEHOLD SAMPLING OF ADMINISTRATIVE UNITS IN NORTHERN UGANDA, A CASE STUDY

Elizabeth R. Zhang[1], Frida Aryemo[2], Natasha Turyasingura[1], Melody Deblasio[3], Christopher Nyeko[2], Sandra Ajolorwot[2], Vivian Nakiwu[2], Amy Bei[1], Sunil Parikh[1], Richard Echodu[4]

[1]Yale School of Public Health, New Haven, CT, United States, [2]Gulu University Multifunctional Research Laboratories, Gulu, Uganda, [3]Yale College, New Haven, CT, United States, [4]Department of Biology, Faculty of Science, Gulu University, Gulu, Uganda

Population-based sampling using census population counts is the gold standard of public health sampling. In low- and middle-income countries, obtaining an up-to-date census at high spatial resolution poses a challenge in conducting population-representative sampling. Conventional methods to randomly selecting households (HH) for cluster sampling designs (e.g. WHO EPI cluster sampling or "random walk") is subject to selection bias and require multiple visits to each cluster. The use of GIS tools can mitigate these biases, preclude the need for a detailed census, and increase study validity by creating a more representative sample. Between August 2022 to January 2023, we successfully implemented a GIS-guided two-stage cluster sampling method GulART Study in Northern Uganda, which aimed to characterize the prevalence of *Pfk13* markers associated with partial resistance to artemisinin-based treatment of malaria in five districts. To the best of our knowledge, prior surveys of *Pfk13* in this region relied on convenience sampling. Our goal was to sample n=660 children <5 years of age. To do so, (1) we randomly selected n=33 parishes, stratifying by district; (2) we next obtained spatial population maps of each selected parish by masking a LandScanTM population density raster with parish boundaries obtained from Humdata in ArcGIS; (3) we used the Create Balanced Spatial Points tool to draw random points weighted by population density; points were then matched to Google Earth satellite imagery to select a human habitation within a 5km radius for a total of n=20 HHs per parish. HHs were oversampled by 1.5 times to account for unsuccessful encounters. To protect HH's geoprivacy, hand-drawn maps of parishes were used to locate sampled HHs. In our experience, GIS-guided sampling located an eligible HH participant in 70% of selected HHs and was feasible to use in field sampling. Rigorous implementation of our sampling protocol

abrogates common biases associated with "random walk" sampling, and linkage of participants and geo-location facilitates additional downstream analyses.

8054

DEVELOPING A ROADMAP FOR THE IMPLEMENTATION OF MALARIA GENOMIC SURVEILLANCE IN AFRICA

Abdoulaye Djimde[1], Alfred Amambua-Ngwa[2], Anita Ghansah[3], Collet Dandara[4], Charles Wondji[5], Isabella Oyier[6], Francis F. Chikuse[7], Nyasha Sithole[7], Aquillah Kanzi[8], Olivo Miotto[9], Victoria Simpson[10], Sofonias Tessema[7]

[1]University of Science, Techniques and Technologies of Bamako, Bamako, Mali, [2]MRC Unit The Gambia at the London School of Hygiene and Tropical Medicine, Banjul, Gambia, [3]Noguchi Memorial Institute for Medical Research, University of Ghana, Accra, Ghana, [4]University of Cape Town & South African Medical Research Council (SAMRC), South Africa, Cape Town, South Africa, [5]Centre of Research in Infectious Diseases (CRID), Yaoundé, Cameroon, [6]KEMRI-Wellcome Trust Research Programme (KWTRP), Nairobi, Kenya, [7]Africa CDC, Addis Ababa, Ethiopia, [8]African Society of Laboratory Medicine, Gauteng, South Africa, [9]Oxford University, Oxford. Mahidol-Oxford Research Unit, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand, [10]Genomic Surveillance Unit, Wellcome Sanger Institute,, Cambridge, United Kingdom

Genomics for global health with a focus on outbreaks and endemic disease has been a long term investment by researchers and public health professionals around the world. Interest and investment in the area of genomic surveillance has accelerated in recent years, including the potential for pathogens with pandemic and epidemic potential, as shown previously. However, there has been little translation of genomics for malaria policy-decision making to date. The power of genomic surveillance when applied to endemic diseases, such as malaria, has a dual purpose - to accelerate the elimination of the disease and as a source for pandemic preparedness for future events. Africa CDC commissioned- a technical working group in April 2022 to identify public health priority use cases and develop a roadmap for the implementation of malaria genomic surveillance in Africa which is to be delivered in 2024. With a focus on sustainability, harmonisation of laboratory approaches and interoperability of data, the roadmap aims to balance the need for country leadership with a continent wide strategy. Providing an end-to-end genomic surveillance framework developed for malaria, but adaptable to other pathogens and vectors, the phased approach encourages a national strategic plan informed by and aligned with regional and continent-wide objectives. It also aims to empower a continental network of institutions for malaria genomic surveillance such as reference laboratories, regional hubs and centres of excellence and national nodes for malaria genomic surveillance. Importantly, an enduring focus on the roadmap is on sustainability and inclusion of national funding as a key part of a diversified funding landscape. While ambitious, the roadmap is also pragmatic. It aims to build on existing knowledge, partnerships and infrastructure for the overarching goal of an integrated ecosystem that accelerates malaria elimination and contributes to global health security.

8055

DRUG PHENOTYPE ASSESSMENT TO VALIDATE DRUG RESISTANCE MARKERS CHANGING AMONG NATURAL SENEGALESE *PLASMODIUM FALCIPARUM* ISOLATES

Yaye Die Ndiaye[1], Katelyn Vendrely Brenneman[2], Wesley Wong[2], Imran Ullah[2], Stephen Schaffner[3], Abdoulaye Tine[1], Mouhammad Sy[1], Tolla Ndiaye[1], Amy Gaye[1], Mame Fama Ndiaye[1], Mariama Touré[1], Nogaye Gadiaga[1], Aita Séne[1], Awa Bineta Deme[1], Baba Dieye[1], Mamadou Samb Yade[1], Younousse Diedhiou[1], Daba Zoumatrou[1], Fatou Ba Fall[4], Doudou Séne[5], Medoune Ndiop[4], Ibrahima Diallo[5], Jules François Gomis[1], Aida Sadikh Badiane[1], Mamadou Alpha Diallo[1], Ibrahima Mbaye Ndiaye[1], Bronwyn MacInnis[6], Sarah Volkman[2], Daouda Ndiaye[1], Dyann Wirth[2]

[1]International Research and Training Center in Applied Genomics and Health Surveillance (CIGASS), Cheikh Anta Diop University, Dakar, Senegal, [2]Harvard T.H. Chan School of Public Health, Boston, MA, United States, [3]3Broad Institute, Cambridge, MA, United States, [4]National Malaria Control Program, Avenue Aimé Cesaire, Dakar, Senegal, [5]National Malaria Control Program, Avenue Aimé Cesaire,, Dakar, Senegal, [6]Broad Institute, Cambridge, MA, United States

Senegal has implemented multiple antimalarial drug-based strategies over the past two decades, including intermittent preventive treatment for pregnant women, artemisinin-based combination therapies as artemether-lumefantrine, artesunate-amodiaquine (AS-AQ) for case management and seasonal malaria chemoprevention (SMC) using SP-AQ. Previously, we profiled several known drug resistance markers (*Pfcrt, Pfmdr1, Pfdhfr, Pfdhps,* and *Pfkelch13*) using single nucleotide polymorphism (SNP) molecular surveillance and whole genome sequence collected from febrile patients with malaria at health facilities across Senegal between 2000-2022. Our molecular surveillance revealed changes in *Pfcrt, Pfdhfr* and *Pfdhps* allele frequencies over time. Of note was a decrease in the *Pfcrt* K76T allele frequency between 2003 and 2014, declining from 76% to 26% coincident with chloroquine (CQ) withdrawal as a primary first line drug. Interestingly, this trend was reversed between 2014 and 2022 with an increase in *Pfcrt* K76T allele frequency reaching a Senegal-wide frequency of 57% in 2022. Whole genome sequencing analyses suggested that this increase was associated with the emergence of a new selective sweep. We hypothesized that these changes on *Pfcrt* K76T in 2014 reflects emerging amodiaquine (AQ) resistance or amodiaquine-mediated changes in parasite fitness due to AQ use in SMC (SP-AQ) or in AS-AQ treatment. To test this hypothesis, we culture-adapted parasites with and without *Pfcrt* K76T and phenotyped them for drug susceptibility to chloroquine (CQ) and mono-desethyl-amodiaquine (MD-AQ), the active metabolite of AQ. Parasites with *Pfcrt* K76T had significantly increased CQ EC50 ($p<0.0001$) and MD-AQ EC50 ($p<0.0013$) relative to wildtype *Pfcrt* parasites. Phenotypic assessment and genetic validation using gene editing in a Senegalese background will be done to assess the impact of *Pfcrt* K76T mutation on MD-AQ susceptibility. However, these findings raise the question of the duration of AQ efficacy and suggest a need for ongoing monitoring using molecular surveillance and genetic validation to guide drug policy.

8056

DEVELOPING AN OPEN SOURCE, FREE, AND GENERALIZABLE SAMPLE AND DATA MANAGEMENT SYSTEM TO ENABLE SCALABLE AND SUSTAINABLE GENOMIC SURVEILLANCE IN SENEGAL

Katherine DeRuff[1], Bassirou Ngom[2], Jules Gomis[2], Elizabeth Curtis[1], Anna Y. Burkhard[3], Kairon Shao[3], Mariama Touré[2], Mouhamad Sy[2], Mamadou Alpha Diallo[2], Yaye Die Ndiaye[2], Chérif Younouss El Amin Lath Diouf[2], Younousse Diedhiou[2], Katherine Battle[4], Jonathan Livny[1], Dyann Wirth[3], Daouda Ndiaye[2], Sarah Volkman[3], Bronwyn MacInnis[1]

[1]Broad Institute, Cambridge, MA, United States, [2]International Center for Research and Training in Applied Genomics and Health Surveillance (CIGASS), Dakar, Senegal, [3]Harvard T.H. Chan School of Public Health, Boston, MA, United States, [4]Institute for Disease Modeling in Global Health, Seattle, WA, United States

Scalable and sustainable pathogen genomic surveillance, and more broadly any sizable sample or data handling, necessitates robust systems for sample and data management. Commercial solutions exist but are often expensive and inflexible to local contexts and needs, while bespoke solutions are often challenging to develop, scale, and sustain. Here we describe a sample and data management system using free and open access tools in the Google Suite (namely Google Sheets), developed to meet the needs of malaria genomic surveillance efforts in Senegal, but available and generalizable to the wider community. The system was initially developed at the Broad Institute in Boston for large-scale sample processing and management and adapted to support large-scale COVID genomic surveillance, and has several features that make it ideal for broader use, including in lower resource settings, such as integration with existing sample and data management systems, familiarity with Google tools and ease of uptake, and being an open source and free solution. Like other labs

scaling surveillance activities, CIGASS historically used several commercial and bespoke tools for smaller scale sample and data management. We are able to maintain functioning and familiar tools and seamlessly integrate them into this new system due to the flexibility of Google tools. Unlike tools that require some level of coding skills to navigate, such as a SQL database, Google tools are often familiar to users. At CIGASS, they already use a Google Workspace to manage all of their office activities including email and file sharing, which made the shift to this Google-based system fairly seamless. Google tools are free and open source, enabling generalizability to a broad range of settings. Google tools meet the highest standards of data security and privacy and access for sharing is controlled at the level of the individual user. This system has proven to be an effective tool for scaling and conducting genomic surveillance at a country-level at CIGASS and is generalizable, adaptable, and openly available to be used for other pathogens and laboratory settings.

8057

IMPACT OF A REWARD SYSTEM AND CONSISTENT FEEDBACK ON REPORTING RATE AND TIMELINESS IN OGUN STATE, SOUTHWEST NIGERIA

Ralph Enushai[1], Oluwatosin Olotu[1], Frederick Ifijeh[1], Chinedu J. Chukwu[2], Isaac Adejo[2], Tomisin Abimbola[2], Serah N. Nweke[3], Victoria Erinle[2], Dozie Ezechukwu[2], Thomas Hall[4], Frank Oronsaye[5], Sonachi S. Ezeiru[5], Cyril Ademu[6], Chukwu Okoronkwo[6], Godwin N. Ntadom[6], Olugbenga A. Mokuolu[7], James Ssekitooleko[8]

[1]Management Sciences for Health, Abeokuta, Ogun State, Nigeria, [2]Management Sciences for Health, Abuja, Nigeria, [3]Management Sciences for Health, Asaba, Delta State, Nigeria, [4]Management Sciences for Health, Arlington, VA, United States, [5]Catholic Relief Services, Abuja, Nigeria, [6]National Malaria Elimination Programme, Abuja, Nigeria, [7]University of Ilorin, Ilorin, Kwara State, Nigeria, [8]The Global Fund to Fight AIDS, Tuberculosis and Malaria, Geneva, Switzerland

The timeliness and reporting rates of data reports are key components of any health system aiming to ensure quality data. In Ogun State, Nigeria, as of 2017, the average annual reporting and timeliness rates of data reports was 40% and 31% respectively among the 20 Local Government Areas (LGA). In 2018, Management Sciences for Health began implementing a seven-step approach to address this challenge, with the aim of getting the timeliness and reporting rates above the 90% national target. Working with the State team, we adopted the following steps: established a data control room to track reporting and timeliness rates and other data quality issues; trained the control room team on the use of District Health Information Software v.2 (DHIS2) to download and track data; divided LGAs among control room members for better accountability; shared daily reporting with LGAs and stakeholders from 8th to 14th of each month; rewarded/celebrated best performing LGA each quarter; presented a letter from the Permanent Secretary of the Ministry of Health to the best performing LGA over the past year; and, supported cleaning and validation of the DHIS2 data reports and having a health facility registry. The results show a steady increase from 2018 through 2023 with the average reporting and timeliness rates increasing from 40% and 31% to 71% and 65% respectively. There was a slight dip in 2021 due to the migration to DHIS2. While the combined effect of the seven-step approach appears to have yielded good results, more study is required to ascertain which of the steps are the most critical and whether the intervention can be sustainably supported by the State. In conclusion, MSH implementation in Ogun State has led to a steady increase in reporting rate and timeliness, although the state still falls slightly below the national target of 90%. However, a dip in 2021 was due to the migration from DHIS version 2013 to 2019, affecting reporting rates and timeliness. Further cleaning on DHIS is needed to remove duplicate and non-functional facilities, which also affect reporting rates.

8058

ENHANCING WEEKLY EPIDEMIOLOGICAL SURVEILLANCE DATA COMPLETENESS ACROSS KARAMOJA REGION OF UGANDA: A QUALITY IMPROVEMENT APPROACH

Derrick Nabongho[1], Badru Gidudu[1], Christine Lodungokol[1], Stephen Kigongo[2], Richard Ongom Opio[1], Angela Kateemu[1], Edward Mugwanya[1], Ronald Kimuli[3], Amy Casella[4], Aliza Hasham[4], Benjamin Binagwa[1], Nancy Brady[4]

[1]USAID/PMI Uganda Malaria Reduction Activity; JSI, Kampala, Uganda, [2]USAID/PMI Uganda Malaria Reduction Activity; MCD, Kampala, Uganda, [3]Ministry of Health, National Malaria Control Program, Kampala, Uganda, [4]USAID/PMI Uganda Malaria Reduction Activity; JSI, Boston, MA, United States

In Uganda's Karamoja region, a review of key malaria indicators revealed significant incompleteness in the weekly epidemiological surveillance report (HMIS 033B), particularly in the commodity section, which is crucial for malaria tracking at health facility and district levels. At baseline in week 40 of 2023, HMIS 033B report completeness was only 67%, well below the required 95% completeness. To address data quality issues, the PMI Uganda Malaria Reduction Activity (PMI MRA) conducted a desk analysis of the report, focusing on completeness, consistency, accuracy, and integrity. Further inquiry revealed inadequate knowledge among health workers on how to complete the HMIS 033B and an unclear understanding of roles regarding who should fill which report section and when. Consequently, PMI MRA worked with Karamoja's 9 district local governments using a systematic quality improvement approach, including regular monitoring, mentorship, data validation, and joint support supervision of malaria activities at the health facility level, along with weekly desk-based generation of malaria indicator dashboards. Forty-two district health technical resource persons were trained in constructing and using malaria surveillance charts and filling the HMIS 033B report, who subsequently trained 448 health facility workers, followed by continuous monthly coaching, monitoring, and supervision for 6 months. The reports also helped district health teams and leadership identify 60 overstocked and 7 stocked out facilities for appropriate commodity redistribution. The proportion of completed HMIS 033B reports improved from 67% in week 40 of 2023 to 97% in week 10 of 2024, following intense data quality checks, and emphasizing completing reports during performance review meetings. Intense data quality improvement efforts in response to incomplete reporting resulted in improvements in reporting rates and data use in Karamoja region.

8059

SOCIODEMOGRAPHIC STUDIES AND THE SPATIAL DISTRIBUTION OF MALARIA EPISODES IN DANGASSA, KATI DISTRICT FROM 2014 TO 2016

Oumar Thiero[1], Aissata Massambou Sacko[2], Kola Cisse[2], Soumba Keita[3], Seydou Doumbia[3]

[1]Tulane/FMOS, New Orleans, LA, United States, [2]FMOS/DER SP, Bamako, Mali, [3]FMOS/UCRC, Bamako, Mali

One of the main characteristics of malaria epidemiology is its heterogeneity in malaria-endemic areas, especially in semi-urban areas such as Dangassa in Mali. This study evaluates the risk factors associated with the occurrence of multiple episodes of malaria in Dangassa from 2014 to 2016 and their spatial distribution. This was a longitudinal study with the ICEMR1 cohort in Dangassa from 2014 to 2016. In the study, participants were malaria-free during the cross-sectional round and were followed according to the occurrence of malaria episodes between the passages. The risk of multiple episodes was determined by ordinal logistic regression with SPSS 25.0 software. Arc-GIS version 10.2 software was used to analyze the spatial distribution of malaria episodes. The risk of a high number of malaria episodes was higher in children aged 5 to 9 years compared to those under 5 years of age (OR=1.33(1.06; 1.66). This risk was greater during periods of high transmission OR=2.05(1.74; 2.42) and varied by year (lower in 2016) OR= 2.69 (2.21; 3.3) and 2.93(2.44; 3.52). The malaria episodes were scattered throughout the village with a high concentration to the west

where the Niger River passes about 4 km away. Our results showed that there would likely be malaria transmission hotspots in Dangassa and that vulnerability related to malaria occurrence was higher among children aged 5 to 9 years compared to those less than 5 years of age.

8060

IMPROVING MALARIA EPIDEMIC SURVEILLANCE IN UGANDA'S WEST NILE REGION THROUGH HEALTH WORKER CAPACITY STRENGTHENING AND REUSABLE MALARIA SURVEILLANCE CHARTS

Felix Manano[1], Robert Abiriga[1], Angela Kateemu[1], Richard Ongom Opio[1], Felix Omania[1], Immaculate Mujawimana[2], Edward Mugwanya[1], Ronald Kimuli[3], Amy Casella[4], Aliza Hasham[4], Benjamin Binagwa[1], Nancy Brady[4]

[1]USAID/PMI Uganda Malaria Reduction Activity; JSI, Kampala, Uganda, [2]Terego District Health Office, Ministry of Health, Kampala, Uganda, [3]Terego District Health Office, Ministry of Health, Kampala, Kampala, Uganda, [4]USAID/PMI Uganda Malaria Reduction Activity; JSI, Boston, MA, United States

Malaria remains a significant public health challenge in Uganda, with varying prevalence rates across high-burden regions, namely: 22% in West Nile, 34% in Karamoja, 21% in Busoga, 13% in Lango, and 12% in Acholi (Malaria Indicator Survey, 2019). In West Nile, there was limited monitoring and tracking of malaria cases between July and September 2022, with weekly epidemiological surveillance reporting (HMIS 033B) consistently at 78%, just below the 82% annual national target in financial year 2022/2023 (UMRESP 2020-2025). To strengthen surveillance in the region, reusable malaria surveillance boards were procured and distributed to all 13 district health offices, 358 health facilities, and two emergency operation centers. Additionally, 279 health workers were trained-including district health officers, biostatisticians, HMIS focal persons, malaria focal persons, district medicines management supervisors, and surveillance focal persons to construct, plot and update, interpret, and use the charts to monitor weekly malaria case trends, set incidence thresholds, and trigger epidemic alerts and response. Of the 378 malaria surveillance charts distributed in health facilities across the region, 94 in six districts successfully plotted and constructed the malaria normal channel charts after training. As a result, the weekly epidemiological surveillance reporting rates increased by 16%, from 76% in week 1 to 92% in week 9 of 2024, indicating improved reporting in the region. Given that malaria epidemics are often localized, the surveillance charts prove most effective when completed and interpreted at the health facility level. Using malaria epidemiological surveillance charts is critical for enhancing the weekly epidemiological surveillance reporting rate and triggering rapid response.

8061

INTEGRATION OF COMMUNITY DATA WITH ROUTINE HEALTH FACILITY DATA TO GENERATE INSIGHTS INTO MALARIA EPIDEMIOLOGY AND SERVICE DELIVERY IN BUIKWE DISTRICT IN UGANDA

Ruth N. Kigozi[1], John Baptist Bawnika[1], Stella Bakeera[1], Rutayisire Medi[2], Solomon Muhumuza[2], Anthony Nuwa[1], Emily Goodwin[1], Godfrey Magumba[1], Hanna Edwards[3]

[1]Malaria Consortium, Kampala, Uganda, [2]Ministry of Health, Kampala, Uganda, [3]Malaria Consortium, London, United Kingdom

While routine surveillance is a key component in control, prevention and elimination of diseases, use of this data for decision making is still limited. This study sought to understand how data from community and health facility-based systems in Buikwe district, Uganda, can be utilized to better-inform decision making. The study reviewed analyzed monthly outpatient and community data from Buikwe district for the period Jan - Aug 2023 to assess service uptake, malaria testing rates, number of confirmed malaria cases, and crude incidence for this period. Completeness of data from health facilities was high with over 90% of the expected reports submitted monthly, however, community data completeness was lower ranging from 33% (Feb) to 75% (Jul) of expected reports submitted. Monthly data trends showed that, as the number of confirmed malaria cases seen at the community increased, the number of confirmed cases seen at the health facilities reduced. At the community, there was 349% increase in the number of cases in May 23 compared those seen Aug 23, while a 114% decrease in the number of confirmed cases was seen at health facilities in the same period. Similar observations are seen with results for crude malaria incidences. Diagnosing malaria at community level reduced the number of cases seen at health facilities. Solely using health facility data to monitor trends in malaria cases could have led to misinterpretation of the prevailing situation. This study showed that combining health facility-based and community surveillance data can provide a more holistic picture of the malaria situation in a given geography.

8062

DIGITALIZATION THROUGH DHIS2 TRACKER PROGRAMS AT HOUSEHOLD AND INDIVIDUAL LEVELS FOR 2023 SEASONAL MALARIA CHEMOPREVENTION CAMPAIGNS IN CÔTE D'IVOIRE

Alexis Serge Aimain[1], Luigi Nuñez[2], Amadou Donapoho Soro[3], Eric Akkatia[3], Melly Aissatou Traore[3], Yao Koffi[3], Mea Antoine Tanoh[1], Collette Yah Epse Kokrasset[1], Patricia L. Yepassis-Zembrou[4], Pascal Zinzindohoue[5], Blaise Kouadio[5], Melaine Tape[5]

[1]Côte d'Ivoire National Malaria Control Program, Abidjan, Côte D'Ivoire, [2]Populuation Services International, Washington, DC, United States, [3]Population Services International Côte d'Ivoire, Abidjan, Côte D'Ivoire, [4]U.S. President's Malaria Initiative, Centers for Disease Control and Prevention, Abidjan, Côte D'Ivoire, [5]U.S. President's Malaria Initiative, U.S. Agency for International Development, Abidjan, Côte D'Ivoire

The PMI Stop Djekoidjo project, funded by the U.S. President's Malaria Initiative, supported the Ivorian Ministry of Health's National Malaria Control Program (NMCP) to launch its first seasonal malaria chemoprevention (SMC) campaign in two health districts in 2023. The NMCP DHIS2 instance, separate from the national Health Management Information System, was used to digitally collect and analyze the campaign data. The goal was to ensure the availability of data to enable course correction during the campaign, reduce workload burden on health workers and community health workers (CHWs), and minimize the data quality issues experienced in previous campaigns using paper-based tools. Data collection tools were first configured to work with DHIS2 Tracker and indicators to monitor performance within a DHIS2 dashboard were created. User acceptance testing was then conducted, and necessary corrections were made to the data collection tools and the dashboard based on feedback. Supervisors, district management teams, and CHWs were trained on the collection of household-level data using a QR code using tablets equipped with the DHIS2 Android Capture application. Training also included conducting analyses and data visualizations within the DHIS2 dashboard. During the SMC campaign itself, data were entered after scanning unique QR codes, which households received during registration. Using QR codes provided instantaneous information to health workers and CHWs than searching children in a register that would take on average five minutes. Digitization of data allowed for more efficient data entry and an overall faster campaign, since data entry took less time per household. Data were submitted every day, allowing near real-time monitoring across the entire campaign. The first and second cycles of the SMC campaign covered 86% and 90% of eligible children, respectively, who received tablets of sulfadoxine-pyrimethamine+amodiaquine (SPAQ). This digitization provided improved data quality, ease of coverage rates monitoring, and reduction of workload burden on health workers and CHWs.

8063

STREAMLINING THE MEDICINE REGISTRATION SYSTEM TO IMPROVE ACCESS TO QUALITY MALARIA COMMODITIES IN MADAGASCAR, 2018 - 2024

Jean René Randriasamimanana[1], Fanja Rakotomanana[2], Hoby Sitraka Ravelomampianina[2], Soafara Andrianome[3], Antonia Stéphanie Rakotoniaina[1], Aline Mukerabirori[1], Aishling Thurow[4], Jane Briggs[4], Thomas Hall[4], Luz Razafimbelo[1], Laurent Kapesa[5]

[1]IMPACT Program, Management Sciences for Health, Antananarivo, Madagascar, [2]Madagascar Medicines Regulatory Authority, Antananarivo, Madagascar, [3]Madagascar Central Medical Store (SALAMA), Antananarivo, Madagascar, [4]Management Sciences for Health, United States of America, Arlington, VA, United States, [5]U.S. President's Malaria Initiative, United States Agency for International Development, Antananarivo, Madagascar

Strengthening the essential medicine registration system is critical to improving availability of malaria commodities in Madagascar. Registration of antimalarial commodities funded by donors to allow their importation and presence on the market has typically taken at least six months, compromising their availability. To address this, the U.S. Agency for International Development (USAID)-funded IMPACT program began supporting the Malagasy Ministry of Public Health (MOPH) in 2019 to harmonize the Madagascar Medicines Regulatory Authority (AMM) market authorization (MA) process, by applying a quality assurance system for the Madagascar Central Medical Store (SALAMA) and donors to prequalify vendors. In 2021, a multi-stakeholder registration committee was established by the AMM to analyze pending dossiers and clear the backlog of MA requests submitted by SALAMA and donors. Monthly meetings have been organized since 2022 with the committee to evaluate the dossiers and grant MA letters for products that fulfill the criteria to be registered. From 2018 to 2024, 91 dossiers of MA requests were submitted to the AMM for malaria medicines, and after technical assessment by the committee, 76 (84%) of the dossiers met the requirements to be assessed for MA. Sixty of the 76 (79%) received MA, and MA requests were processed (dossiers reviewed and, if approved, MA letters issued), on average, in a period of two months (an estimated four months less than before the IMPACT program) from receipt of dossier and payment for combinations of artemether-lumefantrine, artesunate-amodiaquine, and sulfadoxine-pyrimethamine. Implementing a harmonized system of prequalification of and MA processes for malaria commodities streamlines their registration, thereby helping facilitate their availability on the market and ensure quality. Harmonized and streamlined review processes for registration of malaria products is a key strategy to strengthen the medicine regulatory system and improve access to safe, quality antimalarial products, and can be considered for scale up in other low- and-middle income countries.

8064

ESTABLISHING ROBUST, OPEN, ACCESSIBLE BIOINFORMATICS TOOLS FOR MALARIA GENOMIC DATA ANALYSIS AND REPORTING, IMPLEMENTED IN THE TERRA CLOUD-BASED ANALYSIS PLATFORM

Jonathan T. Smith[1], Stephen Schaffner[1], Bassirou Ngom[2], Wesley Wong[3], Christine Loreth[1], Katherine DeRuff[1], Elizabeth Curtis[1], Shadi Zaheri[1], Jorge-Eduardo Amaya-Romero[3], Angela Early[1], Daniel Park[1], Dyann Wirth[3], Daouda Ndiaye[2], Kiran Garimella[1], **Bronwyn MacInnis**[1]

[1]Broad Institute, Cambridge, MA, United States, [2]International Research Training Center on Genomics and Health Surveillance (CIGASS), Dakar, Senegal, [3]Harvard T. H. Chan School of Public Health, Boston, MA, United States

Bioinformatic analysis capacity remains a significant challenge in advancing the implementation and impact of malaria genomic surveillance. Here we share progress in developing validated genomic data analysis tools (workflows) to serve common use cases for Plasmodium falciparum (Pf), and the implementation of these workflows in Terra, a secure, user-friendly, open access, cloud-based data analysis platform. We describe the development of a workflow for high confidence SNP variant calling from short read whole genome sequence data, using the current gold standard genomic analysis toolkit (GATK 4.5.0) and state-of-the-art methods in alignment (BWA-MEM2), variant calling (HaplotypeCaller with De Bruijn graphs), and filtration (GATK VETS). The variant filtration process leverages the MalariaGEN Pf7 data resource, which provides broad representation of global Pf genetic diversity to optimize filter correctness, and has been validated against well characterized samples, including the Pf genetic crosses datasets. Openly accessible in the Terra cloud platform, this workflow offers robust whole genome variant calling regardless of local compute infrastructure or computational expertise. It is part of a larger data analysis ecosystem being developed to provide accessible and reliable tools and support for the malaria genomics community. Additional workflows currently available in Terra will also be featured, including SNP-based drug resistance determination and genetic relatedness inference from short read sequence data, deconvolution of polygenomic infections and hrp-2/3 deletion determination from long read data, and denoising and analysis of amplicon sequence data. We also show the application of these tools to the analysis of Pf genomic surveillance data from Senegal, including local workflow development, data analysis, and NMCP reporting. Practical considerations for the use of these tools and of the Terra platform by the malaria genomics community will also be covered.

8065

COMPARATIVE ANALYSIS OF INDIVIDUAL-BASED MALARIA MODELS: CHARACTERIZING MODEL BEHAVIOR FOR ENHANCED CONFIDENCE IN MODEL-INFORMED DECISION MAKING

Manuela Runge[1], Ricky Richter[1], Narimane Nekkab[2], Aurélien Cavelan[2], Tom Brewer[3], Peter Winskill[3], Melissa Penny[4], Jaline Gerardin[1]

[1]Northwestern University, Chicago, IL, United States, [2]Swiss Tropical and Public Health Institute, Basel, Switzerland, [3]Imperial College London, London, United Kingdom, [4]Telethon Kids Institute, Nedlands, Australia

Mathematical models are increasingly used to support global and national malaria policy decision making. It is unclear how the use of different models may affect supporting model evidence for decision making, however, no exhaustive comparison of model behavior, including perturbations, exists. We use three widely used individual-based models of malaria to characterize model behavior and compare relationships in outcome measures across varying age groups at equilibrium or after perturbations that approximate common interventions used (preventive therapies, vector control, and vaccination). The models were aligned as much as possible on critical input parameters, such as transmission intensity, case management, and diagnostic performance while maintaining structural model differences. The models produce daily, monthly, and yearly clinical outcomes by flexible age groups as well as indicators of transmission for varying scenarios. We describe the relationships between transmission intensity, prevalence, and clinical or severe incidence, in specific age groups or trends by age. While these epidemiological relationships were generally similar across the models at equilibrium and under perturbation, differences were apparent, for extreme levels of low or high transmission, by disease outcome, and for perturbations affecting immunity acquisition. The results support transparent and improved understandings of performance and behavior of the three models assessed. Ultimately this type of comparison increases confidence of model users and decision makers in the modeling results.

8066

EVALUATING SUB-NATIONAL TAILORING OF MALARIA INTERVENTIONS

Adam Bennett[1], Peder Digre[1], Hana Bilak[2], Hannah Slater[1], John Miller[3]

[1]PATH, Seattle, WA, United States, [2]PATH, Geneva, Switzerland, [3]PATH, Lusaka, Zambia

In an environment of limited financial resources for malaria control, directing those resources in the most cost-effective way to maximize reductions

in malaria burden is critical. As a result, data-driven sub-national tailoring (SNT) of malaria interventions has become a key component of developing national strategies and applying for funding from the Global Fund (GF) and other funders. While this process is increasingly driven by funding organizations, the World Health Organization, and partners, it requires strong country leadership and ownership to be truly successful. Country programs also need guidance on how best to implement SNT under the current funding conditions. We completed an in-depth assessment of the effectiveness of the SNT process conducted for the past two GF cycles in seven countries (Central African Republic, Democratic Republic of the Congo, Ethiopia, The Gambia, Nigeria, Senegal, and Zambia) to understand key challenges, gaps, and best practices. We first created a conceptual framework to identify key steps in the SNT process, including improving surveillance data quality, creating a repository of intervention and related data, convening a technical working group, conducting stratification and intervention targeting based on country-defined criteria, obtaining adequate funding, and implementing and evaluating the SNT plan outcomes with allocated funding. For each country we reviewed and collated data on each of these steps from the two most recent GF grant cycles (6 and 7), national strategic and operational plans, intervention coverage, and routine malaria surveillance data. In addition, we conducted 25 in-depth interviews with key national malaria program and partner organization staff to document perspectives of challenges and bottlenecks encountered and successes achieved. We present results of this analysis where a systems approach was used to characterize factors associated with a successful SNT process, focusing on efficiency, equity, country ownership and value for money. Both country specific and cross-country themes will be presented.

8067

RAPID MOLECULAR MONITORING OF *KELCH13* OF *PLASMODIUM FALCIPARUM* SHOWS LOW DIVERSITY AND LACK OF ARTEMISININ RESISTANCE-ASSOCIATED MUTATIONS ON BIOKO ISLAND, EQUATORIAL GUINEA

Thomas C. Stabler[1], Salome Hosch[1], Elizabeth Nyakarungu[2], Johanna Giger[1], David S. Galick[2], Carlos A. Guerra[3], Guillermo A. Garcia[3], Tobias Schindler[4], Joana C. Silva[5], Claudia Daubenberger[1]

[1]SwissTPH, Allschwil, Switzerland, [2]MCD Global Health, Malabo, Equatorial Guinea, [3]MCD Global Health, Silver Spring, MD, United States, [4]Diaxxo AG, Zurich, Switzerland, [5]Institute of Genome Sciences, Baltimore, MD, United States

In 2023, the Bioko Island Malaria Elimination Project (BIMEP) conducted their annual malaria indicator survey (MIS) on Bioko Island (BI), Equatorial Guinea, revealing 12.9% *Plasmodium* species (Pspp) prevalence by RDT over all age groups. As BIMEP pushes towards pre-elimination, monitoring malaria for drug resistance markers, including low parasite density infections, becomes a high priority. With the aim of developing a pre-screening workflow to monitor for drug resistance markers, we analyzed 1,500 dried blood spot samples collected from individuals with positive (n=1400) and negative (n=100) RDTs for the presence of malaria parasites. Utilizing PlasmoPod, a novel, cartridge-based, rapid PCR diagnostic device, samples were tested in the research laboratory on BI, for the presence of Pspp using 18S rDNA/rRNA RT-qPCR. Further, a subset (n=209) was assessed by qPCR for *kelch13* mutations R561H, M579I and C580Y in the propeller region, signals known to be associated with artemisinin resistance in SE Asia. No resistant mutations were found at target sites among these samples. Nanopore sequences from the 2023 MIS are being generated and analyzed on BI providing more detail on currently circulating variations in drug resistance sites of the *kelch13* propeller region. Analysis of *P. falciparum* sequence data from the 2019 MIS (n=90) show nucleotide diversity in the *kelch13* coding region to be low (π = 0.001 ± 0.0001). While most mutations occur in the coiled-coil-containing and BTB (Bric-a-brac, Tramtrack and Broad complex) domains, some SNPs appear in the propeller region. However, these are not known to be associated with resistance, but are common alleles appearing in African isolates. As BI transitions to a low-transmission area, BIMEP will need to conduct continuous surveillance to monitor the potential expansion of drug-resistant strains due to antimalarial-related selective pressure. Employing a qPCR-based screening protocol locally for key *kelch13* mutations with Plasmopod, improves cost-efficiency without compromising PCR accuracy and allows for close, rapid monitoring of *P. falciparum* strains.

8068

ASSESSEMENT OF QUALITÉ OF MALARIA CASE MANAGEMENT AND PREVENTION USING MICROSTRATIFICATION METHOD

Roseline Maimouna Y. Maimouna Bamouni

Clinton health access initiative, Ouagadougou, Burkina Faso

Although there has been a 10% drop in incidence over the past 5 years despite the multitude of interventions implemented to reduce malaria burden, malaria remains the leading cause of mortality in Burkina Faso, accounting for 14% of deaths in 2022. In 2023, the NMCP carried out a microstratification analysis with the aim to assess the quality of malaria services. A two-prong approach was used to carryout this assessment as guided by WHO. Firstly, 17 indicators for malaria management and prevention services were calculated using routine data from health facilities. Secondly, using this 17 indicators, 4 composite indicators were generated to mesure management of uncomplicated malaria, management of malaria (uncomplicated and complicated), routine prevention interventions and a composite indicator of overall malaria program performance. All indicators were then classified into low, medium and high performance. Overall, all the health facilties (3843) were included, analysis of the 4 composite indicators showed that : 13% had a high performance for the management of uncomplicated malaria, 24% for the implementation of routine preventive services, 19% for the total composite indicator. Data on the management of severe malaria were not collected in the health information system. Among the 12 simple indicators, the one with the best performance was the rate of treatment of uncomplicated malaria with an ACT, with a high performance for 27% of health facilities. Prevention through the distribution of LLINS to children under 5 had the lowest performance, with 8% of health facilities with high performance.According to our analysis, the quality of malaria case management and prevention service provision in health facilities faces challenges. These results are in line with those of the SARA survey carried out in 2018, which highlighted the challenges of implementing malaria treatment guidelines. The implementation of routine microstratification analysis using routine data and using the results to inform the targeting of interventions such as supportive supervision to health facilities will greatly improve the quality of service

8069

ADVANCING EARLY WARNING SYSTEMS FOR MALARIA, PROGRESS, CHALLENGES, AND FUTURE DIRECTIONS

Donnie Mategula[1], Judy Gichuki[2], Karen Barnes[3], Emanuele Giorgi[4], Dianne Jannete Terlouw[1]

[1]Malawi Liverpool Wellcome Programme, Blantyre, Malawi, [2]Institute of Healthcare Management, Strathmore University, Nairobi, Kenya, [3]Division of Pharmacology, University of Cape Town, Cape Town, South Africa, [4]Lancaster Medical School, Lancaster University, Lancaster, United Kingdom

Malaria early warning systems (EWS) are predictive tools that often use climatic and environmental variables to forecast malaria risk and trigger timely interventions. Despite their potential benefits, the development and implementation of EWS for malaria face significant challenges and limitations**.** We reviewed the current status of EWS for malaria, including their settings, methods, performance, actions, and evaluation. We conducted a comprehensive literature search using keywords related to EWS and malaria in various databases and registers. We included primary research and programmatic reports focused on developing and implementing EWS for malaria. We extracted and synthesized data on the characteristics, outcomes, and experiences of EWS for malaria. After reviewing 5,535 records, we identified 30 studies from 16 countries that met our inclusion criteria. The studies varied in their transmission settings, from pre-elimination to unstable, and their purposes, ranging from outbreak detection to resource allocation. The studies employed

various statistical and machine-learning models to forecast malaria cases, often incorporating environmental covariates such as rainfall and temperature. The most common mode used is the time series model. The performance of the models was assessed using measures such as the Akaike Information Criterion(AIC), Root Mean Square Error (RMSE), and adjusted R squared(R^2). The studies reported actions and responses triggered by EWS predictions, such as vector control, case management, and health education. The lack of standardized criteria and methodologies limited the evaluation of EWS impact. This review provides a comprehensive overview of the current status of EWS for malaria, highlighting the progress, challenges, and gaps in the field. The review informs and guides policymakers, researchers, and practitioners in enhancing EWS and malaria control strategies. The review also underscores the need for further research on the integration, sustainability, and evaluation of EWS for malaria, especially in light of ongoing climate change**.**

8070

STRAIN-TRANSCENDING ANTI-AMA1 HUMAN MONOCLONAL ANTIBODIES NEUTRALIZE MALARIA PARASITES INDEPENDENT OF DIRECT RON2L RECEPTOR BLOCKADE

Palak N. Patel[1], Ababacar Diouf[1], Thayne H. Dickey[1], Wai Kwan Tang[1], Christine S. Hopp[2], Boubacar Traore[3], Carole A. Long[1], Kazutoyo Miura[1], Peter D. Crompton[1], Niraj H. Tolia[1]

[1]National Institutes of Health, Bethesda, MD, United States, [2]Bernhard Nocht Institute for Tropical Medicine, Hamburg, Germany, [3]University of Sciences, Techniques and Technologies of Bamako, Bamako, Mali

Malaria remains one of the most fatal and prevalent infectious diseases globally. Apical membrane antigen 1 (AMA1) is a promising vaccine and therapeutic antibody target to prevent blood-stage malaria infection. However, AMA1 alleles in endemic areas are highly polymorphic. These polymorphisms serve as an immune evasion strategy to circumvent strain-transcending protection, preventing the development of effective strain-transcending vaccines based on AMA1. AMA1 interacts with rhoptry neck protein 2 (RON2) during merozoite invasion into red blood cells, and this essential interaction is conserved among apicomplexan parasites. While extensive research has focused on antibodies that neutralize parasite growth by disrupting the direct interaction between AMA1 and RON2, no monoclonal antibodies have yet been identified that neutralize parasites through alternative mechanisms. In this study, we investigated a panel of naturally acquired human monoclonal antibodies (hmAbs) specific to AMA1, derived from individuals living in malaria-endemic areas. Our approach utilized structural biology and biophysical tools, along with parasite growth inhibition assays. We evaluated the specificity and binding kinetics of human antibodies using enzyme-linked immunosorbent assay and biolayer interferometry. Epitope binning experiments revealed that two potent neutralizing hmAbs engage AMA1 without disrupting RON2 binding. Co-crystal structures of AMA1 with these neutralizing hmAbs were determined, revealing novel and distinct conformational epitopes. One of the hmAbs neutralized diverse parasite strains, and the combination of these hmAbs showed synergistic enhancement of parasite neutralizing activity. Importantly, this work underscores the significance of neutralization mechanisms for AMA1 hmAbs that are independent of RON2 blockade. These findings highlight a novel, strain-transcending surface targeted by naturally acquired human antibodies that hold promise for the development of broadly protective vaccines and therapeutics.

8071

PRE-CLINICAL STUDY ON VIRAL-VECTORED *PLASMODIUM FALCIPARUM* MULTISTAGE VACCINE EFFECTIVE BOTH FOR PROTECTION AND TRANSMISSION-BLOCKADE IN RHESUS PRIMATES

Yutaro Yamamoto[1], Naho Shinmura[1], Wakaba Kanamura[1], Yuna Sato[1], Ammar Abdurrahman Hasyim[1], Kartika Hardianti Zainal[1], Takuto Katayama[1], Sora Niwa[1], Manaka Ono[1], Hibiki Naruse[1], Yuma Asaki[1], Iyori Mitsuhiro[2], Hiroaki Mizukami[3], Hisatoshi Shida[4], Tomoyuki Miura[4], Shigeto Yoshida[1]

[1]Kanazawa University, Kanazawa city, Japan, [2]Musashino University, Tokyo, Japan, [3]Jichi Medical University, Shimono, Japan, [4]Kyoto University, Kyoto, Japan

We have established an innovative and efficacious vaccine platform (m8Δ/AAV1) that consists of two viral vectors. The m8Δ/AAV-based malaria vaccine is based on a proven viral-vectored vaccine platform, consisting of a highly attenuated vaccinia strain; LC16m8Δ (m8Δ), and adeno-associated virus type1 (AAV1) expressing *P. falciparum* Pfs25-PfCSP fusion protein. The vaccine named m8Δ/AAV1-Pf(s25-CSP) is specifically designed to synergize with the WHO Expanded Program on Immunization (EPI) for infants. A heterologous m8Δ-prime/AAV1-boost immunization regimen has successfully been proven to be highly effective both for protection and transmission blocking in a murine model. Crucially, this activity is long-lasting in comparison with other anti-malarial vaccines tested in the same assays.The present study addressed its safety and vaccine efficacy to a non-human primate model. Four rhesus monkeys were immunized with a heterologous m8Δ-prime/AAV1-boost regimen. The immunized monkeys induced high PfCSP- and Pfs25-specific IgG antibody titers. Remarkably, the persistence of vaccine-induced immune responses were over 6 months and additionally provided *in vitro* sporozoite neutralizing activity against transgenic PfCSP/Pb sporozoites and transmission-blocking efficacy against transgenic Pfs25/Pb. Thus, our vaccine has extensive high-quality pre-clinical data and clear efficacy with a robust antibody response and substantial efficacy against malaria's pre-erythrocytic and sexual stages in non-human primates. Our vaccine would be worth proceeding to a clinical trial as a novel alternative to Protein-in-Adjuvant vaccines such as RTS, S and R21.

8072

R21/MATRIX-M™PHASE III TRIAL: FURTHER FOLLOW-UP AND ASSESSMENT OF AN ADDITIONAL BOOSTER DOSE

Alassane Dicko[1], Mainga Hamaluba[2], Ally Olotu[3], Halidou Tinto[4], Jean-Bosco Ouédraogo[5], **Mehreen S. Datoo**[6]*, Emma Beaumont[7], John Bradley[7], Sandesh Bharati[8], Prasad S. Kulkarni[8], Umesh Shaligram[8], Adrian V S Hill[6], R21/Matrix-M Phase III Trial Group[9]*

[1]Malaria Research and Training Centre, Department of Epidemiology of Parasitic Diseases, Faculty of Medicine, Pharmacy and Dentistry, University of Sciences, Techniques, and Technologies of Bamako, Bamako, Mali, [2]Kenya Medical Research Institute Centre for Geographical Medicine Research–Coast (KEMRI-CGMRC), Kilifi, Kenya, [3]Ifakara Health Institute, Bagamoyo Research and Training Centre, Bagamoyo, United Republic of Tanzania, [4]Unité de Recherche Clinique de Nanoro, Institut de Recherche en Sciences de la Santé, Nanoro, Burkina Faso, [5]Institut des Sciences et Techniques (INSTech), Bobo-Dioulasso, Burkina Faso, [6]Jenner Institute, University of Oxford, Oxford, United Kingdom, [7]London School of Hygiene & Tropical Medicine, London, United Kingdom, [8]Serum Institute of India Pvt. Ltd, Pune, India

R21/Matrix-M™ received WHO and several national approvals for use in African children using a four-dose regime in 2023. Deployment of this vaccine is expected from May 2024. Due to the low-cost per dose ($3.9) and a manufacturing commitment from Serum Institute of India Pvt. Ltd (SIIPL) of up to 200 million doses annually, all of the target population, comprising at least 40 million children per year in sub-Saharan Africa, should soon receive R21/Matrix-M™, significantly reducing malaria morbidity and mortality. The phase III trial of R21/Matrix-M™ is continuing, not only assessing long-term safety and efficacy but also the potential added value of additional annual or biennial boosters to maintain efficacy

in childhood. Participants in the malaria vaccine group were further randomised to receive an additional zero, one or two annual or biennial R21/Matrix-M™ boosters, resulting in them receiving a total of four, five or six doses of R21/Matrix-M™. Prior to this, participants aged 5-36 months had received 3 doses, 4 weeks apart, followed by a booster dose a year later of either R21/Matrix-M™ or a control vaccine. At 24 months following the primary series of vaccinations, evaluation of time to first clinical malaria episode demonstrated vaccine efficacy (VE) of 73% [70-76] at the seasonal administration sites with VE of 77% [72-81] in 5-17 month olds. VE was similar on assessment of multiple malaria episodes: 71% [68-74], and 75% [70-79] in the younger age group. R21/Matrix-M™ also demonstrated significant efficacy against severe malaria: 18 episodes were recorded at 18 months of follow-up across all sites and VE was 62% [6-85]. Further safety and efficacy data from the third year of follow-up will be presented, with the impact on vaccine efficacy of an additional booster dose following a third malaria season. These results all contribute to the growing body of data on R21/Matrix-M™ which will assist policy-makers in judging the optimal use of this low-cost, widely-accessible and high-impact vaccine.

8073

STRUCTURE GUIDED DESIGN OF A MRNA VACCINE TARGETING APICAL MEMBRANE ANTIGEN 1 IN PLASMODIUM FALCIPARUM

Sean Yanik[1], Varsha Venkatesh[1], Deepti Sarkar[1], Kazutoyo Miura[2], Carole Long[2], Martin Boulanger[3], Prakash Srinivasan[1]

[1]Johns Hopkins, Baltimore, MD, United States, [2]NIH, Bethesda, MD, United States, [3]University of Victoria, Victoria, BC, Canada

Previous clinical trials of vaccines targeting apical membrane antigen 1 (AMA1) in *P. falciparum* suffer from low induction of neutralizing antibodies against parasites homologous to the vaccine and offer almost no protection against heterologous parasites. While AMA1 is highly immunogenic, many of the antibodies induced by AMA1 immunization target non-neutralizing and polymorphic epitopes. We employed a stepwise approach to engineer an AMA1 vaccine capable of overcoming these limitations. *In vitro* results show that elimination of AMA1 domain 3 from the vaccine construct may focus the immune response on more neutralizing epitopes on domains 1 and 2 (D12). A *baculovirus* expressed AMA1 (D12) vaccine provides near complete protection of mice challenged with lethal *P. yoelii* parasites. Next, we show that production of this AMA1 (D12) construct in a mRNA LNP platform produces higher antibody titers, more avid antibodies and a higher proportion of mouse IgG2a/IgG1 antibodies than an Addavax adjuvanted protein vaccine. Membrane anchoring this mRNA AMA1(D12) construct induces even higher antibody titers and more avid antibodies than the previous secreted mRNA construct. Interestingly, introduction of the transmembrane region (TM) appears to focus the immune response on the apical end of AMA1, where most known neutralizing monoclonal antibodies bind. While highly neutralizing against homologous parasites, this AMA1(D12)-TM mRNA vaccine still suffers from low *in vitro* efficacy against heterologous parasites. To develop a more conserved vaccine, we designed a fusion protein of the AMA1(D12)-TM construct fused to the RON2L peptide, the parasite derived binding partner of AMA1. Immunization with the AMA1(D12)-RON2L-TM construct enhances the production of cross neutralizing antibodies against heterologous parasites. We have developed a *P. berghei Pf* AMA1 RON2L model to test this vaccine. Currently, we are employing glycoengineering to introduce novel N-glycosylation sites on our construct to further direct the immune response to conserved, neutralizing epitopes.

8074

SAFETY OF THE RTS,S/AS01$_E$ MALARIA VACCINE ONE YEAR AFTER THE PRIMARY VACCINATION IN REAL-LIFE SETTINGS IN THREE SUB-SAHARAN AFRICAN COUNTRIES: INTERIM RESULTS

Martina Oneko[1], *RTS,S Epidemiology EPI-MAL-003 study group*[2]

[1]KEMRI CGHR Kisumu, Kisumu, Kenya

In 2021, WHO recommended the use of the RTS,S/AS01$_E$ malaria vaccine for the prevention of *Plasmodium falciparum* malaria in children living in regions with moderate to high malaria transmission. In the WHO-coordinated Malaria Vaccine Implementation Programme (MVIP), a surveillance study (EPI-MAL-003, NCT03855995) is conducted in Ghana, Kenya and Malawi with the main objective to evaluate the safety signals described in the RTS,S phase 3 trial (NCT00866619). This study includes a prospective cohort event monitoring (home visits, outpatient visits and hospitalizations) in exposed clusters where the RTS,S/AS01$_E$ vaccine was introduced compared to unexposed clusters where the vaccine was not offered. Incidence rates (IR) of malaria, meningitis and mortality were monitored in children under 5 years old. RTS,S/AS01$_E$ vaccinated children in exposed clusters were compared to unvaccinated children in unexposed clusters. We report the safety outcomes one year after the 3-dose primary vaccination. This interim analysis (IA) included 44,912 children uniformly distributed between exposed and unexposed clusters. The primary RTS,S/AS01$_E$ vaccination coverage was 85% in the exposed clusters. IR per 100,000 person-years (PY) of etiology-confirmed meningitis were similar in vaccinated (4.1, 95% confidence interval [CI]: 0.1-23.0) and unvaccinated children (4.0, 95% CI: 0.1-22.6), with IR ratio (IRR) of 1.02 (95% CI: 0.06-16.29, p=0.990). There were 3 cases of cerebral malaria in vaccinated and 2 cases in unvaccinated children (IRR: 1.53, 95% CI: 0.26-9.15, p=0.642). IR per 100,000 PY of all-cause mortality were 659.7 (95% CI: 561.5-770.3) in vaccinated vs 724.5 (95% CI: 622.3-838.8) in unvaccinated children and with similar IR in both genders. Overall, the RTS,S/AS01$_E$ vaccine was not associated with any safety signals previously observed in the phase 3 study, using an at-risk period of one year after the primary vaccination, which confirms the MVIP IA results. Meningitis and cerebral malaria were rare and distributed equally among vaccinated and unvaccinated children. Mortality rates were comparable between boys and girls.

8075

OFF-TARGET ANTIBODY RESPONSES TO BLOOD STAGE ANTIGENS ARE ASSOCIATED WITH CROSS-REACTIVE ANTIBODIES TO THE MAJOR AND MINOR REPEATS OF THE *PLASMODIUM FALCIPARUM* CIRCUMSPOROZOITE PROTEIN IN AFRICAN CHILDREN PARTICIPATING IN THE RTS,S VACCINE TRIALS

Luis M. Molinos-Albert[1], Didac Macia[2], Elisa Fuentes[1], Chenjerai Jairoce[3], Maximilian Mpina[4], David Dosoo[5], Alfons Jimenez[1], Marta Vidal[1], Ruth Aguilar[1], Ross L. Coppel[6], Ben Gyan[5], Claudia Daubenberger[7], Joe J. Campo[8], Gemma Moncunill[1], **Carlota Dobaño**[1]

[1]ISGlobal, Barcelona, Spain, [2]CIBER de Enfermedades Infecciosas, Barcelona, Spain, [3]Centro de Investigação em Saúde de Manhiça (CISM), Manhiça, Mozambique, [4]Ifakara Health Institute, Bagamoyo Research and Training Centre, Bagamoyo, Tanzania, United Republic of, [5]Kintampo Health Research Centre, Kintampo, Ghana, [6]Infection and Immunity Program, Monash Biomedicine Discovery Institute, Department of Microbiology, Monash University, Melbourne, Australia, [7]Swiss Tropical and Public Health Institute, Basel, Switzerland, [8]Antigen Discovery, Inc (ADI), Irvine, CA, United States

Malaria remains a major global health issue, with the largest disease burden caused by *Plasmodium falciparum* (*Pf*), predominantly in children from sub-Saharan Africa. Current malaria vaccines are partially effective and their correlates of protection are not fully understood. Thus, further studies focusing on the mechanisms mediating potent immune responses are warranted to inform next generation vaccines. RTS,S/AS01 is the most advanced malaria vaccine and targets the pre-erythrocytic stage of *Pf*

by presenting a truncated form of the circumsporozoite protein (*Pf*CSP) composed of 18.5 NANP major repeats and the C-terminal domain. We previously reported that an off-target antibody response to blood-stage antigens is associated with *Pf*CSP reactivity and an estimated lower incidence of clinical malaria in a fraction of vaccinated African children during the RTS,S/AS01 phase 3 trial. To gain further insights of this phenomenon as a potential correlate of protection, we selected 60 RTS,S vaccinees displaying equivalent *Pf*CSP IgG antibody levels and differential off-target profiles. Competition ELISA experiments to MSP5, one of the most relevant off-target antigens previously identified by us, showed an abrogation of antibody signals in presence of *Pf*CSP, confirming the recognition of a common epitope. Binding experiments to *Pf*CSP truncated proteins revealed that individuals with high off-target scores presented a superior CSP_{NANP}/CSP_{Cterm} IgG antibody ratio. Surprisingly, a strong decrease of the avidity index to CSP_{NANP} was detected in those individuals presenting the lowest off-target scores. Notably, ELISA experiments using overlapping peptides encompassing the *Pf*CSP sequence revealed that plasma from donors with high off-target scores were enriched in antibodies recognizing the N-terminal junction of *Pf*CSP. Therefore, high off-target profiles in RTS,S vaccinees are associated with a strong cross-reactivity to CSP major and minor repeats.

8076

GENOTYPIC INFECTION ENDPOINT ANALYSIS TO UNDERSTAND EFFICACY AND ESCAPE POTENTIAL OF THE MALARIA MONOCLONAL ANTIBODY CIS43LS

Philipp Schwabl[1], Amadou Niangaly[2], Jorge-Eduardo Amaya-Romero[1], Katrina Kelley[1], Gail Potter[3], Kassoum Kayentao[2], Peter D. Crompton[3], Daniel E. Neafsey[1]

[1]Harvard University, Boston, MA, United States, [2]University of Bamako, Bamako, Mali, [3]NIH, Rockville, MD, United States

The development of malaria infection-blocking monoclonal antibodies (mAbs) has advanced rapidly in recent years. Several mAb candidates have entered field trials to validate safety and efficacy characteristics established in controlled infection experiments. Field trial efficacy measurement typically uses blood microscopy or qPCR to determine parasite presence/absence in study subjects sampled at regular time points after administration of the study agent or placebo. Time to first malaria infection is then compared between study arms. There is clear potential to enhance efficacy measurement and characterize intervention outcomes in greater detail by using genotypic endpoints that specify which strains are circulating among infected study subjects and whether parasite genetic polymorphisms may contribute to present or future intervention escape. This work applies high-sensitivity antigen genotyping to longitudinally track strain diversity in all *P. falciparum* malaria infections detected among the study subjects of a recent phase 2 trial assessing low and high-dose applications of the mAb CIS43LS. Our genotyping results distinguish several events of recrudescence from uncleared baseline infection, amending original efficacy interpretations based on binary endpoints. We observe dose-dependent reductions in strain diversity within individual subjects and discuss new ways to quantify efficacy using metrics based on complexity of infection (COI; number of strains per infection) and molecular force of infection (molFOI; number of newly acquired strains over time). We also observe significant nucleotide and structural variation in the circumsporozoite protein (CSP) N-terminus and in CSP regions flanking the CIS43LS epitope. The observed polymorphisms are not correlated to study arm and thus unlikely associated with antibody escape. Our work demonstrates the value of complementing current trial designs with genotypic endpoints and also highlights various methodological innovations we have applied to boost assay sensitivity and integrate false-positive detection in a high-throughput context.

8077

COMPARATIVE IMMUNOGENICITY OF THE R21/MATRIX-M MALARIA VACCINE ACROSS AGE GROUPS AND GEOGRAPHIES

Samuel Provstgaard-Morys[1], Caroline Bundy[2], Melissa Kapulu[2], Mainga Hamaluba[2], Alison Elliott[3], Eugene Ruzagira[3], Ousmane Traore[4], Umberto D'Alessandro[5], Angela M. Minassian[6], Yekini Olatunji[5], Sophie Roetynck[5], Annette Erhart[5], Sara Silk[6], Lorenz von Seidlein[7], Amelia Bajer[1], Katerina Rapi[1], Katie Ewer[8], Adrian V. S. Hill[1], Lisa Stockdale[1]

[1]Jenner Institute, University of Oxford, Oxford, United Kingdom, [2]Kenya Medical Research Institute Centre for Geographical Medicine Research–Coast, Kilifi, Kenya, [3]MRC/UVRI and LSHTM Uganda Research Unit, Entebbe, Uganda, [4]Unité de Recherche Clinique de Nanoro, Institut de Recherche en Sciences de la Santé, Nanoro, Burkina Faso, [5]MRC Unit The Gambia at LSHTM, Serrekunda, Gambia, [6]Department of Biochemistry, University of Oxford, Oxford, United Kingdom, [7]Mahidol Oxford Tropical Medicine Research Unit, Bangkok, Thailand, [8]Institute for Global Health (Global Health Vaccines R&D), GSK, Siena, Italy

The R21 vaccine was recommended for use by the World Health Organisation in 2023 for the prevention of malaria in children aged 5-36 months. Transmission of the causative pathogen, *Plasmodium falciparum* is not limited to children. Malaria elimination therefore cannot succeed without global eradication of the disease, necessitating vaccination of all age groups. An understanding of vaccine efficacy in older age groups and across geographies is vital in tackling the disease. Immunoglobulin G (IgG) levels specific to the R21 vaccine central repeat region (NANP) have been shown to broadly correlate with vaccine-induced protection. Here, we will show immunogenicity data for the R21 malaria vaccine across different age groups and geographic regions, offering insights into its potential as a universal malaria vaccine. The analysis will compare IgG antibody responses to four constituents of the R21 malaria vaccine, utilizing data from clinical trials conducted across four countries with distinct malaria endemicity profiles. The studies include three age groups: adults, children, and infants in studies conducted in the UK, Thailand, Kenya, Mali, Burkina Faso, Uganda, and The Gambia. Each trial administered three doses of the R21 vaccine with Matrix M adjuvant, one month apart. The objective was to analyse and compare the immunogenicity of the vaccine between these cohorts at baseline and post-vaccination, by assessing antibody responses measured by a validated multiplexed ELISA-based assay to four constituents of the R21/Matrix-M vaccine; Hepatitis B surface antigen, the central NANP repeat, full length R21 construct, and the C-terminus region. The standardisation of data across different cohorts for this comparative analysis involved the validation of the multiplex ELISA, ensuring consistency and accuracy in the interpretation of the immunogenicity results across the cohorts.

8078

R21/MATRIX-M MALARIA VACCINE PHASE 3 CLINICAL TRIAL IMMUNOGENICITY

Lisa Stockdale[1], Emma Beaumont[2], Samuel Provstgaard-Morys[1], Amelia Bajer[1], Katerina Rapi[1], Benedict Hollingdale[1], Mehreen Datoo[1], Almahamoudou Mahamar[3], Alassane Dicko[4], Ousmane Traoré[5], Halidou Tinto[5], Serge Yerbanga[6], Jean-Bosco Ouédraogo[6], Melissa Kapulu[7], Francis Ndungu[7], Mainga Hamaluba[7], Rose Paul[8], Ibrahim Sasamalo[8], Ally Olotu[8], Fernando Ramos Lopez[1], Sophie Weston[1], Katie Ewer[1], Adrian V S Hill[1]

[1]Jenner Institute, Oxford, United Kingdom, [2]LSHTM, London, United Kingdom, [3]Clinical Research Unit of Bougouni-Ouelessebougou, Malaria Research and Training Centre, University of Sciences, Techniques, and Technologies of Bamako, Bamako, Mali, [4]Clinical Research Unit of Bougouni-Ouelessebougou, Malaria Research and Training Centre, University of Sciences, Techniques, and Technologies of Bamako,, Bamako, Mali, [5]Unité de Recherche Clinique de Nanoro, Institut de Recherche en Sciences de la Santé, Nanoro, Burkina Faso, [6]Institut des Sciences et Techniques (INSTech), Bobo-Dioulasso, Burkina Faso, [7]Kenya Medical

Research Institute Centre for Geographical Medicine Research–Coast (KEMRI-CGMRC), Kilifi, Kenya, [8]Ifakara Health Institute, Bagamoyo Research and Training Centre, Bagamoyo, Tanzania, United Republic of

R21/Matrix-M pre-erythrocytic malaria vaccine, a circumsporozoite protein-based nanoparticle with no surface-exposed hepatitis B antigen, was recommended for use by WHO in October 2023, and prequalified in December 2023 following Phase 3 clinical trial efficacy estimates in 5-36 month olds of 75% in seasonal malaria transmission sites and 68% in 'standard' perennial malaria transmission sites. In this Phase 3 efficacy trial, 4800 children aged 5-36 months were enrolled in 5 sites in 4 African countries. Seasonal sites included Burkina Faso and Mali, and standard sites included Burkina Faso, Tanzania and Kenya. Children were randomised 2:1 to receive 3 doses of R21 or a control (Rabies) vaccine in the primary series, plus a booster dose 1 year after the primary series. Fifty per cent (2400) infants were enrolled into an immunogenicity cohort. IgG antibodies specific to the central repeat region of R21 (NANP) have been shown to broadly correlate with vaccine-induced protection. Over 12 months, higher NANP-specific IgG was observed in the younger children (5-17 month age group) compared with older children (18-36 month age group). This younger age group also had higher 12-month vaccine efficacy on time to first clinical malaria episode at both seasonal and standard sites: 79% [95% CI 73-84] p<0.001 at seasonal sites, and 75% [65-83] p<0.001 at standard sites. Here, we report updated data on vaccine-elicited IgG from the immunogenicity cohort post booster dose to four R21 antigens: NANP, C-terminal, full length R21 vaccine construct, as well as the vaccine backbone, Hepatitis B surface antigen using Meso Scale Discovery (MSD). We observe geographical, age and sex variation in vaccine-elicited antibodies before and after primary series and booster dose administration. We also observe differences between sites in rates of decay of NANP-specific antibodies after primary series vaccinations.

8079

A CONJUGATED PFS230D1 VACCINE INDUCES ANTIBODIES THAT DIRECTLY PREVENT FERTILIZATION AND COMPLEMENT ENHANCES NEUTRALIZATION

David Narum[1], Kelly M. Rausch[1], Lynn E. Lambert[1], Karine Reiter[1], Thayne Dickey[1], Nada Alani[1], Vu Nguyen[1], Richard L. Shimp, Jr.[1], Beth Chen[1], Martin Burkhardt[1], Raul Herrera[1], Sachy Orr-Gonzalez[1], Emma K. Barnafo[1], Sofia Nakuchima[1], Sundar Ganesan[2], Francisco Otaizo-Carrasquero[2], Craig Martens[2], Olga Muratova[1], Bruce Swihart[3], Irfan Zaidi[1], Robert D. Morrison[1], Yimin Wu[1], Sara A. Healy[1], Nicholas J. MacDonald[1], Niraj H. Tolia[1], Justin Y.A. Doritchamou[1], Tim G. Myers[2], Jennifer C.C. Hume[1], Patrick E. Duffy[1]

[1]Laboratory of Malaria Immunology and Vaccinology, NIAID, NIH, Bethesda, MD, United States, [2]Research Technology Branch, NIAID, NIH, Bethesda, MD, United States, [3]Biostatistics Research Branch, NIAID, NIH, Bethesda, MD, United States

Malaria imposes a global public health burden. The delivery of the WHO-approved malaria vaccines, RTS,S/AS01 and R21/Matrix-M, which reduce human infection and associated clinical disease, will aid in the control of the global disease burden. Development of a combination vaccine that also disrupts mosquito infection and subsequent transmission events holds even greater promise to control disease. We developed a conjugated Pfs230D1 vaccine that forms nanoparticles which induce antibodies that block mosquito transmission, including in humans. In preclinical studies conducted in rhesus monkeys, conjugated Pfs230D1 formulated with various adjuvants (Alhydrogel, GLA-LSQ, GLA-SE, and AS01) induced varied immunological responses; conjugated Pfs230D1/AS01 induced one of the most robust antibody responses. Transcriptome profiling of fine needle aspirates of draining lymph nodes revealed the induction of blood transcription modules related to antibody production including enrichment in monocytes, neutrophils, and TLR and inflammatory signaling, among other unique adaptive responses. Next, we examined the role of antibodies and complement in preventing parasite development within the mosquito. Antibodies against Pfs230D1 generated in rabbits, rhesus, and human volunteers blocked mosquito infectivity in the absence of complement, indicating disruption of a protein-protein interaction required for sexual development. Subcellular localization of Pfs230 which forms a complex with the glycosylphosphatidylinositol anchored Pfs48/45 on the gamete surface demonstrated that Pfs230D1 and Pfs48/45 domain 3 (D3) are in close proximity to each other by fluorescence resonance energy transfer, even though Pfs48/45D3 specific antibodies only block fertilization independent of complement. Pfs230D1 appears to be a critical transmission blocking vaccine component, as antibodies prevent fertilization alone with enhanced neutralization activity by complement, which together increase the duration of killing and wholistically limit vaccine selection.

8080

FORCED DEGRADATION STUDIES WITH CONJUGATED PFS230D1-EPA DRUG PRODUCT PROVIDE A BASIS FOR EVALUATING ACCELERATED STABILITY

Sofia Nakuchima[1], Karine Reiter[2], Kelly M. Rausch[2], Emma K. Barnafo[1], Fernando Cabezas-Mejia[2], Olga Muratova[2], Martin Burkhardt[2], Albert Jin[1], Lauren Dang[3], Michael Fay[4], Jennifer C.C. Hume[2], Patrick E. Duffy[2], David L. Narum[2]

[1]National Institute of Biomedical Imaging and Bioengineering, NIH, Bethesda, MD, United States, [2]Laboratory of Malaria Immunology and Vaccinology, NIAID, NIH, Bethesda, MD, United States, [3]Biostatistics Research Branch, NIAID, NIH, Bethesda, MD, United States, [4]Biostatistics Research Branch, NIAID, NI, Bethesda, MD, United States

Malaria is a life-threatening disease that affects 249 million people each year. Currently, two WHO-approved vaccines are indicated to prevent clinical disease and target pre-erythrocytic stages of the *Plasmodium* parasite. Development of a transmission-blocking vaccine (TBV) that targets sexual stages in mosquitoes may prevent spread of infection within a community. Combining an effective TBV with a current vaccine would form a promising multi-stage vaccine for use in control and elimination efforts. The leading TBV candidate is a conjugated nanoparticle called Pfs230D1(M)-EPA; in a Phase 2 safety and immunogenicity trial in Mali (NCT03917654), Pfs230D1-EPA formulated with AS01 induced high levels of antibodies with functional activity, and conferred significant reduction (>75%) in mosquito infection. In anticipation of phase 3 clinical trials and integration into a multi-stage vaccine, evaluation of unformulated Pfs230D1-EPA drug product (DP) stability is critical. To this end, forced degradation studies of conjugated Pfs230D1-EPA DP (heating at 80°C for 15 minutes) have shown a significant loss of functional activity (assessed by standard membrane feeding assay) following immunization of mice with mixtures of denatured and non-denatured Pfs230D1-EPA DP. No marked change was observed in the solubility while significant biophysical changes in the secondary structure were observed by circular dichroism (CD) spectra that were effectively replicated in assays to evaluate binding using Pfs230D1 conformation-dependent mAbs. Next, we determined significant changes could be determined in the CD spectra using mixtures of force degraded and non-degraded DP (0:100 to 25:75 with increments of 5%). We aim to correlate the statistical changes in CD spectra to corresponding changes in ELISA titration curves using conformation-dependent mAbs. Subsequently, the CD spectra and/or an ELISA may be used to evaluate changes in conjugated Pfs230D1-EPA DP in an accelerated stability following WHO guidelines (40°C for 14 days, and 2 - 8°C and 25°C for 6 months).

8081

DESIGN, CHARACTERIZATION, AND EFFICACY OF TWO UNIQUE MRNA-BASED BLOOD-STAGE MALARIA VACCINES

Amy C. Ott, Patrick J. Loll, James M. Burns, Jr.

Drexel University College of Medicine, Philadelphia, PA, United States

The rapid deployment of COVID mRNA vaccines represents a significant achievement. The mRNA platform has several advantages over recombinant antigen formulations, including ease of construction and scalability. mRNA-lipid nanoparticles (LNPs) can be easily modified to deliver antigen to both exogenous and endogenous processing pathways to drive broad humoral and cellular immunity. Here, we evaluate the mRNA platform

for delivery of a blood-stage malaria vaccine. Using the *Plasmodium yoelii* model, we focused on the 19-kDa fragment of merozoite surface protein 1 ($MSP1_{19}$) fused to merozoite surface protein 8 (MSP8). Two EGF-like domains within $MSP1_{19}$ are the target of neutralizing antibodies, although T cell recognition of $MSP1_{19}$ is weak. We previously reported that fusion of recombinant $MSP1_{19}$ to MSP8 provided strong MSP8-specific CD4+ T cell help for production of merozoite neutralizing antibodies. Immunization with r*Py*MSP1/8 formulated with Quil A adjuvant afforded significant protection against lethal *P. yoelii* 17XL malaria. We designed a mRNA vaccine construct that targeted *Py*MSP1/8 for secretion (*Py*MSP1/8-sec). The mRNA was encapsulated into LNPs and outbred mice were immunized three times at a 3-week interval. Comparator mice were immunized with r*Py*MSP1/8 formulated in Quil A adjuvant. The *Py*MSP1/8-sec mRNA vaccine induced high titers of antigen-specific antibodies, significantly higher than those induced by the recombinant antigen formulation. Two weeks following the final immunization, mice were challenged with *P. yoelii* 17XL parasitized RBCs. The *Py*MSP1/8-sec vaccine was remarkably protective; all mice survived an otherwise lethal infection, and 5/10 immunized animals did not develop detectable blood-stage parasitemia. We designed a second *Py*MSP1/8 mRNA-based vaccine (*Py*MSP1/8-mem) that encodes a GPI anchor signal sequence and demonstrated successful expression of *Py*MSP1/8 on the surface of transfected cells. Studies are ongoing to compare the immunogenicity and efficacy of secreted versus membrane-bound *Py*MSP1/8 to inform related work focused on *Plasmodium falciparum*.

8082

INTRODUCTION OF MALARIA VACCINE IN BURKINA FASO: LESSONS LEARNED

Mwinmalo Ines Evelyne DA[1], Rene Didace Bakouan[2], Anissa Sidibe[3], Christelle Neya[2], Soumeya Ouangraoua[1], Francine Ouedraogo[1], Erward Kenyi[3], Gladys Tetteh[3], Meg Sreevatsava[4], Ousmane Badolo[1], Christopher Morgan[3]

[1]jhpiego, Ouagadougou, Burkina Faso, [2]Minister of health, Ouagadougou, Burkina Faso, [3]jhpiego, Baltimore, MD, United States, [4]OMS AFRO, Brazzaville, Congo, Republic of the

In October 2021, the World Health Organization recommended RTS,S/AS01 vaccine as a new way for the prevention of malaria. Burkina Faso made the critical decision to introduce the malaria vaccine into its vaccination program, declared interest in roll-out to GAVI and finalized its implementation plan in January 2023. A Malaria Vaccine Introduction Committee was created to spearhead and monitor the introduction, which was occurred on February 5th, 2024. The target population for this vaccine is children aged 5 to 23 months with a vaccination schedule of the first three doses administered at 5, 6, and 7 months, followed by the 4th dose at 15 months. We conducted a comprehensive review of the vaccine introduction process using the WHO's Malaria Vaccine Introduction Readiness Assessment tools. We also analyzed through relevant documents several areas such as planning, training communication, logistic. It took 12-month from December 2022 to January 2023 to introduce the RTS,S/AS01 malaria vaccine. The process began with a strong commitment from the country's top government officials. Ten months before the scheduled introduction, 31% of the preparation activities were completed. By the six-month, the completion rate of all activities required had increased (78%) with the establishment of technical groups. A month ahead of schedule, communication activities, were not conducted due to funding constraints. This led to the postponement of the introduction by 10 days. A month after the introduction, districts with proactive awareness campaigns among community leaders achieved high coverage rates (>90%), while those without had lower coverage rates (<50%), despite the security context.Burkina Faso introduction of the RTS,S/AS01 vaccine demonstrates a commitment to reducing malaria mortality. Lessons learned from this process include the importance of establishing technical working groups, ensuring timely funding for communication activities, and actively involving relevant stakeholders from the outset. Moving forward, these insights guide future vaccine introductions, ensuring a more successful rollout process

8083

FUNCTIONAL EFFICACY OF NANOPARTICLE CONJUGATED *PLASMODIUM VIVAX* CIRCUMSPOROZOITE PROTEIN SUBDOMAIN VACCINE

Pradeep Annamalai Subramani[1], Surendra Kumar Kolli[1], Francis B. Ntumngia[1], Gregory P. Howard[2], Samantha Barnes[1], Justin Nicholas[1], Madison M. Ogbondah[1], Hai-Quan Mao[2], John H. Adams[1]

[1]University of South Florida, Tampa, FL, United States, [2]Johns Hopkins University, Baltimore, MD, United States

A vaccine against vivax malaria is a high priority, due to its global prevalence, relapse, and its socio-economic burden. The circumsporozoite protein (CSP) is the most abundant molecule on the surface of *Plasmodium* sporozoites and is considered a leading pre-erythrocytic stage vaccine candidate. CSP is essential for sporozoite gliding motility, cell traversal activity and entry into the liver parenchyma. Anti-CSP antibodies can prevent sporozoite migration and infection of hepatocytes. The immunodominant central repeat region of CSP is considered important target of protection that is observed with CSP vaccines. Inhibitory monoclonal antibodies specific to the dominant Bc epitopes of two *P. vivax* CSP repeats (VK210 and VK247) show no cross reactivity with the different *P. vivax* variants. Therefore, this dimorphism represents a challenge to developing a broadly neutralizing strain transcending CSP-based vaccine targeting primarily the repeat region. This study aims at exploring the flanking N- and C-terminal domains of PvCSP for induction of broadly neutralizing inhibitory antibodies. Mice were immunized with different recombinant CSP subunits formulated with CpG-1018 as adjuvant and surface conjugated to PLGA nanoparticles and the immunogenicity was evaluated. NP conjugated rCSP subunit formulations induced high titer antibodies to the respective rCSP antigens that could recognize the native antigen on the sporozoite. Preliminary studies revealed that the antibodies produced by NP conjugated rPvCSP sub-domains showed inhibition of transgenic *P. berghei* sporozoites expressing PvCSP liver stage development *in vitro*.

8084

DIRECT SKIN FEEDING ASSAY IN MALARIA TRANSMISSION BLOCKING VACCINE STUDIES - STANDARDIZATION, SAFETY, TOLERANCE, AND SCALABILITY FOR USE IN PHASE 2 AND PHASE 3 CLINICAL TRIALS

Heather Goodman[1], Daman Sylla[2], Adama Sacko[2], Issaka Sagara[2], Sara A. Healy[1], Patrick E. Duffy[1], Jen C. Hume[1]

[1]LMIV/NIAID/NIH, Bethesda, MD, United States, [2]MRTC/USTTB, Bamako, Mali

Malaria Transmission Blocking Vaccines (TBVs) are vaccines designed to reduce the number of infected mosquitoes circulating in a community by blocking the sexual stages of the *Plasmodium* parasite from developing within mosquitoes. For decades, the Standard Membrane Feeding Assay has been the gold standard for measuring activity of these vaccines; however, this assay requires cultured *Plasmodium* parasites to test sera, is time consuming and has relatively low throughput. Logistically this poses many issues for large scale clinical trials and due to the intricacies of performing the assay, oftentimes it isn't conducive to tight timelines where the quick turnaround of results is needed for decision making. Consequently, the Direct Skin Feeding (DSF) and Direct Membrane Feeding (DMFA) Assays are the preferred assays in the field. However, DMFA has its own limitations, and its set-up and execution can be challenging in a field setting. Because of this the DSF has become the leading assay for use in TBV studies as there are fewer limitations to performing them and is the assay closest to mimicking what is naturally seen in the field. Here we will show over 10 years of safety data from over 34,000 DSFs performed across multiple study sites in Mali. We will evaluate acceptability and tolerance of the assay looking at study withdrawal and refusal rates as well as adverse events across studies. We will compare assay logistics and data from recent studies that paired DMFA and DSF and highlight the

reasons DSF is the superior assay. We will also discuss the steps taken to standardize the DSF assay for use in a Phase 2 multi-component vaccine trial in Mali, and what this means in terms of scalability (colony mosquito production and post -feed processing). Lastly, we will discuss how we propose to transfer the assay to multiple sites across Africa and how this assay will be implemented in a multisite Phase 3 clinical trial.

8085

COMPARABILITY OF THE STANDARD MEMBRANE FEEDING ASSAY (SMFA) ACROSS DIFFERENT VACCINE STUDIES, STUDY SITES, AND TIME

Jen C. Hume[1], Jennifer Kwan[2], Olga Muratova[1], Heather Goodman[1], Edward Owen[1], Holly Torano[1], Sara A. Healy[1], Issaka Sagara[3], Patrick E. Duffy[1]

[1]LMIV/NIAID/NIH, Bethesda, MD, United States, [2]LCIM/NIAID/NIH, Bethesda, MD, United States, [3]MRTC/USTTB, Bamako, Mali

The Standard Membrane Feeding Assay (SMFA) is utilized widely to assess the efficacy of malaria transmission blocking vaccines (TBV). The assay is performed by feeding cultured *P. falciparum* gametocyte parasites to *Anopheles* mosquitoes in the presence of test sera and measuring the resulting midgut oocyst infections against a naïve control. The activity of vaccine-induced antibodies to prevent mosquito infection can be expressed as both transmission reducing activity (TRA) where the percent reduction in oocyst count per mosquito against the naïve control is calculated and transmission blocking activity (TBA) where the percent reduction in infection prevalence against the naïve control is calculated. Here we assemble data from the comparator arms of several recent TBV studies (Pfs230D1-EPA and Pfs25-EPA in alhydrogel, Pfs230D1-EPA in AS01 in adults, Pfs230D1-EPA in AS01 in a community setting and Pfs230D1-EPA in Matrix M) to assess the variability in the baseline/control values of SMFAs performed on individuals residing in malaria endemic areas. TRA and TBA data for each study were assembled along with attributes of sites, demographics of study population, and month and year of study in order to examine these control data to determine what differences in the baseline data exist. A total of 681 samples from 289 participants were analyzed using Generalized Estimating Equation (GEE) models fitted with offsets for the number of samples each individual contributed to the analysis. Results of individual variability, within study and cross study variability will be contrasted for both TRA and TBA.

8086

IMMUNOGENICITY OF A *PLASMODIUM VIVAX* BLOOD STAGE NANOPARTICLE VACCINE

Francis B. Ntumngia[1], Gregory P. Howard[2], Samantha Barnes[1], Hai-Quan Mao[3], John H. Adams[1]

[1]Center for Global Health and Interdisciplinary Research, College of Public Health, University of South Florida, Tampa, FL, United States, [2]Department of Biomedical Engineering, Johns Hopkins School of Medicine, Baltimore, MD, United States, [3]Institute for NanoBioTechnology, Johns Hopkins University, Baltimore, MD, United States

The *Plasmodium vivax* Duffy binding protein (DBP) is essential for invasion of human reticulocytes during blood stage infection and development. Region II of DBP (DBPII), contains the critical residues important for binding to its cognate receptor, the Duffy antigen receptor for chemokines (DARC), during the invasion process. Naturally acquired anti-DBPII antibodies block *P. vivax* merozoites invasion of reticulocytes and are associated with protection against disease. These features of DBPII makes it a prime target for vaccine mediated immunity against blood stage vivax malaria. Despite its functional role in the invasion process, allelic variation in dominant B-cell epitopes may complicate vaccine efficacy. An engineered rDBPII based protein, DEKnull-2, with altered variant Bc epitopes, retains conserved, neutralizing epitopes and is reactive with long-term memBc and stable binding inhibitory antibodies from natural *P. vivax* infections. Challenges with conventional vaccines such as low immunogenicity, instability, and the need for multiple doses, are limitations to vaccine efficacy. Innovative formulations and technologies such as nanoparticle vaccines (NPV) show great potential as an alternative to conventional sub-unit vaccines. In this study, the immunogenicity of a rDBPII based NPV was evaluated in BALB/c mice. The vaccine was highly immunogenic in mice, eliciting antibodies reactive with variant DBPII alleles and recognize native DBP on merozoites. Ongoing studies are evaluating the vaccine induced antibodies for inhibition erythrocyte invasion by transgenic *P. knowlesi merozoites* expressing *P. vivax* DBP *in vitro.* Data obtained from this study will determine the suitability of NPVs as a delivery system for a DBP based vaccine compared to traditional subunit vaccine formulations.

8087

NOVEL ASSAY PREDICTS STANDARD MEMBRANE FEEDING RESULTS FOR MALARIA TRANSMISSION BLOCKING VACCINE PFS230D1-EPA/AS01

Cristina A. Meehan[1], Robert Morrison[1], Matthew Cowles[1], Jen C. Hume[1], Issaka Sagara[2], Sara A. Healy[1], Jonathan P. Renn[1], Patrick E. Duffy[1]

[1]Laboratory of Malaria Immunology and Vaccinology, Division of Intramural Research, National Institute of Allergy and Infectious Disease, National Institute of Health, Bethesda, MD, United States, [2]Malaria Research and Training Center, University of Sciences, Techniques and Technologies, Bamako, Mali

In 2024, malaria affects half the global population, with ~250 million cases and more than 600,000 deaths annually. Resistance to drugs and insecticides has made effective vaccines crucial. Transmission-blocking vaccines (TBVs) like Pfs230-EPA are designed to stop malaria transmission through mosquitoes and are moving towards Phase 3 trials. Traditional mosquito-based assays such as the Standard Membrane Feeding Assay (SMFA) are low-throughout, labor-intensive, and limited in detection range, prompting the need for new assays to measure vaccine-induced immune responses that correlate to efficacy. This necessitates the development of cost-effective, scalable tests for large-scale trials. We developed a competitive ELISA (cELISA) platform using human monoclonal antibodies (hmAbs) isolated from Malian adults vaccinated with Pfs230D1-EPA. The assay incorporates single-chain variable fragments that block functional epitopes to quantify levels of antibody (Ab) that react to epitopes targeted by functional hmAbs. A pilot study was run to analyze 185 serum samples collected during a Pfs230D1-EPA/AS01 trial that compared efficacies of full and fractional dosing regimens delivered in a Month 0-1-6-17 schedule. Samples collected 3 months post doses 3 and 4 were assessed in five novel epitope-specific cELISAs that measured different Ab parameters (total IgG, IgG1, IgG3, IgG4, c1q). Immune responses were evaluated for their ability to predict SMFA mosquito assay endpoints. Ab responses for standard ELISA and cELISA (total IgG, IgG1, IgG3, c1q) were significantly higher in the full versus fractional dose group post-dose 3, while all Ab responses were similar between groups post-dose 4. Multivariate logistic regression analysis showed significant relationships to SMFA results for cELISA total IgG and IgG1 assays. Receiver Operator Curve analysis confirmed the strong predictive value of the standard ELISA as well as cELISA total IgG and IgG1 assays for SMFA results, with AUC over 75% at both study time points. These findings lay the foundation for novel assays to assess Ab activity and durability induced by Pfs230D1 in large-scale trials.

8088

ABUNDANT NON-NEUTRALIZING, SYNERGIZING IGG LINEAGES PLAY A CRUCIAL PROTECTIVE ROLE IN MALARIA-NAÏVE UNITED KINGDOM ADULTS VACCINATED WITH BLOOD-STAGE VACCINE CANDIDATE RH5.1/AS01$_B$

Jeffrey Marchioni[1], Kirsty McHugh[2], Jordan R. Barrett[2], Allison Seeger[1], Jessica Kain[1], Cassandra Rigby[2], Doris Quinkert[2], Ana Rodrigues[2], Dimitra Pipini[2], Randall S. MacGill[3], George Georgiou[1], Gregory Ippolito[1], Simon J. Draper[2], Jason Lavinder[1]

[1]The University of Texas at Austin, Austin, TX, United States, [2]Oxford University, Oxford, United Kingdom, [3]Center for Vaccine Innovation and Access, PATH, Washington, DC, United States

Reticulocyte Binding Protein Homologue 5 (RH5) is a *P. falciparum* merozoite surface protein that has low polymorphism frequencies and is an

essential component of a non-redundant erythrocyte invasion pathway. The Draper Laboratory (Oxford) clinically tested RH5.1, an engineered variant of RH5, with $AS01_B$ adjuvant (GSK) to induce long-lasting, protective antibody titers. In this study, we evaluated United Kingdom malaria-naïve adult volunteers (n=5) who received three monthly doses of the RH5.1/$AS01_B$ vaccine and subsequently demonstrated significant reductions in parasite multiplication rate (NCT02927145). Recombinant monoclonal antibodies (mAbs) derived from RH5-specific B cell receptors (BCRs) of volunteers were discovered that neutralize merozoite invasion *in vitro*. In comparison, polyclonal plasma IgG of volunteers exhibited an average neutralizing potency ~10-fold greater than that of mAbs cloned from B cells, highlighting a disconnect between the BCR and circulating IgG repertoires. To address this, we completed high-throughput BCR sequencing coupled with plasma IgG proteomics, followed by subsequent recombinant mAb expression and functional characterization. In four of five donors, the most abundant RH5.1-specific plasma IgG lineage is non-neutralizing *in vitro*, targeting epitopes like the N-terminus, while lower abundance lineages exhibit neutralizing properties. In one donor, all top six lineages (~59% relative abundance) target non-neutralizing epitopes. To explore the contributions of individual mAbs within a polyclonal setting, we generated an artificial plasma IgG repertoire of one donor by pooling together 22 recombinant mAbs at relative abundances (~72% relative abundance total) and evaluated them in an *in vitro* parasite growth inhibition assay. By systematically removing mAbs from this repertoire, we uncovered a synergistic relationship between two mAbs that alone are non-neutralizing. The ability of non-neutralizing antibodies to synergize with each other alongside neutralizing mAbs may reduce the burden of high antibody titers, influencing future RH5 vaccine engineering efforts.

8089

ELICITATION OF POTENT LIVER-STAGE IMMUNITY BY NANOPARTICLE IMMUNOGENS DISPLAYING *PLASMODIUM FALCIPARUM* CSP-DERIVED ANTIGENS

Mark D. Langowski[1], Nicholas K. Hurlburt[2], Alex Roederer[1], Justas Rodarte[2], Gretchen Harms Pritchard[3], Connor Weidle[2], Rashmi Ravichandran[1], Lais Da Silva Pereira[4], Barbara J. Flynn[4], Brian Bonilla[4], Patience Kiyuka[4], Joseph Francica[4], Marion Pepper[3], Azza Idris[4], Robert A. Seder[4], Marie Pancera[5], Neil P. King[1]

[1]Institute for Protein Design, University of Washington, Seattle, WA, United States, [2]Vaccine and Infectious Disease Division, Fred Hutchinson Cancer Research Center, Seattle, WA, United States, [3]Department of Immunology, University of Washington School of Medicine, Seattle, WA, United States, [4]National Institutes of Health, Vacine Research Center, Bethesda, MD, United States, [5]Fred Hutchinson Cancer Center, Seattle, WA, United States

The circumsporozoite protein (CSP) of *Plasmodium falciparum* is the major surface antigen of the sporozoite stage, and is the target of two WHO-recommended vaccines, RTS,S/AS01 and R21/Matrix-M. Though these vaccines offer promise for reducing malaria burden, their rapidly waning antibody titers may affect long-term efficacy. Recent studies have elucidated structures of epitopes not included in RTS,S or R21 that target the junctional NPDP motif and NVDP minor repeat motifs of the CSP repeat region, and the addition of these epitopes may improve long-term potency of CSP-based vaccines. Here, we first stabilized full-length CSP by mutating a proteolytic cleavage site. We then produced a shortened version, named SAmut-5/3-CSP, that displays the 3D7 strain "junctional" region as its repeat region, conjugated it to protein nanoparticles of various valencies, and found that our conjugate to a computationally designed nanoparticle, I53-50, offered the greatest protection against challenge. We also tested genetic fusions of the junctional region, major repeats, and the CSP C-terminal domain (CTD) to I53-50, and compared these to an RTS,S-like benchmark, RT-I53-50. We found that though our immunogens exhibited greater responses toward the junctional region, immunogens with higher major repeat content were associated with improved protection in a transgenic parasite challenge model, with RT-I53-50 being the most protective. To further improve on these constructs, we evaluated I53-50 immunogens that displayed non-native repeat cadences [e.g., $(NANPNVDP)_9$]. These immunogens showed improved cross-reactivity toward junctional region epitopes, but again did not outperform RT-I53-50 liver burden reduction after challenge. Finally, we performed experiments that compared RT-I53-50 to R21 in a head-to-head challenge study and we observed equivalent reductions in liver burden after 3 immunizations. However, subsequent experiments with a titrated, 2-dose regimen showed that R21 was slightly superior. Overall our results support further development of CSP-based vaccines on our clinically validated I53-50 nanoparticle platform.

8090

ASSESSMENT OF THE BURDEN AND RISK OF TYPHOID FEVER USING AVAILABLE DATA TO INFORM VACCINE INTRODUCTION IN RWANDA

Zimy Wansaula[1], Yesser Sebeh[2], Rosette Nahimana[3], Helene Balisanga[4], Axel P. Karamage[4], Alain Zimulinda[5], Edson Rwagasore[4], Katrin Sadigh[1], Matthew Mikoleit[1], Musa Y. Hindiyeh[6], Carol Tevi-Benissan[6], Jenny Walldorf[6], Anna A. Minta[6], Adwoa Bentsi-Enchill[6], Lucy B. Nagle[1]

[1]U.S. Centers for Disease Control and Prevention, Atlanta, GA, United States, [2]CDC Foundation, Atlanta, GA, United States, [3]World Health Organization, Kigali, Rwanda, [4]Rwanda Biomedical Center, Ministry of Health, Kigali, Rwanda, [5]Independent Consultant, Kigali, Rwanda, [6]World Health Organization, Geneva, Switzerland

Since 2018, WHO has recommended typhoid conjugate vaccine (TCV) for use in typhoid-endemic countries, prioritizing those with high disease burden or a high burden of antimicrobial resistance. However, the burden of typhoid fever is often unknown due to poor surveillance. To address this challenge, we piloted the Burden and Risk Assessment of Typhoid (BRAT) framework, a tool developed by CDC, WHO and typhoid experts, to systematically collect and interpret available typhoid data from 2018–2022 in Rwanda. We identified incidence, outbreak, and risk factor data through a desk review and collected prevalence, antimicrobial resistance (AMR), and intestinal perforation data from 13 health facilities, including at least one facility per province. We identified 290 *S.* Typhi isolates from patients in > 18 of Rwanda's 30 districts, with four districts accounting for 45% of *S.* Typhi isolates, indicating geographic variation. Overall, 40%–65% of isolates were resistant to at least one first-line antimicrobial (ampicillin, chloramphenicol, cotrimoxazole), while <40% were resistant to second-line antimicrobials (fluoroquinolones and third-generation cephalosporins). Resistance to fluoroquinolones, the antimicrobials of choice in Rwanda, increased from 38% in 2018 to 70% in 2022. Twenty-four percent of isolates were resistant to all first-line drugs, and no isolates were resistant to all first- and second-line drugs. A total of 360 cases of intestinal perforation were reported, of which 26% were diagnosed as typhoid-associated and resided in > 20 districts. Nationally, 56% of households had access to basic water and 57% had access to basic sanitation. No incidence or outbreak data were found. Using the BRAT framework, we rated the likely burden for prevalence and intestinal perforation as moderate, AMR as high, and WASH risk factors as high at the national level. We determined that typhoid fever is endemic in Rwanda, documented increased antimicrobial resistance and potentially unrecognized typhoid outbreaks. We conclude that Rwanda meets the criteria for moderate evidence to support TCV introduction.

8091

AEROMONAS HYDROPHILA AS A CAUSE OF ACUTE DIARRHEA FROM WESTERN AND COASTAL REGIONS IN KENYA

Janet Ndonye, Mary Kirui, Erick Kipkirui, Ronald Kirera, Nancy Kipkemoi, Margaret Koech, Kirti Tiwari, Elizabeth Odundo

Kenya Medical Research Institute / Walter Reed Army Institute of Research-Africa, Kericho, Kenya

Aeromonas hydrophila group are emerging pathogens that cause gastroenteritis. Nonetheless *Aeromonas spp* can also cause wound infections and septicemia in humans in both developing and developed countries. The reservoirs include, aquatic environment, stored drinking and sewage water and in raw milk, vegetables and meat (food products). This

study tested stool samples for *Aeromonas hydrophila* group and associated phenotypic antibiotic resistance profiles. *Aeromonas hydrophila* group was isolated from stool samples collected from an ongoing case (symptomatic)-control (asymptomatic) diarrheal study. Standard microbiological culture and biochemical tests were performed, followed by identification and antimicrobial susceptibility testing using NC 66 panels and ascertained using the Microscan Walkaway 40 Plus automated identification platform. The drug susceptibility results were interpreted using the CLSI guidelines. According to the study, there were significantly more *Aeromonas hydrophila* isolates in symptomatic individuals (15/19; 79%) than in asymptomatic subjects (4/19; 21%; p=0.01). The isolates were resistant to trimethoprim/sulfamethoxazole 9/19 (47%), amoxicillin/k clauvanate 7/19 (37%), ampicillin sulbactam 5/19 (26%), aztreonam 5/19 (26%), cefepime 2/19 (11%), ceftazidime 2/19 (11%), cefoperazone 2/19 (10%) and meropenem 1/19 (5%). All isolates were susceptible to gentamicin, levofloxacin and piperacillin/tazobactam. The isolation of *Aeromonas hydrophila* is indicative that it may be a potential pathogen that causes acute diarrhea. The isolates were also found to be more resistant to the sulfonamide and beta lactams hence possible transfer to other gut pathogens or normal flora leading to increased antimicrobial resistance.

8092

PHENOTYPIC RESISTANCE OF CIPROFLOXACIN AND AZITHROMYCIN RESISTANT *CAMPYLOBACTER* SP. ISOLATES FROM PERU TO AN EXTENDED PANEL OF ANTIBIOTICS

Katia Manzanares Villanueva[1], Francesa Schiaffino[2], Lucero Romaina Cachique[1], Maribel Paredes Olortegui[1], Pablo Penataro Yori[3], Evangelos Mourkas[4], Ben Pascoe[4], Kerry K. Cooper[5], Craig T. Parker[6], Margaret Kosek[3]

[1]Asosciacion Benefica Prisma, Iquitos, Peru, [2]Universidad Peruana Cayetano Heredia, Lima, Peru, [3]University of Virginia, Charlottesville, VA, United States, [4]University of Oxford, Oxford, United Kingdom, [5]University of Arizona, Tucson, AZ, United States, [6]United States Department of Agriculture, Albany, CA, United States

Antimicriobial resistance jeopardizes the effectiveness of prevention and treatment of an increasingly wide range of infections caused by viruses, bacteria, fungi, and parasites. In 2017, the WHO published a list of bacteria with high antimicrobial resistance. *Campylobacter* was included in this list as a high-priority pathogen due to its progressive, alarming, and high resistance to fluoroquinolones worldwide. During the years 2021, 2022, and 2023, a cohort study was conducted in children aged zero to two years in the city of Iquitos, Peru, with the aim of estimating the disease burden and transmission dynamics. Additionally, it aimed to evaluate antibiotic resistance attributable in Campylobacter in humans and livestock. Stool samples were collected from participants once a month and whenever they had diarrhea. Campylobacter culture was performed on every stool sample and antibiotic resistance was tested using traditional Kirby-Bauer methods. A total of 997 *Campylobacter* spp. strains were isolated, of which 8% (83 strains) were resistant to Azithromycin, 59.3% (591 strains) showed resistance to Ciprofloxacin, and 7.3% (73 strains) were resistant to both. For the strains resistant to both antibiotics, an extended antibiogram battery was performed, consisting of Clindamycin, Fosfomycin, Ampicillin, Tigecycline, and an Azithromycin E-Test. Resistance to Clindamycin was 100%, as well as the Azithromycin E-test. Resistance to Ampicillin was 74% to Ampicillin, 41% to Fosfomycin, and finally Tigecycline proved to be 100% sensitive. This extended, nontraditional antibiogram panel will be useful to evaluate potential alternative antibiotics when Azithromycin and Ciprofloxacin show phenotypic resistance.

8093

APPLICATION OF THE RAPID DIAGNOSTIC TEST BASED ON LOOP-MEDIATED ISOTHERMAL AMPLIFICATION (RLDT) FOR *SHIGELLA* AND ENTEROTOXIGENIC *ESCHERICHIA COLI* (ETEC) DETECTION IN CHILDHOOD DIARRHEA IN BURKINA FASO

Alimatou Héma[1], Samuel S. Sermé[1], Jean W. Sawadogo[1], Amidou Diarra[1], Amidou Z. Ouédraogo[1], Issa Nébié[1], Alfred B. Tiono[1], Sophie Houard[2], Subhra Chakraborty[3], Alphonse Ouédraogo[1], Sodiomon B. Sirima[1]

[1]Groupe de Recherche Action en Santé (GRAS), Ouagadougou, Burkina Faso, [2]European Vaccine Initiative (EVI), Heidelberg, Germany, [3]Johns Hopkins Bloomberg School of Public Health, Baltimore, Baltimore, WA, United States

Developing countries face major challenges in diagnosing and monitoring enteric infections, particularly shigellosis and ETEC diarrhoea. The lack of rapid, accessible, and sensitive diagnostic tools complicates the timely identification and management of these infections, exacerbating their impact on public health. In response to this pressing need, the application of the RLDT has emerged as a promising solution. This study aimed to compare the performance of RLDT with conventional culture methods for detecting of cases of Shigella and ETEC.This study focuses on the implementation and efficacy of the RLDT for detection of *Shigella* and ETEC in a cohort of children under the age of five living in the peri-urban area of Ouagadougou, Burkina Faso, shedding light on its potential to address diagnostic challenges in resource-limited settings. To enable comparison with RLDT-*Shigella* results, conventional culture methods were employed to isolate *Shigella* strains from stool samples. However, since culture alone proved inadequate for detecting ETEC, multiplex PCR was used to identify ETEC toxin genes in a subset of *Escherichia coli* colonies. Of the 165 samples analysed for ETEC, 24.9% were positive by the RLDT compared with 4.2% by culture followed by PCR. The distribution of ETEC toxins by the RLDT was 17.6% for heat-stable enterotoxin porcine (STp), 11.5% for heat-labile enterotoxin (LT) and 8.5% for heat-stable enterotoxin human (STh). From the 263 samples tested for *Shigella*, the RLDT showed a positivity rate of 44.8% compared with 23.2% using culture. Since RLDT is more sensitive than culture, when comparing the RLDT with culture, the sensitivity and specificity for *Shigella* were determined to be 93.44% and 69.8%, respectively, while for ETEC, they were 83.7% and 77.9%, respectively.These results highlight the significant underdiagnoses of *Shigella* and ETEC by bacterial culture-dependent tools and demonstrate the potential of RLDT to improve the estimation of the burden of enteric disease. This method could guide future efforts to prevent and control enteric bacterial infections in children under five years of age in Burkina Faso.

8094

ASSOCIATION OF THE HUNGER SEASON AND MALNUTRITION WITH DIARRHEA ETIOLOGY AND POOR OUTCOMES AMONG CHILDREN HOSPITALIZED WITH DIARRHEA IN HAYDOM, TANZANIA

Stephanie A. Brennhofer[1], Godfrey Guga[2], Sifaeli Katengu[2], Restituta P. Mosha[2], Joyce A. Huchet[2], Mariamu H. Temu[2], Petro M. Gidahing[2], Kelvin M. Msoka[2], Bernadetha P. Hhando[2], Fredrick N. Habiye[2], Yotham Z. Michaeli[2], Rosemary G. Bukhay[2], Jie Liu[3], James A. Platts-Mills[1], Estomih R. Mduma[2], Elizabeth T. Rogawski McQuade[4]

[1]University of Virginia, Charlottesville, VA, United States, [2]Haydom Lutheran Hospital, Haydom, Tanzania, United Republic of, [3]Qingdao University, Qingdao, China, [4]Emory University, Atlanta, GA, United States

Children from agrarian communities in low resource settings with one annual harvest are at risk for malnutrition during the pre-harvest hunger season. Preliminary data was analyzed on 423 children (females: n=185, mean age: 14 months ± 10 months) hospitalized with diarrheal illness at Haydom Lutheran Hospital in Haydom, Tanzania from September

2022-March 2024. Of the 101 acutely malnourished children, 52 were severely (mid upper arm circumference (MUAC) <11.5 cm, weight for height/length z score (WHZ/WLZ) <-3, or bilaterial pitting edema) and 49 were moderately (MUAC ≥11.5 but <12.5 cm or WHZ/WLZ ≥ -3 but <-2) malnourished. Log binomial regressions adjusted for sex and season examined associations between malnutrition, season of admission, diarrheal etiology, and poor outcomes (death or 90-day re-hospitalization). Children with acute malnutrition and diarrhea were 1.74 (RR: 1.74, CI: 0.99, 3.08) times more likely to have a poor outcome, 1.57 (RR: 1.57, CI: 1.01, 2.44) times more likely to have *Shigella* attributable diarrhea (Ct<29.8) and 49% (RR: 0.51; CI: 0.27, 0.94) less likely to have rotavirus attributable diarrhea (Ct<31.8) compared to children with diarrhea but without acute malnutrition. Children admitted with diarrhea during the hunger season (November-March) were 1.28 (RR: 1.28, CI: 0.91, 1.80) times more likely to be malnourished, 2.11 (RR: 2.11, CI: 1.35, 3.29) times more likely to have *Shigella* attributable diarrhea, and were 71% (RR: 0.29, CI: 0.17, 0.52) less likely to have rotavirus attributable diarrhea compared to children admitted during the non-hunger season (April-October). There was no association between hospital admission season and poor outcomes. Rotavirus exhibited seasonality from August-November, while *Shigella* and acute malnutrition tracked closely together throughout the year, peaking from November-June. There was no association between pathogen attributable diarrhea and poor outcomes. Acute malnutrition, not hospital admission season, was a risk factor for poor outcomes, which may underscore the need for vigilant nutrition interventions both during and outside the hunger season.

8095

RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY ON THE EFFICACY AND SAFETY OF CAMPETEC HYPERIMMUNE BOVINE COLOSTRUM (HBC) FOR THE PREVENTION OF *CAMPYLOBACTER*-MEDIATED DIARRHEAL DISEASES

Kawsar Talaat[1], Chad K. Porter[2], Rediet Tekalign[1], Barbara DeNearing[1], Subhra Chakraborty[1], A. Louis Bourgeois[1], Courtney Swisher[1], Brittany L. Feijoo[1], Kamal Dhanjani[1], Jade Lewis[1], Fatema-Tuz Johura[1], Sandra D. Isidean[3], Kayla J. Testa[3], Christina L. Gariepy[3], Dilara Islam[3], Vicky L. Chapman[3], Renee M. Laird[4], Joanne L. Casey[5], Jerry Kanelos[5], Frederic M. Poly[3]

[1]Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, United States, [2]Naval Medical Research Command, Silver Spring, MD, United States, [3]Naval Medical Research Command, Henry M. Jackson Foundation for the Advancement of Military Medicine, Silver Spring, MD, United States, [4]Naval Medical Research Command, Henry M. Jackson Foundation for the Advancement of Military Medicine, Walter Reed Army Institute of Research, Silver Spring, MD, United States, [5]Immuron Limited, Victoria, Australia

Campylobacter causes significant diarrheal disease morbidity in children in low- and middle-income countries, travelers, and deployed military, and is a major cause of foodborne illness worldwide. Growing antibiotic resistance of *Campylobacter* makes improved prevention and control measures imperative. Given the prolonged and expensive nature of vaccine development, passive prophylaxis using oral administration of Hyperimmune Bovine Colostrum (HBC) was explored. CampETEC HBC is derived from cows immunized with a *C. jejuni* HS23/36 capsule polysaccharide (CPS) conjugated to CfaEB, a recombinant fusion protein of the major tip adhesin and subunit of CFA/I from enterotoxigenic *Escherichia coli*. CampETEC contains a high concentration of CPS-specific IgG which bind to HS23/36+ *C. jejuni* strains. Protective efficacy of CampETEC HBC was evaluated following a challenge with *C. jejuni* strain CG8421 (serotype HS23/36) in a randomized, double-blind, placebo-controlled, human infection model. Twenty-seven eligible participants were admitted to the inpatient facility and randomly assigned to receive 1g of CampETEC HBC or placebo (milk powder) thrice daily before meals. After 2 days of product consumption, participants were challenged with 1.67 x 10^5 colony-forming units of *C. jejuni*; they were monitored clinically and continued the CampETEC HBC for an additional 5 days. All participants were treated with azithromycin and ciprofloxacin when they met campylobacteriosis criteria or prior to discharge. CampETEC HBC was well-tolerated by participants, with no moderate or severe product-related adverse events. Study data remain blinded. Preliminarily, 17 of 27 (63%) met criteria for campylobacteriosis; 14 (52%) with moderate-severe diarrhea and 3 (11%) with fever and other symptoms. Twelve participants (71%) with campylobacteriosis required early treatment. Fever 100.8°F was present in 9 (33%) participants. Stool culture data aligned with clinical findings. Final determination of campylobacteriosis will be adjudicated by an independent committee. The protective efficacy of the CampETEC HBC will be determined upon unblinding.

8096

GENOMIC SURVEILLANCE OF ANTIMICROBIAL RESISTANCE IN CHILDREN WITH DIARRHEA AT A COMMUNITY-LEVEL HEALTH FACILITY IN MALI

Antoine Dara, Hinda Doucoure, Boi Kone, Bintou Diarra, Lassina Timbine, Mamadou Tekete, Abdoulaye Djimde

Pathogens genomics Diversity Network Africa, Bamako, Mali

Diarrheal diseases are amongst the most common causes of death in children in Africa. The treatment of diarrhea caused by *Enterobacteria* are often comprised by the emergence of drug resistant strains. Antimicrobial resistance (AMR) remains one of the biggest threats to global health and specially to resource limited countries such as Mali. The extent of AMR burden at the community level is not known. To better gain insights on the extent of AMR at the community health center level, we have performed a whole genome and metagenomic sequencing respectively on isolated bacteria and uncultured stools samples from children with diarrhea. Antibiotics sensitivity tests were performed, and phenotypic data were used to select samples. Genomic and metagenomic analyses have been carried out to detect AMR genes, virulence factors as well as unculturable pathogens. Our results indicate that multi-drug resistant bacteria, mainly *Salmonella* and *E. coli* are circulating at the community level. More importantly, *Enterobacteriaceae* carrying New Delhi metallo-β-lactamase genes (NDM) associated with carbapenem resistance were detected at the community level. Mobile genetic elements harboring AMR genes were detected suggesting them as potential drivers of the spread of AMR genes. We are analyzing metagenomic sequence data to better capture unculturable bacteria that might be involved in the pathogenesis of diarrhea in children. In addition, analyses are underway to fully characterize the pattern of transmission of AMR genes. Our results will inform healthcare workers and policy makers on a rational use of antibiotics.

8097

INTESTINAL MICROBIOME AND IMPLICATIONS ON MATERNAL HEALTH AND BIRTH OUTCOMES

Rachel H. Boone[1], Rebecca M. Carpenter[2], Meghan Garety[3], Rashidul Haque[4], William A. Petri[1]

[1]University of Virginia, Charlottesville, VA, United States, [2]University of Texas Medical Branch, Galveston, TX, United States, [3]University of Pennsylvania, Philadelphia, PA, United States, [4]ICDDR,b, Dhaka, Bangladesh

Unfavorable birth outcomes, such as low birth weight and preterm birth, can have detrimental impacts on a child's prognosis and later development. This concern is greatest in low-middle income countries in Asia and sub-Saharah Africa where pre-term birth rates are highest and there are less resources for post-natal care. Despite the need, there is still a lack in understanding what maternal factors contribute to these outcomes. Using randomly selected mother-child dyads from the Global Network Maternal Neonatal Health (MNH) registry in the Tangail district of Bangladesh, potential causes of unfavorable birth outcomes were investigated. It was found that in a sub-cohort of 376 mother-child dyads, elevated inflammatory cytokines (i.e. CRP and AGP) during the first trimester were correlated with preterm birth (OR = 2.23; 95% CI: 1.03, 5.16). Additionally, presence of aEPEC was significantly associated with increased odds of preterm birth (OR = 2.36; 95% CI: 1.21, 4.57), and higher loads of aEPEC were associated with increased odds of preterm birth (OR = 0.92 ;95% CI: 0.86, 0.98). When these models were adjusted for elevated AGP, the

strength of association was slightly attenuated. It may be hypothesized that elevated AGP captures a history of enteropathogenic infection or colonization in very early pregnancy. To further understand how the intestinal environment influences maternal health and birth outcomes, 16s sequencing was performed on 368 maternal stool samples from the same sub-cohort. Microbiome diversity, community composition, and multivariate analysis were performed. With this data, the correlation between intestinal microbiome, maternal health, and birth outcomes were evaluated.

8098

ISOLATION AND GENOMIC CHARACTERIZATION OF *CAMPYLOBACTER* SPECIES AND IDENTIFICATION OF ANTIBIOTIC RESISTANT *ESCHERICHIA COLI* AND *KLEBSIELLA PNEUMONIA FROM ZIMBABWE*

Marya Carmolli[1], Elizabeth Ross Colgate[1], Korin Eckstrom[1], Beth D. Kirkpatrick[1], Lisa Langhaug[2], Benjamin Lee[1], Kuda Mutasa[2], Robert Ntozini[2], Andrew Prendergast[2], Naume Tavengwa[2], Matthew J. Wargo[1]

[1]University of Vermont, Burlington, VT, United States, [2]Zvitambo Institute for Maternal and Child Health Research, Harare, Zimbabwe

During a study to determine reservoirs of *Campylobacter* in Zimbabwe, stool samples from symptomatic and asymptomatic children and mothers were grown in selective Campylobacter media. In addition to isolating *Campylobacter* species, we identified multiple significantly antibiotic resistant *Escherichia coli* and *Klebsiella pneumoniae* strains. We report on genomic characterization and antimicrobial susceptibility of the isolated strains from a region where few genomic sequences are known. Samples were plated on mCCDA plates in microaerophilic conditions at 42ºC to enrich for *Campylobacter spp*. Putative *Campylobacter* were isolated and sequenced via a combination of Oxford Nanopore Technologies (ONT) long read sequencing and Illumina short read sequencing. Assembled genomes were profiled using MLST typing, genomic distance with Mashtree. Antimicrobial resistance (AMR) gene profiles and select virulence genes and serotypes were identified using abricate, ECTyper, and Kleborate. We identified and sequenced 40 *Campylobacter* isolates; 28 *C. jejuni*, 10 *C. coli*, and 2 other. In addition, isolates of *E. coli* (n=41) and *K. pneumoniae* (n=14) grew on Campylobacter selective media, which included cefoperazone. *E.coli* isolates had predicted encoding of antimicrobial resistance genes (ARG) including TEM-1, TEM-141, CTX-M, and beta lactamase. *K. pneumoniae* was classified via Kleborate with resistance to yersiniabactin, colibactin or both, with evidence of ARG transfer via the genes AGly, Phe, Tet, TMT, Bla, and BlaESBL. Comparison to previously published genomes, the Campylobacter isolates sequenced in this study represent novel populations with significant genetic distance from existing resources. Genomic analysis of *E. coli* and *K. pneumoniae* also suggest that strains are distinct from most sequenced clinical isolates and align with relatively few genome sequences derived from Africa. This study contributes to our understanding of *Campylobacter spp*., *E. coli*, and *K. pneumoniae* genome characteristics in Zimbabwe and contributes to our understanding of antimicrobial resistance patterns in the region.

8099

PATHOGENS CAUSING DIARRHEA IN CHILDREN UNDER FIVE AMONG A VACCINATED POPULATION IN COASTAL GHANA

Delia Akosua Benewah Bandoh[1], Ernest Kenu[1], Mawuli Dzodzomenyo[1], Francis Dennis[2], Duah Dwomoh[1], Edwin Andrew Afari[1], George Armah[3]

[1]University of Ghana School of Public Health, Accra, Ghana, [2]Noguchi Memorial Institute for Medical Research, Accra, Ghana, [3]Noguchi Memorial Institute for Meidcal Research, Accra, Ghana

Diarrhoea remains a leading cause of morbidity and mortality globally. Rotavirus A vaccine was introduced almost 20 years ago to reduce the incidence of diarrhoea among children under five years. Since Ghana adopted the rotavirus A vaccine in 2012, coverage has been very high, 94% in 2022, yet diarrhoea still persists with a prevalence of 13% in under-fives. We conducted a pilot study to assess the possible pathogens causing diarrhea in under-fives in a high prevalent coastal district in Ghana. A case was an under-five confirmed with diarrhoea. Hospitalized diarrhoea cases(38) in Anloga district over an 8-month period were tested. Information on immunization status, WASH practices, and socio-demographics was also obtained. We extracted total nucleic acid of their stool samples. Pathogen detection was performed using quantitative PCR with customized TaqMan Array cards identifying 23 pathogens (10bacteria, 6parasites and 7viruses). Findings were presented in tables and charts. Median age was 21.5(IQR:30,12)months, 55.3%(21/38) with being male. Fully vaccinated were 97.4%(37/38). Diarrhoea pathogens were found in 94.7%(36/38). Of the 23 pathogens tested, 15 were identified. More viruses were identified (71.4%, 5/7) than bacteria (70%, 7/10). Rotavirus A was found in 5.3%(2/38). Other viruses identified were Saprovirus (23.7%, 9/38); Norovirus(26.3%, 10/38); bacteria pathogens identified included: Shigella/ Enteroinvasive Escherichia coli 50%(19/38); Enterotoxigenic Escherichia coli(23.7%, 9/38); Enteroaggregative Escherichia coli(52.6%, 20/38). Almost all (97.4%, 37/38) had access to improved water sources, Hand washing practices among caregivers was poor (28.9%, 11/38) and most children 89%(30/38) did not use household toilet facility. Vaccination was high. Aside known pathogens (Rotavirus A), other diarrhoea pathogens are present. WASH practices were poor. Interventions to improve WASH practices mainly handwashing among caregivers and child use of household toilets are needed. Long term recommendations could consider diarrhoea vaccines which target other pathogens in addition to Rotavirus A.

8100

USING A VACCINATION REGISTER TO MINIMIZE THE RISK OF MISCLASSIFICATION OF CHOLERA VACCINATION STATUS IN THE DEMOCRATIC REPUBLIC OF THE CONGO

Espoir Bwenge Malembaka[1], Patrick Musole Bugeme[1], Chloe Hutchins[2], Jules Jackson[1], Pengcheng Fang[1], Jaime Mufitini Saidi[3], Jean-Marie Chirhonda[4], Joël Mashauri Zigashane[4], Faraja Masembe[4], Delphin Rukakiza[5], John Kazana[6], Laddys Bodiongo Landu[7], Jackie Knee[2], Andrew S. Azman[1]

[1]Johns Hopkins University, Baltimore, MD, United States, [2]London School of Hygiene & Tropical Medicine, London, United Kingdom, [3]Division Provinciale de la Santé Publique du Sud-Kivu, Zone de Santé d'Uvira, Uvira, Congo, Democratic Republic of the, [4]Oxfam DRC, Uvira, Congo, Democratic Republic of the, [5]Programme Elargi de Vaccination (PEV), Division Provinciale de la Santé du Sud-Kivu (DPS), Uvira, Congo, Democratic Republic of the, [6]Division Provinciale de la Santé du Sud-Kivu, Ministry of Health, Prevention and Hygiene, Bukavu, Congo, Democratic Republic of the, [7]PNECHOL-MD, Kinshasa, Congo, Democratic Republic of the

Oral cholera vaccines (OCV) are a key component of the global cholera control strategy. Today, none of the available vaccines have gone through Phase III clinical trials and all have been licensed (and WHO approved) based on immunological bridging studies. Gold-standard field clinical efficacy studies are ethically and logistically challenging with the current vaccine landscape. Phase IV observational studies, like case-control and case-cohort studies, have and will likely continue to serve as the primary source of new data on protection from these and newer OCVs though they are often challenged by misclassification of vaccination status, due to social desirability- and recall bias, and unreliable records. In Uvira, a cholera-endemic city of ~315,000 inhabitants in the eastern DR Congo, one dose of Euvichol-plus was administered to individuals ≥12 months old during a vaccination campaign in December 2023/January 2024. As part of a vaccine impact evaluation in Uvira, we implemented a paper-based vaccine register to record data on all vaccine recipients. We used artificial intelligence algorithms and developed a custom data validation pipeline to digitalize the paper-registers to allow for the validation of vaccination status in participants of cholera vaccine studies. We also conducted a representative household survey 2 months post-vaccination to estimate the vaccination coverage and to compare to the register. We recorded 250,102 vaccine recipients, yielding an estimated administrative vaccination coverage of 79.3% compared to 72.5% coverage measured in the survey.

We are finalizing the data validation at the time of writing this abstract. We will present estimates of the true vaccine coverage in the population based on both the survey and register data using a latent class model and will quantify the biases related to self-reporting vaccination status. We expect the results from our study to provide important and actionable insights for future observational field studies of vaccines, like OCV.

8101

USING CLINICAL PREDICTION TO IDENTIFY CHOLERA IN SEVERELY DEHYDRATED CHILDREN WITH DIARRHEA

Sharia M. Ahmed[1], Anna Jones[1], Ashraful I. Khan[2], James A. Platts-Mills[3], Karen L. Kotloff[4], Eric Nelson[5], Daniel Leung[1]

[1]University of Utah, Salt Lake City, UT, United States, [2]International Centre for Diarrhoeal Disease Research, Bangladesh, Dh, Bangladesh, [3]University of Virginia, Charlottesville, VA, United States, [4]University of Maryland, Baltimore, MD, United States, [5]University of Florida, Gainesville, FL, United States

Cholera remains an important cause of infectious disease deaths, primarily through severe dehydration due to acute watery diarrhea. Because of the lack of reliable diagnostic testing in low and middle-income countries (LMICs), the World Health Organization (WHO) Integrated Management of Childhood Illness (IMCI) and the Global Task Force on Cholera Control (GTFCC) provide antibiotic prescribing guidelines based primarily on symptom presentation. However, severe dehydration can occur with other enteric pathogens. Our goal was to develop a clinical prediction rule to identify severely dehydrated children with cholera. We used clinical and demographic data from the Global Enteric Multicenter Study (GEMS) of the incidence, etiology, and outcome of moderate-to-severe diarrhea (MSD) among children aged 0-59 months to build predictive models to identify severely dehydrated children (as defined by the IMCI and GTFCC guidelines) with MSD attributable to cholera. We screened variables using random forests, and assessed predictive performance with random forest regression and logistic regression using 5-fold cross-validation. External validation via additional prospective data is pending Fall 2024. Of the 2,284 children randomly selected for qPCR testing and classified as severely dehydrated, 101 (4.4%) had MSD attributable to cholera. Top predictors ranked from most predictive included age (months), mid-upper arm circumference (MUAC), respiratory rate per minute, axillary temperature, and if the child is currently breastfed. We were able to achieve an area under the receiver operating curve (AUC, discriminative performance) of 0.69 (95% CI: 0.65, 0.73) with only 2 predictive variables (age, MUAC), and AUC of 0.83 (95% CI: 0.80, 0.85) with 10 predictor variables. Our findings indicate that clinical prediction rules may help identify children suffering severe dehydrating diarrhea as a result of cholera. Antibiotics are indicated and efficacious for children with cholera and MSD. Improved targeting of cholera diagnostics and antibiotic usage has the potential to aid patient outcomes and stewardship of limited resources.

8102

SHIGELLA SPECIFIC DIARRHEAL BURDEN OVER A DECADE IN THE GAMBIA

Bakary Conteh[1], Hannah Atlas[2], Helen Powell[3], Erika Feutz[2], Sean R. Galagan[2], Henry Badji[1], Mehrab Karim[1], Alhagie Manneh[1], Musa Jallow[1], Ramatoulie Jawara[1], Belali Keita[1], Bubacarr E. Ceesay[1], Sheikh Jarju[1], Abdoulie M.J. Jabang[1], Samba Juma Jallow[1], Ousman Secka[1], Martin Antonio[1], Sharon M. Tennant[3], Milagritos D. Tapia[4], Umberto D'Alessandro[1], Patricia B. Pavlinac[2], Karen L. Kotloff[3], M. Jahangir Hossain[1]

[1]Medical Research Council Unit The Gambia at the London School of Hygiene and Tropical Medicine, Fajara, Gambia, [2]Department of Global Health, University of Washington, Seattle, WA, United States, [3]Center for Vaccine Development and Global Health, University of Maryland School of Medicine, Baltimore, MD, United States, [4]Department of Pediatrics, University of Maryland School of Medicine, Baltimore, MD, United States

The Gambia participated as study site of the Enterics for Global Health (EFGH) *Shigella* Surveillance study (August 2022-December 2024), Vaccine Impact on Diarrhea in Africa (VIDA, 2015-2018) and Global Enteric Multicentre Study (GEMS, 2007-2011). This abstract presents the burden of *Shigella* spp. in young children spanning over a decade in The Gambia. VIDA and GEMS enrolled children aged 0-59 months with medically-attended acute moderate-to-severe diarrhea (MSD) while EFGH enrolled children aged 6-35 months with medically-attended acute diarrhea. *Shigella* spp. was detected by microbiological culture and TaqMan assay (qPCR). In all three studies, Population Enumeration and Health Care Utilization Surveys were done to estimate population-based *Shigella* spp. incidence. Among diarrhea cases, *Shigella* isolation by culture was 116/1029 (11.3%), 217/1678 (12.9%) and 90/929 (9.7%) from GEMS, VIDA and EFGH respectively. *Shigella* spp. detection by qPCR from GEMS, VIDA and EFGH was 36.9%, 45.9% and 33.0%, respectively. *Shigella* spp. incidence per 100-child years by qPCR in 0-11, 12-23 and 24-59 months was 1.0, 6.5 and 0.7 respectively in GEMS; 3.4, 8.8 and 2.1 in VIDA, and 36.9 in 6-35 month-olds in EFGH. The highest incidence was observed in 6-35 month-olds and peaked in toddlers (12-23 months) in all three studies. Attributable shigellosis was high in the rainy season (June to October). *Shigella flexneri* was the leading serogroup in GEMS, VIDA and EFGH, accounting for 69.0%, 67.6% and 57.3% of isolates, respectively, followed by *S. sonnei* (20.7%, 18.2%, 36.9%). The most prevalent *S. flexneri* serotypes were 1b, 2a, 6, 3a and 4a in all three studies. *Shigella* spp. is a significant diarrhea pathogen in The Gambia in EFGH and the second most common in GEMS and VIDA. The highest incidence was amongst 6 to 35 month-old children. *Shigella* spp. peaked in the rainy season. *S. flexneri* and *S. sonnei* serogroups accounted for >90% shigellosis. Quadrivalent *Shigella* vaccines could be an important preventive measure in The Gambia in addition to improved hygiene practices.

8103

ENTERIC PATHOGEN PREVALENCE, INCIDENCE AND CLEARANCE RATES, AND SHEDDING INTENSITY IN URBAN KENYAN INFANTS FROM MOLECULAR TESTING OF SEQUENTIAL FECAL SAMPLES

Daniel K. Sewell[1], Fanta Gutema[1], Sheillah Simiyu[2], Phylis Busienei[2], Collins Ouma[3], Christine Amondi[2], John Agira[2], Bonplace Okoth[2], Marsha Marsha[3], Jairus Abuom[3], Alexis Kapanka[1], Blessing Mberu[2], Daniel Kakou[1], Kelly Baker[1]

[1]University of Iowa, Iowa City, IA, United States, [2]African Population and Health Research Center, Nairobi, Kenya, [3]Maseno University, Maseno, Kenya

Prior studies have highlighted a high burden of enteric infection in infants living in low- to middle-income countries, but there is a dearth of information on the incidence and clearance of symptomatic and asymptomatic enteric infections in this susceptible population. This information is imperative for improving modeling efforts aimed at determining the relative importance of transmission pathways as well as for intervention assessments. Additionally, is it not known how various pathogens lead to diarrheal symptoms. This study's goals were two-fold. First, we aimed to estimate prevalence, 2-week incidence, and clearance rates, as well as shedding intensity for 19 types of enteric pathogens in infants 0-12 months of age living in urban settings in Kenya. Second, we investigated whether shedding intensity of these pathogens was predictive of caregiver-reported infant diarrhea. To achieve these goals, a total of 266 infants in Nairobi and Kisumu were recruited into the PATHOME study. For each infant, 5 fecal samples were taken over the course of 14 days and analyzed via TaqMan Array cards for 23 indicator genes of 19 viral, bacterial, and protozoan pathogens. Infant diarrhea was assessed using a 14-day caregiver self-report calendar. Point prevalence and 2-week incidence rates were estimated for each pathogen. Clearance rates for the more prevalent pathogens were estimated via accelerated failure time models. Using complete data from 133 Nairobi infants, prevalence and incidence was found to vary widely across pathogens, age groups, and neighborhood SES, with prevalence rates as high as 0.75 and incidence rates as high as 0.45. Median clearance rates for pathogens ranged from 4 days (Shigella) to 9 (Salmonella). Ct values patterns over 14 day periods were examined, shedding light on the natural history of infections. Using XGBoosting with SMOTE upsampling, pathogens' Ct

values marginally improved predicting diarrhea ±1 day from models only using age, achieving an F1 score of 0.745. Forthcoming data from an additional 133 Kisumu infants will bolster strength of these observations.

8104

ASSEMBLY AND PERFORMANCE OF A CHOLERA RAPID DIAGNOSTIC TEST PROTOTYPE THAT DETECTS BOTH *VIBRIO CHOLERAE* AND BACTERIOPHAGE

Md. Abu Sayeed[1], Imrul K. Nabil[2], Piyash Protik[2], Karen Kelly[1], Yasmin A. Begum[2], Taufiqur R. Bhuiyan[2], Firdausi Qadri[2], Ashraful I. Khan[2], **Eric J. Nelson**[1]

[1]University of Florida, Gainesville, FL, United States, [2]International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b), Dhaka, Bangladesh, Dhaka, Bangladesh

Virulent bacteriophage are associated with compromised performance of cholera rapid diagnostic tests (RDTs). We hypothesized that an enhanced cholera RDT that detects the common virulent bacteriophage ICP1 might serve as a proxy for pathogen detection when the phage are present. We previously developed a monoclonal antibody (mAb) to the ICP1 major capsid protein and demonstrated target specificity. However, the approach for the RDT design (single versus duel mAb sandwich for ICP1) and assembly were outstanding. Our objective herein is to demonstrate a proof of concept for the design and assembly on an RDT that targets both a bacterial pathogen and associated virulent bacteriophage. Candidate mAbs were expanded to increase design options and evaluated by immuno-assays (ELISA; western blot). A subset of mAbs were selected for gold conjugation and printing on the RDT. The limit of detection (LOD) of prototype RDTs were determined in diarrheal stools with and without the addition of ICP1. Three mAb candidates were developed and evaluated for the capsid decoration protein (GP123) and tail fiber protein (GP93), and the prior mAb for the major capsid protein (Gp122). A single mAb sandwich RDT prototype for Gp122 was able to detect ICP1; RDTs with mAbs to GP123 and GP93 failed to detect ICP1 in single or dual sandwich configurations. Biologically meaningful LODs for ICP1 were achieved only with boiling of stool with ICP1; electron microscopy demonstrated increased epitope availability after boiling. In this study, we demonstrate a proof of concept for an RDT that can detect a virulent bacteriophage as a proxy for pathogen detection. Preparation by boiling the substrate increased the limit of detection, however further optimization is required before scaled implementation.

8105

INTEGRATION OF ANTIMICROBIAL RESISTANCE DIAGNOSTICS IN BOKÉ REGIONAL HOSPITAL LABORATORY: GUINEA, JULY-DECEMBER 2023.

Siba Michel Grovogui[1], Julie Rae Sinclair[1], Boubacar Ibrahima Diallo[1], Danielle T. Barradas[1], Varough Deyde[2]

[1]Centers for Disease Control and Prevention, Conakry, Guinea, [2]Centers for Disease Control and Prevention, Atlanta, GA, United States

According to WHO, 1.27 million deaths worldwide in 2019 were attributable to multidrug-resistant bacteria. However, hospital laboratories in Guinea are facing major challenges in detecting antimicrobial resistance (AMR). This abstract describes the steps involved in integrating AMR detection into the essential activities of the Boké Regional Hospital Laboratory in Guinea. Between July and December 2023, we conducted the following to introduce AMR testing at the Boké Regional Laboratory: assessment using an adapted WHO Stepwise Laboratory Quality Improvement Process Towards Accreditation Checklist (SLIPTA); training and mentorship of two bacteriology technicians on AMR detection, provision of laboratory equipment, reagents and consumables; and external quality assessment. Performance data were collected and analyzed to describe the effectiveness of the integration. Means and proportions were calculated using Excel (2013). The laboratory scored an average of 72% across 11 quality indicators assessed in the adapted SLIPTA tool. After training, theorical and practical performance of the technicians improved from 40% to 63% and from 28% to 75%, respectively. Accuracy for bacterial culture and microscopy reached 83% and 50%, respectively. From July to December 2023, 85 public health samples were received, and pathogens were isolated in 29 (34.1%) samples. 28 were pathogens under surveillance., *E. coli* was the most prevalent pathogen identified (n=17, 60.7%). Additionally, 25 (89.3%) of the isolated pathogens showed AMR. AMR prevalence was 16.2% for Ofloxacin, 16.2% for Imipenem, 11.8% for Tobramycin, 10.3% for Ciprofloxacin, 10.3% for Ampicillin, 8.8% for Ceftazidime and (8.8% for Gentamicin.This study highlights the effectiveness of training and mentorship on improving integration of AMR detection into clinical testing in a hospital laboratory setting. The obtained results are crucial for raising awareness among authorities and the population about AMR as a public health issue and for serving as a model for expansion to other healthcare facilities.

8106

INITIAL ISOLATION AND WHOLE GENOME SEQUENCING OF *CORYNEBACTERIUM HINDLERAE* IN ISIOLO, KENYA.

Bryson B. Kimemia[1], Lillian Musila[1], Solomon Langat[2], Erick Odoyo[1], Stephanie Cinkovich[3], Samoel Khamadi[2], Jaree Johnson[4], Elly H. Ojwang[5], Timothy E. Egbo[5], Eric C. Garges[5], Fredrick L. Eyase[1]

[1]Walter Reed Army Institute of Research-Africa (WRAIR-Africa)/Kenya Medical Research Institute (KEMRI), Nairobi, Kenya, [2]Centre for Virus Research, Kenya Medical Research Institute (KEMRI), Nairobi, Kenya, [3]United States Armed Forces Health Surveillance Division, Global Emerging Infections Surveillance Branch, Silver Springs, MD, United States, [4]United States Armed Forces Pest Management Board, Silver Springs, MD, United States, [5]Walter Reed Army Institute of Research-Africa (WRAIR-Africa), Kisumu, Kenya

Corynebacteria, also known as Coryneforms, are a diverse group of gram-positive bacilli with a high G+C content in their genomes. Once dismissed as contaminants, recent research has indicated them as opportunistic pathogens, particularly in immunocompromised individuals and nosocomial infections. *Corynebacterium hindlerae*, a relatively recent addition to the genus, has garnered attention due to its isolation from only clinical sources. This study focuses on the isolation and genomic characterisation of *C. hindlerae* from an unexpected source - *Hyalomma truncatum* ticks collected from cattle in Isiolo County, Kenya. This marks the first reported instance of *C. hindlerae* in Kenya and from a non-human host. The isolation was guided by 16S rRNA metagenomics analysis of tick homogenates. It was identified from a pool of 8 ticks. The homogenate was cultured on 5% Sheep Blood Agar to obtain pure cultures of the bacterium. Following DNA extraction, libraries were prepared using the Illumina Nextera XT DNA Library Preparation Kit. Sequencing was performed on an Illumina MiSeq platform. Reads were filtered and trimmed using BBduk. Kraken2 and PubMLST were used for speciation. *De novo* assembly and annotation were performed in Unicycler and Prokka respectively. A genome map was then drawn using Proksee. Read mapping onto a reference genome using BBmap revealed that the sequenced genome had a coverage of 95.92% and an average depth of 15X. This isolation of *C. hindlerae* highlights the potential role of ticks in the circulation of emerging bacterial pathogens. *C. hindlerae* has so far only been isolated from humans in two different continents, its isolation from ticks in Africa suggests that the bacterium may be more diversely distributed. This points to a pressing need for further research to determine its ecological niche, transmission dynamics, pathogenicity, and potential public health risks.

8107

DIAGNOSTIC PERFORMANCE OF ANTIGEN F1-BASED RAPID DIAGNOSTIC TEST AT THE BEDSIDE ON-SITE AND AT REFERENCE LABORATORY FOR BUBONIC PLAGUE IN HIGH ENDEMIC SETTINGS IN MADAGASCAR

Mihaja Raberahona[1], Minoarisoa Rajerison[2], Rindra Vatosoa Randremanana[2], Josephine Bourner[3], Ravaka Randriamparany[2], Tsinjo Rasoanaivo[2], Lisy Hanitra Razananaivo[2], Gabriella Zadonirina[2], Theodora Mayouya-Gamana[2], Reziky Tiandraza Mangahasimbola[2], Tansy Edwards[4], Elise Pesonel[3], Rivonitina Andry Rakotoarivelo[5], Mamy Jean de Dieu Randria[1], Peter W. Horby[3], Piero L. Olliaro[3]

[1]CHU Joseph Raseta Befelatanana, Antananarivo, Madagascar, [2]Institut Pasteur de Madagascar, Antananarivo, Madagascar, [3]University of Oxford, Oxford, United Kingdom, [4]London School of Hygiene and Tropical Medicine, London, United Kingdom, [5]CHU Tambohobe, Fianarantsoa, Madagascar

Madagascar contributes >80% of global plague cases. Plague occurs seasonally in rural areas in the central highland during August-April. Early detection and treatment in the community prevents death. As per national guidelines, an antigen-based rapid diagnostic test (F1RDT) is routinely used at peripheral health centres and confirmed at the central reference laboratory (RL) by culture and qPCR (gold standard, GS). As part of the IMASOY trial (NCT04110340), we assessed the performance of F1RDT for bubonic plague conducted on-site before treatment (D1) and at the RL vs GS in 45 healthcare centres. Serology was also tested on D1, 11, 21 on blood samples. F1RDT performance was assessed against two GSs (culture and qPCR regardless of serology (GS1); and culture, qPCR and serology (GS2)) in 441 suspected bubonic cases: 59% male, 41% female, median age 12 years (range 0-72). Among them, 192 (44%) were confirmed bubonic cases with GS1 and 220 (50%) with GS2. Serology data were available for 426 participants and identified 28 (7%) additional cases (seroconversion or 4-fold titre increase).The sensitivity (Se), specificity (Sp), positive (PPV) and negative predictive value (NPV) of the on-site F1RDT against GS1 (%, 95% CI) were 93.8 (89.3, 96.7), 73.5 (67.6, 78.9), 73.2 (67.2, 78.6) and 93.8 (89.5, 96.8) respectively, and 89.1 (84.2, 92.9), 77.0 (70.8, 82.4), 79.7 (74.1, 84.5) and 87.4 (81.9, 91.8) respectively against GS2. The Se, Sp, PPV and NPV of the F1RDT at RL against GS1 were 92.2 (87.4, 95.6), 97.6 (94.8, 99.1), 96.7 (93.0, 98.8) and 94.2 (90.6, 96.7) respectively, and 82.3 (76.6, 87.1), 99.1 (96.7, 99.9), 98.9 (96.1, 99.9) and 84.6 (79.6, 88.8) respectively against GS2. The head-to-head comparison of the F1RDT on-site and at RL showed agreement (83%) with a Phi coefficient of 0.666. There was no apparent difference in performance of F1RDT by age (<15, ≥15 years). Current practice of combining on-site testing of suspected bubonic plague with F1RDT and confirmatory tests at RL is effective in identifying plague. Serology would identify few more but it would not be feasible in routine practice.

8108

VARIATIONS IN NASOPHARYNGEAL MICROBIOTA ACCORDING TO COVID-19 SEVERITY STATES

Hugo Carrillo-Ng[1], Juana del Valle-Mendoza[2], Ronald Aquino-Ortega[2], Wilmer Silva-Caso[2], Carmen Tinco-Valdez[2], Yordi Tarazona-Castro[1], **Miguel A. Aguilar-Luis**[2]

[1]Instituto de Investigacion Nutricional, Lima, Peru, [2]Universidad Peruana de Ciencias Aplicadas, Lima, Peru

Coronavirus disease 2019 (COVID-19), caused by the SARS-CoV-2 virus, is affected by a variety of factors. Evidence suggests a relationship between COVID-19 and the nasopharyngeal microbiota. This study compares the diversity and taxonomic composition of the nasopharyngeal microbiota with clinical outcomes of COVID-19. A descriptive and comparative study was performed on patients classified into four groups according to their disease severity. For each study group, 26 patients were recruited: patients hospitalized in the intensive care unit (G1), hospitalized in regular hospitalization wards (G2), those without hospitalization and with mild or no symptoms with SARS-CoV-2 (G3), and healthy patients (G4). SARS-CoV-2 was tested on all patients using RT-PCR. The nasopharyngeal microbiota was characterized by PCR, targeting 13 genera of bacteria. Some bacteria were significantly more frequent in hospitalized patients (G1, G2) compared to the non-hospitalized patients (G3 y G4). This is the case with *Lactobacillus* (G1=96.2% of cases, G2=92.3%, G3=23.1%, G4=15.4%). Similarly, *Prevotella* (G1=96.2%, G2=80.8%, G3=3.8%, G4=23.1%). In the same way, *Veillonella* (G1=92.3%, G2=96.2%, G3=7.7%, G4=11.5%) presented a similar distribution. However, some bacteria were detected more frequently in healthy and asymptomatic subjects, such as Others Bacteroidetes (OB) and Others Firmicutes (OF). Similarly, relative abundance shows similar results to percentage frequency. There are several alterations in the nasopharyngeal microbiome associated with SARS-CoV-2 infection status and disease severity, reported in this study. The presence of *Lactobacillus*, *Prevotella*, *Veillonella*, and the Proteobacteria division were higher in critical and hospitalized patients, compared to asymptomatic and healthy subjects. On the other hand, others Bacteroidetes and species of Firmicutes were predominant in the groups of asymptomatic and healthy subjects. The nasopharyngeal microbiota should be studied in the future as a therapeutic, diagnostic, and prognostic tool in COVID-19.

8109

MOLECULAR DIAGNOSIS OF *SHIGELLA* SPP. IN CHILDREN WITHOUT CLINICAL SYMPTOMS IN A RURAL AND URBAN AREA OF NORTHERN PERU

Miguel A. Aguilar-Luis[1], Ronald Rodriguez-Alfaro[1], Yimi Arnaldo Rosa-Mori[1], Juana del Valle-Mendoza[1], Ronald Aquino-Ortega[1], Wilmer Silva-Caso[1], Jorge Bazan-Mayra[2], Carmen Tinco-Valdez[3], Yordi Tarazona-Castro[3]

[1]Universidad Peruana de Ciencias Aplicadas, Lima, Peru, [2]Direccion Regional de Salud Cajamarca, Cajamarca, Peru, [3]Instituto de Investigacion Nutricional, Lima, Peru

According to the World Health Organization (WHO), *Shigella* spp. infection is, in general, the most common cause of dysentery and the second most common cause of diarrhea. Bacterial dysentery due to *Shigella* spp. is an important morbidity and mortality cause, which accounts for 188 million diarrhea or dysentery cases caused annually by *Shigella* spp. around the world and 164,000 deaths related to this pathogen. In low- and middle-income countries, the most affected population is children under five years old. The purpose of this study is to assess the prevalence of *Shigella* spp. and determine the factors related to school-age children from urban and rural communities of the department of Cajamarca in Peru. Descriptive, cross-sectional study with a chunk sampling based on convenience. The study was conducted in 4-to-14-year-old children 14-year-old children from the districts of Baños del Inca (Urban zone) and San Pablo (Rural zone) in Cajamarca. Amplification by PCR assay for the detection of *Shigella* spp. was carried out using the primers and conditions previously described. The prevalence of *Shigella* spp. was 9.1% in the rural community and 3.6% in the urban community. It was found that the consumption of salads (p=0.24) and handwashing before eating (p=0.008) were factors associated to *Shigella* spp. infection. This study found a higher prevalence of *Shigella* spp. in the rural community and, therefore, we suggest implementing interventions to prevent the infection by this gastrointestinal bacterium It was found that a higher prevalence of *Shigella* spp. in the rural community in school-age children. Despite their healthy lifestyles, such as washing their hands before eating and after using the bathroom, they may be infected by this bacterium. In addition, in rural communities, all infected individuals lack sanitary facilities, so some intervention strategies could be recommended.

8110

A MULTIPLEX REAL-TIME PCR ASSAY FOR DETECTION OF THE FOUR MAIN CAUSES OF BACTERIAL MENINGITIS

Simon Tiemélé Laurent Amoikon[1], Kanny Diallo[1], Firmin Kouassi Missa[1], Jérémie Kolotioloman Tuo[1], Odile B. Harrison[2], Martin CJ Maiden[3]

[1]Centre Suisse de Recherches Scientifiques en Côte d'Ivoire, Abidjan, Côte D'Ivoire, [2]Nuffield Department of Population Health, University of Oxford, Oxford, United Kingdom, [3]Department of Biology, University of Oxford, Oxford, United Kingdom

Strengthening diagnostic capabilities and monitoring circulating pathogens are essential to effectively combat meningitis. Current multiplex assays cannot detect all four WHO priority pathogens for meningitis diagnosis, i.e. *Neisseria meningitidis, Haemophilus influenzae, Streptococcus pneumoniae* and *Streptococcus agalactiae*. This work developed multiplex real time PCR assay capable of simultaneously detecting these pathogens. A total of 45 DNA test samples were used, including appropriate specimens from the National Collection of Type Cultures (NCTC). Specific real-time PCR primers and probes targeting *sodC*, to detect *N. meningitidis, dmsA* for *H. influenzae, SP2020* for *S. pneumoniae*, and *cfb* for *S. agalactiae* were tested individually (monoplex) and in combination (multiplex). Standard curves were generated using tenfold dilutions of DNA extracted from reference DNA samples and the limit of detection (LLD), slope, intercept and R2 were determined. In addition, sensitivity, specificity, and positive/negative predictive value (PPV/NPV) of the multiplex assays were calculated. The monoplex and multiplex real-time PCR assays showed the same sensitivity, specificity, PPV and NPV for each of the four bacterial species, indicating that multiplexing did not alter individual assay performance. The assay sensitivities were all 100%, with specificities between 91.7% (*sodC*) and 100%, PPVs were between 72.7% (*sodC*) and 100%. All NPVs were 100%. The multiplex assay showed high efficiency and robust amplification for each target genes. The LLD ranged from 2 (*S. pneumoniae*) to 66 (*H. influenzae*) genome copies/µl. The multiplex assay showed good performance for rapid and accurate detection of meningitis associated bacteria. This test has application for improved diagnosis of meningitis, particularly for group B Streptococci, which remains underdiagnosed in LMIC. However, field validation with clinical specimens is required before implementation.

8111

EFFICACY OF MACOZINONE AND SUTEZOLID AGAINST *MYCOBACTERIUM LEPRAE*

Vino T. Cheriyan, Nashone Ray, Vilma Marks, Patrick Kyle Andrews, Linda B. Adams, Ramanuj Lahiri

DHHS, HRSA, HSB, National Hansen's Disease Program, Baton Rouge, LA, United States

Mycobacterium leprae (M. leprae), the principal etiological agent of Hansen's disease infects the peripheral nerves, mucous membranes, and skin. The present anti-leprosy multi-drug therapy (MDT) requires prolonged treatment duration (6 to 24 months), and has unpleasant side-effects: causing reduced compliance, increasing the risk of relapse, transmission opportunities, and drug resistance. Therefore, there is a clear need to explore new therapeutic interventions against leprosy, which can effectively shorten treatment duration, without increasing adverse reactions. To test the efficacy of Macozinone and Sutezolid against *M. leprae* in vitro as well as in the mouse foot pad (MFP) model. *M. leprae*, freshly harvested from nude mouse foot pads (FP) were incubated at 33ºC with Macozinone and Sutezolid at different concentrations, Radiorespirometry (RR) assay was used to determine bacterial β-oxidation rate as a measure of viability. Mouse bone marrow derived macrophages were infected with *M. leprae* and were treated with different drug concentrations. The cells were lysed and RR was performed on released *M.* leprae to measure bacterial *viability.* To evaluate the efficacy of Macozinone and Sutezolid against *M. leprae* in vivo, athymic nude mice hind FP were inoculated with $3x10^7$ *M. leprae* and infection was allowed to progress for 2 months. Then drugs were administered by gavage as either a single dose, 5 daily doses or 20 doses (5x4weeks). FPs were harvested one month post-treatment and *M. leprae* viability determined by measuring normalized expression of *esxA* transcripts. Results show that Macozinone and Sutezolid are effective against *M. leprae* both in vitro (axenic and intracellular) and in vivo (MFP). Therefore, Macozinone and Sutezolid, having different modes of action, should be tested in combination with other first and second line drugs to explore new shorter treatment regimens for leprosy.

8112

DETECTING NOVEL MECHANISMS OF CARBAPENEM RESISTANCE: AN INNOVATIVE SCREENING SYSTEM IN LIMA, PERU

Grace Tan[1], George Lawson[1], Omar Romero Rodriguez[2], Diego Taquiri Diaz[2], Lucero Mascaro Rivera[2], Lucero Merino Castaneda[2], Candy Leon Palomino[2], Alice Osmaston[1], Luis Alvarado Ruis[3], Patricia Sheen Cortavarria[2], Mirko Zimic Peralta[2], James Hatcher[1], Ioannis Baltas[1], Robert H. Gilman[4], Monica Pajuelo Travezaño[2], Louis Grandjean[1]

[1]Section of Infection, Institute of Child Health, University College London, London, United Kingdom, [2]Department of Molecular Biology, Universidad Peruana Cayetano Heredia, Lima, Peru, [3]Laboratorio Clinico Roe, Lima, Peru, [4]Johns Hopkins Bloomberg School of Public Health, Department of International Health, Baltimore, MD, United States

The global spread of Carbapenem Resistant Klebsiella pneumoniae (CRKP) presents a severe public health threat, yet research on the genetic mechanisms of carbapenem resistance, particularly in developing nations, remains limited. Robust screening strategies are therefore urgently needed to address this issue. We implemented a high-throughput, novel screening strategy to detect novel carbapenem resistance mechanisms in Lima, Peru. Over 3 years, 200 000 isolates were screened by the regional reference laboratory. Antimicrobial susceptibility was assessed using Kirby-Bauer disc diffusion, and Minimum Inhibitory Concentration testing was conducted with VITEK® 2. Carbapenem-resistant isolates then underwent immunoassay screening (OKNVI Resist-5, Blue-Carba). We identified 3 CRKP isolates from 3 different patients which exhibited carbapenem resistance, but with no known carbapenemases on immunoassay. These isolates were whole genome sequenced (WGS) using Oxford Nanopore Technology. Bioinformatic analysis utilised Resistance Gene Identifier v6.0.3 and Comprehensive Antibiotic Resistance Database v3.2.8. WGS identified OXA-1, SHV-11, Mdtq, LptD, OmpK37, KpnH, KpnG, and marA resistance genes; none individually known to be associated with high level carbapenem resistance. Notably, although all 3 samples were genotypically identical, 2 isolates showed low level resistance, potentially explained by the antimicrobial resistance gene combinations identified. However, 1 isolate exhibited unexplained high-level resistance. WGS of these strains with unexplained carbapenem resistance, identified by our screening strategy, revealed a combination of beta-lactamase genes, and the Mdtq porin. Mdtq has not been previously associated with high-level carbapenem resistance, but could partially explain our findings. We anticipate that as combined genotypic and phenotypic testing among gram negative bacteria gains prominence, treatment dilemmas will increasingly arise due to genotype-phenotype differences.

8113

EXPLORING POTENTIAL ASSOCIATION BETWEEN LOW BODY MASS INDEX AND MID-UPPER ARM CIRCUMFERENCE WITH LEPROSY: A CASE-CONTROL STUDY IN ADDIS ABABA, ETHIOPIA

Lawrence Dela Cruz[1], Elleni Zeleki[2], Hatem Mohamed[1], Yosef Wubshet[3], Liya Sesay Getachew[1], Aemon Fissha[4], Biruk Debebe[4], Ytbarek Gebremedhin[4], Jessica K. Fairley[1], Kidist Bobosha[2], Shimelis Nigusse[4]

[1]Emory University, Atlanta, GA, United States, [2]Armaur Hansen Research Institute, Addis Ababa, Ethiopia, [3]Addis Ababa University, Addis Ababa, Ethiopia, [4]All Africa Leprosy Rehabilitation and Training Center (ALERT), Addis Ababa, Ethiopia

Leprosy is classified as a neglected tropical disease (NTD) that affects about 200,000 annually. Factors associated with poverty, like undernutrition, have been associated with leprosy, but research is limited on the extent of this association. We aimed to determine if low body mass index (BMI) and low mid-upper arm circumference was more common in those with leprosy compared to controls in Addis Ababa, Ethiopia. Individuals attending the outpatient clinics at ALERT hospital in Addis Ababa, Ethiopia were recruited and evaluated for the case control study. Leprosy cases, diagnosed within 1 year, were recruited through convenience sampling of the leprosy clinic within ALERT while controls were recruited from neighboring clinics within the hospital. Controls were tested for antibodies against PGL1, phenoglycolipid-1, a specific *Mycobacterium leprae* antigen, and were included in this study if they tested negative. Height, weight and mid-upper arm circumference (MUAC) were measured and body mass index (BMI), calculated. An analysis was conducted to test the association between BMI and MUAC and leprosy, controlling for age, sex, and education level (as an indicator of socioeconomic status). There were 201 controls and 61cases; 56% were females. Univariate analysis showed that a MUAC less than or equal to 22cm was associated with leprosy [OR = 3.85, 95% CI (1.80, 8.26)] while an underweight BMI, defined by a BMI < 18.5, was not significantly associated, although had a high odds ratio [OR = 2.19, 95% CI (0.87, 5.42)]. A stepwise regression was then conducted to control for factors such as age, sex, and education status (as an indicator for SES), and found MUAC to still be significantly associated with leprosy [aOR = 2.46, 95% CI (1.01, 5.99)]. This study demonstrated the association with undernutrition, adding to the body of knowledge on the likely contribution of low nutrition to the development of disease. Further research, such as longitudinal studies and mechanistic studies, can help elucidate the role of poor nutrition and determine interventions that could potentially prevent clinical disease in at risk individuals.

8114

SEROPOSITIVITY TO IGG ANTIBODY OF *RICKETTSIA SPP*. IN A ENDEMIC AREA OF SOUTHEAST MEXICO

Edgar Villarreal-Jimenez[1], **Nina Mendez-Dominguez**[1], Audey Arnal[2], Fernando Puerto-Manzano[3], Henrry Noh-Pech[3], Karla Dzul-Rosado[3]

[1]Hospital Regional de Alta Especialidad de la Península de Yucatán, Mérida, Mexico, [2]International Joint Laboratory IRD/UNAM ELDORADO, Mérida, Mexico, [3]Centro de Investigaciones Regionales "Dr. Hideyo Noguchi". Universidad Autónoma de Yucatán, Mérida, Mexico

Rickettsioses are tick-borne diseases caused by Gram-negative intracellular bacteria of the genus *Rickettsia.* The state of Yucatan has had a history of rickettsial diseases with the presence of *R. rickettsii* and *R. parkeri* both belonging to the spotted fever group (SFG) and *R. typhi* from the typhus group (TG). Seroprevalence in the states is 5.6% of SFG (*R. akari).* Yucatán has experienced urban growth which contributes to deforestation in areas with wildlife that is an important host for the transmission of this group of diseases. The present study aims to identify IgG antibodies to Rickettsia in participants of three geographic regions of Yucatan. Serum samples were collected from 60 participants. The IgG antibody titers were determined by indirect immunofluorescence assay (IFA), slides were fixed with antigens of *R. typhi* (TG), *R. rickettsii*, *R. parkeri*, and *R. conorii (SFG),* positive results were considered as titers IgG 1:64. For 60 participants 55% were female, 22% were older than 65 year the mean age was 51.4 (+16.16). 75% of participants were seropositive for *Rickettsia spp*., 17% (10/60) were seropositive for *R. typhi*, 15% (9/60) for *R. rickettsii*, 15% (9/60) for *R. parkeri* and 14% (8/60) for *R. conorii*,17% (10/60) presented cross-reaction between SFG and TG and 12% (7/60) cross-reaction between SFG. In t student test mean age was significantly difference between positive and negative patients ($p<0.001$). Chi-square test of independence reveals no significant differences in seropositivity for *Rickettsia spp* by gender ($p=0.635$). These preliminary results indicate high seropositivity to Rickettsia *spp*. in a representative sample of three geographic regions of Yucatan, which contrasts with previous investigations where the estimated seroprevalence in the state is 5.6%. Epidemiological studies of rickettsiosis are relevant because the changes in the ecosystem in recent decades as a result of human activity may impact the observed increase. A study with a larger sample size is important to determine the current seroprevalence.

8115

EVALUATION OF AN ELECTRICITY-INDEPENDENT METHOD FOR IS2404 LOOP-MEDIATED ISOTHERMAL AMPLIFICATION (LAMP) DIAGNOSIS OF BURULI ULCER IN RESOURCE LIMITED SETTING

Evans Kwame Ahortor

3D BioFibR Inc., Halifax, NS, Canada

Buruli ulcer (BU) is a devastating necrotic skin disease. PCR, recommended for confirmation of BU by WHO, requires an equipped laboratory, which often delay timely diagnosis and treatment of BU patients in remote settings. This study aims to evaluate a simple rapid syringe DNA extraction method (SM) in comparison with an elaborate conventional DNA extraction method (CM) followed by loop mediated isothermal amplification (LAMP) assay targeting IS*2404* for the detection of MU, either using a pocket warmer (pw) or a heat block (hb) for incubation. Secondly, we aim to also explore the diagnostic workflow for BU at a community-based health centre in an endemic area in rural Ghana as an example of a potential target setting, using interviews with researchers and health care workers (HCWs). A protocol using SM for DNA extraction followed by IS*2404* PCR (IS*2404* PCR^{SM}) was able to identify MU DNA in 73 out of 83 BU clinical specimens submitted for diagnosis. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of IS*2404* PCR^{SM} were 90.12%, 100%, 100% and 65.21% respectively, as compared to the reference standard IS*2404* PCR in combination with a standard extraction protocol for mycobacterial DNA. Evaluation of the LAMP assay on 64 SM DNA extracts showed a sensitivity, specificity, PPV and NPV of 83.6%, 100%, 100% and 50%, respectively, using either pocket warmer (pwLAMP SM) or heat block (hbLAMP SM) for incubation of the reaction, as compared to the same reference standard. In terms of the limit of detection, the pwLAMP^{SM} could detect 30 copies of the IS*2404* target. Interviews confirmed that a diagnosis at the PoC, in addition to screening based on clinical criteria, would be advantageous to prevent delays and loss to follow-up. The high diagnostic and analytic accuracy of the pwLAMP, evaluated by us in combination with the SM, supports its potential use for the rapid detection of MU in suspected BU samples at the community or primary health care level without reliable electricity supply. Further optimization needs include a lysis buffer, evaluation directly at the PoC and other sites and assessing staff training requirements.

8116

POOR WASH, UNDERNUTRITION, AND FOOD INSECURITY IS ASSOCIATED WITH ANTI-PGL1 POSITIVITY, MARKER OF LEPROSY INFECTION, IN ADDIS ABABA, ETHIOPIA

Hatem Mohamed[1], Liya Sisay Getachew[1], Elleni Zeleke[2], Lawrence Dela Cruz[1], Ytbarek Gebremedhin[3], Biruk Debebe[3], Yosef Wubshet[4], Aemon Fissha[3], Shimelis Nigusse[3], Jessica K. Fairley[1], Kidist Bobosha[2]

[1]Emory University, Atlanta, GA, United States, [2]Armaur Hansen Research Institute, Addis Ababa, Ethiopia, [3]All Africa Leprosy Rehabilitation and Training Center (ALERT), Addis Ababa, Ethiopia, [4]Addis Ababa University, Addis Ababa, Ethiopia

Given stagnant global leprosy cases, more needs to be done for elimination and halting local transmission. The use of anti-PGL1, a specific IgM antibody to *Mycobacterium leprae* infection, can identify individuals exposed to infection at increased risk of developing disease and identify factors related to infection. We conducted a cross-sectional study to determine the prevalence of anti-phenoglycolipid-1 (PGL1) seropositivity among communities near the ALL-African Leprosy, Tuberculosis Rehabilitation Center (ALERT),a former leprosy hospital, and to identify factors associated with seropositivity. Individuals without a present or past history of leprosy were recruited from the outpatient clinics at ALERT hospital from May till December 2023. A questionnaire about sociodemographic, environmental (WASH), and nutritional factors was administered. Height, weight, and mid-upper arm circumference (MUAC) were measured and blood samples tested for anti-PGL1 IgM using a point-of-care lateral flow (ML Flow). Of the 319 participants, 36.8% (n=118) were positive for anti-PGL1 IgM. The majority of participants had improved water sources and sanitation facilities, however 71% reported sharing toilets with other household. Among the study population, 6.6% were categorized as underweight(BMI<18.5), and 12% had low MUAC (< 22 cm). Factors associated with positive PGL-1 IgM included owning agriculture land (aOR 2.95, 95% CI [1.22: 7.51]), unimproved bathing water source (aOR 3.85, 95% CI [1.57: 10.2]) , dirt floors (aOR 1.64, 95% CI [0.97: 2.77]; p=0.065), lower MUAC (< 22 cm) (aOR 1.98, 95% CI [0.97:4.09) and a higher frequency of not eating for an entire day within the past year (aOR 1.77, 95% CI[0.95: 3.29];p=0.071), controlling for age, sex, source of income and education. Our study identified a high prevalence of PGL1-IgM in community members that highlights the likelihood of occult transmission in this region. Associated environmental and nutritional factors also show the likely roles of both the environment and the host in the exposure-infection-disease model in leprosy and should be further investigated.

8117

EPIDEMIOLOGICAL FACTORS ASSOCIATED WITH *MYCOBACTERIUM LEPRAE* SEROPOSITIVITY AND HISTORY OF HANSEN'S DISEASE IN A HIGHLY ENDEMIC AREA OF MINAS GERAIS, BRAZIL

Audra Bass[1], Heloine M. Leite[2], Pedro HF Marçal[3], Lorena B.P. Oliveira[4], Marcos D.S. Pinheiro[2], José A. Ferreira[5], Julie Clennon[1], Thomas R. Ziegler[1], Jeffrey M. Collins[1], Lance A. Waller[1], Lucia A. O. Fraga[2], Jessica K. Fairley[1]

[1]Emory University, Atlanta, GA, United States, [2]Universidade Federal De Juiz de Fora - Campus GV, Governador Valadares, Brazil, [3]Georgia Institute of Technology, Atlanta, GA, United States, [4]Universidade Vale do Rio Doce, Governador Valadares, Brazil, [5]Unifenas, Belo Horizonte, Brazil

Many of Hansen's disease (leprosy) endemic areas are also endemic to helminth infections and studies have shown associations of helminths and mycobacterial infections. Therefore, we assessed the overlap of *Mycobacterium leprae* infection (as measured by antibodies to the LID-1 antigen) and Hansen's disease (HD) with parasitic infections. Children and adults were recruited from high-endemic municipalities in eastern Minas Gerais, Brazil, enrolled, and blood taken by fingerstick. A multiplexed bead assay (MBA) tested for antibodies and questionnaires on demographics and infection history were administered. Data were analyzed multivariable logistical regression with both anti-LID-1 antibody and history of HD as outcomes in separate models. Exposures in the analysis included history of parasites (both antibody results and self-reports) and several pertinent socio-demographics like area of residence (i.e. urban vs. rural). Of 1311 enrollees, 72 (5.5%) reported a history of HD, 94 (7.2%) positive for anti-LID-1, 836 (63.8%) reported having parasitic diseases in the past, 153 (11.7%) tested positive for SEA antibody, and 69 (5.3%) for NIE antibody. There was an association between rural residence and history of HD (aOR, 1.97, CI: 1.14 – 3.38) as well as rural residence and anti-LID-1 positivity (aOR 1.79, CI: 1.07- 3.38). While not statistically significant, there was a positive association between anti-LID-1 and strongyloides serology (aOR 1.57, CI: 0.69-3.57), and a negative one with SEA antibodies (aOR 0.79, CI: 0.38 - 1.61). This differed for those with a history of HD where SEA antibodies was positively associated (aOR 1.26, CI: 0.63-2.50); and NIE seroreactivity negatively associated (aOR, 0.40, CI: 0.09-1.70). There were no statistically significant associations with reported history of parasite infections and either anti-LID-1 or past HD. While we did not find a significant overlap for these infections, we did find statistical significance related to residency in rural places and both anti-LID-1 antibody and history of HD. This suggests an epidemiologic connection with rural residence and HD and deserves further investigation.

8118

SEASONALITY AND ENVIRONMENTAL ASSOCIATION OF MELIOIDOSIS IN NORTHERN VIETNAM

Morgan C. Metrailer[1], Quyen Tran Thi Li[2], Treenate Jiranantasak[1], Andrew Bluhm[1], Tan Luong[1], Khang Pham[3], Ha Thi Thu Hoang[3], Hoa Minh Luong[3], Ngoc Bich Do[3], Hai Thanh Pham[3], Michael H. Norris[4], Trung Thanh Trinh[2], Jason K. Blackburn[1]

[1]University of Florida, Gainesville, FL, United States, [2]Vietnam National University, Hanoi, Vietnam, [3]National Institute of Hygiene and Epidemiology, Hanoi, Vietnam, [4]University of Hawaii, Honolulu, HI, United States

Burkholderia pseudomallei is the causative bacterium of melioidosis, a potentially fatal disease primarily affecting people in the tropics and sub-tropics. This bacterium is environmentally mediated, infecting hosts through contact with contaminated soil and water. *B. pseudomallei* is endemic across Southeast Asia. Vietnam has a high hospital burden of melioidosis in its central region. Despite the history in Central Vietnam and the endemicity in nearby Thailand, melioidosis is not a nationally reportable disease and little is known regarding epidemiology of melioidosis in Northern Vietnam. The objective of this study is to investigate melioidosis distribution, associated environmental and geographic conditions, and determine its seasonality in Northern Vietnam. An ELISA assay with high specificity and selectivity for the detection of *B. pseudomallei* exposure was used to determine melioidosis seroprevalence from febrile patients of unknown cause reporting to hospital (2020-2023). Case data were aggregated to commune (sub-district) for spatial Bayes rate smoothing, local Moran's I, and spatial regression. A presence/absence analysis was performed to elucidate the relationship between environmental/physical conditions and seroprevalence. Blood culturing and WGS of a subset of patient samples was performed. A phylogenetic analysis revealed close genetic relationships between the isolated species, all of which persist in similar environments as *B. pseudomallei*. This study found that *B. pseudomallei* exposure was identified in all six provinces but spatially clustered. Seroprevalence was related to established soil conditions associated with *B. pseudomallei* persistence and increased cropland. A relationship between seasonality and melioidosis seropositivity was established, with the wet season having high seroreactivity. Healthcare accessibility was impactful to the melioidosis seropositivity, indicating that an improvement in public health surveillance regionally would be beneficial. Isolation of genetically similar opportunistic pathogens can be useful for informing clinicians.

8119

ECOLOGY AND EPIDEMIOLOGY OF *SARCINA TROGLODYTAE*, A NOVEL BACTERIUM ASSOCIATED WITH A LETHAL DISEASE IN CHIMPANZEES (*PAN TROGLODYTES*) IN SIERRA LEONE

Emily Dunay[1], Ismail Hirji[2], Leah A. Owens[1], Gregory A. Barrett-Wilt[1], Konkofa Marah[2], Naomi Anderson[2], Maria Ruiz[3], Rebeca Atencia[3], Johanna R. Elfenbein[1], Tony L. Goldberg[1]

[1]University of Wisconsin-Madison, Madison, WI, United States, [2]Tacugama Chimpanzee Sanctuary, Freetown, Sierra Leone, [3]Jane Goodall Institute Congo, Pointe-Noire, Congo, Republic of the

Bacteria of the genus Sarcina (family Clostridiaceae) have been associated with gastrointestinal disease in animals, including humans, since 1842. Although commonly thought to be opportunistic pathogens associated with delayed gastric emptying, evidence is emerging that, like the genus Clostridium, Sarcina consists of a diverse complex of species, some of which may be frank pathogens. Recently, a novel species, Sarcina troglodytae, was identified and epidemiologically associated with epizootic neurologic and gastroenteric syndrome (ENGS), a lethal disease of chimpanzees that has killed at least 56 chimpanzees at a sanctuary in Sierra Leone since 2005. Here, we describe the isolation of S. troglodytae from the brain of an affected chimpanzee and determined viable in vitro growth conditions allowing for further species characterization and elucidation of fermentation byproduct(s) with potential clinical relevance. Additionally, we have developed a species-specific diagnostic PCR which we used to test fecal and environmental samples from chimpanzees in sanctuaries and the wild. Our results demonstrate that S. troglodytae is more prevalent in sanctuary chimpanzees in the affected population in Sierra Leone than elsewhere where, to our knowledge, ENGS has not been observed. We also detected S. troglodytae in environmental samples, primarily soil, which combined with evidence of sporulation in vitro suggests a potential environmental reservoir. Reports in the literature of similar Sarcina-associated pathology in humans and other animals have increased dramatically in the last 15 years, suggesting that bacteria in this genus may be responsible for more morbidity and mortality than is generally appreciated. Clinicians, researchers, conservation biologists, and public health officials should consider certain members of the genus Sarcina to be potential pathogens of interest.

8120

OUTCOME AND PREDICTORS OF MORTALITY AMONG NEWBORNS WITH SEPSIS IN FOUR HEALTH FACILITIES IN MALI A COHORT STUDY

Fatoumata Bintou Traore[1], Cheick Sidya Sidibe[2], Alhassane Diallo[3], Sidikiba Sidibe[4], Bienvenu Salim Camara[4], El Hadj Marouf Diallo[5], Alexandre Delamou[5], Hamadoun Sangho[6]

[1]National Institute of Public Health, Bamako, Mali, [2]Athena Institute for Research on Innovation and Communication in Health and Life Sciences, Vrije Universiteit, Amsterdam, Netherlands, Amsterdam, Netherlands, [3]University of Montpellier, Montpellier, France, Montpellier, France, [4]Department of Public Health, Gamal Abdel Nasser University of Conakry, Conakry, Guinea, Conakry, Guinea, [5]African Centre of Excellence for the Prevention and Control of Communicable Diseases, University of Conakry, Conakry, Guinea, Conakry, Guinea, [6]Faculty of Medicine and Stomatology; University of Sciences, Techniques and Technology of Bamako, Bamako, Mali, Bamako, Mali

Neonatal sepsis is a is a major cause of neonatal mortality and morbidity. No prospective study has been conducted on the survival of newborns with sepsis in Mali. This study aims to analyze the survival of newborns with sepsis and assess possible predictors of mortality in four health facilities in Mali.A prospective cohort study was conducted among neonates diagnosed with sepsis in four health facilities in two regions of Mali from December 2022 to January 2023. The data were analyzed using R software version 4.3.1. Kaplan-Meier estimators with log-rant test were used to estimate the survival time of the neonates. Bivariate and multivariate Cox proportional hazards models were used to show associations between possible predictors and survival time. Variables which p value < 0.05 in multivariable analysis were declared as statistically significant predictors of mortality.The study involved 152 neonates with their respective mothers. The median age of the mothers was 28 years [22-34], and for neonates, it was 2 days [2-8]. Male sex represented (74) 48% of the total. The neonates were followed for a median of 4 days [4-6]. Of the total, (62) 40% were mothers with positive sepsis. The survival rate at 15 days was 63% (50-79). At the end of this follow up 33 (21%) of the neonates died, with incidence of 21.30 per 100 neonates admitted with sepsis. Prematurity [P = 0.001, AHR = 8.81, 95% CI: (1.79, 43.26)], male sex [P = 0.02, AHR = 2.32, 95% CI: (1.08, 4.98)], admission in the hospital [P = 0.02, AHR = 2.48, 95% CI: (1.09, 5.96)], were the independent predictors of mortality among neonates admitted with neonatal sepsis**.**It is important to note that this conclusion is based on objective data analysis and not subjective evaluations. The risk of mortality was high among neonates with sepsis. The prematurity, sex male and the admission in the hospital were identified as predictors of mortality. The intervention focusing on the predictive factors identified could have an effect on mortality.

8121

INFLUENCE OF HIV INFECTION ON COMMON BACTERIA CAUSING SEPSIS AND ASSOCIATED SUSCEPTIBILITY PATTERNS IN CHILDREN AT A PEDIATRIC HOSPITAL IN ZAMBIA

Jonathan Gwasupika

Tropical Diseases Research Centre, Ndola, Zambia

Sepsis, a condition of global public health concern, is a major cause of morbidity and mortality. There is a rise in antimicrobial resistant (AMR) bacteria attributed to sepsis. This study aims to determine the etiology and antibiotic resistance patterns among children admitted with clinical features suggestive of sepsis at Arthur Davison Children's Hospital (ADCH) in Ndola, Zambia and assess the influence of HIV infection on sepsis etiology. This is an ongoing prospective longitudinal study of children aged 2 years admitted at ADCH with clinical sepsis defined as the presence of 2 of the following conditions: temperature 38.0°C, respiratory rate ≥20/minute, and pulse ≥90/minute. Blood collected from each participant is inoculated into BACTEC culture bottles and incubated for 5 to 7 days. Positive cultures are inoculated onto culture media for subculture followed by species identification and antibiotic susceptibility testing. Ethical clearance and approval has been granted by the Tropical Diseases Research Centre ethics committee (TDRC-EC 092/07/23) and National Health Research Authority. Of the 95 participants (63.3% of 150 target sample size) of who have been recruited, 44.2% (42/95) are females and the mean age at admission is 9.8 (SD 6.8) months. About 30.5% (29/95) have had positive blood cultures and 17/29 are probable (true) pathogens with *Staphylococcus aureus* being the most common (10/17). About 6/17 of the true pathogenic bacteria isolated were Gram negative rods (GNR) *(*2 *Klebsiella pneumoniae,* 2 *Pseudomonas aeruginosa,* 1 *Escherichia coli* and 1 *Yersinia pestis*). Approximately 60% of the *S. aureus* isolates were methicillin-resistant (MRSA); multidrug resistance (MDR) was noted in *Klebsiella pneumonia* and *Pseudomonas aeruginosa*. Analysis of association with HIV status is ongoing.*S. aureus* is a common cause of pediatric sepsis and is resistant to penicillins, the first line agent along with gentamicin. Similarly, all GNRs isolated were MDR so strengthening microbiology laboratory capacity is needed and the use of more potent antibiotics such as clindamycin should be encouraged in a low resource setting like ADCH.

8122

AUSTRIAN SYNDROM : A RARE CASE REPORT

Kamena Mwana-Yile Hassan[1], Samia Ejjebli[2], Hanane Badi[1], Jean Claude Bucumi[1], Kamal El Filali Marhoum[1]

[1]Infectious Diseases Department, Ibn Rochd University Hospital, Faculty of Medicine and Pharmacy of Casablanca, HASSAN II University, casablanca,

Morocco, [2]Cardiology Department, Ibn Rochd University Hospital, Faculty of Medicine and Pharmacy of Casablanca, HASSAN II University, casablanca, Morocco

Austrian syndrom is a rare and fatal triad of pneumonia, meningitis and endocarditis caused by streptococcus pneumoniae, with a mortality rate of 60%. Pneumococcus is responsible for less than 3% of native valve endocarditis, but causes rapid valve destruction. A few published cases of austrian syndrome were confirmed by blood cultures.we report a case of austrian syndrome in a 59-year-old patient with a history of arterial hypertension on angiotensin-2 receptor antagonist therapy for five years, presenting with prolonged fever associated with loss of conscience without respiratory or cardiac signs, in whom purulent bacterial meningitis with positive gram stain, infective endocarditis with mitral and aortic localization and interstitial pneumonitis were demonstrated with negative blood cultures. Although the mortality rate is very high, early management aof austrian syndrome can improve the patient's quality of life

8123

WHOLE GENOME SEQUENCING OF EXTENSIVELY DRUG-RESISTANT *ENTEROBACTER HORMAECHEI* CLINICAL ISOLATES FROM A SECONDARY HOSPITAL IN MOROCCO WITH *HSV* AND *NDM* CARBAPENEMASE GENES

Ahmed Belmouden[1], Fatima Moustaoui[1], Mohamed Aghrouch[2], Youssef Idaghdour[3], Zohra Lemkhente[1], Maryama Barhoine[1], Fatima Boubrik[1]

[1]Ibnou Zohr University, Agadir, Morocco, [2]Ministry of Health, Hassan II Hospital, Agadir, Morocco, [3]New-York University Abu Dhabi, Abu Dhabi, United Arab Emirates

The *Enterobacter cloacae* complex (*Ecc*) comprises enteric Gram-negative bacteria responsible for nosocomial outbreaks, primarily affecting immunocompromised patients. These infections are often fatal due to the high-level multidrug resistance of *Ecc* isolates. Despite their clinical significance, little is known about their virulence and pathogenicity. To understand the patterns and mechanisms of antibiotic resistance in three carbapenem-resistant bacterial isolates (EC254, EC256, EC83) selected from a biobank at a hospital in Agadir, genomic DNA was extracted and sequenced using the Illumina MiSeq platform. Hybrid assembly was utilized with Unicycler v0.4.2, and annotation was done via PATRIC version 3.6.6. Resistome and plasmid analyses were conducted using CARD and Plasmid Finder 2.0, respectively. Phylogenetic analyses were performed using MEGA version 10.1.7. The Genome sizes were 4.88Mb (EC83), 5.28Mb (EC256), and 5.29Mb (EC254). BLASTn alignment analysis using the *16S rRNA* gene showed high similarity to *Enterobacter hormaechei* subsp. *xiangfangensis* strain 10-17, with 99.2% and 100% identity for EC83 and both EC254/EC256, respectively. Multilocus Sequence Typing (MLST) (*dnaA*, *fusA*, *gyrB*, *leuS*, *pyrG*, *rplB*, *rpoB*) was assigned as follows: 49/20/19/44/*/24/32 for EC83 and 10/21/9/44/*/4/32 for both EC254 and EC256. Annotation of the assembled genomes indicated the presence of various antimicrobial resistance genes to aminoglycosides, β-lactams, fosfomycin, macrolides, sulfonamides, and fluoroquinolones. Notably, the strain EC83 was identified to carry seven main carbapenemase genes (*SHV-64, TEM-1*, *NDM-1*, *ACT-20*, *CMY-4*, *OXA-1*, and *OXA-48*). For EC254-EC256, five main carbapenemase genes were identified (*CTX-M-15*, *TEM-1*, *ACT-25*, *OXA-1*, and *OXA-48*). Plasmid detection revealed the presence of at least two large (~400 kb total) incompatibility group plasmids belonging to *IncF*, *IncH*, and *IncI1*. Phylogenetic analysis showed that EC254, EC256, and EC83 are closely related. The study generated draft genome sequences that provide valuable information for tracking antibiotic resistance in nosocomial outbreaks.

8124

SUCCESSFUL APPLICATIONS OF PHAGE THERAPY TO OVERCOME MULTIDRUG RESISTANT BACTERIAL INFECTIONS

Biswajit Biswas

Naval Medical Research Command / BDRD, Fredrick, MD, United States

Abstract: Antimicrobial resistance (AMR) is a growing threat for public health around the globe. This threat is currently more pronounced due to ad libitum use of antibiotics. The selection pressure generated by the overuse of antibiotics has led to the rapid spread of AMR in our environment. Additionally, recent overuse of antibiotics during the COVID-19 pandemic has exacerbated these circumstances. Currently, conditions are so unmanageable that an alternative treatment must be developed and implemented. Phages are the most abundant biomolecules on the surface of the earth and a natural predator for bacteria, regardless of whether those bacteria are susceptible or resistant to conventional antibiotics. In this regard, a properly formulated phage mixture would be highly effective for overcoming the AMR problem for any class of bacteria. Unfortunately, two of the hindrances related for rapid implementation of phage therapy are associated with (i) host specificity of phage against the targeted bacteria and (ii) development of phage resistant bacteria during phage therapy. Recently, in our lab we have developed a rapid phage screening system to overcome both problems. This system allowed us to implement the phage therapy and successfully overcome several MDR bacterial infections in humans. In each case, using the system to evaluate the bacteriolytic nature of phages in a liquid environment, we were able to generate an effective therapeutic phage mixture. This liquid-based assay system allowed for the real-time evaluation of the kinetics of bacterial growth and the development of phage resistance over the course of the observation. Additionally, the system was also used for monitoring phage-bacterial interactions in the presence of antibiotics and the subsequent changes in the antibiotic resistance patterns of MDR bacteria under the selective pressure of the lytic phages. The details of the selection and characterization of the phages for these treatments along with treatment outcomes will be described in this presentation.

8125

BURKHOLDERIA PSEUDOMALLEI: A NEGLECTED 'NEGLECTED TROPICAL DISEASE'?

Ashleigh Hale

University Hospitals Coventry and Warwickshire, Coventry, United Kingdom

Neglected tropical diseases (NTDs) are a group of preventable and treatable diseases caused by a range of pathogens, each capable of causing significant morbidity and mortality. Over the years, the list of NTDs has grown. However, *Burkholderia pseudomallei* has not been included thus far. *B. pseudomallei* is a gram-negative, soil-dwelling bacteria which is the causative agent of melioidosis. It is endemic in tropical and subtropical regions with a higher incidence in low-income settings. Infection can cause severe health complications, such as pneumonia, sepsis and multi-organ abscesses. An extensive review of published cases and publicly available information was conducted to identify reoccurring presenting symptoms, comorbidities, average time to diagnosis and treatment outcomes. A meta-analysis was carried out and a literature summary table was constructed. Results showed delays in diagnosis frequently occurred due to the resemblance of symptoms to other conditions, coupled with the similarity of *Burkholderia* organisms to *Pseudomonas* in laboratory settings, thereby predisposing to misidentification. No single presenting symptom was indicative of melioidosis, suggesting a strong clinical suspicion is required to help with prompt diagnosis. Therefore, it is essential for healthcare workers to have awareness of disease and specific areas of endemicity. Approximately 165,000 individuals are diagnosed with melioidosis each year, with an estimated 89,000 deaths. This represents a higher disease burden and greater mortality rate than many other recognised NTDs, such as dengue and leptospirosis. Although *B. pseudomallei* is not formally recognised as a NTD, the case studies examined in this investigation

demonstrate that melioidosis is a major global health concern. The addition of *B. pseudomallei* on the NTD list would significantly increase awareness amongst healthcare professionals, and drive crucial research, leading to improved diagnostic tools, surveillance, treatment, and patient care.

8126

GENOTYPIC AND PHENOTYPIC PROFILES OF ANTIMICROBIAL RESISTANCE IN PATHOGENIC BACTERIA ISOLATED FROM SEPTICEMIC PATIENTS IN WESTERN KENYA

Joseph Khamisi Kaingu[1], James Nonoh[2], Carolyne Kifude[3], Kimita Gathii[3], Amos Onditi[3], Kirti Tiwari[3], John Waitumbi[3]

[1]WRAIR-AFRICA/Maseno University, Kisumu, Kenya, [2]Maseno University, Kisumu, Kenya, [3]WRAIR-AFRICA, Kisumu, Kenya

Antimicrobial resistance (AMR) is a significant global health threat, causing approximately 700,000 deaths annually. Traditional phenotypic antimicrobial susceptibility testing (AST) methods are limited by delays and result in delayed treatment with appropriate antibiotic therapies. We compared phenotypic AST with whole genome sequencing (WGS) in septicemic patients. WHO-GLASS pathogenic bacteria were retrospectively analyzed (2022-2023) from Western and Lake region referral hospitals. BD Bactec9050 and BD Phoenix 100 facilitated blood culture incubation, identification, and AST. DNA extraction and WGS were performed using the Oxford Nanopore Technologies platform, with EDGE Bioinformatics for bacterial identification and abritAMR/RGI for AMR gene identification. Among 960 blood cultures, 12.8% (123) showed bacterial growth, with 17 pathogenic bacteria identified by BD Phoenix. There were 13 Gram-negative bacteria (4 *E. coli*, 8 *Salmonella typhi* and 1 *Salmonella spp*.), and 4 gram-positive bacteria (3 *Staphylococcus aureus*, 1 *Streptococcus pneumoniae*). WGS revealed discrepancies between phenotypic and genotypic identifications, identifying *S. typhi* as *S. typhimurium,* probably due to phenotypic similarities. Two *E. coli* isolates were phenotypically susceptible but interestingly, multidrug-resistant (MDR) efflux genes were detected by WGS. Salmonella isolates displayed resistance to various antibiotics with MDR efflux genes detected. Notably, Salmonella isolates clustered with *S. typhimurium* global sequences, confirming their misidentification by BD Phoenix. *S. aureus* exhibited resistance to several antibiotics, while *S. pneumoniae* was generally susceptible, although genotypic AMR was evident but could not be confirmed due to low reads. In conclusion, the study identified disparities in bacterial identification and AST between phenotypic and genotypic methods, emphasizing the importance of incorporating both techniques for accurate AMR prediction.

8127

INFORMING ECOLOGICAL NICHE MODELS OF *BACILLUS ANTHRACIS* WITH CONSTRAINED DIVERSITY INDICES AND PHYLOGENIES FOR TEXAS AND VIETNAM

Jason K. Blackburn[1], Morgan A. Walker[1], Morgan C. Metrailer[1], Tan Luong[1], Treenate Jiranantasak[1], Andrew P. Bluhm[1], Thi Thu H. Ha Hoang[2], Van Khang Pham[2], Ted L. Hadfield[1], Diansy Zincke[3], Martin E. Hugh-Jones[4], Michael H. Norris[5], Jose Miguel Ponciano[1]

[1]Emerging Pathogens Institute, Gainesville, FL, United States, [2]National Institute of Hygiene and Epidemiology, Hanoi, Vietnam, [3]UF ICBR, Gainesville, FL, United States, [4]Louisiana State University, Baton Rouge, LA, United States, [5]University of Hawaii at Manoa, Honolulu, HI, United States

Ecological niche models (ENMs), including GARP, MaxEnt, Random Forest, and Boosted Regression Trees, are used to prediction the distribution of *Bacillus anthracis* from local to global scales. *Bacillus anthracis,* the bacterial cause of anthrax, has a near global distribution limited by specific soil and environmental conditions constraining its range. As a spore-former, *B. anthracis* can persist for years resulting in repeat outbreaks in areas meeting these ecological conditions. Phylogenetically, *B. anthracis* is divided into five major lineages and 12 to 19 sub-lineages (defined by single nucleotide repeats [SNPs]). Within these sub-lineages, *B. anthracis* can be differentiated into several genotypes using many typing systems, including variable number tandem repeats (VNTR) in a multi-locus VNTR analysis (MLVA) and core genome multi-locus strain typing (cgMLST). While cgMLST is promising for tracking evolution in local populations, a much smaller subset of strains has been whole genome sequenced, limiting cgMLST value in mapping *B. anthracis*. In contrast, available MLVA data reflect a larger population of *B. anthracis* strains in the global collection. Some studies informed ENMs with MLVA-specific sub-lineages and showed environmental and spatial differences. No models have examined which specific VNTRs differentiate spatially. Here, we use ENMs, MLVA-25 phylogenies, and constrained-Simpson Indices to model local patterns of *B. anthracis* lineages in Texas and Vietnam, two regions with endemic anthrax affecting animals and humans. This integrative approach improved model performance and better explained diffusion and evolutionary patterns on both landscapes and across a diversity of sub-lineages.

8128

SEROEPIDEMIOLOGY OF TRACHOMA IN A LOW PREVALENCE REGION RECEIVING ANNUAL MASS AZITHROMYCIN DISTRIBUTION IN MARADI, NIGER

Abdou Amza[1], Boubacar Kadri[2], Beido Nassirou[2], Ahmed Arzika[3], Elisabeth Gebreegziabher[4], Huiyu Hu[4], Lina Zhong[4], Cindi Chen[4], Danny Yu[4], Thomas Abraham[4], YuHeng Liu[4], Thuy Doan[4], Benjamin F. Arnold[4], Thomas M. Lietman[4], **Catherine Oldenburg**[4]

[1]Programme National de Sante Oculaire, Niamey, Niger, [2]Programme National de Santé Oculaire, Niamey, Niger, [3]Centre de Recherche et d'Intervention en Santé Publique, Niamey, Niger, [4]University of California, San Francisco, San Francisco, CA, United States

Trachoma programs use the indicator trachomatous inflammation-follicular (TF) to monitor indication for and response to treatment for trachoma at the community level. Alternative indicators, including serologic responses, are increasingly being evaluated for trachoma surveillance. We evaluated seroprevalence to IgG antibody responses to the Pgp3 antigen in two districts in Maradi, Niger thought to have low TF prevalence. Data were collected as part of the baseline assessment of the Azithromycin Reduction to Reach Elimination of Trachoma (ARRET) trial in September 2021. A random sample of 80 communities were selected from Mayahi and Guidan Roumdji districts, both of which had TF prevalence <20% at their most recent trachoma surveillance survey in 2018. A random sample of 50 children per community were sampled. We collected field grades, conjunctival swabs for processing PCR for ocular *Chlamydia trachomatis*, and dried blood spots for serologic assessment. The most recent mass drug administration prior to sample collection was in March 2020, 18 months prior. Of 3,994 children sampled in 80 communities, 49% were female and median age was 4 years. Overall TF prevalence was 4.6% (95% CI 3.5 to 5.8%) and trachomatous inflammation-intense (TI) prevalence was 0.6% (95% 0.3 to 0.9%). The prevalence of ocular chlamydia was 0.03% (95% CI 0.08%). Seroprevalence with Pgp3 was 6.3% (95% CI 5.5 to 7.1%) in 1-9-year-olds and 3.7% (95% CI 2.9 to 4.4%) in 1-5-year-olds. TF and Pgp3 seroprevalence were more strongly correlated in 1-5-year-olds (correlation coefficient 0.29) compared to 1-9-year-olds (correlation coefficient 0.09). In this low trachoma prevalence setting in Niger, serologic responses to Pgp3 were consistent with little ongoing transmission of *C. trachomatis*.

8129

THE RE-EMERGENCE OF TRACHOMA INFECTION AMONG CHILDREN IN KONGWA DISTRICT, TANZANIA, POSES A THREAT TO YEARS OF PROGRESS

Hamisi Rashid Msagama, Ritah Mutagonda, Aboubakari Mlinga, Getrude Dahaye

Muhimbili Univesity of Health and Allied Sciences, Dar es Salaam, Tanzania, United Republic of

Kongwa District, historically burdened by high trachoma prevalence, witnessed a notable decline from 60% in 1986 to 10% in 2010, further plummeting to less than 5% in 2019 before resurging in late 2020 despite the implementation of SAFE intervention measures. By 2021, the Trachomatous follicular prevalence reported to be 7.1% higher than the

reported baseline. To explore predictors for this resurgence, we conducted a cross-sectional study from January to June 2022 among children aged 1-9 in five villages. Enrolling 247 participants, aligned with the Kongwa Trachoma community outreach program, we managed to obtain clinical data on the disease. Most participants (57.5%) were aged 1-5, with only 22.7% of the school age children enrolled in primary school. While 99.2% had pit latrines, 52.5% reported poor water quality and infrastructure and 47% use open field for waste disposal near household. Univariate analysis revealed risks including larger household size, lack of face washing with soap, poor water quality, and open field waste disposal. Multivariate analysis identified household size (AOR 17.5, 95% CI: 5.5-54.9), absence of face washing with soap (AOR 13.69, 95% CI: 3.5-36.0), and improper waste disposal (AOR 17.9, 95% CI: 4.4-73.5) as continuous risk factors for trachoma infection. Despite SAFE intervention, sustained exposure to risky behaviours and environments perpetuates reinfection. In previous years, absence of pit latrines and distance to water sources were mitigated through a national campaign, suggesting potential for similar strategies to influence hygiene and waste management behaviours. Therefore, our findings have a potential to inform key actors on the need for sustainable approaches in trachoma elimination interventions and further research in other endemic areas.

8130

THE ROLE OF ANTIBODY DATA FOR IMPROVED UNDERSTANDING OF RECRUDESCENT ACTIVE TRACHOMA IN NEBBI DISTRICT OF UGANDA

Rapheal Opon[1], Prudence Beinamaryo[1], David Oguttu[1], Alfred Mubangizi[1], Charles Kennedy Kissa[1], Paul Akampurira[1], Joyce Achan[2], Stephen Begumisa[2], Sharone Backers[2], Stella Agunyo[2], Katherine Gass[3], Mohamed Bah[3], Katrina Farber[3], Sarah Gwyn[4], Diana L Martin[4], Mabula Kasubi[5], Sarah Boyd[6], Ana Bakhtiari[6], Cristina Jimenez[7], Michelle Taylor[7], Anthony W Solomon[8], Emma M Harding-Esch[9], Upendo Mwingira[10], William E Oswald[10], Jeremiah M Ngondi[10]

[1]Ministry of Health Headquarters, Kampala, Uganda, [2]Research Triangle Institute International, Kampala, Uganda, [3]NTD Support Center,Task Force for Global Health, Atlanta, GA, United States, [4]Centers for Disease Control and Prevention, Atlanta, GA, United States, [5]Muhimbili University of Health and Allied Sciences, Dar es salaam, Tanzania, United Republic of, [6]International Trachoma Initiative, Task Force for Global Health, Atlanta, GA, United States, [7]Sightsavers,, Haywards Heath, United Kingdom, [8]Global Neglected Tropical Diseases Program, World Health Organization, Geneva, Switzerland, [9]London School of Hygiene and Tropical Medicine, London, United Kingdom, [10]Research Triangle Institute International, Research Triangle Park, NC, United States

Uganda has progressed towards elimination of trachoma with 92% of 61 endemic evaluation units (EU) having attained trachomatous inflammation—follicular (TF) prevalence of <5%. However, trachoma remains persistent or recrudescent in five districts. Nebbi district was recrudescent after a trachoma surveillance survey (TSS) in 2019 reported a TF prevalence >5%. After restarting MDA, Nebbi had a TF prevalence <5% during next impact survey. At a subsequent TSS in 2023, we included serological testing into standard surveys to evaluate evidence of community transmission of ocular chlamydia. Dried blood spots (DBS) were taken from 1-9-year-olds and tested for antibodies to the *Chlamydia trachomatis* antigen Pgp3 using a lateral flow assay (LFA). Analysis was undertaken to estimate the prevalence of TF, TT, pgp3 antibody (seroprevalence), and pgp3 seroconversion rate (SCR) per 100 children per year. In Nebbi East, 1400 children 1-9 years were examined, of whom 1119 were sampled for DBS; and 1490 adults ≥15 years were examined. In Nebbi West, 1273 children 1-9 years were examined, of whom 1199 were sampled for DBS; and 1530 adults ≥15 years were examined. In Nebbi East children aged 1-9 years had a TF prevalence of 1.9% (95% CI [confidence interval] 1.0-2.7), seroprevalence of 8.2 %(95% CI 6.0-10.9), and SCR of 2.0 (95% CI 1.5-2.8). In children aged 1-5 years the seroprevalence was 4.1% (95% CI 2.5-6.5), and SCR was 1.3 (95% CI 0.8-2.2). In Nebbi West children 1-9 years had a TF prevalence of 1.0% (95% CI 0.3-1.9), seroprevalence of 7.6% (95% CI 5.5-9.9) and SCR of 1.7 (95% CI 1.2-2.3). In children 1-5 years, the seroprevalence was 4.6% (95% CI 3.1-6.6) while the SCR was 1.6 (95% CI 1.1-2.3). Among people ≥15 years, TT prevalence was 0.18% and 0.25% in Nebbi East and Nebbi West, respectively. The trachoma seroprevalence and seroconversion rates in both EUs are consistent with the TF prevalence of <5% reported in Nebbi East and Nebbi West. Based on these findings, on-going community transmission of ocular chlamydia is unlikely.

8131

SOCIAL-ECONOMIC AND CULTURAL PRACTICES INFLUENCING TRACHOMA TRANSMISSION AMONG RESIDENTS IN NORTHERN KENYA

Caroline Wangui Njoroge[1], Samson Nzou[1], John Gachohi[2], Joseph Mutai[1], Mathew Mutinda[1], Robinson Irekwa[1], Tonny Teya[1], Anne Mwangi[1], Peter Rotich[1], Joanne Jepkemei[1]

[1]KEMRI, Nairobi, Kenya, [2]Jomo Kenyatta University of Agriculture and Technology, Nairobi, Kenya

Trachoma is a neglected tropical illness caused by Chlamydia trachomatis. It is a leading cause of avoidable blindness. It creates a severe public health challenge in Kenya's northern region. The problem is widespread, with Turkana being one of the places with the highest trachoma prevalence due to the area being socio-economically disadvantaged. The study employed a descriptive cross-sectional design, recognizing the qualitative nature of the investigation. The results from the study captured a prevalence of 46.8% for trachoma within the past year from a sample size of 444. Based on the binary logistic regression analysis conducted sex, settlement type and occupation were significantly associated with disease transmission in the multivariable level. The qualitative analysis revealed that cultural practices were associated with Trachoma Transmission in Turkana West sub-County. These were inclusive associated with water access, prioritization of animals over household chores, water scarcity had a significant impact on bathing frequency among children, disorganization on waste disposal and unawareness of water treatment methods and poor hygiene practices. The prevalence of Trachoma in Turkana west subcounty is relatively high as such the need for immediate interventions that focus immediate healthcare service delivery, community sensitization and interventions to increase the access of water. They relate with other studies conducted in Baringo and Ethiopia. The recommendation from the findings would be to develop policies like Tailored Education programs, Water and sanitation infrastructure investment and cross-border collaboration.

8132

RESULTS FROM TRACHOMA PREVALENCE SURVEYS IN SENEGAL AS IT NEARS ELIMINATION

Mouctar D. Badiane[1], Rose Monteil[2], Babacar B. Diallo[2], Serigne Niang[2], Emma Harding-Esch[3], Mawo Fall[4], Jeremiah Ngondi[5], Anthony W. Solomon[6], Stephanie L. Palmer[7]

[1]Programme National de Sante Oculaire, Dakar, Senegal, [2]FHI 360 Senegal, Dakar, Senegal, [3]Clinical Research Department, London School of Hygiene & Tropical Medicine, London, United Kingdom, [4]RTI International, Maputo, Mozambique, [5]RTI International, Cambridge, United Kingdom, [6]Department of Control of Neglected Tropical Diseases, World Health Organization, Geneva, Switzerland, [7]FHI 360, Washington, DC, United States

Senegal is a country at the extreme west of Africa with a climate varying from desert in the north to tropical savannah in the south. In 2000, a national trachoma prevalence survey revealed that trachoma was a public health problem in 6/8 regions included in the survey; two regions were not included due to insecurity. In 2004-2021, district -level trachoma baseline surveys were conducted in 69/79 districts. Following these surveys, Senegal's National Eye Health Program scaled up the SAFE strategy (Surgery, Antibiotics, Facial cleanliness, Environmental improvement) where warranted. Trachoma impact surveys (TIS) and surveillance surveys (TSS) have been conducted in all endemic districts. This presentation will present results from trachoma prevalence survey and outline the last steps the country must take to eliminate trachoma. The surveys used a two-stage cluster random sampling design for each evaluation unit (EU). An EU corresponded to one or more health districts (HD) or a proportion

of an HD. In each EU, a list of villages was made and 30 systematically selected using probability proportional to size. In selected households, all consenting individuals aged ≥1 year had their eyelids examined. Trachomatous inflammation—follicular (TF) prevalence was calculated for children aged 1-9 years; trachomatous trichiasis (TT) prevalence was calculated for adults aged ≥15 years. From 2014, surveys were carried out with GTMP or Tropical Data support. District-level baseline mapping initially indicated that 27 districts had TF≥5%; remapping in 8 districts showed TF<5%. A total of 46 districts had TT ≥0.2%. TIS were completed between 2014-2018; all but 5 districts showed that TF had fallen to <5% after SAFE strategy implementation. In those 5 districts, additional years of SAFE were conducted and upon 2nd TIS, TF was <5%. TSS were conducted between 2017-2021; TF remained <5% in all districts. However, TT remains a public health problem in 4 HD/7 EU. Senegal has made great progress towards the elimination of trachoma as a public health problem. However, continued TT case-finding and management are required for elimination validation.

8133

INTER-LABORATORY VALIDATION OF A MULTIPLEX BEAD ASSAY USING A CHIMERIC MONOCLONAL ANTIBODY AGAINST PGP3

Sarah Gwyn[1], Karana Wickens[1], Helena Brazal Monzo[2], Chris Drakeley[2], Stephane Pelleau[3], Michael White[3], Henry Kanyi[4], Sammy M. Njenga[4], Diana L. Martin[1]

[1]Division of Parasitic Diseases and Malaria, Centers for Disease Control and Prevention, Atlanta, GA, United States, [2]Department of Infection Biology, London School of Hygiene and Tropical Medicine, London, United Kingdom, [3]Pasteur Institute, Paris, France, [4]Kenya Medical Research Institute, Nairobi, Kenya

A multiplex bead assay (MBA) that tests for antibodies against the *Chlamydia trachomatis* (Ct) antigen Pgp3 is used for population level serosurveillance for trachoma, the leading infectious cause of blindness. CDC laboratories generated a human/mouse chimeric monoclonal antibody (mAb) against Pgp3 that was used for the inter-laboratory validation of the assay. CDC and three external laboratories, two of which use different MBA protocols than CDC, ran a standard curve (with a typical linear range between 15.6 - 16,000 ng/mL depending on instrument type) along with 3 spiked "unknowns" (high, medium, and low concentrations of mAb) on 3 to 5 different days. Testing was performed by 5 different operators and on 3 different instrument types, giving 7 unique laboratory/operator/instrument conditions for assessment. Values for unknowns were interpolated into concentrations based on each laboratory's standard curve to estimate test accuracy (interpolated value / known value x 100) and inter-laboratory precision (%CV of interpolated values on plates run between different labs). While the absolute median fluorescence intensity signal varied across labs due to the different assay conditions and instruments used, the concentrations interpolated from the standard curve showed accuracy for all medium and low positive unknowns within 80—120% (the acceptable range for accuracy) in each setting. The high positive sample was within range for accuracy in 4/7 conditions. The inter-lab precision of interpolated concentrations for medium and low positive samples was <5% and the high positive sample was 20.6%. While accurate quantitation of antibody levels is not necessary for prevalence studies—the intended use case of the Pgp3 MBA—these results show the Pgp3 MBA is a robust assay with high reproducibility across different laboratories, assay conditions and instruments. The data also point toward the Pgp3 mAb is a useful reagent for inter-laboratory standardization, and generating similar control reagents may be useful for the growing field of serosurveillance more generally.

8134

A NOVEL BEHAVIOR APPROACH TO SUPPORT ELIMINATION OF TRACHOMA IN NOMADIC POPULATIONS

Joyce Christian Lyamuya[1], Agnes Lucumay Agnes Lucumay[1], George Kabona[2], Anyitike Mwakitilima[2], Mpoki Daudi[3]

[1]Helen Keller Intl, Dar es salaam, Tanzania, United Republic of, [2]Ministry of Health, Dodoma, Tanzania, United Republic of, [3]Ngorongoro Coucil, Arusha, Tanzania, United Republic of

Impact assessments conducted between 2012 - 2022 by the Tanzania Neglected Tropical Disease (NTD) Control Program revealed that nine nomadic councils in Arusha, Manyara, Dodoma and Rukwa regions had persistent or recrudescent high prevalence of Trachoma Follicular (TF). Another assessment supported by the Ministry of Health (MoH) and Helen Keller International (2016-2018) revealed overall lower uptake of the National Sanitation Campaign in nomadic communities. These results prompted development of a more holistic approach to implementing the Surgery, Antibiotics, facial cleanliness and environmental improvement (SAFE) strategy for trachoma, with a renewed focus on face cleanliness and environmental improvement (F&E). In 2020, Helen Keller supported the MOH to create innovative interventions to influence the F&E behaviors in these nomadic populations. One of the interventions identified and tested in seven wards of Ngorongoro district for twelve months included promoting the use of games and activity books in primary schools to enhance learning hygiene behaviors and sanitation practices. This intervention was assessed through key informant interviews and observations. Findings indicated that this school-based gaming approach had successful results including: the activation of school-based WASH clubs (SWASH Clubs) which excited and engaged the students, increased understanding of trachoma and its association with poor hygiene and sanitation by students, and creation and use of local waste bins to encourage hygiene and cleanliness in schools. Overall, there was an increased number of handwashing facilities at schools and improved personal hygiene among students participating in SWASH clubs. These interventions were well received by the students, and led to reduction of absenteeism, improved use of toilets, and improvement of hygiene and sanitation practices in the households of students. These results support the need for interventions targeting nomadic populations to include innovative approaches that engage communities in new ways to achieve the greatest impact.

8135

PATHWAYS TO PROGRESS: ENHANCING INFECTIOUS DISEASE DETECTION IN THE PERUVIAN AMAZON

Karin Francesca Perez Garcia[1], Paul Garcia Bardales[1], Wagner V. Shapiama Lopez[1], Tackeshy Pinedo[1], Mario Güimack Fajardo[1], Cesar Ramal Asayag[2], Francesa Schiaffino[3], Josh M. Colston[4], Pablo Peñataro Yori[4], Maribel Paredes Olortegui[1], Margaret N. Kosek[4]

[1]Asosciacion Benefica Prisma, Iquitos, Peru, [2]Universidad Nacional de la Amazonia Peruana UNAP, Iquitos, Peru, [3]Universidad Peruana Cayetano Heredia, Lima, Peru, [4]University of Virginia, Charlottesville, VA, United States

Loreto, Peru, annually reports one of the highest rates of infectious diseases in Peru, and it continues to be the site of the discovery of novel agents of infectious diseases. Because of this plethora of tropical infectious illnesses, Iquitos has become the base for many international infectious diseases research programs, including the Etiology of Acute Febrile Illness in the Peruvian Amazon as determined by modular formatted quantitative PCR: A Protocol for RIVERA, a Health Facility-Based Case-Control Study. This study aims to establish a stable annual surveillance system over four years (2021-2023) for 32 pathogens that cause acute febrile illness using the TaqMan Array Cards. This sub-analysis of the RIVERA study aimed to identify the time and method of delivery of qPCR-based results to enrolled patients. Until December 2023, the study enrolled over 1600 cases through facility-based surveillance and 1600 community-based controls. After enrollment, 51% (1588/3362) of participants received test results between days 2 and 4. Results were delivered both in digital and printed formats.

For the remaining 49% (1545/3362) of participants, the delivery timeline was extended between day 5 to day 10. Results are also systematically distributed to the respective epidemiology departments within each health center. Comprehensive documentation of these actions is diligently maintained, capturing pertinent details such as the date of dissemination, personnel involved, and the results delivery method. Through meticulous sample collection and efficient result delivery processes, the study underscores the importance of timely information dissemination for effective disease management. This concerted effort not only enhances healthcare services but also signifies a significant step towards combating emerging diseases in the region, ultimately improving public health outcomes in Iquitos.

8136

DEVELOPMENT, IMPLEMENTATION, AND CLINICAL VALIDATION OF AN ISOTHERMAL CAS12A BASED QUANTITATIVE ASSAY FOR CONGENITAL CYTOMEGALOVIRUS VIRAL LOAD DETERMINATION

Karissa Chao[1], Monika L. Dietrich[1], Jon Arizti Sanz[2], Sameed Siddiqui[2], Pardis Sabeti[2], Robert F. Garry[1]

[1]Tulane University School of Medicine, New Orleans, LA, United States, [2]Broad Institute of MIT and Harvard, Boston, MA, United States

Congenital CMV (cCMV) is the leading cause of nongenetic infant hearing loss and accounts for more cases of life-long disabilities than more commonly known conditions. In West Africa, the prevalence of CMV is largely unknown due to resource limitations reducing capacity to perform laboratory tests. For the United States, there's evidence suggesting the cost effectiveness of universal cCMV screening though only one state (MN) has a program so far. Thus, there's a need for low-cost, non-laborious, sensitive assays to enable CMV research in low- and middle-income countries (LMIC) and decrease barriers to universal testing in high-income countries (HIC). We developed a quick, isothermal DNA quantitative assay that spans the entire sample collection to result pipeline. This platform utilizes a novel extraction method, HUDSON (Heating Unextracted Diagnostic Samples to Obliterate Nucleases) with isothermal amplification (recombinase polymerase amplification, RPA) and detection (CRISPR/Cas12a). We clinically validated this assay using a Sierra Leonean infant cohort and started implementation through laboratory capacity building efforts at the Kenema Government Hospital (KGH). Cost analysis shows reduction of price and time to obtain a result (40 minutes incubation compared to 65 minutes with PCR); and minimal use of extracted sample (2µL) allows for triplicate testing. Limit of detection and quantification (LOD/LOQ) is $10^{2.5}$IU/mL via fluorescence reader. RPA/Cas12a viral load determination from CMV-exposed infant saliva samples is not statistically different from PCR results (paired t-test, p=0.7692, N=101). HUDSON extraction is successful in serum and saliva samples, and compatible with subsequent DNA detection. Initial implementation involved evaluating assay performance in a low-resourced laboratory (KGH) using lateral flow output, which had an LOD of 10^{5}IU/mL. This novel isothermal DNA assay increases the capacity of a low-resourced laboratory for determining viral loads of suspected cCMV cases and/or CMV clinical research by providing results in less time, lower temperatures, and less costs per sample compared to PCR.

8137

SCARCE FOLLOW UP AFTER A LATE DIAGNOSIS: A SURVEY OF KEY STEPS IN CLINICAL CARE AMONG PATIENTS WITH CHRONIC TRYPANOSOMA CRUZI INFECTION IN BOGOTÁ, COLOMBIA

Juan Carlos Villar, Antonia Camacho, Luis David Sáenz, Helena Arango

Fundación Cardioinfantil-Instituto de Cardiología, Bogotá, Colombia

For people with chronic *Trypanosoma cruzi* infection (cTCI) in endemic countries, receiving proper clinical care is challenging. In Colombia, a country with universal health care coverage, most people with cTCI live now in urban centers with no vector transmission and theoretically easier access to health care services. We surveyed *T. cruzi* seropositive individuals living in Bogotá who participated in observational or interventional studies at a referral center for cardiovascular disease since 2016. The aim was to describe key steps of clinical care in diagnosing, stratifying risk, or treating patients with cTCI. From 152 eligible participants, 102 were contacted and 96 gave consent to participate. The mean age was 61.5 years; 51 were women, 67.8% had chronic Chagas cardiomyopathy (CCC) and 24 participated in randomized trials. Age at cTCI diagnosis was 51.4 years (54 for those with CCC versus 46 for CCC-free participants, p<0,001). Fifty (52.1%) participants were diagnosed incidentally: 39 as blood donors, 10 after a family member was diagnosed and 1 after an occupational health assessment. The other 46 were diagnosed after cardiac manifestations suggesting CCC: 17 because of heart failure and 14 for arrythmias/sudden cardiac death. No participants diagnosed with cTCI had gastrointestinal complaints. Risk of CCC was stratified using ECG in 87 participants (95% among those with CCC and 80% for CCC-free, p=0.021) and echocardiogram in 77 (87% with CCC and 64% for CCC-free, p=0.008). Of 27 reporting trypanocidal therapy, 20 (74%) had it as part of interventional studies (Median time diagnosis-to-treatment 4[IQR 3-12] months). Regarding follow-up, 64 participants reported visits at least once a year, whereas 32 (16 with CCC) had none or just occasional visits. In this small series from a referral center in Bogotá, cTCI diagnosis is usually made decades late and, unacceptably, often when cardiac involvement is present. Despite the use of risk stratification tools upon cTCI diagnosis, many patients, even those with CCC, are not properly followed. It is imperative to promote an earlier diagnosis and timely follow-up for those at risk or with cTCI.

8138

COMPLICATED SPINAL CYSTIC ECHINOCOCCOSIS SUCCESSFULLY TREATED WITH SURGERY: 10-YEAR FOLLOW-UP

Gian Luca D'Alessandro[1], Tommaso Manciulli[2], Sofia Frattola[1], Ambra Vola[3], Raffaella Lissandrin[4], Enrico Brunetti[4], Fabrizio Cuzzocrea[5]

[1]WHO Collaborating Centre for the Clinical Management of Cystic Echinococcosis, University of Pavia, Pavia, Italy, Pavia, Italy, [2]WHO Collaborating Centre for the Clinical Management of Cystic Echinococcosis, University of Pavia, Pavia, Italy; Department of Clinical and Experimental Medicine, University of Florence, Florence, Italy, Pavia, Italy, [3]WHO Collaborating Centre for the Clinical Management of Cystic Echinococcosis, University of Pavia, Pavia, Italy; Department of Virology and Microbiology, IRCCS Policlinico San Matteo, Pavia, Italy, Pavia, Italy, [4]WHO Collaborating Centre for the Clinical Management of Cystic Echinococcosis, University of Pavia, Pavia, Italy; Department of Infectious and Tropical Diseases, IRCCS Policlinico San Matteo, Pavia, Italy, Pavia, Italy, [5]Department of Orthopedics and Traumatology, IRCCS Policlinico San Matteo, Pavia, Italy, Pavia, Italy

Spinal Cystic Echinococcosis (CE) is a devastating form of *Echinococcus granulosus* infection, with a poor prognosis due to the infiltrative growth of the parasite larva in the bone, as no cleavage plan exists. Surgery is the standard treatment, but complete resection of infiltrating cysts remains difficult and recurrence is the rule. We report a case of vertebral and paravertebral Cystic Echinococcosis, successfully treated with sequential surgery. A 47 y.o. woman from Italy sought medical attention for the onset of dorsal-lumbar pain, lower limb paraesthesia and claudication. A CT scan of the spine showed a hypodense fluid-filled mass in the paravertebral and retroperitoneal space at D12-L1 level, measuring 9x9x5 cm. The mass infiltrated the iliopsoas muscle and was adjacent to the aortic wall. Destruction of the D12-L1 intervertebral disc was noted, with osteolysis of the adjacent vertebras and extension into the vertebral canal. Differential diagnosis included vertebral osteomyelitis and spinal Cystic Echinococcosis. Serology for Cystic Echinococcosis (Western blot) was positive. In October 2012, a posterior surgical decompression by laminectomy, intradural lavage with hypertonic saline and stabilization was performed. The next month, a second intervention was performed to remove all the pathologic tissue and for cage positioning. Pathological examination confirmed *E.*

granulosus infection. The patient recovered after surgery and is still disease-free after 10 years. While this outcome is exceptional for spinal CE, it shows that successful management is possible in a referral center.

8139

HIGH PREVALENCE OF UNDIAGNOSED ACUTE FEBRILE ILLNESS IN THE PERUVIAN AMAZON

Katherine Torres[1], Alonso Cruz-Echevarría[1], Freddy Alava[2], Cristina Burga[2], Berónica Infante[3], Dionicia Gamboa[4], Michael Berg[5], Mary Rodgers[5], Francisco Averhoff[5], Gavin Cloherty[5], Joseph Vinetz[6]

[1]Laboratorio de Malaria, Laboratorios de Investigación y Desarrollo, Facultad de Ciencias e Ingeniería, Universidad Peruana Cayetano Heredia, Lima, Peru, [2]Laboratorios Teodoro E. Gildred, Universidad Peruana Cayetano Heredia, Lima, Peru, [3]Laboratorio ICEMR-Amazonia y Enfermedades Infecciosas Emergentes, Laboratorios de Investigación y Desarrollo, Facultad de Ciencias e Ingeniería, Universidad Peruana Cayetano Heredia, Lima, Peru, [4]Laboratorio de Malaria: Parásitos y Vectores, Laboratorios de Investigación y Desarrollo, Facultad de Ciencias e Ingeniería, Universidad Peruana Cayetano Heredia, Lima, Peru, [5]Abbott Pandemic Defense Coalition, Chicago, IL, United States, [6]Section of Infectious Diseases, Department of Internal Medicine, Yale School of Medicine, New Haven, CT, United States

The Peruvian Amazon has a heavy burden of arbovirus infections and is an important location to maintain vigilance for early detection of emerging pathogens. The Abbott Pandemic Defense Coalition (APDC) and Universidad Peruana Cayetano Heredia (UPCH) are conducting acute febrile illness (AFI) surveillance in hospitals and health centres in Iquitos city and San Lorenzo region screening with (rapid diagnostic test) RDTs for malaria, COVID-19, and dengue. Between September 2023 and April 2024, 608 participants were enrolled in the study with a confirmed diagnosis for 129 (21.22%) participants including malaria 54 (8.88%), COVID-19 21 (3.45%), and dengue 52 (8.55%) single infections. We report a high prevalence of undiagnosed cases of febrile illness of 78.78% (n=479). Overall, 50.82% (309/608) were female and had a median age of 27.02 years old (IQR: 12.75 - 41.31 years old). The participants with and without a confirmed diagnosis did not differentiate relative to sex and age. However, we report that there is an association between the reported occupation and the diagnosis status by Fisher's exact test (p=0.023). The undiagnosed group did report working proportionately more on wildlife (2.33% vs 0.21%) and farming (9.30% vs 2.51%) in comparison to the group with a confirmed diagnosis while the latter had other non-health-related occupations (29.46% vs 40.08%). Additionally, the confirmed cases shared a triad of general symptoms: sickness, fever/chills, and headache, and had a disease-specific pattern of specific symptoms. The commonly screened diseases have an undifferentiated clinical manifestation making a clinical diagnosis troublesome and thus there is a high burden of febrile cases with unknown etiology. It is important to have the capacity to study unknown cases with next-generation sequencing, particularly those with unusual or serious clinical manifestations, as part of surveillance for the detection of emerging pathogens.

8140

MALARIA RETINOPATHY IS ASSOCIATED WITH WORSE LONG-TERM COGNITION IN UGANDAN CHILDREN WITH SEVERE MALARIAL ANEMIA

Kagan A. Mellencamp[1], Ruth Namazzi[2], Caitlin Bond[1], Robert O. Opoka[2], Andrea L. Conroy[1], Paul Bangirana[2], Chandy C. John[1]

[1]Indiana University School of Medicine, Indianapolis, IN, United States, [2]Makerere University College of Health Sciences, Kampala, Uganda

Severe malarial anemia (SMA) and cerebral malaria (CM) due to *Plasmodium falciparum* are both associated with long-term neurocognitive impairment (NCI) in children. Malaria retinopathy is an important clinical feature of CM, caused by sequestration of parasitized erythrocytes in retinal blood vessels, reflecting sequestration in the vasculature of the brain. However, long-term NCI in children with CM does not correlate with malaria retinopathy. The presence of retinopathy in children with SMA has rarely been evaluated, and the association of retinopathy in SMA with long-term NCI is not known. We evaluated the association of malaria retinopathy with long-term cognitive outcomes (overall cognition, attention, and associative memory) among children ages 6 months to 4 years with CM (n=41) or SMA (n=101). Malaria retinopathy was assessed by medical officers on admission and cognitive outcomes were measured one year after admission. On admission, 7.2% of children with SMA and 45% of children with CM exhibited retinopathy. In children with SMA, retinopathy was associated with worse overall cognition ($p<0.001$) but was unrelated to attention or associative memory ($p=0.67$ and $p=0.53$, respectively). In children with CM, retinopathy was not associated with overall cognition or associative memory ($p=0.94$ and $p=0.71$, respectively), but was associated with better attention scores ($p=0.04$). Among children with SMA, neither continuous *P. falciparum* histidine-rich protein-2 (*Pf*HRP2) level nor *Pf*HRP2 level >1700 ng/mL was associated with overall cognition or attention, but both were associated with worse associative memory ($p=0.01$ and $p=0.02$, respectively), while in children with CM, neither *Pf*HRP2 level nor level >1700 ng/mL was associated with any cognitive outcomes. Scores in overall cognition were lower in children with CM or SMA, irrespective of retinopathy, than in 108 asymptomatic community children. The study findings suggest that sequestration of *P. falciparum*-infected erythrocytes occurs in the brain vasculature of a subset of children with SMA and is strongly associated with worse long-term cognition in these children.

8141

SAFETY, IMMUNOGENICITY AND EFFICACY OF THE SHIGELLA VACCINE - A SYSTEMATIC REVIEW

Salman Haq

Aga Khan university, Karachi, Pakistan

Shigella infections present a significant global health challenge, especially in low- and middle-income countries where antimicrobial resistance is increasing. Vaccination is a promising approach to address this threat, but the immunogenicity, efficacy, and safety of Shigella vaccines undergoing phase 1 and phase 2 trials require thorough evaluation. This systematic review aims to assess the effectiveness and safety of Shigella vaccines. Following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, experimental trials comparing Shigella vaccines with placebo or other vaccines in adults and children were included.Five trials were included, two of which used oral and three parenteral vaccines. Adverse events were lower with oral vaccines as compared to parenteral ones. Comparison of ZF0901 (bivalent Shigella conjugate vaccine) with the existing approved HIB vaccination as a control showed no significant adverse events linked to vaccinations after half, one, or two doses. In all three age groups, similar rates of adverse events were seen at each injection, with fever accounting for most of these occurrences.Regarding immunogenicity, the ZF0901 vaccine caused a statistically significant increase in type-specific IgG antibodies against S. flexneri 2a and S. sonnei 30 days after immunization in all vaccine groups, regardless of the amount or number of injections. More than half of the recipients exhibited >4-fold seroconversion across all age categories. No substantial dose impact between 10 µg and 5 µg was detected. Likewise, SF2a-TT15 (Monovalent vaccine) was compared with and without alum A single injection of non-adjuvanted 10 µg oligosaccharide resulted in a 27-fold increase in IgG GMT (5080 vs 189) vs the non-adjuvanted 2 µg oligosaccharide dose, which showed a 5-fold increase (1411 vs 283) compared to baseline. The existing data from included trials provide promising and interesting results regarding the efficacy, safety and immunogenicity of the Shigella vaccines. However, data from phase 3 trials is needed to develop recommendations for use in public health.

8142

CLINICO-EPIDEMIOLOGICAL STUDY OF SNAKEBITE: AN AUDIT OF THIRTEEN YEARS DATA FROM A COMMUNITY-BASED TREATMENT CENTRE OF EASTERN NEPAL

Srista Manandhar[1], Sunit Chhetri[1], **Arun Gautam**[1], Rohan Basnet[1], Urza Bhattarai[1], Madhav Bhusal[2], Sanjib Kumar Sharma[1]

[1]B.P. Koirala Institute of Health Sciences, Dharan, Nepal, [2]Devdaha Medical College, Rupandehi, Nepal

Snakebite envenomation is a global public health concern, especially in tropical and subtropical regions where venomous snakes are endemic. We describe the demography, clinical presentation, management and prevalence of traditional practices for snake bites in eastern Nepal. This study involves 13,825 patients who received snakebite treatment in Damak Red Cross Snakebite Treatment Centre (DRSTC) situated in eastern Nepal, over a period of thirteen years (2008-2021). The median age of the victims was 29 years (IQR: 18-43) with farming and agriculture (39.53%) being the most affected occupation. Most snake bite incidents occurred outdoors, notably during the monsoon season (61.72%). Cobras (Naja spp.) were the predominant species identified, often resulting in lower limb bites (69.24%). Most patients were asymptomatic. The predominant symptom was pain at the bite site (14.2%). Local remedies like application of chili powder and tourniquets were common (91.7%) and 0.8% of victims consulted traditional healers prior to seeking treatment at DRSTC. Antivenom was infused for 3.25% of victims. Motorcycles (57.9%) were the primary mode of transport and significantly decreased time in reaching healthcare centres in comparison to other means ($p<0.001$). We conclude that Snakebites are a common problem in eastern Nepal. Tourniquet application as a part of first aid is common. Neurotoxic envenomation, inflicted by common cobra predominates in this region.

8143

IDENTIFYING ADDITIONAL RISK FACTORS FOR DEVELOPING CHRONIC KIDNEY DISEASE

Sandy Hoar

George Washington University, Washington, DC, United States

Chronic Kidney Disease(CKD) is an increasing global problem with significant morbidity and mortality. Immigrants to the United States frequently work in hot environments without sufficient access to water, and often have poorly controlled diabetes (DM) and /or hypertension (HTN), all possible risk factors for the development of CKD. All patients seen in a clinic for the uninsured by 1 provider during a 4 month period with either a reduced glomerular filtration rate (eGFR) and/or proteinuria (albumin-to-creatinine ratio ACR), were interviewed for current and past hot occupational environments and the availability of water. Fifty patients were evaluated; 28 were female, 6 were aged 30-40 years old (yo), 13 40-50 yo, 17 50-60 yo, 13 60-70 yo, 1 70-80 yo. Twenty-five patients had DM, 41 had HTN, 19 patients had both DM and HTN. Thirty-five had worked in a hot environment, 27 did not have any or easy access to water, including 1 person who worked in a cold environment, 24 patients worked in both a hot environment and did not have access to water. Twenty-six had a lowered eGFR, 10 sufficient to diagnose CKD, including 2 who were in kidney failure (<15), 26 patients had both lowered eGFR and moderate to severe proteinuria. Two patients were from Africa, 3 from the Caribbean, 45 from the Americas. Patients arrived in the US from the 1960s to the 2020s, the majority in the 2000s. Examining the 30-40 year old cohort, 4 were female, 1 had both DM and HTN, 4 worked in a hot environment, 3 did not have water, 2 had both a low eGFR and proteinuria, all 6 were from C Am, 2 arrived in the 2000s, 2 in the 2010s, 1 in the 2020s. Females were more common than males, the youngest cohort had the worst eGFR, and none had worked as migrants. Patients frequently are asked their current job but not always asked their current or past working conditions. Asking a patient their current and past work environment and their current/past access to water, can help identify those who may need additional occupational counseling for cooling and rest breaks and a need for increased water intake, evaluation and monitoring to prevent or identify CKD, and the risks of heat stress.

8144

DISCORDANCE BETWEEN IMMUNIZATION HISTORY AND SEROLOGIC IMMUNITY TO VACCINE-PREVENTABLE INFECTIONS AMONG ASYLUM SEEKERS IN THE US

Christian Olivo-Freites[1], Patricia Miguez-Arosemena[2], Cristina Olivo-Freites[3], Deborah Edelman[2], Kayla Leschly[1], Jayme Leschly[1], Amir M. Mohared[4]

[1]Ryan Health, New York, NY, United States, [2]Icahn School of Medicine at Mount Sinai, New York, NY, United States, [3]Department of Hematology and Oncology, University of Texas Health Science Center, Houston, TX, United States, [4]Center for Global Health, Massachusetts General Hospital, Boston, MA, United States

In the past year, nearly 2 million people have entered the US through irregular routes of migration, most to seek asylum. Outbreaks of vaccine-preventable infections, such as measles and varicella, have been reported in migrant shelters across the US. We sought to determine the susceptibility of this population to vaccine-preventable infections. We conducted a cross-sectional study of unhoused asylum seekers in New York City from January 1- November 30, 2023. We measured serologic evidence of immunity against varicella, measles, mumps, rubella, hepatitis A, and hepatitis B. We used multivariable logistic regression to determine the adjusted odds ratio (aOR) for susceptibility. In the subset of individuals who provided written vaccine records from their countries of origin, we analyzed their vaccination history and evaluated for discordance between reported vaccination history and serologic immunity. Among 1147 people (53.2% female, median age 13), nearly one-third were susceptible to measles(26.9%, 95% CI: 24.3-29.5%), varicella (32.0%, 95% CI: 29.3-34.8%), and hepatitis A (32.0%, 95% CI: 29.3-34.8%). Almost half were susceptible to hepatitis B (41.6%, 95% CI: 38.7-44.5%). Susceptibility to measles was more likely in children (aOR 1.69, 95%CI: 1.24- 2.30) and adolescents (aOR 2.10, 95%CI: 1.37-3.19) compared with adults. Susceptibility to varicella was more likely in children (aOR 9.85, 95%CI: 6.81-14.59) and adolescents (aOR 4.90, 95%CI: 3.02-8.01) compared with adults and in men (aOR 1.35, 95%CI: 1.02-1.78) compared with women. We found that 195 people (17.0%) provided documented completion of the two-dose MMR vaccine series in their country of origin, of whom 53 (27.2%) did not have serologic evidence of immunity against measles. People with discordant vaccine records and immunity were most commonly from Ecuador (35.9%), Colombia (26.4%), and Venezuela (15.1%). In summary, a high number of unhoused asylum seekers are not immune to vaccine-preventable infections. People with documented history of vaccination against measles prior to entering the US were no more likely to have serologic evidence of immunity against measles.

8145

STRENGTHENING INTEGRATED COMMUNITY CASE MANAGEMENT COMMODITY AVAILABILITY IN UGANDA

PETER PA Anyumiza[1], Phellister PN Nakamya[1], Rebecca Babirye[1], Geoffrey Nuwamanya[1], Samantha Herrera[2], Catherine Maiteki Sebuguzi[3], Maureen Amutuhaire[3], Jimmy Opigo[3]

[1]1.Programme for Accessible Health Communication and Education (PACE), Kampala, Uganda, [2]PATH, Kampala, WA, United States, [3]Ministry of Health, Ministry of Health, Uganda National Malaria Control Division, Kampala, Uganda

The Integrated Community Case Management (iCCM) program is a key strategy for delivering life-saving interventions for malaria, pneumonia and diarrhoea to populations with poor access to health services mainly targeting children under 5 years of age. The program has been implemented in Uganda since 2010, reaching 70% of districts by 2023 though Village Health Teams (VHTs). However, stagnation in achieving malaria testing and treatment targets at the community level has been noted due to frequent stockouts of commodities, hindering its effectiveness. To address this issue, the Ministry of Health, in partnership with PACE and

PATH-PMI Insight, conducted a Landscape Assessment to investigate iCCM commodity stockouts in Uganda. A mixed-methods approach was utilized, involving forty in-depth interviews conducted at national, district, and health facility levels, alongside eight focus group discussions with VHTs. Inductive qualitative analysis using QSR International's NVivo software explored community-level barriers to iCCM stock availability. Document review offered insights into VHT service provision, while District Health Information System (DHIS2) data analysis using STATA version 14 assessed commodity stockouts. Additionally, a design workshop engaged key stakeholders to craft intervention strategies. Stockouts of key commodities such as ACTs, ORS+ Zinc, and Amoxicillin were prevalent. The proportion of villages with ACT stockouts increased from 52.6% in 2020 to 62.9% in September 2023. DHIS2 data for 2023 revealed significant stockouts of iCCM commodities, with 62.9% of villages experiencing stockouts. Challenges in the commodities supply chain were identified at various levels, including national, district, health facility, and community levels. Key reasons for stockouts included governance issues, management challenges, human resource constraints, and data quality gaps indicating a systemic issue. Strengthening iCCM stock availability requires government leadership, civil society engagement, reliable medicine supply, and improved governance.

8146

THE PREDICTIVE VALUE OF SIRS AND Q-SOFA SCORES AS MEASURES OF SEPSIS SEVERITY AMONG PATIENTS IN A PRIVATE HOSPITAL IN LAGOS, NIGERIA: RESULTS FROM THE R JOLAD SEPSIS STUDY

Abiola Fasina-Ayoola[1], Adebisi Adeyeye[2], Abigail Obi[2], Francis Olajide[2], Joao Vissoci[3], Oludoyinmola Ojifinni[4], Catherine Staton[3]

[1]R JOLAD Hospital/Emergency Healthcare Consultants, Lagos, Nigeria, [2]Emergency Healthcare Consultants, Lagos, Nigeria, [3]Global Emergency Medicine Innovation and Implementation Research Center, Duke University, Durham, NC, United States, [4]School of Clinical Medicine, Faculty of Health Sciences, University of the Witwatersrand,, Johannesburg, South Africa

In sepsis, systemic inflammatory response syndrome (SIRS) and quick Sepsis-related Organ Failure Assessment (qSOFA) scores are used to screen patients and predict mortality in sepsis. Studies have documented their predictive value, notably in high-income countries. There is little data on their efficacy in low-resource, high-malaria settings. This study evaluated SIRS and qSOFA for septic patient screening at a Lagos, Nigeria, private hospital. A sepsis registry was established at R-Jolad Hospital. Septic patients meeting at least two SIRS criteria were enrolled in the registry. Data on qSOFA scores generated from the vital signs, patient disposition, malaria co-infection, and management, including the use of vasopressors and mortality outcomes were recorded. Frequencies, chi-square tests, and regression analyses were used to assess the relationship between these outcomes and the SIRS and qSOFA scores.230 sepsis patients aged ≥ 18 were enrolled from September 2023 to April 2024. 57.8% were outpatients, 41.8% emergencies, and 0.4% admitted. Fifty percent of enrolled patients met two SIRS criteria, 42.7% met three, and 7% met four. The average qSOFA score was 0.9 (SD ±0.6). 77.6% of 215 hospitalized patients were discharged, 11.2% were referred, 6.8% were discharged against medical recommendation, and 4.4% died in hospital. SIRS and qSOFA did not significantly affect patient disposition, vasopressor use, or hospital stay. 74.3% of patients had malaria co-infection, of which 10.3% and 1.2% had qSOFA scores of 2 and 3. 48.5% of this group met 2 SIRS criteria, 42.7% met 3, and 8.2% met 4. The qSOFA score may better screen for severe illness in malaria-endemic areas than SIRS. In our resource-constrained environment, neither SIRS nor qSOFA accurately predicted the severity of sepsis or the likely final disposition of admitted patients. Though half of patients enrolled in the registry presented with an SIRS score >2, the majority were discharged. Further studies are required to determine a suitable sepsis clinical severity score in similar environments with high endemic malaria transmission.

8147

CLINICAL PRESENTATION OF ACUTE ARBOVIRAL INFECTIONS DURING THE 2023 OUTBREAK IN THE TIRS PROJECT COHORT

Gloria Abigail Barrera-Fuentes[1], Henry Puerta-Guardo[1], James Earnest[2], Oscar Kirstein[3], Azael Che-Mendoza[1], Guadalupe Ayora-Talavera[1], Pilar Granja-Perez[4], Salha Villanueva[4], Matthew H. Collins[2], Hector Gomez-Dantes[5], Pablo Manrique-Saide[1], Gonzalo Vazquez-Prokopec[2], Norma Pavia-Ruz[1]

[1]Universidad Autónoma de Yucatán, Mérida, Mexico, [2]Emory University, Atlanta, GA, United States, [3]Ministry of Health, Jerusalem, Israel, [4]Secretaría de Salud de Yucatán, Mérida, Mexico, [5]National Institute of Public Health, Cuernavaca, Mexico

Aedes borne diseases (ABD) are caused by viral infections transmitted to humans through bites of infected Aedes aegypti. The increase in the incidence and geographical distribution of ABDs is a major public health problem in the Region of the Americas. The year 2023 had the highest historical record of dengue cases in the continent, with more than 4.1 million new infections. Mexico was within the regions with the highest cumulative incidence and both total number and severe number of cases. Within the country, Yucatan state reported 19% of Mexico's cases. The aim of this study was to describe the clinical characteristics of the ABD cases from the last active surveillance season during the outbreak (July-December 2023) in the TIRS trial cohort of ~4600 children aged 2-15 at enrollment in Merida, Yucatán, Mexico. Through household visits, phone calls, phone messages and a toll-free line, 822 reports of potential ABD symptoms were observed. Of these, 558 (68%) were considered suspected ABD cases. A total of 488 participants provided a blood sample. From these, 310 cases were detected (64% attack rate) by PCR or IgM results. Dengue represented 82% of the cases (n=254), followed by Zika 12% (n=37) and coinfections 6% (n=19). Patients with confirmed ABD were slightly older than the negatives but there were no significant differences between age nor sex. The clinical presentation of the cases was diverse, with fever (100%), headache (79.8%-84.6%) and myalgia (78.9-84.6%) as the most common signs/symptoms reported regardless the diagnosis. A total of 15 patients presented alarm signs and were referred to ER consultation. No ABD severe cases were observed. All the patients recovered satisfactorily. These results describe the variable array of symptoms involved in DENV infections and reinforce the importance of strengthened surveillance and laboratory diagnosis to detect silent ZIKV transmission during a DENV outbreak.

8148

ASSESSMENT OF HOME BASED RAPID DIAGNOSTIC TESTING UPTAKE TOWARDS INCREASING COMMUNITY-BASED ACCESS TO CARE IN KENYA, SOUTH AFRICA, AND ZAMBIA

Anna Winters[1], *DASH Study Consortium*[2]

[1]Akros, Lusaka, Zambia

Rapid diagnostic tests (RDTs) offer a cost-effective solution for early disease detection, public health screening, and surveillance; however, their uptake remains sub-optimal. We sought community members' perspectives on the distribution and administration of RDTs to increase testing and treatment uptake for health priorities. In this qualitative study, we conducted 60 in-depth interviews and 11 focus group discussions with community members in rural and urban settings in Kenya, South Africa, and Zambia. Interviewers collected written informed consent and audio-recorded interviews. They distilled key information in structured memos capturing context, perspectives, and recommendations. We conducted rapid thematic analyses using analytic memos and debriefs with country research teams. All participants prioritized HIV, TB, and malaria for rapid testing. South African participants wanted to self-test for malaria in facility-based settings due to low confidence in interpreting results. All participants had a strong preference for home delivery of RDTs and medication by CHWs, despite concerns of increased workload. Though most were confident

about self-testing, participants generally preferred having a CHW present for pre-/post-test counseling, consultation, and linkage to treatment and prevention. Kenyan participants had mixed feelings about HIV self-testing at home due to perceived need for counseling and medical attention. If unfacilitated self-testing, participants preferred audio-visual demonstrations and pictorial brochures to follow at their own pace. If reactive, participants preferred phone consultation with a professional healthcare worker to get personalized advice on medication, lifestyle, and being fast-tracked for medicine pick-ups at a private pharmacy or health facility. A non-reactive result could prompt online information seeking or care-seeking if feeling unwell. Convenience, access, easy-to-follow instructions and personalized guidance through testing and accessing care pathways should be prioritized for the implementation of RDTs.

8149

HIGH-RISK *APOL1* VARIANTS ARE ASSOCIATED WITH REDUCED LONG-TERM SURVIVAL FOLLOWING SEVERE MALARIA

Claire D. Liepmann[1], Ruth Namazzi[2], Kagan A. Mellencamp[1], Giselle Lima-Cooper[1], Anthony Batte[2], Paul Bangirana[3], Marco Abreu[1], Tae-Hwi Schwantes-An[1], Robert Kalyesubula[2], Robert O. Opoka[2], David S. Hains[1], Chandy C. John[1], Andrea L. Conroy[1]

[1]Indiana University School of Medicine, Indianapolis, IN, United States, [2]Makerere University College of Health Sciences, Kampala, Uganda, [3]Makerere University Institute of Psychology, Kampala, Uganda

Acute kidney injury (AKI) is an emerging complication of clinical importance occurring in 24-59% of children hospitalized with severe malaria. Survivors of AKI are at increased risk of post discharge mortality and chronic kidney disease (CKD). High-risk variants in the apolipoprotein-L1 (*APOL1*) gene account for ~70% of increased risk of kidney disease in people of African descent. G1 and G2 variants of *APOL1* are protective against African trypanosomiasis but confer increased risk of kidney disease. We hypothesized that children with severe malaria, subsequently at risk for AKI, and who carry high-risk *APOL1* variants have increased risk of long-term mortality and CKD. Analysis is nested in an established prospective cohort study of children under 5 years hospitalized with severe malaria at 2 sites in Uganda. Array genotyping determined *APOL1* status of 564 children. Children were followed for 1 year then recontacted and consented to kidney function assessment at 4-9 years using serum creatinine and urine albumin to creatinine ratio using the Kidney Disease Improving Global Outcomes (KDIGO) guidelines. G1 frequency was 7.4% and G2 frequency was 8.9%. 2.7% (15/564) of children were considered high-risk if they have 2 *APOL1* risk variants (G1G1/G1G2/G2G2). There was no difference in age, sex, patient characteristics, or disease severity at presentation (p>0.05 for all) between kidney risk groups. In-hospital mortality was 20% in the high-risk group (3/15) versus 6.9% (38/549) in the low-risk group (p=0.088). All-cause mortality among children at 4-9 years was 58.3% (7/12) versus 19.4% (85/438), corresponding to a hazard ratio of 3.71 (95% CI 1.72 - 8.03, p=0.001). Among surviving children, with long-term follow-up available, the odds of CKD was 3.70 times higher among children with high-risk *APOL1* (95% CI 0.40 - 33.74, p=0.247). There were no differences in mean eGFR or specific KDIGO CKD risk categories (p>0.05) between kidney risk groups. Efforts to validate mortality risk among children with high-risk *APOL1* variants living in malaria endemic regions are ongoing.

8150

POSTMORTEM CHARACTERIZATION OF GASTROSCHISIS ASSOCIATED UNDER-5 DEATHS IN MOZAMBIQUE: INSIGHTS FROM CHILD HEALTH AND MORTALITY PREVENTION SURVEILLANCE (CHAMPS)

Elisio Xerinda[1], Rosauro Varo[2], Milton Kincardett[1], Arlindo Malheia[1], Portia Mutevedzi[3], Dianna Blau[3], Cynthia Whitney[3], Marcelino Garrine[1], Quique Bassat[4], **Inacio Mandomando**[1]

[1]Centro de Investigação em Saúde de Manhiça, Maputo, Mozambique, [2]Barcelona Institute for Global Health, Barcelona, Spain, Barcelona, Spain, [3]Emory University, Atlanta, GA, United States, [4]ISGlobal, Hospital Clínic – Universitat de Barcelona, Barcelona, Spain, Barcelona, Spain

The Child Health and Mortality Prevention Surveillance (CHAMPS) Network performs advanced minimally invasive tissue sampling (MITS) postmortem techniques in deceased children, providing a unique opportunity to investigate in depth causes of death (CoD), including rare conditions like gastroschisis, in Africa and South Asia. Gastroschisis is a congenital malformation associated with increased risk of mortality in settings with limited resources for prenatal diagnosis and surgical intervention. Here we present CHAMPS CoD findings in children who died from gastroschisis in Mozambique (Manhiça and Quelimane). A panel of multidisciplinary specialists reviews MITS pathology and microbiology results together with clinical records and verbal autopsy to determine the immediate, underlying, and comorbid CoD using ICD-10 codes. Of 1312 cases DeCoded betwen 2016 and 2022, 1.4% (n=19) had gastroschisis as the underlying CoD. All but one start with were perinatal deaths: 2 stillbirths (10.5%), 3 deaths in less than 24 hours (15.8%), and 13 deaths between 1-7 days (68.4%). The non-perinatal death e was 47-month-old child born with gastroschisis and submitted to sugery three days post-birth who developed postosurgery complications (rectovaginal fistula) and died due to sepsis. The immediate CoD among those cases were sepsis (47.4%), pneumonia (10.5%), peritonitis (5.3%), hyaline membrane disease (5.3%), and intrauterine hypoxia (5.3%). *Klebsiella pneumoniae* (44%), *Escherichia coli*, and *Pseudomonas aeruginosa* (11%) were the main etiology of sepsis. The maternal conditions grastroschisis-associated were young maternal age (15.8%), HIV exposure (5.3%), pre-term rupture of membranes (5.3%), chorioamnionitis (5.3%), twin pregnancy (5.3%), and maternal anaemia (5.3%). Our findings provided a snapshot of the impact of a rare condiction in the early child mortality in Mozambique, calling for the urgent need of improving antenatal care including ultrasound check and surgical capacities and improve targeted infection control and clinical management in high-risk groups

8151

IMPORTANCE OF CLINICAL EXPERTISE IN DIAGNOSIS OF LEPROSY AND AMERICAN CUTANEOUS LEISHMANIASIS: INSIGHTS FROM CLINICAL PROFILES IN EASTERN MINAS GERAIS, BRAZIL

Anabella Almeida[1], **Lorena Bruna Pereira de Oliveira**[2], André Otaviano[3], Daisy Santos[1], Weverton Ferreira[1], Giselle Ramos[1], José Geraldo Neto[1], Karolina Campos[1], Isabel Moreira[1], Cristina Oakis[1], Clara Rodrigues[1], Mathias Garcia[1], Pedro Henrique Ferreira Marçal[2], Jessica Fairley[4], Lucia Fraga[1]

[1]Universidade Federal de Juiz de Fora, Governador Valadares, Brazil, [2]Universidade Vale do Rio Doce, Governador Valadares, Brazil, [3]Secretaria Municipal de Saúde, Inhapim, Brazil, [4]Emory University, Atlanta, GA, United States

Leprosy and American Cutaneous Leishmaniasis (ACL) are neglected tropical diseases (NTDs) with considerable prevalence and morbidity rates in Brazil. Conventional laboratory techniques for leprosy exhibit suboptimal sensitivity, leaving diagnosis to the clinical assessment of physicians, often a challenging task. Similarly, clinical examination for ACL lacks sensitivity and specificity, leading to underdiagnosis and delayed treatment. Furthermore, the broad spectrum of immune responses leads to a diverse array of clinical presentations. We present, therefore, four cases of these two NTDs

from eastern Minas Gerais, Brazil, demonstrating the diversity of clinical presentations making diagnosis challenging. Two individuals diagnosed with MB leprosy exhibited disparate disease phenotypes. One patient initially presented with right forearm pain and neural thickening, subsequently developing hypochromic skin lesions with sensory deficits several years later. The second patient manifested hypochromic patches with sensory loss. Notably, while the bacilloscopic index for this individual was negative, suggestive biopsy findings confirmed the clinical suspicion. For the ACL cases, one patient displayed suspicion of cutaneous involvement with a localized lesion, while the other exhibited cutaneous involvement with a localized lesion and reactive lymphadenitis in the adjacent region. The inconclusive diagnosis in the latter ACL suspect was attributed to a negative parasitological examination. Subsequently, a lesion sample was obtained for molecular diagnosis (PCR). Accessibility to this diagnostic tool posed challenges in patients' cities, far from reference centers. Therefore, the development of rapid diagnostic tests holds promise for accurately diagnosing infections with reduced technological complexity, facilitating effective control of new cases and highlighting the critical need for improved diagnostic methods. Moreover, enhancing physicians' training to recognize clinical cases without reliable tests is imperative for timely intervention and management.

8152

RENIN RELEASE IS ASSOCIATED WITH ACUTE KIDNEY INJURY AND PREDICTS MORTALITY IN CHILDREN WITH SEVERE MALARIA

Daniel Adan Jr[1], Ruth Namazzi[2], Caroline Kazinga[3], Anthony Batte[2], Kagan A. Mellencamp[1], Natalja N. Stanski[4], Caitlin Bond[1], Robert O. Opoka[5], Chandy C. John[1], Andrea L. Conroy[1]

[1]Indiana University School of Medicine, Indianapolis, IN, United States, [2]Makerere University, Kampala, Uganda, [3]CHILD Laboratory, Kampala, Uganda, [4]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, United States, [5]Aga Khan University Medical College, Nairobi, Kenya

Renin has been identified as a biomarker of acute kidney injury (AKI) in critical illness. In a two-site prospective cohort study, we assessed plasma renin levels in 594 children with severe malaria (SM). Community children renin levels were used to establish a population reference with the 99th percentile as the cut-off for elevated renin. The mean age of children was 2.1 years and 44.3% were female. Children with SM had substantially higher renin levels than community children, with 26.9% of children with SM having elevated renin. We compared the relationship between elevated renin with clinical complications of SM and mortality. Children were separated into two groups, those who met a specific research definition of SM (n=275) and children who did not (n=319). Irrespective of SM definition, children with elevated BUN and acidosis were more likely to have elevated renin ($p<0.001$). In the subset of children who did not meet the specific definition of SM, complications related to volume status (shock, cold peripheries, vomiting) metabolic complications (severe AKI, hyponatremia) and hematologic complications (severe anemia, blackwater fever) were strongly associated with elevated renin ($p<0.001$ for all except hyponatremia and vomiting, $p=0.001$ for both). In addition, elevated renin was associated with increased mortality irrespective of malaria definition after adjusting for age, sex, site and the presence of severe AKI at enrollment ($p=0.002$). We evaluated pathways of host response in both groups of children. While significant in both groups of SM, markers of kidney injury, stress and hemolysis were more strongly associated with elevated renin in children who did not meet a specific definition of malaria. Together, these findings suggest that elevated renin is a shared biomarker of mortality in children with SM. However, the pathways of renin induction may vary depending on the underlying cause of illness and may be affected by the timing that children seek care and by pretreatment with antimalarials. Additional studies are needed to understand whether interventions targeting renin could be beneficial in SM.

8153

SEVERE AND FATAL LASSA FEVER - OBSERVATIONS IN 19 ICU PATIENTS TREATED IN NIGERIA

Cyril Erameh[1], Sylvanus Okogbenin[1], Ephraim Ogbaini[2], Osahogie Edeawe[3], Jerome Christian[2], Joseph Okeguale[2], Christian Erohubie[2], Matin Kohsar[4], Hannah Müller[4], Benevolence Ohomoime[2], Rita Esumeh[2], Sule Pius[3], Ludmila Unrau[4], Ester Orban[4], Reuben Eifediyi[2], Stephan Günther[4], Michael Ramharter[4], Lisa Oestereich[4], **Till F. Omansen**[4]

[1]Irrua Specialist Teaching Hospital, Irrua, Niger, [2]Irrua Specialist Teaching Hospital, Irrua, Nigeria, [3]Irrua Specialist Teaching Hospital, Hamburg, Nigeria, [4]Bernhard Nocht Institute for Tropical Medicine, Hamburg, Germany

Lassa fever (LF) is a viral hemorrhagic fever (VHF) classified as priority disease by WHO. Due to the high case fatality rate, lack of adequate vaccine and treatment, urgent improvement of the therapy is needed. The pathophysiology of LF is poorly understood and complicated by biosafety restrictions. After extensive capacity building and employment of a glovebox laboratory setup and point-of-care devices we here characterized 19 cases of severe Lassa fever patients admitted to the intensive care unit (ICU) of the VHF isolation ward at Irrua Specialist Teaching Hospital in Edo State, Nigeria. Cases were recruited during the current seasonal outbreak between January and April 2024. All cases had RT-PCR confirmed LF. The mean age was 40.7 years and 36% were female. Eight (42%) of the 19 cases died during admission. The most frequently observed severe complication was hepatitis. Acute liver failure was rare and mainly occurred in advanced stages. Acute kidney injury (AKI) was common, often requiring hemodialysis. Relevant hemorrhage was not observed commonly. However, upon ultrasonography, we consistently noted pleural effusions in severe and fatal patients resulting in respiratory insufficiency. In some cases, this could be attributed to hypervolemia in the case of AKI with reduced urinary output. However, in most cases, patients were hypovolemic. Coagulation parameters were usually only mildly deranged until late stage, when we observed thrombocyte dysfunction and DIC. We thus conclude that the picture of severe and fatal LF is hallmarked by hepatitis, AKI and pleural effusions, most likely due to vascular leak syndrome. In two patients we noted secondary bacterial sepsis due to *E. coli* and *K. pneumoniae* with highly elevated Il-6, procalcitonin and C-reactive protein results compared to other cases, further indicating that not hyperinflammation and viral sepsis, but vascular leak drives pathophysiology in LF. We henceforth recommend case management and research for LF focuses on host-directed therapies to address vascular leak and improvement of coagulopathy to enable invasive drainage of effusions to aid the compromised respiration.

8154

ASSOCIATION OF DENGUE VIRUS SEROTYPES AND THE CLINICAL SEVERITY OR MORTALITY IN TAIWAN'S LARGEST DENGUE OUTBREAK

Jih-Jin Tsai[1], Li-Teh Liu[2], Chun-Hong Chen[3]

[1]Kaohsiung Medical University Hospital, Kaohsiung, Taiwan, [2]Department of Medical Laboratory Science and Biotechnology, College of Medical Technology, Chung-Hwa University of Medical Technology, Tainan city, Taiwan, [3]National Institute of Infectious Diseases and Vaccinology, National Health Research Institutes, Miaoli County, Taiwan

Dengue virus serotype 2 (DENV-2) was the major serotype in the 2015 dengue outbreak in Taiwan, while DENV-1 and DENV-3 were dominant between 2005 and 2014. We aimed to investigate whether DENV-2 contributed to disease severity and mortality in the outbreak in Kaohsiung city, Taiwan. We collected serum samples from dengue patients to detect the presence of DENV and determine the serotypes by using quantitative reverse transcription-polymerase chain reaction. Our cohorts comprised 105 DENV-1-infected cases and 1,550 DENV-2-infected cases. Demographic data, DENV serotype, and comorbidities were covariates for univariate and multivariate analyses to explore the association with severity and mortality. The results suggested that DENV-1 persisted and circulated, while DENV-2 was dominant during the dengue outbreak that occurred

between September and December 2015. However, DENV-2 did not directly contribute to either severity or mortality. Aged patients and patients with diabetes mellitus (DM) or moderate to severe chronic kidney disease (CKD) had a higher risk of developing severe dengue. The mortality of dengue patients was related to a higher Charlson comorbidity index score and severe dengue. Among DENV-2-infected patients and older patients, preexisting anti-dengue IgG, DM, and moderate to severe CKD were associated with severe dengue. Moreover, female sex and severe dengue were associated with a significantly higher risk of death. Our findings highlight the importance of timely serological testing in elderly patients to identify potential secondary infections and focus on the meticulous management of elderly patients with DM or moderate to severe CKD to reduce dengue-related death.

8155

SEPSIS ENDOTYPES IDENTIFIED BY HOST GENE EXPRESSION ACROSS GLOBAL COHORTS

Josh G. Chenoweth[1], Joost Brandsma[1], Deborah Striegel[1], Pavol Genzor[1], Elizabeth Chiyka[1], Subramaniam Krishnan[1], Gary Fogel[2], Christopher Woods[3], Carlo Colantuoni[4], George Oduro[5], Te Vantha[6], Andrew Letizia[7], Kevin Schully[8], Danielle Clark[1]

[1]Henry M. Jackson Foundation for the Advancement of Military Medicine Inc., Bethesda, MD, United States, [2]Natural Selection Inc., San Diego, CA, United States, [3]Duke University School of Medicine, Durham, NC, United States, [4]Johns Hopkins School of Medicine, Baltimore, MD, United States, [5]Komfo Anokye Teaching Hospital, Kumasi, Ghana, [6]Takeo Provincial Referral Hospital, Takeo, Cambodia, [7]Naval Medical Research Unit EURAFCENT Ghana detachment, Accra, Ghana, [8]Biological Defense Research Directorate, Naval Medical Research Command, Frederick, MD, United States

Sepsis is a global health priority accounting for 47 million deaths in 2017. The signs and symptoms of sepsis are highly variable and the failure to develop effective therapeutics is attributed to clinical and immunological heterogeneity. Disease endotypes defined by shared phenotypes have shown promise for precision medicine approaches that address complicating heterogeneity in sepsis. The human host response to infection is highly sensitive and specific, enabling the use of gene expression measures in blood to delineate patient endotypes. There is an urgent need to characterize sepsis endotypes in diverse populations to facilitate new and better prognostic and therapeutic solutions in low- and middle-income countries that carry the greatest burden for sepsis. Here we analyze host gene expression in a prospective multi-site international sepsis cohort (n=494) in West Africa (Ghana), Southeast Asia (Cambodia), and the United States (North Carolina) as part of the Austere environments Consortium for Enhanced Sepsis Outcomes (ACESO). We employ soft-clustering decomposition of host RNA sequencing data to identify discrete and overlapping clusters within high-dimensional gene expression data. We identify four sepsis subtypes differentiated by 28-day mortality. A low mortality "immunocompetent" group is specified by features that describe the adaptive immune system. In contrast, three high mortality groups show elevated clinical severity. The "immunosuppressed" group members show signs of a dysfunctional immune response, the "acute-inflammation" group is set apart by molecular features of the innate immune response, while the "immunometabolic" group is characterized by metabolic pathways such as heme biosynthesis. Using latent space exploration techniques with these data and public datasets we further describe the cell type-specific molecular phenotypes that underly these endotypes including a dysregulated myeloid compartment shared between sepsis and COVID-19. Taken together our data supports endotype-driven immunotherapeutic interventions for sepsis and identifies biomarkers that predict outcomes.

8156

INTEGRATED SEROLOGICAL SURVEILLANCE FOR MULTIPLE INFECTIOUS DISEASES IN VANUATU

Mohamad Assoum[1], Elizabeth Nguyen[1], Arunasingam Abayasingam[1], Prudence Rymill[2], Fasihah Taleo[3], Mackline Katenga[2], Stephanie Tabe[2], Eithandee Aung[1], Fernando Santiago[4], Gladymar P. Chacon[1], Claire Dyer[1], David Kennedy[1], Md S. Islam[5], Dorothy Machalek[1], Nicodemus Tedla[4], Julie Jacobson[6], John Kaldor[1], Susana Vaz Nery[1]

[1]The Kirby Institute, UNSW, Kensington, Australia, [2]Ministry of Health, Port-Vila, Vanuatu, [3]WHO Western Pacific Regional Office, Port Vila, Vanuatu, [4]School of Medical Sciences, UNSW, Kensington, Australia, [5]School of Population Health, UNSW, Kensington, Australia, [6]Bridges to Development, Seattle, WA, United States

Vanuatu's population is at risk of neglected tropical diseases (NTDs) and vaccine-preventable diseases (VPDs). Serological surveys that measure the prevalence of antibodies are a strategy for monitoring current or past exposure to infectious pathogens. Integrated serosurveillance using novel multi-bead assays that can detect ~100 different disease-specific antibodies from a single dried blood spot, and has the potential to provide information on the distribution of a wide range of infections, including estimating vaccine coverage.Between 2021 and 2023, we conducted integrated serological surveys to assess the seroprevalence of IgG antibodies against multiple VPDs, NTDs, and other infectious diseases in 92 villages in Vanuatu's Tafea, Sanma and Shefa provinces. After obtaining informed consent, approximately 2000 participants aged >1 year of age provided a finger prick blood sample to prepare a dried blood spot (DSB) that was analysed using the Luminex technology. Seroprevalence was defined as the proportion of patients with positive IgG results in DBS specimens. Here, we report the overall estimated cluster-adjusted seroprevalence in 501 participants across Sanma (N=245), Tafea (N=243) and Shefa (N=13). Seroprevalence of *Chlamydia trachomatis* was 28.6% by pgp3 (95%CI 23.0-35.0%) and 12.6% (95%CI 9.3-16.8%) by CT694; *Brugia malayi* 3.6%, (95%CI 1.0-11.9%) and *Wuchereria bancrofti* 3.3% (95% CI 1.8-5.9%). Seroprevalence of measles was 35.6% (95%CI 27.6-22.5%), rubella 72.7% (95%CI 61.7-81.5%), tetanus toxoid 76.7% (95%CI 64.6-85.6%), and diphtheria toxoid 57.2% (95%CI 44.9-68.7%). The seroprevalence of SARS-CoV-2 spike protein was 29.9% (95%CI 17.8-45.6%). An additional 648 samples are being analysed and will be presented. Our preliminary results provide a promising measure of effective population-level immunity and exposure to multiple infectious diseases, with the advantage of being cost-effective, scalable, acceptable, and able to target hard-to-reach and high-risk populations. Additional analysis by age groups has been conducted, and comparisons with national immunisation coverage surveys are pending.

8157

OVERCOMING DIAGNOSTIC CHALLENGES WITH ACUTE FEBRILE ILLNESS IN NIGERIA: WHAT CAN WE LEARN FROM THE SURVEILLANCE OF AFI AETIOLOGIES IN NIGERIA (SAFIAN) STUDY?

Lauren Courtney[1], Jean Kim[1], Jay Samuels[2], Philippe Chebu[2], Onyia Ejike[3], Ikponmwosa Odia[4], Claire Quiner[1], Ephraim Ogbaini[4], Vivian Kwaghe[3], Cyril Erameh[4], Eke Ofuche[2], Femi Owolagba[2], Blessed Okira[4], Ikponmwosa Odia[4], Jacqueline Agbukor[4], Julius Imoyera[4], Kat Asman[1], Adamu Ephraim[1], Osas Edeawe[4], Nankpah Vongdip[3], Emmanuel Oga[1]

[1]RTI International, Research Triangle Park, NC, United States, [2]APIN Public Health Initiatives, Abuja, Nigeria, [3]University of Abuja Teaching Hospital, Abuja, Nigeria, [4]Irrua Specialist Teaching Hospital, Irrua, Nigeria

Undiagnosed acute febrile illness (AFI) is a serious public health concern, with cases often remaining undiagnosed, or misdiagnosed and treated as malaria. Insufficient laboratory capacity for routine diagnosis is a common limitation for timely and accurate diagnosis of the cause of AFI. We established a hospital-based surveillance study to generate data to support

decisions on which pathogens should be prioritized for routine screening. In this presentation we aim to assess the operational lessons learned to improve AFI diagnosis and surveillance. The Surveillance of AFI Aetiologies in Nigeria (SAFIAN) study introduced a new technology, TaqMan Array Card (TAC) to screen patients presenting with AFI for 25 pathogens at two tertiary hospitals in Nigeria, expanding the hospital's diagnostic capacity. TAC is an efficient and accurate multiplex PCR allowing for simultaneous testing of multiple pathogens. RedCap was used to collect medical record abstraction and patient self-reported demographic and risk behaviors. We trained hospital clinical and laboratory staff and provided regular technical assistance to resolve issues. Study teams monitored supply management; reagents required frequent replenishments since they had a shorter shelf-life than the study length, and TAC required repeated runs for failed samples due to routine laboratory issues; 15.1% (114/754) of samples were repeated, along with 12.3% (15 of 122) of cards. The procurement process for the TAC-specific supplies was complex, expensive and lengthy. Efficient study operations management was critical to track RedCap data management issues and resolve in real time. Steady communication and regular monitoring were key to addressing critical study issues. Lessons learned highlight the importance of integrating innovative diagnostic tools and training in laboratory practices. Strengthening laboratory capabilities and adopting advanced diagnostic methodologies are crucial for enhancing public health responses to AFIs in Nigeria, but this will require sustainable investment in diagnostic infrastructure.

8158

A CASE OF PRE-EXTENSIVELY DRUG-RESISTANT TUBERCULOSIS IN KWAZULU-NATAL, SOUTH AFRICA

Jessica Tuan[1], Francois Eksteen[2]

[1]Yale University School of Medicine, New Haven, CT, United States, [2]Church of Scotland Hospital, Tugela Ferry, South Africa

A 35-year-old man from KwaZulu-Natal, South Africa with HIV [CD4 unknown; viral load 6,368,115 copies/mL (6 months prior), improved to 283,791 copies/mL (3 months prior)] and presumptive treatment for pulmonary & extrapulmonary multi-drug-resistant (MDR) tuberculosis (TB) with left neck TB abscess status-post abscess aspiration (3 months prior), presented to clinic for follow-up. He received 3 months of presumptive MDR-TB treatment and felt overall well and in good health. He reported unintentional 14 kg weight gain over 3 months. He denied fever, chills, weight loss, cough, hemoptysis. He was adherent to medications and TB clinic appointments. He was generally well-appearing, in no acute distress. He was afebrile. He weighed 83 kg. Skin exam revealed a left neck 3-cm length healed, clean, dry scar. The remainder of his exam including pulmonary exam was normal. GeneXpert testing of sputum culture (on initial presentation): *Mycobacterium tuberculosis* with Rifampicin resistance. A recent chest X-ray demonstrated left-sided nodular lesion (2 cm) and few, scattered sub-cm calcifications bilaterally. The chest X-ray was improved his prior chest X-ray 3 months prior, demonstrating scattered infiltrates, nodules, and calcifications bilaterally. His sputum culture (on initial presentation) later resulted with *M. tuberculosis*: *Resistant* - Isoniazid (INH), Rifampin, Fluoroquinolones, Second-line injectables. His prior left neck abscess aspirate culture (on initial presentation), later demonstrated growth of *M. tuberculosis*: *Resistant* - INH, Rifampin, Fluoroquinolones, Second-line injectables. For the management of at minimum pre-extensively drug-resistant TB, he was to restart/continue linezolid for 1 year; start delamanid for 0.5-1 year; continue bedaquiline for 1 year; stop ethambutol, pyrazinamide, and high-dose isoniazid. Levofloxacin was continued given patient's overall clinical improvement with monitoring. Also, the plan was to add clofazimine and terizidone for 18 months. This is a challenging case of diagnosed pre-XDR TB, which has a nuanced and complex management that providers should recognize and understand.

8159

IMPLEMENTING NEUROCOGNITIVE ASSESSMENT TOOLS - A PILOT STUDY COMPARING NEUROCOGNITIVE FUNCTION OF EBOLA SURVIVORS WITH NON-INFECTED CONTROLS IN SIERRA LEONE

Emily J. Engel[1], Nell G. Bond[1], Tucker Challay[2], Doris A. Fofanah[2], Ibrahim Sumah[2], Robert J. Samuels[2], Alex C. Birdsill[1], John S. Schieffelin[1]

[1]Tulane University School of Medicine, New Orleans, LA, United States, [2]Kenema Government Hospital, Kenema, Sierra Leone

Neurocognitive issues often follow viral infections, both acute and chronic including mental illness, hearing loss, and depression. The Ebola virus (EBOV) continues to pose a significant global health threat, notably highlighted by the 2013-2016 West African outbreak, which infected over 28,600 people and claimed more than 11,300 lives, surpassing previous outbreaks combined. Consequently, an estimated 17,000 West Africans are now EVD survivors. These survivors seem to suffer from a variety of post-Ebola sequelae, which is now characterized as Post-Ebola Syndrome (PES). PES encompasses a range of persistent health issues, including rheumatologic, ophthalmologic, psychologic, and neurologic conditions. In a study conducted in Eastern Sierra Leone, EVD survivors were found to be significantly more likely than age- and sex-matched controls to report difficulties such as sleep disturbances (14.2% vs 1.6%, p<.001), depression (12.5% vs 2.7%, p<.001), anxiety (8.9% vs 3.2%, p<.001), and hallucinations (11.3% vs 1.6%, p<.001), 2.5 years post-recovery. To delve deeper into these discrepancies, we conducted a pilot study involving 50 adult participants, split evenly between EVD survivors and matched controls. Employing Neurocognitive Assessment tools, we evaluated specific types of neurocognitive dysfunction approximately eight years after EVD recovery. Participants underwent a battery of validated neurocognitive tests covering processing speed, attention, executive functioning, and memory domains. Using linear regression and controlling for the effects of age, sex, and education, the group of EVD survivors performed significantly worse than controls on measures of attention (β=.32, p=.01), executive functioning (β =-.38, p=.01), and immediate memory (β =-.29, p=.04). There was no notable group difference observed in delayed memory recall (β=.14, p=.34). These initial findings are instrumental in deepening our comprehension of neurocognitive impairment among adult EVD survivors and elucidating the true impact of PES on this population.

8160

DISCREPANCY ANALYSIS BY USING DATA QUALITY ASSESSMENT AT COMMUNITY LEVEL IN RWANDA

Nyabugande Aimable

Rwanda Biomedical Center, Kigali city, Rwanda

Introduction:since 2013, malaria data reported through rwanda routine under the health information system. however prior supervisory assessments have revealed concerns regarding the accuracy and reliability of aggregated data from public health facilities across the country. system. Methods:This study was conducted in two districts such as Rulindo and Gisagara, under six health facilities, with 12 cells covered 24 villages. data were collected from January to March 2023. the key indicators such as malaria cases, RDT test and acts based on SISCom were compared to the same indicators based on records from chws data reported through the system for the same time period. We used T-test for data analysis.Result: In rulindo district, the malaria cases reported in the system out of chws data we found 3.0% (52/50) and acts reported in the system out of CHWs data were 1.0% (51/50) both level of discrepancy was acceptable, contrary to RDT reported into the system out of CHWs data 13.0% (52/40) where the level of discrepancy is not acceptable. Although, in Huye district, the malaria cases reported in the system out of CHWs data was 0.2% (1544/1539), ACT reported in the system out of CHWs data was 0.2% (1544/1537) and RDT reported in the system out of CHWs data were 0.2% (1543/1537), all discrepancies were acceptable.Conclusion:Our study found non significant different in the discrepancies observed for malaria indicators such as

malaria case,RDT and ACT within the system is acceptable based on WHO, there is a significant different for ACTs with P=0.0026 in the discrepancies observed in Rulindo district.However,discrepancy was increased for RDT reported both in the system and CHWs. Thus, we suggest that the improvement in working conditions for CHWs ,to respect malaria data validation meeting before reporting system.

8161

MOLECULAR DETECTION AND SEQUENCING OF GENES ENCODING THE PREDICTED AMIDASE, NADH UBIQUINONE OXIDOREDUCTASE AND SODIUM NEUROTRANSMITTER SYMPORTER ENZYMES IN *ONCHOCERCA VOLVULUS* PARASITE

Anabel Acheampong[1], Kenneth Bentum Otabil[1], John Asiedu Larbi[2], Prince Nyarko[2], Prince-Charles Kudzordzi[2], Godbless Owusu Adjei[1], Paulina Pokua Oduro[1]

[1]University of Energy and Natural Resources, Sunyani, Ghana, [2]Kwame Nkrumah University of Science and Technology, Kumasi, Ghana

Current evidence shows that mass drug administration of ivermectin alone may not be sufficient to achieve elimination of transmission of onchocerciasis by 2030 in some highly endemic foci. Drug repurposing may offer a cheaper and faster route of new drug development considering the ambitious timelines for elimination championed by the World Health Organization. However, there is insufficient knowledge on the metabolism and chokepoint metabolic enzymes which could serve as targets for repurposed drugs. This study set out to identify and sequence three previously predicted genes encoding amidase, NADH ubiquinone oxidoreductase and Sodium symporter in the *Onchocerca volvulus*, the causative agent of onchocerciasis. These potentially chokepoint enzymes are predicted to be encoded in the genome of the worm and may be inhibited by analgesics and other existing drugs. Briefly, extracted DNA from the parasites was amplified using the Proflex PCR system. The PCR products were visualized using gel electrophoresis and then sequenced via Sanger sequencing. The sequences were then compared with the predicted sequences. The amino acid sequences of the sequenced genes were determined using the Expasy translate tool and SWISS model was used to create the 3-dimensional alpha folding structures. Clustal Omega was used to determine the similarity between the enzymes in the parasite and other species. It was confirmed that the previously predicted genes encoding the three enzymes were present in the genome of adult *O. volvulus* parasite. The sequences of the genes amplified in this study were 100% identical to the sequences predicted previously and available in GenBank. From the 3-dimensional alpha fold structure of the proteins, we inferred that *O. volvulus* amidase is a single-pass membrane protein whilst NADH ubiquinone oxidoreductase and Sodium neurotransmitter symporter are multi-pass membrane proteins with roles in transport across the membranes Sequence analysis showed high similarity with *O. ochengi* for amidase and NADH ubiquinone oxidoreductase, and with *Caenorhabditis elegans* for sodium neurotransmitter symporter.

8162

INFECTION STAGE L3 OF *LOA LOA* AS POTENTIAL TARGET FOR PROTECTIVE IMMUNITY

Roland Dieki, Jean Paul AKUE

Centre International de Recherche Médicales de Franceville (CIRMF), Franceville, Gabon

Loa loa is a neglected filarial which has drawn attention this last thirty years. This is due to its negative impact on the WHO control program on mass chemotherapy in region where this filarial is co-endemic with *O. volvulus* or *W. bancrofti*, also a reduced life span has been observe in these area with individual carrying high density of *L. loa* microfilaria. Previous studies have shown that *L. loa* L3 might be linked to concomitant immunity. In order to search for potentiel protective molecule. L3 were harvest from natural infected *Chrysop* in different village of endemic region of Gabon and L3 isolated according to modified Baerman technique. The immunogenicity of L3 extract was evaluate after a separation by SDS-PAGE and probe by western blot with IgG1 and IgG4 of individual infected or exposed to *L. loa* from endemic country. In parallel to these experiments, *Brugia pahangi* adult extract was digested with *N-glycanase* or not digested. These extract were also probe with the IgG1 and 4 of the same individuals. Primers were designed from *B. pahangi ALT*-1, *ALT*-2 and *chitinase* genes follow by PCR using *L. loa* DNA as template. The result show that both IgG1 and IgG4 react with different L2 antigen with different molecular weight (from 8-110 kDa and 10-100 kDa respectively). The adult *B. pahangi* extract react with the same probe whether de glycosylated or not, suggesting that the reactivity is linked to peptide backbone. The amplification: using *L. loa* DNA as a template generate amplicon with size of 1200 bp for both *ALT*-1 and *ALT*-2 a supplementary band of 600 bp for *ALT*-2 while primers from chitinase generate amplicon of 1500 bp.Our results suggested that the natural *L. loa* L3 are immunogenic. The cross reactivity observe between *L. loa* and Lymphatic filarial is Linked to peptide backone. The amplicon generated with lymphatic filarial show the existence of homologue antigens for *ALT*-1,-2 and *chitinase* in *L. loa*. The extension of these homologies will be clarified after the ongoing sequencing of these amplicons.

8163

INFLAMMATION AND FIBRINOLYSIS IN LOIASIS PATIENTS BEFORE AND AFTER IVERMECTIN TREATMENT: POTENTIAL MECHANISM UNDER POST-IVERMECTIN SEVERE ADVERSE EVENTS

Tristan Lepage[1], Narcisse N. Toche[2], Lucie Nkwengoua[3], Hugues C. Nana-Djeunga[2], Sebastien D S Pion[4], Joseph Kamgno[2], Charlotte Boullé[4], Jérémy T. Campillo[5], Michel Boussinesq[4], Claude Tayou[3], **Cédric B. Chesnais**[4]

[1]Montpellier University Hospital, Montpellier, France, [2]Higher Institute for Scientific and Medical Research, Yaoundé, Cameroon, [3]University Teaching Hospital Yaounde, Yaoundé, Cameroon, [4]Institut de recherche pour le développement, Montpellier, France, [5]Inserm, Montpellier, France

Loiasis is often regarded as a relatively benign disease, but recent evidence suggests an association with excess mortality. In addition, there have been documented instances of thrombosis and micro-emboli formation in capillary vessels, both spontaneously and as part of post-ivermectin serious adverse events (SAEs). However, the hemostatic profile of individuals with loiasis has never been studied. A biological pilot study was conducted in a rural area of Cameroon to assess the impact of loiasis and the treatment with ivermectin on hematological, hemostatic, and biochemical blood parameters. A total of 38 adult participants were enrolled and categorized into four balanced groups based on their *Loa loa* microfilarial densities (Group A (N=10): 0 mf/ml, Group B (N=11) : 20-4160 mf/ml, Group C (N=7): 5380-19,580 mf/ml, Group D (N=10): 21,300-39,870 mf/ml). Subsequently, the 18 microfilaremic patients from groups B and C received ivermectin treatment. At baseline, no significant differences in hemostasis and inflammation parameters were found among the groups. However, a positive correlation was observed between microfilarial densities and granulocyte ($p=0.012$) as well as eosinophil ($p<0.001$) counts. Four days off treatment, a significant increase in D-dimer levels, from 725 ng/mL to 1276 ng/mL ($p=0.024$), was recorded. Prothrombin fragment 1+2 levels rose from 315 to 435 pmol/L, but this difference was not statistically significant ($p=0.313$). C-reactive protein, fibrinogen, and alpha-1-globulin levels also showed significant increases. Eosinophil counts markedly increased from 225/µL to 1807/µL ($p<0.001$). Ivermectin treatment appeared to induce inflammation and pronounced fibrinolysis, indicative of coagulation activation. These preliminary findings shed light on potential biological mechanisms underlying SAEs following ivermectin treatment in loiasis. Further comprehensive studies investigating the hemostatic profile in loiasis are warranted for a better understanding of this complex disease and its management.

8164

IMPACT OF THE FILARIAL INFECTIONS *ONCOCECA VOLVULUS, LOA LOA* AND *MANSONELLA PERSTANS* ON THE METABOLIC PROFILE OF LEAN, OVERWEIGHT AND OBESE INDIVIDUALS IN CAMEROON (FIMMIP)

Benjamin Lenz[1], Anita Obi Bate Ebob[2], Fanny Fri Fombad[2], Amuam Andrew Beng[2], Manuel Ritter[1], Indulekha Karunakaran[1], Narcisse Victor Tchamatchoua Gandj[2], Lucy Cho Nchang[2], Jayagopi Surendar[1], Chang Wang[1], Ute Klarmann-Schulz[1], Arcangelo Ricchiuto[1], Janina M. Kuehlwein[1], Ambe Marius Ngwa[2], Tatiana Djikeussi Katcho[2], Achim Hoerauf[1], Samuel Wanji[2], Marc P. Hübner[1]

[1]University Hospital Bonn, Bonn, Germany, [2]Universtiy of Buea, Buea, Cameroon

Type 2 diabetes is among the ten leading causes of death as identified by the WHO in 2019 with the prognosis that type 2 diabetes prevalence will increase the strongest in sub-Saharan Africa reaching an 134% increase by 2045. The FIMMIP study was designed to investigate the impact of filarial infections on metabolic diseases in rural Cameroon. In this open label pilot trial, 1619 participants infected with the filarial nematodes *Onchocerca volvulus* (n=359)*, Loa loa* (n=54)*, Mansonella perstans* (n=117), multiple filarial species (n=165) or filariae-free endemic participants (n=924), being lean (BMI <25), overweight (BMI 25-30) or obese (BMI ≥30) were analysed for their parasitological, anthropomorphic and metabolic profile. Filariae-infected participants had significantly reduced levels of circulating liver enzymes (ALP, ALT, AST and γGT) as well as increased markers associated with kidney health (urine microalbumin, serum creatinine). Similarly, C-reactive protein, a marker associated with obesity-derived inflammation, was significantly reduced in filariasis patients. Strikingly, glycated hemoglobin (HbA1c) values were significantly reduced in filariasis patients and diabetes prevalence (HbA1c >48 mmol/mol Hb) was 2.3 times lower in the filariasis patients (31% vs. 13.4%). Furthermore, comparing the impact of *O. volvulus, L. loa* and *M. perstans* infection indicated filarial-species dependent differences with *M. perstans* infections inducing the strongest beneficial impact on liver enzymes, CRP levels, kidney markers, and lowest rate of diabetes prevalence (9.4%). Ongoing analyses include multiplex assays to assess the immunological profile, insulin and adipokine levels as well as the comparison of the metabolic and immunological profile 12 and 18 months following doxycycline treatment in *O. volvulus* and *M. perstans*-infected participants. Taken together, our study suggests that filarial infections improve metabolic parameters and protect against the development of type 2 diabetes with *M. perstans* infected individuals showing the most striking effects.

8165

DOXYCYCLINE TREATMENT REDUCES IMMUNE ACTIVATION OF CD4$^+$ T CELLS AS WELL AS CLINICAL SIGNS OF INFLAMMATION IN PATIENTS WITH FILARIAL LYMPHEDEMA IN TANZANIA

Anja Feichtner[1], Sacha Horn[1], Abdallah Ngenya[2], Max Demetrius[2], Winifrida John[2], Ndekya Urio[2], Jubin Osei-Mensa[3], Ute Klarmann-Schulz[4], Janina Kuehlwein[4], Manuel Ritter[4], Achim Hoerauf[4], Michael Hoelscher[1], Linda Batsa Debrah[3], Alexander Debrah[3], Upendo Mwingira[2], Akili Kalinga[5], **Inge Kroidl**[1]

[1]University Hospital of the University of Munich (LMU), Munich, Germany, [2]National Institute for Medical Research (NIMR)-, Dar es Salaam, Tanzania, United Republic of, [3]Kumasi Centre for Collaborative Research in Tropical Medicine (KCCR), Kumasi, Ghana, [4]Institute of Medical Microbiology, Immunology and Parasitology (IMMIP), University Hospital of Bonn (UKB), Bonn, Germany, [5]National Institute for Medical Research (NIMR)-, Dar es Salaam, Ghana

Filarial lymphedema (LE) is caused by chronic infection with *Wuchereria bancrofti* (WB), a mosquito-borne nematode. Around 51 million people worldwide are infected with WB, and 15 million suffer from filarial LE. As part of an ongoing clinical trial to test the efficacy of doxycycline, people were recruited in Tanzania as part of the TAKeOFF-LEDoxy-trial. Four hundred and twenty participants were randomized to receive either doxycycline, 100 mg or 200 mg per day, or placebo for 6 weeks. The average age of the participants was 51 years and 67% were female. In addition to clinical characteristics, immunological aspects of the different treatment groups were measured at baseline, end of doxycycline treatment (day 42) and after 6 and 24 months in a subgroup of participants. In total, whole blood from 42 patients was analyzed for the presence of regulatory T cells (Tregs) and immune activation markers (CD38/HLADR) on CD4$^+$ T cells. All 42 participants were recruited in the dry season, the 6-month visit took place in the rainy season, and the 24-month visit took place in the dry season. In terms of immune parameters, the values for all treatment groups on day 42 were comparable to the baseline results of CD38$^+$/HLADR$^+$ and regulatory CD4$^+$ T cells. In contrast, the 6-month visit showed a significant increase in immune activation parameters and a decrease in Tregs for participants of the placebo group, but not for the doxycycline 200mg group. Interestingly, these results were consistent with the clinical data, as after 6 months the placebo group had a significantly higher number of individuals with acute adenolymphadenitis (ADL), an acute clinical manifestation characterized by recurrent attacks of fever that is associated with inflammation caused by secondary bacterial infection that enter the body via wounds and damaged skin. This difference resolved at subsequent visits, most likely due to the effect of intensive and regular hygiene training, which prevented wounds, inflammation and with that progression of LE in all treatment groups. Similar to those clinical findings at 24 months, all groups showed reduced immune activation.

8166

EVALUATION OF THE BIOLOGICAL ACTIVITY OF CHEMICAL CONSTITUENTS FROM THE STEMBARK OF *KIGELIA AFRICANA*, A CAMEROONIAN MEDICINAL PLANT, AGAINST *ONCHOCERCA OCHENGI* PARASITES

Ghansenyuy Salome Yuwong[1], Yemback Piere[1], Eyong Kenneth Oben[1], Gabriel Ngosong Folefoc[1], Fidelis Cho Ngwa[2]

[1]University of Yaounde 1, Yaounde, Cameroon, [2]University of Buea, Buea, Cameroon

Onchocerciasis is the second leading infectious cause of blindness, with about 21 million people infected and 120 million persons at risk of infection worldwide. It is caused in man by the filarial worm, *Onchocerca volvulus*. For over 30 years, Mass treatment with ivermectin has been the mainstay control/elimination strategy for this disease. In recent years, moxidectin has been approved for the treatment of onchocerciasis. Both drugs are only effective against the microfilarial form of *O. volvulus*, but not the adult worms which may live for upto 15 years in patients. Also, the emergence of resistance to ivermectin in parasitic nematodes of veterinary importance raises serious concerns that this may extend to the human *O. volvulus.* Therefore, the search for new and highly effective filariacides is imperative. About 50 % of drugs used in modern medicine are of plant origin and about 80 % of Africa's population relies on medicinal plants for their health needs. *Kigelia africana* is described in the Cameroon national herbarium and is used locally to treat skin diseases including onchodermatitis, a symptom of onchocerciasis. To investigate the potential of *Kigelia africana,* fractions (hexane-ethyl acetate 10 %, hexane-ethyl acetate 25 %, and ethyl acetate 100 %) were extracted and pure compounds (lapachol, 2-(1-hydroxyethyl-2-acetylnaphtho [2,3-b] furan-4,9-dione and 2-acetyl-naphto [2,3-b]furan-4,9-dione) were isolated from the stembark of this plant against *Onchocerca ochengi*, a bovine onchocerciasis parasite closely related to *O. volvulus*. The pure compounds belong to the quinone class. The hexane-ethyl acetate 25 % fraction showed the best activity, having a 100 % inhibition at a concentration of 125 µg/ml meanwhile, all the pure compounds were found to be very active, showing complete inhibition at a concentration of 5 µg/ml. All the tested fractions and pure compounds showed varying degrees of toxicity on the monkey epithelial cells which served as hosts for the filarial parasites. These findings open new avenues on research and development of new therapeutic agents for the treatment of onchocerciasis.

8167

EVALUATION OF SLASH AND CLEAR COMMUNITY-DIRECTED ONCHOCERCIASIS VECTOR CONTROL INTERVENTION IN THE TROPICAL RAINFOREST OF LIBERIA

Dawn Blackburn[1], Elizabeth M. Wendt[1], Sonnie Z. Gbewo[2], Larry Gee[2], Ben Masiira[3], Andrew Abbott[1], Paul Cantey[1], Thomson L. Lakwo[3], Karsor K. Kollie[2]

[1]Centers for Disease Control and Prevention, Atlanta, GA, United States, [2]Department of Health Services, Ministry of Health-Liberia, Monrovia, Liberia, [3]African Field Epidemiology Network (AFENET), Kampala, Uganda

Onchocerciasis is caused by a parasitic worm known as *Onchocerca volvulus* that is transmitted by repeated bites of *Simulium* blackflies. Onchocerciasis programs rely on mass drug administration of ivermectin, which may be insufficient to eliminate the parasite. Slash and clear (S&C) is the removal of trailing vegetation to which blackfly larvae attach. It has significantly reduced *Simulium damnosum* sp. biting rates in some settings. We evaluated the effectiveness of S&C in reducing the biting rate of *Simulium yahense* in the tropical rainforest of Liberia. We identified two comparable control (Baila) and intervention (Gargar) sites along River St. John in Bong County. Baseline fly collection was conducted by human landing catching for 7 days at each site followed by S&C at the intervention site in November 2022. Flies were then collected 2 times per week from December 2022 until November 2023 at both sites. Daily biting rates (DBR) were calculated by dividing the number of flies collected by number of days of collection. Independent sample T-tests were used to show differences in DBR at control and intervention sites. After S&C, DBR progressively decreased at the intervention site, with a significant difference from baseline at 4 months post S&C ($p < 0.05$), while in the control site there was an initial increase in DBR followed by a downward trend over the same period. There was a maximum reduction from baseline of 79% at 4 months post S&C compared to an increase of 7% at the control site, which is significant ($p<0.05$). By 7 months post S&C, daily biting rates at both sites returned to baseline levels, after which the Gargar (intervention) site DBR increased until again falling below pre-S&C levels while the Baila (control) site DBR steadily increased until plateauing. The change in biting rate at the intervention site was not as pronounced, time to decline was slower, and suppression was not as sustained as what was reported in savanna grassland settings. Adjusting the timing and frequency of S&C is planned to evaluate these differences. S&C is a low-cost, community-directed intervention that may reduce *S. yahense* biting rates in Liberia.

8168

PARASITOLOGICAL INDICATORS SUGGESTS THAT ONCHOCERCIASIS MIGHT LIKELY NEVER BEEN ELIMINATED IN THE YABASSI HEALTH DISTRICT (LITTORAL REGION, CAMEROON) USING IVERMECTIN SOLELY: URGENT NEED OF COMPLEMENTARY INTERVENTIONS

Laurentine Sumo[1], Gabriella S. Ondoua Nganjou[2], Narcisse Nzune Toche[2], Louis-Rolph Bamou Heumou[2], Arnauld Efon Ekangouo[2], Linda Djune Yemeli[2], Yannick Emalio[2], Jean Bopda[2], Jeanne C. Sondi Dissake[2], André Domche[2], Shannon M. Hedtke[3], Warwick N. Grant[3], Flobert Njiokou[4], Joseph Kamgno[2], Hugues C. Nana Djeunga[2]

[1]University of Ebolowa, Ebolowa, Cameroon, [2]Higher Institute for Scientific and Medical Research (ISM), Yaoundé, Cameroon, [3]La Trobe University, Melbourne, Australia, [4]University of Yaoundé I, Yaoundé, Cameroon

Ivermectin has been the mainstay of the control of onchocerciasis through annual mass administration under community directives. This strategy has been successful in transmission elimination of onchocerciasis in certain foci in Africa, leading to the shift of the paradigm of the fight against onchocerciasis from control to elimination. Despite this sustained effort, hotspots for transmission of the infection have been identified in certain foci, as it was the case in 2015 in the Yabassi Health District where onchocerciasis was still meso-endemic after more than 15 years of uninterrupted ivermectin based-mass treatments. This study therefore aimed to assess prevalence and intensity of *Onchocerca volvulus* infection in the Yabassi Health District after 10 additional annual rounds of mass drug administration. A cross-sectional survey was therefore conducted in first- and second-line communities of the Yabassi Health District. All volunteers aged 5 years and above underwent clinical and parasitological examinations. Two skin snips were collected from the posterior iliac crest of each participant using a 2mm corneoscleral Hold-type punch and examined for *O. volvulus* microfilaridermia. Of the 572 enrollees, 181 (31.6%; 95% CI: 28.0% - 35.6%) presented with microfilariae under the skin, with the mean microfilarial density estimated at 8.13 (standard deviation, SD: 34.5) mf/ss. In the sentinel communities visited in 2015, *O. volvulus* parasitological indicators remained unchanged, from 43.8% (95% CI: 37.7% - 50.1%) to 38.8% (95% CI: 33.0% - 45.0%), after 10 additional yearly rounds of uninterrupted treatment with ivermectin (Chi-square: 1.49; df: 1; *p*: 0.222). These results indicate that ivermectin solely might not be enough to eliminate transmission of onchocerciasis as predicted by mathematical models, and call for introduction of targeted complementary/alternative interventions to accelerate the elimination of this debilitating disease.

8169

REBOUND IN PREVALENCE AND INTENSITY OF ONCHOCERCA VOLVULUS INFECTION FIVE YEARS AFTER CESSATION OF ALTERNATIVE TREATMENT STRATEGIES IN THE MASSANGAM HEALTH DISTRICT, WEST REGION, CAMEROON: NEED FOR COORDINATED AND SUSTAINED EFFORTS

Gabriella Sandrine Ondoua Nganjou[1], Laurentine Sumo[2], Narcisse Nzune Toche[3], Arnauld Efon Ekangouo[3], Linda Djune Yemeli[3], Yannick Emalio[4], Jean Bopda[4], Jeanne Crescence Sondi Dissake[1], André Domche[1], Ivana Youmbi Kammogne[1], Shannon Hedtke[5], Warwick Grant[5], Flobert Njiokou[1], Joseph Kamgno[6], Hugues Clotaire Nana Djeunga[4]

[1]Department of Animal Biology and Physiology, Faculty of Science, University of Yaoundé I, Yaoundé, Cameroon, [2]Department of Animal Biology and Physiology, Faculty of Science, University of Ebolowa, Ebolowa, Cameroon, [3]Department of Biochemistry, Faculty of Science, University of Yaoundé I, Yaoundé, Cameroon, [4]Higher Institute for Scientific and Medical Research (ISM), Yaoundé, Cameroon, [5]Department of Environment and Genetics, La Trobe University, Melbourne, Australia, [6]Department of Public Health, Faculty of Medicine and Biomedical Sciences, University of Yaoundé I, Yaoundé, Cameroon

The control of onchocerciasis currently relies on yearly distribution of ivermectin to at-risk populations. To tackle onchocerciasis in hotspots and achieve elimination of transmission, several complementary/alternative strategies (biannual ivermectin, doxycycline-based test-and-treat and vector control) have been implemented in Massangam Health District (HD), and short-term impact evaluation showed significant reductions in the endemicity levels in three focal hotspot communities (Makouopsap, Makankoun, and Njinja-Njingouet). Since this three-years pilot initiative stopped, this study therefore aimed to assess the situation of onchocerciasis in the focal hotspot communities five years after the cessation of alternative strategies. A quantitative cross-sectional survey was conducted in December 2023 in the three focal hotspot communities. Participants underwent a comprehensive assessment that involved interviews, clinical examinations and skin snipping to establish *Onchocerca volvulus* microfilaridermia. The overall prevalence of *O. volvulus* infection in the three focal communities was 18.8% (95% CI: 13.8-24.3), the highest prevalence (30.8%) being found in the community Makankoun. The intensity of infection was 3.136 (standard deviation, SD: 19.3099) mf/ss, ranging from 5.218 mf/ss (Mankakoum community) to 2.840 mf/ss (Njinja-Njingouet community). The parasitological indicators significantly increased five years after the cessation of Alternative Treatment Strategies (ATS) in all three focal communities ($\chi^2 = 4.18$; df = 2; $p = 0.0409$) compared with their baseline levels (end of ATS implementation). These findings indicate a rebound in onchocerciasis transmission and underscore the need for coordinated and

sustained efforts, which can be implemented in a transmission zone as recommended by the WHO, to achieve the elimination goals outlined in the 2021-2030 roadmap to end the neglect and achieved SDGs.

8170

ADMINISTRATION OF THE SUPERVISOR'S COVERAGE TOOL TO ASSESS THERAPEUTIC COVERAGES OF MASS DRUG ADMINISTRATION FOR ELIMINATION OF NEGLECTED TROPICAL DISEASES IN 3 LGAS OF AKWA IBOM STATE, NIGERIA

Aliyu Mohammed[1], Kingsley C. Azu[1], Salisu Ahmad[1], Unyime Ekpoudia[1], Louise Makau-Barasa[2], Ellie Leaning[2]

[1]Hellen Keller International, Abuja, Nigeria, [2]The END Fund, New York, NY, United States

Between June and July 2023, mass drug administration (MDA) for the control and elimination of schistosomiasis (SCH), onchocerciasis (oncho), and lymphatic filariasis (LF) were conducted in 15 SCH endemic LGAs, 4 oncho endemic LGAs, and 1 LF endemic LGA in Akwa Ibom state, Nigeria. Directly following the MDA, the WHO's Supervisors Coverage Tool (SCT) was administered in 3 LGAs (Ibeno, Udung Uko and Ini) to ascertain the status of the SCH, LF and Oncho therapeutic coverage rates following the MDA, identify gaps in treatment, and inform an action plan to emergent and reported challenges. The SCT followed the approved WHO methodology, including training activities, a survey using an open data kit, and the WHO Decision Rule guide to determine coverage. The result of the SCT indicated the status of the MDA as well as the treatment coverage in the 3 LGAs and recommended actions to improve NTD programming in the state. The main gaps identified during the SCT were (1) the absence of target individuals during MDA implementation, (2) issues of over/underreporting, and (3) Praziquantel/drug paucity. These gaps could be addressed by adjusting the timing of MDA delivery in the communities to conduct MDAs in the morning and evening when the majority of families are in the house, increased advocacy to the key stakeholders and/or training to the medicine distributors and supervisors, and improved coordination between stakeholders.

8171

MANAGEMENT PRACTICES AND THEIR ASSOCIATED FACTORS AMONG LYMPHOEDEMA PATIENTS ATTENDING LYMPHOEDEMA CLINICS IN SELECTED ENDEMIC DISTRICTS FOR LYMPHATIC FILARIASIS IN SRI LANKA

Sithija S. Perera[1], Nipuni K. Shilpeswarage[2], **Indeewarie E. Gunaratna**[2]

[1]Regional Filariasis Unit, Puttalam, Sri Lanka, [2]Anti Filariasis Campaign, Colombo 05, Sri Lanka

<Lymphatic filariasis is one of the main causes of lymphoedema in tropical endemic countries. Sri Lanka reports around 500-900 lymphoedema patients annually despite validation as eliminating the disease in 2016. Majority of new patients reported are in the early stages. Good management practices can prevent disease progression to disabling complications. Therefore, this study was conducted to determine factors associated with morbidity management practices among lymphoedema patients attending lymphoedema clinics in three filariasis endemic districts in Sri Lanka. This was a clinic-based cross-sectional study conducted among 405 lymphoedema patients selected through consecutive sampling. A pre-tested interviewer-administered questionnaire was used to collect data. The chi-square test was used to determine the association of all factors with the practices of lymphoedema management. The sample consisted of 51.4% of males, 88.1% had unilateral lymphoedema and 58.5% were in the early stages. The knowledge of skincare (58.6%), compression (74.9%) and management of acute attacks (64.2%) was good among most patients. The attitude was good among 94.1%. More than half the patients had good practice in skincare, use of topical antibiotics, elevation, wearing comfortable footwear and compression. Age and civil status were associated with the practice of exercise (P<0.05) and elevation (P<0.01). Level of education and income were associated with all practices (P<0.001) except skincare. Having a good knowledge of the same practice showed a statistically significant association in the practice of hygiene and skin care (P<0.001), footwear (P=0.001) and compression (P<0.001). Good attitudes were significantly associated with the practice of elevation (P<0.001). Quality of life was associated with all practices (P<0.001). Awareness programs should be organized for patients and health staff to improve practices. Prospective studies with control groups would establish the impact of interventions of morbidity management practices.>

8172

ADAPTIVE BASKET TRIAL TO ASSESS THE EFFICACY AND SAFETY OF OXFENDAZOLE AS PAN-NEMATODE CANDIDATE IN ONCHOCERCIASIS, LOIASIS, MANSONELLOSIS AND TRICHURIASIS PATIENTS

Marc P. Hübner[1], Sonja Zehetmayer[2], Jennifer Keiser[3], Ghyslain Mombo-Ngoma[4], Dieudonne Mumba Ngoyi[5], Michael Ramharter[6], Samuel Wanji[7], Marta Bofill Roig[2], Fabrice Lotola Mougeni[2], Annina S. Schnoz[3], Rella Zoleko Manego[4], Lidwine Badjina[6], Benjamin Lenz[1], Alexander Kazakov[1], Ivan Scandale[8], Frederic Monnot[8], Achim Hoerauf[1], Martin Posch[2], Sabine Specht[8]

[1]Institute for Medical Microbiology, Immunology and Parasitology, University Hospital Bonn, Bonn, Germany, [2]Center for Medical Data Science, Medical University of Vienna, Vienna, Austria, [3]Swiss Tropical and Public Health Institute, Basel, Switzerland, [4]Centre de Recherches Médicales de Lambaréné (CERMEL), Lambaréné, Gabon, [5]Institute National de Recherche Biomédicale (INRB), Kinshasa, Congo, Democratic Republic of the, [6]Bernhard Nocht Institute for Tropical Medicine (BNITM), Hamburg, Germany, [7]University of Buea, Buea, Cameroon, [8]Drugs for Neglected Diseases initiative (DNDi), Geneva, Switzerland

Oxfendazole is a broad-spectrum veterinary anthelmintic that offers a number of advantages that are desirable for a new anthelmintic agent for human use. The safety and broad spectrum efficacy of oxfendazole are consistently demonstrated in intestinal helminth infections in animals, as well as tissue-dwelling larval cestode and trematode infections in diverse animal species. First-in-human safety and pharmacokinetic data have shown its safety in humans at acceptable exposure. In experimental filarial infections, oxfendazole acts against adult worms, but not the microfilarial stage, which is expected to prevent microfilariae-induced adverse events in onchocerciasis and loiasis patients. Thus, oxfendazole represents a promising candidate to expand the limited portfolio of anthelmintic drugs available. A field-applicable formulation for early studies in infected patients was developed and confirmed its safety and tolerability via the EU HELP consortium. Via EU EDCTP3 funding, the eWHORM consortium is now conducting a "basket trial" approach for the first time in NTDs, assessing efficacy and safety in onchocerciasis, loiasis, mansonellosis and trichuriasis patients at the same time in four sub-Saharan African countries. To harmonize procedures among different study sites and diseases, a master protocol was developed and data simulations were used to design this adaptive basket trial, which includes an interim analysis six months after oxfendazole treatment. Based on the results from the interim analyses, midcourse adaptions will drop non-efficacious treatment arms and allocate additional study participants to the efficacious treatment arms or initiate a new treatment arm. This patient centric approach allows for the first time not only the inclusion of co-infected patients, but at the same time to detect country-specific differences in efficacy. Such an adaptive basket trial design avoids costly repetitions, allows quicker decisions and expedites drugs to market. The eWHORM consortium aims to provide the proof of concept of oxfendazole as pan-nematode drug candidate for future registration studies.

8173

RESULTS OF STOP TREATMENT ASSESSMENTS FOR ONCHOCERCIASIS IN SEVEN DISTRICTS OF LOWER MADI MID NORTH FOCUS, UGANDA

Annet T. Khainza[1], David W. Oguttu[2], Lauri Bernard[3], Edridah Tukahebwa Muheki[1], Edson Byamukama[1], Christine Nahabwe[2], Monica Ngabirano[2], Alfred Mubangizi[2], Thomas R. Unnasch[4], Frank O. Richards[3], Gregory S. Noland[3]

[1]The Carter Center, Kampala, Uganda, [2]The Ministry of Health, Kampala, Uganda, [3]The Carter Center, Atlanta, GA, United States, [4]The University of South Florida, Tampa, FL, United States

In Uganda, onchocerciasis was initially reported in 17 foci. The largest of these foci, the Madi Mid North (MMN) focus, comprising 11 districts and one city in northern Uganda bordering the Republic of South Sudan, is one of two foci where mass drug administration (MDA) with ivermectin remains ongoing. In 2019, the Uganda Onchocerciasis Elimination Expert Advisory Committee (UOEEAC) classified MMN as "transmission suspected interrupted" after the focus passed initial entomological and epidemiological sentinel site assessments. Stop-MDA entomological (2021-2023) and epidemiological (2023) assessments were conducted in the seven southernmost districts of MMN that are thought to be at lower risk of reintroduction of onchocerciasis as they do not share a border with South Sudan. None of the 3,499 blood samples from children under 10 years of age tested positive (95% upper confidence limit [UCL] <0.001) for Ov16 antibodies by ELISA, and none of the 293 pools of 19,537 collected *Simulium* black flies caught were positive for parasite O-150 DNA (95% UCI, 0.2/2000) by PCR, thus meeting WHO stop-MDA criteria of <0.1% Ov16 prevalence and <1/2000 infective black flies with 95% confidence. Based on this evidence, the UOEEAC recommended in August 2023 to halt MDA and begin post-treatment surveillance (PTS) in the seven districts of lower MMN with a population of 1,121,520 people—the single largest stop-MDA recommendation in the history of Uganda's onchocerciasis elimination program. PTS will continue until transmission elimination is achieved in the entire MMN cross-border focus.

8174

BARRIERS TO MORBIDITY MANAGEMENT AND DISABILITY PREVENTION (MMDP) CARE IN BENISHANGUL GUMUZ REGION, ETHIOPIA

Wasihun E. Toli[1], Belete Mammo[1], Shambel Belete[1], Abebual Yilak[1], Alyssa R. Lindrose[2], Elizabeth Sutherland[3], Misbah Noor[3], Fikre Seife[4], Merga Mekonnon[4], Meagan Meekins[3], Biruck Kebede[1], Tibebu Alemayehu[3], Molly Brady[5]

[1]RTI International, Addis Ababa, Ethiopia, [2]RTI International, Washington, DC, United States, [3]RTI International, Research Triangle Park, NC, United States, [4]Ministry of Health, Addis Ababa, Ethiopia, [5]RTI International, Indianapolis, IN, United States

Despite achievements in scaling up preventive measures in lymphatic filariasis (LF) endemic regions in Ethiopia, access to lymphedema and hydrocele care remains low in many areas. This assessment evaluated areas previously targeted for LF morbidity management and disability prevention (MMDP) service provision and explored barriers to MMDP services. A modified Direct Inspection Protocol (DIP) and Hydrocele Surgery Facility Assessment Tool (HSFAT) were conducted in three woredas of Benishangul Gumuz Region in March 2024 across 6 health facilities, 2 hospitals, and 8 health posts. Key informant interviews (KIIs) were held with patients, service providers, program officers and managers and Community-Based Health Insurance (CBHI) Officers. The average DIP score was 61%, with 2 facilities only slightly below the 75% benchmark. While health facility staff were able to correctly identify aspects of MMDP care in the DIP, KIIs reported lack of adequate MMDP knowledge and skills arising from poor continuity of training, staff turnover/workload, and lack of job aids and guidelines. While Ethiopia has integrated MMDP indicators into the health system database, half of facilities and both hospitals showed weak documentation of MMDP in registration books and patient charts. Use of Ethiopia's CBHI benefit package was weak and non-standardized in the woredas visited. Few facilities provide services for MMDP through CBHI for those enrolled. Affected persons are often obliged to pay high costs out of pocket for hydrocelectomies and medicines. However, both hospitals generally possessed the infrastructure, capacity, and supplies needed for hydrocele surgery. Findings in Benishangul Gumuz highlight the need for strengthened integration of MMDP case management in CBHI and improving overall implementation of CBHI as a strategy for sustainable financing, universal health coverage and equity. To further scale up and enhance accessibility, affordability, and service quality for MMDP services, strengthened integration and ownership, as well as financial, technical, and logistical support are needed.

8175

PROGRAMMATIC IMPLEMENTATION OF THE TRIPLE DRUG MASS DRUG ADMINISTRATION FOR LYMPHATIC FILARIASIS ELIMINATION IN HAITI

Farah-Nelhy M. Momprevil1[1], Marc-Aurele Telfort[1], Mérilien Jean-Baptiste[1], Lali Chania[2], Katina Sommers[2], Wedsanley Jean Philippe[3], Tara Brant[4], Jennifer Akamboe[4], Emily Dodd[4], Jamal Choice[4], Caitlin M. Worrell[4], Mary Kamb[4], Andreas M. Nshala[4]

[1]Nationaux de Malaria et de Filariose Lymphatiqe, CPNMFL, Ministry of Public Health and Population, Port-au-Prince, Haiti, [2]IMA World Health, Washington, DC, United States, [3]IMA World Health, Port-au-Prince, Haiti, [4]Centers for Disease Control and Prevention, Atlanta, GA, United States

Haiti is one of four countries in the Americas endemic for lymphatic filariasis (LF). Haiti recently adopted the WHO-recommended triple drug strategy for mass drug administration (MDA) using ivermectin, diethylcarbamazine, and albendazole (IDA) to accelerate elimination of LF. We report on program results for the first Haitian commune implementing IDA MDA. In September 2023, Le Ministère de la Santé Publique et de la Population (MSPP) conducted a 10-day MDA campaign using IDA in Limonade, a semi-urban commune in the North department. A one-month community mobilization and sensitization preceded the MDA. Trained community drug distributers distributed IDA to all eligible individuals through door-to-door and fixed posts. School-aged children were reached either at home or in schools. All MDA participants were dosed by weight. Adverse events were managed at local health facilities. Treatment data were recorded electronically and monitored daily. Among 60,815 inhabitants living in Limonade, 45,568 (74.9%) were offered the medications and 45,265 (74.4%) swallowed them. Of people accepting treatment, 98.6% reported being residents of Limonade and 1.4% were from neighboring communes. Treatment coverage was similar among females (47.1%) and males (52.9%). One third of the people treated were school-aged children. Overall, 0.7% (n=303) of people offered treatment refused the MDA. Most common reasons for refusal were fear of side events and the desire to take pills at home. A total of 23,061 (50.9%) people were treated via door-to-door approach, 17,990 (39.7%) in fixed posts, and 4,214 (9.3%) in schools. Mop-up treatments were given to 1,845 (4%) out of all people treated. Only 44 (0.1%) people reported an adverse event, usually (nausea or headache); no serious adverse events were reported following treatment. The high coverage and overall success of IDA MDA in Limonade demonstrates its feasibility in other Haitian communes. The challenges and successes in Limonade can serve as a blueprint for scale-up in all endemic communes and in other country LF elimination programs.

8176

THE HEALTH AND WELLNESS IMPACT OF HOPE GROUPS FOR PEOPLE WITH LYMPHATIC FILARIASIS IN EBONYI STATE, NIGERIA: PATIENT DATA AT BASELINE

Abel Eigege[1], Jenna E. Coalson[2], Christopher Nwuzor[1], Samuel Ifeanyichukwu[1], Bulus Mancha[1], Lindsay Rakers[2], Emily Griswold[2], Emmanuel Miri[1], Gregory S. Noland[2], Hyacinth Ebenyi[3], Ifeanyi Nwofoke[3], Ngaji Ogaji[3], Edwin Okpani[3], David Nweke[4], Martha Nwiboko[5]

[1]The Carter Center, Jos, Nigeria, Nigeria, [2]The Carter Center, Atlanta, GA, United States, [3]Ebonyi State Ministry of Health, Abakaliki, Nigeria, Nigeria, [4]Alex Ekwueme Federal University Teaching Hospital, Abakaliki, Nigeria, Nigeria, [5]Ebonyi State University, Abakaliki, Nigeria, Nigeria

Lymphatic filariasis (LF) is a chronic disease that is highly stigmatized in Nigeria, the third most LF-endemic country globally by prevalent case count. The Carter Center has used "Hope Groups," nurse-led support groups, in Plateau and Nasarawa states of Nigeria since 2003 to provide ongoing support to people living with LF as part of morbidity management and disability prevention (MMDP). We aim to evaluate the impact of this program on a cohort of adult LF cases as it is newly introduced in Ebonyi state, Nigeria. Baseline data were collected on demographics, physical manifestation of LF, disability status (WHO Disability Assessment Schedule [WHODAS] 12-item tool), depression status (Patient Health Questionnaire [PHQ]-9 tool, social support (Oslo social support scale), and perceived stigma. Of 197 total participants, 67.5% were male. Sixty-nine (35%) had hydrocele and 128 (65%) had lymphedema, of which 43 (33.3%) had ulcer complications and 27 (21.1%) had fungal infection from lymphedema. Disability scores were moderate, averaging 35.7 (sd 13.5) on a scale from 12 (mild) to 60 (extreme). PHQ-9 scores indicated poor depression status in the cohort; 95% met the criterion for depression requiring mental health care referral (score 10+) and 71% met the criterion for severe depression (scores 20-27). Disconcertingly, 57% of the participants reported considering self-harm nearly every day in the prior two weeks. Most participants (59%) reported poor social support (Oslo support score 3-8), 27% had moderate support (scores 9-11), and only 13% reported strong support (scores 12-14). Most (68%) also responded in the affirmative to all three dichotomous stigma questions. Based on the high PHQ-9 scores, additional support is needed beyond the initial Hope Group plan. The intervention will incorporate WHO's Mental Health Gap Action Program (mhGAP) training for the Hope Group facilitators to enhance care.

8177

MASS SURGERY WEEKS FOR TREATMENT OF HYDROCELE DUE TO LYMPHATIC FILARIASIS IN PLATEAU AND NASARAWA STATES, CENTRAL NIGERIA, 2020 - 2021

Abel Eigege[1], Nuhu K. Dakum[2], Christian Agbo[2], Henry Embu[2], Sumi Benjamin Garkuwa[3], Bulus S. Mancha[1], Samuel Audu Kwarsen[3], Mafwalal Bunah Masok[3], Philemon Dagwa[3], Ibrahim Adamu[4], Jacob Danboyi[4], Emmanuel Davies[5], Nseobong Akpan[5], John Umaru[1], Lindsay Rakers[6], Emily Griswold[6], Frank O. Richards[6], Gregory S. Noland[6], Emmanuel S. Miri[1]

[1]The Carter Center, Jos, Nigeria, [2]Jos University Teaching Hospital, Jos, Nigeria, [3]Plateau State Ministry of Health, Jos, Nigeria, [4]Nasarawa State Ministry of Health, Lafia, Nigeria, [5]Federal Ministry of Health, Abuja, Nigeria, [6]The Carter Center, Atlanta, GA, United States

Lymphatic filariasis (LF) is a neglected tropical disease with high burden in Nigeria. Despite significant progress in interrupting transmission, people with past lymphatic damage from LF can continue to suffer severe morbidity. Hydrocele is a common manifestation which can require surgery to treat, but sufferers often live in areas with limited access to surgeons. We report the results of a program of mass surgery weeks (MSW) between 2020 and 2021 supported by the Carter Center to provide hydrocelectomy services to men with filarial scrotal hydrocele in Plateau and Nasarawa states in central Nigeria. Patients were mobilized to five general hospitals by Local Integrated Health Team members in the catchment areas using their patient line-listings, which included telephone numbers. Patients were pre-screened on arrival at the hospitals for hydrocele surgery eligibility by physical examination and ultrasound. Approved patients had the hydrocelectomy surgical procedure and postoperative follow-up explained to them. In general, the operation was performed under local anesthesia using lignocaine infiltration of the scrotal skin and spermatic cord. If general anesthesia was needed, intravenous ketamine was administered with local lignocaine. The technique used was making a vertical (median raphe) skin incision to deliver the sac for hydrocelectomy, or making oblique incision along the affected groin down to the spermatic cord for hernia. Local general practitioners supervised by two urologists performed 492 surgical repairs (hydrocele 430; hernia 62) in 378 men over seven MSW in five semi-urban Nigerian community hospitals with excellent outcomes. Postoperative complications were uncommon among the 93% who returned for recommended follow-up, including hematoma (1%) and infection (2%). MSW can be a safe and effective method of delivering LF morbidity management in remote areas if candidates are preoperatively screened and surgeons are supervised by qualified urologists.

8178

DETERMINING THE FUNCTION OF AN APICOPLAST-LOCALIZED GTPASE IN *TOXOPLASMA GONDII*

Michael B. Griffith, Victoria L. Robinson, Aoife T. Heaslip

University of Connecticut, Storrs, CT, United States

The apicomplexan phylum contains a diverse group of obligate intracellular parasites which are the causative agents of medically relevant diseases including malaria and toxoplasmosis. Many of these parasites contain a four-membraned non-photosynthetic plastid organelle, termed the apicoplast, which produces several essential metabolites that the parasite cannot scavenge from the host. As loss of the apicoplast is lethal to the parasite, characterization of apicoplast proteins provides valuable insight into novel pathways of apicoplast biology which can be targeted for therapeutic intervention. While the apicoplast genome encodes multiple proteins, most apicoplast-localized proteins are nuclear encoded and trafficked to the apicoplast. Despite their importance, many apicoplast proteins remain uncharacterized. Our lab has identified a homolog of a prokaryotic translational GTPase(trGTPase) BipA in *Toxoplasma gondii*, termed TgBipA. Based on high-throughput proteomic and genomic screens, this protein is predicted to localize to the apicoplast and be essential for parasite survival. Through immunofluorescence assays, we demonstrate that TgBipA is in fact localized to the apicoplast lumen. To investigate the function of this protein, we created a TgBipA inducible knockout (KO) line using Cre recombinase-based methodology. TgBipA KO parasites do not form plaques indicating an essential role for TgBipA in parasite growth. 72 hours after TgBipA KO, 50% of parasites do not contain an identifiable ring-shaped apicoplast and nuclear-encoded apicoplast proteins are found in vesicular structures in the parasite cytosol. Ultrastructure expansion microscopy reveals a shrunken apicoplast prior to dissolution. Taken together, this data shows that TgBipA is essential for apicoplast upkeep. Our future goal is to examine the mechanistic role of TgBipA by mutating conserved residues found to be essential for GTP hydrolysis and ribosome binding in BipA and determining if these mutants are sufficient to rescue a wildtype TgBipA KO, providing valuable insight into the functional domains of TgBipA and its role as a potential trGTPase.

8179

COMPARISON OF CARDIAC FIBROSIS CAUSED BY *TRYPANOSOMA CRUZI* IN THE CHRONIC PHASE IN IN VIVO MODELS OF MICE (BALB/C, SWISS), AND *CAVIA PORCELLUS*

Josselyn K. Vaca[1], **Carlos Javier Neyra Palacios**[1], Edith M. Málaga Machaca[1], Manuela R. Verástegui[2], Solange B. Custodio[1], Robert B. Gilman[1]

[1]Universidad Peruana Cayetano Heredia, LIMA, Peru, [2]Universidad Peruana Cayetano Heredia, Lima, Peru

Chagas disease, caused by *Trypanosoma cruzi*, necessitates effective animal models for study. This research evaluates Balb/C mice, Swiss mice, and guinea pigs (*Cavia porcellus*) for their utility in modeling Chagas disease's cardiac aspects. We compared parasitological, histopathological, and immunological responses among these models after infecting them with *T. cruzi*. Balb/C and Swiss mice showed higher parasitemia and more significant electrocardiographic changes compared to guinea pigs, indicating greater susceptibility to *T. cruzi*. Histopathological analysis confirmed more extensive cardiac fibrosis in these mice. Swiss mice, in particular, demonstrated heightened susceptibility and severe clinical signs, suggesting they may serve as more relevant models for studying human Chagas disease. This study highlights Swiss mice's potential as suitable models for investigating Chagas disease pathogenesis and testing new treatments due to their pronounced response to *T. cruzi* infection.

8180

SUCCESSFUL REPURPOSING OF FDA-APPROVED DRUGS AGAINST *LEISHMANIA* PARASITES PREVIOUSLY PREDICTED THROUGH A MACHINE LEARNING APPROACH

Rafeh Oualha, Yosser Zina Abdelkrim, Ikram Guizani, Emna Harigua-Souiai*

Institut Pasteur of Tunis, Tunis, Tunisia

Drug repurposing holds significant promise in the search for new treatments against Neglected Tropical Diseases, as it drastically reduces cost and time through the drug discovery process. In previously published work, we developed a Machine Learning (ML) pipeline to repurpose FDA-approved drugs against Leishmaniases. We herein provide validation of such approach through *in vitro* experiments, evaluating the antileishmanial effects of 10 ML-predicted drug candidates. We assessed the activity of these drugs against promastigotes from two strains of *L. infantum* and one of *Leishmania major*, each associated with distinct clinical manifestations, using an MTT assay. Among them, 5 molecules exhibited an effect against the *Leishmania* strains, including Acebutolol, Prilocaine, and Phenylephrine, newly identified in this study, with IC50 values ranging from 67 to 200 µg/mL. Dibucaine and Domperidone demonstrated potent activity, consistent with previous *in vivo* studies. None of the 5 compounds displayed notable cytotoxic effects on THP-1 derived macrophages. Intracellular *L. major* forms were also susceptible to these compounds, displaying enhanced IC50 values compared to those observed against the promastigotes. Notably, Dibucaine and Domperidone showed IC50 values < 2 µg/mL, comparable to Amphotericin B. Acebutolol, Prilocaine, and Phenylephrine exhibited IC50 values ranging from 17 to 57 µg/mL. Additionally, all compounds demonstrated satisfactory to high selectivity indexes. Our previously established Computer-Aided repositioning pipelines identified Dibucaine and Domperidone as promising candidates, reinforcing prior *in vivo* findings. In conclusion, this study brings confirmation of the potential of Dibucaine and Domperidone as promising candidates through *in vitro* tests against two prevalent *Leishmania* species in Africa and the Middle East, reinforcing previous *in silico* and *in vivo* findings. More importantly, we herein uncovered Acebutolol, Prilocaine and Phenylephrine as novel drug candidates against Leishmaniases, underscoring the relevance of our computational approach and warranting further investigation.

8181

CONSIDERATION OF FEXINIDAZOLE AS A NOVEL TREATMENT OPTION FOR RHODESIENSE-HUMAN AFRICAN TRYPANOSOMIASIS

Rebecca J. Chancey

CDC, Atlanta, GA, United States

Human African Trypanosomiasis (HAT) is caused by the protozoan parasites *Trypanosoma brucei rhodesiense* and *Trypanosoma brucei gambiense*. It is endemic in 36 sub-Saharan African countries and efforts for elimination are ongoing. Treatment options have been unchanged for decades until the new drug fexinidazole was included in the 2019 WHO interim guidelines for the treatment of gambiense HAT. Fexinidazole has antitrypanosomal activity against both *T.b. rhodesiense* and *T.b. gambiense*. Therefore, fexinidazole is now being considered as a treatment option for rhodesiense HAT for patients >6 years or >20kg. Fexinidazole is an oral medication and has fewer adverse effects than currently recommended treatment options, although vomiting and nausea can be significant. Risk of relapse in patients with gambiense HAT is higher after fexinidazole compared to nifurtimox-eflornithine combination therapy. Data on the efficacy of fexinidazole in rhodesiense HAT are limited. Preliminary data from an unpublished clinical trial on the efficacy and safety of fexinidazole in patients with rhodesiense HAT show positive outcomes, although with a small sample size. Patients treated with fexinidazole should be monitored closely for relapse. The US Food and Drug Administration (FDA) approved fexinidazole for treatment of gambiense HAT in 2023. The European Medicines Agency (EMA) approved fexinidazole for use in the treatment of rhodesiense HAT in 2023. Current treatment guidelines for HAT were reviewed by WHO in February 2024 and updated WHO guidelines to expand fexinidazole use in HAT treatment are in development. Fexinidazole is available in the US by contacting Sanofi Customer Service or Medical Affairs at 1-800-372-6634 or customersupport@sanofi.com. In nonendemic countries outside the US, it may be obtained for compassionate use from WHO. WHO continues to track cases closely as elimination efforts are ongoing. US physicians are encouraged to discuss management of patients with suspected HAT with subject matter experts at Centers for Disease Control and Prevention who can provide treatment guidance and report confirmed cases to WHO.

8182

CLINICAL PRESENTATION AND MANAGEMENT OF CUTANEOUS LEISHMANIASIS AMONG NEWLY ARRIVED AFGHAN EVACUEE CHILDREN

Alexandra Linn[1], Lauren Palladino[2], Alexandra Vinograd[2], Rachel Martin-Blais[3]

[1]Beth Israel Deaconess Medical Center/Boston Children's Hospital, Boston, MA, United States, [2]Children's Hospital of Philadelphia, Philadelphia, PA, United States, [3]Nationwide Children's Hospital, Columbus, OH, United States

In 2021, over 80,000 Afghan citizens were evacuated to the U.S., half of them children. As part of a larger retrospective cross-sectional analysis of all pediatric Afghan evacuees referred for care at an urban quaternary children's hospital and associated community hospital system between 08/2021 and 02/2022, we identified children diagnosed with complex cutaneous leishmaniasis (CL). Children were referred for management by physicians on a military base and in the emergency department due to concern for complex CL (i.e. lesions in areas at high risk of mucosal involvement, multiple or large lesions). The majority of these children presented for a joint dermatology/infectious diseases clinic, which was cross-referenced for inclusion. Chart reviews were conducted by study clinicians and abstracted into a REDCap database. Of 477 children in the larger study, nine cases of complex CL were identified. The age range was 11 months to eight years. Eight cases (89%) were female. Seven children (78%) had facial lesions. Seven (78%) had PCR positivity. *Leishmania tropica* was the most commonly identified species (56%). One child was diagnosed with leishmaniasis recidivans (presumed *L. tropica*) based on morphologic characteristics, history of previous intralesional

therapy, and positive PCR (speciation unable to be performed). Treatment was chosen based on patient's clinical presentation, social factors, and available resources. Two children were treated with fluconazole for presumed *L. major*, two with miltefosine, and one with LAmB, all (56%) with good responses to therapy. Three children (33%) were resettled before initiating treatment. One child (11%) was lost to follow up prior to diagnostic testing or treatment. The number of children identified likely represents an underestimation of total cases of CL. It is likely that some cases were misdiagnosed as impetigo and simple cases were not referred to subspecialty care. This case series highlights both the challenge of recognizing unfamiliar diseases and the difficulty of connecting evacuee children to subspecialty care and ensuring appropriate follow-up.

8183

TARGET-BASED 6-5 FUSED RING HETEROCYCLIC SCAFFOLDS DISPLAY BROAD ANTIPARASITIC POTENCY *IN VITRO*

Boniface Pone Kamdem[1], Darline Dize[1], Mariscal Brice Tchatat Tali[1], Cyrille Armel Njanpa Ngansop[1], Rodrigue Keumoe[1], Eugenie Aimée Madiesse Kemgne[1], Lauve Rachel Tchokouaha Yamthe[2], Patrick Valere Tsouh Fokou[3], Katsura Hata[4], Fabrice Fekam Boyom[1]

[1]Anti-Microbial & Biocontrol Agents Unit, Laboratory for Phytobiochemistry & Medicinal Plants Studies Department of Biochemistry Faculty of Science-University of Yaounde 1, Yaounde, Cameroon, [2]Institute for Medicinal Research and Medicinal Plants Studies, PO Box 6163, Yaounde, Cameroon, [3]Department of Biochemistry, Faculty of Science, University of Bamenda, PO Box 39, Bambili, Bamenda, Cameroon, [4]Global Health Research Section, hhc Data Creation Center, Eisai Co., Ltd., 1-3, Tokodai 5-chome, Tsukuba-shi, Ibaraki, Japan

Malaria, leishmaniasis, and African trypanosomiasis are protozoan diseases, which represent major global health problems, mainly in developing countries; however, the development of drug resistance coupled with the toxicity of current treatments has held up their management. The implication of certain enzymes (dihydrofolate reductase [DHFR]) or proteins (potassium channels) in the pathogenesis of these protozoan diseases is undeniable. In this study, a series of three DHFR inhibitors (6-5 fused heterocyclic derivatives X, Y, and Z) and one K+ channel blocker (E4031) were screened for their inhibitory effects on *Leishmania donovani*, *Plasmodium falciparum*, and *Trypanosoma brucei*. A resazurin assay was used to assess the antitrypanosomal and antileishmanial effects of the test compounds, whereas the antiplasmodial activity was evaluated through the SYBR Green I assay. Moreover, the cytotoxicity of the test compounds was evaluated in Vero, Raw 264.7, and HepG-2 cells using a resazurin-based assay, while their pharmacokinetic properties were predicted using the online tool, pkCSM. As a result, compound Y exhibited selective (selectivity index range: from 2.69 to >61.4; Vero, Raw 264.7, and HepG-2 cells) and broad-spectrum antiprotozoal activity against *L. donovani* promastigotes (IC_{50}: 12.4 µM), amastigotes (IC_{50}: 4.28 µM), *P. falciparum* (IC_{50}: 0.028 µM) and *T. brucei* brucei (IC_{50}: 0.81 µM). In addition, compound X inhibited the growth of *P. falciparum* (IC_{50}: 0.0052 µM) and *T. brucei* brucei (IC_{50}: 6.49 µM). *In silico* screening of the active antiprotozoal compounds demonstrated positive drug likeness scores, as none of the criteria for Lipinski's rule were violated by these compounds. However, in-depth pharmacokinetic and mechanistic studies are warranted to support the discovery of novel antiprotozoal agents against malaria, leishmaniasis, and African trypanosomiasis by repurposing K+ channel blockers and DHFR inhibitors.

8184

IMMUNOMODULATION EFFECT OF HOOKWORM PROTEINS ON CHRONIC CHAGASIC LIVER MODELS

Maria Jose Villar, Cristina Poveda, Bin Zhan, Kathryn M. Jones

Baylor College of Medicine, Houston, TX, United States

Chagas disease, caused by the protozoan parasite *Trypanosoma cruzi*, affects nearly 7 million people globally. Its chronic stage often induces inflammatory cardiac and digestive immunity, posing significant challenges for treatment. Unfortunately, patients with Chronic Chagas disease lack a definitive cure, relying instead on managing symptoms with drugs like Benznidazole and Nifurtimox which have serious side effects of toxicity. Given the liver's pivotal role in drug metabolism and parasite control, understanding hepatic immunity in Chronic Chagasic models is imperative. In this context, exploring immunomodulatory strategies becomes paramount. Hookworm-derived recombinant proteins, AIP-1 and AIP-2, have demonstrated efficacy in reducing inflammation in mouse models of inflammatory diseases, including cardiac inflammation due to *T. cruzi* infection. We previously showed that both AIP-1 and AIP-2 reduced inflammatory cell infiltrate into the heart and decreased several inflammatory cytokines including IFNγ and IL-6. Here we evaluated the impact of these two proteins on liver inflammation. Female BALB/c mice were infected with bioluminescent *T. cruzi* H1 strain trypomastigotes for 70 days. Following infection, mice received a seven-day treatment regimen of 1mg/kg AIP-1 or AIP-2 protein via intraperitoneal injection. Control groups remained untreated or received a 14-day regimen of 25mg/kg aspirin in their drinking water. At 84 days post-infection, samples of hepatic tissue were collected for comprehensive evaluation. Both AIP-1 and AIP-2 significantly reduced pSTAT3 levels in the liver, indicating the reduced inflammation pathway. We will discuss further the immunomodulatory effects of AIP-1 and AIP-2 specifically on hepatic immunity in a mouse model of Chronic *T. cruzi* infection.

8185

IMPROVED TREATMENT OUTCOME FOLLOWING THE USE OF A WOUND DRESSINGS IN CUTANEOUS LEISHMANIASIS LESIONS

Camila I. De Oliveira[1], Pedro Borba[1], Jamile Lago[1], Thainã Lago[1], Mariana Araújo-Pereira[1], Artur Queiroz[1], Hernane Barud[2], Lucas Carvalho[1], Paulo Machado[3], Edgar Carvalho[1]

[1]FIOCRUZ, Salvador, Brazil, [2]Uniara, Araraquara, Brazil, [3]UFBA, Salvador, Brazil

Leishmaniasis, caused by *Leishmania* parasites, is a neglected tropical disease and Cutaneous Leishmaniasis (CL) is the most common form. Despite the associated toxicity and adverse effects, Meglumine antimoniate (MA) remains the first-choice treatment in Brazil, pressing the need for the development of better alternatives. Bacterial Nanocellulose (BNC), a biocompatible nanomaterial, has unique properties regarding wound healing. In a previous study, we showed that use of topical BNC + systemic MA significantly increased the cure rate of CL patients, compared to treatment with MA alone. Herein, we performed a study comparing the use of wound dressings, BNC or placebo, in CL caused by *Leishmania braziliensis, versus* use of systemic MA alone. We show that patients that made use of topical wound dressings (BNC or placebo) showed improved cure rates and a decreased need for rescue treatment, compared to patients treated with systemic MA alone. Of note, time-to-cure was significantly improved with the use of a wound dressing (BNC or placebo). Assessment of the immune response showed that patients treated with wound dressings displayed a downmodulation in the production of immune mediators, in comparison to those treated with MA alone, particularly in inflammatory mediators such as IL-1. This study shows that topical application of a wound dressing, in addition to the standard systemic use of MA, can improve chemotherapy outcome in CL caused by *L. braziliensis*.

8186

IMPROVING THE LEISHMANICIDAL ACTIVITY OF MILTEFOSINE USING SPRAYABLE DRESSINGS BASED ON NANOFIBERS OF PVP/TETRONIC®/CYCLODEXTRINS

Zeinab Dirany[1], Paolo Ginatta[2], Javier González-Benito[3], Gustavo González-Gaitano[1], **Paul Nguewa**[2]

[1]Dept. of Chemistry, School of Sciences, University of Navarra, Pamplona, Spain, [2]Dept. of Microbiology and Parasitology, University of Navarra, Pamplona, Spain, [3]Dept. of Materials Science and Engineering and Chemical Engineering, Universidad Carlos III de Madrid, Madrid, Spain

Miltefosine (MF) is a well-known amphiphilic zwitterionic alkylphospholipid used in clinic for the treatment of leishmaniasis. This pathology is a neglected tropical disease, caused by *Leishmania species* and transmitted by the bite of sandflies. Leishmaniasis presents different clinical forms, of which the cutaneous one is the most prevalent. Despite being the only oral antileishmanial drug, MF is restricted by dose-limiting gastrointestinal side effects, a high cost compared to other drugs, teratogenicity, and potential of drug resistance due to long treatment duration. Currently, the development of effective therapies against leishmaniasis is of utmost importance. Our approach to the improvement of the leishmanicidal activity of MF has been its formulation in the form of sprayable dressings, based on submicrometric fibers of MF with polyvinylpyrrolidone (PVP), a biocompatible hydrophilic polymer. The fibers are produced by solution blow spinning, (SBS) an emerging method for the manufacturing of non-woven materials made of nanometric fibers. Cyclodextrins (CDs), which have demonstrated to reduce the hygroscopicity of PVP and to improve its stability, have been also incorporated in the formulation, along with Tetronic® 1307, an amphiphilic block copolymer that improves the antileishmanial action of MF. The release profile of the drug from the fibers was tested to correlate the performance with the composition, degree of functionalization and morphology of the material. The cytotoxicity on macrophages and the antileishmanial (*Leishmania major*) activity were evaluated to assess the biological and therapeutic effects of these new formulations of MF. Therefore, in addition to the possible oral and intravenous administrations, our results prove the effectiveness of this new in-situ delivery of MF on affected areas such as skin lesions of cutaneous leishmaniasis.

8187

A VALID 96-WELL-PLATE-ENZYMATIC ASSAY FOR *LEISHMANIA* METHYLTHIOADENOSINE PHOSPHORYLASE MTAP PROTEIN, A CANDIDATE DRUG TARGET

Yosser Zina Abdelkrim[1], Isleme Khalfaoui[2], Mourad Barhoumi[2], Sonia Abbess[2], Thouraya Mejri[2], Abid Hela[2], Emna Harigua-Souiai[2], Ikram Guizani[2]

[1]Laboratory of Molecular Epidemiology and Experimental Pathology, Institut Pasteur de Tunis – University Tunis el Manar / Process Engineering Department, Institut Supérieur de Etudes Technologiques de Bizerte, Direction Générale des ISETs, Tunis/Bizerte, Tunisia, [2]Laboratory of Molecular Epidemiology and Experimental Pathology, Institut Pasteur de Tunis – University Tunis el Manar, Tunis, Tunisia

The Leishmania infantum methylthioadenosine phosphorylase (LiMTAP) protein is the unique enzyme capable of metabolizing the MTA. Identified as highly druggable by the Tropical Disease Research database, it has ~35% identity to the human MTAP (huMTAP), so considered as a Leishmania drug target. We previously cloned and expressed the protein as a bacterial recombinant. Our goal is to develop a feasible, rapid, and coupled-enzyme assay in a format of 96-well-plate for the MTAPase activity. The test is critical for biochemical studies e.g. kinetic experiments to determine enzyme parameters, and biochemical screenings to discover Leishmania inhibitors. Thus, we used the plasmid constructs to purify the recombinant LiMTAP on Nickel based columns and developed an LiMTAPase 96-well plate assay. Based on our previous established tube-assay in crude extracts and on published work on huMTAP, we varied the reaction volume [50-100µl], temperature [25-37°C], time [0-180min], MTA concentrations [0-250µM], and DMSO rates [0-10%]. Enzymatic activity was monitored at 305nm based on a reference curve generated from the adenine conversion using 2 commercial xanthine oxidase (XO) sources [MedChemExpress and Sigma] and various concentrations [0.08-0.4 units per reaction]. Reaction mixtures contained 10ng/µl LiMTAP, 50mM potassium phosphate (pH7.4). We found experimental conditions to be highly reproducible using an MTA concentration range of [75-150µM], 5-10 % DMSO percentage, between 90-120 minutes, in 100 µl. We used MTAPase kinetics to determine Michaelis Menten kinetic parameters to select for the best XO. We found comparable Kcat mean value (Vmax/[LiMTAP]) of ~4.5 min-1, when we considered the conditions where the XO conversion rates were comparable. In conclusion, we have developed effective conditions to set a miniaturized LiMTAP biochemical assay adapted for multiple and single points enzymatic tests. Currently, a cost-effectiveness comparison is ongoing to further improve the assay for the screenings of novel inhibitors of this protein, and thus accelerating discovery of promising anti-Leishmania molecules.

8188

OPTIMIZING THE MULTI-FACETED PIPELINE OF AI-BASED DRUG DISCOVERY AGAINST INFECTIOUS DISEASES

Ons Masmoudi, Emna Harigua-Souiai

Laboratory of Molecular Epidemiology and Experimental Pathology, Institut Pasteur de Tunis, Université de Tunis El Manar, Tunis, Tunisia

Artificial Intelligence (AI) has now gained a wide interest in the field of drug discovery due to the increasing availability of large datasets useful in training AI models to predict properties and activities of chemical compounds, and design novel drug candidates. The AI-based pipeline encompasses: the dataset, the model and the prediction task as main components. The present work is focused on optimizing the different components of such a pipeline towards providing robust predictive tools of chemical compound activities against five infectious diseases, including Malaria, AIDS, Tuberculosis and Trypanosomiases.For each disease of interest, we retrieved bioassays datasets from the PubChem database. All datasets are highly imbalanced towards the inactive class. Data balancing was applied to all datasets through targeted strategies in order to identify optimal ratios. We used different molecular fingerprints and graph-convolution methods to encode the chemical structures from these libraries. Then, we trained two Machine Learning (ML) and four Deep Learning (DL) algorithms to assess the anti-pathogen potential of chemical entities. Investigating the impact of the data imbalance on the ML and DL models performances demonstrated a consensus ratio of 1:9 as optimal across all simulations. Among the evaluated models, Random Forest (RF), Multi-Layer Perceptron (MLP), Graph Convolution Network (GCN) and Attentive Fingerprint (AFP) demonstrated the best performances on specific datasets, and were optimized through hyperparameter tuning. At this stage, we identified the optimal balancing ratio and predictive model for each dataset. We then assessed the generalization power of each model to unseen data (external validation). Although no particular model could exhibit optimal performances on all datasets, MLP provided a superior ability to accurately identify the active molecules, with the best trade-off between the True Positive and False Positive rates. We aim at further automating the optimized pathogen-specific pipelines on our open source platform https://cidalsdb.streamlit.app/ for use by the scientific community.

8189

FEXINIDAZOLE IN PATIENTS WITH HUMAN AFRICAN TRYPANOSOMIASIS DUE TO *TRYPANOSOMA BRUCEI RHODESIENSE,* TOWARDS AN ARSENIC FREE FIRST LINE THERAPY

Olaf Valverde Mordt[1], Westain Tizgo Nyirenda[2], Anthony Eriatu[3], Marshal Lemerani[4], Charles Wamboga[5], Elisabeth Baudin[6], Deolinda Alves[1], Enock Matovu[7]

[1]Drugs for Neglected Diseases initiative, Genève, Switzerland, [2]Malawi Ministry of Health, Rumphi, Malawi, [3]Uganda Ministry of Health, Lwala

(Kaberamaido), Uganda, [4]Malawi Ministry of Health, Lilongwe, Malawi, [5]Uganda Ministry of Health, Kampala, Uganda, [6]Epicentre, Paris, France, [7]Makerere University, Kampala, Uganda

Rhodesiense human African trypanosomiasis (r-HAT) is the zoonotic, acute, and fatal form of sleeping sickness in Eastern Africa. To date neurotoxic melarsoprol is the only drug available for treatment of the advanced meningo-encephalitic stage. A new oral treatment could simplify HAT elimination as proposed by the World Health Organization. In 2022, a clinical trial to test fexinidazole, a new, safer, highly effective, short-course treatment, was completed in Malawi and Uganda for r-HAT as an alternative to the toxic existing treatment. Fexinidazole has now received a positive scientific opinion from the European Medicines Agency to treat both forms of HAT, first the chronic *gambiense* form in 2018 and in 2023 the acute *rhodesiense* HAT. The last trial for the clinical development of fexinidazole for HAT was designed as a single arm benchmark study comparing observed to unacceptable fatality rates at the end of hospitalization, due to the low number of detected r-HAT cases. The principal endpoint was defined as an unacceptable attributable fatality rate equal or greater than 8.5% . Additional study objectives were treatment failure (including relapses) or deaths at the end of hospitalization or during 12 months follow-up, and safety, pharmacokinetics, and molecular assessments. The sample size, defined according to the principal objective was of 34 evaluable patients in advanced stage complemented by the available number of patients in early stage. The primary efficacy result was achieved, with no related deaths during hospitalisation: 0 C.I. (0.0-8.43%) in any of the 45 patients who were included, of which 34 were evaluable in the advanced stage of illness. Safety was acceptable; one patient relapsed. Full results will be communicated during the presentation, including all secondary endpoints and safety data. After its addition to the treatment arsenal for gambiense HAT, fexinidazole has now been shown to be a good first-line treatment alternative to replace melarsoprol and suramin for the oral treatment of both stages of r-HAT.

8190

IN VITRO EVALUATION OF THE ANTI AMOEBIC ACTIVITY OF BENZOTHIAZOLE BT3 AGAINST *ENTAMOEBA HISTOLYTICA*

Maritza Velásquez-Torres[1], José G. Trujillo-Ferrara[2], Aldo A. Reséndiz-Albor[3], Ivonne M. Arciniega-Martínez[3], Nadia M. Pérez-Vielma[4], Rosa A. Jarillo-Luna[5], **Judith Pacheco-Yepez**[1]

[1]Sección de Estudios de Posgrado e Investigación, Escuela Superior de Medicina, Instituto Politécnico Nacional, Ciudad de México, Mexico, [2]Laboratorio de Investigación en Bioquímica, Escuela Superior de Medicina, Instituto Politécnico Nacional, Ciudad de México, Mexico, [3]Laboratorio de Inmunidad de Mucosas, Sección de Estudios de Posgrado e Investigación, Escuela Superior de Medicina, Instituto Politécnico Nacional, Ciudad de México, Mexico, [4]Centro Interdisciplinario de Ciencias de la Salud, CICS, Santo Tomás, Instituto Politécnico Nacional, Ciudad de México, Mexico, [5]Coordinación de Ciencias Morfológicas, Escuela Superior de Medicina, Instituto Politécnico Nacional, Ciudad de México, Mexico

Due to the side effects of the available anti-amebic drugs, it is necessary to seek new compounds. Since previous studies have demonstrated the anti-parasitic activity of benzothiazoles, the aim of the current contribution was to evaluate the *in vitro* effect of BT3 (4-[5-(trifluoromethyl)-1,3-benzothiazol-2-yl] benzoic acid) against *Entamoeba histolytica* and during the interactions of the amoebae with hamster neutrophils (a model of susceptibility). *E. histolytica* trophozoites were treated with different concentrations of BT3 for 5 h and viability was examined by using the WST-1 reagent. The 50% inhibitory concentration (IC_{50}) was obtained by linear regression between the concentration of the compound and the percentage of inhibition. The cytotoxicity of BT3 was assessed on the Vero cell line. Additionally, determination was made of ROS production with a 2', 7'-dichlorodihydrofluorescein (DCF) ROS Assay Kit (Ab238535, Abcam, Cambridge, UK) and of NO production with a NO Assay Kit (Ab272517, Abcam, Cambridge, UK), based on the conventional Griess method. The *in vitro* results showed that the viability of trophozoites treated with BT3 was significantly decreased in a dose dependent manner, while BT3 did not show any cytotoxic effect on the Vero cell line. The IC_{50} of BT3 was 117.5 µM at 5 h. The test compound triggered the production of reactive oxygen species and nitric oxide by the neutrophils. These prooxidant species, which were found in the supernatant of amoebae-neutrophils interactions, could possibly contribute to amoebic damage.

8191

FACTORS ASSOCIATED WITH RELAPSE IN VISCERAL LEISHMANIASIS: AN INDIVIDUAL PATIENT DATA META-ANALYSIS USING THE INFECTIOUS DISEASES DATA OBSERVATORY DATA PLATFORM

Prabin Dahal[1], Rishikesh Kumar[2], Sauman Singh-Phulgenda[1], Abdalla Munir[3], Niyamat Ali Siddiqui[2], James Wilson[1], Gemma Buck[1], Caitlin Naylor[1], Matthew Brack[1], Manju Rahi[4], Paritosh Malaviya[5], Monique Wasunna[6], Francois Chappuis[7], Koert Ritmeijer[8], Carlos Costa[9], Gustavo Romero[10], Vassiliki Syriopoulou[11], Ahmed Musa[12], Fabiana Alves[13], Kasia Stepniewska[1], Philippe J. Guerin[1], Krishna Pandey[2]

[1]University of Oxford, Oxford, United Kingdom, [2]ICMR - Rajendra Memorial Research Institute of Medical Sciences (RMRIMS), Patna, India, [3]Infectious Diseases Data Observatory (IDDO), Oxford, United Kingdom, [4]Indian Council of Medical Research (ICMR), New Delhi, India, [5]Infectious Disease Research Laboratory, Department of Medicine, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India, [6]Drugs for Neglected Diseases initiative, Nairobi, Kenya, [7]Division of Tropical and Humanitarian Medicine, Geneva University Hospitals, Geneva, Switzerland, [8]Médecins Sans Frontières, Amsterdam, Netherlands, [9]Department of Community Medicine, Federal University of Piauí, Piauí, Brazil, [10]Center for Tropical Medicine, University of Brasilia, Brasilia, Brazil, [11]Infectious Diseases and Chemotherapy Research Laboratory, Medical School, National and Kapodistrian University of Athens, Athens, Greece, [12]Institute of Endemic Diseases, University of Khartoum, Khartoum, Sudan, [13]Drugs for Neglected Diseases initiative (DNDi), Geneva, Switzerland

A significant geographical variation is observed in the efficacy of existing drugs used for treating visceral leishmaniasis (VL). Elucidating factors that explain some of this variation can provide valuable insights regarding treatment response across different endemic settings. An individual patient data meta-analysis (IPD-MA) using data from 33 studies (published 2000-19) was therefore undertaken to explore the predictors of relapse using hierarchical logistic regression models fitted separately by geographical region. Of the 9,353 patients included, 5,924 (63.3%) were from the Indian sub-continent (ISC), 2,929 (31.3%) from Eastern Africa (EA), 377 (4.0%) from Brazil and 123 (1.3%) from Greece. Treatment administered included: miltefosine (n=2,109, 22.5%), pentavalent antimony (n=1,871, 20.0%), amphotericin B deoxycholate (n=2,669, 28.5%), liposomal amphotericin B (n=485, 5.2%), paromomycin (n=712, 7.6%), a combination of these drugs (n=977, 10.4%), or other (n=530, 5.7%). Overall, 4.0% (376/9,353) of patients relapsed following initial treatment response: 4.4% (260/5924) in the ISC and 3.3% (97/2929) in EA. In a multivariable model from the ISC that included age, sex and treatment, age <15y was the only factor associated with an increased relapse risk (adjusted odds ratio (AOR) [95% confidence interval (CI)]: 1.6 [1.2-2.0]; reference ≥15y]. In EA, variables associated with increased relapse risk in a multivariable model that included age, sex, anaemia (defined using WHO's age and sex specific threshold) and treatment included: male sex (AOR: 3.4 [1.5-7.8]), age<5y (AOR: 5.9 [1.9-18.4]) and 5-15y (AOR: 3.3 [1.3-8.0] (reference ≥15y), and severe anaemia at presentation (AOR: 2.8 [1.4-5.3]). This IPD-MA demonstrates young age, male sex, and severe baseline anaemia are predictors of relapse; potentially explaining some of the observed heterogeneity in treatment response. Studies in this IPD-MA often excluded patients with complicated disease and pregnant/lactating women which could have potentially biased the conclusions. Further work is underway to assess the factors associated with all-cause mortality.

8192

LEVERAGING MACHINE LEARNING (ML) AND DEEP LEARNING (DL) MODELS FOR DRUG REPURPOSING: A SUCCESSFUL CASE STUDY ON LEISHMANIA PARASITES

Emna Harigua Souiai, Ons Masmoudi, Rafeh Oualha, Mohamed M. Heinhane, Ines Tej-Abdeljaoued, Yosser Z. Abdelkrim, Oussama Souiai, Ikram Guizani

Institut Pasteur de Tunis, Tunis, Tunisia

Computer-Aided Drug Discovery has gained momentum with recent advances in data analysis and artificial intelligence (AI). In this context, disposing of reliable datasets is of utmost importance. We herein report our efforts in collating targeted and manually curated datasets and the implementation of highly reliable AI models in the frame of Ligand-Based Drug Discovery against COVID-19 and Leishmaniases, among others. Extensive literature search for biologically active or inactive molecules was backed-up with data retrieval from PubChem and other chemical databases. For each pathogen, manually curated datasets of up to 4,000 molecules could be consolidated. Then, we implemented 4 machine learning (ML) and 4 deep learning (DL) algorithms that were trained and optimized on both disease-specific datasets. Our results highlighted the importance of injecting literature-issued data points within larger screening datasets towards obtaining optimal performances of the ML and DL models. Interestingly, ML models exhibited the highest scores (accuracy>0.85 and ROC-AUC>0.90), across all simulations as compared to DL models. Nonetheless, through external validation (unseen data) on the FDA-approved drugs, DL algorithms demonstrated higher generalization power and accurate activity predictions with True Positive rates>50%.As an ultimate validation of our approach, we used the Leishmania-specific models herein optimized (RF, MLP & GCN) to select the most potentially active compounds within the FDA-approved drugs. We opted for molecules commonly predicted as active by all 3 models with>80% confidence. Out of 71 predicted molecules, 21 were previously described in the literature as antileishmanial agents. Out of the remaining 50, 10 drugs have never been described before; and were thus purchased towards their validation as effectors on Leishmania parasites in vitro. The present research leverages the potential of AI within a data-driven approach that capitalizes on the team's expertise in Computer-Aided Drug Discovery to deliver an optimal strategy for a cost-effective therapeutics discovery against infectious diseases.

8193

EVALUATION OF TCNMT OF NOVEL IN-SILICO INHIBITORS AGAINST *TRYPANOSOMA CRUZI* N-MYRISTOYLTRANSFERASE

Diana C. Gonzalez Garcia[1], Priscila S.G. Farani[1], Angel Torres[1], Juan Carlos E. Silva[1], Miguel Beltran[1], Frida Lara[1], Sayonara De Melo Viana[1], Alan Talevi[2], Rosa A. Maldonado[1]

[1]University of Texas at El Paso, El Paso, TX, United States, [2]Universidad Nacional de La Plata, Buenos Aires, La Plata, Argentina

Chagas disease (CD) is caused by the protozoan parasite *Trypanosoma cruzi.* Although originally endemic to South and Central America, the disease prevalence has increased in non-endemic regions such as the United States, Europe, Japan, and Australia. CD is hard to detect during the acute phase, progressing to the chronic phase, where it may cause damage to organs such as the heart and digestive system. Current standard serologic diagnostics lack enough sensitivity and specificity. In addition, treatment is long, with a high rate of adverse effects in patients. N-myristoylation is a posttranslational modification of proteins that is specific to the alpha-amino group of an N-terminal glycine residue and catalyzed by N-myristoyl transferase (NMT). It is known to play a role in cellular regulation and signal transduction in eukaryotes and parasite survival. NMT has been shown to be a chemotherapeutic target candidate in other protozoan parasites close to the *T. cruzi* family, such as *Plasmodium falciparum, Leishmania donovani,* and, more closely, *T. brucei*. In our study, it was purified the recombinant NMT enzyme from *T. cruzi* (TcNMT) and tested against newly designed in silico NMT inhibitors. First, we isolated the gDNA from *T. cruzi* CL-Brener strain parasites, followed by PCR to obtain the gene that codes for TcNMT. Subsequently, it was cloned into a pET15b expression plasmid. The recombinant protein 6xHis-TcNMT (TcNMT) in Rossetta-gami cells. The recombinant enzyme TcNMT was purified by affinity, ion exchange, and size exclusion chromatography. Next, the enzymatic activity of the recombinant TcNMT was characterized, followed by the evaluation of the inhibitors DA, QU, and DI. We also assessed the cellular cytotoxicity of our inhibitors in human cardiomyocytes AC16; the compounds the DA, QU, and DI showed an IC50 of 23.6 µM, 34.5 µM and 18.6 µM, respectively. Currently, we are assessing the efficacy of the inhibitors against intracellular amastigotes at 24, 48, and 72 hours after treatment, monitoring the infection in the Bio Tek Cytation 7.

8194

HEAT SHOCK PROTEIN TCJ2: A NOVEL MRNA VACCINE CANDIDATE FOR CHAGAS DISEASE IDENTIFIED THROUGH IMMUNOPEPTIDOMICS

Leroy Versteeg, Rakesh Adhikari, Jungsoon Lee, Brian Keegan, Cristina Poveda, Maria Jose Villar, Kathryn Jones, Maria Elena Bottazzi, Peter Hotez, Edwin Tijhaar, Jeroen Pollet

Baylor College of Medicine, Houston, TX, United States

Globally around 6-7 million people are infected with the protozoan parasite *Trypanosoma cruzi*, the causative agent of Chagas disease. A subset of these people has the risk of developing cardiomyopathy as a symptom of chronic Chagas disease. Efforts to develop prophylactic and therapeutic vaccines against *T. cruzi* infection are ongoing, but no vaccine is currently available to prevent or treat Chagas disease. Developing effective vaccines requires targeting parasitic antigens presented on major histocompatibility complex-I (MHC-I) molecules, which can stimulate *T. cruzi*-specific CD8+ cytotoxic T cells and eliminate infected cells. However, no systematic screening has been done to evaluate which antigen targets are presented by *T. cruzi* - infected cells during natural infection and can be detected by antigen-specific CD8+ T cells. In our study, we employed mass spectrometry-based immunopeptidomics to analyze which *T. cruzi* peptides were presented on MHC-I of infected host cells. From dozens of *T. cruzi* peptides that were identified, multiple peptides from duplicate experiments traced back to Tcj2, which is a trypanosome chaperone protein and member of the DnaJ (heat shock protein 40) family. Protein sequence identity analysis showed that Tcj2 was very conserved between different *T. cruzi* strains, while human and mouse orthologs showed considerable differences. Next, an mRNA construct encoding for Tcj2 protein was developed and showed translation of Tcj2 protein *in vitro*. When Tcj2 mRNA was formulated into LNPs and tested as an mRNA vaccine candidate in mice, it induced cytotoxic CD8+ T cells, along with a Th1-skewed humoral antibody response. Splenocytes of Tcj2-immunized mice showed a much stronger reduction in replication of *T. cruzi* in an *in vitro* co-culture with *T. cruzi* infected cells, compared to co-cultures with splenocytes from naïve mice, demonstrating the protective potential of Tcj2 as a vaccine target. Our findings demonstrate the potential of immunopeptidomics to identify new vaccine targets for Chagas disease, and revealed Tcj2 as a promising new mRNA vaccine candidate.

8195

IMMUNOTHERAPY WITH TSA-1 C4 COMBINED WITH BZN INDUCES DIVERGENT IMMUNE RESPONSE BUT CONFERS PROTECTION AGAINST TRYPANOSOMA CRUZI INFECTION

Julio V. Cruz-Chan[1], Landy M. Pech-Piste[1], Victor M. Dzul-Huchim[1], Jaime Ortega-López[2], Peter J. Hotez[3], Maria E. Bottazzi[3], Liliana E. Villanueva-Lizama[1]

[1]University Autonomous of Yucatan, Merida, Mexico, [2]Centro de Investigación y Estudios Avanzados IPN, Ciudad de Mexico, Mexico, [3]Baylor College of Medicine, Houston, TX, United States

Chagas disease, caused by *Trypanosoma cruzi*, affects 6-7 million people worldwide. The infection progress to chronic chagasic cardiomyopathy in

30% of patients driving death by cardiac failure. The current treatments induce side effects and have poor efficacy during the chronic phase. Here, we propose the evaluation of TSA-1.C4 and the adjuvant TLR-4 agonist plus a low dose of BNZ. According to our data, Balb/c mice showed a protective effect mediated by a reduced peripheral blood parasitemia, and prevention of cardiac inflammation was observed in TSA-1.C4+TLR-4 agonist+Low BNZ treated mice. In addition, significant IFNy+CD4+ producing T cells, IL-2 and IL-4 cytokines were observed in vaccine-linked chemotherapy treated mice. This is the first report demonstrating the beneficial effect of a vaccine-linked chemotherapy formulated with the recombinant TSA-1.C4 protein and TLR-4 agonist adjuvant and all these results suggests a promising therapeutic option for further studies.

8196

VALIDATION OF *TRYPANOSOMA CRUZI* MULTI-EPITOPE RECOMBINANT PROTEIN IN INDIVIDUALS WITH HLA-A*02 ALLELE AS A HUMAN CHAGAS DISEASE VACCINE CANDIDATE

Christian Teh-Poot[1], Andrea Alfaro-Chacón[1], Landy Pech-Pisté[1], Miguel Rosado-Vallado[1], Asojo Oluwatoyin Ajibola[2], Liliana Villanueva-Lizama[1], Eric Dumonteil[3], Julio Cruz-Chan[1]

[1]Universidad Autónoma de Yucatán, Merida, Mexico, [2]Hampton University, Hampton, VA, United States, [3]Tulane University, New Orleans, LA, United States

Chagas disease is the most significant neglected tropical disease affecting individuals in the Americas, caused by the protozoan *Trypanosoma cruzi.* Available drugs are toxic and ineffective in chronic phase and the development of a Chagas disease vaccine is hampered by the complexity of parasite and HLA polymorphisms. Epitope-specific $CD8^+$ T cells are necessary to confer a robust immune response and protection against intracellular parasites such as *T. cruzi* by producing IFN-γ and perforin. Thus, the antigen(s) for the development of a Chagas vaccine or immunotherapy must include $CD8^+$ T cell epitopes. In this study, we aimed to develop a multi-epitope recombinant protein as a novel human vaccine for Chagas disease. Sixteen database programs were used to predict *de novo* 40 potential epitopes for HLA-A*02:01. Nine out of 40 predicted epitopes were able to elicit IFN-γ in PBMC from chagasic patients. Molecular docking revealed a good binding affinity among the epitopes with diverse HLA molecules. A recombinant multi-epitope protein including nine nonamers *T. cruzi* $CD8^+$ epitopes was expressed and able to recall an antigen-specific immune response in *ex-vivo* assay using PBMCs from chagasic patients with HLA-A*02 allele.

8197

IMPACT OF MALNUTRITION ON THE EFFICACY OF LMCEN-/- VACCINE

Lais Da SilvaPereira, Laura Klenow, Hannah Markle, Nazli Azodi, Thalia Pacheco-Fernand, Sreenivas Gannavaram, Hira Nakhasi

Food and Drug Administration, Silver Spring, MD, United States

Globally, malnutrition is the most frequent cause of immunodeficiency and significant risk factor for the development of visceral leishmaniasis. The susceptibility to and severity of *Leishmania* infection can be altered by the host's body weight and serum levels of micronutrients. In murine models, malnutrition leads to failure of the draining lymph node and a reduction in the number of immune cells that prevent the dissemination of *Leishmania*. However, there is a gap in our understanding of how malnutrition affects the development of a specific immune response to a *Leishmania* vaccine. Our laboratory has developed a promising *Leishmania major* live attenuated vaccine with a Centrin gene-knockout (*LmCen*$^{-/-}$), which has been shown to be safe and efficacious against *Leishmania donovani* and *L. major* challenges in animal models of visceral leishmaniasis and cutaneous leishmaniasis respectively. Nevertheless, how malnutrition affects the immune response to *LmCen*$^{-/-}$ vaccine remains unknown. This study aimed to determine whether the efficacy of the *LmCen*$^{-/-}$ vaccine is abrogated in the malnourished host. We used a murine model of malnutrition to assess the *LmCen*$^{-/-}$ vaccine's efficacy in both well-nourished (WN) and poly nutrients-deficient (PND) mice. The control mice group (WN) received a diet of normal mouse chow containing 17% protein, 100 ppm iron, and 30 ppm zinc. The test mice group (PND) received a chow with decreased protein (3%), iron (10 ppm), and zinc (1 ppm). Mice are fed with WN or PND diets, 4 weeks before the start of immunizations and throughout the challenge with *L. donovani*. We evaluated whether malnutrition status has a significant impact on neutrophils, macrophages, and dendritic cellularity at the local and systemic levels. In addition, we assessed the nutritional markers in the lymph node barrier and splenocytes. Results from the series of experiments assessing how malnutrition affects Leishmania burden and whether it abrogates LmCen-/- vaccine efficacy will be presented.

8198

FACTORS AFFECTING COMMUNITY DIRECTED INTERVENTION VOLUNTEERS' PERFORMANCE IN ONCHOCERCIASIS AND LYMPHATIC FILARIASIS ELIMINATION PROGRAMS, ETHIOPIA

Anley Haile Abate[1], Aderajew Mohamed[1], Yewondwossen Bitew[1], Tewodros Seid[1], Fetene Mihretu[2], Yohannes Eshetu[3], Abdo Aliyi[1], Abey Mezgebu[4], Geremew Haileyesus[1], Fikresilasie Samuel[1], Fikre Seife[5], Kadu Meribo[5], Emily Griswold[6], Zerihun Tadesse[1], Jenna E. Coalson[6], Frank O. Richards Jr.[6], Gregory S. Noland[6]

[1]The Carter Center, Addis Ababa, Ethiopia, [2]The Carter Center, Bahir Dar, Ethiopia, [3]The Carter Center, Bonga, Ethiopia, [4]The Carter Center, Gambella, Ethiopia, [5]Ministry of Health, Addis Ababa, Ethiopia, [6]The Carter Center, Atlanta, GA, United States

In Ethiopia, the onchocerciasis program started with control in 2001 and shifted to elimination in 2012. The lymphatic filariasis (LF) program began in 2009. The Carter Center was significant in integrating the community-directed treatment with ivermectin/albendazole (CDTI/A) approach into the primary health care system throughout RB/LF endemic areas in the country. Over 500,000 community drug distributors (CDDs) and community supervisors (CSs) work for the CDTI/A program in Ethiopia, but their level of quality, commitment, and dedication varies. To monitor the program, we conducted a desk review and a mixed-methods cross-sectional community-based study. We randomly selected two kebeles from 12 woredas from seven regions. Then, we randomly selected CDDs in these selected kebeles, resulting in 402 samples. We also conducted 44 key informant interviews and 24 focus group discussions in all targeted kebeles. Consistent with qualitative data, the CDD to population ratio of 1:67 among surveyed CDDs is below the national standard of 1:50. High attrition has led to few active CDDs/CSs in most woredas in Amhara, Gambela, and Benishangul Gumuz regions. These woredas have substandard recruitment and selection processes. Per national guidelines, CDDs should be chosen by community members, but 46% of surveyed CDDs were appointed by kebele leaders. Moreover, 55% of CDDs received only 1-2 hours of training before their last MDA round while half a day is recommended. Qualitative data indicated that pastoral/agro-pastoral areas have tried to improve MDA coverage by directly involving health professionals rather than community volunteers and recruiting more male CDDs to combat high attrition rates for female CDDs. Training and recruitment practices that do not align with national recommendations may contribute to CDD attrition in some parts of Ethiopia. We should evaluate different modes of CDD recruitment, provide quality CDD training, and consider targeted recruitment strategies in pastoralist areas with high attrition rates, particularly for female CDDs.

8199

IMPACT OF MASS DRUG ADMINISTRATION FOR LYMPHATIC FILARIASIS AND YAWS ELIMINATION ON ATTENDANCES FOR SKIN DISEASE IN RURAL HEALTH CENTERS IN WEST NEW BRITAIN PROVINCE, PAPUA NEW GUINEA

Simon Westby[1], Joycelyn Salo[1], Wendy Houinei[2], Joseph Nale[2], Jastina Kakul[2], Grace Michael[1], Julie Jacobson[3], Moses Laman[1], Christopher L. King[4]

[1]Papua New Guinea Institute of Medical Research (PNGIMR), Goroka, Papua New Guinea, [2]West New Britain Provincial Health Authority, Kimbe, Papua New Guinea, [3]Bridges to Development, Vashon, WA, United States, [4]Center for Global Health and Diseases, Case Western Reserve University School of Medicine, Cleveland, OH, United States

Papua New Guinea (PNG) is highly endemic for lymphatic filariasis (LF) and yaws. Other skin diseases such as scabies, crusted scabies, fungal and bacterial infections are some of the most common reasons for visits to rural health centers (HCs) in PNG. Recently, PNG started mass drug administration (MDA) to eliminate lymphatic filariasis (LF) and yaws and control scabies and STH with ivermectin, diethylcarbamazine, albendazole (IDA), followed by azithromycin. West New Britain Province (WNBP) in PNG is the first province to receive MDA with IDA and azithromycin, which began in December 2023. Using the PNG National Health Information System (NHIS), we show a significant drop in HC visits for skin diseases and yaws-like lesions two months following MDA compared to the previous six months before MDA. For the 23 HCs reporting complete records in the NHIS for the periods mentioned above, pre-MDA HC visits for all skin diseases excluding yaws-like lesions had a median = 63 (48, 93 IQR) that declined to a median = 42 (26, 55 IQR, p<0.001 Wilcoxon rank-sum test) post-MDA. For yaws-like lesions, there was a median of 24 (13, 30 IQR) visits pre-MDA that declined to a median = 12 (6, 17 IQR, p<0.001) post-MDA. There were no significant changes in non-skin disease HC visits during this period (pre-MDA median = 501 (337,693 IQR) versus post-MDA median = 493 (400,733 IQR, p=0.41). These results show that MDA with IDA and azithromycin can dramatically reduce the burden of skin diseases seen at HCs, with benefits beyond treatment for LF and yaws alone, and that significant decreases in HC visits for skin disease are detectable shortly after MDA. These effects could increase treatment acceptability within the health system and help sustain the high drug coverage in the population necessary to achieve elimination targets for LF and yaws. We will continue to conduct active surveillance of skin-neglected tropical diseases in WNBP to see how long the reduction in HC visits persists after MDA and better evaluate participants' perceptions of the MDA program.

8200

EMPOWERING YOUTH AGAINST LYMPHATIC FILARIASIS: A GAME-CHANGING APPROACH TO URBAN DRUG COMPLIANCE

Rajshree Das, Anjali Singh, Ranpal Singh, Somnath Banerjee, Kiran Agrahari

Project Concern International-India, New Delhi, India

Lymphatic Filariasis (LF) is a significant public health challenge in India, accounting for 43% of global infections. Across 339 endemic districts, approximately 650 million people are at risk. Mass drug administration (MDA) targets 402 million individuals annually for directly observed therapy (DOT). While rural DOT rates have improved from 18% in 2018 to 49% in 2023, urban areas struggle, with only 33% DOT rate in 2023 due to limited number of drug administrators (DAs), residents' unavailability during work hours, low risk perception and limited interface with the DAs. Within urban areas, the assessments have shown poor DOT among youth aged 18-23 years, and among individuals with higher education. Youth, comprising 12% of the total population, offer a potential solution. Engaging youth volunteers from the National Service Scheme during the 2023 MDA increased DOT from 34% to 43% in urban areas. Leveraging this, the Department of Higher Education sensitized nearly 3 million university students across five states namely Uttar Pradesh, Bihar, Jharkhand, Odisha and Chhattisgarh during the Feb 2024 MDA. During Feb 2024 MDA, booths were placed in 343 colleges across 67 districts of 5 states. The records showed 49% college going students consumed filaria prevention drugs at dedicated booths. Further assessment revealed 81% of youth consumed filaria prevention drugs during the Feb 2024 MDA, with 65% consuming at booths and 35% at home. More than 64% students informed about MDA at their home and reported that their parents or siblings consumed anti-LF drugs. Odds of DOT were over 5 times higher (OR: 5.4, p:0.00, 95% CI: 3.1-9.3) when youth received LF/MDA information and over 9 times higher (OR: 9.9, p:0.00, 95% CI: 4.2-23.1) with the knowledge of preventive drug consumption. These findings indicate the potential of youth-focused interventions to significantly improve urban DOT rates when coupled with comprehensive information dissemination about MDA. Implementing activities such as interactive campaigns, social media challenges, and recognition programs to motivate youth involvement can yield encouraging results in elimination efforts.

8201

PARTICIPATORY ACTION RESEARCH TO ENHANCE EQUITABLE HEALTH SEEKING FOR PERSONS AFFECTED BY SKIN NTDS IN LIBERIA

Hannah Berrian[1], Rosalind McCollum[2], Emerson Rogers[3], Shahreen Chowdhury[2], India Hotopf[2], Wede Tate[1], Jerry Kollie[1], Colleen Parker[3], John Solunta Smith Jr.[1], Karsor Kollie[3], Zeela Zaizay[4], Lucas Sempe[5], Maaike Seekles[2], Tia Akpan[6], Anna Wickenden[7], Maneesh Phillip[7], Sally Theobald[2], Laura Dean[2]

[1]UL-PIRE Africa Center, Monrovia, Liberia, [2]Liverpool School of Tropical Medicine, Liverpool, United Kingdom, [3]Ministry of Health, Monrovia, Liberia, [4]Actions Transforming Lives (ACT), Monrovia, Liberia, [5]Queen Margaret University, Edinburgh, United Kingdom, [6]American Leprosy Missions (ALM), Greenville, SC, United States, [7]Effect Hope, Ontario, ON, Canada

Persons affected by skin neglected tropical diseases (NTDs) often experience barriers toseeking timely, quality care across their care - seeking journey. The literature predominantlyfocuses on curative care, with little emphasis on holistic care (such as physical rehabilitationand psychosocial support). Spiritual beliefs about the causation of NTDs impact both ability toperceive the need to seek care. Health workers, friends, and family can stigmatise personsaffected, impeding their treatment, participation and inclusion. We sought to understand howan intervention bundle influences the health-seeking pathway of persons affected by skin NTDsusing the Levesque Pathway. REDRESS centred lived experience within intervention design.Persons affected, informal providers and health actors co-developed a bundle of interventionswhich sought to strengthen person-centred integrated case management for skin NTDs.To understand the impact of such health systems reform on the lived experience of personsaffected, we used a series of participatory methods including photovoice (20), focus groupdiscussions (6) and in-depth interviews (12) to document their health seeking journey from thedemand side.Many participants expressed pain, discomfort, and difficulties managing their conditions,particularly at baseline. They experienced stigma and neglect and were not included indecision-making relating to their health. Health-seeking journeys often oscillated betweentraditional and formal practices. Barriers to their ability to seek and reach care, includingdistance, poor roads, cost of transportation persisted throughout the intervention period. PeerSupport Groups impacted their mental wellbeing through mutual experience-sharing. Familyand community support enabled healthcare seeking. Support from family and friends and peersupport groups are key to engagement of persons affected by stigmatising diseases, particularlyin remote rural settings. We find using a person-centred approach for integrated casemanagement strengthens engagement across the patient pathway, promoting their participationand inclusion.

8202

THREE GEOSPATIAL APPROACHES OFFER INSIGHTS INTO PLANNING EFFECTIVE MDAS FOR NTDS IN WEST AFRICA

Maureen K. Headland[1], Kaustubh Wagh[1], Andres Martinez[2], Vance Harris[2], Caleb Parker[2], Elisabeth Chop[3], Brian Fuller[3], Diana Stukel[1]

[1]FHI 360, Washington, DC, United States, [2]FHI 360, Durham, NC, United States, [3]Helen Keller International, New York, NY, United States

Effective mass drug administration (MDA) is the cornerstone of preventive chemotherapy (PC) neglected tropical disease (NTD) programs. USAID's Act to End NTDs | West program supports Ministries of Health to eliminate or control five PC NTDs across 11 West African countries by assisting with MDAs and disease specific assessments. Coverage evaluation surveys (CES) are used to validate treatment coverage shortly after MDA. Non-treated populations (MDA eligible people in endemic districts who do not participate in the most recent treatment campaign) are of concern as they may enable ongoing transmission of infection. If these populations can be identified, programs can take more precise actions to identify and target them for treatment. Geospatial patterns of non-treated populations are identified by mapping CES data from five surveys (29,501 MDA-eligible respondents) conducted in 16 districts (879 villages) across Niger, Senegal, and Sierra Leone. Clusters of sampled villages with high rates of non-treatment are identified on the maps, as well as locations where disproportionately more men (or women) were not treated. Further, a geospatial analysis describing the travel time between households and health facilities was conducted, and the results are used as a proxy to measure village remoteness. The geospatial maps reveal clusters of high levels of non-treatment associated with remote populations in Sierra Leone and with mobile populations in both Senegal and Niger. One district-level map reveals a distinct pattern of high non-treatment villages located along district administrative boundaries. This research shows how conducting geospatial analyses of varying complexity can be used to refine NTD MDA programs. During program planning, GIS-generated travel time maps could support programs to ensure areas physically more remote from the health system receive additional support in subsequent rounds of MDA. During program evaluation, maps provide crucial insights into the effectiveness of interventions, enabling adjustments to improve microplanning ultimately contributing to the successful elimination or control of NTDs.

8203

ROLES OF COMMUNITY DRUG DISTRIBUTORS FOLLOWING THE HALT OF MASS DRUG ADMINISTRATION FOR ONCHOCERCIASIS IN UGANDA

Stella Neema[1], John Bosco Asiimwe[1], Edridah Muheki Tukahebwa[2], Harriet Sengendo[3], Annet T. Khainza[2], Lauri Bernard[3], Gregory S. Noland[3], **Jenna E. Coalson**[3]

[1]Makerere University, Kampala, Uganda, [2]The Carter Center, Kampala, Uganda, [3]The Carter Center, Atlanta, GA, United States

Mass drug administration (MDA) with ivermectin is key to onchocerciasis elimination. In Uganda, community drug distributors (CDDs), typically volunteers selected by other community members, mobilize communities for MDA, increase disease awareness, and distribute and report treatments. At peak in 2009, The Carter Center trained 77,600 CDDs in Uganda, but as transmission is interrupted, MDA is no longer required. We conducted a mixed methods, cross-sectional study in late 2023 to describe the involvement of former CDDs in other community health and development activities in formerly endemic foci that have stopped MDA. We randomly selected two subcounties per district and two parishes per subcounty, then surveyed ~162 former CDDs from the parish rosters. Twenty-two focus group discussions, 33 in-depth interviews, and 90 key informant interviews were also conducted. About 78% of 1,580 surveyed former CDDs reported that they had opportunities for service after MDA stopped, and 70.6% reported engaging in such health or development services. Nearly all (90%) felt their CDD service equipped them with skills for other service roles, and 94% reported increased interest in such work. Other activities they had performed included mosquito net distribution, health education and community sensitization, sanitation improvement, immunization, and integrated community case management. Of the 29.4% of former CDDs who did not engage in health and development after their CDD service, lack of opportunity stood as the primary barrier for 68%. The national and district Ministry of Health officers highlighted the value of CDDs' previous training and good reputations in their communities and reported integrating them where possible into health programs, though several noted that educational barriers and poor rosters of former CDDs can be practical limitations. Ultimately, this study has demonstrated that many former CDDs have been integrated into continued service activities in their communities when opportunities arose. Additional opportunities, cross-training, and improved documentation would help maximize their contributions.

8204

EFFECT OF MOBILE POPULATIONS ON STOPPING MDA FOR LYMPHATIC FILARIASIS/ONCHOCERCIASIS IN CROSS RIVER STATE

Kemisola R. Fagbohun[1], Chukwuemeka Makata[2], Chinwe Okoye[2], Fatai Oyediran[2], Omeji Godwin Okeagu[3], Veronica Mark Onem[3], Wangeci Thuo[1], Nnanke Etimita[1], Chukwuma Okonkwo[1], Scott McPherson[1], Danielle Epps[1]

[1]RTI, Research Triangle Park, NC, United States, [2]NTD Control Division, Federal Ministry of Health, Abuja, Nigeria, [3]NTD Control Program, Cross River State Ministry of Health, Calabar, Nigeria

The mobility of populations presents a significant challenge in reaching milestones to stop Lymphatic Filariasis (LF) and Onchocerciasis (OV) mass drug administration (MDA). These NTDs affect communities in remote or underserved areas where populations may be highly mobile due to factors like seasonal migration, economic opportunities, or displacement from conflict or environmental disasters. Nigeria, particularly Cross River State, borders Cameroon. In both 2019 and 2023, refugees camped in six LGAs (Aamkpa, Boki, Bakassi, Etung, Ogoja and Obanliku) in the state, staying in the camps with some later integrating into host communities. As of 2023, only Ogoja, and Etung LGAs continued to host refugees supported by UNHCR. Refugee camps often experience high population turnover as people arrive, depart, or move between camps. This mobility complicates efforts to track and treat individuals for LF and OV, as it may be challenging to ensure consistent coverage of MDA. This is further worsened by limited access to health facilities, constrained by logistical requirements or reluctance to seek medical care due to cultural or religious reasons. From 2020 till date, the state NTD program identified the LGAs and communities where refugee populations were located and collaborated with UNHCR and other International Organization to provide targeted treatments to these camps, this was further strengthened by continuous monitoring of MDA and use of members of refugees as medicines distributors (community implementers). As a result, 21,314 refugees were treated from 30,483 persons in 2020 for Oncho/LF MDA in five camps (Adagom 1, Adagom 3, Ukende, Agbokim, and Ajassor) across 2 LGAs (Ogoja and Etung), with 100% geographical coverage and 70% therapeutic coverage. The 2023 treatment was for OV only due to Implementation Units (IU) fulfillment of criterion to stop LF MDA (passed Transmission Assessment Survey TAS 1). A total of 14,804 refugees were treated, from 21,487 persons, in five camps across 2 LGAs thereby achieving 100% geographical coverage and 69% therapeutic coverage.

8205

ELIMINATING ONCHOCERCIASIS IN NIGERIA: SUCCESSES, FAILURES, AND LEARNINGS FROM CROSS RIVER STATE

Chukwuma Okonkwo[1], Wangeci Thuo[1], Joseph Mfon[1], Nnanke Etimita[1], Kemisola R. Fagbohun[1], Fatai Oyediran[2], Chukwuma Makata[2], Veronica Mark Onem[3], Omeji Godwin Okeagu[3], Scott McPherson[1], Danielle Epps[1]

[1]RTI, Research Triangle Park, NC, United States, [2]NTD Control Division, Federal Ministry of Health, Abuja, FCT, Nigeria, [3]NTD Control Program, Cross River State Ministry of Health, Calabar, Nigeria

This paper explores past successes and failures of Onchocerciasis program in CRS and identifies few hypotheses on why the state is yet to reach elimination goal. Onchocerciasis prevalence mapping was completed in 1998, confirming that 15 of the 18 LGAs in CRS were endemic. After more than 20 years of Mass Drug Administration (MDA), CRS conducted epidemiological assessments in 2009, 2012, 2017 and 2023 to evaluate progress towards elimination. A 2017 assessment indicated the state had reached elimination target; 3,193 DBS samples collected in 2017, were analyzed in 2019, showing zero positive case. The NOEC recommended a repeat of the epidemiological assessment due to delays in completion of laboratory analysis. A repeat of the assessment in 2023 unexpectedly confirmed disease prevalence; 100 children aged 5-9 years of consenting parents/guardians were targeted in 34 purposively selected endemic communities; a total of 3,260 DBS samples were collected on labelled filter papers using sterile lancet needles to prick the children's fingers. The blood samples, spotted on the filter papers, and stacked onto pencil sticks, were allowed to dry completely before storage in humid-free bags packed with desiccants. Samples were analyzed using OV-16 ELISA serological test to determine presence of IgG4 antibodies. A total of 56 positive cases were found in 15 communities across 8 LGAs, resulting to 1.72% OV prevalence in the state. This result reveal evidence of ongoing OV transmission in CRS with the following hypothesis - ineffective MDA coverages formed reservoir for transmission; influx of refugees from endemic regions of Cameroun increased transmission rate and spread; populations living in hard-to-reach areas missed treatment during MDAs; there are cross border transmission from neighboring endemic communities; and there is change in vector distribution due to shifts in waterways and breeding sites over the years. Two years of additional MDA has been recommended. As we explore approaches to strengthen MDA to reach all vulnerable populations, it is crucial to consider factors like climate change and cross border movements in our future programming.

8206

LEAVING NO ONE BEHIND: STRENGTHENING MASS DRUG ADMINISTRATION CAMPAIGNS AGAINST NEGLECTED TROPICAL DISEASES THROUGH THE IMPLEMENTATION OF SUPERVISOR COVERAGE TOOL IN ANGOLA

Cecilia de Almeida[1], Elsa P. Mendes[1], José Franco Martins[2], Luis Lufunda[3], Xavier Badia Rius[4], Ana Direito[3], Teresa Nobrega[3], **Ercilio Jive**[3]

[1]National NTD Control Program, Ministry of Health, Luanda, Angola, [2]National Malaria Control Program, Ministry of Health, Luanda, Angola, [3]The Mentor Initiative, Luanda, Angola, [4]The Mentor Initiative, haywards heath, United Kingdom

Mass Drug Administration (MDA) is one of the recommended public health strategies to control and eliminate preventive chemotherapy neglected tropical diseases (NTDs) in endemic regions. However, ensuring comprehensive coverage of target populations remains a challenge, particularly in resource-constrained settings and hard to reach populations. In Angola, improvement of campaigns reach has been the main focus of the Ministry of Health. In 2018, Supervisor Coverage Tool (SCT) started to be implemented alongside MDA campaigns to identify areas not reaching optimal treatment coverage thresholds. The main objective of the SCT is to identify areas not reaching optimal treatment coverage thresholds and to improve the coverage when the campaign is still ongoing. Trained supervisors used the results of the tool to direct mop-up activities to recover areas where individuals were missed, ensuring that no one is left behind. Data collected through the SCT is used to assess gaps in access, tailor outreach efforts, and optimize resource allocation for future campaigns. In 2024, SCT was implemented in 3 provinces, 13 municipalities and 52 villages. Implementation of the SCT in Angola has resulted recovering of more than 7,400 treatments during ongoing campaigns. The impact results on MDA coverage are being analyzed and will be presented. The tool has enhanced the accountability and efficiency of MDA campaigns, enabling health authorities to track and monitor adherence in real-time and adjust strategies as needed. The SCT proved to be of great support to improve MDA management and increase coverage of interventions. The tool is also used to inform ongoing campaign implementation and gaps encountered during campaigns, therefore contributing to continuously improving MDA planning and implementation.

8207

HYPERENDEMICITY OF SOIL-TRANSMITTED INFECTIONS IN CHILDREN OF THE HONDURAS TROPICAL RAINFOREST

Gabriela Matamoros[1], Maria Esther Araujo[1], Ana Sanchez[2]

[1]Instituto de Investigaciones en Microbiologia, Facultad de Ciencias, Universidad Nacional Autonoma de Honduras, Tegucigalpa, Honduras, [2]Department of Health Sciences, Faculty of Applied Health Sciences, Brock University, St. Catharine's, ON, Canada

The Honduran Moskitia, located in the eastern region of the country, is one of the most isolated and remote geographies in Central America, as well as one of the last remaining tropical forests in the continent. Populated by Afro-Caribbean Garífuna and indigenous Miskito communities, La Moskitia inhabitants are plagued by poverty and lack of basic water and sanitation; situation conducive to intense transmission of soil-transmitted helminths (STH). According to the Ministry of Health, mass drug administration (MDA) is provided to schoolchildren twice a year, but the efficacy of this strategy is unknown. The present study aimed to undertake a rapid assessment of the prevalence of STH in a small group of schoolchildren living in the community of Kaukira in the Honduran Moskitia. The formol-ether concentration (FEC) technique was used to detect STH, and a qPCR was evaluated as a screening diagnostic tool. A total of 54 samples were analyzed by both FEC and qPCR. Two multiplex qPCR protocols were tested, each including specific primers and probes for STH identification. Following DNA detection, a spiking experiment was performed to assess the limit of detection of the qPCR for *A. lumbricoides* and *T. trichiura*. Using both methods, an overall STH prevalence of 98.2 % (CI 95%: 94.6-100%) was observed; the highest STH prevalence reported to date in Honduras. *T. trichiura* was the most prevalent parasite, followed by *A. lumbricoides, N. americanus, and S. stercoralis,* with prevalences of 92.6%, 57.4%, 37% and 7.4%, respectively. In comparison to the FEC, the qPCR demonstrated higher sensitivity, with the advantage of detecting *S. stercoralis*. The spiking experiment showed that the qPCR can detect 1 egg/100 mg of stool for both parasites. The findings of this study demonstrate that, despite undergoing bi-annual anthelminthic therapy, STH prevalence in this region is remarkably high. They also highlight that measuring achievement of the STH elimination target by 2030 requires the implementation of sensitive diagnostic techniques that allow effective surveillance, specially in regions where MDA is the single strategy for STH control.

8208

COMMUNITY LEADERS ACTION GROUP: A SOCIAL CATALYST TO INCREASE MASS DRUG ADMINISTRATION COVERAGE AND COMMUNITY SUPPORT FOR COMMUNITY-DIRECTED DISTRIBUTORS

Emmanuel Emukah[1], Adamu Sallau[2], Lazarus Nweke[2], Raymond Ogieva[1], Ross Hegtvedt[3], Marquita McMichael[3], Ileana Resendez[3], Lindsay Rakers[3], Emily Griswold[3], Jenna E. Coalson[3], Emmanuel Miri[4], Ifeoma Otiji[5], Owen Eguasa[6], Efeomon Eseigbe[6], Happy Poko[6], Solomon Adelamo[4], Izebhua Blessing Ikponmwosa[1], Samuel Ifeanyichukwu[2], Egeonu Attamah-Isiani[2], Emalee Martin[3], Chukwuemeka Makata[7], Fatai Oyediran[7], Frank O. Richards, Jr.[3], Gregory S. Noland[3]

[1]The Carter Center, Benin City, Nigeria, [2]The Carter Center, Enugu, Nigeria, [3]The Carter Center, Atlanta, GA, United States, [4]The Carter Center, Jos, Nigeria, [5]Enugu State Ministry of Health, Enugu, Nigeria, [6]Edo State Primary Health Care Development Agency, Benin City, Nigeria, [7]Federal Ministry of Health, Abuja, Nigeria

Onchocerciasis is a neglected tropical disease endemic in Nigeria for which a key intervention strategy is mass drug administration (MDA) with ivermectin. It is possible to interrupt transmission with 12-15 rounds of MDA; however, onchocerciasis transmission has persisted after 28 years of MDA in four districts of Edo and Enugu states, Nigeria. These two states have had low MDA coverage, with community leaders' disengagement from the MDA program having led to low community support and ownership and reduced support to community directed distributors (CDDs) of ivermectin. This study examined the impact of the "Community Leaders Action Group" (CLAG) innovation, where committed community leaders were trained to engage non-committed leaders in both their own and nearby communities to step up support for the CDDs and MDA. CLAG members acted as social catalysts to improve incentives to CDDs. Forty community leaders with histories of supporting CDDs were engaged and asked to encourage other leaders to follow suit. We reviewed reported MDA coverage data from the treatment rounds before and after the CLAG intervention in the study area, in November 2021 and December 2022, respectively. Results showed significant increase in proportion of communities offering incentives to support CDDs from 370 communities (36.3%) before CLAGs to 580 (56.9%) after ($p<0.001$). Surveys of CDDs showed that community support to CDDs (financial or gifts) increased from 616 CDDs (34.8%) to 882 CDDs (49.9%). Fewer communities had inadequate (<65%) therapeutic coverage after CLAGs (249 communities, 24.4%) than before (417 communities, 40.9%), a 40.3% risk reduction (95% confidence interval [CI] 31.9-47.6%). CLAGs remain active and reported coverage rates have remained >65% for the two years after the study. CLAGs were successful in engaging community leaders and improving MDA delivery in these Nigerian districts with persistent onchocerciasis. We recommend the CLAG training in all endemic communities to improve ownership and sustainability of NTD elimination efforts and accelerate progress toward disease elimination.

8209

A PROGRAMMATIC OVERVIEW OF THE GULF SOUTH VECTOR EDUCATIONAL CENTERS FOR TRAINING, OUTREACH, AND RESOURCES (VECTOR) COLLABORATIVE

Claudia Riegel[1], Janet Hurley[2]

[1]City of New Orleans Mosquito, Termite and Rodent Control Board, New Orleans, LA, United States, [2]City of New Orleans Mosquito, Termite and Rodent Control Board, Texas A& M, TX, United States

Vector-borne diseases have increased in the past two decades at rates beyond what current infrastructure can manage. To protect public health, we must increase and strengthen our front-line defenses, which are mosquito abatement districts and public health workers. This is particularly important in the Gulf South of the United States because of its intersection of health and economic disparities with a climate that is susceptible to vectors and pathogens. The Gulf South Vector Education Center for Training, Outreach, and Resources (Gulf South VECTOR) was funded in 2023 by the Centers for Disease Control and Prevention (NC50CK000638). This is a regional partnership of public and private organizations led by the City of New Orleans Mosquito, Termite, and Rodent Control Board, Louisiana, United States. The goal of this project is to strengthen partnerships across public and private sectors. The Gulf South VECTOR Collaborative will coordinate training and evaluation of pest management, vector control districts, public health, sanitary, and animal health professionals in these fields to achieve an integrated workforce to mitigate community vector-borne disease risk in the Gulf Coast region of the United States. The project will aim to address critical gaps in information exchange, resources, infrastructure, evaluation methods, and training standards. Specifically, this project will train and evaluate students and professionals. We will create and test educational content that highlights procedural best practices. The core curriculum will be standardized and replicated across the region, and will be offered to students, working professionals, and trainees across audiences with diverse backgrounds. This project will break down silos and promote interdisciplinary training and create partnerships through regional and national cooperation that is desperately needed to build resiliency and protect people and animals from vector-borne disease. A summary of the progress will be presented.

8210

OSELTAMIVIR, A NON-METRONIDAZOLE CLASS OF COMPOUND, AFFECTS RAFT ASSEMBLY, VESICLE BIOGENESIS, AND HOST-PARASITE INTERACTIONS BY *GIARDIA*

Breanna Pence[1], Julio Rangel[1], Harrison VanKoten[2], James Klinkenberg[2], Steven Patterson[2], Siddhartha Das[1]

[1]University of Texas at El Paso, El Paso, TX, United States, [2]University of Minnesota, Minneapolis, MN, United States

Giardia lamblia is a protozoan parasite responsible for intestinal illness, worldwide. Symptoms of giardiasis include diarrhea, abdominal pain, and malnutrition in children. Metronidazole is a common treatment for giardiasis, but toxicity and resistance has been reported. Being a non-invasive parasite, the mechanisms by which *Giardia* causes infection are unclear. Recent reports have suggested that *Giardia* releases nanoscale lipid particles, called extracellular vesicles (EVs). EVs exist as two subtypes: microvesicles (MVs) and exosomes (EXOs), both of which carry virulent factors that paralyze the host's immune defenses. We reported earlier that oseltamivir (Osm, Tamiflu®), an anti-viral compound, inhibits the attachment of trophozoites to intestinal epithelial cells and cyst production *in vitro*. Osm also disassembles giardial lipid rafts (LRs) and alters the production of EVs by *Giardia*. In the current study, we optimize the anti-*Giardia* activity by synthesis of Osm analogs. The analogs were evaluated for their inhibition of giardial growth, attachment to Caco-2 cells, cyst production, LR assembly, and EV biogenesis. LR assembly was assessed using confocal microscopy. EVs were isolated by ultracentrifugation (15,000 x g for MVs and 100,000 x g for EXOs), then EV size and concentration was assessed using nanoparticle tracking analysis. Four analogs were found to reduce the growth of trophozoites (IC_{50} ~30-50 μM), attachment (IC_{50} ~65-102 μM), cyst production (IC_{50} ~40-50 μM), LR assembly, and the EV production (~20 μM). Some compounds demonstrated selective activities on MVs and EXOs, suggesting that EV subtypes are structurally and functionally distinct. We found that the release of cytokines such as CCL20, CCL2, and PLAUR was reduced by our analogs, implicating that these compounds are effective in modulating the immune response by host cells. This is the first successful targeting of EVs and demonstration of the potential of EV production as a drug target. We propose that these synthetic Osm analogs should be effective in treating metronidazole-resistant giardiasis alone or in combination with other anti-giardial agents.

8211

TRUST IN THE HEALTHCARE SYSTEM AND NATIONAL CONTROL PROGRAMMES IN A RURAL SETTING IN CAMEROON: AN ECONOMIC EXPERIMENT

Sergi Alonso[1], Poppy HL Lamberton[1], Louis-Albert Tchuem Tchuente[2], Justin Komguep Nono[3]

[1]School of Biodiversity, One Health and Veterinary Medicine & Wellcome Centre for Integrative Parasitology, University of Glasgow, Glasgow, United Kingdom, [2]Centre for Schistosomiasis and Parasitology & Laboratory of Biology and Ecology, Department of Animal Biology and Physiology, Faculty of Science, University of Yaoundé, Yaoundé, Cameroon, [3]Unit of Immunobiology and Helminth Infections, Laboratory of Molecular Biology and Biotechnology, Institute of Medical Research and Medicinal Plant Studies (IMPM), Ministry of Scientific Research and Innovation, Yaoundé, Cameroon

Healthcare-seeking levels are low in the sub-Saharan Africa (SSA), where patients still confront weak health systems and face several barriers to access. This is partly why the current mainstay control of schistosomiasis and other neglected tropical diseases (NTDs) is based on community-targeted mass drug administration (MDA), irrespective of individual diagnosis. Asymmetry of information, such as the lack of trust, is a determining factor for healthcare behaviours and treatment compliance in rural SSA, and is influenced by interpersonal and institutional factors. We elicited trust among patients actively seeking care at health facilities and is the first study to compare it to trust levels measured among households eligible to receive MDA treatment through community outreach. We further analysed socio-economic and health predictors of trust, controlled by provider-specific characteristics. In the Bafia district (Cameroon), we recruited 108 adults eligible for MDA treatment and 11 MDA providers (January 2024); and 116 adults seeking care at district health facilities and 18 health providers (February 2024). We conducted a trust experiment where patients and providers received endowments and faced the decision to share them (or not) between one another in a three-stage economic experiment. We also conducted socio-economic questionnaires and interviews with clinical vignettes to assess providers' clinical competence on schistosomiasis and other common health issues. Results will be presented and discussed in the context of tackling NTDs where treatment coverage is a combined measure of MDA access and treatment compliance, with the latter likely driven by trust in the healthcare system and the effectiveness of such campaigns. Inadequate coverage translates to reduced effectiveness of control strategies, which perpetuates disease transmission and hinders the World Health Organization objective of eliminating the disease as a public health problem by 2030. This study sheds light on the relevance of trust in healthcare settings and parasitic helminth interventions, which has never been evaluated before.

8212

ENHANCING COMMUNITY LEADER ENGAGEMENT IN THE FIGHT AGAINST NTDS IN CAMEROON: UNDERSTANDING KEY DETERMINANTS

Emilienne Epee[1], Diawara Aissatou[2], Shona Wynd[3], Ebene Clarisse[4], Nana Hughes[5], Nko Ayissi Georges[4], Ngo Likeng Julienne Louise[6], Ndzana Bertrand[7]

[1]University Of Yaounde 1, Yaounde, Cameroon, [2]Glide, Abu Dhabi, United Arab Emirates, [3]Glide, Abudhabi, United Arab Emirates, [4]Moh Cameroon, Yaounde, Cameroon, [5]Ism, Yaounde, Cameroon, [6]Ucac, Yaounde, Cameroon, [7]University of Ebolowa, Ebolowa, Cameroon

Onchocerciasis, a neglected tropical disease, remains a significant public health challenge due to its persistence. Despite the implementation of community-based control strategies, certain community groups continue to remain uninvolved, presenting barriers to its elimination. There is an urgent need for a critical review of community health implementation principles to ensure consistent and active community participation. This study aimed at exploring the factors associated with the non-implication of community leaders in the fight against NTDs in Cameroon. We conducted a qualitative and descriptive study using a pre-designed interview guide. Focus groups involving community leaders from 32 hyperendemic communities across four regions were analyzed. Quantitative data were processed using SPSS, while Nvivo facilitated transcription and content analysis for qualitative data. Among the selected communities, community leaders included members of dialogue structures, traditional chiefs, and religious leaders. Knowledge about onchocerciasis remained limited and misconceptions negatively impacted awareness and communication related to Mectizan. Interestingly, in certain villages, leaders attributed onchocerciasis to supernatural causes. Although traditional authorities are aware of Mectizan as a treatment, they do not actively participate in its implementation. Additionally, feedback on program evolution is lacking, as well as an overview of the entire fight against NTDS, particularly onchocerciasis. Efforts to effectively engage community leaders in the fight against NTDs, especially onchocerciasis, require addressing misconceptions, enhancing awareness, and fostering active participation. Feedback mechanisms and comprehensive program evaluations are essential for successful elimination strategies.

8213

INTEGRATION OF HYGIENE MEASURES FOR LYMPHEDEMA MANAGEMENT INTO COMMUNITY HEALTH CENTERS' MINIMAL PACKAGE OF ACTIVITIES IN TWO RURAL SETTINGS, MALI

Moussa Sangare[1], Yaya Ibrahim Coulibaly[2], Abdoul Fatao Diabate[3], Diadje Tanapo[3], Sekou Oumarou Thera[3], Oumar Coulibaly[3], Housseini Dolo[3], Siaka Yamoussa Coulibaly[3], Salif Seriba Doumbia[3], Fatoumata Traore[4], Binta Sall[3], Mahamoud Mahamadou Koureichi[3], Michel Emmanuel Coulibaly[3], Lamine Soumaoro[3], Abdallah Amadou Diallo[3], Seydou Doumbia[3], Alison Krentel[5], Thomas B Nutman[6]

[1]International Center for Excellence in Research, | University of Sciences, Techniques and Technologies; School of Epidemiology and Public Health, University of Ottawa, Bamako, Mali, [2]International Center for Excellence in Research, | University of Sciences, Techniques and Technologies; Dermatology Hospital of Bamako, Bamako, Mali, [3]International Center for Excellence in Research, | University of Sciences, Techniques and Technologies, Bamako, Mali, [4]International Center for Excellence in Research | University of Sciences, Techniques and Technologies, Bamako, Mali, [5]Bruyere Research Institute; School of Epidemiology and Public Health, University of Ottawa, Ottawa, ON, Canada, [6]National Institute of Allergy and Infectious Diseases, Bethesda, MD, United States

Lymphedema (LE) impedes people from carrying out their daily activities, exacerbating poverty, social exclusion, and stigmatization. Evidence demonstrates the effectiveness of routine hygiene practices in managing LE. with a reported improvement of patient's living standards. To ensure sustainability of hygiene activities, we identified obstacles to integrating LE management into community health centers' minimal package of activities. A mixed-method study was conducted in the health districts of Kolondieba and Kolokani, enrolling LE patients involved in a doxycycline trial with hygiene care in both arms. A questionnaire was administrated to participants to identify barriers and facilitators to the integration of hygiene care into the minimal package of activities. Additionally, 24 in-depth interviews and 8 focus group discussions were conducted with patients and health workers. SPSS V26 and NVivo V14 were used for quantitative and qualitative data analysis respectively. In total, we enrolled 192 LEDoxy patients with mean age of 56±11 years and a sex ratio of 0.15. Most of the participants 83% (160/192) stated that they would like to have hygiene measures integrated into the minimal package of activities. Among the 35 obstacles to the integration reported, 14 (40%) and 11 (31%) respectively the poor quality of management and the lack of qualified health workers. Lack of resources for clinicians and patients/families, high cost of treatment at health centers and the low level of knowledge of the condition by health workers were the main obstacles reported by interviewees. Key reported integration facilitators include overcoming LE stigma, enhancing workforce capacity, promoting LE self-management and families' support. Resource scarcity, patients perceived low level of knowledge of the condition by heath workers, were identified as main barriers to hygiene measures integration

into community health centers' minimal package of activities in these rural settings. Overcoming these obstacles could help in implementing a sustainable integration system

8214

LEVERAGING FULL GEOGRAPHICAL COVERAGE APPROACH TO TRACHOMATOUS TRICHIASIS CASE FINDING AND MANAGEMENT WITH CATARACT TO SUSTAIN SERVICES IN TANZANIA

Athuman Tawakal[1], Joyce Lyamuya[1], Bernadeta Shilio[2], Regina Noh[3], Nick Kourgialis[4], Barnabas Mshangila[5]

[1]Helen Keller International, Dar es Salaam, Tanzania, United Republic of, [2]Ministry of Health, Dar es Salaam, Tanzania, United Republic of, [3]Cure Blindness/Himalayan Cataract Project, US, NY, United States, [4]Helen Keller International, US, NY, United States, [5]Mbeya Zonal Referal Hospital, Mbeya, Tanzania, United Republic of

Tanzania is one of the highest burden countries for trachoma. TT elimination program aims to provide sight saving surgeries to more than 48,000 people with Trachomatous Trichiasis in Tanzania. Neglected Tropical Disease Control Program of the Ministry of Health through collaboration with Helen Keller Int'l, Sightsavers International adapted Full Geographical Coverage Approach targeting all regions and districts with high endemicity of TT for case finding and organize surgical camps at the community level to offer treatment to confirmed cases. The approach focuses on leaving no one behind for case finding and management by ensuring it is reaching everywhere and everyone in the districts where the program is being implemented. Trained community case finders are used to identify, counsel, and refer people with TT for confirmatory screening and surgical care through surgical outreach camps. Initial screenings are conducted on a house-to-house basis using community case finders. Free surgeries are offered by qualified technical teams at health facilities within the targeted regions, thus ensuring easy access to care. The approach has proven efficiency in reaching all villages in each targeted districts resulting in high coverage of households and screening majority of marginalized population groups including women and disabled people living in remote areas and also experienced high acceptance rate of surgical services. The FGC approach was further leveraged with case finding of cataract cases in the same villages, using the same case finders and screening same population which was piloted in Mbarali district on Mbeya region and similarly witnessed high coverage in reaching the population for cataract case finding and treatment and demonstrated effectiveness in increasing the reach and highly contributing to saving many people from preventable blindness caused by Trachomatous Trichiasis and cataracts as well created sustainability in the service provision in the region.

8215

THE INFLUENCE OF RUMORS AND MISINFORMATION ON ONCHOCERCIASIS ELIMINATION - EVIDENCE FROM CROSS BORDER REGION OF MALI

Dukharmel Nazaire[1], Abdoul Fatao Diabate[2], Diadje Tanapo[2], Mahamoud Mahamadou Koureichi[3], Sekou Oumarou Thera[2], Siaka Yamoussa Coulibaly[2], Salif Seriba Doumbia[2], Moussa Sangare[2], Yaya Ibrahim Coulibaly[2], Alison Krentel[1]

[1]Bruyere Research Institute, Ottawa, ON, Canada, [2]International Center for Excellence in Research (ICER-MALI) | University of Sciences, Techniques and Technologies of Bamako, Bamako, Mali, Bamako, Mali, [3]International Center for Excellence in Research (ICERMALI) | University of Sciences, Techniques and Technologies of Bamako, Bamako, Mali, Bamako, Mali

After more than 15 years of mass administration of ivermectin against onchocerciasis, Mali has succeeded in pre-stop survey of onchocerciasis in most areas except for the transmission zone KA05, a cross border area that includes three health districts. To inform the mass drug administration cycle in 2024, a study was carried out in February 2023 in 6 villages of KA05 using a mixed methods approach. This abstract will present the qualitative findings from 24 individual in-depth interviews (5 women and 19 men) and (10 focus group discussions (5 women's groups and 5 men's groups). Participants were 18 years and older and were purposively selected according to the following identities: gold miners, local community members, self-identified as never treated, people with high mobility, former community drug distributors and healthcare providers. Results showed that some participants believed that the existence of onchocerciasis in KA05 was "fake news" while others reported that onchocerciasis is the result of a "curse". Other rumors included the belief that it is only adult men who are at risk of contracting onchocerciasis while some participants believed that the tablets themselves distributed during MDA bring onchocerciasis to the communities. Themes related to side effects showed that some participants confused the side effects of praziquantel (used to treat schistosomiasis) with those of ivermectin, as the two campaigns have been conducted in close proximity in the past. Others refused the treatment out of fear of being skin snipped, as had been done in previous onchocerciasis detection campaigns. This research demonstrates the strength of rumors in KA05 communities in Mali and their potential for influence on people's acceptability of mass drug administration for onchocerciasis. Despite many years of mass drug administration in the region, it is clear from this research that new social mobilization approaches are needed. It is recommended that regular adaptations are made to health awareness and education messages to address misinformation and currently circulating rumors.

8216

THE THERAPEUTIC EFFICACY OF ALBENDAZOLE AND IVERMECTIN AGAINST SOIL-TRANSMITTED HELMINTH INFECTIONS IN RWANDA

Jean Bosco Mbonigaba

Rwanda Biomedical Centre/ Ministry of Health, City of Kigali, Rwanda

By 2030, WHO has set a new goal of eliminating soil-transmitted helminthiasis (STH) as a public health problem in 96 out of 101 countries (96%). To achieve this goal, the tools targeting both the agent and host must exhibit optimal efficacy and effectiveness. Rwanda's neglected tropical diseases (NTD) program has been implementing mass deworming campaigns in communities and schools since 2008. However, there is persistence of high prevalence of STH in many districts, with a high proportion of moderate to high intensity infections (MHI). The National NTD Program is currently conducting a community trial to *(1)* determine and quantify the force of each of the drivers behind that persistence of MHI in order to inform the design of proportional treatment, behavioral and water, sanitation and hygiene interventions; and *(2)* test different integrated interventions package to determine the most impactful package capable of accelerating the elimination of STH as a public health problem. Here we are presenting the findings of efficacy study. In November 2023, we performed efficacy testing of a single dose of albendazole chewable (400 mg) alone and a single dose of albendazole chewable (400 mg) combined with ivermectin 200 mcg/ kg body weight. Each treatment regimen was administered by directly observed therapy (DOT). Before administering medications, a stool sample was collected from each study subject and screened for helminth eggs using duplicate kato-katz technique and egg count was performed. On the 14th day after drug administration, a follow-up stool sample was analyzed. The results showed Trichuris Trichiura mean eggs per gram (EPG) reduction of 76% by ALB+IVM compared to 17% by ALB alone. The cure rate was 45% by combined treatment compared to 13% by ALB alone. These findings showed the superior therapeutic efficacy of albendazole when combined with ivermectin to treat Trichuris Trichiura. The same evidence was demonstrated in pemba island and Laos. The scale-up of this combination treatment should be piloted to inform the large scale-up in all districts endemic to Trichuris Trichiura.

8217

UNDERSTANDING PERCEPTIONS OF SCHISTOSOMIASIS AND ITS CONTROL AMONG HIGHLY ENDEMIC LAKESHORE COMMUNITIES IN MAYUGE; UGANDA

Lazaaro Mujumbusi[1], Lucy Pickering[2], Edith Nalwadda[1], Sande Slivesteri[1], Agnes Ssali[1], Mary Nanzala[3], Keila Meginnis[2], Janet Seeley[4], Poppy H. L Lamberton[2]

[1]Medical Research Council/Uganda Virus Research Institute & London School of Hygiene & Tropical Medicine Uganda Research Unit, Entebbe, Uganda, [2]University of Glasgow, Glasgow, United Kingdom, [3]Makerere University –Johns Hopkins University Research Collaboration, Kampala, Uganda, [4]London School of Hygiene and Tropical Medicine, London, United Kingdom

Over 240 million people have schistosomiasis, of which the majority live in Africa. In Uganda, over 4 million people are infected, and 55% of the population is at risk. Praziquantel mass drug administration is the WHO-recommended control strategy, but coverage is often low. How perceptions of schistosomiasis shape prevention and treatment practices and their implications for control measures are not well understood. Rapid ethnographic appraisals were performed for six weeks using structured observations, transect walks, participant observation, sixty in-depth interviews, and 19 focus group discussions. Data were analyzed thematically using iterative categorization. Community members had varied perceptions about how one can catch and transmit schistosomiasis and these perceptions affect prevention and treatment practices. Observations revealed open defecation as a common practice, low latrine numbers, and all communities largely depend on lake water and contact it daily. Perceptions that a swollen stomach was a sign/symptom of '*ekidada'* (caused by witchcraft) resulted in some people rejecting free praziquantel in favour of herbal treatment from traditional healers at a fee. Others rejected praziquantel because of its perceived side effects. People who perceived that schistosomiasis is caught from drinking unboiled lake water did not seek to minimize skin contact with infected water sources. These findings exhibit knowledge gaps and misconceptions that impacted control, necessitating a contextualized health education programme, alongside MDA, and improved WASH practices. Therefore, we co-developed a set of interventions with community members and developed education messages tailored to community needs through community meetings, local radios, drama, posters/banners, videos and training VHTs for sustainability. These education programs have improved knowledge, led to reduced misperceptions, water processing, and increased demand for praziquantel. Therefore, working with the community to co-develop tailored education messages can lead to improved knowledge and prevention practices.

8218

OUTBREAK OF *PLASMODIUM VIVAX* INFECTION IN A NATIVE COMMUNITY OF CONDORCANQUI PROVINCE, AMAZONAS, PERU IN 2023

Miguel Bernal[1], Deybi J. Huamán Maicelo[2], Milagros L. García Cordova[2], **Milagros Saavedra-Samillán**[2], Stella M. Chenet[2]

[1]Red de Salud Condorcanqui, Amazonas, Peru, [2]Instituto de Investigación de Enfermedades Tropicales, Universidad Nacional Toribio Rodríguez de Mendoza de Amazonas (UNTRM), Chachapoyas, Peru

Amazonas ranks as the second department in Peru with the highest incidence of malaria, affecting native communities within Condorcanqui province. In 2022, an increase in P. vivax cases (1,436) was reported, followed by P. falciparum cases (203). On June 6, 2023, the first seven malaria cases were detected within the native community of Alto Kashap and on June 9 the Condorcanqui Health Network coordinated an intervention to control the outbreak. The aim of this study was to describe the intervention during the malaria outbreak in Alto Kashap within the jurisdiction of the Atzakus Health Post, which provides coverage to 236 inhabitants. During the intervention, a total of 205 patients were evaluated. A total of 23 cases of P. vivax were diagnosed by microscopy, of which 15 were confirmed using qPCR. This revealed a positivity rate of 11.22% and an annual parasitic index of 83.03%, indicating a high risk of transmission in the area. Additionally, it was observed that 52.17% of the cases were men and more than 85% were under 27 years old. All positive patients were symptomatic and received on-site treatment, consisting of a seven-day course of chloroquine and primaquine, according to technical guidelines for malaria treatment in Peru. On the other hand, although the vector species was not identified during the intervention, outdoor residual spraying was carried out in all households (77) in the community as a preventive measure. In conclusion, the intervention played a critical role in the control of the malaria outbreak in Alto Kashap and contributed to the identification of housing and geographical factors involved in the transmission of the disease. These factors include the lack of basic services, such as limited access to drinking water, insufficient sanitation systems and limited medical care. Moreover, the community's proximity to the Kashap stream increases the risk of creating habitats conducive to vector proliferation. The study emphasizes the need for continuous research and coordinated efforts, as well as the implementation of new strategies to effectively control and mitigate the spread of malaria in other communities of Condorcanqui.

8219

GEOSPATIAL MODELLING TO PREDICT SOIL-TRANSMITTED HELMINTH RISK IN SCHOOLCHILDREN IN DAK LAK PROVINCE, VIETNAM

Tin Pham[1], **Adam W. Bartlett**[1], Dinh Ng_Nguyen[2], Katrina Blazek[1], Susana Vaz Nery[1]

[1]University of New South Wales, Sydney, Australia, [2]Tay Nguyen University, Dak Lak, Vietnam

Soil-transmitted helminth (STH) infections pose an ongoing public health problem in Vietnam despite long-running preventive chemotherapy (PC) programs. We used parasitological data (N=10,048) collected during a trial comparing the impact of school-based PC vs community-wide mass drug administration (MDA) on STHs in schoolchildren, in conjunction with open-source environmental and climatic data. We then conducted geospatial modelling to provide STH risk predictions at baseline (October 2019) and follow-up (November 2020) throughout Dak Lak province, Vietnam. Environmental and climate variables were selected through multivariate regression models that provided the lowest Akaike information criterion without co-linearity. Semi-variograms were then used to evaluate residual spatial autocorrelation and inform use of non-spatial or spatial risk prediction models to develop STH risk prediction maps for overall risk and risk of moderate-heavy intensity infections. The overall risk prediction maps demonstrated persisting STH hotspots in south and southeast corners of the province at baseline and follow-up. These hotspots were consistently demonstrated on risk prediction models stratified by control strategy (school-based PC vs community MDA). At baseline, there were considerable areas where the predicted moderate-heavy intensity infection risk was >2%, however at follow-up most of the province was predicted to have <2% moderate-heavy intensity infection. This analysis demonstrates that whilst the burden of STH infections, as measured by infection intensity, has reduced throughout the province, there remain persistent STH hotspots in the south and southeast of the province that require further evaluation for STHs and targeted interventions.

8220

ACCEPTABILITY OF INTEGRATED NEGLECTED TROPICAL DISEASES SURVEYS AND MASS DRUG ADMINISTRATION IN VANUATU

Md S. Islam[1], Elizabeth Nguyen[2], Fasihah Taleo[3], Gladymar P. Chacon[2], Prudence Rymill[4], Mackline Katenga[4], Stephanie Tabe[4], Denny Manvoi[5], Clare Dyer[2], David Kennedy[2], Lindah Peter[5], Julie Jacobson[6], John Kaldor[2], **Susana Vaz Nery**[2]

[1]School of Population Health, UNSW Sydney, Australia, [2]The Kirby Institute, UNSW Sydney, Australia, [3]World Health Organization, Port Vila, Vanuatu, [4]Ministry of Health, Port Vila, Vanuatu, [5]Vanuatu Red Cross Society, Port Vila, Vanuatu, [6]Bridges to Development, Seattle, WA, United States

Soil-transmitted helminths, scabies, and yaws are neglected tropical diseases (NTDs) endemic in Vanuatu. To control and eliminate these

diseases, the Vanuatu Ministry of Health implemented an integrated control program including mass drug administration (MDA) with albendazole, azithromycin and ivermectin. Community acceptability of integrated MDA was assessed between February 2023-April 2024 in a mixed-methods study that included questionnaires, focus group discussions with residents, and in-depth interviews with community leaders. Results of Tafea and Sanma province activities are presented here, while those for Shefa province are underway.

Questionnaire data revealed 88% (35/40) of respondents in Tafea and 91% (61/67) in Sanma recalled having received MDA. Predominant factors for residents' participation in MDA were prevention of intestinal worms (Tafea: 27%[15/56]; Sanma: 37%[39/105]) or skin infections (Tafea: 27%[15/56]; Sanma 38%[40/105]). Absenteeism and forgetfulness were the main reasons for not taking the medicines in both provinces. Most respondents were happy with the number of pills they took during the integrated MDA (Tafea: 86%[30/35]; Sanma 90%[55/61]), though fewer reported liking the taste (Tafea: 71%[25/35]; Sanma 48%[29/61]). A single visit (integrated MDA) was preferred to multiple visits by most respondents (Tafea: 79%[30/38]; Sanma 83%[55/65]). Qualitative findings confirmed that communities believed they had been suffering from multiple NTDs, and that the distribution of medication would reduce NTDs in their community. Misperceptions surrounding scabies were discovered during discussions, with some perceiving acid rain to be the cause of scabies. Participants expressed that sharing results of serosurveillance and stool sample analysis with the community would improve awareness of NTD causes and prevention mechanisms. In conclusion, this study suggests that the integrated MDA was acceptable to the community. Strategies to engage local communities in both awareness creation and medicine distribution can further improve participation of the communities and MDA acceptability.

8221

PILOTING INTEGRATION OF HUMAN, ANIMAL AND ENVIRONMENTAL ANTIMICROBIAL RESISTANCE (AMR) SURVEILLANCE TO MONITOR ESBL-PRODUCING *E. COLI* USING A ONE HEALTH APPROACH IN BANGLADESH

Mahbubur Rahman[1], Rezaul Hasan[1], Farjana Jahan[1], Tahmidul Haque[1], Afroza Jannat Suchana[1], Kazi Saiful Islam[1], Mohammad Mehedi Hasan[2], Rizwana Khan[3], Aninda Rahman[4], Zahid Hayat Mahmud[5], Mohammed Badrul Amin[6], S.M. Shahriar Rizvi[4], Fahmida Chowdhury[3], Abdullah Al Mamun[7], Emily Kate Rousham[8], Mohammad Aminul Islam[9], Leanne Unicomb[1], Mahbubur Rahman[10], Zakir Hossain Habib[10]

[1]Environmental Health and WASH, Health System and Population Studies Division, International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b), Dhaka, Bangladesh, Dhaka, Bangladesh, [2]Environmental Health and WASH, Health System and Population Studies Division, International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b), Dhaka, Bangladesh, Dhaka, Bangladesh, Dhaka, Bangladesh, [3]Infectious Diseases Divison (IDD), International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b), Dhaka, Bangladesh, Dhaka, Bangladesh, [4]Communicable Disease Control (CDC) Program, Directorate General of Health Services (DGHS), Dhaka, Bangladesh, Dhaka, Bangladesh, [5]Laboratory of Environmental Health, Health System and Population Studies Division, International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b), Dhaka, Bangladesh, Dhaka, Bangladesh, [6]Food Safety and One Health Laboratory, Nutrition Research Division, International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b), Dhaka, Bangladesh, Dhaka, Bangladesh, [7]Department of Environment, Ministry of Environment, Forest and Climate Change, Bangladesh, Dhaka, Bangladesh, [8]Loughborough University, Loughborough, United Kingdom, [9]Paul G. Allen School for Global Health, College of Veterinary Medicine, Washington State University, USA, Washington, WA, United States, [10]Institute of Epidemiology, Disease Control, and Research (IEDCR), Directorate General of Health Services (DGHS), Dhaka, Bangladesh, Dhaka, Bangladesh

One Health approaches have gained prominence in global antimicrobial resistance (AMR) surveillance but such approaches are currently limited in Bangladesh. We present a protocol and scoping results on integrated One Health (human, animal and environmental) AMR surveillance to monitor extended-spectrum β-lactamase (ESBL) producing *Escherichia coli* (Ec)) in Bangladesh. Our protocol uses the WHO integrated global surveillance on ESBL-Ec "One Health" approach (Tricycle protocol) for samples from Mymensingh and Chattogram metropolitan areas Bangladesh (July 2023 to December 2025). We will collect human (blood, n=2846 and rectal swabs of healthy pregnant women, n=120), environmental (wastewater, n=120) and animal (chicken caecum, n=240) samples to test and compare the prevalence of ESBL-Ec. Environmental and animal samples will be collected by icddr,b field team and human samples by IEDCR a government agency responsible for human AMR surveillance. Human samples will be tested in local medical college hospitals, animal samples in the central disease investigation laboratory of the Department of Livestock and environmental samples at icddr,b laboratory. The results will be in a single platform used by three labs to estimate the burden of ESBL- *Ec*. To date, we have conducted a preliminary environmental surveillance for ESBL-Ec along with physicochemical properties of wastewater and river water samples including community, hospital and poultry markets. We collected a total of 59 samples of wastewater, river water and drinking water from Mymensingh (n=24) and Chattogram (n=35). We detected ESBL-Ec in all wastewater and river water samples and *Ec* in 60% of drinking water samples in Chattogram. ESBL-Ec abundance was highest in poultry wastewater. ESBL-Ec counts were significantly correlated with all the physicochemical parameters ($p<0.05$). Integrated surveillance of AMR using a One Health approach can provide valuable insights when we have human, animal data to examine the sources and transmission routes of AMR organism. This information is crucial for designing effective interventions to address this global public health challenge.

8222

MOLECULAR CHARACTERIZATION OF EXTENDED SPECTRUM BETA LACTAMASE PRODUCING ESCHERICHIA COLI AMONG CHILDREN AND FARM ANIMALS IN AGOGO, ASANTE AKIM MUNICIPAL, GHANA

Md Neyaz Ahmed Khan

Bernhard Nocht Institute for Tropical Medicine, Hamburg, Germany

ESBL-producing *Escherichia coli* are a growing global concern, particularly in sub-Saharan Africa, including Ghana. Overuse of antibiotics in healthcare and agriculture contributes to the prevalence of ESBL resistance in both humans and livestock. The prevalence of ESBL in *E. coli* across human, animal, and hospital settings underscores Ghana's one health challenge. This study in Agogo, Ghana, aims to comprehensively investigate ESBL-producing E. coli, including genetic diversity, transmission patterns, antimicrobial resistance, and virulence genes, employing a holistic one-health approach. This cross-sectional study was conducted from June to December 2019 in the Ashanti region of Ghana. Whole genome sequencing was performed on ESBL-producing *E. coli* isolates previously identified from children with and without diarrhoea below 5 years of age and farm animals from Agogo and its nearby communities. Raw reads were assembled using TORMES pipeline. Kraken2 was used for species classification, and ResFinder to screen for antibiotic resistance genes. MLST was conducted with PubMLST schemes, while SNPs were identified via SAMtools.This study sequenced 117 ESBL-producing *E. coli* genomes: 44 from healthy children, 30 from children with diarrhea, and 43 from animals. Among them, 55.6% were typed by MLST, with the rest yielding unknown profiles. The prevalent STs were ST-2 (23.1%), ST-8 (13.8%), and ST-535 (9.2%). Eight STs were shared between humans and animals. 47 antimicrobial resistance (AMR) genes were identified, with blaCTX-M-15 present in 87.0% of isolates. Additionally, 197 virulence genes were found, crucial for bacterial pathogenicity, including invasion, adhesion, biofilm formation, and secretion of toxins. In conclusion, we identified prevalent antimicrobial resistance genes such as blaCTX-M-15 and a myriad of virulence genes, indicating the potential for heightened pathogenicity. Shared sequence types between humans and animals indicates potential transmission. Further investigation into transmission dynamics is imperative to develop targeted interventions and mitigate the spread of resistant strains.

8223

DETECTION OF POTENTIAL ZOONOTIC PATHOGENS FROM BAT BLOOD SAMPLES COLLECTED IN BELIZE, CENTRAL AMERICA

Michele M. Adams[1], Benedicte Fustec[1], Brooke Rodriguez[1], Kara Linder[1], Lauren Lock[2], M. Brock Fenton[3], Nancy B. Simmons[4], Nicole L. Achee[1], John P. Grieco[1], Daniel Becker[2]

[1]Department of Biological Sciences, Eck Institute for Global Health, University of Notre Dame, Notre Dame, IN, United States, [2]School of Biological Sciences, University of Oklahoma, Norman, OK, United States, [3]Department of Biology, University of Western Ontario, London, ON, Canada, [4]Department of Mammalogy, Division of Vertebrate Zoology, American Museum of Natural History, New York, NY, United States

The Remote Emerging Disease Intelligence-NETwork (REDI-NET) is an expert Consortium engaged in emerging infectious disease surveillance efforts. We use Oxford Nanopore Technologies (ONT) Next-Generation Sequencing (NGS) technology for metagenomic sequencing of varied environmental, invertebrate, and non-human vertebrate sentinel sample types for rapid identification of microorganisms that may represent zoonotic spillover threats to humans. Here we report outcomes from NGS testing of 85 blood samples (FTA cards) taken from 18 bat species collected in 2019 at the Lamanai Archeological Reserve, Orange Walk District, Belize, as a part of a longitudinal ecological study of infection within and between members of the diverse bat community. Our sequencing outputs indicate the presence of 55 microorganisms previously documented to cause disease in humans across three major taxa groups: bacteria (52), eukaryotic parasites (helminths; 2), and fungi (1). All 18 bat species harbored at least one of these bacteria, while helminths were unique to Lasiurus ega and Sturnira parvidens, and fungi found only in Lasiurus ega bats. No known blood-borne pathogens or viruses were detected despite PCR positivity in some of the same samples. These results are intended to guide One Health efforts and public health decision-making in Belize, and highlight the need for further development of an optimized approach to pathogen surveillance in such sample types using NGS technology.

8224

DYNAMIC SURVEILLANCE OF MULTIDRUG-RESISTANT LARGE SPECTRUM B-LACTAMASE PRODUCING ENTEROBACTERIACEAE IN SEMI-URBAN POULTRY FARMS FOR PROSPECTIVE ZOONOTIC RISKS ASSESSMENT, ABIDJAN, CÔTE D'IVOIRE

Bertin Kipre Guede, Valerie Carole Gbonon, Anatole Abale Toty, Fernique Konan Kouadio, Félicité Beudjé, Safiatou Teninba Mariko, Bertin Konan Tiekoura, Nathalie Aya Guessennd-Kouadio, Mireille Carmen Dosso-Bretin

Institut Pasteur Cote D'Ivoire, Abidjan, Côte d'Ivoire

Zoonotic pathogens' surveillance is a global health issue, especially in Limited-and-Medium Income Countries. Among these infectious disease drivers, are Large Spectrum β-Lactamase producing Enteric bacteria that could spill over from poultry into humans, and as a result pose inherent health risks to domestic animals along with pathogen transmission in urban communities and hospitals. The current study therefore, aims at detecting reservoirs of these bacteria in semi-urban poultry farms for dynamic qualitative surveillance. For this pilot study over the 2023-year period, 40 faeces samples were collected from small scale poultry sites in Bingerville; a suburb of Abidjan. Then, bacteria were primarily seeded in physiological fluid before culture on selective agar Eosin Methylene Blue (EMB), isolation by Gram staining test, identification by Leminor serial tests, and antimicrobial susceptibility test using disk diffusion method as well as E-test, with both incubation temperatures 37°C, and 44°C to determine Inhibition Diameters and Minimum Inhibition Concentrations (EUCAST; CA-SFM 2021). Results showed 20 (50%) positive *Escherichia coli* culture, out of which 13 (65%) where Large Spectrum β-Lactamase producing enteric bacteria detected at 44°C, while 07 (35%) positive E. coli were detected as wild phenotype at 37°C. In conclusion, findings demonstrated a large amount of both Cephalosporinase, and Penicillinase enzyme producing bacteria circulating over the farming sites investigated. Current study, which is carried out yearly, is extended to nineteen (19) other sites for a successful implementation of integrated surveillance, and consequently contribute to curb emergence of zoonotic pathogens due to lack of hygiene, and biosecurity over small scale farms.

8225

SPILLOVER OF HIGH PATHOGENICITY AVIAN INFLUENZA A (H5N1) VIRUS IN INDIAN FLYING FOX (*PTEROPUS MEDIUS)* BATS IN BANGLADESH

Ariful Islam[1], Mohammad Enayet Hossain[2], Emama Amin[1], Shariful Islam[1], Md Arif Khan[1], Abdullah Al-Mamun[1], Sarah Munro[3], Tahmina Shirin[4], Mohammed Ziaur Rahman[2], Marcel Klaassen[5], Jonathan H Epstein[3]

[1]EcoHealth Alliance, Dhaka, Bangladesh, [2]One Health laboratory,International center for diarrheal disease research (icddr,b), Dhaka, Bangladesh, [3]EcoHealth Alliance, New York, NY, United States, [4]Institute of Epidemiology, Disease Control and Research (IEDCR), Dhaka, Bangladesh, [5]Centre for Integrative Ecology, School of Life and Environmental Sciences, Deakin University, Geelong, Victoria, Australia

High pathogenicity avian influenza (HPAI) outbreaks raise concerns due to pandemic potential, socioeconomic impact, and wildlife conservation risks. Here, we report unusual mortality of Indian flying fox (*Pteropus medius)* bat populations due to spillover of H5N1viruses. We monitored house crow (*Corvus splendens*) mortality events in Dhaka city between 2017 and 2023. During investigation, we observed crows and Indian flying fox bats cohabiting in the same roost and occasionally observed dead bats in the affected roosts. We collected swab and tissue samples from dead crows and bats and tested for the presence of AIV matrix gene, followed by the H5, H7, and H9 subtyping using rRT-PCR. Aside from house crows, we found 11 Indian flying foxes infected with HPAI H5N1. We detected the H5N1 virus in tissue samples (trachea, kidney, liver, lungs, and brains) of these bats, indicate the systemic infection with H5N1 and could be the reason for the bats' mortality, and potential risk of HPAI viruses to mammalian hosts. Phylogenetic analysis revealed that bat sequences belonged to the 2.3.2.1a clade, closely related to sequences from house crows and ducks in Bangladesh. The 2.3.2.1a clade comprises two major lineages: G1 and G2 and the bat sequences cluster within the G2 lineage indicating continuing evolution that have resulted segregating multiple distinct subclusters in Bangladesh. We found bat H5N1 sequences contain several amino acid mutations and genetic markers of mammal adaptation. We report the first detection of HPAI H5N1 viruses in bats in Bangladesh, concurrent with H5N1 in sympatric wild birds. Our findings suggest acute disease caused by the virus as the likely cause of mortality events in bats cohabiting with infected crows. This underscores the potential of HPAI virus to cross host barriers and infect mammals, posing a significant public health concern for future pandemics if not controlled.

8226

SEROPREVALENCE OF BACTERIAL ZOONOSES IN A BIODIVERSITY HOTSPOT: A CROSS-SECTIONAL STUDY FROM MEGHALAYA, INDIA

Rajiv Sarkar[1], Melari S. Nongrum[1], Barilin Dkhar[1], Worthing Yanglem[1], Mercylin Lyngdoh[1], Kirti Chauhan[1], Peter J. Marbaniang[1], Mahesh Moorthy[2], Sitara S. R. Ajjampur[2], John A. J. Prakash[2], Mark L. Wilson[3], Sandra Albert[1]

[1]Indian Institute of Public Health Shillong, Shillong, India, [2]Christian Medical College, Vellore, India, [3]University of Michigan, Ann Arbor, MI, United States

Zoonotic diseases (ZDs) remain a major global public health threat, with approximately 60% of infectious diseases considered to be of zoonotic origin. The northeast region (NER) of India, which is within the Indo-Burma biodiversity hotspot, is a region of concern for ZDs due to its unique ecology, cultural practices, dietary preferences (including bushmeat consumption), agricultural practices (slash-and-burn agriculture, mixed farming) and high animal-to-human ratio. However, the risk of ZDs is

largely undetected due to a paucity of infectious-disease surveillance. We conducted a population-based serosurvey in three ecologically distinct field sites of Meghalaya (a hilly, forested and predominantly tribal state in NER) to estimate the seroprevalence of three common bacterial ZDs: scrub typhus, leptospirosis, and brucellosis. A total of 1,328 participants from 30 village-clusters were included, using age-structured sampling; 1,307 (98.4%) provided blood samples. Serum samples were tested for pathogen-specific IgG using commercially-available immunoassays. Weighted seroprevalences were calculated using sampling weights that accounted for non-response. The overall (IgG) seroprevalences of *Orientia tsutsugamushi* (scrub typhus), *Leptospira* spp. and *Brucella* spp. were 12.1% (95% CI: 10.2-14.2%), 9.1% (95% CI: 7.4-11.2%) and 4.4% (95% CI: 3.2-6.1%), respectively. Village-level seroprevalence varied considerably: 0-43.9% for *Orientia* (intraclass correlation coefficient [ICC]: 0.214), 1-27.7% for *Leptospira* (ICC: 0.115) and 0-15.6% for *Brucella* (ICC: 0.182). The seroprevalences increased with increasing age ($P<0.001$ for *Orientia* and *Leptospira*, and $P=0.020$ for *Brucella*), and differed between males (15.4%) and females (10.2%) for *Orientia* ($P=0.001$), but not for *Leptospira* (8.1% vs. 9.6%, $P=0.419$) and *Brucella* (4.0% vs. 4.7%, $P=0.563$). The complex bio-socio-environmental drivers of ZD transmission need further exploration. Our findings highlight an under-reported burden of ZDs in Meghalaya and underscore the importance of heightened surveillance in areas with close human-animal contact.

8227

DETECTION OF *TRYPANOSOMA LEWISI* FROM *RATTUS RATTUS* AND *RATTUS NORVEGICUS* IN TOLIARA, ON THE SOUTHWESTERN COAST OF MADAGASCAR

Dina Ny Aina Liantsoa Randriamiarinjatovo[1], Marius Paul Hubert Rakotondratsima[2], Tovoson Randriamiadana[3], Mercia Rasoanoro[1], Ibrahim Antho Youssouf Jacky[3], Milijaona Randrianarivelojosia[1]

[1]Institut Pasteur de Madagascar, Antananarivo, Madagascar, [2]The Peregrine Fund Madagascar Program, Antananarivo, Madagascar, [3]Université de Toliara, Toliara, Madagascar

In the island of Madagascar, over the last two decades, different studies have described the presence of *Trypanosoma lewisi* infection in *Rattus rattus* in the central highlands and on the island's eastern cost. With the aim to update the parasite inventory in small mammals, we undertook the detection of *Trypanosoma* in rodents in the southwestern part of the island. For this preliminary study, rat trapping was carried out during transversal field trips at four sites (Amborogony, Maninday in town; and at two rural villages Andranomanintsy, Amboaboaka 45 km north of Toliara) in 2022 and 2023. For each captured rat, thin blood smears were prepared, stained with Giemsa and microscopy examined on site for *Trypanosoma* detection. Blood spots were collected on Whatmann 3MM CHR filter paper and sent to the Institut Pasteur de Madagascar for *Trypanosoma* identification by PCR. DNA was extracted with the Qiagen kit. Nested PCR was performed to amplify the *Trypanosoma rRNA* gene. The PCR products of positive samples were shipped to Genoscreen (Lille, France) for sequencing. The sequences obtained were analyzed on Geneious Prime to identify *Trypanosoma* species. In total, 173 small mammals including 144 *R. norvegicus,* 25 *R. rattus* and 4 *Mus musculus* were captured. Microscopically, *Trypanosoma* was found in seven rats [4.1%; 95% CI: 1.8-8.5%] (in one *R. rattus* and in 6 *R. norvegicus*). Additionally, PCR followed by sequencing confirmed that all of these infected rats harbored *T. lewisi.* Our results demonstrate for the first time the presence of *T. lewisi* in *R. rattus* and in *R. norvegicus* in the sub arid southwestern part of Madagascar. We plan to expand our investigation to type the population of *T. lewisi* that may infect small mammals living in forests in the island's southwestern areas.

8228

TICKS AND TICK-BORNE PATHOGENS IN GHANA: A SIGNIFICANT RISK OF ZOONOTIC PATHOGEN INFECTIONS

Seth Offei Addo[1], Michael E. DeWitt[2], Ronald Essah Bentil[1], Christopher Nii Laryea Tawiah-Mensah[1], Jane Ansah-Owusu[1], Stacy Amoah[1], Richard Odoi-Teye Malm[1], John W. Sanders[3], Joseph W. Diclaro II[4], Samuel K. Dadzie[1]

[1]Noguchi Memorial Institute for Medical Research, Accra, Ghana, [2]Department of Internal Medicine, Section on Infectious Diseases, Wake Forest University School of Medicine, Winston-Salem, NC, United States, [3]Department of Internal Medicine, Section on Infectious Diseases, Wake Forest University School of Medicine, Wiston-Salem, NC, United States, [4]Navy and Marine Corps Force Health Protection Command; Center for Disease Control Detachment, Atlanta, GA, United States

Ticks and tick-borne diseases negatively impact human and livestock health. In Ghana, diverse tick species are present with the occurrence of tick-borne pathogens of zoonotic and veterinary importance. To reduce future human risk for tick-borne diseases, it is imperative to identify the variables influencing tick population dynamics and tick-borne pathogens. Therefore, the purpose of this study was to determine the relationship between season, climate variables, and land use on the prevalence of ticks and tick-borne pathogens in Ghana. In addition, we predict the likelihood of detecting zoonotic tick-borne pathogens in the nation. The data from tick collections done in 2020, 2022, and 2023 were geocoded and associated with available climate data from 2012-2022. Each data point was associated with its corresponding land use category label. All analyses were performed in R version 4.1.3. A total of 3864 ticks were collected with *A. variegatum* (49.25%) as the predominant species which was more likely to be abundant in the wet season (IRR=2.40, 95%CI=2.13-2.71, $p<0.001$). The overall prevalence of pathogens in all tick species was 56.24% with zoonotic tick-borne pathogens recorded as *R. africae* (34.76%), *R. aeschlimannii* (11.03%), *C. burnetii* (2.49%), *A. capra* (0.47%) and CCHFV (0.47%). *Rickettsia africae* was more likely to be detected in ticks sampled in the wet season (OR=3.50, 95%CI=2.57-4.81, $p<0.001$). It was also observed that precipitation (OR=106, 95%CI=0-172, $p<0.001$) was highly associated with tick pathogen positivity. Land use had a significant impact on the abundance of tick species and the distribution of identified pathogens. Using multivariable logistic models, we predict that there is an increased risk of detecting zoonotic tick-borne pathogens in Northern Ghana. Our research sheds light on the intricate relationship of climate and land use on the distribution and prevalence of ticks and tick-borne pathogens in Ghana and indicates the need for increased surveillance to develop efficient control and preventive strategies.

8229

DESCRIPTIVE ANALYSIS OF ZOONOSES ACQUIRED BY TRAVELERS RETURNING TO CANADA FROM 2013-2023

Jill Blackmore[1], Andrea Boggild[2], Erin Schillberg[3]

[1]Public Health Agency of Canada, Toronto, ON, Canada, [2]University of Toronto, Toronto, ON, Canada, [3]Public Health Agency of Canada, Winnipeg, MB, Canada

Zoonoses account for the majority of established and emerging infectious diseases across the globe. Climate change has enhanced the burden of zoonoses due to vector range expansion. Globalization impacts travelers' potential for exposure to novel or rare pathogens and the introduction to an immunologically naïve population upon return. Understanding the zoonoses acquired abroad and imported into Canada is essential to inform effective public health guidance. This study aims to describe the travel-acquired zoonoses diagnosed in Canadian residents from 2013 to 2023 using data from the Canadian cohort of GeoSentinel, the Canadian Travel Medicine Network (CanTravNet). CanTravNet is comprised of 7 sites and is estimated to represent 15-20% of all ill travelers in Canada. For the purpose of this study, only patients who were residents of Canada at time of visit to a CanTravNet site were included. Zoonotic disease was defined as pathogens with a primary transmission route of direct or indirect animal or arthropod exposure. Among the 20,459 visits made to a CanTravNet

site from 2013-2023, preliminary results indicate that 12% (n= 2,392) resulted in at least one zoonotic diagnosis. Based on the available data, the proportion of zoonotic diagnoses increased over the study period from 9% in 2013 to 19% in 2023. Of the zoonoses diagnosed, the most frequent regions of acquisition were: Sub-Saharan Africa (37%), Central America (9%) and the Caribbean (9%). The majority (98%) of zoonoses diagnosed over the study period were vector-borne, specifically mosquito-borne (77%). Malaria and dengue were the top two zoonoses diagnosed every year of the analysis except in 2021 when filariasis replaced dengue. These preliminary findings suggest mosquito-borne diseases are the primary risk for zoonotic infections among Canadian travelers. As vectors continue to expand their range and the magnitude of vector-borne outbreaks increase, this risk is expected to increase. A better understanding of which zoonoses are acquired by Canadian travelers and from where, can help inform public health education and mitigate the risk of introducing novel pathogens into Canada.

8230

BABOON-HUMAN CONFLICT, COEXISTENCE AND COMMON BABOON MICROBIOME IN AL-BAHA REGION, SAUDI ARABIA

Ghanem M. AlGhamdi

Al-Baha University, AlAqiq, Saudi Arabia

Papio hamadryas existence in Al-Baha Region in areas of human proximity has been observed for several decades. Such coexistence has its impact on people health and finance. The goal was to investigate areas of hot spots conflicts between people and baboon. Our data showed that baboons occur on various districts of Al-Baha Regions with social, financial and ecological impact on people. Various number of divers microbes were detected in examined faecal samples. Further work is required to understand the relevance of microbes to the ecosystem and people in the rea.

8231

PLASMODIUM SPP. AND FILARIAL INFECTIONS IN MACAQUES IN BELITUNG DISTRICT, INDONESIA

Irina Diekmann[1], Taniawati Supali[2], Balbir Singh[3], Paul CS Divis[3], Peter U. Fischer[1]

[1]Infectious Diseases Division, Department of Medicine, Washington University School of Medicine, St. Louis, MO, United States, [2]Department of Parasitology, Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia, [3]Universiti Malaysia Sarawak (UNIMAS) Malaria Research Centre, Kota Samarahan, Sarawak, Malaysia

Until recently Belitung District in Indonesia was thought to be free of human malaria and to have eliminated lymphatic filariasis (LF) caused be *Brugia malayi* in humans by mass drug administration. Surveillance surveys showed later that *B. malayi* is still endemic in the area and that in some villages up to 5% of the adult residents are infected. *B. malayi* and *Plasmodium knowlesi* are mosquito transmitted, blood borne, pathogens that infect humans and macaques. Therefore, we decided to explore the role of macaques (*Macaca fascicularis*), that are abundant in Belitung, as a reservoir host for filarial and plasmodial parasites. We collected blood samples from 163 macaque in five different villages and tested the samples by real-time PCR for filarial and *Plasmodium* infection. Filarial and *Plasmodium* DNA was found in 30.1% and 79.8% of the samples, respectively. *B. malayi* DNA was detected in 13.5% of the macaques, while other filarial DNA was detected from a *Dirofilaria* species. Co-infections with both *Plasmodium* and filarial parasites were observed in 27% of the macaques, indicating that most macaques infected with filarial parasites were also infected with *Plasmodium* spp. Sanger sequencing of the partial plasmodial small subunit rRNA (SSUrRNA) gene region confirmed the presence of at least three different *Plasmodium* species: *P. knowlesi*, *P. cynomolgi* and *P. inui*. Population genomic studies have indicated that macaques and humans share the same *B. malayi* genomic profiles in Belitung. However, it is unclear whether *P. knowlesi* in macaques are transmitted to humans in this area. This study has shown that macaques in Belitung are infected with filarial and *Plasmodium* species that can infect humans. Further research will be needed to better understand the epidemiology of both infections in macaques and their potential role as a source for human infections. This information could inform strategies to prevent transmission of these zoonoses to humans.

8232

COMMUNITY PRACTICES CONTRIBUTING TO MAGNITUDE AND RECURRENCE OF ANTHRAX OUTBREAK IN MURANG'A COUNTY IN KENYA, FEBRUARY 2024

Jane A. Eregae, Matheka M. Matheka, Owiny M. Maurice, Odhiambo F. Fredrick

Kenya Field Epidemiology and Laboratory Training Program, Nairobi, Kenya

Globally, Up to 100,000 Humans Get Infected with Anthrax Annually. Kenya Reports an Average of 10 Outbreaks Every Year. Murang'a County Has Had Recurrence of Anthrax With the Most Recent in February 2024 When County Health Department Reported 18 Suspected Human Cases That Were Linked to Cow That Had Died of Unknown Cause. The Magnitude of The Outbreak and the Drivers of Recurrence Were Unknown. We Sought to Characterize Anthrax Cases and Identify Possible Drivers of Recurrence in Murang'a. We Conducted Active Case Search in Health Facilities and in Community in February 14-21, 2024. Suspected Animal Case Was Sudden Death With Non-Clotting Bleeding from Body Orifices and Confirmed Case Was Positive for *Bacillus Anthracis* by Gram Stain. Suspect Human Case Was a Case With Painless Skin Lesion (Eschar) or Abdominal Pain and Diarhoea after Exposure to a Suspected Animal Case. Cases Were Interviewed and Data Collected Were Subjected to Descriptive Analysis. We Identified 14 Animals (13 Suspected and One Confirmed) With 8.8/100,000 Attack Rate and 71 Human Cases (22 From Health Records and 49 at the Community). Of those Interviewed, 62.7%(37/59) Had Gastrointestinal Form While the Cutaneous Was 52.5%(31/59) with One Community Death; Case Fatality Rate=1.4%(1/71). Attack Rate Among Humans Was 14.3/100,000 Population Contributed by Three Of Seven Sub Counties with Kigumo Sub County Recording 31.4/100,000 Population. The Age Group in Humans 10-19 Years Were the Majority at 23.9%(17/71). Of the Animal Cases, 85.7%(12/14) Were Buried Without Following Recommended Guidelines, 7.1%(1/14) Were Fed to Dogs and 7.1%(1/14) Was Consumed by Humans. Of the Respondents That Owned Livestock 82.4%(14/17) Would Neither Disinfect Slaughter Sites Nor Vaccinate Their Livestock. We Linked the Outbreak Among the Humans to Poor Handling and Consumption of Livestock Carcasses. Improper Disposal of Carcasses Leading of Environmental Contamination and Poor Attitude Towards Livestock Vaccination Could be Contributing to the Recurrence of Anthrax Outbreaks in Murang'a. We Recommend Enhanced Community Engagement on Handling of Anthrax Cases and Livestock Vaccination.

8233

AN ANALYSIS OF RICKETTSIAL INFECTIONS AMONG FEBRILE PATIENTS IN NIGERIA

Cyril Erameh[1], Vivian Kwaghe[2], Jean Kim[3], Jay Samuels[4], Lauren Courtney[3], Claire Quiner[3], Kat Asman[3], Adamu Ephraim[3], Osas Edeawe[1], Ephraim Ogbaini[1], Philippe Chebu[4], Nankpah Vongdip[2], Victoria Orok[2], Oladimeji Matthew[2], Emmanuel Oga[3]

[1]Irrua Specialist Teaching Hospital, Irrua, Nigeria, [2]University of Abuja Teaching Hospital, Abuja, Nigeria, [3]RTI International, Research Triangle Park, NC, United States, [4]APIN Public Health Initiatives, Abuja, Nigeria

Rickettsial infections are underrecognized yet significant public health threats in Nigeria. Because Rickettsial infections are rarely diagnosed in Nigeria, our study offers a critical insight by reviewing confirmed cases to improve understanding of its symptoms, distribution and the factors influencing its transmission across different Nigerian regions. Data from 55 PCR-confirmed Rickettsial infection cases collected through the SAFIAN study from September 2023 to April 2024 were analyzed. Participants were recruited from Gwagwalada (Federal Capital Territory), a suburban area, and Irrua (Edo State), a rural setting. The analysis focused on patient

demographics, clinical symptoms, risk factors, and outcomes. Of the 55 cases analyzed, 76% (42 cases) were reported in suburban Gwagwalada, and 24% (13 cases) in rural Irrua. The affected individuals were predominantly females (53%), with ages ranging from 5 to 80 years (mean: 32 years, SD: 18.4). The symptom profile included fever (100%), headache (58%), nausea/vomiting (25%), abdominal pain (15%), diarrhea (12%), cough (18%), arthralgia (16%), muscle pain (13%), and infrequently, rash (2%) and unusual bleeding (4%). Environmental risk factors were prominent, with 35% of cases reporting contact with domestic animals, 10% recent visits to forested areas, 35% reporting recent insect bites, and 55% noting inadequate vector control measures. Participants with occupations associated with extended outdoor stays such as farmers, artisans, miners and traders accounted for 27% of the sample. There was PCR-confirmed coinfection with malaria in 27% of the sample. The mortality rate was approximately 6%. The study highlights a significant burden of Rickettsial infections in both rural and suburban settings of Nigeria, with a notable prevalence of infections in suburban areas adjacent to dense vegetation and domestic animal habitats. These findings emphasize the need for targeted surveillance, vector control, and community education to mitigate the risk of Rickettsial diseases and enhance public health outcomes in endemic regions.

8234

A ONE HEALTH APPROACH TO ASSESSMENT OF PATHOGEN EXPOSURE ACROSS INFORMAL SETTLEMENTS: APPLICATION OF BOOT SOCK SAMPLING AND SOURCE TRACKING METHODS

Lamiya Nerose Bata

Monash University, Clayton, Australia

Rapid urbanisation often results in informal settlements, lacking the infrastructure necessary for separating human and animal reservoirs of disease. A One Health approach to assessing pathogen exposure, and subsequent disease risk, requires reevaluating traditional methodological approaches. In the case of pathogen exposure via soil surfaces, grab sampling provide limited spatial representation, and may not accurately reflect pathogen transmission risk. In this study, we compared traditional grab sampling of soil with a novel bootsock method. The bootsock method is a composite technique used to capture microbial data, purported to better reflect human-pathogen interactions in real world environments. Bootsock sampling outperformed grab sampling in detecting *E. coli* in laboratory experiments and measuring average *E. coli* levels in field experiments within Fijian informal settlements. Power analysis suggested that bootsock sampling demonstrated spatial representation, allowing us to assess contamination on a settlement-level scale that was time and cost-effective. 16S amplicon sequencing data was collected over two years as part of the RISE (Revitalising Informal Settlements and their Environments) program to assess sources of microbial contribution in bootsock and grab samples from Fijian and Indonesian informal settlements. Sourcetracker analysis showed a significant dominance of animal fecal contributions over human feces. In Fijian soils, dog feces made up 7.8% of the predicted microbial contribution in bootsocks, compared to the 1.1% from human feces. In grab samples, dogs accounted for 4.8%, whereas human contributions were at 2.9%. In Indonesian soils, human fecal contributions were ~0.1% in bootsocks and 0% in grab samples, while duck feces accounted for up to 20% of microbial presence in bootsocks and 12% in grab samples. Overall, the application of the bootsock method demonstrably improved the assessment of enteropathogen contamination in soils, compared to grab sampling, highlighting the potential risk of human exposure to fecal pathogens associated with animals in soil environments.

8235

RAPID CLADE REPLACEMENT AND IMPACT OF VACCINE DEPLOYMENT IN THE SPATIOTEMPORAL CIRCULATION OF SARS-COV-2 VARIANTS IN SAO PAULO, BRAZIL

Cecilia A. Banho[1], Beatriz C. Marques[1], Lívia Sacchetto[1], Maisa C. P. Parra[1], Maria C. Elias[2], Sandra C. Sampaio[2], Marta Giovanetti[3], Fernando R. Spilki[4], Benjamin M. Althouse[5], Nikos Vasilakis[6], Maurício L. Nogueira[1]

[1]Faculdade de Medicina de São José do Rio Preto, São José do Rio Preto, Brazil, [2]Butantan Institute, São Paulo, Brazil, [3]Instituto Oswaldo Cruz, FIOCRUZ, Rio de Janeiro, Brazil, [4]Instituto de Ciências da Saúde, Universidade Feevale, Novo Hamburgo, Brazil, [5]New Mexico State University, Las Cruces, NM, United States, [6]niversity of Texas Medical Branch, Galveston, TX, United States

Since 2021, the emergence of variants of concern (VOC) has led Brazil to experience record numbers of COVID-19 cases and deaths. The increased spread of the virus, combined with a low vaccination rate, has contributed to the emergence of new mutation that may enhance viral fitness leading to the disease persistence of the disease. Due to limitations in the real-time genomic monitoring of new variants in most Brazilian states, we aimed to investigate whether genomic surveillance, coupled with epidemiological data and spatiotemporal spread of SARS-CoV-2 variants in a smaller region, can reflect the progression of the pandemic at the national level. Our findings revealed three SARS-CoV-2 variant replacements in 2021 and early 2022, corresponding
to the introduction and rise in frequency of Gamma, Delta and Omicron variants, as indicated by peaks of the Effective Reproductive Number (Reff). These distinct clade replacements triggered two waves of COVID-19 cases, which were influenced by the increasing vaccine uptake over time. Our results indicated that the effectiveness of vaccination in preventing new cases during the Delta and Omicron circulation was six and eleven times higher, respectively, than during the period when Gamma was predominant, and it was highly efficient in reducing the number of deaths. Furthermore, we demonstrated that continuous genomic monitoring in a smaller region of Brazil can reflects the national trends in the spread and evolution of SARS-CoV-2.

8236

ASSESSING PYRAZINOIC ACID EFFLUX VELOCITY, UNVEILING THE IMPACT OF RV1258C AND RV0191 ON PYRAZINAMIDE RESISTANCE IN MYCOBACTERIUM TUBERCULOSIS

Carlos Alonso Flores Bancayan, Kiara Beatriz Aricoche del Campo, Mirko Zimic Peralta, Patricia Sheen Cortavarria

Universidad Peruana Cayetano Heredia, Laboratorio de Bioinformática, Biología Molecular y Desarrollos tecnológicos, Lima, Peru

Tuberculosis, predominantly caused by Mycobacterium tuberculosis, remains a significant global health concern due to the emergence of drug-resistant strains. Pyrazinamide is crucial in shortening the standard treatment duration from 9-12 months to six months. Resistance to this drug typically results from mutations in the pncA gene, impairing the pyrazinamidase enzyme required for converting pyrazinamide to its active form, pyrazinoic acid. Additionally, the role of efflux pumps in resistance, particularly in the absence of pncA mutations, is poorly understood and remains underexplored. This study aims to investigate the function of the efflux pumps Rv0191 and Rv1258c and their impact on pyrazinamide resistance. Specifically, we examine how these pumps alter the dynamics of pyrazinoic acid expulsion. To achieve this, we genetically engineered the modified H37Rv Mycobacterium tuberculosis by inactivating and suppressing both genes using the techniques of Oligonucleotide-mediated Recombineering followed by Bxb1 integrase Targeting (ORBIT), and CRISPR interference. Our results reveal that the two genes confer a unique efflux pattern for pyrazinoic acid in the modified strains over six days, differing significantly from the wild-type. Using linear regression, we observed statistically significant differences in the efflux profiles at

all evaluated time points (0-140 hours), with marked reductions in the genetically modified strains. A significant reduction in both the rate and quantity of pyrazinoic acid efflux was observed following the inactivation of both genes (p<0.0001) and when Rv1258c was suppressed (mRNA level 0.195, 95% CI 0.136 - 0.254, with a p=0.0037). Future work will assess the susceptibility of these strains to pyrazinamide and pyrazinoic acid. The discovery of two involved in pyrazinamide resistance suggests a In the near future, we will test the susceptibility to pyrazinamide and pyrazinoic acid. The identification of two efflux pumps involved suggests that resistance is multifactorial in nature, improving our understanding and informing future therapeutic treatment strategies against tuberculosis.

8237

THE DECEPTIVE LUNG: PULMONARY TUBERCULOSIS MIMICKING INTERSTITIAL LUNG DISEASE

Santhosh S C, Rajat Ranka, Prasan Kumar Panda, Venkatesh Srinivasa Pai

AIIMS Rishikesh, Rishikesh, India

Tuberculosis (TB) can present as a variety of pulmonary manifestations, many of which are similar to other respiratory illnesses. We present a case of 25-year-old woman from rural North India presented with a one-month history of persistent intermittent fever, progressive shortness of breath, and dry cough. On admission, she had type 1 respiratory failure requiring noninvasive ventilation. High-resolution computed tomography (HRCT) of the chest was suggestive of diffuse ground-glass opacities and interstitial thickening, raising suspicions of ILD. She was worked up for connective tissue diseases and other causes of ILD, which were inconclusive. However, bronchoalveolar lavage (BAL) was done and BAL fluid GeneXpert PCR identified Mycobacterium tuberculosis without rifampicin resistance. The patient was diagnosed with pulmonary tuberculosis and initiated on anti-tubercular therapy. Subsequently there was dramatic clinical and radiological improvement. This case highlights the need of considering tuberculosis when making a differential diagnosis of unusual radiological findings, especially in TB-endemic areas. Early and accurate diagnosis is critical for commencing appropriate treatment and avoiding complications.

8238

SALIVA SAMPLE FOR WEEKLY SURVEILLANCE OF SARS-COV-2 IN A PERI-URBAN COMMUNITY STUDY IN LIMA-PERÚ

Mayra R. Ochoa[1], Bia Peña[1], Omar Flores[1], Ana I. Gil[1], Rubelio Cornejo[1], Lucie Ecker[1], Leigh M. Howard[2], Carlos G. Grijalva[3], Claudio F. Lanata[4]

[1]Instituto de Invesigación Nutricional, Lima, Peru, [2]Vanderbilt University and Vanderbilt University Medical Center, Nashville, TN, United States, [3]Division of Pharmacoepidemiology, Departments of Health Policy, Vanderbilt University Medical Center; Department of Biomedical Informatics, Vanderbilt University Medical Center, Vanderbilt University, Nashville, TN, United States, [4]Instituto de Invesigación Nutricional; Department of Pediatrics, School of Medicine, Vanderbilt University, Lima, Peru

Nasopharyngeal swab samples (NPS) and nasal swabs samples (NSS) have been the most common respiratory samples used to identify SARS-CoV-2 infections during the COVID-19 pandemic. However, some previous cross-sectional studies have shown that saliva could be used as an alternative sample for SARS-CoV-2 infection identification. This alternate approach may be particularly useful for longitudinal community-based surveillance studies that require frequent and repeated collection of respiratory samples. In this study, we evaluated the sensitivity and specificity of saliva samples (SLS) for detection of SARS-CoV-2 compared with NSS and NPS in a community-based cohort study conducted in San Juan de Lurigancho in Lima, Peru during 2021. We selected NPS, NSS and SLS samples (425 of each type) that were collected simultaneously on the same day on the same person from 132 participants (including 44 children and 88 adults), with or without respiratory symptoms, studied over a 2-month period. All samples were tested by RT-PCR at a research laboratory. Using NSS as reference, SLS had a sensitivity of 95%, specificity of 97% and agreement= 96.94%, with Kappa = 0.75 (CI95%: 0.62 - 0.88). Using NPS as reference, SLS had a sensitivity of 79%, specificity of 97% and agreement= 95.53%, with Kappa = 0.64 (CI95%: 0.50 - 0.79). We did not find differences in viral load between SLS and NSS (*p*= 0.22) or between SLS and NPS (*p*= 0.71). We conclude that SLS demonstrated excellent diagnostic performance and could be used for longitudinal surveillance of SARS-CoV-2 in both children and adults in community settings.

8239

PENICILLIN NON-SUSCEPTIBILITY IN PNEUMOCOCCAL CARRIAGE ISOLATES FROM PATIENTS WITH ACUTE RESPIRATORY ILLNESS IN KENYA, 2017 - 2020

Godfrey Momanyi Bigogo, Terry Komo, Arthur Odoyo, Joshua Auko

Kenya Medical Research Institute (KEMRI), Kisumu, Kenya

Vaccines can combat antimicrobial resistance (AMR). Penicillin non-susceptible pneumococcus is a global AMR threat. Kenya introduced 10-valent pneumococcal conjugate vaccine Synflorix™ (GlaxoSmithKline, $PCV10^{GSK}$) in 2011, and switched to Pneumosil™ (Serum Institute of India, $PCV10^{SII}$) in 2022. We examined penicillin non-susceptibility in pneumococci isolated from nasopharynxes of patients with acute respiratory illness (ARI) 6-9 years after $PCV10^{GSK}$ introduction. Nasopharyngeal swabs from patients meeting a standardized ARI case definition presenting to surveillance facilities in Kibera (Nairobi informal settlement) and Asembo (rural western Kenya) were cultured for pneumococci. Specimens with <10 colonies of any bacterial growth were excluded. Serotyped isolates were tested for susceptibility to penicillin (oral non-meningitis cutoff) by broth microdilution; intermediate or resistant results were classified as non-susceptible. We combined data from the two sites and described susceptibility of the isolates to penicillin and by PCV10 product. Among 3,905 ARI patients enrolled from January 2017 to April 2020, 1,807 (46.3%) were colonized with pneumococci; AMR data were available for 922 (51.0%) isolates, including 817 (88.7%) from Asembo. Penicillin non-susceptibility was observed in 85.7% (790) of all isolates, including 92.6% (263/284) of $PCV10^{GSK}$-type, 96.0% (243/253) of $PCV10^{SII}$-type, and 82.6% (519/628) of non-PCV10 serotypes. Among 271 non-susceptible PCV10-type isolates, 52.4% (142) are included in both $PCV10^{GSK}$ and $PCV10^{SII}$ (19F [n=64], 14 [n=39], 23F [n=25], 9V [n=7], 1 [n=6], 6B [n=1]), and 45.0% (122) in $PCV10^{SII}$ only (6A [n=96], 19A [n=26]). Among 519 non-susceptible non-PCV10 serotypes, the most common serotypes were 3 (n=64), 11A (n=53), 35B (n=44). We observed high penicillin non-susceptibility in pneumococcal carriage isolates, particularly among vaccine serotypes, in the context of a mature PCV program. The recently introduced $PCV10^{SII}$ that contains 6A may be useful in combating AMR.

8240

EXPLORING THE ASSOCIATION OF COMMUTING PATTERNS AND TUBERCULOSIS INCIDENCE IN LIMA, PERU: INSIGHTS FROM NETWORK ANALYSIS AND GENERALIZED ADDITIVE MODELS

Diego Villa, Kasandra Ascuña-Durand, Martina Guillermo-Roman, Gabriel Carrasco-Escobar

Health Innovation Laboratory, Institute of Tropical Medicine "Alexander von Humboldt", Universidad Peruana Cayetano Heredia, Lima, Peru

One-third of the population of Lima, Peru, lives in peripheral areas and relies on overcrowded public transportation for commuting, creating a suitable environment for TB transmission. To explore the association between commuting patterns and the cumulative incidence rate (CIR) of TB in Lima, the students and workers commuting flows were extracted from the 2017 National Census data and were analyzed using network analysis techniques. An analysis at a subregion level revealed that Central Lima was the only sub-region where the out-flow of commuters was less than the in-flow, coinciding with having the lowest CIR registered (88.53/100k ppl.). The remaining subregions exhibited the inverse commuting pattern, with Eastern Lima registering the highest CIR (131.91/100k ppl.). At a district

level, correlation analysis revealed a moderate positive association between certain centrality metrics of district importance in the commuting flows and the CIR. Notably, the out-degree centrality—the number of districts residents of a particular district commute to—in the students commuting flow was the one that showed the greatest association with the CIR (r = .55, 95% CI [.26, .74]). Next, we build generalized additive models (GAM) to model the district CIR as a function of the non-linear effects of poverty indices and pollutant concentration measures, and evaluate whether the addition of any of the centrality metrics improved model fit. The best-performing GAM according to the Akaike information criterion included the percentage of households with unsatisfied basic needs, the standardized CO concentration, and the intra-strength centrality (ISC)—the percentage of commuters that do not leave their district of residence—in the students commuting flow (P < .001). After adjusting for the other predictors, the ISC showed a positive non-linear association with the CIR with greater magnitude in the predictor's distribution tails. These findings highlight a relevant association between commuting patterns and TB incidence at a sub-region and district level in the province of Lima, Peru.

8241

EQUITABLE AND REAL-WORLD ASSESMENT OF TUBERCULOSIS CATASTROPHIC COSTS

Paula P. Carballo-Jimenez[1], Sumona Datta[1], Rosario Montoya[2], Eric S. Ramos[3], Luz Quevedo Cruz[1], Matthew J. Saunders[1], Carlton A. Evans[1]

[1]Innovation For Health and Development, London, United Kingdom, [2]Innovación Por la Salud Y Desarrollo, Lima, Peru, [3]Innovation For Health and Development, Lima, Peru

One of the 3 World Health Organization priorities for ending tuberculosis (TB) by 2035 is the elimination of catastrophic costs due to TB. These are defined as costs exceeding 20% of pre-illness household annual income, because these are usually too expensive for TB treatment completion to be affordable. Surveys of costs due to TB usually interview randomly-selected patients once during treatment, recording their costs from the previous 30 days and extrapolating these to their total illness duration. These surveys take more than an hour to complete, require specially trained researchers and inevitably exclude patients who could not afford to continue TB treatment. We developed and evaluated a more equitable approach that empowered TB program staff and/or community health workers to record patients' costs data cumulatively from the time of TB diagnosis, including the more vulnerable patients who could not complete TB treatment. In place of extrapolated estimations, we recorded data on all actual costs experienced throughout the TB illness. For 174 patients, our approach showed that pretreatment costs due to TB occurred over a median 30 (interquartile range, IQR=7-78) days. When pre-treatment costs were recently recalled, the median total was $437 (IQR=95-1450). These totals costs constituted lost income $202 (IQR=0-600), medical expenses $167 (IQR=50-640) and non-medical expenses $68 (IQR=0-110). During treatment, TB-related costs totaled a further $782 (IQR=210-3,200). Thus, pretreatment plus during treatment total household costs due to TB constituted a median 12% (IQR=5-29) of pre-illness annual household income (that was median $15,960 IQR=10,200-24,000). Consequently, 34% (IQR=27-41) of households experienced catastrophic costs due to TB. When pre-treatment costs were instead assessed by late recall at the end of treatment a median 184 (IQR=157-220) days later, these estimates were very similar (all p>0.1). Our approach empowered program staff to collect important data and ensured that data assessing catastrophic costs due to TB equitably included the most vulnerable patients for whom they have greatest importance.

8242

HOST IMMUNOTHROMBOSIS BIOMARKER ANALYSIS TO PREDICT COVID-19 CLINICAL OUTCOMES

Freyda Mannering[1], Dylan Allen[1], Bochra Tourki[2], Thomas Keller[1], Jose Herazo-Maya[2], Iset Vera[1], Kami Kim[1]

[1]University of South Florida, Dept of Internal Medicine, Division of Infectious Disease and International Medicine, Tampa, FL, United States, [2]University of South Florida, Ubben Center for Pulmonary Fibrosis Research, Tampa, FL, United States

Strategies to improve clinical management identification of risk factors for severe COVID-19 patients are greatly needed. Hyperactivation and dysregulation of the hemostatic and immune systems contribute to the pathophysiology of COVID-19. In this study we analyzed a panel of soluble host immune markers from hospitalized COVID-19 patients (N=140) to identify a biomarker signature attributable to severe clinical presentation. For analysis, we included factors associated with immunothrombosis - Resistin, Myeloperoxidase (MPO), soluble Supression of tumorigenicity 2 (sST2), Tissue Factor (TF), Angiopoietin 2, Interleukin 8 (IL-8), Thrombomodulin, host cell-free DNA (h-cfDNA), and mitochondrial cell-free DNA (m-cfDNA). Plasma soluble biomarkers were analyzed by ELISA or Luminex assays. Cell free DNA measurements were obtained via quantitative PCR or fluorometry. Clinical biomarkers, obtained from patient chart review, included D-dimers, C-reactive protein (CRP), fibrinogen, ferritin, lactate dehydrogenase (LDH), white blood cell count (WBC), platelet count, and total neutrophils. We conducted binary logit analysis to predict the probability of either survival (N=97), death (N=20), or mechanical ventilation (N=22). Levels of h-cfDNA were higher in deceased versus survived patients (p=0.02) and in ventilated versus non-ventilated patients (p=0.0001). Levels of the neutrophil effector molecule, Resistin, were also higher in patients under mechanical ventilation (p=0.02). Our binary logit analysis also pointed to sex (males; p=0.04) and total neutrophil count (p=0.03) as predictive factors of a fatal outcome or ventilator use. In future studies, we will complement our analysis with supervised (Random Forest Analysis) and unsupervised machine learning approaches to identify patterns distinguishing the outcome models and incorporate additional biomarkers into our study. Our results indicate that neutrophil processes are at play in disease progression and that such biomarkers should be tested further to determine their suitability as a part of the standard clinical work up.

8243

RIFAMPIN HETERORESISTANCE, AN IMPORTANT KEY FACTOR TO CONSIDER IN THE TUBERCULOSIS DETECTION

Katherine J. Vallejos, Jorge Coronel, Diego Taquiri, Omar Romero, Patricia Sheen, Mirko Zimic

Universidad Peruana Cayetano Heredia, Lima, Peru

This study underscores the significance of identifying heteroresistant infections in comprehensive tuberculosis (TB) diagnostics, emphasizing the coexistence of drug-resistant and susceptible *Mycobacterium tuberculosis* (MTB) populations. A retrospective analysis of 2,916 MTB whole genomes, obtained from the Tuberculosis Group in Peru from 1999 to 2020 and analyzed using TBprofiler software, was conducted. Among these genomes, 39% exhibited at least one drug resistance, 18.8% were multidrug-resistant, 1.95% displayed mixed infections with different lineages, 4.7% were heteroresistant to at least one drug, and 0.75% were specifically heteroresistant to rifampin, comprising 22 isolates. The objective was to phenotypically and genotypically characterize clinical isolates identified as rifampin heteroresistant based on their whole-genome sequencing (WGS). Four rifampin-resistant (RR-MTB) and four sensitive MTB strains were cultured using the agar proportion method (APM) and test endpoint assay (TEMA) for minimum inhibitory concentration (MIC) determination. Three colonies from each MTB isolate were selected from 7H10 solid media in both the absence and presence of rifampin (1 µg/ml). MIC determination and sequencing of the *rpoB* gene were performed for each colony. Phenotypic analysis confirmed that all MTB isolates were

rifampin heteroresistant by APM; however, only one MTB isolate was categorized as RR-MTB by TEMA (MIC_RIF >1 µg/ml). Colony isolates from rifampin-free and rifampin-supplemented media showed different MIC values and *rpoB* SNPs, indicating selective growth of strains. Colonies from rifampin-supplemented media displayed high resistance (MIC >1 µg/ml) and mutations such as S450L, while those from rifampin-free media exhibited sensitivity (MIC < 1 µg/ml) with D435Y, L452P, and L430P mutations, and some retained the wild type. Among the tested sensitive strains, no mutations in the *rpoB* gene or variations in MIC were observed. This study confirmed the coexistence of both sensitive and resistant populations within the same clinical isolate, corroborating the WGS analysis.

8244

REDUCTIONS IN THE DETECTION OF POTENTIAL RESPIRATORY PATHOGENS DURING SARS-COV-2 PANDEMIC LOCKDOWN: EVIDENCE FROM TWO COHORT STUDIES IN LIMA, PERÚ

Bia Peña[1], Mayra Ochoa[1], Ana I. Gil[1], Omar Flores[1], Rubelio Cornejo[1], Lucie Ecker[1], Leigh M. Howard[2], Carlos G. Grijalva[3], Claudio F. Lanata[4]

[1]Instituto de Investigación Nutricional, La Molina, Peru, [2]Department of Pediatrics, Vanderbilt University Medical Center, Nashville, TN, United States, [3]Division of Pharmacoepidemiology, Departments of Health Policy, Vanderbilt University Medical Center; Department of Biomedical Informatics, Vanderbilt University Medical Center, Vanderbilt University, Nashville, TN, United States, [4]Instituto de Investigación Nutricional; Department of Pediatrics, School of Medicine, Vanderbilt University, La Molina, Peru

During the COVID-19 pandemic, laboratory efforts mainly focused on detecting SARS-CoV-2 infections, rarely searching for other co-pathogens. The TrueMark™ Respiratory Panel 2.0 TaqMan Array Card (TAC) allows simultaneous detection of up to 41 pathogens, including SARS-CoV-2. We collected weekly nasopharyngeal samples (NPS), from household members enrolled in two cohorts in the same district in Lima, Peru, before (Dec-2019 to Mar-2020) and during the pandemic (Dec-2020 to Mar-2021). NPS were collected regardless of symptoms. A subset of NPS from both cohorts was selected for TAC analysis. The first group consisted of 58 NPS from the pandemic cohort 21 with positive to SARS-CoV-2 by RT-PCR, and 37 with respiratory symptoms and negative for SARS-CoV-2; the second group consisted of 18 NPS from the pre-pandemic cohort, paired with 18 NPS negative for SARS-CoV-2 from the pandemic group. We found a decline in the detection of 1 or more potential pathogens other than SARS-CoV-2 in the NPS from the pre-pandemic from 72.2% (13/18) to 29.3% (17/58) in the pandemic (p=0.002). In the pre-pandemic, the pathogens most commonly detected were human *Rhinovirus* (4/18; 22.2%), *H. influenzae* (4/18; 22.2%), *S. pneumoniae* (3/18; 16.7%), and *Moraxella catarrhalis* (3/18; 16.7%); while in the pandemic group, were human *Rhinovirus* (6/58; 10.3%), *S. pneumoniae* (3/58; 5.2%) and *Cytomegalovirus* (3/58; 5.2%). In the pandemic group, the detection of potential pathogens had a small decline from 32.4% in SARS-CoV-2 negative NPS (12/37) to 23.8% in SARS-CoV-2 positive NPS (5/21) (p>0.05). We found a higher detection of potential pathogens in NPS from participants ≤18 years of age (19/29, 65.5%, CI95%: 46.1-80.9) than in >18 years of age (11/47, 23.4%, CI95%: 13.3-37.9, p<0.005), suggesting that children were the main carriers. Our study indicates that the pandemic lockdown in Peru, that included 2 years of school closures, was associated with an important reduction in the detection of potential respiratory pathogens in the nasopharynges.

8245

RISK FACTORS FOR ILLNESS SEVERITY AMONG HOSPITALIZED CHILDREN <5 YEARS IN PERU, 2017—2018

Candice Romero

U.S. Naval Medical Research Unit SOUTH, Lima, Peru

It is important to establish the timing, incidence, and clinical evolution of RSV among children under 5 years old, an RSV vaccine target group. We enrolled 489 children, of which 84% (411/489) had RNA or DNA from 1 or more pathogens identified. RSV was identified in 34% (165/489) of children; 74% (133/181) of children enrolled during April—June 2018 tested positive for RSV. Of all enrolled, 21% (103/489) required supplemental oxygen therapy, 47% of which tested positive for RSV. Infants under 1 year old were at greater risk for severe illness compared to children of 1 or more years old (PR: 2.36 [95% CI: 1.02-5.49], p=0.046). Children with laboratory-confirmed RSV illness (2.05 [1.44—2.94], p<0.001), household exposure to biomass fuel embers (3.16 [1.77—5.66], p<0.001), and neurological disease (3.32 [1.61—6.83], p<0.001) were at increased risk for severe illness as compared to children with other pathogens, without biomass fuel exposure, and without neurological disease, respectively. Among SARI cases, risk factors for severe illness were RSV illness, infancy, household biomass fuel exposure, and preexisting neurological disease. These findings may help to identify children disproportionately at risk for severe illness and guide clinical care and will help to prioritize future vaccination among risk groups which include military population.

8246

OUT-OF-SEASON RESPIRATORY VIRUS INFECTIONS DURING THE PANDEMIC PERIOD OF SARS-COV-2 TRANSMISSION IN BRAZIL

Juan Pablo A. Ticona[1], Luciane Santos Amorim Santos[2], Meng Xiao[3], Nivison Nery Jr[2], Emilia M. M. Andrade Belitardo[2], Mariam O. Fofana[4], Renato Victoriano[2], Jaqueline Cruz[2], Laise Eduarda Paixão de Moraes[2], Mitermayer G. Reis[2], Federico Costa[1], Ricardo Khouri[2], Derek A. Cummings[5], Albert I. Ko[4]

[1]Instituto de Saúde Coletiva, Universidade Federal da Bahia, Salvador, Brazil, [2]Instituto Gonçalo Moniz, Fundação Oswaldo Cruz, Ministério da Saúde, Salvador, Brazil, [3]Department of Laboratory Medicine, State Key Laboratory of Complex Severe and Rare Diseases, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China, [4]Department of Epidemiology of Microbial Diseases, Yale School of Public Health, New Haven, CT, United States, [5]Department of Biology, University of Florida, Gainesville, FL, United States

Evidence from multiple countries suggests that the COVID-19 pandemic disrupted transmission of other respiratory viruses. We aimed to characterize respiratory virus transmission post the emergence of SARS-CoV-2 in a cohort in Salvador, Brazil, a region that typically experienced an annual peak of influenza in winter.From Nov2021 to Oct2022, we conducted biweekly household visits to screen individuals with respiratory symptoms in an urban informal settlement, in Salvador. Symptomatic individuals and their contacts underwent interviews and nasal swab collection. Virus identification was performed by RT-PCR or multiplex PCR to detect SARS-CoV-2, influenza (Flu), and respiratory syncytial virus (RSV), followed by metagenomic analysis among participants with cough or fever who had PCR(-) results.In total, 3174 residents in 1174 households were screened ≥1 times during the study period, among which, 669 symptomatic episodes were reported. We identified 108(16%) SARS-CoV-2, 28(4%) Flu A, 14(2%) human Parainfluenza virus (HPIV), 10(1%) Rhinovirus, and 5(1%) RSV cases. Flu, HPIV, and RSV infections peaked in Nov and Dec 2021 (summer), during which low transmission of the Delta variant occurred. Whole Genome Sequencing revealed the emergence of the Omicron BA.1 variant in Jan2022. Furthermore, Flu and RSV exhibited low transmission during the winter months. The most prevalent influenza genotype was H3N2. The secondary attack rate (SAR) among house contacts was 25% (95%CI 10-47%) for Flu and 50.0% (95%CI 38-62%) for Omicron BA.1. Flu cases presented similarly to SARS-CoV-2 clinically, while HPIV-infected participants were younger (p<0.01) and experienced more symptoms (p<0.01).Our genomic surveillance for respiratory viruses during the pandemic identified an off-season summer Flu wave of transmission. This wave followed a prolonged period of low transmission and may have been caused by relaxed respiratory hygiene measures post the Delta variant transmission decline and before the emergence of Omicron variant. Finally, the household SAR for influenza was lower than the Omicron BA.1 variant, reflecting its lower transmissibility.

8247

VIRAL ETIOLOGY AND EPIDEMIOLOGIC INVESTIGATION OF PATIENTS WITH SEVERE ACUTE RESPIRATORY ILLNESS IN GHANA, JANUARY 2021-MAY 2022

Bernard Nkrumah[1], Ivy Asantewaa Asante[2], Yaw Awuku-Larbi[2], Selassie Kumordzie[3], Bright Agbodzi[3], Stephen Nyarko[2], Lorreta Kwasah[2], Linda Boatemaa[2], Emmanuella Awedana Apuri[4], Danielle E. Gill[5], Danielle T. Barradas[6], Ernest Kenu[7]

[1]African Field Epidemiology Network (AFENET), Accra, Ghana, [2]Virology Department, Noguchi Memorial Institute for Medical Research, Accra, Ghana, [3]US Naval Medical Research Unit, EURAFCENT, Accra, Ghana, [4]African FieVirology Department, Noguchi Memorial Institute for Medical Research, Accra, Ghana, [5]Global Respiratory Viruses Branch, National Center for Immunization and Respiratory Diseases, US Centers for Disease Control and Prevention, Atlanta, GA, United States, [6]Global Health Security Program, Division of Global Health Protection, U.S. Centers for Disease Control and Prevention, Accra, Ghana, [7]School of Public Health, University of Ghana, Accra, Ghana

Severe acute respiratory illness (SARI) is prevalent in sub-Saharan Africa (SSA), contributing to approximately 77% of hospitalizations. In Ghana, limited diagnostic tools have hindered understanding of SARI etiologies. Our study aimed to determine the etiologies among individuals with SARI in Ghana. Archived oropharyngeal and nasopharyngeal specimen (n=307) collected from 29 SARI surveillance sentinel sites across Ghana during January 2021 to May 2022 were tested at the National Influenza Center using the Fast-Tracked Diagnosis Respiratory Pathogens 21 real-time quantitative polymerase chain reaction (RT-qPCR) kit and the Illumina Respiratory Pathogen ID/AMR enrichment panel for multi-pathogen detection. These specimens had previously tested negative for influenza virus and SARS-CoV-2 using the RT-PCR. Sequencing data were analyzed using the Explify Respiratory Pathogen ID/AMR Enrichment Panel application. Chi-squared analyses were used to assess statistically significant associations ($p<0.05$) between pathogens and sex, age, and symptoms. Etiology was determined for 56% (171/307) of specimens, identifying 14 viral pathogens, including adenovirus (20%), human rhinovirus (13%), human coronavirus (8%), and respiratory syncytial virus (4%). Multiple pathogens were detected among 24% (41/171) of positive specimens. Adenovirus and rhinovirus (19%, (8/41)) co-infection was the most common. Cytomegalovirus was detected most frequently among cases aged <5 years (13.8%, $p=0.005$) whilst adenovirus was most prevalent among 5-24 age group ($p=0.046$). Epstein-Barr virus detection varied by sex ($p=0.035$). Adenovirus was detected among patients with cough (28%, $p=0.060$)) and sore throat (37%, $p=0.054$). Human rhinovirus was predominant in cases with difficulty in breathing (24%, $p=0.803$). This study demonstrates the need to expand pathogen detection methods for surveillance of SARI to better understand respiratorydisease burden and to inform policy and resource allocation for medications, vaccination, and early detection of outbreaks.

8248

INCIDENCE OF ACUTE RESPIRATORY ILLNESSES IN CHILDREN IN A PERIURBAN COMMUNITY OF LIMA, PERU

Lucie Ecker[1], Carlos G. Grijalva[2], Leigh M. Howard[2], Bia Peña[1], Mayra Ochoa[1], Ana I. Gil[1], Omar Flores[1], Rubelio Cornejo[1], Stefano Rios[1], Claudio F. Lanata[1]

[1]Instituto de Investigación Nutricional, Lima, Peru, [2]Division of Pharmacoepidemiology, Departments of Health Policy, Vanderbilt University Medical Center, Nashville, TN, United States

Acute respiratory illness (ARI) is among the leading causes of morbidity and mortality among children each year, and most occur in low- and middle-income countries. Traditional studies of common acute respiratory infections are mainly carried out in primary healthcare centers, emergency departments, and hospitals, but those do not reflect the real burden of infection within households and communities. We conducted a prospective household-based cohort study in a peri-urban community of Lima, Peru. Eligible households included at least one child 5 to 60 months of age at enrollment, which were followed through weekly home visits to identify symptoms of ARI defined as the presence of cough and/or runny nose with fever. 119 children were enrolled and followed from October 2019 to February 2020, accruing 10576 child-days at risk. Incidence rate of ARI was 5.5 episodes child/year. Higher incidence was found in female children 6.0 episodes/child/year vs. 5.1 episodes/child/year in males. The highest incidence was found in children less than 12 months with 7.8 ARI episodes/child/year (8.3episodes/child/year in female and 7.2 episodes/child/year in male) and in children between 2 and 3 years of age (6.2 episodes/child/year). Median duration of symptoms was 6 days (IQR 3-35). The most common ARI symptoms were cough (92.5%) and runny nose (81.3%), followed by fever (38.8%), difficulty breathing (25%) and wheezing (7.5%). In 49.3% episodes of ARI, caregivers sought medical attention at an outpatient clinic and 4 (0.025%) cases were treated at an emergency room. Antibiotics were used in 46 (28.8%) cases, prescribed mainly by physicians (82.6%). Our findings demonstrate a high incidence of ARI in children less than 5 years in this peri-urban community in Lima and highlights the amount of disease that remains undetected at healthcare units and the high, mostly unjustified, use of antibiotics. Further studies are needed to evaluate the burden of ARIs at the community level, their impact on child development, and the cost to society.

8249

TUBERCULOSIS: MEN DIE MORE

Luz Quevedo Cruz[1], Matthew Saunders[2], Paula P. Carballo-Jimenez[2], Rosario Montoya[2], Maribel Rivero[2], Jonathan Gomez[2], Pilar Tapia[2], Maria Haro[2], Jessica Franco[2], Rosario Sosa[2], Carlton A. Evans[3], Sumona Datta[2]

[1]Cayetano Heredia University, Lima, Peru, [2]Prisma NGO, Lima, Peru, [3]Imperial College London, Lima, Peru

Tuberculosis (TB) is still one of the largest killers in low-middle income countries. The World Health Organization estimates that there are more cases in men. This is thought to be due to a combination of care-seeking, biological and behavioral factors, such as increased smoking, alcohol consumption, drug use and HIV infection. The objective of this analysis was to evaluate gender-related risk to TB mortality. We invited all patients above 15 years old who started treatment for tuberculosis from 32 community health centers in Callao, Peru to participate in the Prevent TB cohort study (http://www.isrctn.com/ISRCTN17820976). They were followed-up for 18 months post recruitment during household visits. If a participant died during this time, a verbal autopsy was performed with family members .Date of death was confirmed from multiple sources including TB treatment records or death certificates. For participants who were alive, survival analysis was censored on the day of the follow-up interview or the last day someone saw the participant. 2283 participants were recruited between 07/2016 and 11/2018 with 2028 (89%) having follow-up data available for survival analysis. Males were 1.7-times more likely than females to have TB. There were 132 deaths over 1,765,504 person-years, with males 2.6-times more likely to die compared with females in this follow-up period. Therefore, time-to-event analysis with the Cox Proportional Hazard Model demonstrated that males had approximately 1.5-times higher hazard of death compared to females (HR:1.53, 95%CI:1.04-2.24,$p<0.005$). In models adjusted for age, comorbidity, rifampicin resistance treatment, diagnostic delay and disease severity (HR:1.81, 95%CI:1.08-3.02,$p<0.005$). These findings suggest that males have an increased risk of death during TB treatment independent of comorbidities, and behavioral factors that are associated with increased death. These sex differences require more research and could be explained by anything from PK/PD, adherence and immunological differences between sex.

8250

INCIDENCE OF SARS-COV-2 INFECTION IN A COMMUNITY COHORT IN PONCE, PUERTO RICO

Chelsea G. Major[1], Dania M. Rodríguez[1], Neal Alexander[2], Liliana Sánchez-González[1], Tatiana Morales-Ortíz[3], Carolina Torres[4], Kamalich Muniz Rodriguez[1], Nicole A. Medina-Lópes[1], Rafael Tosado-Acevedo[1], Jorge Muñoz-Jordán[1], David Mabey[2], Laura E. Adams[1], Vanessa Rivera-Amill[3], Gabriela Paz-Bailey[1]

[1]Centers for Disease Control and Prevention Dengue Branch, San Juan, PR, United States, [2]London School of Tropical Medicine and Hygiene, London, United Kingdom, [3]Ponce Health Sciences University, Ponce, PR, United States, [4]Kāpili Services, LLC, Orlando, FL, United States

Characterizing the incidence of SARS-CoV-2 infections is important to estimate morbidity and mortality rates, identify high-risk groups, and inform mitigation efforts. Asymptomatic and mild infections often go undetected, complicating the estimation of infection rates from surveillance reports. In 2020, we implemented a community-based cohort study in Ponce, Puerto Rico (PR) to assess local SARS-CoV-2 transmission dynamics. All participants provided weekly self-collected anterior nasal swabs (ANS); additional ANS were collected from those reporting COVID-like symptoms or contact with an infected person. ANS were tested for SARS-CoV-2 by RT-PCR to identify incident infection events. Participant demographics, preventive and health care-seeking behaviors, and acute symptom data were collected using standardized questionnaires. We used Poisson regression to estimate overall and univariate infection incidence rates. Among 1,030 participants enrolled, mean age was 35.9 (range 1-97) years, 99.6% identified as Hispanic/Latino, and 37.9% had an annual household income <$20,000. In Jun 2020-Apr 2022, we detected 262 SARS-CoV-2 infection events, of which 83 (31.7%) were asymptomatic, participants sought care for 19 (10.2%), and 1 (0.4%) was fatal. Overall incidence was 3.56 (95%CI: 3.13-3.98) infections per 1,000 person-weeks (PW). Incidence was lower among participants ≥65 years (0.94, 95%CI: 0.32-1.56 per 1,000 PW) than in all other age groups. Incidence increased dramatically beginning in Dec 2021 after the Omicron variant was introduced in PR, from 0.91 (95%CI: 0.68-1.15) to 11.87 (95%CI: 10.26-13.48) infections per 1,000 PW. There was no evidence of infection rate differences by sex, employment status, household income, or COVID-19 vaccine or infection history. The frequency of mild infections and low rate of health care seeking in our cohort suggest that routine surveillance severely underestimates regional SARS-CoV-2 burden. Analyses are underway to assess the potential role of mobility, preventive behaviors, and other time-varying factors on SARS-CoV-2 infection risk.

8251

ASSOCIATION OF PRE-EXISTING ANTIBODY RESPONSES AND THE RISK OF SARS-COV-2 INFECTION IN A HIGHLY EXPOSED BRAZILIAN COHORT DURING THE OMICRON BQ.1 EPIDEMIC WAVE

Mariam O. Fofana[1], Juan Pablo Aguilar Ticona[2], Nivison Nery Jr[1], M. Catherine Muenker[1], Joseph Q. Lu[3], Homegnon Antonin Ferreol Bah[2], Emilia Andrade Belitardo[2], Jaqueline Silva[2], Gabriel Ribeiro dos Santos[1], Renato Victoriano[2], Ricardo Khouri[2], Stephen Thomas[3], Adam Waickman[3], Federico Costa[4], Mitermayer G. Reis[2], Derek A.T. Cummings[5], Albert I. Ko[1]

[1]Yale School of Public Health, New Haven, CT, United States, [2]Instituto Goncalo Moniz (Fiocruz Bahia), Salvador, Brazil, [3]SUNY Upstate Medical University, Syracuse, NY, United States, [4]Universidade Federal da Bahia, Salvador, Brazil, [5]University of Florida, Gainesville, FL, United States

Post-vaccination neutralizing antibodies were found to be a correlate of protection against symptomatic illness in clinical trials of COVID-19 vaccines. However, the association between neutralizing antibodies and subsequent infection risk remains poorly characterized for variants of concern, including Omicron BQ.1, which emerged in 2022. We conducted serial household-based serosurveys in a cohort of informal settlement residents in Salvador, Brazil, in March-August 2022 ("pre-BQ.1 period"), and in November-December 2022 after the emergence of BQ.1. We identified cases of incident PCR-confirmed SARS-CoV-2 infections during the BQ.1 period. Each case was matched by age and sampling time with one PCR-negative control. We measured BQ.1-specific serum antibody responses using a pseudo-neutralization electrochemiluminescence assay (Meso Scale Discovery) and compared cases vs. controls using linear regression adjusted for age, sex, and vaccination history. Of 511 participants who underwent PCR testing in the BQ.1 period, 95.2% had at least one prior exposure to SARS-CoV-2 infection or vaccination. Of 59 PCR-positive cases, 33 (55.9%) had symptomatic illness and 34 had serum collected in the pre-BQ.1 period. Unexpectedly, in pre-BQ.1 sera collected a median 7.4 (interquartile range [IQR] 6.8-7.7) months prior to PCR testing, median pseudo-neutralization against BQ.1 was higher among cases (71.2%, IQR 38.9-86.4%) than controls (39.9%, IQR 25.9-70.9%). In contrast, there was no statistically significant difference in median pseudo-neutralization among cases (58.7%, IQR 38.5-72.6%) and controls (51.4%, IQR 27.9-83.0%) whose sera were collected at the time of PCR testing in the BQ.1 period. The lack of association between BQ.1 antibody responses and incident infection suggests that neutralizing antibodies may no longer be a meaningful correlate of protection and raises questions about their relevance for immunogenicity bridging trials of COVID-19 vaccines. The observed association of pre-BQ.1 pseudo-neutralization with higher risk of infection may reflect a combination of high attack rates and delayed time to infection.

8252

BIOMARKER DISCOVERY AND ASSAY DEVELOPMENT TO DETECT ANTIBODIES TO *SCHISTOSOMA HAEMATOBIUM*

Yong Wang, Maurice Royal, Sylvia Ossai, Maria Ulke, Kimberly M. Won, Sukwan Handali, Willam E. Secor

CDC, atlanda, GA, United States

While a number of recombinant antigens have been described for detection of *Schistosoma mansoni* and *S. japonicum* infections, antigens specific for *S. haematobium* diagnosis are limited. Antibody testing is not necessarily appropriate for the monitoring and evaluation use case described in WHO's target product profiles (TPP) for schistosomiasis but it still has potential as a screening tool in the use case for determining transmission interruption and post-verification surveillance. In addition, *S. haematobium*-specific antibody tests may be helpful to support diagnosis of female genital schistosomiasis (FGS). To this end, we have identified and qualified two antibody biomarkers, rSh_SAP1 and rSh_quadruplet, for *S. haematobium.* The sensitivity and specificity of combined antigens in a multiplex bead assay (MBA) that detects total IgG (including IgG4) were 88% and 97%, respectively. As these tests met the TPP criteria as the screening assay for interruption of transmission, we conducted validation of the MBA based on these two antigens. Using a set of defined sera from paristologically-confirmed positive individuals, negative individuals, and from people who had parasitic infections that might cross-react with *S. haematobium*, the sensitivity and specificity of the MBA were 88% and 97% for rSh_quadruplet and 88% and 92% for rSh_SAP1. Combining both antigens gave a sensitivity of 92% and a specificity of 97%. Cross-reactivity was detected mostly sera from individuals infected with *Fasciola hepatica* and *Paragonimus westermani*. Next steps will include evaluation in an independent laboratory and evaluation of these antigens in a lateral flow rapid diagnostic test. Such a test could contribute to a diagnostic algorithm for FGS by identifying a history of *S. haematobium* infection in women presenting with urogenital symptoms.

8253

UNDERSTANDING THE IMPACT OF *SCHISTOSOMA HAEMATOBIUM* INFECTION AMONG GAMBIAN SCHOOL-AGED CHILDREN: EPIDEMIOLOGICAL AND IMMUNOLOGICAL INSIGHTS

Aradhana Singh[1], Haddy Bittaye[2], John Archer[3], Bonnie L. Webster[3], Jason P. Mooney[1]

[1]Institute of Immunology and Infection Research, Edinburgh, United Kingdom, [2]Medical Research Council Unit in The Gambia at the London School of Hygiene and Tropical Medicine, Fajara, Gambia, [3]Wolfson Wellcome Biomedical Laboratories, Science, Natural History Museum, London, United Kingdom

Schistosomiasis, caused by blood fluke of the genus *Schistosoma*, is the second deadliest parasitic disease and is found mostly in Sub-Saharan Africa. In The Gambia, infection is predominantly caused by *S. haematobium* which causes urogenital schistosomiasis, with 10% of adolescents in 2015 found to be infected by urinary egg microscopy. To assess level of infection and associated morbidity, a cross-sectional study was performed to determine the prevalence of anaemia, haematuria and *S. haematobium* infection. First, 1650 healthy children from 29 villages in Upper River region in 2018 were screened. Next, 308 children were surveyed two months later to provide longitudinal data on infection and quantitative assessment of associated morbidity. Persistent anaemia unrelated to malaria infection and/or *S haematobium* infection were identified. Prevalence of moderate to severe anaemia was 33.7% (557/1650), while 41.5% (622/1498) had urinary haematuria and 17.3% (121/698) were positive for *S. haematobium* eggs detected by microscopy. The distribution of *S. haematobium* infection exhibited a localized pattern, within two specific villages, Nyamanari and Dingiri, with the high prevalence levels, 66.9% (81/121). Overall, the intensity of infection was low, with a median of 4 eggs/10mL urine. Urinalysis of the follow-up cohort found that the prevalence of haematuria did not change across the time points (41%). Proteinuria and leukocyturia was less evident, 11% and 4% respectively. IL-6 was detected in urine and was significantly higher in those with haematuria (p=0.01). Further work includes quantification of plasma inflammatory cytokines and diagnosis of *S. haematobium* by qPCR for more accurate levels of infection. In pilot work (n=24/308), infection was found in microscopy-negative samples using qPCR. Together, these data show high levels of anaemia, haematuria and *S. haematobium* infection in The Gambia than previously reported. Therefore, using a more sensitive diagnostic to detecting low-density infections, coupled with targeted interventions in persistent areas of infection could help lead to elimination or transmission interruption

8254

PREVALENCE AND CHARACTERIZATION OF HEPATIC FIBROSIS AND PORTAL HYPERTENSION AMONG INDIVIDUALS LIVING IN AN *SCHISTOSOMA JAPONICUM* ENDEMIC REGION OF THE PHILIPPINES

Mario A. Jiz[1], Ralph Aniceto[1], Hannah Wu[2], Jonathan D. Kurtis[2], Veronica Tallo[1], Andreas Neumayr[3], Christoph Hatz[3], Jennifer Friedman[2], Joachim Richter[4]

[1]Research Institute of Tropical Medicine, Manila, Philippines, [2]Center for International Health Research, RI Hospital and Alpert Medical School of Brown University, Providence, RI, United States, [3]Swiss Tropical and Public Health Institute, Allschwil, Switzerland, [4]Institute of Tropical Medicine and International Health, Charité Universitäts Medizin, Berlin, Germany

The Niamey protocol was developed to characterize hepatic fibrosis due to *Schistosoma mansoni*. Similar guidelines do not exist for *S. japonicum* and little is known with respect to response to Praziquantel treatment for *S. japonicum*. As a part of an NIH funded longitudinal study designed to assess the impact of annual treatment (three years) for *S. japonicum* on hepatic fibrosis, we screened individuals from endemic villages in Leyte, The Philippines. We enrolled N = 288 subjects ages 14-60 with *S. japonicum* infection who were invited to the field laboratory where history and physical exam, serum chemistries, hepatitis B antigen assay, and ultrasound of the liver and spleen using a modified Niamey protocol were conducted. Individuals with Hepatitis B and those with ultrasound findings of cirrhosis or fatty liver due to other causes such as alcohol intake were excluded. Individuals with Image Pattern A or B were considered not to have fibrosis. Individuals with Image Pattern C-F were considered to have Periportal Fibrosis and individuals with Image Pattern G were considered to have Interseptal Fibrosis. The presence or absence of portal hypertension was assessed based on the portal vein quotient (portal vein diameter/height < 7.5). Of N=203 subjects after exclusions for hepatitis B or cirrhosis (N=10, 74 respectively) fibrosis of any type due to *S. japonicum* was found in 118 (58%) of subjects. Specifically, Periportal Fibrosis was demonstrated in 70 (33%), Interseptal Fibrosis in 85 (42%), and 37 subjects (18%) had evidence of both. Men were almost twice as likely to have any type of fibrosis and over four times as likely to have both patterns. Nine subjects (4%) had evidence of portal hypertension, a significant risk factor for bleeding. All individuals with portal hypertension were male and none had purely Interseptal Fibrosis. Subjects with any type of fibrosis were treated, enrolled, and will be treated annually and followed to determine responsiveness of types of fibrosis to treatment. Interseptal Fibrosis is uniquely seen in *S. japonicum* and we will examine its responsiveness to treatment over three years.

8255

FEMALE GENITAL SCHISTOSOMIASIS (FGS) KNOWLEDGE GAPS AND NEEDS IN SUB-SAHARAN AFRICA: ANALYSIS AND REVIEW OF ACTION PLANS GENERATED FROM A PEER-TO-PEER EDUCATION METHOD

Maria Victoria Dreher Wentz[1], Anastasia Pantelias[2], Amaya L. Bustinduy[3], Julie Jacobson[2]

[1]Ontario HIV Treatment Network, Toronto, ON, Canada, [2]Bridges to Development, Vashon, WA, United States, [3]London School of Hygiene and Tropical Medicine, London, United Kingdom

Female Genital Schistosomiasis(FGS) is a neglected gynecological manifestation of schistosomiasis, affecting girls and women in sub-Saharan Africa. Misdiagnosis is common due to lack of awareness and the similarity of symptoms to other sexually-transmitted infections leaving chronic manifestations and indicating a need to increase awareness and knowledge of FGS. This mixed-method research included an inductive thematic analysis of action plans, developed by participants attending the 2021 FGS Accelerated Scale Together (FAST) Packaged virtual workshop hosted by Bridges to Development and the Geneva Learning Foundation, aimed to identify key challenges and solutions to address FGS. This study conducted quantitative analyses of baseline and endline surveys, descriptive statistics and the McNemar test, to evaluate the peer-to-peer methodology used during the workshop. The peer-to-peer education methodology was well received by participants and was associated with an increase in participant awareness, knowledge, and confidence (p<0.001). Five predominant themes describing challenges emerged: lack of awareness, misdiagnosis, lack of knowledge, lack or inadequate preventative measures and high exposure risk. Within solutions, six key themes emerged: sensitization, knowledge and education, capacity strengthening, increasing awareness, intersectoral collaboration and implementation of preventative measures. This study presents the results of a novel virtual workshop, and confirms its success and effectiveness. This study sheds light on the multifaceted challenges and potential solutions surrounding FGS, in the eyes of those who work in the target regions, highlighting the essential participation of local professions when developing projects. The training generated a holistic approach that was highlighted by multiple participants, and it is deemed essential in tackling FGS issues in multiple sub-Saharan countries. Furthermore, the peer-to-peer virtual approach is a highly effective tool for raising awareness of FGS, with the possibility of being used with NTDs.

8256

PREVALENCE AND INFECTION INTENSITIES OF *SCHISTOSOMA MANSONI* IN VILLAGES DESIGNATED PERSISTENT HOTSPOTS AND NON-PERSISTENT HOTSPOTS IN WESTERN KENYA

PETER RARIEYA OLILAH[1], Susan Musembi[2], Winka Le Clec'h[3], Timothy J. Anderson[3], Frédéric D. Chevalier[3], Eric Ndombi[1]

[1]Kenya Medical Research Institute, KISUMU, Kenya, [2]Kenyatta university, Nairobi, Kenya, [3]Texas Biomedical Research Institute, San Antonio, TX, United States

Efforts have lately been intensified to control schistosomiasis using preventive chemotherapy using praziquantel mass drug administration (MDA) in most countries where the disease is prevalent. Previous have reported the existence of 'persistent hotspots,' villages where schistosomiasis prevalence and infection intensities remained high despite years of preventive chemotherapy. Western Kenya is one of the regions where such persistent hotspots were reported. Many years later, following implementation of school-based deworming in western Kenya, it has not been established whether further gains have been made in reducing infection prevalence and intensities. This study sought to determine whether persistent hotspot remain following years of school-based deworming program by comparing the prevalence and infection intensity of *Schistosoma mansoni* between five randomly selected persistent hotspot and non-hotspot regions in Siaya County, Western Kenya. We carried out a cross sectional study involving 500 participants (250 from the persistent hotspots, and the other 250 from non-hotspots villages) who were recruited into the study between May and September 2023. The average prevalence in the persistent hotspot villages was significantly higher than in the non-hotspot villages, *P=0.0006*. Children <18-years were 0.99 times more at risk of infection compared to adults, OR 0.99(95% CI 0.98-1). Males also had a higher risk of infection of 0.99 times compared to females, 0R 0.99(95% CI 0.98-1).The overall prevalence in the selected ten villages was 39.2%, quite significant proportion of the sampled population despite ongoing control efforts. The most notable finding of this study is the continued existence of persistence hotspots, first described in 2017, despite continuation of mass drug administration especially in school children. This finding necessitates a rethink of the control strategies currently in use, including incorporating vector control and other sanitation and hygiene (WASH) based control measures in the persistent hotspots.

8257

A FRAMEWORK FOR UNDERSTANDING AND ADDRESSING BIOLOGICAL AND OPERATIONAL HOTSPOTS IN SCHISTOSOMIASIS CONTROL

Rivka M. Lim[1], Thomas M. Arme[2], Amy B. Pedersen[1], Joanne P. Webster[3], Poppy HL Lamberton[2]

[1]University of Edinburgh, Edinburgh, United Kingdom, [2]University of Glasgow, Glasgow, United Kingdom, [3]Royal Veterinary College, Hatfield, United Kingdom

Recognition of both biological and operational hotspots is crucial for effective schistosomiasis control, as each requires distinct mitigation strategies and resource allocation. To achieve the World Health Organization's (WHO) goal of eliminating schistosomiasis as a public health problem by 2030, a greater understanding of what is driving persistent high transmission, prevalence and morbidity in endemic regions is needed. Persistent 'biological hotspots', are areas which meet specific prevalence and treatment intervention targets, but transmission persists. Establishing universal thresholds to define these hotspots and effectively allocate interventions such as biannual mass drug administration and snail control, along with regular surveillance for drug resistance, can be challenging due to the inconsistency in definitions, and region-specific complexities. Recognising that there could also be 'operational hotspots', particularity stemming from insufficient treatment coverage due to factors such as a lack of access, community compliance, along with the challenge of accurately measuring treatment coverage, is vital to understand alternative drivers of ongoing transmission. In light of these challenges, we conducted an extensive literature review to evaluate WHO's current provisional definition of a persistent hotspot. We then interviewed stakeholders in the field and, using insights from both sources, proposed modifications to the definition of a biological persistent hotspot. Using this definition and the WHOs own recommendation for routine monitoring for effective treatment coverage, we produced a definition framework that aims to guide decision-making by introducing regional flexibility to the thresholds and identifying regions that require additional investigations and support to address treatment shortfalls, thereby designating regions for targeted control initiatives. By acknowledging and addressing both biological and operational drivers of transmission, we believe that the effectiveness of schistosomiasis control efforts can be enhanced toward achieving the WHO's goal of elimination.

8258

THE IMPACT OF EXTREME RAINFALL EVENTS ON SCHISTOSOMIASIS TRANSMISSION IN COMMUNITIES LIVING AROUND MANOMBO SPECIAL RESERVE, MADAGASCAR

Laura Braun[1], Herizo Randrianandrasana[2], Nina Finley[3], Andry Tsirimanana[4], Mandranto Rasamoelina[5], Sakib Burza[6]

[1]London School of Hygiene and Tropical Medicine, London, United Kingdom, [2]Health In Harmony, Farafangana, Madagascar, [3]Health in Harmony, Portland, OR, United States, [4]Health in Harmony, Farafangana, Madagascar, [5]Centre d'Infectiologie Charles Merieux, Antananarivo, Madagascar, [6]Health In Harmony, Portland, OR, United States

Schistosomiasis is a parasitic disease affecting over 200 million people worldwide. Madagascar ranks among the countries with the highest prevalence, with up to 52% of the population at risk. Infection occurs through contact with contaminated freshwater bodies that contain schistosome-infected aquatic snails, and is directly linked to frequency and duration of water contact, with hygiene activities and rice paddy farming being key risk factors. Climate change, through increased global temperature and extreme precipitation, can create new habitats suitable for schistosome snails, thereby potentially shifting or expanding transmission zones in Madagascar. Importantly, climate change may also affect the risk of infection by influencing the frequency and duration of water contact with freshwater bodies. This project is determining how extreme rainfall events are affecting water-based hygiene activities and schistosomiasis infection in communities living around the Manombo Special Reserve in south-eastern Madagascar. 10 rural rainforest villages with known *Schistosoma mansoni* prevalence were enrolled in this study. Microbial water contamination and snail presence was assessed in a total of 19 freshwater bodies used by villages for water contact activities. This included rivers, ponds and rice paddy fields. Additionally, we assessed *S. mansoni* prevalence and infectivity in 40 school-aged children and high-risk adults per village using duplicate Kato-Katz. Stool sample collection was paired with household surveys about water, sanitation and hygiene (WASH) infrastructure and practices. Sampling is repeated twice, in the dry season and after extreme rainfall at the beginning of the rainy season. Data collection is ongoing, and results will be available mid-2024. This project enables an in-depth assessment of how extreme rainfall events affect WASH infrastructure and practices, freshwater quality, schistosomiasis prevalence, and snail densities across a range of water sources contacted by high-risk rainforest communities.

8259

A PUBLIC DATABASE CATALOGING GEOGRAPHICAL, SEQUENCE AND FUNCTIONAL VARIATION IN TRPM$_{PZQ}$, A CANDIDATE LOCUS FOR PRAZIQUANTEL RESISTANCE.

Claudia Rohr, Sang-Kyu Park, Jonathan Marchant

Medical College of Wisconsin, Milwaukee, WI, United States

The drug praziquantel (PZQ) is used to treat NTDs caused by parasitic flatworms such as schistosomiasis, a disease that afflicts over 200 million people. While PZQ has been used clinically for four decades, heavy reliance on a single drug poses concerns related to drug resistance. This is

compounded by the lack of knowledge about the parasite target of PZQ. A parasite target of PZQ has finally been identified - a transient receptor potential ion channel in the melastatin family known as $TRPM_{PZQ}$. $TRPM_{PZQ}$ is a key locus that underlies variation in praziquantel susceptibility in the laboratory, such that it is reasonable to infer that different $TRPM_{PZQ}$ channel variants will be associated with varied sensitivities to PZQ in the field, and potentially differential treatment outcomes. Effort to detail standing and *de novo* variation in $TRPM_{PZQ}$ and correlating this genetic diversity with the functional sensitivity of $TRPM_{PZQ}$ to PZQ, and ultimately treatment outcomes, is now a priority. Here, the functional consequences of $TRPM_{PZQ}$ sequence variants from both laboratory and field studies performed by various groups have been compiled into a publicly available database (trptracker.live). This database aggregates the functional impact of each variant in a resource that allows users to assess the impact of mutations throughout the channel sequence. Each variant has been profiled in a standardized Ca^{2+} reporter assay under identical conditions enabling cross comparison of functional effects relative to the accession sequence. For field studies, geographic information is also integrated. This portal enables rapid assessment of the PZQ sensitivity of sequenced variants, and thereby prioritization of 'variants for concern' in the context of surveillance for the emergence and/or spread of variants that could underpin PZQ resistance. Users are also able to request functional profiling of any sequence variants isolated from their own data in natural schistosome populations, expanding the scope of this community-driven database to various schistosome species that infect humans and animals.

8260

DETECTION OF *NEORICKETTSIA SPP*. IN SUSCEPTIBLE OR RESISTANT *FASCIOLA HEPATICA* OBTAINED FROM NATURALLY INFECTED CATTLE IN CUSCO, PERU

Carol Alexandra Castro[1], Martha Vanessa Fernandez- Baca[1], Rodrigo Alejandro Ore[1], Maria Luisa Morales[1], Miguel M. Cabada[2]

[1]Sede Cusco - Instituto de Medicina Tropical Alexander von Humboldt - UPCH, Cusco, Peru, [2]Infectious Diseases Division, Internal Medicine Department, University of Texas Medical Branch, Galveston Texas USA., Cusco, Peru

The genus *Neorickettsia* comprises obligate intracellular bacteria present in digeneans and capable of causing disease in animals and humans. *Fasciola hepatica* obtained from sheep in Oregon and Uruguay have been shown to harbor Neorickettsia. The role of this endosymbiont on Fasciola's lifecycle is unknown. Our study objective was to describe the prevalence of Neorickettsia sp. in adult F. hepatica with different susceptibility patterns to triclabendazole obtained from naturally infected cattle in Cusco, Peru. A total of 409 Fasciola were collected from three slaughterhouses in Cusco city, transported to the laboratory, and incubated at 37°C with 5% CO2 for 48 hours. Fully motile Fasciola were exposed to triclabendazole at a concentration of 15ug/ml. Parasite motility as a proxy of viability was evaluated at 24 and 48 hours to determine sensitivity to triclabendazole. Parasites with motility score of zero at 24 hours were considered sensitive and parasites with a motility score of 2 or 3 after 48 hours were considered resistant. DNA was extracted from adult parasites using the E.Z.N.A.® Tissue DNA Kit following the manufacturer's instructions. *Neorickettsia sp*. DNA was detected by real-time PCR targeting the bacteria heat shock protein gene (GroEL). Sixty-one parasites were classified as sensitive and 87 as resistant. The prevalence of Neorickettsia was 27.8% in sensitive and 51.5% of resistant parasites (p= 0.004). Our results suggest that Neorickettsia infection occur more often in triclabendazole resistant parasites. Further research should confirm these results and explore the potential role of Neorickettsia in resistance to triclabendazole.

8261

COMMUNITY PREFERENCES FOR INTERVENTIONS TO REDUCE HUMAN TO SNAIL TRANSMISSION OF SCHISTOSOMIASIS IN MAYUGE DISTRICT UGANDA

Moses Arinaitwe[1], Sande Silvesteri[2], Lazaaro Mujumbusi[2], Lucy Pickering[3], Edith Nalwadda[2], Agnes Ssali[2], Keila Meginnis[4], Poppy H L Lamberton[5], Janet Seeley Seeley[2]

[1]Vector Borne and Neglected Tropical Diseaes Division, Kampala, Uganda, [2]Medical Research Council/Uganda Virus Research Institute and London School of Hygiene & Tropical Medicine Uganda Research Unit, Entebbe, Uganda., Entebbe, Uganda, [3]School of Social & Political Sciences, University of Glasgow, UK, Glasgow, United Kingdom, [4]School of Biodiversity, One Health, and Veterinary Medicine, University of Glasgow, UK, Glasgow, United Kingdom, [5]University of Glasgow, UK, Glasgow, United Kingdom

Over 240 million people have schistosomiasis. *Schistosoma mansoni* transmission occurs when eggs in faeces enter fresh water, hatch into miracidia, penetrate intermediate snail hosts, which releases infective cercariae. Governments have deployed praziquantel mass drug administration to control schistosomiasis. However, alternative interventions are required for communities to reach the WHO 2030 goal. Understanding community preferences for control interventions will help improve uptake and sustainable use. This study elicited community's preferences for interventions aimed at minimizing human to snail transmission. Stakeholder workshops, with school-age children, women, fisherfolks and opinion leaders, were held in three highendemicity communities in Mayuge, Uganda. The life cycle and interventions, previously suggested by rapid ethnographic appraisals, were presented. Enforcing fines for open defecation, constructing latrines at the lake, market, within a five minute walk from homes and maintaining latrines to higher standard were discussed and prioritized by popularity, affordability and preferred attributes. Facilitators for the use of the top two were discussed. Latrines by the lake and market were the most preferred interventions, followed by open defecation fines. Latrines with many stanzas, working hand washing facilities, cleaning materials and easily accessed were the most reported preferences. Forming open defecation committees, Having bylaws and sensitizing community members on dangers of open defecation. Facilitators included hand washing facilities, well maintained, having a caretaker, and open defecation fines. Stakeholders emphasized community member sensitization as facilitators. Findings indicate preferences of communities who live around infected water bodies that are popular, affordable and sustainable for interventions that reduce human to snail transmission. These would improve on routine usage and coupled with enforcing open defecation would contain excreta from reaching water bodies reducing disease transmission.

8262

UNRAVELLING THE TRUE IMPACT OF SCHISTOSOMIASIS: REDEFINING THE WHO ELIMINATION AS A PUBLIC HEALTH PROBLEM TARGET

Derick Osakunor[1], Sergi Alonso[1], Sandra Jumbe[2], Poppy Lamberton[1]

[1]University of Glasgow, Glasgow, United Kingdom, [2]Queen Mary University of London, London, United Kingdom

Schistosomiasis remains a global health challenge, affecting millions worldwide. Current strategies for morbidity control and targets for elimination as a public health problem (EPHP) are based on the intensity of infection, the latter focusing on having <1% heavy-intensity infections. However, evidence suggests that associations between intensity and morbidity are not linear, and as the distribution of schistosomiasis morbidity moves towards more subtle rather than severe disease, correlations between intensity and morbidity become even more complex. Additionally, conventional diagnostic methods, relying on egg counts in urine or faeces, are inadequate in detecting low-intensity infections or predicting long-term morbidity. The delayed onset of symptoms further complicates early diagnosis and intervention. In this context, does the concept of EPHP and

the emphasis on egg counts have true meaning to those affected by the disease? We performed a comprehensive review to highlight the impact of schistosomiasis, extending beyond the established physical health consequences, as well as the pitfalls in current research to address the complexity of schistosomiasis and its far-reaching impacts. We provide a broader perspective to inform more effective public health interventions and policy frameworks and how to monitor them. We discuss how incorporating novel biomarkers and assessing the broader and "true" impact of schistosomiasis on overall quality of life, including physical, psychosocial, downstream economic and societal aspects, and spillover opportunity costs, can offer promising avenues for deeper insights into the lived experiences of those grappling with the disease. There is a need for a holistic approach to schistosomiasis control, one that embraces advanced diagnostics, and expands morbidity metrics. Only by addressing these challenges head-on can we ensure that interventions are not only effective but also equitable and responsive to the needs of individuals and communities, improving global health outcomes.

8263

MAPPING AND VALIDATION OF MICROSATELLITE MARKERS FOR *SCHISTOSOMA HAEMATOBIUM*: INSIGHTS FROM POOLED SAMPLES IN SENEGAL AND GABON

Kathleen Maria Kuesters[1], Souleymane Doucouré[2], Lady Charlène Kouna[3], Sandrine Lydie Oyegue-Liabagui[3], Jean-Bernard Lekana-Douki[3], Bruno Senghor[2], Cheikh Sokhna[2], Doudou Sow[4], Ronald E. Blanton[1]

[1]Tulane University, New Orleans, LA, United States, [2]Campus International IRD-UCAD de Hann, Dakar, Senegal, [3]Centre Interdisciplinaire de Recherches Médicales de Franceville, Franceville, Gabon, [4]Université Gaston Berger, Saint-Louis, Senegal

Understanding the population genetics of *Schistosoma haematobium* transmission within and between communities is crucial for identifying transmission agents, monitoring resistance and reinfections, and evaluating mass treatment effectiveness. Microsatellite markers have proven effective in estimating these measures. While 10 markers are sufficient, 15-20 markers are ideal for *S. mansoni*. Therefore, we aimed to create and validate a catalog of published microsatellite markers for *S. haematobium*. A literature review compiled published *S. haematobium* tri- and tetramer microsatellite markers, which were then mapped in silico to the karyotyped Shae.V2 *S. haematobium* reference genome using Geneious software. Marker characteristics, including chromosomal location, orientation, repeat region presence, uniqueness, and overlap, were recorded. Selected markers were validated using both a lab strain and pooled field samples from Senegal and Gabon, with fragment analysis employed to observe allele presence and proportions.Results: Of the 41 published markers, 10 are on the sex chromosome, rendering them unsuitable for some population genetic analyses, 7 have primer sites on different chromosomes, 3 enclose a complex repeat region which leads to more difficult interpretation than for simple repeats, 3 do not contain a repeat region, and 2 overlap with another 2 so we can only use one for each overlap. There are 16 published microsatellite markers suitable for population genetic analyses. Fragment analysis revealed 87 alleles across these markers in a laboratory strain. The presence and proportions of alleles were compared between a lab strain and 125 samples from human infections from Senegal and Gabon. Not all published microsatellite markers are useful for population genetic analyses of *S. haematobium*. Pooled samples demonstrate efficacy in estimating diversity and differentiation measures for *S. haematobium* infrapopulations, paralleling findings from previous studies on *S. mansoni* communities in Brazil. In silico analyses may change with subsequent versions of the genomic sequence.

8264

EFFECT OF *SCHISTOSOMA MANSONI* INFECTION ON GUT MICROBIOTA IN PRE-SCHOOL AGED CHILDREN IN ALBERTINE REGION, UGANDA.

Andrew Edielu[1], John Kelvin Mugerwa[1], Gloria Oduru[1], Jacent Nassuuna[1], Hannah W. Wu[2], Susannah Colt[2], Emily L. Webb[3], Jennifer F. Friedman[2], Patrice Akusa Mawa[1], Amaya L. Bustinduy[3], Martin Holland[3]

[1]MRC/UVRI & LSHTM Uganda Research Unit, Entebbe, Uganda, [2]Rhode Island Hospital, Center for International Health Research, Providence, RI, United States, [3]London School of Hygiene & Tropical Medicine, London, United Kingdom

Schistosomiasis is associated with changes in gut microbiota, a key player in egg transit as evidenced from experimental mouse models. Microbial diversity is widely considered a measure of gut health. We present comparison of microbial communities between *S. mansoni* infected (*Sm+)* and non-infected Pre-school aged children (PSAC) using 16S-amplicon sequencing. We further offer a clinical perspective on the observed effects of infection on gut microbiota community structure and function. PSAC aged 12–47 months were recruited from Albertine region of Western Uganda. *S.mansoni* infected samples were from the Praziquantel in Pre-schoolers (PIP) dose finding trial. Non-infected controls were recruited from the same region. Stool microbial DNA was extracted using QIAamp® Fast DNA Stool Mini Kit. A V4-16S-rRNA-amplicon library was generated by PCR amplification and sequenced using the Illumina MiSeq v3 Reagent kit. The data were analysed/visualised using box plots, Principal Coordinates Analysis, UniFrac and other functional parameters. A total of 114 participants were recruited with equal numbers between the groups. Median age was 30.0 months (IQR 27.0 – 34.4) and 42.4% were female. (Sm+) was associated with higher species relative abundance, increased alpha diversity – Shannon Index (p-value<0.001) and Simpson Index (p-value=0.002); increased beta diversity – Bray Curtis distances (p-value=0.001). In the Sm+ group, Oscillospirales, *Prevotella* and *Oscillospiraceae* were expanded while *Bacilli, Enterobacteriaceae, Lactobacillales*, Lachnospirales and *Lachnospiraceae* were reduced. PiCrust2 analysis inferred that pyruvate synthesis, starch metabolism and amino acid synthesis were downregulated. We report increased abundance and diversity of microbial communities in *Sm+* PSAC. While these alterations aid schistosome egg passage, the reduction in pyruvate, amino acids and starch metabolism are likely to have adverse effects on nutrition and cognition, both of which are clinical entities associated with schistosomiasis. Research exploring further clinical perspectives is required.

8265

CHARACTERIZATION AND FUNCTIONAL ANALYSIS OF THE MICROBIOTA OF THE INTERMEDIATE HOSTS OF SCHISTOSOMES

Peter McCann[1], Julianne Megaw[1], Cinzia Cantacessi[2], Karen Siu-Ting[1], Geoffrey Gobert[1]

[1]Queen's University Belfast, Belfast, United Kingdom, [2]University of Cambridge, Cambridge, United Kingdom

Aquatic snails act as the important intermediate hosts of schistosome helminths. Snail haemolymph has been shown by others to have a diverse microbiome, but the impact of a helminth infection has not yet been reported. Since the host microbiome has the potential to influence the transmission of the parasites we sought to investigate this area of host-parasite-bacteria interactions. Here, we characterised the bacterial species and abundance comprising the whole snail microbiota using 16S rRNA sequencing. Naïve, "infection failed" and patent snails were examined for *Biomphalaria glabrata* and *Schistosoma mansoni* parasites. The results of our study show that there are significant differences in beta diversity metrics based on infection status and highlighted key genera with linear discriminant analysis. Additionally, we carried out predicted functional analysis on these reads using PICRUSt2 to highlight key metabolic pathways between infected and uninfected snails. Based on these results

we further explored the *B. glabrata* microbiome using metagenomics. Snail homogenates containing microorganisms were added to microbiological growth media and gDNA extracted for shotgun sequencing. Our results present a new view on the unique interplay between the aquatic snail host, the schistosome infection and the bacteria present. From this information we a better understanding of mutualism between parasites and bacteria, as well as better understanding of the biology of the schistosome lifecycle during the aquatic transmissible stages.

8266

DNA METHYLATION PROFILES IN UROTHELIAL BLADDER CANCER TISSUES AND CHILDREN WITH SCHISTOSOMIASIS FROM EGGUA, OGUN STATE NIGERIA

Chiaka I. Anumudu[1], Cephas A. Akpabio[2], Rachel P. Ebuh[2], Oluwaseun E. Fatunla[3], Henrietta O. Awobode[4]

[1]Cellular Parasitology Programme Departement of Zoology, University of Ibadan, Ibadan, Nigeria, [2]University of Ibadan, Ibadan, Nigeria, [3]Department of Pathology, University College Hospital, Ibadan, Nigeria, [4]Department of Zoology, University of Ibadan, Ibadan, Nigeria

Squamous cell carcinoma, the most frequent kind of bladder cancer in regions where schistosomiasis is endemic, has been connected to chronic schistosomiasis. In this study, we set out to evaluate early promoter DNA methylation in a few genes linked to bladder cancer associated with schistosomiasis. In the Eggua Community of Ogun State, 159 school-age children provided urine samples, which were then analysed by microscopy to check for Schistosoma haematobium eggs. A subset of 34 (21.1%) urine samples positive for *S. haematobium*, was age and sex-matched with negative urine samples. These samples, together with 16 formalin-fixed paraffin-embedded bladder cancer tissues from University College Hospital Ibadan, were all processed using DNA isolation and bisulphite DNA conversion techniques. The methylation status of APC, RARβ2, and other target genes was assessed using quantitative methylation-specific PCR. Schistosomiasis positive samples had higher levels of methylation of the genes RARβ2 (67.7%), RASSF1A (38.2%), and TIMP3 (52.9%) compared to negative urine samples and bladder cancer tissues. In comparison to the matched controls, the positive urine samples had promoter DNA methylation that was 1.4, 13.3, 3.4, and 3.8 times greater in *APC, RARβ2, RASSF1A, and TIMP3*, respectively. Although there were no significant associations, the odds of promoter methylation were expected to increase with age group for *APC* (OR: 1.615) and *TIMP3* (OR: 2.000); sex for *TIMP3* (OR: 2.644); and haematuria for *RARβ2* (OR: 1.094), *RASSF1A* (OR: 1.143), and *TIMP3* (OR: 1.842). In patients with schistosomiasis, gene promoter DNA methylation was observed in tumour suppressor genes. Thus, children with active schistosomiasis may experience promoter DNA methylation. This might serve as an early non-invasive biomarker to detect and hint at the risk of developing schistosomiasis-associated bladder cancer later in life.

8267

DEEP HUMORAL PROFILING COUPLED WITH MACHINE LEARNING REVEALS NOVEL DIAGNOSTIC AND MORBIDITY BIOMARKERS FOR SCHISTOSOMIASIS PATHOPHYSIOLOGY

Pedro Marcal[1], Maurice R. Odiere[2], E. A. Kavere[3], R. Kiplimo[3], A. Eleveld[3], A. Mwaki[3], Sukwan Handali[4], William E. Secor[4], Aniruddh Sarkar[1]

[1]Georgia Institute of Technology, Atlanta, GA, United States, [2]Centre for Global Health Research, Kenya Medical Research Institute, Kisumu, Kenya, [3]Safe Water and AIDS Project, Kisumu, Kenya, [4]Centers for Disease Control and Prevention, Atlanta, GA, United States

Schistosomiasis continues to cause substantial morbidity in endemic regions. Current diagnostic methods relying on parasite egg detection or existing antibody (Ab) tests do not provide a way to detect disease-associated morbidity. Here we use a multiplexed 'Ab-omics' platform to obtain a comprehensive array of anti-helminth humoral profiles (isotypes, FcR-binding, and glycosylation). We apply machine learning to this high-dimensional data to reveal unique Ab signatures predictive of infection and morbidity. Serum from subjects (n=60, from Kenya), with and without abdominal ultrasound-detectable morbidity, previously screened for parasite eggs (Kato-Katz), were characterized with the Ab-omics workflow with multiple *S. mansoni* antigens (SEA, Sm25, Sm29, MEG, CD63, Calumenin) and other helminth and non-helminth antigens. Antigen-coated barcoded beads were incubated with serum and probed. Overall, a complex interplay with increases in both activating (IgG1) and inhibitory subclasses (IgG4) and pro-inflammatory (FcR2A, FcR3A) and anti-inflammatory (FcR2B, galactosylation) changes in antigen-specific Abs were seen in Egg+ vs Egg- sera. With a total of 144 measured features (12 Ab Fc probes x 12 antigens) from each patient, application of a LASSO-SVM machine learning model, revealed a minimal Ab signature capable of differentiating Egg+ from Egg- individuals accurately (AuC>0.9). This included both antigen-specific Ab titer (SEA-IgG) and Fc receptor binding (Sm29-FcR1, SEA-FcR2b). Within the Egg+ subset, interestingly reduced IgG1 but increased IgG4 was seen in those with morbidity. While neither Ab titer nor egg counts were predictive of ultrasound morbidity, the machine learning model revealed a distinct Ab signature, including IgG1 Abs against Sm29, and Fc receptor binding (Calumenin-FcR1, Sm25-FcR3b), that was able to distinguish those with and without morbidity (AuC>0.8). Our findings suggest that a purely Ab-based biomarker can achieve accurate diagnosis of both schistosome infection and associated morbidity in endemic areas.

8268

THE ROLE OF INTESTINAL MORBIDITY IN THE PATHOGENESIS OF ANEMIA AMONG YOUNG CHILDREN FROM LAKE ALBERT, UGANDA WITH *SCHISTOSOMA MANSONI* INFECTION

Susannah Colt[1], Andrew Edielu[2], Gloria Kakoba Ayebazibwe[3], Rachael Nakyesige[3], Hannah Wu[1], Kanika Men[1], Elise Kurtis[1], Patrice Mawa[3], Emily Webb[2], Amaya Bustinduy[2], Jennifer Friedman[1]

[1]Center for International Health Research, RI Hospital and Alpert Medical School of Brown University, Providence, RI, United States, [2]London School of Hygiene and Tropical Medicine, London, United Kingdom, [3]Medical Research Council-London School of Hygiene & Tropical Medicine Research Unit, Entebbe, Uganda

There is a significant global burden of disease due to anemia among individuals living in low- and middle-income countries. Schistosomiasis has been shown to cause both iron deficiency anemia (IDA) and non-iron anemia (NIDA), the latter largely due to anemia of inflammation. Though the presence of worms and eggs in the vasculature and tissues are thought to drive inflammation, it is possible that disruptions in the gut wall as eggs pass from the sterile bloodstream to the intestines also contribute, specifically, through microbial translocation (MT) as microbial products enter the blood stream culminating in inflammation. In this study, 345 Ugandan children aged 12-48 months infected with egg patent Schistosoma *mansoni* were recruited from villages along Lake Albert, Uganda. Infection intensity was determined by Kato Katz. WHO age adjusted cutoffs for hemoglobin (< 11 g/dL) were used to determine presence of anemia. Among anemic children, serum ferritin levels were used to classify children as having IDA (≤ 30 ng/mL) or NIDA (> 30 ng/mL). Biomarkers capturing gut wall integrity/MT [occult blood loss and serum endotoxin core antibody (EndoCAb)], epithelial damage [serum intestinal fatty acid binding protein (I-FABP)], gut inflammation (fecal calprotectin), and epithelial permeability [fecal alpha-1 antitrypsin (AAT)] were assessed. We used multivariable regression models to assess the relationship between markers of intestinal morbidity and anemia type. Higher schistosomiasis intensity was associated with increased risk of both IDA (OR 1.36, 95% CI 1.12-1.65, p=0.002) and NIDA (OR 1.23, 95% CI 1.03-1.46, p=0.02) compared to no anemia after adjusting for confounders. Calprotectin and AAT were associated with increased risk of IDA (OR 1.36, 95% CI 1.02-1.81, p = 0.03; OR 1.25, 95% CI 0.99-1.58, p = 0.06, respectively). Further, both AAT and calprotectin were associated with occult blood loss, suggesting intestinal morbidity culminates in IDA due to occult blood loss in the stool.

8269

SCHISTOSOMIASIS JAPONICUM INFECTION IN THE PHILIPPINES: LOW PREVALENCE AMONG CHILDREN AGED 1-4 YEARS AND CORRELATION BETWEEN HELMINTH BURDEN AND INTESTINE INFLAMMATION

Ralph Aniceto[1], Jennifer Friedman[2], Hannah Wu[3], Mario Antonio Jiz[1], Veronica Tallo[1], Marianette Inobaya[1], Marianne Joy Sagliba[1], Amabelle Joy Moreno[1]

[1]Research Institute for Tropical Medicine, Muntinlupa, Philippines, [2]Browne Universiy, Providence, RI, United States, [3]Browne University, Providence, RI, United States

Schistosomiasis remains a public health problem in endemic areas in the Philippines. Infection with *Schistosoma japonicum* in children is associated with poor nutritional status. Preventive chemotherapy, through annual mass drug administration (MDA) of praziquantel has been conducted in endemic provinces among 5-65 years old. There is limited data on clinical trials on praziquantel for children under 5 years old. This age window coincides with the "praziquantel treatment gap," which highlights the fact that this age group remains excluded from preventive chemotherapy campaigns, which represent the primary approach to reducing infections in endemic regions globally. We screened 1081 participants in 64 barangays. 975 participants submitted three stool samples for Kato-Katz and 17 (1.74%) turned positive for *S. japonicum* which was eventually recruited for treatment and follow up. Mean age was 2.29 years and 70% (12) were males. Co-infection with *Ascaris lumbricoides* was found in five participants and three participants had *Trichuris trichiura*. Stool calprotectin test was used to check for inflammation in the gastrointestinal tract, elevated calprotectin concentration (> 80 ug/g) was at 64% (11). All 17 participants tested negative for fecal occult blood test. Elevated white blood cell count (WBC), in the absence of other concomitant infection was found in 64% (11) of the participants. One participant with schistosomiasis, ascaris and trichuris coinfection had a hemoglobin of 9 g/dL. Our study has several limitations including the sample size, light intensity of infection, limited inflammatory markers used among others. Despite the considerable size of our study population and light intensity of infection we observed an elevated calprotectin and WBC in our study participants. Follow up of participants is being done to determine whether treatment of schistosomiasis and STH infection would result in significant changes in the markers and to monitor for possible reinfection. Future work to investigate schistosomiasis burden and treatment in this age group would significantly decrease the morbidity and end organ complications.

8270

SCHISTOSOMA MANSONI INFECTION IN THE SNAIL *BIOMPHALARIA GLABRATA*, IS ASSOCIATED WITH EXPRESSION PERTURBATION OF CARBONIC ANHYDRASE, THE HIV TRANS-ACTIVATOR OF TRANSCRIPTION, AND TELOMERASE

Gabriela Lewis, Simone Parn, Matty Knight

University of the District of Columbia, Washington, DC, United States

Telomerase is a ribonucleoprotein complex that maintains telomeres at the proximal ends of chromosomes, adding repeats to the 3' chromosome end. Human telomerase (hTERT) regulation is tightly linked to the cell cycle and cell differentiation states governing both malignancy and senescence. The HIV Trans-Activator of Transcription (HIV-TAT) is used by HIV to upregulate viral transcription, thus increasing viral transmission between cells. TAT proteins also alter cell membrane selective permeability by rearranging phospholipid bonds; these altered cells have ultimately shown resistance to apoptosis and necrosis. Carbonic anhydrases (CA's) govern intracellular conversions of carbon dioxide into bicarbonate ions and protons. CA's combine with proton transporters to move ions across the cell membrane to maintain homeostatic intracellular pH. In cancer cells, CA's favor proton-expelling activity, creating an acidic extracellular environment which promotes cancer cell growth and tumor proliferation. Cancer development resembles parasitic disease as it depends on the host's biochemical and molecular pathways to progress. The snail/schistosome relationship provides a model to examine the regulation of cancer-associated genes, such as the gastropod homologs of hTERT, CA, and TAT. To test this hypothesis in relation to the development of *Schistosoma mansoni* in *Biomphalaria glabrata*, we identified *B. glabrata's* hTERT, CA, and TAT homologs and studied their expression by qPCR. A temporal-dependent regulation of CA, TAT, and snail TERT during the progression of *S. mansoni* infection was observed; these transcripts were upregulated in *B. glabrata* 30 minutes post-infection. Treating susceptible snails with anti-telomerase drugs BPPA and BIBR before infection blocked parasite cercariae shedding in the drug-treated snails, and treating susceptible snails with sodium salicylate before infection resulted in CA downregulation and prevented cercariae shedding. These findings indicate that as in malignancy, regulation of TERT, CA, and TAT may be critical for the intra-molluscan stage of development in the *B. glabrata* snail host.

8271

TROGOCYTOSIS: A POTENT MECHANISM FOR HOST RESISTANCE TO SCHISTOSOMIASIS

佳 沈

Sun Yat-Sen University, Guangzhou, China

Host specificity is the outcome of long-term coevolution between pathogens and their hosts, and remains an area of paramount importance extensively studied within the field of disease ecology, yet many mechanisms are still enigmatic. *Schistosoma japonicum* exhibits a typical host specificity, being susceptible to humans and most mammals (including mice), while *Microtus fortis* exhibits natural anti-schistosome characteristics. Thus, comparison of schistosome infection in *M. fortis* with the infection in laboratory mice provides a unique perspective for exploring and understanding host specificity. In this study, we found that a large number of immune cells adhered to the surface of schistosomes in *M. fortis*, a phenomenon that was not observed in mice. By isolating immune cells attached to the parasite surface for single-cell RNA-sequencing, most of these cells were identified as macrophages. We further confirmed that the *M. fortis* macrophages kill schistosomes through a novel pathway known as "trogocytosis". This is the first report of host immune cells using "trogocytosis" to kill multicellular pathogens. Furthermore, we demonstrated that the adherence of *M. fortis* macrophages to the surface of the schistosomes and their subsequent trogocytosis are mediated by complement C3 and complement receptor 3 (CR3). We also clarified that the activation of the Ca^{2+}/NFAT signaling is a key regulator enabling macrophages to perform "trogocytosis". These findings not only elucidate a novel anti-schistosome mechanism in *M. fortis* but also provide a better understanding of host-parasite interactions, host specificity and the potential generation of novel strategies for schistosomiasis control.

8272

THE INTERACTION OF HOP, STRESS PROTEINS, AND PIWI IN THE MECHANISM OF CANALIZATION UNDERSCORES THE SUSCEPTIBILITY OF *BIOMPHALARIA GLABRATA* TO *SCHISTOSOMA MANSONI* INFECTION

Oumsalama Elhelu[1], Matty Knight[2], Clarence Lee[1]

[1]Howard University, Washington, DC, United States, [2]University of the District of Columbia, Washington, DC, United States

Schistosoma mansoni is a parasitic flatworm that is the causative agent for the chronic debilitating disease schistosomiasis. *Biomphalaria glabrata*, is the obligatory intermediate host of this parasite, enabling the larval forms to develop into infectious cercariae. With praziquantel being the single drug for schistosomiasis, which is only effective in killing adult parasites but not any larval stages. There is an impetus towards developing new remedies against schistosomiasis. To develop new intervention tools to eradicate schistosomiasis, emphasis has been placed on interrupting the development of the parasite in the snail. Thus far, results have shown that the early induction of stress, manifested by the induction of heat shock proteins (HSPs), such as Hsp70 and Hsp90, is a prerequisite step in juvenile

snail susceptibility to parasite infection. To determine the involvement of HSPs in the snail-schistosome interaction, we hypothesized that stress inhibitor drugs, such as curcumin and PU-H71, affecting Hsp70 and Hsp90, respectively, would affect the outcome of infection in susceptible snails. Results show that treatment of susceptible snails with these drugs inhibited parasite infection (no cercariae shedding) after 6-weeks post-exposure in drug-treated snails. To determine the effect of these drugs in inhibiting *S. mansoni* infection in the snail host, we examined the regulation of the specific transcripts encoding Hsp70, Hsp90, HOP, and PIWI in drug-treated versus non-treated infected snails. In addition, we examined whether the mechanism of canalization, involving the expression of HOP concurrent with the expression of the stress encoding transcripts underscores *B. glabrata* susceptibility to *S. mansoni* infection. By using gene silencing studies with siRNA corresponding to HOP, results showed that suppressing the expression of HOP prevented schistosome infection in the snail host. This data provides evidence that the interaction of HOP with Hsp70, Hsp90, and PIWI maintains cell homeostasis by a mechanism known as canalization in the snail-schistosome relationship.

8273

COMMUNITY AND INDIVIDUAL PREFERENCES FOR A NEW WATER INFRASTRUCTURE FOR NON-DRINKING ACTIVITIES IN A SCHISTOSOMIASIS ENDEMIC AREA

Raheema Chunara[1], Lazaaro Mujumbusi[2], Edith Nalwadda[3], Moses Arinaitwe[4], Lucy Pickering[1], Michael Templeton[5], Poppy Lamberton[1]

[1]University of Glasgow, Glasgow, United Kingdom, [2]Medical Research Council/Uganda Virus Research Institute & London School of Hygiene and Tropical Medicine Uganda Research Unit Uganda, Entebbe, Uganda, [3]Medical Research Council / Uganda Virus Research Institute | MRC/UVRI, Entebbe, Uganda, [4]Ministry of Health, Kampala, Uganda, [5]Faculty of Engineering, Department of Civil and Environmental Engineering, Imperial College London, London, United Kingdom

Schistosomiasis is a water-borne parasitic disease affecting 240 million people worldwide. Schistosomes sexually reproduce in humans releasing eggs through urine/faeces which infect freshwater snails, where they reproduce asexually releasing hundreds of cercariae/day. These cercariae burrow directly into humans on contact with contaminated water. Mass drug administration has been the WHO recommended strategy for nearly 20 years, and whilst successful in some areas, there are hotspots across Africa. Additional non-pharmaceutical interventions are needed to meet the WHO goal of eliminating schistosomiasis as a public health problem by 2030 such as improved access to safe water, sanitation and hygiene (WaSH). Non-governmental organisations (NGOs) play a vital role in implementing WaSH infrastructure in low-income countries, however 30-50% of WaSH projects implemented cease to be used after 2 – 5 years. To increase access, both uptake *and* sustainability of WaSH infrastructure needs to be considered. Qualitative research can provide valuable insights into community needs and help co-design solutions that effectively address these needs. In February 2023, data were collected from community members in Bugoto, a high-endemicity community in Uganda, through in-depth interviews (IDIs) (n=21) and focus group discussions (FGDs) (n=4). Thematic analysis using NVIVO14 software was employed to code the data into themes, followed by iterative characterization to analyse selected themes. Insights gained from this research shed light on non-drinking water usage patterns, as well as facilitators and barriers to accessing various water sources within the community. Furthermore, preferences for future water infrastructure for non-drinking purposes were identified resulting in five major themes. These findings, combined with observational data gathered during the researcher's time in Bugoto, will inform the design of future interventions tailored to the community's preferences and requirements.

8274

ASSOCIATIONS BETWEEN INDICATORS OF WATER, SANITATION AND HYGIENE (WASH) AND MALARIA RISK: A STUDY OF URBAN SETTLEMENTS IN NIGERIA

Gift Wilfred Enang[1], Ifeoma D. Ozodiegwu[1], Bamgboye Eniola[1], Laurette Mhlanga[1], Yusuf Jamiu[1], Ikeoluwapo Ajayi[2]

[1]Loyola University Chicago, Maywood, IL, United States, [2]University of Ibadan, Ibadan, Nigeria

While global efforts have made strides in malaria control, Nigeria's rapid urban growth, along with other challenges of urbanization, often outpaces infrastructure development. This leads to inadequate access to clean water, sanitation facilities, and proper hygiene practices, thereby increasing the risk of infectious diseases like malaria. Consequently, there is a pressing need for further investigation into the relationship between Water, Sanitation, and Hygiene (WASH) practices and malaria infection in urban settlements. A cross-sectional survey conducted in Ibadan metropolis during the 2023 wet season investigated the impact of WASH practices on malaria across formal, informal, and slum settlements. Water and sanitation variables were categorized into improved (e.g., piped water sources, flush toilets) and unimproved (e.g., rainwater, pit latrines without slabs). Hygiene practices were derived using Principal Component Analysis (PCA) based on environmental factors, identifying ineffective hygiene practices below the median PCA. Malaria presence was assessed using rapid diagnostic tests, adjusting for age, gender, and insecticide-treated net (ITN) presence through multiple linear regression. Of 7123 individuals tested, weighted malaria rates were 3.45%, 3.96%, and 12.16% in formal, informal, and slum areas, respectively. Poor WASH practices were more prevalent in slums (87%) than formal (63%) and informal (79%) settlements. Across all areas, unimproved sanitation and poor hygiene correlated with higher malaria risk (unimproved sanitation facilities: aOR 1.74, 95% CI 1.30–2.32, $P < 0.0002$; ineffective hygiene: aOR 1.41, 95% CI 1.12–1.78, $P < 0.004$). Due to the correlation between WASH practices and malaria risk observed in this study, suggested interventions to boost urban WASH infrastructure include upgrading water sources, enhancing sanitation facilities, and promoting hygiene. Strategies may include building or renovating sanitation facilities, installing piped water systems, and distributing water purification tablets or hygiene kits, thereby reducing malaria and enhancing public health.

8275

ASSOCIATIONS BETWEEN MICRONUTRIENT STATUS, HORMONES, AND IMMUNE STATUS DURING PREGNANCY AND CHILD GROWTH IN RURAL BANGLADESH

Belinda Chen[1], Chih-Hsien Lin[1], Andrew Mertens[1], Sophia T. Tan[2], Farheen Jamshed[1], Diego Figueroa[1], Caitlin Hemlock[3], Zachary Butzin-Dozier[1], Lia C. H. Fernald[1], Christine P. Stewart[4], Alan E. Hubbard[1], Md. Ziaur Rahman[5], Shahjahan Ali[6], Benjamin F. Arnold[7], Firdaus S. Dhabhar[8], Douglas Granger[9], Mahbubur Rahman[10], Stephen P. Luby[2], Jack Colford[1], Audrie Lin[11]

[1]UC Berkeley School of Public Health, Berkeley, CA, United States, [2]Division of Infectious Diseases and Geographic Medicine, Stanford University, Stanford, CA, United States, [3]Department of Environmental and Occupational Health Sciences, University of Washington, Seattle, WA, United States, [4]University of California Davis, Institute for Global Nutrition, Davis, CA, United States, [5]University of California, Santa Cruz, Department of Microbiology and Environmental Toxicology, Santa Cruz, CA, United States, [6]Department of Epidemiology, Colorado School of Public Health, University of Colorado,, Denver, CO, United States, [7]Francis I. Proctor Foundation, University of California San Francisco, San Francisco, CA, United States, [8]Department of Psychiatry & Behavioral Sciences, Department of Microbiology and Immunology, Sylvester Comprehensive Cancer Center, Miller School of Medicine, University of Miami, Miami, FL, United States, [9]Institute for Interdisciplinary Salivary Bioscience Research, University of California, Irvine, Irvine, CA, United States, [10]Environmental Health and WASH, Health System and Population Studies Division,

International Centre for Diarrhoeal Disease Research, Dhaka, Bangladesh, [11]Department of Environmental and Occupational Health Sciences, University of Washington, Santa Cruz, CA, United States

Poor growth in early childhood is associated with increased mortality, impaired cognitive development, and reduced adult economic productivity, which may result in higher risks of social immobility and intergenerational poverty. This observational study used data collected from the WASH Benefits trial in rural Bangladesh to examine associations between maternal hormones (CRP, AGP, cytokine-sum-score), immune status (plasma cortisol, estriol), and micronutrient status (Vitamin D, ferritin, sTfR, RBP) during the first and second trimesters of pregnancy and subsequent measures of child growth. Length-for-age z-score (LAZ) weight-for-length z-score (WLZ), and insulin-like growth factor 1 (IGF-1) at 3, 14, and 28 months were measured as the primary outcomes. All outcomes were adjusted for confounding variables, and the p-values were adjusted using the Benjamini-Hochberg procedure. We used generalized additive models, adjusted for covariates, and reported the mean difference in outcomes between the 25th and 75th percentile of the exposure distribution. In this substudy (n=575), maternal prenatal α1-acid glycoprotein (AGP), the cytokine sum score, retinol binding protein (RBP), and estriol were associated with child growth. AGP was inversely associated with WLZ at age 14 months. The cytokine sum score was inversely associated with WLZ at 28 months. RBP was positively associated with WLZ at 3 months and 14 months. Estriol was positively associated with LAZ and IGF-1 at 14 months. Identifying early interventions aimed at optimizing the *in-utero* milieu may be a helpful strategy for promotion of healthy growth trajectories throughout childhood.

8276

WEATHER AND SEASON PREDICTORS OF INFANT DIARRHEAL ILLNESS AND HOUSEHOLD STORED WATER CONTAMINATION IN CLIMATE-VULNERABLE, URBAN, COASTAL MOZAMBIQUE

Rebecca Kann

University of Washington, Seattle, WA, United States

Improvements in water, sanitation, and hygiene (WASH) have the potential to reduce the global burden of diarrhea, a leading cause of mortality for under-5 children. However, extreme weather events associated with climate change may compromise the effectiveness of WASH infrastructure to reduce the risk of diarrhea. We quantified associations between weather conditions, drinking water quality, and infant diarrhea in a climate-vulnerable low-income urban setting. We leveraged the data from a cluster-matched cohort study in Beira, Mozambique, that followed 642 mother-child dyads from pregnancy through 12 months old. We collected information on demographics and health using household surveys, tested for bacterial contamination in household stored water, and obtained weather data from a land surface station. We used generalized linear mixed-effects models to evaluate associations between (1) weather (i.e. season [rainy vs. dry], heavy rainfall events [presence vs. absence of 95th percentile rain event], ambient temperature [continuous (°C)], and flooding [presence vs. absence of flooding around household (reported)]) and stored water quality, (2) weather and infant diarrhea, and (3) stored water quality and infant diarrhea. We found that heavy rainfall (aOR: 1.66; 95% CI: [1.09, 2.51]), temperature (β: 1.40 [1.27,1.55]), and season (aOR: 1.95 [1.58,2.40]) were all associated with higher odds of stored water contamination. Rainy season was associated with a 32% higher period prevalence of infant diarrhea (aOR: 1.32 [1.01,1.73]), and there was a 10% increase in infant diarrhea per 1 °C of ambient temperature. We did not find an association between stored water quality and infant diarrhea. Our findings suggest associations of season and extreme weather on stored water quality and infant diarrhea, highlighting the importance of integrating climate resiliency into WASH strategies for reducing the burden of diarrhea, particularly in low-income urban settings.

8277

PROCESS EVALUATION FOR THE DELIVERY OF A WATER, SANITATION AND HYGIENE MOBILE HEALTH PROGRAM IN THE DEMOCRATIC REPUBLIC OF THE CONGO: RANDOMIZED CONTROLLED TRIAL OF THE PREVENTIVE INTERVENTION FOR CHOLERA FOR 7 DAYS (PICHA7) PROGRAM

Presence Sanvura[1], Kelly Endres[2], Jean-Claude Rusanga[1], Lucien Bisimwa[1], Jamie Perin[2], Camille Williams[2], Cirhuza Cikomola[1], Justin Bengehya[3], Ghislain Maheshe[1], Alain Mwishingo[1], Christine Marie George[2]

[1]Catholic University of Bukavu, Bukavu, Congo, Democratic Republic of the, [2]Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, United States, [3]Bureau de l'Information Sanitaire, Surveillance Epidémiologique et Recherche Scientifique, Division Provinciale de la Santé Sud Kivu, Bukavu, Congo, Democratic Republic of the

In the Democratic Republic of the Congo (DRC), there over 85 million diarrhea episodes annually. Effective and scalable water, sanitation, and hygiene (WASH) interventions are needed to reduce diarrheal diseases. Mobile health (mHealth) reminders of public health information has been shown to reduce disease morbidity and increase health-protective behaviors. Given the high household mobile phone coverage in DRC (>80%), WASH mHealth programs present a promising approach to improve WASH behaviors. The objective of the Preventive-Intervention-for-Cholera-for-7-days (PICHA7) study was to develop evidence-based WASH interventions to reduce severe diarrheal diseases in DRC using a combination of mHealth and in-person visits. The PICHA7 mHealth program delivered weekly voice, text, and interactive voice response (IVR) quiz messages to diarrhea patient households promoting handwashing with soap, water treatment, and safe water storage over a 12-month period. The randomized controlled trial (RCT) of the PICHA7 program was in urban eastern DRC from November 2021 to November 2023. The objective of this study was to assess the implementation of the PICHA7 mHealth program in delivering mHealth messages during this RCT. During the PICHA7 RCT, 1196 participants received weekly text, voice and IVR quiz messages from the PICHA7 mHealth program over the 12-month program. Outcome indicators included unique text, voice, and IVR messages received (fidelity) and % of unique messages fully listened to (dose). Unique text messages were received by 84% of program households, and 85% of unique voice and 77% of unique IVR messages answered were fully listened by at least one household member. Less than 2% of mobile messages failed. These findings show high fidelity and dose of mobile messages delivered for the PICHA7 mHealth program. This demonstrates the feasibility of delivering the PICHA7 mHealth program in eastern DRC and provides important insights for delivering WASH mHealth programing in low- and middle-income countries globally.

8278

SYSTEMATIC REVIEW OF THE ASSOCIATION BETWEEN COLIFORM BACTERIA IN DRINKING WATER AND DIARRHEA

Amber Jacobsen[1], Sara dos Santos Almeida[2], Peter Jensen[2]

[1]University of South Carolina School of Medicine Greenville, Greenville, SC, United States, [2]University of Copenhagen, Copenhagen, Denmark

In this systematic review, we challenge whether *Escherichia coli* (E. coli) and fecal coliforms in water predict disease outcomes. Our objective was to review existing observational studies and assess the impact of water quality on various health indicators, including diarrhea, nutritional status, and gastrointestinal diseases in low- and middle-income countries. We searched using PRISMA guidelines on PubMed and web of science to identify the relevant articles using search criteria that identified studies that included water quality, health outcomes, and coliforms. We included peer-reviewed observational studies in low and middle-income countries that explored the relationship between fecal coliforms and/or E. coli in water and health outcomes. 18 studies were used for data extraction. Furthermore,

we included the relevant articles from a previous systematic review. Based on our inclusion criteria, an additional 11 studies were included from Gruber et al., totaling 29 studies included in our systematic review. The final search was performed on June 22nd, 2023. Of the thirty-one studies, only six had significant results (20.7% of all), one studied fecal coliforms, and five studied E.coli. Even within the studies with significant results, some did not control for confounding, others only sampled water at the source in the public domain and not in the domestic or personal domain, the time between sampling and diarrhea cases was weeks (up to 12), and seasonality was not considered. These results undermine the association between E.coli and fecal coliforms as proxies for health outcomes related to water quality in observational studies. Based on our systematic review of available literature, despite tradition, there is limited evidence to support using E.coli and fecal coliforms as proxy measures for human health outcomes. Based on this systematic review, future research should focus on the effects of water quantity, animal proximity, food, and water storage practices to establish a more concrete link to human health outcomes.

8279

UNIVERSITY STUDENT AWARENESS OF INTESTINAL PARASITES AND PREVENTIVE BEHAVIOR IN EASTERN SAUDI ARABIA

Sarah A. Alshuhaib[1], Maryam M. Alnasser[1], Mehwish Hussain[1], **Ayman A. El-Badry**[2]

[1]College of Public Health, Imam Abdulrahman Bin Faisal University, Dammam, Saudi Arabia, [2]Cairo University Kasr Al-Ainy Faculty of Medicine, Egypt & Imam Abdulrahman Bin Faisal University, Saudi Arabia, Cairo, Egypt - Dammam, Saudi Arabia -, Egypt

Good awareness and preventive behaviors among populations mitigate the prevalence of intestinal parasitic infection (IPI). A cross-sectional study was conducted from January to May 2023 to assess and compare the awareness and preventive behaviors towards IPIs among 1,829 students from health (562) and non-health (1,267) colleges, at Imam Abdulrahman bin Faisal University. Data on student characteristics were collected through questionnaires. Nearly half (48.9%) of the students delineated good awareness about IPIs, students from health faculty had higher awareness than non-health faculty (P<0.001). Female students were more aware of intestinal parasites than males (P<0.001). There was no significant association between student academic year and parent's education level, on student awareness of IPIs and preventive behavior. The majority of the students possessed poor intestinal parasite preventive behavior. Interestingly, students from non-health faculty had better intestinal parasite preventive behavior than students from health faculty (P<0.05), and male students had better prevention behavior than female students (P<0.05). Strategies and curricula must be developed to reinforce preventive behavior and promote awareness of IPIs in university students.

8280

INFLUENCE OF MATERNAL AND CHILD FUT2 SECRETOR STATUS ON GROWTH AND ON THE EFFICACY OF WATER, SANITATION, HANDWASHING, AND NUTRITION INTERVENTIONS ON ENVIRONMENTAL ENTERIC DYSFUNCTION IN RURAL BANGLADESH

Ronit Gupta[1], Andrew N. Mertens[2], Akram Ullah[3], Tahmeed Ahmed[4], Rashidul Haque[3], Mamun Kabir[3], Mondar M. M. Ahmed[3], Mustafa Mahfuz[4], Shahjahan Ali[5], Mohammad Alauddin[6], Md. Ziaur Rahman[7], Jessica Grembi[8], Abul K. Shoab[9], Mahbubur Rahman[9], Leanne Unicomb[9], Benjamin F. Arnold[10], Syeda L. Famida[3], Salma Akther[3], Md. Saheen Hossen[3], Palash Mutsuddi[3], Alan E. Hubbard[11], Christine P. Stewart[12], John M. Colford Jr.[11], Stephen P. Luby[8], Audrie Lin[7]

[1]Department of Biostatistics, T.H. Chan School of Public Health, Harvard University, Boston, MA, United States, [2]Division of Epidemiology, School of Public Health, University of California, Berkeley, Berkeley, CA, United States, [3]Infectious Diseases Division, International Centre for Diarrhoeal Disease Research, Bangladesh, Dhaka, Bangladesh, [4]Nutrition Research Division, International Centre for Diarrhoeal Disease Research, Bangladesh, Dhaka, Bangladesh, [5]Department of Epidemiology, Colorado School of Public Health, University of Colorado, Denver, CO, United States, [6]Department of Chemistry, Wagner College, Staten Island, NY, United States, [7]Department of Microbiology and Environmental Toxicology, University of California, Santa Cruz, Santa Cruz, CA, United States, [8]Division of Infectious Diseases and Geographic Medicine, Stanford University, Stanford, CA, United States, [9]Health System and Population Studies Division, International Centre for Diarrhoeal Disease Research, Bangladesh, Dhaka, Bangladesh, [10]Francis I. Proctor Foundation, University of California, San Francisco, San Francisco, CA, United States, [11]Division of Epidemiology and Biostatistics, School of Public Health, University of California, Berkeley, Berkeley, CA, United States, [12]Department of Nutrition, University of California, Davis, Davis, CA, United States

The fucosyltransferase-2 (FUT2) gene indicates blood group secretor status, which can affect risk of infection, possibly affecting child growth. We investigated whether maternal and child secretor status are risk factors for poor child growth and whether they are effect modifiers of interventions on child environmental enteric dysfunction. In the WASH Benefits trial in rural Bangladesh, 720 clusters of 5551 pregnant women were randomized to 7 arms. We assessed 4 arms: control; combined water, sanitation, and handwashing intervention (WSH); nutrition intervention (N); and combined N+WSH. Across 1499 children, 68.2% were secretors (S), 21.5% non-secretors (NS), and 10.3% inconclusive; across 1379 mothers, 64.8% were S, 22.3% NS, and 12.9% inconclusive. Measurements were taken at ages 3, 14, and 28 months, analyzed using generalized linear models adjusted for baseline confounders. Child NS status was associated with 0.10 SD lower length-for-age Z score (-0.15, -0.05), 15% higher risk of stunting (1.06, 1.24), and 25% higher risk of severe stunting (1.02, 1.53). NS status was associated with 0.06 SD lower weight-for-age Z score (WAZ) (-0.11, -0.01) and 0.09 SD lower head circumference Z score (-0.15, -0.04). By measurement round, maternal NS status was associated with 0.13 SD higher WAZ at 3 months (0.05, 0.20). Child and maternal NS status were both associated with 0.10 log ng/ml lower child myeloperoxidase [(-0.14, -0.05), (-0.15, -0.06), respectively]. Maternal S status was a significant modifier of the effect of WSH on child alpha-1 antitrypsin at 14 months (p=0.03) and the effects of WSH and N on child myeloperoxidase at 28 months (p=0.01, p=0.03, respectively). Child S status was a significant effect modifier of WSH on myeloperoxidase at 14 months (p=0.02). Overall, we report mixed associations: maternal NS status was associated with lower child gut permeability and inflammation and child NS was associated with lower gut inflammation, but child S had improved growth outcomes. FUT2 secretor status was not a significant effect modifier of interventions on most outcomes, but future studies using targeted genomics may find new associations.

8281

USE OF SOLAR DISINFECTION WITH ALUMINUM TO IMPROVE WATER QUALITY IN RURAL AREAS OF THE NORTHERN ANDES OF PERU

Jesús Rascón[1], Fátima Burgos[1], Lily del Pilar Juarez-Contreras[2], Oscar Gamarra-Torres[2]

[1]Instituto de Investigación de Enfermedades Tropicales, Universidad Nacional Toribio Rodríguez de Mendoza de Amazonas (UNTRM), Chachapoyas, Peru, [2]Instituto de Investigación para el Desarrollo Sustentable de Ceja de Selva (INDES-CES), Universidad Nacional Toribio Rodríguez de Mendoza de Amazonas (UNTRM), Chachapoyas, Peru

The Calo River basin, situated in the Amazon region within the montane forests of the Andes in Northeastern Peru, serves as a crucial hub for livestock activities. Extensive cattle ranching constitutes the primary economic activity in this region, with cattle having unrestricted access to water sources for drinking. However, this unregulated leads to significant environmental and health issues, impacting environmental sustainability and public health. The main objective of this study was to assess the efficacy of employing solar water disinfection (SODIS) with commercial aluminum to enhance water quality sustainably while evaluating its suitability for use by livestock and the general population. The most important parameters for water quality were established and variations of these

parameters were analyzed based on the type of SODIS and season. Simultaneously, the study compared these parameters against national and international standards for water quality targeting animal and human consumption. It was determined that parameters such as fecal coliforms, Escherichia coli, turbidity, ammonium, iron, calcium, lead, and arsenic are essential for the study. By applying Principal Component Analysis (PCA), it was demonstrated that all models of the SODIS system incorporating photocatalysis are viable options for treating water intended for animal consumption which was particularly evident during the dry season, spanning from June to November. Conversely, regarding water for human consumption, although the levels of contaminants were reduced, certain parameters such as fecal coliforms, E. coli, lead, and arsenic remained above regulatory limits. Therefore, it is recommended to employ SODIS with commercial aluminum as a complement to other treatment systems, such as multiple filtration systems. Finally, the implemented systems have proven to be effective in producing water suitable for animal consumption after undergoing one month of treatment.

8282

SEVEN YEARS OF EXPOSURE TO A HIGHLY FECAL CONTAMINATED ENVIRONMENT: A STUDY IN 24 INFORMAL SETTLEMENTS IN THE ASIA-PACIFIC REGION

Yussi Marlene Palacios Delgado[1], Maghfira Saidfuddaolah[2], Vina Waqa[3], S. Fiona Barker[1], Rebekah Henry[1], Brandon Winfrey[1], Karin Leder[1]

[1]Monash University, Melbourne, Australia, [2]Hasanuddin University, Makassar, Indonesia, [3]Fiji National University, Suva, Fiji

People living in urban informal settlements of the Global South are at high risk of contractingdiarrhoeal disease, which causes 500,000 deaths among children every year. Globally, a billion peoplelive in informal settlements, where they are underserved by critical infrastructure including water andsanitation services – giving rise to environmental contamination. Determining the scale of faecalcontamination in water sources and soil that residents interact with is crucial for understandingimpacts on their health and wellbeing. Since 2018, the Revitalising Informal Settlements and theirEnvironment (RISE) program has collaborated with 24 informal settlements in Fiji and Indonesia toassess the impacts of a nature-based intervention for managing wastewater on human exposure tofaecal contamination. The intervention, a treatment train consisting of pressure tanks and constructedwetlands, aims to reduce environmental faecal contamination in these communities. Approximately1200 water samples and 1100 soil samples have been collected longitudinally between 2018 and 2024,prior to completion of the intervention. We found that more than 90% of recreational water samplesshowed *E. coli* levels to be above good quality inland water guidelines, indicating persistent exposureto human and/or animal faecal waste over the 7-year pre-intervention period. Well samples, which areused for washing, bathing, or drinking, failed to meet WHO drinking water guidelines, also implyingpotential exposure to faecal pathogens. Soil samples collected from the local environment also showed*E. coli* contamination, reaching 10^4 MPN/g (dry weight). Our study provides novel insights into the scaleof contamination in a wide variety of water sources and soil, expanding our understanding of humanexposure to faecal contamination in informal settlements in Asia-Pacific.

8283

MATERNAL ESTRIOL DURING EARLY GESTATION IS ASSOCIATED WITH CHILD DEVELOPMENT IN RURAL BANGLADESH

Nicol Hernandez, Arlene Tan

WASH Benefit Trials, Santa Cruz, CA, United States

Maternal factors during pregnancy may affect child development during the postnatal period. This study investigated the potential associations between maternal hormones, immune status, micronutrient status, and child development. This was an observational substudy nested in a randomized controlled trial that took place in rural areas in Bangladesh (n=516). We examined maternal cortisol, estriol, micronutrient status, C-reactive protein (CRP), alpha-1-acid glycoprotein (AGP), and 13 cytokines during the first and second trimesters of pregnancy. Child development outcomes were assessed using the WHO gross motor milestones module at age 1 year, the MacArthur-Bates Communicative Development Inventories, and the Extended Ages and Stages Questionnaire. For the data analysis, we constructed generalized additive models and reported the mean difference in the outcome between the 25th and 75th percentile of the exposure after adjusting for covariates. Maternal estriol during pregnancy was positively associated with the sum score of WHO gross motor milestones at age 14 months (an adjusted difference of 0.22 more motor milestones attained in the 75th percentile compared to the 25th [95% confidence interval 0.07, 0.38]). This result remained significant after the Benjamini-Hochberg procedure was used to determine the false discovery rate (FDR correction) ($p = 0.04$). There were no significant associations between maternal cortisol, CRP, AGP, interferon gamma (IFN-γ) as a measure of the inflammatory process, cytokine sum score, vitamin D (25-hydroxy-D [25(OH)D]), ferritin, soluble transferrin receptor (sTfR), retinol binding protein (RBP), and child development at ages 14 and 28 months. Maternal estriol levels during pregnancy may play an important role in a child reaching their motor milestones during the first year of life.

8284

MONITORING ANTIBIOTIC RESISTANCE GENES ACROSS NEW ORLEANS RIVER AND LAKE WATERS

Claire E. Schwarze, Jessica M. Blanton, Ronald E. Blanton

Tulane University, New Orleans, LA, United States

The World Health Organization's list of priority pathogens highlights *Enterobacteriaceae* resistant to carbapenems and 3rd generation cephalosporins as a critical threat to human health. These bacteria cause severe disease and systemic infection, posing significant danger to care facilities, particularly when first-line antibiotics prove ineffective. *E. coli* and *Klebsiella*, specifically, are gut commensals that can be found in highly contaminated surface waters and have high potential for developing resistance. The Mississippi River receives organic waste from sources such as agriculture and human excretion, making it a favorable environment for the development and exchange of antibiotic resistance genes (ARGs). This study investigates the water microbiome of two shoreline sites on the Mississippi River and a site on the more brackish Lake Ponchartrain, all of which see a high flux of visitors year-round. In this study, abundance and composition of resistant bacteria are evaluated by coliform count estimates and cultivation of resistant *E. coli* and *Klebsiella.* Additionally, we evaluate the presence/absence of ARGs responsible for 3rd generation cephalosporin and carbapenem resistance. Fecal contamination levels are measured using qPCR of markers for both human and ruminant indicative *Bacteroidales* and *Lachnospiraceae.* Microbiome diversity is assessed by 16S rRNA gene sequencing. We hypothesize that there is a quantifiable difference in counts of antibiotic resistant bacteria and ARGs across the three sites. Over a one-year time scale, the highest levels and diversity, over the year, are expected in the river at Jackson Square, a high-density urban area. Preliminary data show similar counts of resistant bacteria at the two river sites, yet the lake exhibits higher counts. Of importance, all sites show much lower levels of fecal contamination indicators and resistant bacteria than urban sites in Brazil, for example. This study establishes a baseline for antibiotic resistance in New Orleans waters that will inform future monitoring efforts.

8285

DETECTION OF *SALMONELLA* TYPHI AND *BLA*$_{CTX-M}$ GENES IN DRINKING WATER, WASTEWATER, AND ENVIRONMENTAL BIOFILMS IN SINDH PROVINCE, PAKISTAN

Ayesha Tajammul[1], Scott Benson[2], Jamil Ahmed[3], Jim VanDerslice[2], **Windy Tanner**[4]

[1]U.S. Pakistan Center for Advanced Studies in Water, Mehran University of Engineering and Technology, Jamshoro, Pakistan, [2]University of Utah, Salt Lake City, UT, United States, [3]Rashid Latif Khan University Medical College, Lahore, Pakistan, [4]Yale University, New Haven, CT, United States

Typhoid fever poses a significant public health risk, particularly in low- and middle-income countries where access to clean water and improved sanitation may be limited. In Pakistan, this risk is especially serious given the emergence of an extensively drug-resistant (XDR) *Salmonella* Typhi strain, a strain attributed to *S*. Typhi acquisition of the *bla*$_{CTX-M-15}$ gene. This now-dominant XDR *S.* Typhi strain, non-XDR *S.* Typhi strains, and *bla*$_{CTX-M}$ genes are readily disseminated via drinking water and wastewater in Pakistan and may also be present in biofilms associated with these environmental sources. This study investigates the presence of *S*. Typhi and *bla*$_{CTX-M}$ genes within these environmental compartments. Drinking water (n=35) or wastewater samples (n=35) and samples of their associated biofilms were collected from Karachi and Hyderabad, Pakistan. Samples were tested by PCR for *S*. Typhi and *bla*$_{CTX-M}$ group 1 genes as a proxy for *bla*$_{CTX-M-15}$. Heterotrophic plate counts (HPC) were conducted to assess sample microbial load. *S*. Typhi was detected by PCR in one bulk wastewater sample and one drinking water biofilm. *Bla*$_{CTX-M}$ group 1 genes were detected in all sample types and were detected more frequently in bulk wastewater (n=13/35) than in drinking water (n=2/35) and more frequently overall in biofilm samples (n=22/70) versus bulk water (n=15/70). Detection of *bla*$_{CTX-M}$ in biofilm was not significantly associated with detection in the associated bulk water sample. This study marks the first detection of *S*. Typhi in drinking water biofilms and the first report of *bla*$_{CTX-M}$ genes in environmental biofilms in Pakistan. Environmental biofilms, particularly in drinking water systems, may serve as reservoirs for human exposure to *S*. Typhi and drug resistance genes. This study underscores the importance of expanding surveillance strategies to include biofilm sampling, providing valuable insights into pathogen dissemination in water systems, and informing targeted public health interventions to prevent waterborne diseases.

8286

THE INTERPLAY AMONG GLUCOSYLCERAMIDE TRANSFERASE AND ENCYSTATION-SPECIFIC PROTEINS IS IMPORTANT FOR DRIVING THE PROCESS OF CYST FORMATION BY AN ANCIENT PROTOZOAN, *GIARDIA LAMBLIA*

Julio H. Rangel, Breanna C. Pence, Siddhartha Das

The University of Texas at El Paso, El Paso, TX, United States

Giardia lamblia is an intestinal protozoan and the primary cause of waterborne illness known as "giardiasis." *Giardia* cysts, transmit the infection via contaminated water, contain a protective fibrous cyst wall composed of unique N-acetylgalactosamine (GalNAc) polymer and giardial cyst wall proteins (gCWPs). We have demonstrated that encystation stimulation induced the expression of giardial glucosylceramide transferase (gGlcT1) enzyme, while giardial long chain fatty acyl elongase (gFAELO) is expressed in trophozoites and downregulated during encystation. The current study examines how gGlcT1 interacts with the changes in the production of gCWPs and drives the encystation and cyst production process. We are also interested in exploring if gFAELO counteracts the function of gGlcT1 and the possible dynamic interactions between these enzymes, which are critical for continuing the encystation-excystation cycle of this waterborne pathogen. In a novel approach, we assessed gGlcT1 expression during encystation using enzymatic and immunoblot analysis. We also generated gGlcT1 overexpressed, knockdown, and mutant cell lines of *Giardia* to elucidate the role of full-length and truncated gGlcT1 on encystation hall marks. Furthermore, we investigated the possibility of gFAELO affecting gCWP production by overexpressing and coexpressing gFAELO and gGlcT1. We found that the level of CWP expression changed in various gGlcT1 clones, suggesting a possible link between gGlcT1 and CWPs during encystation. Furthermore, changes in expression levels of gGlcT1 alter the morphology of the cyst wall, implicating the importance of gGlcT1 and CWPs interplay for cyst formation and maintaining the cyst morphologies. Overexpression and coexpression of gFAELO changed the expression pattern of gGlcT1, lowered the production of gCWP and reduced cyst-wall thicknesses—indicating the formation of unstable and osmotically sensitive cysts that facilitate the excystation of *Giardia*. The interplay among gGlcT1, CWPs, and gFAELO is critical for triggering the encystation process but is also likely to facilitate the excystation process.

8287

HIGH BURDEN OF ENTERIC PATHOGEN INFECTION IN MOTHER-CHILD PAIRS AND WASH INDICATORS IN RURAL AND PERI-URBAN COMMUNITIES OF BOLIVIA

Cinthia Copeticona-Callejas, Alejandra Gabriela Torrez Mamani, Belen Claudia Choque Pardo, Sonia Guadalupe Jiménez Pacohuanca, Volga Ana Iñiguez Rojas

Instituto de Biologia Molecular y Biotecnologia, La Paz, Bolivia, Plurinational State of

Enteric infections in developing countries are frequent among children who are exposed to poor environmental conditions from an early age. The pathogens associated with acute gastroenteritis (AG) are transmitted by the fecal-oral route and through contaminated food and water, particularly in areas lacking access to WASH services. The objective of this study was to analyze the presence of enteric pathogens and their association with WASH indicators in mother-child pairs from 12 rural and peri-urban communities in the La Paz River Basin. 376 stool samples collected from mothers and children under 5 years of age, were evaluated for 20 enteric pathogens by real-time PCR including viruses (rotavirus, norovirus GI/II, astrovirus, sapovirus, and adenovirus), bacteria (*Salmonella*, *Shigella*, ETEC (estA/eltB) and EPEC (eae/bfpA), *Clostridium difficile* (tcdA/tcdB), *Helicobacter pylori*, and *Campylobacter*), protozoa (*Cryptosporidium parvum*, *Giardia lamblia*, and *Entamoeba histolytica*), and helminths (*Ascaris lumbricoides*, *Necator americanus*, *Strongyloides stercoralis*, *Ancylostoma duodenale*, and *Trichuris trichiura*). 85% of the analyzed population was infected with at least one pathogen. The most frequently found pathogens were *H. pylori* (34%), adenovirus (29%), EPEC (27%), *Giardia* (26%), and *Shigella* (22%). Differences were found between peri-urban and rural communities in relation to WASH indicators, drinking water treatment, and pathogen carriage, highlighting the presence of risk factors associated with hygiene practices and sanitation conditions. Analysis of the distribution of enteropathogens revealed that children carry a higher burden of viral pathogens and protozoa than their mothers. The same pattern was observed in co-infections with ≥ 3 pathogens. In conclusion, these data indicate that the study population carried a high burden of enteric pathogens, considering its asymptomatic status. This suggests a wide circulation of pathogens, and different sources of contamination. These findings, represent one of the first studies of enteric pathogens in peri-urban/rural communities in Bolivia.

8288

"FLORENCE"- A SMARTPHONE COPILOT BASED ON LARGE AI MULTIMODAL MODELS: TESTS IN CÔTE D'IVORE IN PATIENTS WITH SUSPECTED SKIN NEGLECTED TROPICAL DISEASES

Elena Dacal[1], Iago Veiras[1], Oscar Darias[1], Jaime García-Villena[1], Alvaro López-Caro[1], Alejandro Angulo[1], Labiya Toure[2], Ange Théodore Yao Kouakou[2], Aboa Paul Koffi[2], Christian R. Johnson[3], Emma Saéz-López[4], Israel Cruz[5], Miguel Luengo-Oroz[1]

[1]Spotlab, Madrid, Spain, [2]Programme National de Lutte contre l'Ulcère de Buruli, Divó, Côte D'Ivoire, [3]Fondation Raoul Follereau, Paris, France.

University of Abomey-Calavi, Abomey-Calavi, Benin, [4]Department of Microbiology, Paediatrics, Radiology and Public Health, Faculty of Medicine, University of Zaragoza, Zaragoza, Spain. Spanish Network for Research on Respiratory Diseases (CIBERES), Carlos III Health Institute, Madrid, Spain, Zaragoza, Spain, [5]National School of Public Health, CIBERINFEC, Instituto de Salud Carlos III, Spain, Madrid, Spain

Large Multimodal Models (LMMs) present an innovative approach in healthcare leveraging the integration of heterogeneous data types to improve and optimize patient diagnosis and management. This approach shows particular promise for diseases in which combining data is crucial for accurate diagnosis, or when expert personnel are scarce, and the differential diagnosis is complex. Neglected Tropical Diseases (NTDs), particularly skin NTDs such as Buruli ulcer, leprosy, yaws or scabies, represent an optimal scenario in which to apply this methodology, given the need for an early diagnosis, the complex differential diagnosis and the scarcity of dermatologists in rural areas. We developed and tested two assistants for the diagnosis, management and follow-up of patients with suspected skin NTDs in Côte d'Ivoire: i) "Florence," an expert in Skin NTDs; and ii) "Florence Pro," an augmented version of Florence equipped with a guide from World Health Organization on skin NTDs tailored for front-line health workers and the ePilly Trop book on tropical infectious diseases. The configuration of these two assistants has adhered to the CO-STAR framework augmented with one-shot learning. Afterward, these were deployed into a mobile App, MultiSpot, facilitating the combination of clinical data and images of skin lesions. This system was tested at the Divo Regional Hospital in Côte d'Ivoire, where clinicians evaluated its effectiveness in diagnosing simulated cases of patients with skin conditions. Following testing, a performance survey was conducted, measuring system usability and accuracy metrics, reaching promising results. Preliminary findings underscore the potential of this tool in diagnosing and managing patients with suspected skin NTDs, being particularly useful for health workers and individuals with limited expertise in dermatology. Subsequent steps entail implementing a user journey in the assistants, and conducting this study on a larger scale, encompassing a broader spectrum of cases and diverse personnel.

8289

DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF PATIENTS WITH CHROMOBLASTOMYCOSIS AND EUMYCETOMA IN EIGHT MEDICAL CENTERS, UNITED STATES

Dallas J. Smith[1], Vaisak Nair[2], Drashti Shah[3], George R. Thompson[4], Ilan S. Schwartz[5], Harrison White[6], Kaya L. Curtis[6], Poonam Sharma[7], William P. Daley[7], Robert T. Brodell[7], Rachel McMullen[3], Kaitlin Benedict[1], Jeremy A. W. Gold[1], Samantha Williams[1], Shari R. Lipner[6], Avrom S. Caplan[8], Eva Rawlings Parker[9], Peter G. Pappas[3], Paschalis Vergidis[2]

[1]Centers for Disease Control and Prevention, Atlanta, GA, United States, [2]Mayo Clinic, Rochester, MN, United States, [3]University of Alabama at Birmingham School of Medicine, Birmingham, AL, United States, [4]University of California Davis Medical Center, Sacramento, CA, United States, [5]Duke University School of Medicine, Durham, NC, United States, [6]Weill Cornell Medicine, New York, NY, United States, [7]University of Mississippi Medical Center, Jackson, MS, United States, [8]NYU Grossman School of Medicine, New York, NY, United States, [9]Vanderbilt University Medical Center, Nashville, TN, United States

Chromoblastomycosis and eumycetoma, mycoses acquired via traumatic inoculation, are Neglected Tropical Diseases causing substantial disability and stigma. US epidemiologic and clinical data on these diseases are lacking. Monitoring local acquisition and causative organisms for these mycoses is needed given potential climate change- and migration-related shifts in geographic distribution. We reviewed medical records of cases diagnosed 1/1/03-8/1/23 at 8 US medical centers. We identified 48 chromoblastomycosis and 9 eumycetoma cases as of 4/5/24. For chromoblastomycosis, most patients were male (n=37), non-Hispanic (n=41), White (n=33); average age was 62 years. Most (n=36) were immunocompromised; 29 received organ transplantation, and 21 had immunosuppressive therapy. Twenty-eight had no lifetime international travel. Nine recalled traumatic inoculation; 8 had US acquisition (3 in AL, 2 in TN; 1 each in FL, NC, and HI). Sixteen had culture data: 6 *Exophiala* spp; 3 *Cladosporium* spp; 3 *Fonsecea spp*; 1 each *Wangiella* spp, *Phialophora verrucosa*, *Bipolaris* spp, *Rhizopus* spp. Common presentations and symptoms were nodules (n=24), raised and crusted lesions (n=11), and pain (n=11). Most infections were on the upper limbs (n=33) and of mild severity (n=39). Most were treated with itraconazole (n=18); 33 had surgical lesion excision. For eumycetoma, most patients were men (n=7), non-Hispanic (n=9), White (n=4); average age was 57 years. Only 2 were immunocompromised. Three recalled traumatic inoculation location (2 in AL, USA; 1 in Vietnam). Six had culture data: 1 each *Fusarium* spp, *Medicopsis romeroi*, *Scedosporium boydii*, *Trematospheria grisea*, *Exophiala jeanselmei*, *Acremonium* spp. Seven had pain and 8 had lesions on lower limbs. Five received voriconazole treatment, and 5 had local surgical excision. Study limitations were difficulty distinguishing chromoblastomycosis and cutaneous phaeohyphomycosis due to limited histopathology data and causative organism identification gaps. Clinicians should be aware of locally-acquired and travel-associated cases. Continued surveillance could increase disease recognition.

8290

TALAROMYCOSIS IN THE UNITED STATES: AN ANALYSIS OF COMMERCIAL HEALTH INSURANCE CLAIMS AND MEDICAID DATABASES, 2016 TO 2022

Kaitlin Benedict[1], **Dallas J. Smith**[1], Jeremy A. W. Gold[1], Thuy Le[2]

[1]Centers for Disease Control and Prevention, Atlanta, GA, United States, [2]Duke University School of Medicine, Durham, NC, United States

Talaromycosis (formerly penicilliosis), an emerging severe fungal disease caused by the environmental pathogen *Talaromyces marneffei* (formerly *Penicillium marneffei*), is endemic in tropical and sub-tropical parts of Southeast Asia, southern China, and northeastern India. Talaromycosis mainly affects immunocompromised people, particularly those with advanced HIV disease. In the US, data on talaromycosis frequency and patient features are lacking. We leveraged the 2016-2022 Merative™ MarketScan® Commercial/Medicare and Multi-state Medicaid databases, which contain health insurance claims data for >70 million people combined, to identify talaromycosis based on ICD-10-CM code B48.4, excluding rule-out diagnoses. We selected patients with continuous insurance enrollment within -90-30 days of diagnosis and examined demographic characteristics, underlying conditions, and treatment. We identified 99 patients (commercial/Medicare insurance: 77, Medicaid: 22). Median age was 56 years (interquartile range [IQR] 43-65); 66% were female. Among commercial/Medicare insurance patients, 46% were from the South, followed by 25% Midwest, 21% West, and 7% Northeast. Total, 34% were hospitalized (median 8 days, IQR 4-14). Over half (56%) had a documented immunosuppressive condition (18% cancer, 17% primary immune deficiency, 6% immune-mediated inflammatory disease, 6% transplantation, and 3% HIV) and/or immunosuppressive medication use (32%, primarily prednisone). Other co-diagnoses included chronic obstructive pulmonary disease (52%), pneumonia (42%), asthma (37%), diabetes (23%), aspergillosis (19%) and COVID-19 (17%). Outpatient antifungal prescriptions included amphotericin B (19%), itraconazole (14%), and voriconazole (11%). Limitations are possible case misclassification and lack of data on travel, exposure characteristics, laboratory test results, inpatient medications, and mortality. This is the first large-scale description of US talaromycosis cases and underscores the need for US healthcare providers to remain vigilant for the possibility of travel-associated talaromycosis.

8291

IMPORTED LEISHMANIASIS IN THE UNITED KINGDOM: CASE DATA AND OUTCOMES FROM A NATIONAL MULTIDISCIPLINARY TEAM MEETING

Owain Donnelly[1], Ciara Mahon[1], Rachel Southern-Thomas[1], Simran Goyal[1], Adam T. Gray[1], Mark S. Bailey[2], Jonathan Joseph[3], Peter L. Chiodini[4], June Minton[1], Naomi F. Walker[5], Sarah Eisen[6], Laura Nabarro[1], Stephen L. Walker[1], Anna Checkley[1]

[1]Hospital for Tropical Diseases, University College London Hospitals (UCLH) NHS Foundation Trust, London, United Kingdom, [2]Academic Department of Military Medicine, Royal Centre for Defence Medicine, Birmingham, United Kingdom, [3]Department of Rhinology, Royal National ENT and Eastman Dental Hospital, UCLH, London, United Kingdom, [4]Department of Clinical Parasitology, UCLH, London, United Kingdom, [5]Tropical and Infectious Diseases Unit, Liverpool University Hospitals NHS Foundation Trust, London, United Kingdom, [6]Department of Paediatrics, UCLH, London, United Kingdom

Leishmaniasis, caused by the parasitic protozoan *Leishmania*, is a neglected tropical disease which is rare in the UK. Expert clinical guidance is vital for optimal case management, and the national UK Leishmaniasis Multi-Disciplinary Team (UKLMDT) meeting offers a monthly virtual forum to which clinicians across the UK refer cases. Experienced specialists from dermatology, ENT, infectious diseases, tropical medicine, parasitology, and pharmacy advise on diagnosis, treatment, and procuring medications. We describe the caseload and outcomes from the UKLMDT's first two and a half years. Data for patients discussed between November 2021 and April 2024 were extracted from the University College London Hospitals electronic patient record, and referring teams contacted for information on patient outcomes. Data analysed included patient age, location of referring hospital, number of discussions per patient, clinical manifestations, immune status, number of relapses, time since last relapse, causative species of *Leishmania*, and diagnostic results. Over this time, 65 patients were discussed, referred from throughout the UK, as well as four international referrals. Clinical phenotypes included cutaneous (34/65), mucosal (7/65), visceral (22/65), and post-kala-azar dermal leishmaniasis (1/65). The median number of discussions per patient was one (range 1-8); additional discussions were common for relapse, lack of response to treatment, pregnancy, and children (12% of cases). The commonest causative species were *L. donovani* complex (n=26), *L. Viannia* subgenus (n=17), and *L. mexicana* complex (n=4). Seven patients were determined not to have leishmaniasis. Examples of advice given in complex cases, and treatment undergone and clinical outcomes of patients at >6 months post-treatment will be discussed. The UKLMDT is a model for decentralised care of a rare infection, enabling clinicians to access expert advice provide improved, evidence-based care locally. Future considerations include how best to share data and outcomes with international colleagues, with a view to improving diagnosis and case management of leishmaniasis.

8292

CUTANEOUS LEISHMANIASIS IN NORTHERN SYRIA: A ONE YEAR DESCRIPTIVE ANALYSIS OF EPIDEMIOLOGICAL AND CLINICAL DATA

Ayla AlKharrat[1], Owen Bicknell[2], Basel Abdelal[2], Mouhannad Abdulkader[2], **Sergio Lopes**[1], Sara Estecha-Querol[1]

[1]The MENTOR Initiative, Haywards Heath, United Kingdom, [2]The MENTOR Initiative, Gazientep, Syrian Arab Republic

Leishmaniasis remains a serious public health issue in northern Syria. Exacerbated by over a decade of conflict and displacement, cutaneous leishmaniasis (CL) in Syria is a major cause of discrimination, social isolation and economic loss. The MENTOR Initiative has been supporting local static health facilities and mobile clinics to deliver adequate treatment for CL. In this work, we describe key epidemiological characteristics and clinical manifestation of CL in northern Syria.In 2023, a total of 38,077 new CL cases were diagnosed across 11 districts in Northwest Syria (NWS) and 8 districts in Northeast Syria (NES). Areas with the highest number of reported cases were Harim (20.6%), Afrin (12.2%) and Jebel Saman (11.1%) districts in NWS. The CL cases were reported in 6,360 (16.7%) children under 5, 18,485 (48.5%) children (5-17 years), and 13,232 (34.8%) adults. Of these, 18,328 (48.1%) were females. Internally displaced persons (IDPs) accounted for 48.9% of the detected cases, 50.7% of cases were detected among host populations, while the remaining 0.4% were refugees. Most patients presented with lesions on the face (42.6%), upper limb (38.7%), and lower limb (23.7%). The diameter of the lesions ranged between 10 - 160 mm, with an average of 16 mm and a median of 10 mm. Most commonly, lesions were in the shape of nodules (82.6%), followed by papules (13%). Other lesions were in the form of ulcers (2.4%) and plaques (1.9%). The number of lesions detected per patient ranged between 1 - 75, with an average of 1.7. The majority (38.4%) of new cases were diagnosed between January and March. On average, patients presented to health facilities 67 days after noticing the lesion. From the 31,586 cured patients, 31,578 (99.97%) received five or more rounds of treatment with Glucantime and/or Pentostam before being discharged. This study showcases essential epidemiological features of CL cases attending to health facilities/seeking care in Northern Syria. The findings reinforce the need to continue to provide essential medical assistance to affected populations in Syria as CL continues to be a major cause of disability and social discrimination.

8293

PEERING INTO THE CRYSTAL BALL - PREDICTING OUTCOMES IN VISCERAL LEISHMANIASIS

James P. Wilson[1], Forhad Chowdhury[1], Shermarke Hassan[1], Eli Harriss[1], Fabiana Alves[2], Ahmed Musa[3], Prabin Dahal[1], Kasia Stepniewska[1], Philippe J. Guérin[1]

[1]University of Oxford, Oxford, United Kingdom, [2]Drugs for Neglected Diseases initiative, Geneva, Switzerland, [3]University of Khartoum, Khartoum, Sudan

Visceral leishmaniasis (VL) is a neglected tropical disease prevalent in populations affected by poverty, war and famine. In resource limited settings, effective risk stratification is crucial for equitable care, including judicious allocation of hospital beds, medicines, and specific interventions e.g. blood transfusions. We present our work on the application of individual participant data (IPD) from the Infectious Diseases Data Observatory (IDDO) VL data repository, to improve clinical decision making through prediction model research. Specifically, we present evidence gaps highlighted in a novel systematic review of VL prognostic models, and how IPD can be harnessed to predict relapse, supporting the ongoing South Asian Elimination Programme (SAEP). Adhering to best practice guidelines, we reviewed all studies that developed or validated models predicting outcomes in VL patients. Bibliographic databases were searched from database inception to March 2023 with no language restriction. Screening, data extraction and risk of bias assessments were performed in duplicate. Eight studies, published 2003 - 2021, were identified describing 12 models (9 in Brazil, 3 in East Africa). All models predicted mortality (10 models predicting in-hospital mortality, 2 registry-reported mortality). Risk of bias was high for all models, due to small sample sizes or poor reporting of model performance. Importantly, no models predicted treatment failure or relapse, or were developed in South Asia, despite representing the highest global VL case burden prior to 2010. In the context of the ongoing SAEP, and the lack of a non-human disease reservoir, prompt diagnosis and treatment of patients with relapse is needed to limit further transmission. Since 2018, through close collaboration with VL investigators across the world, we have built a repository of over 9,300 prospectively collected IPD from 36 clinical trials, with the majority of patients from South Asia with robust 6-month relapse outcomes. At ASTMH 2024 we look forward to sharing our preliminary relapse model, it's relevance in the elimination programme, and the clinical implications.

8294

EPIDEMIOLOGY, HEALTH-SEEKING BEHAVIORS AND TRADITIONAL PRACTICES RELATED TO SNAKEBITES IN RURAL AND TRIBAL COMMUNITIES IN SOUTHERN INDIA

Rohan Michael Ramesh[1], Ravikar Ralph[1], Mohan Jambugulam[1], Arpitha Anbu Deborah[1], Kumudha Aruldas[1], Sushil Mathew John[1], Judd L. Walson[2], Anand Zachariah[1], Sitara S.R Ajjampur[1]

[1]Christian Medical College Vellore, Vellore, India, [2]Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, United States

Nearly 60,000 people die of snakebites in India annually, accounting for more than half of all global snakebite deaths in 2019. With limited access to healthcare, there is a constant reliance on traditional healers in communities, especially remote tribal areas, due to easier access and high trust. This study describes the epidemiology and health-seeking behaviors of snakebite victims in a rural and tribal block in Tamil Nadu in southern India. During the survey in Timiri (rural block) and Jawadhu hills (inhabited predominantly by tribal groups within a reserve forest), 322 of 151,293 individuals reported a snakebite in the preceding year. When these individuals were followed up with a detailed questionnaire, snakebite incidence was confirmed to be 174/100,000 (64/286) persons in Jawadhu Hills and 194/100,000 (222/286) in Timiri. The proportion of cases belonging to households in the lowest wealth index quintile was higher in Jawadhu Hills (55%) than Timiri (7%). Only 59% (168/286) received first-aid within an hour, mostly with tourniquet application (76%), followed by ingestion of herbal concoctions (23%) more in Jawadhu Hills (90%,45/64) compared to Timiri (69%,82/222). Overall, 80% of all snakebite victims first visited a public hospital or private clinic; however, only 25% in Jawadhu Hills (16/64) first visited a hospital compared to Timiri (88%,195/222). In Jawadhu Hills, 11% initially stayed home after the incident, compared to Timiri (1%). Traditional healers were the first point of contact in 17% (49/286) of snakebites, of which 64% (41/64) were in Jawadhu Hills, and primarily accessed on foot or by motorcycle. The mortality rate was 2.7/100,000 population in the Jawadhu Hills and 4.4/100,000 in Timiri. Our study highlights healthcare access challenges for snakebite envenomation in rural and tribal communities. Key challenges identified include inadequate first aid, reliance on traditional healers, and limited emergency transport. Addressing these requires a multifaceted approach, combining community awareness, collaboration with traditional healers, and infrastructure improvements for timely healthcare access.

8295

SEASONAL TRANSITION OF *ANOPHELES STEPHENSI* AND *AEDES AEGYPTI* LARVAL HABITAT SUPERPRODUCTIVITY IN KEBRIDEHAR, ETHIOPIA

Solomon Yared[1], Dereje Dengela[2], Peter Mumba[3], Sheleme Chibsa[3], Seth Irish[4], Melissa Yoshimizu[5], Sarah Zohdy[6], Meshesha Balkew[2], Gonzalo M. Vazquez-Prokopec[7]

[1]Jigjiga University, Jigjiga, Ethiopia, [2]PMI Evolve Project, Abt Global, Addis Ababa, Ethiopia, [3]U.S. President's Malaria Initiative, USAID, Addis Ababa, Ethiopia, [4](at time of work) U.S. President's Malaria Initiative, Entomology Branch, U.S. Centers for Disease Control and Prevention, Atlanta, GA, United States, [5]U.S. President's Malaria Initiative, USAID, Washington, DC, United States, [6]6.U.S. President's Malaria Initiative, Entomology Branch, U.S. Centers for Disease Control and Prevention, Atlanta, GA, United States, [7]Emory University, Atlanta, GA, United States

The invasion and spread of *Anopheles stephensi*, an Asian native mosquito species, across Africa, poses a significant threat to malaria control and elimination because of its adaptability to urban areas and efficiency in transmitting both *Plasmodium falciparum* and *Plasmodium vivax*. Field observations indicate that *An. stephensi* and *Aedes aegypti* overlap in their larval habitat use of artificial water storage containers. We document the seasonal shift in *An. stephensi* and *Ae. aegypti* in Kebridehar, Ethiopia. Mosquito larvae were sampled for four consecutive months in Nov, Dec 2020 and Jan, Feb 2021. A total of 90 water storage containers identified as potential larval habitats were sampled; 75% were ground level cisterns, followed by tires (13%) and ground level barrels (7%). A total of 13,635 *An. stephensi*, 1,168 *Ae. aegypti* and 757 *Culex* spp. were collected by standard dipping. Habitat positivity for *An. stephensi* increased from 61% (55/90) in November to 82% (63/77) in February, and *Ae. aegypti* habitat positivity decreased from 47% in November to 21% in February. Larval productivity of each container for *An. stephensi* was highly heterogeneous, with a mean number of larvae per 20 dips of 41 (or 2.1 per dip) and a range of 0-700 per 20 dips (or 0-35 per dip). Conversely, *Ae. aegypti* larval productivity was an order of magnitude lower and had a much narrower range (4.3, 0-70 per 20 dips, or 0.22, 0-3.5 per dip). Such heterogeneity was characterized by a negative binomial distribution with parameter $k<0.5$, which indicates strong aggregation. Further, a fit to a Pareto function identified that up to 77% of all larvae originated from only 23% of the larval sites. The 23% of sites, here defined as "superproductive" habitats, increased as the dry season progressed. This study shows that both *An. stephensi* larval productivity is strongly aggregated, leading to opportunities for impactful larval source management, and that *Ae. aegypti* coexists in the same larval sites as *An. stephensi*.

8296

A FOCUSED CASE-RESPONSE APPROACH TO MALARIA VECTOR SURVEILLANCE IN AREAS OF UNSTABLE TRANSMISSION

Sungano Mharakurwa[1], Tanatswa X. Gara-Mundere[1], Trust Nyakunu[1], Brenda Makonyere[1], Tariro Chikava[1], Natasha Mbwana[1], Charmaine Matimba[1], Nobert Mudare[1], Shungu Munyati[2], Lovemore Gwanzura[3]

[1]Africa University, Mutare, Zimbabwe, [2]Biomedical Research and Training Institute, Mutare, Zimbabwe, [3]Biomedical Research and Training Institute, Harare, Zimbabwe

Current mainstay approaches to routine malaria vector surveillance are based longitudinal monitoring on a cohort of fixed, designated households representing a wider area (average population of 200,000 residents). In regions of unstable seasonal transmission, this routine surveillance approach is hampered by several factors, such as but not only the following: (i) transmission occurring in foci that are prone to unpredictable shifts of locale; (ii) eruption of transmission in non-traditional malaria zones amid a backdrop of climate change; (iii) repeated sampling readily depletes the designated households of vector abundance, rendering them no longer representative of the wider area. Thus, upon successive surveys, designated households may reach a point when they capture little or no vectors while malaria transmission is raging in the wider surveillance area. In the present study, routine monthly entomological surveillance based on fixed longitudinal households was compared with a focused case-response approach based on non-fixed households from the village with prevailing highest number of cases for the week in a given health centre catchment. Both routine standard and focused case-response (FRC) approaches were conducted simultaneously every month in 24 health centre catchments of Mutasa district from 2022 - 2023, using regular prokopack aspiration, CDC light trap and larval vector collections. A total of 1,912 mosquitoes were caught through the standard longitudinal approach while the FCR approach yielded 7,149. The FCR approach exhibited 2X higher odds of catching sporozoite-positive vector mosquitoes than the standard approach (OR [95% CI]: 2.1 [1.72 - 2.49], P lt 0.001, N = 9,061). The FCR approach promptly detected non-traditional and outbreak malaria vectors, unlike the standard approach delimited to fixed households. Community fatigue to surveillance activities was encountered with the standard but not the FCR approach. The focused case-response approach can be an effective complementary entomological surveillance approach in regions of unstable transmission or those zeroing towards malaria elimination.

8297

DOES IVERMECTIN IMPAIR ANOPHELES ATTRACTIVENESS TOWARD TREATED HOSTS UNDER FIELDS AND LABORATORY CONDITIONS?

Lamidi Zela[1], Sié Hermann Pooda[2], Angélique Porciani[3], André Barembaye Sagna[4], Malik Bandaogo[1], A. N. Ramzy Kambou[1], Anyirekun Fabrice Somé[5], Christophe Roberge[6], Adrien M.G. Belem[7], Roch K. Dabiré[5], **Karine Mouline**[3]

[1]Centre International de Recherche-Développement sur L'Elevage en zone Subhumide, Bobo Dioulasso, Burkina Faso, [2]Université Ouezzin COULIBALY, Dédougou, Burkina Faso, [3]Institut de Recherche pour le Développement, Montpellier, France, [4]Institut de Recherche pour le Développement, Bobo Dioulasso, Burkina Faso, [5]Institut de Recherche en Sciences de la Santé, Bobo Dioulasso, Burkina Faso, [6]MEDINCELL, Jacou, France, [7]Université Nazi Boni, Bobo Dioulasso, Burkina Faso

Ivermectin administered to hosts as a systemic insecticide is viewed as a complementary tool against malaria vectors. However, whether its metabolization would modify hosts' attractiveness to Anopheles has never been addressed, despite ethical and operational concerns. Hence, the objective of this study was to evaluate, in the fields and the laboratory, if major malarial mosquitoes are more or less attracted to ivermectin-treated vs control hosts. A two-arms design was used: 4 cattle received no treatment (controls) and 4 were treated with a long-acting ivermectin formulation (1mg/kg) from the BEPO® technology (2-3 months efficacy, IMPACT project). Cattle exposures were performed at t=2 days, 1, 2, 3, and 4 months post-treatments, under nets in the fields of Bama, Burkina Faso, and using a dual-choice olfactometer in the laboratory. In the fields, trapped wild mosquitoes were counted and identified. A random subsample of 100 alive, engorged mosquitoes was followed for survival. In the laboratory, colony female *An. coluzzii* were released into the olfactometer and activated females counted according to their choice for treated or control cattle. In the fields, the formulation's efficacy was up to 4 months on wild *An. coluzzii* of all insecticide resistance status. A total of 181,696 mosquitoes was collected for which the cattle treatments did not influence their attractiveness (χ_2^2=0.8791; P=0.3484). For Anopheles spp., treated bovines were more attractant than controls at t=4 months (Z= 0.584; P =0.001). *An. coluzzii* tended to be more trapped around treated than control cattle for all instances but this was not significant. In the laboratory, dual choice-tests on *An. coluzzii* colony showed similar attractiveness whatever cattle treatments (Z=0.215 ; P=0.83). We showed an insecticidal effect for up to 3-4 months on major wild malaria vector, meeting the WHO target product profile for endectocide-based malaria control. Dual-choice experiments with wild mosquitoes may help concluding on potential attractiveness impairment by ivermectin treatments, from which disentangling parts of the princeps molecule and the vehicle will also be needed.

8298

COMPARING ANOPHELES BEHAVIOR WITH INTERCEPTOR® G2'S DUAL VS SINGLE ACTIVE INGREDIENTS: 3D VIDEO TRACKING ANALYSIS

Beatrice Helena Schildknecht, Pie Mueller

SwissTPH, Allschwil, Switzerland

All WHO prequalified insecticide-treated bed nets contain pyrethroids. However, the rise of insecticide resistance in mosquitoes to these pyrethroids presents an imminent threat to the success of malaria vector control. A new net, Interceptor® G2 (BASF), has come to the market that combines alpha-cypermethrin, a pyrethroid, with chlorfenapyr, a pro-insecticide that is bio-activated through the oxidative metabolism within the mosquitoes' mitochondria. Interceptor® G2 has demonstrated increased efficacy against pyrethroid-resistant mosquitoes in large-scale epidemiological field trials. This investigation attempts to clarify how a net with combinations of both active ingredients influence mosquito behaviours from exposures. Implementing the use of flight tunnels, we assessed the influences of a net with both active ingredients of a commercial Interceptor® G2 netting and solo dipped netting with each discrete active ingredient. In the tunnel, mosquitoes had to negotiate an insecticide-treated net with nine 1 cm large holes to reach an artificial host. We recorded the flight paths using a 3D video tracking system and monitored the time to death post-exposure using a set of infrared time-lapse cameras. Data suggest that susceptible mosquitoes are killed mainly by alpha-cypermethrin exposures, while pyrethroid-resistant mosquitoes are primarily intoxicated by the chlorfenapyr with delayed mortality. We will present an in-depth analysis of the flight trajectories and their relationship with mortality, blood feeding and insecticide conversion rates.

8299

VECTORCAM - A NOVEL AI-POWERED DIGITAL TOOL FOR AUTOMATED MORPHOLOGICAL IDENTIFICATION OF MOSQUITO SPECIES, SEX, AND ABDOMINAL STATUS BY VILLAGE HEALTH TEAMS IN UGANDA: A RANDOMIZED CONTROLLED TRIAL

Sunny Patel[1], Marina Rincon Torroella[1], Deming (Remus) Li[1], Atul Antony Zacharias[1], Parthvi Mehta[1], Shreya Raman[1], Kyle Cooper[1], David Onanyang[2], James Kaweesa[2], Kigongo Siriman[2], Jovan Batte[2], Neil Lobo[3], Douglas Norris[4], Catherine Maiteki[5], Jimmy Opigo[5], Peter Waiswa[6], Soumyadipta Acharya[1]

[1]Johns Hopkins University, Baltimore, MD, United States, [2]Vector Borne and Neglected Tropical Diseases Control Division, Ministry of Health, Kampala, Uganda, [3]University of Notre Dame, South Bend, IN, United States, [4]Johns Hopkins University, School of Public Health, Baltimore, MD, United States, [5]National Malaria Control Division, Ministry of Health, Kampala, Uganda, [6]Makerere University School of Public Health, Kampala, Uganda

The shortage of entomological expertise in malaria control programs poses a significant challenge for effective vector interventions. VectorCam, an innovative, cost-effective tool, utilizes deep learning to rapidly identify mosquito species, empowering local health workers. Our ongoing randomized controlled trial in Uganda assesses VectorCam's performance over 12 months, focusing on the accuracy, timeliness, and completeness of surveillance reports by village health teams (VHTs). VHTs were recruited in two districts in Uganda. All VHTs were trained to collect mosquitoes using standard methods, and randomly selected study participants (N = 24) used VectorCam for on-site mosquito identification and data reporting, whereas the control arm assisted in the collection and sent specimens to district vector control officers (VCOs) for morphological identification under microscopy. Molecular analysis confirmed mosquito species, while sex and abdomen status were determined by microscopy to benchmark accuracy. Built-in timestamps in the software measured identification speed, and both arms were reported to DHIS2 for completeness evaluation. Currently, VectorCam reports an average of 93±2% identification accuracy across all current classes for species, 95±2% for sex, and 78%±4% for abdomen status identification. Furthermore, the VHTs analyze mosquitoes with a median time of 16.52 ± 0.21 seconds per mosquito. Real-time dashboards and comprehensive surveillance reports are also generated. Intermediate analysis from the RCT shows better performance on all metrics (accuracy, timeliness, and completeness) as compared to the control arm. VectorCam offers the possibility of enabling task sharing of vector surveillance with VHTs and concurrently generating surveillance reports automatically, thereby helping countries mitigate a crucial expertise and resource constraint in scaling up vector surveillance programs.

8300

GENOMIC EVALUATION REVEALS A STRONG POPULATION STRUCTURE OF *ANOPHELES FUNESTUS* COLLECTED IN COAST AND LAKE MALARIA ENDEMIC REGION IN KENYA

Brian Polo[1], Sylvia Milanoi[1], Diana Omoke[1], Cynthia Awuor[1], Duncan Onguru[2], Sanjay Nagi[3], Alistair Miles[4], Mara Lawniczak[5], Eric Ochomo[1]

[1]Kenya Medical Research Institute, Kisumu, Kenya, [2]Jaramogi Odinga Oginga University Science and Technology, Kisumu, Kenya, [3]Department of Vector Biology, Liverpool School of Tropical Medicine,, Liverpool, United

Kingdom, [4]Wellcome Sanger Genomic Surveillance Unit, Wellcome Sanger Institute, Hinxton, Cambridge, United Kingdom, [5]Wellcome Sanger Institute, Cambridge, United Kingdom

Efforts to reduce malaria impact have been successful through implementation of insecticide-based interventions but rising resistance and mosquito adaptations threaten these gains. Understanding the molecular, ecological, and evolutionary factors behind these changes is crucial for prolonging insecticide effectiveness and developing new vector control strategies. We used whole genome sequenced data of 105 *Anopheles funestus* mosquitoes from genome surveillance MalariaGEN vector observatory project. The samples were collected from Kisumu, Migori and Bungoma counties in Lake malaria endemic region and Kwale county in the Coast malaria endemic regions in Kenya. To investigate their geographical population structure, we used principal component analysis, neighbour-joining tree and fixation index. To understand the demographic history, we computed the genetic diversity summary statistics for mosquito cohorts grouped by geographical region. Selection pressure was analyzed by scanning the whole genome for signal of recent selection using H12 statistics. We found population structure between Lake and Coastal Kenya populations of *An. funestus* based on genetic diversity statistics. *Anopheles funestus* from the Lake region are separated by high differentiation from the Costal population with a mean F_{ST} 0.117. The genetic divergence was low among *An. funestus* from Lake region (F_{ST} < 0.0005) but higher between the Coastal County and the Lake region counties (F_{ST} ~ 0.128-0.138). Additionally, *An. funestus* from Lake region share selection signal at the *CYP6rp1* on the 2RL chromosome and *CYP9k1* at the X chromosome, while Coast (Kilifi) samples had a selection signal near the Esterase and *GSTe1* region on the 2RL chromosome and around the *NADH-cyp* region on the X chromosome. Our findings indicate that *An. funestus* from the Coast are highly differentiated from the population at the Lake region. Due to the regional population diversity of *An. funestus*, targeted approach of intervention should be considered for effective intervention against malaria. Reiterating the need for incorporating genomics in routine vector surveillance in Kenya.

8301

EFFECT OF ECOLOGICAL ZONES AND CLIMATIC CONDITIONS ON MOSQUITO DIVERSITY IN GHANA: A LONGITUDINAL STUDY FROM 2017 - 2022

Eric Behene[1], Seth O. Addo[1], Ronald E. Bentil[1], Mba-Tihssommah Mosore[1], Reham A. Tageldin[2], Patrick Obuam[3], Sandra A. Kwarteng[3], Dorcas Atibilla[4], Bernice Baako[5], Victor Asoala[5], Ellis Owusu-Dabo[3], Naiki Attram[6], **Shirley C. Nimo-Paintsil**[6], Terrel Sanders[6], Andrew G. Letizia[6], Samuel K. Dadzie[1], James F. Harwood[7]

[1]Noguchi Memorial Institute for Medical Research, Accra, Ghana, [2]United States Naval Medical Research Unit EURAFCENT Cairo Detachment, Cairo, Egypt, [3]Kwame Nkrumah University of Science and Technology, School of Public Health, Kumasi, Ghana, [4]Kintampo Health Research Center, Bono East Region, Kintampo, Ghana, [5]Navrongo Health Research Center, Upper East Region, Navrongo, Ghana, [6]United States Naval Medical Research Unit EURAFCENT Ghana Detachment, Accra, Ghana, [7]United States Naval Medical Research Unit EURAFCENT, Sigonella, Italy

Globally, mosquito diversity has been observed to decline due to land use and environmental conditions. However, this decline has not affected all species or geographical locations equally. In Africa, there is an estimated total of 677 mosquito species representing 16 genera. A majority of species and mosquito-borne pathogens are predominantly in West and Central Africa. To determine the influence of ecological zones and weather conditions on changes in mosquito diversity, mosquito surveillance data from three distinct settings in Ghana (Deciduous Forest, Forest-Transition zone, and Guinea Savannah) were analyzed and compared. From 2017 to 2022, mosquitoes were collected using the Centers for Disease Control and Prevention (CDC) light traps with either incandescent or ultra-violet light sources and Biogents Sentinel (BG) traps. Climate data was obtained from the National Aeronautics and Space Administration (NASA) Prediction of Worldwide Energy Resource (POWER) program. A total of 98,127 mosquitoes were morphologically identified as 54 species belonging to 8 genera: *Culex*, *Aedes*, *Anopheles*, *Mansonia*, *Coquillettidia*, *Culiseta*, *Eretmapodites* and *Toxorhynchites* all of which are of medical importance except *Toxorhynchites*. The species diversity was significantly affected by changes in the ecozones (p<0.01). In summary, the species richness in Deciduous Forest (Generalized Linear Mixed Model, GLMM=0.52, p<0.01) and Guinea Savannah (GLMM=0.40, p<0.01) was higher than the Forest-Transition zone. The Deciduous Forest zone (GLMM=-0.05, p<0.01) recorded the lowest species evenness. Additionally, species diversity was significantly higher with the CDC incandescent light traps (p<0.05) than BG traps. Understanding how the various ecological zones affect species diversity could be useful in disease surveillance and public health interventions for controlling mosquito-borne diseases and predicting "hot spots". Further studies investigating the influence ecozones have on mosquito species diversity and their potential implications for disease transmission is needed to inform vector control and prevention strategies.

8302

USING A VARIANT-SPECIFIC, ELECTROCHEMILUMINESCENCE MULTIPLEX SERONEUTRALIZATION ASSAY TO DELINEATE TRANSMISSION DYNAMICS OF SARS-COV-2 AS THE PANDEMIC TRANSITIONED TO ENDEMICITY

Mariam O. Fofana[1], Juan Pablo Aguilar Ticona[2], M. Catherine Muenker[1], Joseph Lu[3], Nivison Nery Jr[1], Homegnon Antonin Ferreol Bah[2], Emilia Andrade Belitardo[2], Jaqueline Silva[2], Gabriel Ribeiro dos Santos[1], Renato Victoriano[2], Ricardo Khouri[2], Federico Costa[4], Stephen Thomas[3], Adam Waickman[3], Mitermayer G. Reis[2], Albert I. Ko[1], Derek A.T. Cummings[5]

[1]Yale School of Public Health, New Haven, CT, United States, [2]Instituto Goncalo Moniz (Fiocruz Bahia), Salvador, Brazil, [3]SUNY Upstate Medical University, Syracuse, NY, United States, [4]Universidade Federal da Bahia, Salvador, Brazil, [5]University of Florida, Gainesville, FL, United States

Understanding the transition of the COVID-19 pandemic to endemicity and implementing surveillance has become increasingly difficult as infections more often are asymptomatic and home-based testing is not routinely reported to health authorities. Estimates from serological surveys may be less prone to under-reporting bias than symptom-based virologic surveillance, but their use has been limited as most populations now have pre-existing antibodies from infection or vaccination.
We conducted serial serological surveys of a community-based cohort in Salvador, Brazil to identify SARS-CoV-2 infections throughout the pandemic. We obtained vaccination history and sera in July-October 2021 and March-September 2022, before and after the peak of BA.1 transmission in Brazil. We identified infections based on increases in variant-specific pseudo-neutralization antibody responses with the Meso Scale Discovery V-Plex assay. To validate our serology-based method, we performed active screening for PCR-confirmed infection by identifying symptomatic individuals during household visits. Of 733 participants who underwent serial testing, 84.0% had detectable anti-SARS-CoV-2 IgG as measured by ELISA before the BA.1 wave. In contrast, median BA.1-specific pseudo-neutralization was low (7.1%, interquartile range [IQR] 3.3-14.9%) and increased to 39.0% (IQR 19.1-80.1%) after the wave. A 5% increase in BA.1-specific neutralization was 81.3% (95% confidence interval 66.9-90.6%) sensitive in identifying individuals with a PCR-confirmed infection. Among those who did not receive a vaccine dose between surveys, 92.0% had increased BA.1-specific neutralization indicative of infection. By measuring variant-specific pseudo-neutralization responses, we found high SARS-CoV-2 incidence during the Omicron BA.1 wave in a population with high pre-existing immunity. We are using this approach to estimate incidence during subsequent waves of Omicron sub-variants, identify immunological factors that drove transmission to endemicity, and inform future surveillance that minimizes bias from limited access to testing and underreporting.

8303

RETHINKING DENGUE PROTECTIVE IMMUNITY: MULTIPLE REPEAT SYMPTOMATIC INFECTIONS IN A SINGLE TRANSMISSION SEASON

Lisbeth Cantarero[1], Miguel Plazaola[1], Jose G. Juarez[1], Karla Gonzalez[1], Reinaldo Mercado-Hernandez[2], Sandra Bos[2], Eva Harris[2], Angel Balmaseda[1]

[1]Sustainable Science Institute, Managua, Nicaragua, [2]Division of Infectious Diseases and Vaccinology, School of Public Health, University of California, Berkeley, Berkeley, CA, United States

Dengue continues to be a major public health threat, with increasing disease burden worldwide. Dengue virus is comprised of 4 serotypes (DENV1-4); primary (1°) infection with one serotype confers lifetime immunity to disease with that serotype and transient immunity towards the other serotypes, typically protecting against infection for at least 6 months to 2 years. In 2022, all 4 DENV serotypes co-circulated in Nicaragua after post-pandemic introduction of new lineages. Leveraging 2 cohort studies in Managua (A2CARES Arbovirus Cohort Study, n=~2,000; Pediatric Dengue Cohort Study, n=~4,000), we evaluated heterotypic repeat symptomatic DENV infections in 2022. All enrolled participants presenting with suspected dengue or undifferentiated febrile syndrome were tested for dengue via real-time RT-PCR and serological tests. DENV-positive samples were serotyped via multiplex real-time RT-PCR. Unexpectedly, we observed 10 patients with repeated symptomatic DENV infections within a single transmission season. We recorded 2nd symptomatic infections as soon as 31 days post-1° infection (mean=94 days, range 31-158). We documented 7 repeat cases of DENV1 followed by DENV4 (6) or DENV3 (1) and 3 2nd infections after an initial DENV-4 case (2 DENV1 and 1 DENV3). All 1st infections were 1°, with 3 classified as Dengue with Warning Signs (DwWS) and 7 as Dengue without Warning Signs (DwoWS). Six 2nd infections were DwoWS and 4 were DwWS. Interestingly, the patient with 2 symptomatic infections 31 days apart presented with DwWS in both episodes. We are currently evaluating the immune profile of each infection series after the first and 2nd infections using a multiplex Luminex-based platform with multiple antigens from DENV1-4 and the related Zika flavivirus as well as focus reduction neutralization tests to DENV1-4 to investigate potential immunological explanations for these clinical/epidemiological observations. Our results demonstrate the need to re-evaluate the protective immunity of DENV after a first infection. These data can help inform public health policy regarding disease transmission risk during epidemics with multiple serotypes.

8304

INAPPARENT PRIMARY DENGUE VIRUS INFECTIONS REVEAL HIDDEN SEROTYPE-SPECIFIC EPIDEMIOLOGICAL PATTERNS AND SPECTRUM OF INFECTION OUTCOME: A COHORT STUDY IN NICARAGUA

Jose V. Zambrana[1], Sandra Bos[2], Elias Duarte[2], Aaron L. Graber[2], Julia Huffaker[2], Carlos Montenegro[3], Lakshmanane Premkumar[4], Aubree Gordon[1], Angel Balmaseda[5], Eva Harris[2]

[1]Department of Epidemiology, School of Public Health, University of Michigan, Ann Arbor, MI, United States, [2]Division of Infectious Diseases and Vaccinology, School of Public Health, University of California, Berkeley, Berkeley, CA, United States, [3]Sustainable Sciences Institute, Managua, Nicaragua, [4]Department of Microbiology and Immunology, University of North Carolina School of Medicine, Chapel Hill, NC, United States, [5]Laboratorio Nacional de Virología, Centro Nacional de Diagnóstico y Referencia, Ministerio de Salud, Managua, Nicaragua

Dengue is the most prevalent mosquito-borne viral disease and a major public health problem worldwide. Most primary infections with the 4 dengue virus serotypes (DENV1-4) are inapparent; nevertheless, prior research has primarily focused on symptomatic infections, limiting understanding of the epidemiological burden and spectrum of disease of each DENV serotype. Our study addresses this bottleneck by providing a new method and a detailed examination of primary (1°) inapparent infections. Here we present (1) the evaluation of a multiplex DENV1-4 envelope domain III multiplex microsphere-based assay (EDIII-MMBA) to serotype 1° symptomatic and inapparent infections and (2) its application leveraging 17 years of prospective sample collection from the Nicaraguan Pediatric Dengue Cohort Study. The EDIII-MMBA demonstrated excellent diagnostic accuracy of symptomatic and inapparent 1° DENV infections when evaluated against gold-standard serotyping methods. After evaluation of the method, we analyzed 46% (N=574) of total inapparent primary DENV infections with the EDIII-MMBA. Remaining infections were inferred using stochastic imputation, taking year and neighborhood of infection into account. Significant within- and between-year variation in serotype distribution between symptomatic and inapparent infections and circulation of serotypes undetected in symptomatic cases were observed in multiple years. We show that a significant majority of 1° infections remained inapparent: 77% for DENV1, 80% for DENV2, and 64% for DENV3. DENV3 exhibited the highest likelihood of symptomatic and severe 1° infections (Pooled OR compared to DENV1 = 2.24, 95% CI 1.33-3.77, and 5.46, 1.50-19.89, respectively), whereas DENV2 had similar likelihood to DENV1 in both analyses. In conclusion, our study indicates that case surveillance skews the perceived epidemiological footprint of DENV and reveals a more complex and intricate pattern of serotype distribution in inapparent infections. Further, the significant differences in infection outcomes by serotype emphasize the importance of serotype-informed public health strategies.

8305

UNVEILING THE DYNAMICS OF DENGUE VIRUS TRANSMISSION ACROSS A GRADIENT OF URBANICITY IN THREE COUNTRIES: INSIGHTS FROM PARALLEL LONGITUDINAL COHORT STUDIES IN ECUADOR, NICARAGUA, AND SRI LANKA

Paulina E. Andrade Proano[1], Lisbeth Cantarero[2], Chandima Jeewandara[3], Sandra Vivero[4], Victoria Nipaz[4], William Cevallos[4], Miguel Plazaola[2], Juan Carlos Mercado[2], Luis Cisneros[2], Gabriel Trueba[5], Shyrar Tanussiya Ramu[3], Saubhagya Danasekara[3], Madushika Dissanayake[3], Lahiru Perera[3], Maneshka Karunananda[3], José G. Juárez[2], Joseph N.S. Eisenberg[6], Neelika Malavige[3], Angel Balmaseda[2], Josefina Coloma[7], Eva Harris[7]

[1]Universidad San Francisco de Quito, Quito, Ecuador, [2]Sustainable Sciences Institute, Managua, Nicaragua, [3]Department of Immunology and Molecular Medicine, University of Sri Jayewardenepura, Colombo, Sri Lanka, [4]Centro de Biomedicina, Universidad Central, Quito, Ecuador, [5]Instituto de Microbiología, Universidad San Francisco de Quito, Quito, Ecuador, [6]Department of Epidemiology, School of Public Health, University of Michigan, Ann Arbor, MI, United States, [7]Division of Infectious Diseases and Vaccinology, School of Public Health, University of California, Berkeley, Berkeley, CA, United States

In recent years, dengue has expanded into rural areas worldwide, challenging its traditional conception as an urban disease. The Asian-American Centers for Arbovirus Research and Enhanced Surveillance (A2CARES) of the NIH Centers for Research in Emerging Infectious Diseases (CREID) Network aims to understand dengue virus (DENV) transmission dynamics and seroprevalence in parallel longitudinal cohort studies across a gradient of urbanicity, encompassing forest edge/remote and urban areas in Ecuador and peri-urban and urban areas in Nicaragua and Sri Lanka. Central to A2CARES is technology transfer and harmonization of DENV serological assays across sites. Here, we implemented the same in-house DENV Capture IgG ELISA across sites and transferred a DENV Inhibition ELISA (iELISA) established in Nicaragua to all partners. Each A2CARES cohort includes ~2,000 participants aged ~2-80 years and yearly serosurveys in inter-epidemic periods in addition to case surveillance. Seroprevalence analysis revealed that forest edge and remote areas in Esmeraldas, Ecuador, have seroprevalence rates (79-92%), as high as urban areas in Managua, Nicaragua (88%), and even Colombo, Sri Lanka (96%), where the population sampled was substantially older and has higher densities. By age 21, nearly all individuals in all three sites had been exposed to DENV, regardless of their rurality/urbanicity status. The average age of infection for Ecuador, Nicaragua and Sri Lanka was 20, 29 and 45 years old, respectively. Analysis of primary and secondary DENV infections using the iELISA revealed that the forest edge/remote area of Ecuador had

the highest number of primary infections (48%) when compared to urban and peri-urban areas in Nicaragua (32%) and Sri Lanka (33%), suggesting more recent introduction of DENV. This study highlights the value of comparative analysis using integrated methods and cohort studies across continents, as well as the need for continued research to understand the evolving dynamics of DENV transmission in different settings. Together, our results fundamentally challenge the concept of dengue as an urban disease.

8306

RESPIRATORY SYNCYTIAL VIRUS (RSV) EPIDEMIOLOGY AND CLINICAL CHARACTERISTICS OF HOSPITALIZED CHILDREN < 2 YEARS OF AGE DURING THE SARS-COV-2 PANDEMIC (OCTOBER 2020-JANUARY 2023) AT KENEMA GOVERNMENT HOSPITAL, SIERRA LEONE

Foday Umaro Turay[1], Troy Moon[1], Gustavo Amorim[2], Robert J. Samuels[3], John S. Schieffelin[1]

[1]Tulane University, New Orleans, LA, United States, [2]Vanderbilt Institute for Global Health, Vanderbilt University, Nashville, TN, United States, [3]College of Medicine and Allied Health Sciences, University of Sierra Leone, Free Town, Sierra Leone

Respiratory Syncytial Virus (RSV) is a leading cause of acute lower respiratory tract infections in children under five years of age, resulting in significant morbidity and mortality worldwide. This study aimed to investigate the prevalence and clinical features of RSV disease in hospitalized infants in Sierra Leone. A prospective study was conducted on children under 2-years of age who were hospitalized at Kenema Government Hospital between October 1, 2020, and January 31, 2023. A total of 912 children participated in the study, with 147 (16.1%) testing positive for RSV. Of these, 106 (72.1%) were attributed to RSV-A, and 41 (27.9%) to RSV-B. The distribution of RSV exhibited distinct seasonal patterns, with fluctuations in transmission rates corresponding to climatic and environmental factors. During the rainy seasons of both 2021 and 2022 (May to November), we observed a surge in RSV cases, particularly those attributed to RSV-A. Conversely, RSV activity during the dry season (December to April) was relatively lower. In multivariable In logistic regression, detection of RSV-B was significantly associated with a higher severity score and increased likelihood of requiring oxygen therapy or referral to the ICU. younger age was significantly associated with a higher likelihood of requiring oxygen therapy, referral to the ICU, and higher severity scores. These findings highlight the importance of early detection and prompt treatment in young children infected with RSV, as they are at a higher risk of developing severe illness. In conclusion, our study provides valuable insights into the epidemiology and clinical characteristics of RSV in hospitalized children under 2 years of age in Sierra Leone. RSV-A was found to be associated with more severe respiratory illness compared to RSV-B, and both types of RSV showed a seasonal pattern, with a peak during the rainy season. These findings highlight the need for continuous surveillance and monitoring of RSV infections, especially during the peak and transitional seasons, to inform public health interventions and reduce the burden of RSV on children's health.

8307

EPIDEMIOLOGICAL CHARACTERISTICS AND HOSPITAL OUTCOMES OF HOSPITALIZED LASSA FEVER CASES DURING THE 2022-2023 OUTBREAK IN LIBERIA

Emmanuel Dwalu[1], Hannock Tweya[2], Mher Beglaryan[3], Chukwuma D. Umeokonkwo[4], Ralph W. Jetoh[1], Bode I. Shobayo[1], Fahn M. Tarweh[1], Philip Owiti[5], Pryanka Relan[6], Shermarke Hassan[7], George W. Goteh[8], Darius B. Lehyen[8], Louis Ako-Egbe[9], Ibrahim F. Kamara[10], Godwin E. Akpan[11], Peter Adewuyi[11], Patrick N. Kpanyen[1], Benjamin T. Vonhm[1], Julius S M Gilayeneh[1]

[1]National Public Health Institute of Liberia, Monrovia, Liberia, [2]International Training and Education Center for Health (I-TECH), Lilongwe, Malawi, [3]Tuberculosis Research and Prevention Centre, Yerevan 0014, Armenia, [4]African Field Epidemiology Network, Lugogo House, Lugogo By-Pass, Kampala, Uganda, [5]Ministry of Health Republic of Kenya, Nairobi, Kenya, [6]WHO Health Emergencies Programme, World Health Organization, Geneva, Switzerland, [7]Infectious Diseases Data Observatory, University of Oxford, Oxford, United Kingdom, [8]Ministry of Health, Monrovia, Liberia, [9]World Health Organization Liberia Country Office, Monrovia, Liberia, [10]World Health Organization Country Office, Freetown, Sierra Leone, [11]African Field Epidemiology Network, Monrovia, Liberia

Lassa fever is an endemic and immediately notifiable disease in Liberia, and one laboratory confirmed case constitutes an outbreak. We described the epidemiological characteristics and hospital outcome of Lassa fever cases hospitalized during the 2022-2023 outbreak in Liberia.We conducted a retrospective cohort study using routine Lassa fever surveillance data from the 2022-2023 outbreak in Liberia. Descriptive statistics were used to summarize the data and log binomial regression to assess the association between epidemiological characteristics and mortality. A total of 439 suspected Lassa fever cases were reported. The median age was 22 (interquartile range: 10-33) years and 233 (53%) were women. The median number of days between symptom onset and admission was 4 (IQR 2-7). Of the 439 cases, 416 (95%) were tested for Lassa fever and 138 were confirmed with 33% positivity rate. The majority, 290 (69%), of confirmed cases were <30 years, 78 (57%) were females, and 81 (59%) were reported during the dry season (October – March). Contact with rodents, 94 (89%), was the commonest mode of exposure. Fever, 128 (93%), malaise, 121 (88%), headache, 114 (83%) and myalgia, 114 (83%) were the most common clinical characteristics. There were 83 (19%) deaths among hospitalized suspected Lassa fever cases - 42 deaths (15%) among 278 individuals who tested negative and 41 among confirmed cases with 30% case fatality rate (CFR). The highest CFR was recorded among those aged 40-49 years, 8 (67%) and those aged≥50, 5 (63%). There was no significant association between epidemiological characteristics and Lassa fever mortality.The outbreak highlighted a high disease burden of Lassa fever with young adults disproportionately infected, and substantial mortality, even among those who tested negative for the virus. This underscores the urgent need for preventive measures like vaccines and health education campaigns.

8308

INCIDENCE OF LASSA FEVER DISEASE AND LASSA VIRUS INFECTION IN FIVE WEST AFRICAN COUNTRIES: A PROSPECTIVE, MULTI-SITE, COHORT STUDY (THE *ENABLE* LASSA RESEARCH PROGRAM)

Anton Camacho[1], *The ENABLE Consortium*[2]

[1]Epicentre, Paris, France, [2] Coalition for Epidemic Preparedness Innovations (CEPI), Oslo, Norway

Lassa fever (LF), a haemorrhagic illness caused by the Lassa fever virus (LASV), is endemic in West Africa causing an estimated 100 000 to 300 000 cases and 5 000 fatalities every year. LF is a WHO priority pathogen for vaccine development due to its pandemic potential. However, vaccine trial design requires accurate prevalence and incidence data, challenging due to asymptomatic infections and varied clinical presentations. The Enable Lassa program aims to estimate LASV infection and LF disease incidences in five West African countries. We conducted a prospective cohort study in communities known to be LF hotspots in Benin, Guinea, Liberia, Nigeria (three sites) and Sierra Leone from 2021 to 2023, with a 24-month follow-up. Household surveys collected demographic and LF risk factors, while blood samples determined LASV IgG serostatus. Febrile cases were tested biweekly with LASV RT-PCR for LF disease, and a subset of participants provided blood samples every six months for IgG serostatus assessment. We enrolled 23,193 participants overall. Baseline seroprevalence was low (<15%) in Benin and one Nigerian site, intermediate (15%-30%) in Guinea and Sierra Leone, and high (>30%) in Liberia and the other two Nigerian sites. Adjusted seroprevalence increased with age (p<0.001). Overall, 39 confirmed LF cases were detected over 2 years: 2 in Benin, 14 in Liberia and 23 in Nigeria, corresponding to an incidence rate of respectively 0.23 (95% CI: 0.03 - 0.81), 1.45 (95% CI: 0.79 - 2.44) and 1.90 (95% CI: 1.20 - 2.85) per 1000 person-years. Serology testing will be completed for ASTMH conference but preliminary results suggest that LASV infection is much more common than LF disease. This is the first epidemiological study

to measure the incidence of LF disease and LASV infection in West Africa. Our results suggest that pre-exposure to LASV may temporarily reduce the risk of LF disease. Finally, we found evidence that children may be at greater risk of LF disease than adults due to lower pre-exposure. Our results are currently being used to inform the design of future vaccine efficacy trials.

8309

THE COMPOUND EFFECTS OF CLIMATIC EXTREMES ON DENGUE RISK IN THE CARIBBEAN: A PREDICTION MODEL FRAMEWORK USING LONG- AND SHORT-LAG INTERACTIONS

Chloe Fletcher[1], Tilly Alcanya[2], Leslie Rollock[3], Cédric J. Van Meerbeeck[4], Laura-Lee Boodram[5], Tia Browne[6], Sabu Best[6], Roché Mahon[4], Adrian Trotman[4], Avriel R. Diaz[7], Willy Dunbar[8], Catherine A. Lippi[9], Sadie J. Ryan[9], Felipe J. Colón-González[10], Anna M. Stewart-Ibarra[11], Rachel Lowe[12]

[1]Barcelona Supercomputing Center, Barcelona, Spain, [2]Centre on Climate Change & Planetary Health and Centre for Mathematical Modelling of Infectious Diseases, London School of Hygiene & Tropical Medicine, London, United Kingdom, [3]Ministry of Health & Wellness, Saint Michael, Barbados, [4]Caribbean Institute for Meteorology and Hydrology, Saint James, Barbados, [5]The Caribbean Public Health Agency, Port of Spain, Trinidad and Tobago, [6]Barbados Meteorological Services, Christ Church, Barbados, [7]International Research Institute for Climate & Society, Palisades, NY, United States, [8]National Collaborating Centre for Healthy Public Policy, Montreal, QC, Canada, [9]Department of Geography, University of Florida, Gainsville, FL, United States, [10]Wellcome Trust, Data for Science and Health, London, United Kingdom, [11]Inter-American Institute For Global Change Research, Montevideo, Uruguay, [12]Catalan Institution for Research & Advanced Studies, Barcelona, Spain

Weather and climate extremes have detrimental health impacts through increased risk of injury, displacement, adverse mental health, food insecurity, respiratory illness and infectious disease. Small islands in the Caribbean are highly vulnerable to increasingly frequent and intense events, which can exacerbate outbreaks of arboviral diseases such as dengue. Disease risk drivers are often complex, delayed and interacting. To date, few operational forecasting tools that consider the compound effects of climatic extremes using long-lag and short-lag interactions have been created. Here, we developed a modelling framework to predict the probability of a climate-sensitive disease outbreak 3 months ahead in a small island setting, focusing on dengue in Barbados. Using confirmed cases from 1999 to 2022, we tested combinations of interacting long- and short-lag meteorological predictors within a Bayesian hierarchical mixed model, controlling for seasonal and interannual variation. We found that a three-way interaction between 3-month averaged mean temperature (lagged 3 to 5 months), 6-month standardised precipitation index (SPI-6) (lagged 5 months) and SPI-6 (lagged 1 month) best predicted dengue risk in Barbados. This is consistent with previous research showing elevated outbreak risk following long-lag dry and short-lag wet conditions using distributed lag nonlinear models. However, our methodology explicitly accounts for the interacting effects of temperature, drought and excessive wetness on dengue outbreaks in Barbados. We used this model to create a dengue prediction framework that estimates the probability of exceeding a predefined epidemic threshold 3 months in advance. These probabilities translate to outbreak risk levels that link to national guidance on public health interventions set by the Barbados Ministry of Health & Wellness. This scheme was adopted for the recently launched climate-integrated dengue early warning system in Barbados to produce monthly forecasts. The framework was also deployed to forecast dengue risk over the Caribbean during the International Cricket Council Men's Twenty20 World Cup 2024.

8310

MASSIVE GLOBAL IMPACTS OF CLIMATE CHANGE ON DENGUE TRANSMISSION

Erin Mordecai[1], Marissa Childs[2], Kelsey Lyberger[1], Mallory Harris[1]

[1]Stanford University, Stanford, CA, United States, [2]Harvard University, Cambridge, MA, United States

Climate change is having pervasive impacts on health, but its impacts on infectious disease transmission are often difficult to quantify, predict, and attribute in the face of multiple concurrent changes. Thermal biology predicts that warming temperatures have a nonlinear effect on mosquito-borne disease transmission, and despite empirical and theoretical support from laboratory studies, evidence of nonlinear effects of warming on disease transmission in the field remains rare. Here, we compiled a global dataset on monthly, sub-country dengue incidence from 21 countries over an average of 11 years and performed a population-weighted Poisson fixed effects panel regression to identify the causal effects of temperature warming on dengue. Supporting predictions from thermal biology, we found that dengue incidence peaked at 28ºC and that warming had the largest effect at 15-20ºC, where temperature is most limiting to transmission. Using a counterfactual historical climate scenario, we found that anthropogenic warming that has already occurred is responsible for 19% of the existing dengue burden, and this ranges up to 30-40% of the burden in some cooler locations in Latin America. After accounting for underreporting, we estimate that climate change is already responsible for over 45 million cases per year. By midcentury under a high emissions scenario (SSP3-7.0), we expect dengue burden to increase by 61% on average and to more than double in some cooler regions, where over 257 million people live. By contrast, mitigating carbon emissions (SSP1-2.6) reduces this increase in dengue by 18%, indicating a substantial public health benefit of slowing climate change. This work paves the way for climate change attribution of infectious diseases and provides some of the first rigorous evidence that warming-driven increases in dengue are already underway.

8311

MAPPING THE GLOBAL ENVIRONMENTAL SUITABILITY FOR SCRUB TYPHUS

Qian Wang[1], Tian Ma[2], Fangyu Ding[2], Nicholas Day[1], Benn Sartorius[3], Richard Maude[1]

[1]MORU, Bangkok, Thailand, [2]Chinese Academy of Sciences, Beijing, China, [3]University of Oxford, Oxford, United Kingdom

Scrub typhus (ST) is a neglected vector-borne infectious disease that causes epidemics in many parts of the Asia-Pacific region. The absence of specific symptoms and lack of awareness lead to underdiagnosis and chronic underreporting. It has seroprevalence of 23.11% among febrile patients and a median mortality of 5.00%. The disease's vectors, larval mites (chiggers), are widespread, exposing vast populations to risk. Recent outbreaks in non-endemic areas underscored significant knowledge gaps regarding the true extent and distribution. Here, we undertook an exhaustive assembly of known human ST occurrence records worldwide and combined it with environmental covariates using an ensemble modelling framework to map the probability of occurrence at 5 × 5-km globally. This dataset compiled 10,586 unique human occurrence locations across 27 countries/regions from 2000 to 2020, along with 28 climatic, geographic, and socio-economic covariates. We employed an ensemble machine learning approach to capture possible nonlinear effects and complex interactions. This approach involved stacking of three sub-models (generalized additive models, boosted regression trees and random forest). The fivefold cross-validation was utilized to improve performance and avoid overfitting. Our findings reveal that ST suitability is highest in moderate to tropical climates, notably extending beyond the classic "tsutsugamushi triangle" into large sections of South America, Central Africa, and Southeast Asia. Based on a suitability probability threshold >0.5, Brazil, Australia, America, India, the Democratic Republic of the Congo, Mexico, Sudan, Indonesia, Argentina, and China were identified as the most at-risk countries, with most never having reported a case, expect Australia, India,

Indonesia, and China. This data assembly and modelled occurrence risk surface provide novel insights into the public health impact of ST, and we foresee this serving as a catalyst for broader discussions regarding the potential global impact of this disease, improve public awareness, drug and vector control methods, and leading to further burden assessment.

8312

HETEROGENOUS SPATIO-TEMPORAL DISTRIBUTION OF COVID-19 PANDEMIC PROGRESSION IN PERU

Kasandra Lizzeth Ascuña-Durand[1], Diego Villa[1], Coralith García[2], Gabriel Carrasco-Escobar[1]

[1]Health Innovation Laboratory, Universidad Peruana Cayetano Heredia, Peru, Lima, Peru, [2]Instituto de Medicina Tropical Alexander von Humboldt, Universidad Peruana Cayetano Heredia, Peru, Lima, Peru

Socioeconomic and demographic factors play a key role in spreading infectious diseases, exhibiting specific geographical and temporal dynamics that contribute to understanding the emergence of a pandemic. Peru, characterized by socioeconomic and health policy divisions, experienced significant impacts during the COVID-19 crisis. Despite government efforts, the pandemic's effects were not uniform across the country. The main objective of this study was to explore epidemiological data to identify clusters that help explain the spatiotemporal heterogeneity in the pandemic's dispersion in Peru. We analyzed Peruvian Ministry of Health data, including COVID-19 cases, deaths, hospitalizations, and vaccine doses. Using agglomerative hierarchical analysis, we identified an optimal number of clusters that best represent the dynamics of Peruvian provinces during the pandemic. Finally, we characterize the clusters using socioeconomic variables. The 196 Peruvian provinces were classified into five clusters, explaining the epidemiological behavior of the pandemic. Significant differences were identified among the clusters, highlighting marked geographic variability. Clusters located in the Peruvian central highland experienced milder pandemic effects, marked by lower economic activity and population density. This likely influenced lower virus spread. More urbanized provinces that have larger populations in main cities with higher economic resources experienced more cases and deaths in their clusters, facing more severe consequences during the pandemic. We also analyzed hospitalization and vaccine dose indicators. This research enables us to categorize and characterize Peruvian provinces using diverse epidemiological indicators and socioeconomic features, revealing trends that could drive a better distribution of resources in low and middle-income countries. Therefore, this scope highlights the potential to integrate this data for a better approach to epidemiological studies and implement adequate strategies for preventing and controlling other infectious diseases developed under similar conditions.

8313

ASSESSING THE IMPACT OF CLIMATE CHANGE ON VECTOR BEHAVIOR AND VECTOR CONTROL STRATEGIES

Emma L. Fairbanks[1], Janet M. Daly[2], Michael J. Tildesley[1]

[1]University of Warwick, Coventry, United Kingdom, [2]University of Nottingham, Nottingham, United Kingdom

Vector-borne diseases constitute about 17% of global infectious diseases, significantly impacting health and economic progress. With climate change and increased global mobility, these diseases increasingly threaten human and animal health, as well as food security. Vectorial capacity, defined as the total number of potentially infectious bites that would eventually arise from all the mosquitoes biting a single host on a single day, quantifies the potential of vector populations to transmit pathogens. Existing models of vectorial capacity vary, typically focusing on singular phenomena such as climatic factors or vector control measures. However, the interplay between these elements remains underexplored. We developed an integrated model of vectorial capacity that synthesises elements from previous models while introducing novel considerations of vector behaviours, including the impact of climate on vector control strategies and the effects of multiple feeding behaviours within a single gonotrophic cycle. Utilising historical climate data this model can then be used to observe historic changes in vectorial capacity and identify effective vector control strategies. Our findings indicate that regions previously free from or only sporadically affected by vector-borne diseases have experienced an increase in vectorial capacity over the past fifty years. This trend suggests a likely increase in the frequency of disease outbreaks in these areas. Effective disease control programs will require enhanced coverage and adherence to mitigate the effects of climate change on disease burden. Our analysis further demonstrates that vector control is particularly effective against vectors that exhibit multiple feeding behaviour per gonotrophic cycle. The increasing vectorial capacity driven by climate change poses significant economic and public health challenges globally. Moreover, our results highlight the increased efficacy of vector control measures against vectors with multiple-feeding behaviours, which could inform the development of more effective disease mitigation strategies.

8314

PRESSURE-TESTING AND PROTOTYPING AI TOOLS FOR ENHANCED QUALITATIVE DATA ANALYSIS IN GLOBAL HEALTH: A CASE STUDY ON DRC VACCINATION SURVEYS

Roy Burstein, Joshua L. Proctor

Bill & Melinda Gates Foundation, Seattle, WA, United States

The Democratic Republic of the Congo is currently facing multiple disease outbreaks driven by low rates of childhood vaccination. Understanding the barriers to immunization services is key to effectively adapting the immunization program. Detailed information on reasons for non-vaccination exists in free-text responses to survey questions but analysis of such data is resource-intensive and often infeasible. This study evaluates the use of large language models (LLMs) to analyze qualitative responses from caregivers, surveyed nationally in three rounds during 2020-2023. The surveys revealed a vaccination rate of 40% and considered 29 categories of reasons for non-vaccination. Approximately 8,000 responses selected 'other' and entered free text, requiring deeper analysis. We employed multiple methodological approaches, ex., combining natural language processing (NLP) techniques with the generative capabilities of GPT-4, to categorize responses and identify novel, emergent themes. The AI-assisted computational workflow can be executed quickly and with an ~85% accuracy rate benchmarked against a human intelligence (HI) evaluation of 1000 responses. The AI assistant successfully classified responses into both existing categories and identified insightful new categories such as "Number of children present does not warrant opening a new vaccination vial". We also identified and quantified the limitations of this approach with regards to choice of LLM, model parameters, and prompt engineering designs. The integration of LLMs like GPT-4 with NLP methodologies presents a promising avenue for analyzing vast amounts of unstructured qualitative data in global health. It facilitates the discovery of nuanced factors influencing vaccination rates, which traditional survey data analysis might overlook. This study demonstrates the potential of AI in streamlining data analysis in global health research and underscores the opportunity for building new data collection instruments that incorporate LLMs to generate more granular insights. The adaptability of AI tools suggests broad applicability across diverse studies.

8315

AN AI ASSISTANT TO SUPPORT DISEASE MODEL BUILDING, SIMULATION, AND ANALYSIS: ACCELERATING MODELING RESEARCH AND DEVELOPMENT IN RESOURCE-CONSTRAINED SETTINGS

Joshua L. Proctor, Guillaume Chabot-Couture

Bill & Melinda Gates Foundation, Seattle, WA, United States

Dynamic disease modeling is an essential tool in understanding and predicting disease patterns, aiding in the planning and implementation of health interventions. However, the complexities involved in building and running these models, including the need for specialized training and software, can be prohibitive, especially in resource-constrained settings. We propose an AI-based modeling assistant, leveraging OpenAI's latest

models and API features, including file retrieval, code analytics, and custom functions. The assistant is designed to leverage existing disease model simulation engines and enable users to either build model and configuration files from natural language prompts or import a document that includes an explicit model description. For this proof-of-concept, we leverage existing and open-source disease simulation engines like the Compartmental Modeling Software (CMS). Our AI assistant facilitates the entire process from characterization to execution and analysis of disease models. It correctly interprets model specifications, produces a syntactically correct model files, runs simulations using a dockerized CMS, and analyzes results with the aid of Code Analytics for plotting and downstream analysis. The AI assistant incorporates expert knowledge and established best practices, offering customized support for users at various skill levels, from those merely model-curious to seasoned disease modelers. We also identify the current limitations of the assistant, i.e., when the assistant begins to hallucinate with the specification of complex system setup. By democratizing access to disease modeling and augmenting existing capacity-building activities such as training and workshops, this AI assistant represents a significant step toward enhancing global disease modeling capabilities. It empowers researchers in resource-limited settings with the ability to rapidly and independently iterate on building models for their own use-cases. This is a novel approach in disease modeling research, with potential broad-reaching implications for global health.

8316

THE MOST FORETOLD HUMAN RABIES CASE IN LATIN AMERICA VIEWED UNDER THE ONE HEALTH APPROACH

Ricardo Castillo-Neyra[1], Lizzie Ortiz-Cam[2], Elvis W. Diaz[2], Sherrie Xie[1], Jorge Cañari[2], Valerie Paz-Soldán[3], Sergio E. Recuenco[4]

[1]University of Pennsylvania, Philadelphia, PA, United States, [2]Universidad Peruana Cayetano Heredia, Lima, Peru, [3]Tulane University, New Orleans, LA, United States, [4]Universidad Nacional Mayor de San Marcos, Lima, Peru

In 2014, a rabid dog was detected in Arequipa, Peru, signaling the first reintroduction of the virus to an area previously declared rabies-free in Latin America. Since then, a combination of reactive ring vaccination, city-wide mass vaccination campaign, community-based and spatially targeted surveillance activities, and education campaigns have been conducted. However, the number of detected rabid dogs has remained constant for years, culminating in the first detected human rabies case reported in October 2023, in Arequipa. We aimed to integrate epidemiological, socio-ecological, and policy data to understand the conditions leading to this human rabies case and potential future cases, threatening the goal of zero dog-mediated human cases by 2030. We conducted multi-year surveys combined with qualitative studies to understand barriers to dog vaccination; visited the 'grout' of the city (e.g., water channels, periphery) to characterize the ecology of free-roaming dogs; and evaluated surveillance efforts, dog rabies incidence, and socio-economic status (SES) to estimate social and spatial inequities associated with rabies. We discovered feral dogs living in caves around the city. We found behavioral, logistical, and geographical barriers that prevent owners from vaccinating their dogs, but also revealed organizational, economic, and operational barriers that impede the optimization of mass vaccination campaigns. We found a strong negative association between SES, rabies incidence, and surveillance efforts, evidencing deep social and spatial inequities associated with rabies. Dog-mediated human rabies remains being neglected globally, potentially due to its elimination from high-income countries. We report for the first time that for dog rabies inequities are also present within very fine spatial scales. Challenges to reaching herd immunity exist both in communities and implementing organizations. The presence of cave-dwelling dogs poses new One Health challenges. Our data show that the persistence of conditions that led to the 2023 human case threatens the prospects of eliminating dog-mediated human rabies by 2030.

8317

ONE HEALTH SURVEILLANCE APPROACH ILLUMINATES SILENT SLEEPING SICKNESS TRANSMISSION HOTSPOTS IN HAMLETS OF OYO STATE, NIGERIA

Rolayo Toyin Emmanuel[1], Yahaya A. Umar[2], Philip A. Vantsawa[2], Deborah M. Dibal[2], Kelly Zongo[3], Olaleye O. Olusola[4], Temitope O. Popoola[4]

[1]Nigerian Institute for Trypanosomiasis and Onchocerciasis Research, Kaduna, Nigeria, [2]Department of Biological Sciences, Faculty of Science, Nigerian Defence Academy, Kaduna, Nigeria, [3]The END Fund, New York, NY, United States, [4]Nigerian Institute for Trypanosomiasis and Onchocerciasis Research, Ibadan, Nigeria

Approximately 55 million individuals in sub-Saharan Africa face the peril of contracting sleeping sickness (SS). Its occurrence is driven by an epidemiologic triad comprising *Trypanosoma brucei gambiense*, tsetse flies, humans, animals, and a propitious environment. Despite advancements in diagnostics, the actual status of SS in Nigeria remains elusive. In our quest for clarity, we embraced a holistic approach: one health surveillance comprising human and animal population surveys, entomological and ecological assessments to illuminate SS transmission hotspots and risk factors in sparsely-populated remote rural hamlets. To do this, we collected blood samples from 72 consenting humans and 145 animals. Furthermore, tsetse flies were captured using odor-baited traps, and species diversity and spatial distribution were assessed. Captured tsetse flies, human and animal blood samples were screened for *T. b. gambiense* infection, and sources of tsetse bloodmeal were identified using colorimetric Loop-mediated amplification respectively. Captured tsetse flies were *Glossina palpalis palpalis* with 16.90% *T. b. gambiense* infection rate. Humans were preferred bloodmeal source (41.67%, p= 0.010). Alaho has the highest tsetse fly density of 10.33 flies/trap/day, highest human-tsetse fly contact and transmission risk index of 80787.31. Anthropogenic activities and ecological conditions were found to impact tsetse fly density ($p < 0.0001$). The prevalence of *T. b. gambiense* among humans and domestic animals was 40.28% and 40.69% respectively. Illiteracy (p= 0.01) and defecation in forests (p= 0.0004) were major determinants of SS occurrence. We identified thirteen SS transmission hotspots. Correlation exist between humans, animals and tsetse fly infection ($p < 0.0001$) depicting one health implication. Silent transmission of SS is ongoing warranting intensified sensitization and surveillance. Animals serve as reservoir hosts aiding persistence of SS in the hamlets. An urgent one health and WASH-guided strategic control approaches are imperative to prevent SS epidemic in the hamlets and devastating resurgence in Nigeria.

8318

MORPHOLOGICAL AND MOLECULAR IDENTIFICATION OF *B. MALAYI* AND OTHER FILARIAL SPECIES IN ANIMALS FROM BELITUNG, INDONESIA: IMPLICATIONS FOR LYMPHATIC FILARIASIS ELIMINATION

Irina Diekmann[1], Kerstin Fischer[1], Taniawati Supali[2], Peter Fischer[1]

[1]Infectious Diseases Division, Department of Medicine, Washington University School of Medicine, St. Louis, MO, United States, [2]Department of Parasitology, Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia

In Indonesia, *Brugia malayi* is the most common filarial parasite causing lymphatic filariasis (LF) in humans. Belitung District was considered free of LF in 2017 after 5 rounds of mass drug administration (MDA) and 3 transmission assessment surveys (TAS). However, surveys in 2021 and 2022 revealed microfilaria (Mf) rates exceeding 1% in some villages. This study investigates the presence of *B. malayi* and other filarial species in potential animal reservoirs comparing microscopy and real-time PCR targeting filarial, *B. malayi*, *Brugia pahangi* and *Dirofilaria immitis* DNA. Blood samples were collected from 495 animals in villages with and without human LF infections. PCR showed a higher detection rate (94%) compared to microscopy (78%) for identifying any filarial infection in blood. It also showed a higher detection rate in identifying different filarial species. Using PCR *B. malayi* was detected in 7.1% (35/495) of all the samples.

Infection rate in cats was 4.1% (12/291), 2.4% (1/41) in dogs, and 13.5% (22/163) in macaques. *B. pahangi* DNA was only found in 5.1% (17/332) of dog and cat samples while *D. immitis* DNA was exclusively detected in 39% (16/41) of the dog samples. Using microscopy an unknown *Dirofilaria* species was found in 20.3% (33/163) of the macaque samples that could not be speciated and has not been characterized molecularly previously. Morphologically, a co-infection in one dog with *B. malayi* and *D. immitis* was observed, but PCR only detected *B. pahangi* and *D. immitis* DNA. By microscopy identified as a single infection, PCR detected dual co-infections in one cat (*B. malayi*/*B. pahangi*) and one dog (*B. pahangi*/*D. immitis*) and a triple co-infection in one dog. The highest mean *B. malayi* Mf density was found in macaques (712 Mf/mL, N=22), which was even higher compared to the mean Mf density in humans (583 Mf/mL, N=42) living in the same area. This study highlights the need for molecular methods to accurately identify Mf, particularly due to multiple filarial species found in animals. In order to eliminate LF in humans enhanced surveillance and intervention may be required in areas with animal reservoirs, especially in those with macaques.

8319

PAN-CANADIAN RESPONSE TO HIGHLY PATHOGENIC AVIAN INFLUENZA (HPAI) A(H5N1): BENEFITS AND CHALLENGES OF A ONE HEALTH APPROACH

Peter A. Buck[1], *Clarice Lulai-Angi*[2], *Cynthia Pekarik*[3], *Yohannes Berhane*[4], *Jennifer Provencher*[5], *Erin Leonard*[6], *Jolene Giacinti*[5], *Andrea Osborn*[7], *Amole Khadilkar*[8], *Nicole Atchessi*[1], *Trevor Thompson*[3], *Michael Brown*[3], *Cathy Furness*[9], *HPAI One Health Fed-Prov-Terr-Indigenous WorkGroup*[10]

[1]Public Health Agency of Canada, Ottawa, ON, Canada, [2]Canadian Food Inspection Agency, Ottawa, ON, Canada, [3]Environment and Climate Change Canada, Gatineau, QC, Canada, [4]Canadian Food Inspection Agency, Winnipeg, MB, Canada, [5]Environment and Climate Change Canada, Ottawa, ON, Canada, [6]Public Health Agency of Canada, Halifax, NS, Canada, [7]Canadian Food Inspection Agency, Parksville, BC, Canada, [8]Indigenous Services Canada, Ottawa, ON, Canada, [9]Canadian Food Inspection Agency, Guelph, ON, Canada

Human and animal health are interdependent and linked to the ecosystems where they coexist. Wild birds, especially waterfowl, are considered natural reservoirs for avian influenza A viruses, such as the currently circulating highly pathogenic avian influenza (HPAI) A(H5N1). This virus was introduced into Canada in Autumn 2021 through wild bird migration and quickly spilled-over into domestic poultry by December 2021. Infections in other species that eat wild birds or are exposed to common contaminated environments such as cats, red foxes, skunks, raccoons, and marine mammals have been reported during the current outbreak. Increased infections in birds and non-human mammals, and the prolonged duration of the epizootic provides more opportunity for replication and mutation of the virus. To date, while human infections with the current strain of A(H5N1) have been rare, the virus has the potential to cause serious disease in people. Concerns regarding A(H5N1) are wide-ranging, and include: animal health and wellbeing; business and employment; food systems, safety and security, including traditional foods of Indigenous and Inuit Peoples; value chain impacts and international trade; wildlife susceptibility in endangered and at-risk species; and, mental health and wellbeing of individuals in many sectors. A One Health approach, involving a network of partners and stakeholders has been taken in Canada through a range of activities, including: development of surveillance plans in wild birds; on-farm response and control; multisectoral research to explore the link between domestic and wild birds; prioritization exercises to inform surveillance and research; development of risk communications and guidance for key audiences, including the public; sharing of intelligence through cross-sector multidisciplinary Working Groups; and, international reporting and collaboration. This presentation will describe a range of benefits and challenges associated with taking a One Health approach for the prevention, response and control of HPAI A(H5N1) in the Canadian context.

8320

A ONE HEALTH APPROACH IN DETECTION OF INFECTIOUS DISEASES IN NORTHERN GHANA

Deborah Narwortey[1], Bernice Baako[1], John Zing[1], Felix Nenyewodey[1], Seth Offei Addo[2], Stephen Kantum Adageba[1], Simon Bawa[1], Michael Bandasua Kaburise[1], Francis Broni[1], Cornelius Debpuur[1], Ali Moro[1], Jane Ansah-Owusu[2], Samuel Dadzie[3], Victor Asoala[1], Patrick Odum Ansah[1], Zahra Parker[4], Abdulwasiu Bolaji Tiamiyu[5], Edward Akinwale[5], Kara Lombardi[6], Leigh Anne Eller[6], Erica Broach[6], Anastasia Zuppe[6], Tsedal Mebrahtu[6], Qun Li[6], Jillian Chambers[6], Nicole Dear[6], Ana Manzano-Wight[6], Jenny Lay[6], Terrel Sanders[7], Robert Hontz[7], David B. Pecor[8], Cynthia L. Tucker[8], Sherri Daye[9], Hee Kim[9], Yvonne-Marie Linton[10], Thierry Lamare Assedi Njatou Fouapon[11], Melanie D. McCauley[6]

[1]Navrongo Health Research Centre, Navrongo, Ghana, [2]Noguchi Memorial Institute for Medical Research, Accra, Ghana, [3]Noguchi Memorial Institute for Medical, Accra, Ghana, [4]Henry Jackson Foundation, Lagos, Nigeria, [5]HJF Medical Research International (HJFMRI), Abuja, Nigeria, [6]Henry M. Jackson Foundation for the Advancement of Military Medicine, Bethesda, MD, United States, [7]U.S. Naval Medical Research Unit-EURAFCENT, Accra, Ghana, [8]Walter Reed Biosystematics Unit (WRBU), Smithsonian Museum Support Center, Suitland, MD, United States, [9]One Health Branch, CIDR, Walter Reed Army Institute of Research, Silver spring, MD, United States, [10]Walter Reed Biosystematics Unit (WRBU), Smithsonian Museum Support Center, Suiltland, MD, United States, [11]One Health Branch, CIDR, Walter Reed Army Institute of Research,, Silver spring, MD, United States

Interactions between a pathogen, host, environment, and habitat disruption can provide opportunities for new or emerging disease spillover events. A collaborative One Health approach is needed to develop appropriate plans for response and control of some of these diseases. We investigated infectious etiologies of febrile illnesses among adults presenting at the War Memorial Hospital in Northern Ghana from May 2022 to June 2023. Those who presented with thermal dysregulation of ≤ 35.5°C or ≥ 38°C with unknown disease origin were enrolled. Confirmed zoonotic febrile cases triggered targeted entomological surveillance activities and enrollees were invited to participate in quantitative household surveys and purposive focal group discussions to investigate animal-rearing practices and socio-behavioral risk factors. In addition, weather monitoring stations were installed at three local senior high schools and data were collected daily as part of the students' science education. Malaria was detected in 50 (50%) of the enrolled febrile patients using the BioFire Global Fever Panel, with a notable increase during the rainy season. Of 2,369 mosquitoes collected using CDC light traps, 1,817 comprised Anopheles (76.7%), followed by Culex (20.7%) and Aedes (2.6%). Plasmodium falciparum infections were confirmed in 15/1185 (1.26%) of Anopheles tested - with positives identified only as An. gambiae s.s. and An. arabiensis by species-diagnostic PCR. Using the BioFire Respiratory Panel, the following viral infections were also detected: Hepatitis C virus (n=6), Influenza virus (n=4), Enterovirus (n=3), Human Immunodeficiency Virus (HIV) (3), Respiratory Syncytial Viruses (RSV) (n=3), Human Metapneumovirus (n=1), Parainfluenza virus (n=1) and SARS-COV-2 (n=3). Based on social surveillance interviews, close-contact animal housing withing within homesteads and uninspected meat consumption were found to constitute potential risks for pathogen transmission. This study illustrates the need for further multidisciplinary approaches that consider social and environmental factors to mitigate human and animal health threats in Ghana.

8321

THE ONE HEALTH INITIATIVE FOR ZOONOTIC DISEASE RESPONSE IN EASTERN UGANDA. OPPORTUNITIES AND AREAS FOR IMPROVEMENT

Richard Ssekitoleko[1], Herbert Isabirye[2], Benjamin Fuller[3], Margaret R Lawrence[3], Solome Okware[1], Annet Alenyo[1], Immaculate Atuhaire[1], Andrew Bakainaga[1], Elizabeth Mgamb[1], Yonas Tegegn Woldemariam[1], Christopher C. Moore[3]

[1]World Health Organization, Kampala, Uganda, [2]Infectious Disease Institute and the National Public Health Emergency Operations Center, Kampala, Uganda, [3]University Of Virginia, Charlottesville, VA, United States

The One Health initiative focuses on linkages of human, animal, and environmental health and is pivotal for global health security. Collaborative efforts in One Health are imperative to effectively address emerging health threats. We conducted an evaluation of the One Health initiative in the districts of Eastern Uganda, January to March 2024, targeting the pillars of zoonotic outbreak response including coordination, case management, surveillance, vaccination, and risk communication. Three outbreaks, anthrax in Bukedea and Kapchorwa, and rabies in Katakwi, occurred in 3 (11%) of 27 districts. Response meetings involving multisectoral teams and partners were conducted regularly, but without the inclusion of One Health plans and committees. Human alerts consistently followed animal alerts, yet Public Health authorities were only notified after alerts from humans. Animal samples were collected only after disease manifestation in humans for anthrax, while no samples were obtained for rabies. The absence of a regional animal laboratory led to improvised sample collection from animals. There were no surveillance dashboards for real-time updates of animal or human surveillance data. Efforts in capacity building focused on surveillance, sample collection, and infection prevention and control, with collaborative support in only Katakwi. Rabies vaccination for animals and humans occurred in Katakwi, whereas there was a shortage of anthrax vaccines. Community engagement lacked coordination across sectors and standardized sensitization activities. Poor refuse disposal practices were observed in Katakwi, while Bukedea and Kapchorwa experienced unregulated cattle movement and meat sale without intervention from the environmental health team. While some aspects of the One Health initiative, including multi-sectoral teams and sample transport, are in place, critical gaps remain, including lack of a regional animal laboratory and the need for improved disease notification systems. Urgent actions are needed to assist districts in One Health planning, and the establishment and operationalization of One Health committees.

8322

A ONE HEALTH APPROACH TO PREVENTION, DETECTION, AND RESPONSE TO CRIMEAN-CONGO HEMORRHAGIC FEVER IN THE KURDISTAN REGION OF IRAQ

Bejan A. Dizayee[1], Aso H. Kareem[2], **Lauren N. Miller**[3], Erin Sorrell M. Sorrell[4], Claire J. Standley[3]

[1]Central Veterinary Laboratory, Ministry of Agriculture, Kurdistan Region, Erbil, Iraq, [2]Ministry of Health, Kurdistan Region, Erbil, Iraq, [3]Georgetown University, Washington, DC, United States, [4]Johns Hopkins University, Baltimore, MD, United States

In 2022, Iraq experienced the largest outbreak of Crimean-Congo hemorrhagic fever (CCHF) in over 40 years, recording 379 human cases and 74 deaths. The stark increase in reported cases, primarily from governorates across the southeast, was attributed to interruptions in vector control and prevention activities during the COVID-19 pandemic. In an effort to prevent additional surges in cases and deaths, the Federal Government of Iraq (GIOI) and the Kurdistan Regional Government (KRG) designed multisectoral, One Health (OH) initiatives for CCHF prevention, detection, and response. In coordination with the GOI, KRG's Ministries of Health (MOH) and Agriculture (MOA) conceived joint activities for implementation in the Soran and Khabat Districts of the Erbil governorate to pilot their targeted interventions. Beginning in spring 2024, awareness campaigns, data collection, and acaricide spraying were applied to households with previously confirmed CCHF cases. Surveys captured information on residential demographics, owned animals, as well as vector presence and concentration. Tick samples were collected by field teams from animals, outdoor shelters, and the surrounding property and transported to the Central Veterinary Laboratory for identification and testing. Acaricide spray was then applied to residences, animals, and any outdoor facilities; follow-up investigations and tick sampling were also performed post-acaricide spray. Finally, educational risk campaigns were conducted to support household and community awareness. KRG's OH approach has also been adopted by the GOI to better integrate multisectoral strategies for tickborne disease threats across the country. This integrated response to CCHF in Iraq is an on-going, evolving collaboration on One Health; however, it highlights the importance of comprehensive surveillance, field research, and evidence-based strategies for tickborne diseases. Actively engaging in multisectoral collaboration has proven effective in aligning priorities, consolidating resources, and implementing disease prevention and control initiatives.

8323

FIRST PILOT RELEASE OF X-RAY STERILIZED MALE *AEDES AEGYPTI* TO CONTROL INVASIVE MOSQUITOES IN SOUTHERN CALIFORNIA: STRATEGY, LESSONS LEARNT AND THE WAY FORWARD

Solomon K. Birhanie, Michelle Q. Brown

West Valley Mosquito and Vector Control District, Ontario, CA, United States

The urban-adapted, daytime-biting *Aedes aegypti* is the primary mosquito vector of dengue and has the potential to transmit several other arboviruses, including Zika, chikungunya, and yellow fever. In California, *Ae aegypti* has spread in over 300 cities within 22 central and southern counties in less than a decade. Due to its cryptic breeding habitats, control efforts have been extremely challenging. Sterile Insect technique (SIT) has brought novel opportunities to strengthen mosquito control programs. The West Valley Mosquito and Vector Control District in southern California has embarked on SIT as part of the integrated vector management to control invasive *Aedes* mosquitoes. Our approach utilizes SIT in targeted *Aedes* hotspots instead of large-scale mass releases. This work aims to assess the impact of targeted X-ray sterilized male mosquito releases on local population dynamics of invasive *Aedes* mosquitoes. In our pilot program, we released X-ray sterilized male *Ae. aegypti* mosquitoes at three locations in southern California. First, a site was selected based on counts from weekly surveillance data using BG Sentinel traps. Baseline (prior to release) and follow-up cluster mosquito trapping was conducted within 100 and 200 yards from each site. A 100-times the number of female *Ae. aegypti* from BG Sentinel traps were released at each site. Follow-up cluster mosquito trapping was conducted at nine sites around each release site for four consecutive weeks. The results indicated a reduction of *Ae. aegypti* population as high as 71% four weeks after release. Preseason sterile mosquito releases are currently underway. Lessons learnt from this pilot program help to optimize SIT as an additional tool in our invasive mosquito control program.

8324

CHANGING PARASITE SPECIES DYNAMICS AND SPECIES-SPECIFIC ASSOCIATIONS OBSERVED BETWEEN *ANOPHELES* AND *PLASMODIUM* GENERA IN SOUTHWEST BURKINA FASO

Paula Lado[1], Lyndsey I. Gray[1], Emmanuel Sougue[2], Anna-Sophia Leon[1], Molly Ring[1], Greg Pugh[1], Jenna Randall[1], Elizabeth Hemming-Schroeder[1], Hannah Sproch[3], A. Fabrice Some[2], Roch K. Dabire[2], Sunil Parikh[3], **Brian D. Foy**[1]

[1]Colorado State University, Fort Collins, CO, United States, [2]IRSS, Bobo Dioulasso, Burkina Faso, [3]Yale School of Public Health, New Haven, CT, United States

The prevalence of malaria parasite species in some parts of Africa is rapidly changing. Relatedly, the natural vector competence and vectorial capacity of African anophelines for human *Plasmodium* species has only been well described for *P. falciparum* and is unclear in the context of mixed and non-falciparum infections. Over the course of the two RIMDAMAL clinical trials (2015 and 2019-2020) testing ivermectin for malaria control in the same region of Burkina Faso, we sampled participants' blood and their households for *Anopheles* spp. mosquitoes and tested these samples for *Plasmodium* species. *Plasmodium* prevalence in participants' samples was high in both trials (>50%). However, *P. falciparum* mono-infections predominated in the 1st trial but infections with mixed and non-falciparum species compromised 11-27% of infections in the 2nd trial with notable changes in species detected in participants over time. Furthermore, while *An. gambiae* s.l. was main vector captured in both trials, *An. funestus* mosquitoes were unexpectedly prevalent in the first season of the 2nd trial. Notably, *An. funestus* had a significantly higher overall sporozoite rate (15.3%; 38/249) over the intervention period than *An. gambiae* s.l. (4.8 %; 122/2528) ($P < 0.0001$) in the 2nd trial. We further found that the *Plasmodium* species detected in abdominal and head+thorax tissues of these two vector species significantly differed; *P. falciparum* sporozoites were more prevalent in *An. gambiae* s.l. ($P < 0.0001$), while *P. ovale* sporozoites were more prevalent in *An. funestus* ($P < 0.0001$). Our field-derived mosquito data suggest differential vector competence or vectorial capacity for *P. falciparum* and *P. ovale* at the field site in two of the most common African *Anopheles* species. Further work is underway to determine the mechanisms underlying these potential differences, as well as how these findings could impact the existing control measures and their resulting efficacy.

8325

EVALUATION OF HUMAN EXPOSURE TO MALARIA VECTORS USING AN IMMUNO-EPIDEMIOLOGICAL BIOMARKER (*ANOPHELES*-GSG6-P1 SALIVARY PEPTIDES) IN FOUR RURAL AREAS IN CAMEROON

Idriss Nasser Ngangue Siewe[1], Paulette Ndjeunia Mbiakop[2], André Sagna Barembaye[3], Jean Arthur Mbida Mbida[4], Christophe Antonio-Nkondjio[5], Franck Remoue[6], Athanase Badolo[7]

[1]University of Douala / OCEAC, Yaounde, Cameroon, [2]University of Yaounde I / OCEAC, Yaounde, Cameroon, [3]MIVEGEC, University of Montpellier, CNRS, IRD, BoBo Dioulasso, Burkina Faso, [4]University of Douala, Douala, Cameroon, [5]OCEAC, Yaounde, Cameroon, [6]MIVEGEC, University of Montpellier, CNRS, IRD, Montpellier, France, [7]JOSEPH KI-ZERBO University, Ouagadougou, Burkina Faso

In some areas of Africa, malaria still poses a threat to the health of urban dwellers. Vector control remains the main strategy to combat this disease. Due to significant limitations in methods currently used to assess human exposure to Anopheles bites, novel indicators assessing human antibody responses to Anopheles salivary peptides (gSG6-P1) represent a promising biomarker tool that could determine human-*Anopheles* contact and malaria risk. This study assessed sociodemographic factors influencing human exposure to *Anopheles* bites in rural cities of Cameroon. The study was conducted in Njombe (NJ), Kekem (KE), Belabo (MB) and Ouami (OU). Information on villages, gender, age, presence of vegetation around the house, bed net use was recorded using a questionnaire, human blood was collected to determine the level of IgG against *Anopheles* gSG6-P1 salivary peptide, using ELISA method. IgG levels to gSG6-P1 varied significantly bites by village. Specifically, IgG levels to gSG6-P1 were significantly higher in Njombé compared to Belabo and Ouami (all $p=0.01$). Age groups, gender, and owning a bed net did not seem to influence the exposure to *Anopheles* in the study area (all $p>0.05$). However, bed net use, condition and presence of vegetation around the house significantly influenced the exposure to *Anopheles*. Study participants who declared using their bed nets had significantly lower IgG responses to the *Anopheles* gSG6-P1 ($p<0.0076$), thus lower exposure to malaria vector bites, than those who declared not using their bed nets. Expectedly, participants who declared using bed nets with holes or reported vegetation around their houses had significantly higher levels towards *Anopheles* (median= 0.269 and 0.269, respectively) compared to those who didn't (all $p<0.05$). Antibody responses towards *Anopheles* gSG6-P1 salivary peptides vary with the village of residence, bed net use and condition and the presence of vegetation around the house. This immunological tool could be relevant to help malaria control programs to evaluate vector control strategies on human-vector contact at national and even international scale.

8326

ASSESSING INSECTICIDE TREATED NETS PERFORMANCE WITH BIOMARKER OF *ANOPHELES GAMBIAE* S.L GSG6-P1 SALIVARY PEPTIDE ANTIGEN: A LONGITUDINAL STUDY IN MALI

Ibrahim Traore[1], Moussa BM Cisse[1], Alou Yacouba Sangare[1], Mariam S. Sangare[1], Aldiana K. Maiga[1], Lazeni Konate[1], Yacouba Dansoko[1], Amadou Diakite[1], Tidiani Sinayoko[1], Alice Dembele[1], Jean Marie Sanou[1], Mamadou Sow[1], Abdourhamane Dicko[2], François D. Traore[3], Franck Remoue[3], Ousmane A. Koita[1]

[1]Laboratoire de Biologie Moleculaire Appliquee, Bamako, Mali, [2]National Malaria Control Program, Bamako, Mali, [3]Institut de Recherche pour le Developpement, Montpellier, France

The Anopheles gSG6-P1 salivary peptide antigen enables the detection of individual and population-wide human exposure levels to Anopheles bites. This represents a novel evaluation tool for assessing insecticide-treated net (ITN) effectiveness for malaria control traditionally performed using entomological and parasitological indicators. This study investigates the correlations among Anopheles biting rate, ITN hole index (HI), and malaria *Plasmodium falciparum* prevalence, alongside the novel use of the Anopheles gSG6-P1 salivary peptide antigen as an indicator of ITN performance. A durability monitoring of ITN was conducted over three years in Kénieba and Kita, western Mali, with a cohort of 549 ITNs (Yorkool and PermaNet 2.0) and 311 children under five. Assessments of ITN physical integrity and *Anopheles* biting rates were conducted annually. Malaria *P. falciparum* prevalence and the immunoglobin G (IgG) response to the gSG6-P1 antigen were assessed alongside net use. An association between ITN physical condition and malaria transmission indicators was observed. *An. gambiae* sl biting rate remained low, under 3 bites/person/night. After three years of usage, when 78% PermaNet 2.0 remained in serviceable condition, malaria prevalence (43%) and the IgG responses to gSG6-P1 (dDO 0.16) were low, and when 50% for Yorkool remaining in serviceable condition, malaria prevalence (65%) and the IgG responses to gSG6-P1 was (dDO 0.35). Higher hole indices of ITN were associated with increased malaria prevalence and elevated IgG anti-gSG6-P1 levels, indicating greater exposure to mosquito bites. The biomarker gSG6-P1 antigen of *An. gambiae* sl was used for the first time in Mali to determine ITN performance, and the results were consistent with physical integrity and parasitological indicators. This biomarker when added to existing traditional indicators may provide a comprehensive view of ITN effectiveness and help in decision-making by the National Malaria Control Program.

8327

CHARACTERIZATION OF LARVAL HABITATS TO ASSESS THE FEASIBILITY OF LARVAL SOURCE MANAGEMENT AS A SUPPLEMENTARY INTERVENTION IN A HIGH MALARIA TRANSMISSION AREA IN NIGERIA AND A LOW MALARIA TRANSMISSION AREA OF ZAMBIA - OPERATIONALIZING THE WORLD HEALTH ORGANIZATION'S THE FEW, THE FIXED. AND THE FINDABLE

Mohamed N. Bayoh[1], Adedayo Oduola[2], Petrus Inyama[2], Kelvin Mwenya[1], Matthias Sikaala[1], Lazarus Samdi[2], Brian Chirwa[1], Alex Chilabi[3], Reuben Zulu[3], Ifeanyi Okeke[2], Godwin Ntadom[4], Mary Esema[4], Muhamad A. Bunza[5], Enerst Mulenga[1], Grace Yina[2], Christina Riley[6], Lilia Gerberg[7], Jules Mihigo[8], Melissa Yoshimizu[7], Allison Belemvire[7], Paul Psychas[9], Daniel Impoinvil[10], Meghan Tammaro[11], Kelley Ambrose[11], Kerri-Ann Guyah[11], Bradley Longman[11], Aklilu Seyoum[11]

[1]PMI Evolve Project - Abt Global, Lusaka, Zambia, [2]PMI Evolve Project - Abt Global, Abuja, Nigeria, [3]National Malaria Elimination Program, Lusaka, Zambia, [4]National Malaria Elimination Program, Abuja, Nigeria, [5]Federal University, Birnin-Kebbi, Nigeria, [6]Akros, Lusaka, Zambia, [7]U.S. President's Malaria Initiative, USAID, Washington, DC, United States, [8]U.S. President's Malaria Initiative, USAID, Abuja, Nigeria, [9]U.S. President's Malaria Initiative, U.S. Centers for Disease Control and Prevention, Lusaka, Zambia, [10]10U.S. President's Malaria Initiative, Malaria Branch, U.S. Centers for Disease Control and Prevention, Atlanta, GA, United States, [11]PMI Evolve Project - Abt Global, Rockville, MD, United States

Malaria remains a major public health concern in Africa, and larval source management (LSM) is (re)emerging as a tool for some National Malaria Programs to supplement contemporary vector control efforts for reducing the burden. In 2022-2023 the U.S. President's Malaria Initiative (PMI) VectorLink project, utilized geospatial tools to assess and map all potential *An. gambiae* s.l. or *An. funestus* s.l. larval habitats in a high-burden rice irrigation farm area of Nigeria - Argungu, Bunza, and Kalgo Local Government Areas in Kebbi State, and in a low-burden area of Zambia- Katete and Chipata districts in Eastern Province. Each habitat was characterized by habitat type, presence of larvae, water longevity in the habitat, size, and other factors. The number of larval habitats enumerated and assessed ranged between 2088-3218 from two surveys in Nigeria and 775-1338 from four surveys in Zambia. In Nigeria, 98.7% of the habitats were permanent or semi-permanent, while in Zambia this number was 90.1%. *Anopheles* larvae were present in the habitats at each survey round in both countries; the highest habitat positivity in Nigeria ranged from 79-87% in August 2022 and 22-74% in Zambia in May 2023. In Kebbi, the main larval habitats were small to large rice basin irrigation farms averaging about 7.5 hectares; in Zambia, habitats were small to medium-sized such as ditches associated with gardens measuring 14-23m in habitat perimeter. More than 90% of the habitats in both countries were accessible. These larval habitats comply with the WHO's "fixed" and "findable" guidance for larviciding. In Zambia, we conducted field simulations to derive an operational definition for "few" habitats. One person doing weekly larviciding in a 10km^2 settlement could cover a 2km^2 area per day each with a total habitat perimeter of 1800m per km^2. We determined that habitats are "few" when there is less than 1800m of habitat perimeter per km^2 of a settlement. All sites in Zambia met this criterion for "few" habitats. An LSM pilot study may demonstrate impact in the high transmission area in Nigeria and possible added acceleration towards elimination in the low transmission area in Zambia.

8328

MODELS TO INFORM THE DESIGN OF FIELD TRIALS OF NOVEL GENE DRIVE INTERVENTIONS TO SUPPRESS MALARIA VECTOR POPULATIONS

Penelope A. Hancock[1], Ace North[2], Tin-Yu J. Hui[1], Adrian W. Leach[1], Andrew McKemey[1], Azize Millogo[3], John Connolly[1], Patric Epopa[3], franck adama Yao[3]

[1]Imperial College London, London, United Kingdom, [2]University of Oxford, Oxford, United Kingdom, [3]Institute de Recherche en Sciences de la Sante, Bobo Dialasso, Burkina Faso

Gene drive technologies are a promising means of malaria vector control with the potential to cause widespread and sustained vector population suppression. Here we consider gene drives that have been engineered in *Anopheles* vector species to target female fertility, suppressing the vector population as the gene drive spreads. Large cage experiments have shown that these gene drives can crash mosquito populations within a year, yet their performance in wild populations remains untested. In preparation for the first field trials, we developed a data-driven mathematical model to estimate the impacts of gene drive releases on vector abundance, malaria prevalence and clinical cases in children. The model parameterisation is specific to candidate release sites in Burkina Faso, considering local vector ecology and species composition, malaria transmission intensity and the historical coverage of vector control and human treatment interventions. We simulated cluster randomised control trials designed to detect gene drive impacts over a range of trial designs, accounting for noise in measurements of mosquito abundance and malaria prevalence and incidence. Trials aiming to detect vector suppression have greater statistical power when gene drives target both *An. coluzzii* and *An. gambiae* rather than targeting *An. coluzzii* only. Regardless of the target vector species, trials have greater power using either malaria prevalence or incidence as the primary endpoint, rather than vector population suppression. We estimated the size of a trial required for 90% power to detect a reduction in malaria prevalence of at least 30%, and determined how this depends on fitness costs incurred by the gene drive on mosquitoes and the spread of the gene drive from release into control clusters. Our results can inform the development of field trial protocols for these novel interventions.

8329

DEVELOPMENT OF SIT FOR *AEDES ALBOPICTUS* CONTROL IN CHINA: A PRELIMINARY FIELD STUDY

Zhang Dongjing

Sun Yat-sen University, Guangzhou, China

Aedes albopictus is the primary vector of dengue fever in mainland China. Vector control is essential for dengue prevention. Due to resistance from overuse of insecticides, there is a critical need for alternative control strategies like *Wolbachia*-based IIT or radiation-based SIT. Previously our team has successfully eliminated *Ae. albopictus* on two isolated islands in Guangzhou using IIT/SIT. Testing these techniques in urban centers is crucial to validate their effectiveness and support area-wide use of technique like SIT for controlling mosquito populations and mosquito-borne diseases. A *Wolbachia*-free *Ae. albopictus* GT strain was developed and its rearing efficiency was optimized under laboratory conditions before its transfer to a mass rearing facility. Standard mass rearing procedures have been established for GT strain with two important indicators: the induced sterility and female contamination rate being >99.0% and <0.1%, respectively. A field trial study performed in Guangzhou, China by releasing irradiated GT males indicated that SIT is effective in reducing the population and the biting rate of *Ae. albopictus* in urban area, where there was a reduction of the population by 40% and of the biting rate by 75%. Expansion of the releases in a larger area is needed in order to assess the cost-effectiveness of SIT for mosquito population control.

8330

A CLINICAL SCORE TO SCREEN CHILDREN IN NEED FOR CHRONIC FASCIOLIASIS TESTING IN CUSCO - PERU

Karen Mozo Velazco[1], Maria L. Morales[1], Martha Pilar Lopez[1], Benicia Baca - Turpo[1], Eulogia Arque[1], Miguel M. Cabada[2]

[1]Instituto de Medicina Tropical Alexander von Humboldt – Universidad Peruana Cayetano Heredia, Peru, CUSCO, Peru, [2]University of Texas Medical Branch, Infectious Diseases Division, Galveston, TX, United States

Fasciola is a trematode hyperendemic in Peru presenting with few and unspecific symptoms particularly among children in the community. Tools to identify children in need for screening are urgently needed. The aim of this study was to determine the sensitivity and specificity of a clinical score to identify children that will benefit from screening for chronic fascioliasis. This is a secondary data analysis of a study evaluating fascioliasis among children 3-16 years in Cusco. We included data collected using a demographic, symptoms, and signs questionnaire and laboratory results from stool microscopy, Fasciola ELISA, transaminases, and complete blood counts. Chronic fascioliasis was defined as having *F. hepatica* eggs in the stool. No infection was defined as not having *Fasciola* or other parasite eggs in the stool and having negative serology. ROC curves and logistic regression were used to determine the sensitivity and specificity of symptoms and laboratory combinations to identify chronic fascioliasis. The analysis included 909 children of which 162 had chronic fascioliasis and 747 had no infection. Half were female and the mean age was 9.6 years (±3.6). Comparing symptoms in children with chronic fascioliasis and no infection, right upper quadrant pain ($p \leq 0.001$), fatigue ($p \leq 0.001$), anorexia ($p=0.006$), vomiting ($p=0.009$), and diarrhea ($p=0.040$) were more common in the former. Similarly, the hematocrit ($p=0.038$), hemoglobin ($p=0.008$), leucocytes ($p=0.043$), and eosinophils ($p \leq 0.001$) levels were different between the groups. Combining right upper quadrant pain, fatigue, and eosinophilia identified children with chronic fascioliasis with 85% sensitivity and 92% specificity. A clinical score applied in the community can identify children that would benefit from stool microscopy testing for fascioliasis. This could simplify screening and allow a better use of triclabendazole.

8331

DIAGNOSTIC ACCURACY OF COLPOSCOPY FOR FEMALE GENITAL SCHISTOSOMIASIS SCREENING AT PRIMARY LEVEL OF CARE

Pia Rausche[1], Jean-Marc Kutz[1], Paule Donven[1], Sonya Ratefiarisoa[2], Olivette Totofotsy[2], Diavolana Andrianarimanana-Koecher[2], Tahinamandranto Rasamoelina[3], Rivo S. Rakotomalala[2], Zoly Rakotomalala[2], Bodo S. Randrianasolo[4], Irina Kislaya[1], Jürgen May[1], Valentina Marchese[1], Rivo A. Rakotoarivelo[5], Daniela Fusco[1]

[1]Department of Infectious Diseases Epidemiology, Bernhard Nocht Institute for Tropical Medicine, Hamburg, Germany, [2]Centre Hospitalier Universitaire Androva, Mahajanga, Madagascar, [3]Centre Infectiologie Charles Mérieux, Antananarivo, Madagascar, [4]Association K'OLO VANONA, Antananarivo, Madagascar, [5]Department of Infectious Diseases, University of Fianarantsoa Andrainjato, Fianarantsoa, Madagascar

Diagnosis of neglected tropical diseases poses a major challenge due to the lack of tools that are adapted to endemic contexts. Among others, Female Genital Schistosomiasis (FGS), caused by persistent infection with *Schistosoma haematobium*, is an excellent example. Left untreated, it can lead to complex gynecological syndromes with consequences such as pelvic pain or infertility. The standard screening for FGS is colposcopy, a complex clinical examination that often cannot be performed in resource-limited contexts due to lack of expertise or insufficiently equipped infrastructures. This study aims to investigate the accuracy of colposcopy to detect FGS by trained midwives at the primary level of care. The study was implemented in the rural region of Boeny, Madagascar, where a prevalence of FGS above 60% is reported. Colposcopy images were collected by trained midwives and re-evaluated by two gynecologists through a blinded reconciliation process. Reference diagnosis was defined as agreement of both gynecologists on the FGS diagnosis; images with a conflicting interpretation were excluded from the analysis. Statistical analysis using R included descriptive statistics, measures of diagnostic accuracy and binary Poisson regression with robust standard errors. Among 660 women enrolled, 631 colposcopy images were collected. A final diagnosis from a gynecologist was available in 598 cases. Preliminary results show sensitivity of 95.9 % (95%CI 93.3-97.5) and specificity of 30.0 % (95%CI 23.7-37.1). Multivariate regression shows a positive influence on diagnostic agreement of increasing colposcopy routine in comparison to the start of the study. One study centre presents a negative influence on the agreement of diagnosis. This study shows the potential of implementing colposcopy at primary level of care as a screening tool for FGS due to the high sensitivity. Implementation could bridge the gap in access to health care in rural regions and holds potential to integrate other colposcopy-based screenings such as for cervical cancer into the service.

8332

TRANSCRIPTOMICS OF THE AFRICAN FRESHWATER SNAIL VECTOR *BIOMPHALARIA SUDANICA S.L.* REVEALS CANDIDATE LOCI FOR SCHISTOSOME RESISTANCE

Tom Pennance[1], Javier Calvelo[2], Jacob A. Tennessen[3], Eric S. Loker[4], Lijun Lu[4], Johannie M. Spaan[1], Andrés Iriarte[2], Maurice R. Odiere[5], Michelle L. Steinauer[1]

[1]Western University of Health Sciences COMP-NW, Lebanon, OR, United States, [2]Universidad de la República, Montevideo, Uruguay, [3]Harvard T.H. Chan School of Public Health, Boston, MA, United States, [4]University of New Mexico, Albuquerque, NM, United States, [5]Kenya Medical Research Institute (KEMRI), Kisumu, Kenya

Biomphalaria sudanica s.l. is a major freshwater snail vector for *Schistosoma mansoni*, the causative agent for intestinal schistosomiasis, in the hyperendemic Lake Victoria basin. The disease afflicts millions of people dependent on this water source, and methods to control snail populations to curb schistosome transmission are impractical to implement. Methods to curtail transmission of the disease could be developed from the snails' naturally occurring genetic resistance, which in some cases can thwart schistosome infection. We have previously identified potential pathogen recognition receptors/effector genes within the *B. sudanica* genome. We hypothesized that genes relevant to parasite resistance will show differential expression following exposure to *S. mansoni*, allowing for more precise identification of key genetic pathways. Here, we compared the differential transcriptomic profiles of 100 *B. sudanica* snails 8, 24 and 72 hours post-exposure to either *S. mansoni* with which they are compatible or incompatible to, or sham exposed (control). Significant differential expression of transcripts was assessed (EdgeR) using pairwise comparisons (control vs. exposed groups at each timepoint). 1,472 of 23,598 genes showed differential expression at one or multiple time points. Eight hours after exposure, snails exposed to the compatible parasite showed no differentially expressed genes to sham exposed snails, whereas snails exposed to the incompatible parasite had both up- (n=41) and downregulated genes (n=175). The highest upregulated genes in both exposed snail groups 8 and 24 hours after exposure were candidate immune genes that had been shortlisted as pathogen recognition receptors prior to this study due to signs of balancing selection in the *B. sudanica* genome. Therefore, these data directly support their involvement in the *B. sudanica* immune response to *S. mansoni* and future experimental work will test their functional role in the resistance pathways of this African snail vector.

8333

AUTOMATED DIAGNOSIS OF *SCHISTOSOMA HAEMATOBIUM* WITH ARTIFICIAL INTELLIGENCE ON HANDHELD DIGITAL MICROSCOPES IN RURAL CÔTE D'IVOIRE

María Díaz de León Derby*[1], Elena Dacal*[2], Daniel Cuadrado*[2], Jean Coulibaly*[3], Jaime Garcia-Villena[2], Carla Caballero[2], Lin Lin[2], David Bermejo-Peláez[2], Miguel Luengo-Oroz[2], Daniel Fletcher[1], Karla Fisher[4], Jason Andrews[5], Kigbafore Silue[3], **Isaac Bogoch**[4]

[1]University of California, Berkeley, Berkeley, CA, United States, [2]SpotLab, Madrid, Spain, [3]Université Félix Houphouët-Boigny, Abidjan, Côte D'Ivoire, [4]Toronto General Hospital, Toronto, ON, Canada, [5]Stanford University, Palo Alto, CA, United States

Schistosomiasis continues to plague over 200 million people globally and disproportionately impacts children in Africa. The World Health Organization has called for novel tools to help monitor schistosomiasis control and elimination programs, and portable digital microscopy with artificial intelligence (AI)-supported diagnostics are a promising tool for these schistosomiasis public health initiatives. We used the computer vision model YOLOv8 to train AI object detection models for the purpose of detecting Schistosoma haematobium eggs in digital images of urine samples. These models were trained with images acquired from an earlier version of the mobile microscope during field studies conducted in Côte d'Ivoire between 2020-2022 We then used the latest generation of our mobile microscopy platform (the "NTDscope") to acquire images of urine samples processed from patients in the Azague region of Côte d'Ivoire, in January of 2024, as part of broader schistosomiasis screening and treatment programs. The digital images were acquired in both brightfield and darkfield contrasts. 75 samples were evaluated on Day 1 and again on Day 2, with an equal distribution of high-intensity and low intensity infection, and non-infected samples. Given the slight changes in optics and illumination on the new NTDscope hardware, we used the images acquired on the first day of the field study to re-train and recalibrate our AI models before the second day in the field. Preliminary sensitivity and specificity of AI models compared to conventional light microscopy was 48-95% and 16-88%, respectively on day 1, and 83-97% and 48-87%, respectively, on Day 2 following AI recalibration. These data suggest that handheld digital microscopy with automated parasite identification may be a helpful tool for schistosomiasis control initiatives.

8334

CHARACTERIZATION AND PROCESS DEVELOPMENT OF A *SCHISTOSOMA HAEMATOBIUM* SERINE PROTEASE INHIBITOR (SHSERPIN-P46): A NEXT GENERATION VACCINE FOR UROGENITAL SCHISTOSOMIASIS

Adebayo Molehin[1], Brooke Hall[1], Leah Sanford[1], Christine Lee[1], Sean Gray[2], Darrick Carter[2], Karleen King[1]

[1]Midwestern University, Glendale, AZ, United States, [2]PAI Lifesciences Inc, Seattle, WA, United States

Urogenital schistosomiasis, caused by *Schistosoma haematobium*, currently affects millions of people in Sub-Saharan Africa. *S. haematobium* eggs trapped in urogenital tissues result in intense inflammation and eosinophilia leading to bladder wall thickening and development of masses and pseudopolyps. Urogenital schistosomiasis is also associated with hydronephrosis, active-stage lesions, cervical scarring, decreased fertility and bladder squamous cell carcinoma. In addition, people infected with *S. haematobium* have significantly higher risks of sexually transmitted infections such as HIV. Furthermore, transmission of a more virulent hybrid strain of *S. haematobium* / *S. bovis* is now being reported in Europe, a region previously considered schistosomiasis free. Hence, an urgent need to develop an effective vaccine for long term protection. Serine protease inhibitors (serpins) are key factors used by many pathogens to evade their host immune responses, and serpin-based vaccines have shown promising results in many parasite systems. In this study, we developed and characterized a candidate vaccine based on a secretory serpin from *S. haematobium* (Shserpin-p46). Transcriptional profiling and proteomics demonstrated that Shserpin-p46 is expressed in the intra-mammalian life cycle stages and localized to the parasite tegument. Recombinant Shserpin-p46 inhibited neutrophil elastase in a dose-dependent manner and was strongly recognized by putative resistant individuals and experimentally-infected rat (naturally-resistant hosts) sera when compared to chronically-infected mouse counterparts, indicating that rShserpin-p46 is not only highly immunogenic, but critically involved in disease resistance. A pilot study evaluating the efficacy of a Shserpin-p46 antigen formulated in proprietary TLR4-agonist-based adjuvants, EmT4™ and LiT4Q™ in hamster model of urogenital schistosomiasis is now underway. An effective schistosomiasis vaccine would play a major role in the overall reduction of disease morbidity thereby improving quality of life for people living in endemic regions.

8335

MULTIPLE ROUNDS OF PRAZIQUANTEL TREATMENTS OF *SCHISTOSOMA MANSONI* HOSTS (MICE AND HUMANS) GRADUALLY RENDER THEM LESS SUSCEPTIBLE TO REINFECTION

Etienne Soh Bayeck[1], Bernard Zambo[2], Leonel Meyo Kamguia[2], Mireille Kameni[2], Brice Owona Ayissi[1], **Justin Komguep Nono**[2]

[1]University of Yaounde 1, Yaounde, Cameroon, [2]Institute of Medical Research and Medicinal Plant Studies, Yaounde, Cameroon

Beyond transient control of the infection, additional benefits of mass drug administration (MDA) of praziquantel in endemic communities have been suggested in communities but yet to be unequivocally demonstrated. Recent studies conducted by our group revealed, in a complementary manner, the benefits of repeated administration of praziquantel. First, using *Schistosoma mansoni* infected mice, repeated infection-treatment cycles led to reduced host susceptibility to reinfection burden, but not to the onset of associated liver fibrosis. This result highlighted the development of an enhanced humoral response in mice following praziquantel treatment leading to resistance to reinfection. Resistant mice displayed higher baseline levels of serum IL-4 and IgE. Secondly, in children from communities endemic for *S. mansoni* in rural Cameroon, that have received different numbers of praziquantel MDA rounds, we similarly observed a reduced reinfection rate and burden, but not that of liver fibrosis onsets, after multiple rounds of praziquantel MDA. This was also associated with higher baseline levels of plasma IgE and IL-4 in children and robustly persisted even after correcting for all possible identifiable confounders such as age, gender, numbers of daily contacts with infested waters, body mass index, length of residence in the endemic area (AOR of the predictor variable numbers of praziquantel rounds in affecting the odds of having heavy reinfection= 0.16; p=0.03) . Taken together, our data reveal that treatment of *S. mansoni*-infected hosts with praziquantel might rewire the immune system to a conformation less permissive to subsequent reinfection under sustained infection pressure, opening up discussions on how this might affect infection prevalence, intensities, associated morbidity and transmission at community levels.

8336

EMPOWER: ENRICHMENT METAGENOMIC PROFILING FOR WOMEN'S REPRODUCTIVE HEALTH

Jennifer Fitzpatrick[1], Rebecca Rockett[2], Juliana Gill[3], Rhoda Ndubani[1], Kwitaka Maluzi[1], Barry Kosloff[4], Kwame Shanaube[1], Cristina Tato[3], Amaya Bustinduy[5], Helen Ayles[1], Tanya Golubchik[2]

[1]Zambart, Lusaka, Zambia, [2]University of Sydney, Sydney, Australia, [3]Chan-Zuckerberg Biohub, San Francisco, CA, United States, [4]Longhorn Vaccines & Diagnostics, Bethesda, MD, United States, [5]London School of Hygiene and Tropical Medicine, London, United Kingdom

Schistosomiasis is a chronic parasitic disease, affecting the health of more than 200 million people, with devastating clinical and socio-economic impact. Female genital schistosomiasis (FGS) is a long-term, debilitating consequence of urogenital *Schistosoma haematobium* infection - estimated to affect up to 56 million girls and women in sub-Saharan Africa. FGS is

associated with significant maternal complications such as sub/infertility, ectopic pregnancy, intrauterine growth restriction and preterm labour, likely increased risk of human papillomavirus (HPV)/cervical cancer and susceptibility to sexually transmitted infections (STIs; including HIV). STIs are another ongoing global health burden, with over one million infections acquired every day worldwide. FGS is frequently misdiagnosed as an STI (symptoms often mimic) - leading to inappropriate antibiotic treatment, furthering antimicrobial resistance, while causing social harms and stigma. In settings where adequate laboratory service is lacking, the coexistence of FGS/STIs poses a significant diagnostic challenge for healthcare providers managing patients with urogenital complaints. Since its advent, Next Generation Sequencing (NGS) has been prohibitively expensive for routine diagnostic/epidemiological use in low- and middle-income countries. We have developed in-country (Zambia), cost-effective enrichment NGS protocols together with computational pipelines, for organism detection, drug resistance and vaginal microbiome analysis. We have designed a targeted metagenomic multi-pathogen sequencing panel (~45, 000 x120 base pair oligonucleotide bait-capture probes), comprising all common STI related viruses, bacteria, and parasites (including S. haematobium). Multi-pathogen and drug resistance analysis will be shown utilizing cervicovaginal swabs from different communities in Zambia. The utilization of this novel technology will EMPOWER vulnerable girls and women, within longer-term public health strategies, to engage with effective rapid diagnostics and treatment, while minimizing stigma and disruption to daily life.

8337

SEROPREVALENCE AGAINST MULTIPLE VIRUSES AT HUMAN ANIMAL INTERFACE IN BUKAVU, DEMOCRATIC REPUBLIC OF CONGO

Junior Bulabula-Penge[1], Antoine Nkuba-Ndaye[1], Chasinga Buharanyi[2], Ayagirwe Basengere[3], David Lupande-Muenebintu[4], Daniel Mukadi-Bamuleka[5], Esperance Tsiwedi Tsilabia[5], Noella Mukanya Mulopo[5], Louis Glénat[6], Frédéric LeMarcis[7], Eric Delaporte[8], Almudena Mari Saez[6], Martine Peeters[6], Steve Ahuka-Mundeke[1]

[1]National Institute of Biomedical Research (INRB), Kinshasa, Congo, Democratic Republic of the, [2]Hôpital Panzi, Bukavu, Congo, Democratic Republic of the, [3]Université Evangélique d'Afrique, Bukavu, Congo, Democratic Republic of the, [4]Hôpital Provincial Général de Bukavu, Bukavu, Congo, Democratic Republic of the, [5]Rodolphe Mérieux INRB-Goma Laboratory, Goma, Congo, Democratic Republic of the, [6]TransVIHMI, Universite de Montpellier, Institut de Recherche pour le Développement, INSERM,, Montpellier, France, [7]TransVIHMI, Universite de Montpellier, Institut de Recherche pour le Développement, INSERM, Montpellier, France, [8]TransVIHMI, Universite de Montpellier, Institut de Recherche pour le Développement, INSERM,, M, France

The Democratic Republic of Congo has a long history of emerging zoonotic infections, such as Ebola and Monkeypox. This study aims to determine the prevalence of serological markers of zoonotic infectious diseases in Bukavu, South Kivu. A cross-sectional study was conducted from April to May, 2023, among humans and domestic animals in Bukavu. Pregnant women, blood donors, and individuals in contact with animals were included. After obtaining their consent, participants completed a questionnaire and provided a blood sample on filter paper. Consent was also obtained to collect blood samples from animals. Samples were stored at -20°C. Detection of antibodies against antigens for Ebolavirus (NP, GP, VP40), SARS-CoV-2 (SP, NP), Arboviruses (ONNV_E2, USUV_NS1, DENV2_NS1, DENV3_NS1, DENV4_NS1, CHKV_E2, ZIKV_NS1, WNV_NS1, WNV_DIII), and Mpox was conducted using previously developed multiplex serology with the Luminex® technique for humans. Adaptation of the assay for domestic samples is in development. Out of 1427 human participants, 1407 provided a blood sample, of which 1181 samples were analyzed. Among them, 62.3% were females and 37.7% males, with a median age of 24 years. The majority (89.9%) were either blood donors or pregnant women, while 10.1% were at-risk workers. The seroprevalence of Ebola virus, considering positivity for at least two Ebola antigens, was 0.2%. No positive cases were detected among individuals in contact with animals. For SARS-CoV-2, the seropositivity was 32.4%. Among arboviruses, the seropositivity for ONNV was 4.2% in the at-risk group and 0.8% in the general population (p=0.0009). The prevalence of WNV was 1.2%. Among farmers and slaughterhouse workers, Mpox seroprevalence was 5% versus 1.8% in the general population (p=0.021). 507 animals were sampled and analysis is ongoing. These preliminary results demonstrate that SARS-CoV-2, ONNV, WNV, and Mpox viruses are the most prevalent in the human population in Bukavu. Expanding research to include animals is crucial for a better understanding of zoonotic infections for more effective prevention strategies, and mitigating future outbreaks

8338

EXPOSURE TO MAYARO VIRUS IN THE IN THE PERUVIAN AMAZON

Amy C. Morrison[1], Adam J. Moore[2], Daniel Strebow[3], Whitney Weber[3], Zachary Streblow[3], Mariana Leguia[4], Jhonny Cordova[5], Jennifer E. Rios Lopez[5], S. Alfonso Vizcarra[5], Alejandra Garcia-Glaessner[4], Breno Muñoz-Saavedra[4], Diana Juarez[4], Patricia Barrera[4], Gabriela Salmon-Mulanovich[4], Tatiana Quevedo[6], Carlos Calvo-Mac[6], Marcela M. Uhart[7], Nicole R. Gardner[7], Christine K. Johnson[7], Christopher M. Barker[1], Lark L. Coffey[1]

[1]Dept. of Pathology, Microbiology, and Immunology, School of Veterinary Medicine, University of California, Davis, Davis, CA, United States, [2]University of California, Davis, Davis, CA, United States, [3]Vaccine & Gene Therapy Institute, Oregon Health & Science University, Beaverton, OR, United States, [4]Laboratorio de Genómica, Pontificia Universidad Católica del Perú, Lima, Peru, [5]Asociacón Benéfica Prisma, Lima, Peru, Iquitos, Peru, [6]Asociacón Benéfica Prisma, Lima, Peru, [7]One Health Institute, School of Veterinary Medicine, University of California, Davis, Davis, CA, United States

Iquitos is the largest urban center (~400K people) in the Peruvian Amazon, an epidemiological island only accessible by boat or air, with a range of nearby communities along three major rivers and a 90-km road. The area has a well-documented history of dengue outbreaks, and low numbers of infections with other arboviruses, including Mayaro virus (MAYV), are detected in residents, with occasional small outbreaks. To assess MAYV circulation in and around Iquitos, we leveraged samples from a 2016-2018 community-based cohort study for *Aedes*-borne viruses (ABV) and a 2022-2024 study conducting concurrent sampling of wildlife, mosquitoes, and humans along a gradient of ecological disturbance. In the first study, we tested sera from 1,575 children in highly urbanized areas in Iquitos. In the second, we tested sera from 416 community participants (ages 3 - 88) in two Amazon River islands with established secondary forest, one peri-urban community with disturbed forest, and homes of Iquitos residents with frequent contact with non-human primates. The ABV cohort was screened by nLUC showed seroprevalence of <1% for MAYV neutralizing (NT) antibody. For the second study, sera were screened by PRNT. A total of 104 of 416 (25%) of participants screened positive for MAYV neutralizing antibody. Endpoint titers ranged from 640 to 5120. Seropositivity was higher in adults (34%) compared to children less than 18 years of age (12%), and highest in the peri-urban area (31%) followed by the more forested sites (21% and 26%) and finally Iquitos City (9%). Household clustering of seropositive people as young as three years of age was observed. Viruses detected in concurrent mosquito and bat collections demonstrate circulation of additional arboviruses. The city has a large human population living near forest ABV cycles, with significant spillover risk. Our large community pediatric cohort suggest no or limited transmission within the city, but evidence of recent infection in at least one island site. One health research programs are required to better understand local transmission cycles and the risk of adaptation to urban disease cycles.

8339

RISK FACTORS FOR ACUTE Q FEVER IN KILIMANJARO, TANZANIA: A PROSPECTIVE OBSERVATIONAL FEBRILE ILLNESS SURVEILLANCE STUDY

Matthew Rubach[1], Thomas Bowhay[2], William Nicholson[3], Jamie Perniciaro[3], Deng Madut[1], Ganga Moorthy[1], Holly Biggs[1], Michael Maze[4], Jo Halliday[5], Kathryn Allan[5], Angelo Mendes[5], Blandina Mmbaga[6], Wilbrod Saganda[7], Bingileki Lwezaula[7], Sarah Cleaveland[5], Venance Maro[6], John A. Crump[1]

[1]Duke University, Durham, NC, United States, [2]University of Otago, Dunedin, New Zealand, [3]US Centers for Disease Control & Prevention, Atlanta, GA, United States, [4]University of Otago, Christchurch, New Zealand, [5]University of Glasgow, Glasgow, United Kingdom, [6]Kilimanjaro Christian Medical Centre, Moshi, Tanzania, United Republic of, [7]Ministry of Health, Moshi, Tanzania, United Republic of

Acute Q fever, caused by *Coxiella burnetii*, is a common cause of febrile illness among patients admitted to hospital in northern Tanzania. We sought to identify risk factors for acute Q fever in a prospective febrile illness cohort. We screened for fever among adults and children presenting to two referral hospitals in Moshi, Kilimanjaro, 2012-14. Medical and pediatric ward inpatients were eligible if they had fever >=38 ° C or report of fever within the previous 72 hours; outpatients were eligible if they had fever >=38 ° C. After consent, a standardized clinical history was obtained, including a risk factor questionnaire on animal exposures, animal husbandry activities, and outdoor activities within 30 days of enrollment. Venous blood was collected at enrollment and at a follow-up visit 4-6 weeks post-enrollment and serum tested for immunofluorescent IgG antibody (IFA) to *C. burnetii* Phase II antigen. Acute Q fever was defined as a participant with >=4-fold increase in reciprocal antibody titer between acute and convalescent serology. Non-cases were defined as participants with paired IFA results that did not meet the case definition. Participant household or village global positioning system (GPS) coordinates were obtained. Environmental co-variates linked to participant GPS coordinates were extracted from open data sources. A multivariable logistic regression model was fitted to identify risk factors. Acute Q fever was identified in 64 (8.3%) of the 773 febrile participants included in this analysis. Median (range) age was 12.5 (0.25-61) years, with 18 (28.1%) cases in children <2 years; 31 (48.4%) cases were female. Cattle density (OR 1.12 [95% CI 1.01-1.24], p=0.031), maximum mean temperature (average of monthly means for the 3 months prior to enrollment, ° C) (OR 0.88 [95% CI 0.80-0.98], p=0.014), and age <2 years (ORs 3.10 to 3.45 compared to other age quintiles, p=0.004 to 0.067) were independently associated with acute Q fever. Our findings suggest next steps to understand Q fever epidemiology should focus on identifying risk factor behaviors and exposures in young children and on the role of climate and livestock exposures.

8340

BAT HUNTING PRACTICES AND HEALTH RISKS: INSIGHTS FROM A BANGLADESHI BAT-HUNTING COMMUNITY

Abdul Khaleque Md. Dawlat Khan[1], Farhana Begum[2]

[1]Institute of Epidemiology, Disease Control and Research (IEDCR), Dhaka, Bangladesh, [2]University of Dhaka, Dhaka, Bangladesh

Bats are natural reservoirs of many emerging infectious diseases that cause significant human morbidity and mortality. Hunting and bat bushmeat can cause serious zoonotic diseases such as a Nipah-like henipavirus in humans. However, bat-hunting is a common practice in Bangladesh. This research aimed to explore bat-hunting practices including socioeconomic factors, cultural beliefs, and related health risks in a bat-hunting community in Bangladesh. The study was conducted in a bat-hunting community in the central part of Bangladesh from May 2017 to April 2018. A qualitative ethnographic approach was employed which included observations of bat-hunting events, and in-depth interviews with 4 bat-hunters, and 20 individuals involved in bat meat processing and selling. Collected data was analyzed using a thematic analysis approach. The bat hunters were involved in hunting when there was no work to earn in winter. They stated that hunting bats is an alternative source of income and lower-cost animal protein compared to domestic animal meats that they could not avail for the higher price. They faced several health risks including falls from trees, bat bites, and scratches during hunting. While no laboratory-confirmed cases of Nipah virus were found among them, one individual exhibited symptoms of Nipah-like encephalitis and died before testing, leading to beliefs in supernatural causes among the community people. They believed that bats don't transmit infections, rather they used bat meat and body parts for treating several illnesses like asthma, heart disease, and sexual vigor. We observed that bat processing was placed at their homestead where family members including children were exposed to bat blood and raw meat and domestic animals like dogs and cats eat the offal of bats. The study findings highlight the statements of livelihood, cultural beliefs, and health risks associated with bat hunting and consumption. The study underscores the urgent need for a culture-sensitive intervention with educational outreach programs aimed at augmenting awareness and economic outcomes of these hunters to reduce the health risks of zoonotic diseases.

8341

MICROBIOMES AND RESISTOMES IN HOUSEHOLD ENVIRONMENTS WITH DOMESTIC ANIMAL COHABITATION: A STUDY IN RURAL BANGLADESH

Jade Benjamin-Chung[1], Gabriella Barratt Heitmann[1], Kalani Ratnasiri[1], Sumaiya Tazin[2], Claire Anderson[1], Suhi Hanif[1], Afsana Yeamin[3], Abul Kasham Shoab[3], Farjana Jahan[3], Md. Sakib Hossain[3], Zahid Hayat Mahmud[3], Mohammad Jubair[3], Mustafizur Rahman[3], Mahbubur Rahman[3], Ayse Ercumen[2]

[1]Stanford University, Stanford, CA, United States, [2]North Carolina State University, Raleigh, NC, United States, [3]icddr,b, Dhaka, Bangladesh

In low- and middle-income countries, frequent cohabitation of domestic animals in rural households leads to household contamination with animal feces. Young children frequently touch and ingest soil and animal feces within household environments. These exposures increase their risk of enteric pathogen and antimicrobial resistant infections. Our objective was to understand whether cow cohabitation in homes with soil floors in rural Bangladesh contributed to pathogen and antimicrobial resistance genes (ARGs) in soil floors. We randomly sampled 10 households with soil floors and cows that resided inside the home in rural Chauhali sub-district, Sirajganj District, Bangladesh and concurrently collected cow dung and household soil floor samples. We extracted DNA, performed shotgun metagenomic sequencing, and used the Chan Zuckerberg Infectious Disease bioinformatics pipeline to detect pathogens and ARGs. We detected 5 pathogens in soil, 14 pathogens in cow dung, and 23 in both soil and cow dung. Pathogens that were present in at least 3 of 10 households in both soil and cow dung were *Acinetobacter baumannii*, *Agrobacterium tumefaciens*, *Bacillus cereus*, *Clostridium botulinum*, *Escherichia coli*, *Elizabethkingia anopheles*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella enterica*, and *Stenotrophomonas maltophilia*. 100% of household floors and cow dung samples contained ARGs against various classes of antibiotics including sulfonamides, rifamycin, aminoglycosides, macrolides, lincosamides, and tetracycline. Paired floor and cow dung samples from the same households shared ARGs against aminoglycosides, cephamycin, lincosomides, macrolides, rifamycin, streptogramin, and tetracycline. Our findings suggest that the cohabitation of animals in homes with soil floors is associated with shared pathogens and ARGs between cow dung and floors, presenting a risk of exposure for household members. Future research is needed to establish whether these exposures are linked to increased enteric infections and antimicrobial resistant infections.

8342

ASSESSING ANIMAL FECAL CONTAMINATION IN FLOORS AND HAND SAMPLES FROM HOUSEHOLDS IN NORTHWESTERN COASTAL ECUADOR

Viviana A. Alban[1], Kelsey J. Jesser[1], Caitlin Hemlock[1], Aldo Lobos[2], Joseph Eisenberg[3], Gwenyth Lee[4], Gabriel Trueba[5], Valerie J. Harwood[2], Karen Levy[1]

[1]University of Washington, Seattle, WA, United States, [2]University of South Florida, Tampa, FL, United States, [3]University of Michigan, Ann Arbor, MI, United States, [4]Rutgers University, New Brunswick, NJ, United States, [5]Universidad San Francis, Quito, Ecuador

Interaction between humans and animals is commonplace in low- and middle-income countries, with animals often sharing living spaces with families. Factors such as hand-to-mouth contact, interaction with contaminated surfaces, and caregivers' hygiene could contribute to infants' exposure to animal feces. To assess animal fecal contamination in household settings, we collected floor swabs and infant and caregiver hand rinses in 141 households from nine communities in coastal Ecuador. We measured four microbial source tracking (MST) markers to assess animal fecal contamination from avian (GFD), canine (DG37), swine (Pig2Bac), and ruminant (Rum2Bac) sources. We found that 43% of floors, 31% of infant hands, and 23% of caregiver hands tested positive for at least one MST marker. Mean $\log_{10}$ concentrations were 1.21, 1.82, and 1.24 gene copies (gc)/cm^2 for floor, infant hands, and caregiver hands, respectively. We used generalized estimating equations with robust standard errors to determine the association between sample type and MST marker prevalence (modified Poisson) and loads (Gaussian). Caregiver and infant hands were 48% (95%CI: 0.37,0.73) and 28% (95%CI: 0.56, 0.94) less likely to test positive for any MST marker compared to floor samples. Specifically, caregiver hands were 69% (95%CI: 0.15, 0.64) less likely to test positive for the avian MST marker and 59% (95%CI: 0.24, 0.70) less likely to test positive for the MST canine marker; no difference was found for other markers. Though floors were more likely to have contamination, we found higher MST loads on infant and caregiver hands. On average, infant hands had 0.6 $\log_{10}$ MST gc/cm^2 (95%CI: 3.80, 4.35), and caregiver hands had 0.03 $\log_{10}$ gc/cm^2 more than floors(95%CI: 1.01, 1,16). Our findings indicate that floors and hands are contaminated with animal feces, with higher concentrations of MST markers detected on infant hands. Both sample types could serve as reservoirs and pathways for contaminant transmission. Understanding the dynamics of animal fecal contamination within households is essential to inform targeted interventions to reduce health risks associated with animals.

8343

DISCOVERY OF NEW SPECIES OF WILD MAMMALS AS POTENTIAL RESERVOIRS IN AMAZONIA OF *COXIELLA BURNETII*, THE AGENT OF Q FEVER

Loïc Epelboin[1], Damien Donato[2], Edith Guilloton[1], Salma Omar[1], Mona Saout[3], Olivier Duron[4], Alizée Raptapopoulo[5], Aurelie Couesnon[5], Elodie Rousset[5], Benoit De Thoisy[2], Anne Lavergne[2]

[1]Centre Hospitalier de Cayenne, Cayenne, French Guiana, [2]Institut Pasteur in French Guiana, Cayenne, French Guiana, [3]Université de Guyane, Cayenne, French Guiana, [4]University of Montpellier, CNRS, IRD, Montpellier, France, [5]ANSES (French Agency for Food, Environmental and Occupational Health and Safety), Sophia-Antipolis, France

Q fever is a ubiquitous bacterial zoonosis due to *Coxiella burnetii* with a worldwide distribution. In most parts of the world, transmission to humans occurs via infected livestock. In French Guiana, a French territory located in Amazonia, the incidence of human Q fever is the highest in the world, but the animal reservoir remains a mystery. The aim of this study was to investigate the reservoir of *C. burnetii* in wild Amazonian mammals. From Feb 2021 to Jan 2023, various mammalian feces, tissues and anal and vaginal swabs were collected from bat captures, roadkill mammal corpses, zoo and animal care centers, feline and forest herbivore droppings collected by the French Biodiversity Office and tissues from collections of the Institut Pasteur in French Guiana. Specific detection of the *C. burnetii* IS_{1111} target was carried out by real-time PCR on extracted DNAs. Over the study period, 2014 samples were analyzed by qPCR (swabs N=218, droppings N=498, urine N=15 and tissues N =1283) from 16 different orders. Thirty-four samples from 29 individuals of 7 different orders and 16 different species were positive for *C burnetii*: 1 artiodactyla (1 *Dicotyles tajacu*), 2 carnivoras (1 *Panthera onca*, 1 *Potos flavus*), 2 chiropteras (1 *Carollia perspicillata,* 1 *Molossus molossus*), 5 marsupialia (4 *Didelphis marsupialis,* 1 *Philander opossum*), 1 xenarthra (*Choloepus didactylus*), 6 primates (1 *Sapajus apella*, 3 *Saimiri sciureus*, 2 *Alouatta macconnelli*), 12 rodents (7 *Rattus rattus*, 1 *Rattus norvegicus*, 1 *Makalata didelphoides*, 1 *Proechimys guyannensis* , 2 Mus musculus). For all samples, bacterial loads were low. Organs were more strongly positive than feces.This study reveals a remarkable diversity of wild mammal species carrying *C. burnetii* in Amazonia, suggesting a complex ecosystem in which *C. burnetii* could spread and maintain itself. Further research into the interactions between wild species and human populations is required to better understand and control the spread of this zoonosis in Amazonia.

8344

TRANSPOSON MUTAGENESIS OF *PLASMODIUM KNOWLESI* REVEALS DETERMINANTS OF ANTIMALARIAL SUSCEPTIBILITY

Brendan Elsworth[1], Sida Ye[2], Sheena Dass[3], Jacob T. Tennessen[3], Basil T. Thommen[3], Aditya S. Paul[3], Marc-Jan Gubbels[4], Kourosh Zarringhalam[5], Manoj T. Duraisingh[3]

[1]Food and Drug Administration, Silver Spring, MD, United States, [2]University of Massachusetts, Boston, MA, United States, [3]Harvard T.H. Chan School of Public Health, Boston, MA, United States, [4]Boston College, Boston, MA, United States, [5]University of Massachusetts Boston, Boston, MA, United States

Forward genetic approaches have been applied to identify essential gene function in two *Plasmodium* species. However, the lack of essentiality data for parasites in the *P. vivax* clade limits the ability to prioritize targets for vaccines and therapeutics for this important group of malaria parasites, especially for large clade-specific gene families. Moreover, zoonotic cases of malaria are increasing in prevalence in Southeast Asia caused by infection with *P. knowlesi* and *P. cynomolgi*, which are closely related to *P. vivax* and serve as powerful models since *P. vivax* cannot be cultured *in vitro*. Here we conduct a transposon mutagenesis screen in *P. knowlesi*, to provide the most complete determination of gene essentiality for blood-stages of any *Plasmodium* spp., informing drug and vaccine development. Our screen has reached near site-level saturation providing the resolution to identify non-essential domains within essential genes. Analysis of the data revealed considerable conservation of the druggable genome within *Plasmodium* spp., as well as divergences in pathways related to the TCA cycle and metabolism. We investigated the utility of transposon mutagenesis in *P. knowlesi* to identify genes that modulate sensitivity to antimalarial drugs in unbiased genome-wide perturbation screens. Selection with the ganaplacide analog, GNF179, enriched 1000-fold for mutants containing insertions in an acetyl-CoA transporter 1 gene, whose deletion confers GNF179-resistance in *P. falciparum*. Artemisinin selection revealed known modulators of susceptibility, including knowpain 3 and hemoglobin digestion, as well as new candidates in known pathways, such as FBXO7 involved in protein ubiquitination, and new genes such as PATPL1, disruption of which leads to increased susceptibility to dihydroartemisinin. The *P. knowlesi* essentiality data and piggyBac transposon system will serve as valuable resources to the community for identifying novel *Plasmodium* biology.

8345

IMPROVING CESTOCIDES THROUGH TARGET-BASED DESIGN

Daniel J. Sprague[1], Sang-Kyu Park[2], Jonathan S. Marchant[2]

[1]Medical University of South Carolina, Charleston, SC, United States, [2]Medical College of Wisconsin, Milwaukee, WI, United States

The anthelmintic drug praziquantel (PZQ) has been used for decades to treat parasitic flatworm infections of clinical and veterinary importance.

Recent identification of $TRPM_{PZQ}$, the parasite target of PZQ, has enabled target-based design opportunities to develop novel anthelmintic chemotypes. Two tantalizing approaches towards this goal are exploitation of (i) binding pocket variation between parasite $TRPM_{PZQ}$ orthologs to target specific diseases, and (ii) metabolically stable PZQ derivatives to prolong target exposure. The latter is challenging for trematode $TRPM_{PZQ}$, as metabolically stable derivatives resulting from cyclohexyl ring modifications typically lose potency at $TRPM_{PZQ}$ owing to the stringent binding pocket architecture. Here, we capitalized on both these strategies to develop potent, metabolically stable ligands targeting cestode $TRPM_{PZQ}$. First, an amino acid difference from trematode $TRPM_{PZQ}$ makes the cyclophyllidean cestode $TRPM_{PZQ}$ binding pocket more sterically accommodating. This allows incorporation of modifications that show greater metabolically stability than PZQ. Second, cestodes possess a histidine residue at a critical position in the binding pocket that can be exploited to enhance ligand potency. Additionally, *in silico* experiments guided the design of new molecules that are potent agonists of pseudophyllidean $TRPM_{PZQ}$, a characteristic lacking in PZQ. This was accomplished through the rational design of molecules that interact with this histidine residue. Pursuing both these target-based design opportunities led to the identification of PZQ derivatives that showed improved potency at cestode $TRPM_{PZQ}$ and stability *in vitro*. Based on these improvements, testing these analogs against various cestode *ex vivo* and *in vivo* models has merit. Ultimately, these studies demonstrate the power of target-based design in improving treatments for cestode infections.

8346

DISCOVERY AND OPTIMIZATION OF ANTHELMINTIC CANDIDATES FOR SOIL TRANSMITTED HELMINTHS

Mostafa A. Elfawal[1], Emily Goetz[1], You-Mie Kim[1], Paulina Chen[1], Leonard Barasa[2], Sergey Savinov[3], Paul R. Thompson[2], Raffi Aroian[1]

[1]Program in Molecular Medicine, UMass Chan Medical School, Worcester, MA, United States, [2]Department of Chemical Biology, UMass Chan Medical School, Worcester, MA, United States, [3]GALY Co, Boston, MA, United States

Soil-transmitted helminths (STH) are among the most common neglected tropical diseases (NTDs), affecting about 1.5 billion people, with children and pregnant women in endemic countries being the most vulnerable. To control STH, Mass Drug Administration (MDA) campaigns are conducted to target preschool and school-aged children using two benzimidazole drugs, albendazole and mebendazole. However, the efficacy of these drugs is not optimal, and new drugs with new modes of action are urgently needed to overcome recalcitrant parasites and inevitable resistance. To find new anthelmintics, we built a novel screening pipeline based on human parasitic nematodes. We screened over 30,000 small molecules covering various compound libraries using human hookworms. We identified novel compounds with broad-spectrum anthelmintic activity against whipworms and hookworms. We further evaluated these compounds using cheminformatics, data mining, and *in vitro* characterization to determine their potency, safety, and speed of action against adult parasites. Based on these criteria, we prioritized over twenty compounds for *in vivo* studies in hamsters infected with the zoonotic hookworm parasite, *Ancylostoma ceylanicum.* We identified multiple lead compounds with significant *in vivo* activity against nematode parasites. Our top candidates, including ones with completely novel anthelmintic scaffolds, were equally potent against the sensitive and resistant isolates of two important veterinary parasites resistant to multiple classes of currently deployed anthelmintics. We then screened analogs of the top anthelmintic candidates to understand the structure-activity relationship and to establish the SAR model for at least four leads. We analyzed cell permeability and intestinal solubility of *in vitro* potent analogs with varying *in vivo* activities to understand the discrepancy between the two. We will present our ongoing studies on these newly emerged anthelmintic candidates, including lead optimization using medicinal chemistry approaches, target deconvolution using click chemistry and pulldown techniques, and mode of action studies.

8347

INVESTIGATING THE MECHANISM OF ACTION FOR THE AMOEBICIDAL AGENT NITROXOLINE AGAINST *BALAMUTHIA MANDRILLARIS*

Kaitlin Marquis[1], Natasha Spottiswoode[2], Angela Detweiler[1], Samuel Lord[2], Norma Neff[1], Dyche Mullins[2], Julia Haston[3], Heather Stone[4], Joseph DeRisi[5]

[1]Chan Zuckerberg Biohub, San Francisco, CA, United States, [2]University of California San Francisco, San Francisco, CA, United States, [3]Centers for Disease Control and Prevention, Atlanta, GA, United States, [4]US Food and Drug Administration, Silver Spring, MD, United States, [5]Chan Zuckerberg Biohub and University of California San Francisco, San Francisco, CA, United States

Balamuthia mandrillaris is a free-living amoeba that causes granulomatous amebic encephalitis, a condition with a mortality rate of 90%. This disease is currently treated with a six-drug regimen of limited efficacy and frequent toxicities. Our lab previously discovered that a quinolone antibiotic, nitroxoline, is a potent *in vitro* inhibitor of *B. mandrillaris.* Nitroxoline has since been used successfully to treat a human patient. In this project, we sought to understand the mechanisms of action of nitroxoline, create a high-quality annotated reference genome for *B. mandrillaris,* and analyze the transcriptional response to nitroxoline as compared to other cellular stressors. We demonstrated that nitroxoline's amoebicidal activity can be rescued by supplementing with iron and copper divalent cations, consistent with nitroxoline's known ability to chelate metals. We next interrogated the mechanism of amoebicidal activity with electron microscopy. *B. mandrillaris* is thought to respond to stressors by encystment. Scanning electron microscopy revealed that nitroxoline acts by undermining the structural integrity of *Balamuthia* cysts and interfering with the encystment process. To interrogate this phenomenon further, we next created a high-quality annotated reference genome by generating extensive Pacbio Hifi reads, Illumina, and HiC datasets. This new genome surpasses its predecessors in completeness, sequence continuity, and telomere-to-telomere coverage for most chromosomes. Finally, building on this resource, we conducted a transcriptomic study that revealed the amoeba's dynamic and distinct responses to nitroxoline, as compared to other triggers of encystment such as galactose and hypoxia. Our findings argue against a common encystment transcriptomic program and highlight nitroxoline's effect on metal-requiring pathways. These insights not only highlight nitroxoline's potential as a transformative therapeutic agent for this rare, but deadly pathogen, but also significantly advance our molecular understanding of *Balamuthia* itself.

8348

GLUCOSE IN - LACTATE OUT: GLUCOSE AND LACTATE TRANSPORT IN *SCHISTOSOMA MANSONI*

David L. Williams[1], Sammy Y. Aboagye[1], Pavel A. Petukhov[2]

[1]Rush University Medical Center, Chicago, IL, United States, [2]University of Illinois, Chicago, Chicago, IL, United States

Only praziquantel is available for treating schistosomiasis, a disease affecting more than 200 million people. Treatment of hundreds of millions of people with praziquantel alone is not sustainable, and new drugs for schistosomiasis treatment are needed. Schistosome worms in the mammalian host use aerobic fermentation of glucose to generate ATP with concomitant production of lactate. Both glucose and lactate are cell impermeable and require specific transport proteins for cell uptake and secretion. Previous studies have found that RNAi suppression of facilitative glucose transporters (GLUTs) resulted in *Schistosoma mansoni* worms with decreased viability.(PMID: 17040830). We present results that inhibitors targeting human GLUTs have LD_{50} < 10 micromolar against *S. mansoni* worms. Because GLUTs are found primarily on the worm surface, we hypothesize that additional glucose transporters must be present on internal worm cells. We have found that two genes encoding proteins with high homology to human sodium-coupled glucose transporters (SGLTs) are present in the *S. mansoni* genome and that both have wide tissue

expression. We present results that compounds clinically used for diabetes treatment by inhibiting human SGLTs are active against *S. mansoni* worms with low micromolar LD_{50}. Excretion of lactate at the schistosome surface has been shown to involve aquaporins.(PMID: 20454673) Excretion of lactate by internal cells has not been characterized. We hypothesize that uncharacterized lactate transporters must be present on internal worm cells. We have identified two genes in the *S. mansoni* genome encoding proteins with homology to human monocarboxylate transporters (MCTs). Both genes have wide tissue expression. We present results that inhibitors targeting human MCTs block lactate excretion from worms and have LD_{50} < 10 micromolar. Identification and validation of schistosome glucose and lactate transporters will provide a solid basis for future studies for target-based drug development for new schistosomiasis drugs.

8349

INDIVIDUAL-LEVEL EFFICACY OF ALBENDAZOLE AND FIXED-DOSE FORMULATION OF IVERMECTIN/ALB (FDC) AGAINST *TRICHURIS TRICHIURA* AND HOOKWORMS IN ETHIOPIA, KENYA AND MOZAMBIQUE. PER PROTOCOL ANALYSIS OF THE ALIVE CLINICAL TRIAL

Pedro E. Fleitas[1], Stella Kepha[2], Woyneshet Gelaye[3], Augusto Messa Jr.[4], Javier Gandasegui[1], Lisette van Lieshout[5], Jaime Algorta[6], Áuria de Jesus[4], Valdemiro Novela[4], Inácio Mandomando[4], Charles Mwandawiro[2], Wendemagegn Enbiale[3], Paula Petrone[1], Jose Muñoz[1], Alejandro J. Krolewiecki[7]

[1]Barcelona Institute for Global Health (ISGlobal), Barcelona, Spain, [2]Eastern and Southern Africa Centre of International Parasite Control, Kenya Medical Research Institute, Nairobi, Kenya, Nairobi, Kenya, [3]Bahir Dar University, College of Medicine and Health Sciences, Bahir Dar, Ethiopia, [4]Centro de Investigação em Saúde de Manhiça (CISM), Maputo, Mozambique, [5]Leiden University Center for Infectious Diseases, Leiden, Netherlands, [6]Departamento Investigación clínica, Laboratorios Liconsa (InsudPharma group), Madrid, Spain, [7]Universidad Nacional de Salta, Instituto de Investigaciones de Enfermedades Tropicales/CONICET, Oran, Argentina

Albendazole (ALB) shows low to moderate efficacy against *Trichuris trichiura (Tt)* and hookworm (Hk) infections. We conducted a per-protocol analysis at individual level of the ALIVE clinical trial, aimed at evaluating a fixed-dose formulation of ivermectin/ALB (FDC) in single doses, and ALB in participants infected with *Tt* (n=369) and Hk (n=226) in Ethiopia, Kenya and Mozambique. We used a mixed model fitted in a Bayesian framework to calculate the percentage of participants with therapeutic failure, defined as those not cured and with an individual egg reduction rate (ERRi) insignificantly different from zero. We evaluated the impact of age, sex, body composition, study site, ivermectin dose, and co-infection with another soil-transmitted helminth (STH) on efficacy. Posterior means and 95% credible intervals (95% CI) of the ERRi were calculated for each participant and covariate. In *Tt*-infected participants, 53.6% (ALB) and 5.7% (FDC) of participants had therapeutic failure. In the ALB arm, an average participant co-infected with *A. lumbricoides* exhibited a superior response (ERRi: 65.0 (95% CI: 30.7,83.8)), compared to an average participant with single infection (ERRi: -49.0 (95% CI: -143.5,0.9), p=0.032). In the FDC arm, an average participant co-infected with *S. stercoralis* displayed a poorer response (ERRi: -25.0 (95% CI: -355.2,77.2)) than an average participant with single infection (ERRi: 95.5 (95% CI: -92.4,97.4), p=0.011), and an average participant from Mozambique exhibited a better response (ERRi: 99.1 (95% CI: 97.0,99.9)) compared to an average participant from Kenya (ERRi: 88.7 (95% CI: 75.1,94.1), p=0.017). Among Hk-infected participants, 14.7% (ALB) and 9.7% (FDC) had therapeutic failure. In the FDC arm, an average participant co-infected with *S. stercoralis* exhibited a poorer response (ERRi: 59.6 (95% CI: 0.1.85.2)) compared to an average participant with single infection (ERRi: 95.7 (95% CI: 91.5.97), p=0.012). Our findings suggest significant improvements in efficacy with FDC compared to ALB in *Tt* infections. Moreover, co-infections may influence treatment responses, warranting further investigation.

8350

A MULTI-COUNTRY COMMUNITY EVALUATION OF THE LONG-TERM PERFORMANCE OF PERMANET 3.0, A LONG-LASTING PYRETHROID-PBO NET

Duncan K. Athinya[1], Patrick K. Tungu[2], Samuel K. Dadzie[3], Raghavendra Kamaraju[4], Maurice Ombok[5], John E. Gimnig[6], Melinda Hadi[7]

[1]Vestergaard Frandsen (EA) Limited, Nairobi, Kenya, [2]Muheza College of Health and Allied Sciences, Muheza, Tanzania, United Republic of, [3]Noguchi Memorial Institute for Medical Research, University of Ghana, Accra, Ghana, [4]National Institute of Malaria Research (Indian Council of Medical Research), New Delhi, India, [5]Kenya Medical Research Institute, Kisumu, Kenya, [6]Centers for Disease Control and Prevention, Division of Parasitic Diseases and Malaria, Atlanta, GA, United States, [7]Vestergaard Sàrl, Lausanne, Switzerland

Pyrethroid-PBO nets have received a WHO recommendation for deployment in place of pyrethroid-only nets where malaria vectors are resistant to pyrethroids. The recommendation is conditional, due to uncertainty around the long-term performance of PBO in pyrethroid-PBO nets. Three-year, multi-country community studies are useful in evaluating long-term performance. This study evaluated PermaNet 3.0, a pyrethroid-PBO net formulated with 25g/kg of PBO and 4g/kg of deltamethrin on the roof. The long-term community studies were conducted in Ghana, India, and Kenya, following the 2013 WHO guidelines. The physical and chemical components were evaluated at 12, 24, and 36 months. Bioefficacy was tested using a pyrethroid susceptible *Anopheles gambiae s.s.* Kisumu laboratory strain. With the development of standard operating procedures for testing with pyrethroid-resistant strains, additional samples of PermaNet 3.0 were collected from Uganda, Tanzania, and Malawi at 3 years of use. The bioefficacy of these additional samples was tested using two well-characterized pyrethroid-resistant laboratory strains of *An. gambiae s.s.*. PermaNet 2.0 was used as a pyrethroid-only positive control for all assessments. PermaNet 3.0 had optimal bioefficacy. The loss of deltamethrin was more gradual than the loss of PBO. PBO had a rapid 38-58% loss in year 1, followed by a more gradual loss in years 2 (20-40% loss) and 3 (19-25% loss). PermaNet 3.0 retained 5-10g/kg of PBO at the 3-year end-of-use period. In the additional samples (Uganda, Tanzania, and Malawi), the PBO content was between 3-10g/kg, comparable with the community studies. Against pyrethroid-resistant mosquitoes, four times higher mortality was observed with 3-year used PermaNet 3.0 relative to the pyrethroid-only net. Fabric integrity and attrition levels were similar for PermaNet 3.0 between all sites. PermaNet 3.0 is a durable pyrethroid-PBO LLIN, that protects against pyrethroid-resistant malaria vectors through three years of use.

8351

RANDOM CONTROLLED TRIALS AND BEYOND - RESULTS FROM THE FIRST MULTI- COUNTRY STUDY OF THE EFFECTIVENESS OF SPATIAL REPELLENTS TO CONTROL VECTOR BORNE DISEASES AMONGST FORCED DISPLACED POPULATIONS IN CONFLICT AFFECTED AREAS OF N. SYRIA, YEMEN AND N. NIGERIA, 2019 - 2024

Richard James Allan[1], Ramona Scherrer[1], Sara Estecha Querol[1], Laura Paris[1], Olivia Wetherill[1], David Weetman[2], Sergio Lopes[1]

[1]The MENTOR Initiative, Haywards Heath, United Kingdom, [2]Liverpool School of Tropical Medicine, Liverpool, United Kingdom

Over 80% of the world's population is affected by one or more vector borne diseases resulting in over 1 million deaths each year. Indeed, 17% of all infectious disease results from pathogens biologically transmitted to humans by blood-feeding sandflies, mosquitoes and others that vector pathogens such as Leishmaniasis, malaria, dengue, their feeding time preferences often correlate with common human behaviour patterns, creating a defined time and context when humans are vulnerable to attack and infection. Frequency and intensity of armed conflicts and extreme weather events have multiplied since the 1960s, disproportionately affecting some regions and displacing 110 million people by 2023. Changes to

the context in which disease vectors, pathogens and humans exist. Extreme events often generate hazardous environmental conditions in which arthropod vectors thrive, human vulnerability increases, and the effectiveness of core vector tools such as ITNs and indoor residual spraying (IRS), are most limited, and death rates rise sharply. The MENTOR Initiative, between 2019 to 2024 conducted a multi-county evaluation of spatial repellent devices (SRD) for control of different vectors and diseases amongst 64,000 displaced people living in temporary shelter camps in N. Syria, Yemen and N. Nigeria. The study findings demonstrate high acceptance and retention (73-98%) for SRD and show the tools ability to exert effective disease control. *Phlebotomine* sandfly density reduced by >74%, incidence of cutaneous leishmaniases was halved (0.52 times lower, 95% CI = 0.37-0.73, p<000); blood fed *aedes* mosquitoes which vector flaviruses were reduced by 89.6% (t test=13.5, p<0.000), and *anopheles* mosquitoes and incidence of malaria reduced. SRD are light weight, low cost, easy to transport, deploy, and use with minimal instruction. Their ability to achieve control both indoors and also in peri-domestic spaces make these tools a vital addition to the expanded vector control toolbox now urgently required. Innovate new tools fit for purpose and approved for use by WHO are vital, but currently missing due to regulatory bottlenecks.

8352

HOUSE MODIFICATIONS USING INSECTICIDE TREATED SCREENING OF EAVE AND WINDOW AS VECTOR CONTROL TOOL: EVIDENCE FROM A SEMI-FIELD SYSTEM IN TANZANIA AND SIMULATED EPIDEMIOLOGICAL IMPACT

Olukayode Ganiu Odufuwa[1], Richard Sheppard[2], Safina Ngonyani[1], Ahmadi Mpelepele[1], Dickson Kobe[1], Agathus Njohole[1], Jason Moore[1], Jastin Lusoli[1], Joseph Muganga[1], Rune Bosselmann[3], Ole Skovmand[4], Zawadi Mageni Mboma[1], Emmanuel Mbuba[1], Rose Philipo[1], Jennifer Stevenson[1], Ellie Sherrard-Smith[2], John Bradley[5], Sarah Moore[1]

[1]Ifakara Health Institute, Bagamoyo, Tanzania, United Republic of, [2]Imperial College, London, United Kingdom, [3]Vegro Aps, Copenhagen, Denmark, [4]MCC47, Montpellier, France, [5]London School of Hygiene and Tropical Medicine (LSHTM), London, United Kingdom

Simple house modification tools that target eaves and windows have the potential to reduce human exposure to mosquito bites in the home. This study assessed the performance of Insecticide Treated Screening (ITS) comprising Eave Nets and Window Screens (ITENs & ITWS), incorporated with deltamethrin and piperonyl-butoxide (PBO) in Tanzania. A randomised Latin square (4 X 4) was conducted in four experimental huts built in a semi-field system (SFS). Four treatment arms were evaluated: 1) new ITS; 2) 12-months naturally-aged ITS; 3) estimated 12 months field-used Olyset® Plus ITNs (Standard-of-Care in Tanzania), and; 4) no treatment for 32 nights using a minimum of 30 mosquitoes per strain per night (a total of 120 per hut). Four laboratory-reared strains were used: transmitters of malaria (*Anopheles arabiensis* and *An. funestus*) and dengue infection (*Aedes aegypti*) and those known for nuisance biting (*Culex quinquefasciatus*). Recaptured mosquitoes were assessed for mortality at 72 hours (M72), blood feeding and hut entry endpoints. A simulation exercise with a modified mechanistic model tracking *Plasmodium falciparum* malaria was used to illustrate the potential epidemiological impact from these products. New ITS induced higher M72 than field-used ITNs against all mosquito species tested [OR: 2.25 (95%CI: 1.65-3.06), p<0.0001], while M72 was similar between aged ITS and field-used ITNs [OR: 0.80 (95%CI: 0.59-1.08), p=0.141]. Both new, and aged ITS reduced more mosquito blood feeding and hut entry than field-used ITNs for all mosquito species tested (p<0.0001). Transmission model estimates indicate epidemiological impacts of ITS may supersede those of ITNs at the population level. The model results indicate that the potency of these impacts depends on assumed intervention percentage cover, durability and mosquito bionomics. ITS is an efficacious tool for controlling vectors transmitting malaria, and dengue, and those known for nuisance biting in a semi-field setting. Given the intervention's simplicity, it should be considered as an additional (or stand-alone) tool.

8353

ENTOMOLOGICAL EFFECTS OF ATTRACTIVE TARGETED SUGAR BAIT STATION DEPLOYMENT IN WESTERN ZAMBIA: VECTOR SURVEILLANCE FINDINGS FROM A TWO-ARM CLUSTER RANDOMIZED PHASE III TRIAL

Javan Chanda[1], Joseph Wagman[2], Benjamin Chanda[3], Kochelani Saili[3], Erica Orange[4], Patricia Mambo[3], Rayford Muyabe[3], Tresford Kaniki[3], Mwansa Mwenya[3], Mirabelle Ng'andu[3], John Miller[1], Annie Arnzen[4], Kafula Silumbe[1], Gift Mwaanga[5], Limonty Simubali[5], Edgar Simulundu[5], Mulenga Mwenda[1], Busiku Hamainza[6], Ruth A. Ashton[7], Thomas P. Eisele[7], Angela Harris[8], Joshua Yukich[7], Laurence Slutsker[9], Thomas Burkot[10], Megan Littrell[2]

[1]PATH, Lusaka, Zambia, [2]PATH, Washington, DC, United States, [3]PATH, Kaoma, Zambia, [4]PATH, Seattle, WA, United States, [5]Macha Research Trust, Choma, Zambia, [6]National Malaria Elimination Centre, Lusaka, Zambia, [7]Centre for Applied Malaria Research and Evaluation, Tulane School of Public Health and Tropical Medicine, New Orleans, LA, United States, [8]Innovative Vector Control Consortium, Liverpool, United Kingdom, [9]Independent Consultant, Atlanta, GA, United States, [10]Australian Institute of Tropical Health and Medicine, Cairns, Australia

Attractive targeted sugar bait (ATSB) stations are a novel tool with potential to complement current approaches to malaria vector control. To assess the public health value of ATSB stations in the context of high coverage with standard malaria vector control, a two-arm cluster-randomized controlled trial was conducted in Western Province, Zambia. The broader trial was designed to measure the effect of Sarabi v1.2 ATSB® station (Westham Ltd., Hod-Hasharon, Israel) deployment on malaria case incidence and infection prevalence over two seven-month deployments. To provide key entomological context for overall interpretation of trial findings, monthly vector surveillance was conducted in 10 intervention and 10 control clusters. Human landing capture (HLC) and ultraviolet light trap (LT) collections were used to monitor *Anopheles funestus* parity, abundance, biting rates, sporozoite prevalence, and entomological inoculation rates (EIR). Over the course of the study, 11,229 female *An. funestus* specimens were collected from control clusters and 9,108 from intervention clusters. The primary entomological outcome was the proportion of *An. funestus* that were non-parous, and a subset of 3,131 specimens collected during HLC were successfully assessed for parity via ovarian dissection. There was no difference in non-parous proportion (NPP) across the study arms: mean NNP was 23.0% (95%CI 18.2% - 28.7%) in the control and 21.2% (95%CI 18.8% - 23.9%) in the intervention, an OR = 1.05 (95%CI 0.82 - 1.34; p = 0.688). A non-significant 35% reduction in LT abundance (RR = 0.65 [95%CI 0.30 - 1.40, p = 0.267]) was associated with ATSB deployment, consistent with the observed epidemiological impact of ATSB reported previously. Human landing rates were highly variable, but model results indicate a similar non-significant trend, with a RR = 0.68 (95%CI 0.22 - 2.00; p = 0.479). There was no observed effect on sporozoite positivity or EIR. Similar trials in Kenya and Mali conclude in 2024 and will provide additional evidence of ATSB efficacy in other settings, but additional research is needed to understand how to maximize the impact of ATSB approaches in Zambia.

8354

FIELD TRIAL RESULTS OF A VOLATILE PYRETHROID SPATIAL REPELLENT USING A TRANSFLUTHRIN ACTIVE INGREDIENT AS A CONTROL INTERVENTION FOR OUTDOOR-BITING *ANOPHELES* MOSQUITOES

Tim Burton[1], Limonty Simubali[2], Lewis Kabinga[2], Lepa Syahrani[3], Dendi H. Permana[3], Ismail E. Rozi[3], Jennifer Stevenson[2], Monicah Mburu[2], Edgar Simulundu[2], Puji Asih[3], Din Syafruddin[3], Neil Lobo[1]

[1]University of Notre Dame, Notre Dame, IN, United States, [2]Macha Research Trust, Macha, Zambia, [3]Eijkman Research Center for Molecular Biology, National Research and Innovation Agency (BRIN), Cibinong, Indonesia

Presently, the most common malaria control tools - i.e. long lasting insecticide-treated nets (LLINs) and indoor residual spraying (IRS) are limited

to targeting indoor biting and resting behaviors of *Anopheles* mosquito species. Few interventions are targeted towards malaria control in areas where transmission is driven or persists due to outdoor biting behaviors. A volatile pyrethroid-based spatial repellent (VPSR) using a transfluthrin active ingredient was designed to address this gap in protection. A collection of one semi-field and three field trials were conducted in communities vulnerable to outdoor biting in Zambia and Indonesia, assessing the protection provided by the VPSR in outdoor spaces where biting is known to occur. The product provided significant protection to users during semi-field trials by reducing observed host-seeking activity by roughly 40% per night and increasing mortality among exposed mosquitoes, with evidence that this effect was under-estimated due to the all-night containment inherent to the semi-field study design. Host-seeking was significantly reduced in structures protected by the VPSR device across the remaining three field trials, with significant nightly reductions of around 70% and similar rates of hourly protection. These results are reported along insights gained from additional field measurements as they relate to product efficacy over the duration of the field trials.

8355

FINAL YEAR RESULTS FROM A FOUR-ARM CLUSTER-RANDOMIZED TRIAL IN TANZANIA COMPARING THE EFFECTIVENESS OF THREE TYPES OF LONG-LASTING INSECTICIDAL NETS (LLINS) - PYRIPROXYFEN-PYRETHROID, CHLORFENAPYR-PYRETHROID, AND PIPERONYL BUTOXIDE-PYRETHROID - VERSUS A PYRETHROID-ONLY LLIN, AGAINST MALARIA

Nancy Matowo[1], Jacklin F. Mosha[2], Manisha A. Kulkarni[3], Eliud Lukole[4], Jacklin Martin[4], Alphaxard Manjurano[4], Immo Kleinschmidt[1], Naomi Serbantez[5], Mark Rowland[1], Franklin Mosha[6], Natacha Protopopoff[1]

[1]London School of Hygiene and Tropical Medicine, London, United Kingdom, [2]National Institute for Medical Research, Mwanza Medical Research Centre, Mwanza, Tanzania, United Republic of, [3]School of Epidemiology and Public Health, University of Ottawa,, Canada, United Kingdom, [4]National Institute for Medical Research, Mwanza, Tanzania, United Republic of, [5]PMI-USAID, Dar es Salaam, Tanzania, United Republic of, [6]5.Department of Parasitology, Kilimanjaro Christian Medical University College, Moshi, Tanzania, United Republic of

New classes of LLINs containing two active ingredients (a.i.) have been recently recommended by WHO in areas where malaria vectors are resistant to pyrethroid. This policy was based on evidence generated by the first two years of our recently published trial in Tanzania. In this paper, we report the final third-year trial findings which are required to assess the lifespan of the new classes of LLIN in the community and the replacement intervals required. A third year of follow-up of a four-arm cluster-randomized controlled trial of dual-a.i. LLINs which was conducted between January 2021 and February 2022 in Tanzania. Restricted randomisation was used to assign 84 clusters to the four LLIN groups (1:1:1:1) to receive either standard pyrethroid (PY)-LLINs (reference), chlorfenapyr-PY LLINs, pyriproxyfen-PY LLINs or piperonyl butoxide (PBO)-PY LLINs. Households received one LLIN for every two people. The field team, laboratory staff, analysis team and study participants were blinded to the allocation. The primary 24 months' endpoint was reported previously; here we present malaria infection prevalence in children 6 months to 15 years old at 36-months post LLIN distribution. Analysis was according to intention-to-treat (ITT). The trial was registered with ClinicalTrials.gov (NCT03554616) and is now completed.Overall usage of study nets was 22% at 36 months' post distribution. In the chlorfenapyr-PY LLIN arm, there was strong evidence of a reduction of malaria prevalence compared to the standard LLIN arm at 36 months (OR 0·57 [95%CI 0·38-0·86] p=0·0069). There was only weak evidence of a difference in malaria prevalence at 36 months in groups receiving pyriproxyfen-PY LLINs and PBO-PY LLINs compared to the standard LLIN.

8356

A CLUSTER-RANDOMIZED CONTROLLED PHASE III EVALUATION OF 3D WINDOW DOUBLE SCREEN (3D-WDS) IN REDUCING MALARIA TRANSMISSION WHEN COMBINED WITH PYRETHROID-TREATED LONG-LASTING INSECTICIDAL NETS IN NORTHEASTERN TANZANIA

Subam Kathet[1], Victor Mwingira[2], Frank S. Magogo[2], Veneranda M. Bwana[2], Hanna Granroth-Wilding[1], Patrick Tungu[2], Tomi Hakala[3], Markku Honkala[3], Mikko Aalto[4], William N. Kisinza[2], Seppo Meri[1], **Ayman Khattab**[1]

[1]University of Helsinki, Helsinki, Finland, [2]National Institute for Medical Research, Muheza, Tanzania, United Republic of, [3]Tampere University of Technology, Tampere, Finland, [4]East Africa University, Bosaso, Somalia

The emergence of insecticide resistance in malaria vectors has prompted the need to develop alternative vector control methods that do not depend on insecticides. The 3D-Screen is an innovative window screen composed of 3D conical structures assembled onto a screen mesh. When installed as a double screen setup in window openings, creating the 3D-Window Double Screen (3D-WDS), its unidirectional design permits mosquitoes to enter from outside and leave from inside the house through the 3D-WDS, effectively trapping them between the double screens. Prior laboratory and experimental hut studies have demonstrated the remarkable efficacy of 3D-WDS in capturing host-seeking mosquitoes. This trial aimed at the elucidation of the epidemiological and entomological impact of implementing 3D-Screens in community settings. A two-armed, cluster randomized controlled trial was undertaken to assess whether houses equipped with both 3D-WDST, and long-lasting insecticidal nets (LLINs) provide superior protection against malaria compared to LLINs alone. In Muheza, Tanzania, fourteen hamlets with similar epidemiological and entomological profiles were randomly assigned to either the treatment or control arm. Seven hamlets received both 3D-WDST and LLINs (the treatment arm), while the remaining seven received only LLINs (the control arm). Epidemiological (malaria and anaemia prevalence in children) and entomological (indoor mosquito densities and the entomological inoculation rate) surveys were conducted at 10-week intervals over a 52-week period of follow-up. The trial findings demonstrated a significant decrease in the entomological inoculation rate of malaria mosquitoes sampled from households with 3D-WDST compared to those without. Additionally, malaria prevalence was significantly reduced in both study arms. Therefore, the 3D-Screen shows promise in reducing malaria transmission and providing a non-insecticidal alternative for mosquito control.

8357

ARTIFICIAL INTELLIGENCE LEVERAGING A VISION FOUNDATION MODEL FOR RECOGNITION OF MULTIPLE BLOOD PARASITES IN MICROSCOPY IMAGES

David Bermejo-Peláez[1], Lin Lin[2], Lucía Pastor[1], Roberto Mancebo-Martin[1], Ramon Vallés-López[1], Elena Dacal[1], Claudia Carmona[3], Victor Anton Berenguer[4], Alexandra Martín Ramírez[3], Maria Flores-Chaves[5], Ana Valeria Soriano[6], Fabiola Gonzales[6], Mary Cruz Torrico[6], Daniel Illanes[6], Jose Miguel Rubio[7], Miguel Luengo-Oroz[1]

[1]Spotlab, Madrid, Spain, [2]Spotlab & Universidad Politécnica de Madrid & CIBERBBN, Madrid, Spain, [3]National Microbiology Centre (Instituto de Salud Carlos III), Madrid, Spain, [4]Microbiology Service (Hospital Universitario Severo Ochoa) & National Microbiology Centre (Instituto de Salud Carlos III), Madrid, Spain, [5]National Microbiology Centre (Instituto de Salud Carlos III) & Fundación Mundo Sano, Madrid, Spain, [6]Universidad Mayor de San Simón, Cochabamba, Bolivia, Plurinational State of, [7]National Microbiology Centre (Instituto de Salud Carlos III) & CIBERINFEC, Madrid, Spain

Blood parasites that cause malaria, filariasis, and Chagas disease remain global health threats. Swift and precise parasite identification is crucial for treatment and epidemiological control. Although microscopy is the main diagnostic tool, its slow process and reliance on skilled experts hinder its effectiveness, especially in areas with less common parasites or resource-limited. In this context, AI for microscopy image analysis can provide a

more rapid and accurate diagnostic. We propose a data-efficient AI-based methodology to disease diagnosis focusing on the blood sample rather than the disease, enabling the identification of multiple parasites. In order to reduce the need for extensive annotated databases to train our method, we first use a self supervised learning (SSL) algorithm, which leverages large unannotated datasets to learn meaningful representations of blood parasites without the need for labels, usually scarce in parasitology. As a result, we came up with a foundation model based on a total of more than 100K microscope images (10x, 40x and 100x magnification, from 4 sites) acquired from thin blood smears of 332 patients. From this database, more than 89K images were used for SSL pretraining. In a subsequent step, the remaining 15K images were labeled (11 parasite species, including 5 filariae, 5 *Plasmodium* species and *T. cruzi*) by experts and used for finetuning with an 80%-20% patient level split. We used a transformer based model, ViT, with DINO as the SSL strategy.Results show that we achieve 95% accuracy (F1 Score) across the 11 parasite species. If just 10% of labeled data is used for finetuning (an average of approx 100 labels per class), we still achieve a high accuracy of 90% across all 11 species-comparable to the performance obtained with all data without using SSL. This shows that further species can be included with a very limited number of labels.Our work presents a generalized AI framework to classify multiple blood parasite species within a single model aligning with the real-world need, and has the potential to be integrated into smartphones facilitating real-time diagnosis and monitoring.

8358

EVALUATING THE ACCURACY OF CLINICAL MALARIA DIAGNOSES USING TAQMAN® ARRAY CARD MOLECULAR DETECTION IN NIGERIA

Emmanuel Oga[1], Claire Quiner[1], Jean Kim[1], Cyril Erameh[2], Vivian Kwaghe[3], Philippe Chebu[4], Lauren Courtney[1], Kat Asman[1], Osas Edeawe[2], Ephraim Ogbaini[2], Nankpah Vongdip[3], Victoria Orok[3], Oladimeji Matthew[3], Onyia Ejike[3], Ikponmwosa Odia[2], Blessed Okira[3], Jacqueline Agbukor[2], Julius Imoyera[2], Adamu Ephraim[1], Jay Samuels[4]

[1]RTI International, Research Triangle Park, NC, United States, [2]Irrua Specialist Teaching Hospital, Irrua, Nigeria, [3]University of Abuja Teaching Hospital, Abuja, Nigeria, [4]APIN Public Health Initiatives, Abuja, Nigeria

In Nigeria, a high malaria endemic region, routine clinical diagnoses frequently attribute acute febrile illnesses (AFIs) to malaria, which may mask the presence of other pathogens. This study assesses the accuracy of these clinical diagnoses compared to molecular detection using the TaqMan® Array Card (TAC) as part of the larger SAFIAN Study, aiming to uncover misdiagnoses and identify undiagnosed pathogens. Participants clinically diagnosed with malaria at two surveillance sites in Nigeria were tested with TAC PCR analysis to detect a broad panel of pathogens. Participant samples from 181 patients with acute febrile illness (AFI), clinically diagnosed with malaria and treated accordingly, were analyzed using TAC PCR to identify *Plasmodium spp.* as well as 24 other pathogens. The study compared clinical diagnoses, hospital laboratory tests (including microscopy or rapid diagnostic tests), and molecular testing results. Of the 181 cases diagnosed clinically with malaria, only 64 (35.4%) were confirmed by PCR for *Plasmodium spp.*, indicating a significant gap in clinical diagnostic accuracy. Additionally, molecular testing identified alternative pathogens in 38 cases (21%). Of these, 17 were viral while 21 were bacterial; including 8 cases (4.4%) of viral hemorrhagic fevers (VHF), 9 cases (5.0%) of other viral infections, and 21 cases (11.6%) of bacterial infections. Notably, 47 patients (26%) had a molecular detection of *Plasmodium spp.* only, suggesting over-treatment based on clinical suspicion alone. There is a marked discrepancy between clinical diagnoses of malaria and molecular confirmation with PCR in this sample of AFI patients in Nigeria. A substantial proportion of patients received malaria treatment despite the absence of *Plasmodium spp.* detection by molecular testing. This misdiagnosis risks masking other significant infections, highlighting the need for improved diagnostic strategies, such as the broader implementation of molecular diagnostics in routine clinical practice to enhance disease surveillance and patient management in malaria-endemic areas, and reduce the overdiagnosis of malaria.

8359

SOLUBLE TRIGGERING RECEPTOR EXPRESSED ON MYELOID CELLS 1 (STREM-1) TO RISK-STRATIFY PEDIATRIC AND ADULT PATIENTS WITH FEBRILE ILLNESS IN SOUTHERN MOZAMBIQUE

Núria Balanza[1], Bàrbara Baro[1], Sara Ajanovic[1], Zumilda Boca[2], Justina Bramugy[2], Anelsio Cossa[2], Elizabeth JA Fitchett[3], Heidi Hopkins[3], David Mabey[3], Tegwen Marlais[3], Hridesh Mishra[4], Campos Mucasse[2], Marta Valente[1], Andrea M. Weckman[4], Shunmay Yeung[3], Kathleen Zhong[4], Kevin C. Kain[4], Quique Bassat[1]

[1]ISGlobal, Barcelona, Spain, [2]Centro de Investigação em Saúde de Manhiça, Maputo, Mozambique, [3]London School of Hygiene and Tropical Medicine, London, United Kingdom, [4]University Health Network, Toronto, ON, Canada

Fever is a leading reason for seeking healthcare globally. Early in the course of illness, it is challenging to identify the subset of patients at risk of severe and fatal infections. However, many life-threatening infections share common pathophysiological pathways. We hypothesized that quantifying plasma biomarkers of immune and endothelial activation at presentation may help identify patients at high risk of adverse outcomes. This study was conducted in the Mozambican cohort of the Febrile Illness Evaluation in a Broad Range of Endemicities (FIEBRE) study. From December 2018 to February 2021, children ≥2 months and adults who presented with fever to two Mozambican hospitals were prospectively enrolled. Levels of Angpt-2, CHI3L1, CRP, IL-6, IL-8, PCT, sFlt-1, sTNFR1, sTREM-1, and suPAR at presentation were retrospectively determined in plasma using Luminex and ELISA. Standard clinical and laboratory parameters were assessed at presentation, and clinical outcomes were evaluated up to ≥28 days later. A total of 1,955 participants were enrolled and had biomarkers measured. Of these, 1,040 were managed as outpatients and 915 were admitted to hospital, with 531 and 509 being children aged <15 years, respectively. 93 deaths occurred in the following 28 days. All biomarkers were elevated in inpatients compared to outpatients and were associated with 28-day mortality (all $p<0.001$). sTREM-1 was the top-performing biomarker for predicting 28-day mortality with an AUROC of 0.82 (95% CI: 0.78-0.86), superior to that of PCT, CRP and lactate. Its prognostic accuracy was consistent across age and sex, but reduced in HIV-positive patients. sTREM-1 added value to clinical severity scores for 28-day mortality. Among inpatients discharged alive, sTREM-1 correlated with length of hospital stay. Among outpatients, sTREM-1 was associated with seeking further care or subsequent admission after being sent home. These findings confirm sTREM-1 as a promising biomarker for risk-stratification of all-age febrile illnesses in resource-constrained settings.

8360

COULD WE USE CONVENTIONAL MALARIA RDT TO IDENTIFY SEVERE MALARIA IN TRAVELERS?

Daniel Camprubí Ferrer, Julia Pedreira, Leire Balerdi-Sarasola, Guillermo Villanueva, Qiuyue Yang, Paula Petrone, Jose Muñoz, Claudio Parolo

ISGlobal / Hospital Clínic Barcelona, Barcelona, Spain

Mortality due to malaria remains unacceptably high, even in non-endemic settings, where WHO criteria for severe malaria (SM) are inaccurate. Therefore, identification of easy to detect biomarkers to discriminate malaria patients at risk of developing SM is key to improve the management of malaria in endemic and non-endemic countries. We performed an observational cross-sectional study of international travellers with fever returning from an international trip. Patients were classified as SM or uncomplicated malaria (UM) based on WHO criteria, except for parasitemia (threshold of 2% parasite density was used according to European and Spanish guidelines). HRP2 and pLDH concentrations were measured in

whole blood samples, extracted at the initial diagnostic workup, through Luminex. Samples were also tested with a dual lateral flow assay (LFA) allowing to detect HRP2 and pLDH (05FK60, Abbott, Chicago, IL, USA). Pictures of the LFA strips were used to quantify the signal of each strip line. We included a total of 121 travelers with febrile illnesses: 75 travelers with malaria (50 with SM and 25 with UM) and 46 travelers with non-malarial fevers. As expected, HRP2 and pLDH resulted undetectable in travellers with non-malarial fevers. In travellers with malaria, the median concentration of HRP2 and pLDH were 8537.4ng/ml and 219.8ng/ml, respectively, and resulted significantly higher in patients with SM ($p<0.001$). HRP2 showed 78% sensitivity and 84% specificity to predict severe malaria (AUC-ROC 0.86), and pLDH showed 80% sensitivity and 88% specificity (AUC-ROC 0.88). Quantification of pLDH signal in LFA also showed a good diagnostic performance to identify SM cases (83% sensitivity, 68% specificity and 0.84 AUC-ROC). In conclusion, besides being good diagnostic tools for the diagnosis of malaria, parasite biomarkers such as HRP2 and pLDH can be useful tools to predict patients at risk of developing severe malaria. Quantification of pLDH signal in rapid diagnostic tests could be a rapid and reliable tool to identify SM in returning travellers.

8361

ADMISSION POINT-OF-CARE TESTING FOR THE CLINICAL CARE OF CHILDREN WITH CEREBRAL MALARIA

Geoffrey Guenther[1], David Wichman[2], Nthambose M. Simango[3], Mengxin Yu[4], Olivia D. Findorff[5], Nathaniel O. Amoah[2], Rohini Dasan[2], Karl B. Seydel[6], Douglas G. Postels[7], Nicole F. O'Brien[8]

[1]Boston Children's Hospital, Boston, MA, United States, [2]The George Washington University School of Medicine and Health Sciences, Washington, DC, United States, [3]Kamuzu University of Health Sciences, Blantyre, Malawi, [4]The Wharton School of the University of Pennsylvania, Philadelphia, PA, United States, [5]University of Virginia College of Arts and Sciences, Charlottesville, VA, United States, [6]Michigan State University College of Osteopathic Medicine, East Lansing, MI, United States, [7]Children's National Hospital / The George Washington University School of Medicine and Health Sciences, Washington, DC, United States, [8]Nationwide Children's Hospital / The Ohio State University College of Medicine, Columbus, OH, United States

Cerebral malaria (CM) continues to be a driver of child mortality and morbidity in endemic regions. Point of care testing (PoCT) is a cost-effective alternative to laboratory-based testing in the clinical care of critically ill children, including those with CM. The lower cost and easy scalability of PoCT may be useful in acute patient management in resource-limited settings (RLS) but little is known about the clinical utility of PoCT in the recognition or management of organ dysfunction in pediatric CM. We evaluated the clinical utility of PoCT in the care of 193 Malawian children with CM hospitalized between March 2019 and May 2023 who had both PoCT and laboratory-based testing. We determined the frequency of abnormal PoCT values of creatinine, lactate, glucose, and electrolytes on hospital admission, and evaluated how often these values resulted in changes in clinical management. We determined if there were associations between abnormal PoCT results and patient outcomes. Overall, 53.6% of all PoCT results were abnormal. Clinical interventions followed 15.1% of abnormal results and were most likely to occur with abnormal results of potassium (32.1%), lactate (22.0%), creatinine (16.3%), or glucose (9.8%). The most frequent interventions were blood transfusions (in response to high lactate or anemia), administration of furosemide (after elevated creatinine or potassium results), administration of fluid boluses (in response to high lactate, low bicarbonate, and low sodium levels), administration of intravenous glucose in those with hypoglycemia, and the initiation of epinephrine infusions after abnormal lactate results with concurrent clinical findings of shock. Children with hyperlactatemia or hypocalcemia had higher mortality rates. PoCT result values largely correlated well with laboratory-based testing results. High rates of abnormal PoCT testing results combined with lower intervention rates suggest the need for further research to develop evidence based diagnostic and treatment algorithms incorporating PoCT testing.

8362

FLUID BOLUS RESUSCITATION INCREASES MORTALITY IN MALAWIAN CHILDREN WITH CEREBRAL MALARIA

Meredith G. Sherman[1], Pallavi Dwivedi[2], Ronke Olowojesiku[3], Rami Imam[4], Kennedy M. Chastang[5], Eduardo A. Trujillo Rivera[2], James E. Bost[2], Amina M. Mukadam[6], Alice Liomba[7], Karl B. Seydel[8], Douglas G. Postels[9]

[1]Global Health Initiative, Children's National Hospital, Washington, DC, United States, [2]Division of Biostatistics and Study Methodology, Children's National Hospital, Washington, DC, United States, [3]Department of General and Community Pediatrics, Children's National Hospital, Washington, DC, United States, [4]The George Washington University School of Medicine, Washington, DC, United States, [5]Howard University, Washington, DC, United States, [6]University of Washington, Seattle, WA, United States, [7]Blantyre Malaria Project, Blantyre, Malawi, [8]Department of Internal Medicine, College of Osteopathic Medicine, Michigan State University, East Lansing, MI, United States, [9]Division of Neurology, Children's National Hospital, Washington, DC, United States

The Fluid Expansion As Supportive Therapy (FEAST) trial conducted in 2011 found that fluid bolus resuscitation in African children with signs of hypovolemia increased mortality risk, including in patients with malaria. However, no specific subgroup analysis was performed in the FEAST study for children meeting the diagnostic criteria for cerebral malaria on admission. We evaluated the association between fluid bolus resuscitation and mortality in Malawian children with CM using a retrospective review of 1674 children admitted to Queen Elizabeth Central Hospital in Blantyre from 2000 to 2018. Informed by the findings of the FEAST trial, we hypothesized children with CM would have increased risk of mortality with fluid bolus resuscitation. Twenty-two patients with missing systolic blood pressure (SBP) measurements, three patients missing data for sex, and five patients with hypotension were excluded from the analysis. Using covariate balancing propensity score weighting, participants who received fluid bolus resuscitation were matched to participants who did not receive the intervention. Our final population included 252 children who received fluid bolus resuscitation and 252 matched children with similar propensity scores who did not. We found that fluid bolus resuscitation in children with CM increased mortality (OR 1.92; 95% CI: 1.36-2.71). Patients with a SBP over 100 mmHg on admission who received bolus fluids had an even higher risk of mortality (OR 3.15; 95% CI: 1.81-5.48). For children with CM and a SBP less than or equal to 100mmHg, there was no statistically significant impact of fluid bolus resuscitation on outcome (OR 1.44; 95% CI: 0.91-2.26). We additionally found that children with CM had decreased survival with hypoglycemia (OR 1.86; 95% CI: 1.05-3.29), deep breathing (OR 1.85; 95% CI: 1.25-2.72), and a lower Blantyre Coma Score on admission (for BCS=1, OR 0.48; 95% CI: 0.29-0.77; for BCS=2, OR 0.36; 95% CI: 0.22-0.60, both compared to BCS=0). Our results support the findings of the 2011 FEAST trial for Malawian children with cerebral malaria and indicate fluid bolus resuscitation has the potential to cause harm in this group.

8363

DEREGULATED IL-10 EXPRESSING T CELLS IN CHILDREN WITH ACUTE *PLASMODIUM FALCIPARUM* MALARIA: IMPLICATIONS FOR ETIOLOGY OF BURKITT LYMPHOMA

Bonface Ariera[1], sidney ogolla ogolla[1], Rosemary Rorchford[2]

[1]Kenya Medical Research Institute-Kenya, Kisumu, Kenya, [2]University of Colorado, Anschutz medical campus, DENVER, CO, United States

Plasmodium falciparum malaria and EBV co-infections in children living in malaria-endemic areas are associated with EBV-linked cancer, endemic Burkitt lymphoma (eBL). EBV infection in most African children occurs before the age of 1 year, yet eBL does not occur until later in childhood. It is postulated that repeated episodes of malaria suppress immunity to EBV, creating a permissive environment for eBL pathogenesis. However, the mechanisms responsible for the suppressed immunity to EBV are not fully understood. Previous studies have characterized the immunological alterations that pathologically link malaria exposure and EBV co-infections to eBL tumorigenesis, but the malaria-driven mechanisms still remain obscure.

To precisely understand how a single episode of acute clinical *P. falciparum* malaria perturbs EBV T cell immunity, we intensely characterized T cell activation, co-inhibitory receptor expression, and cytokine secretion profiles in children with acute clinical *P. falciparum* malaria following antigenic stimulation with EBV and CMV peptides. We observed upregulated levels of CD69 and OX40 in both CD4+ and CD8+ T cell subsets in children with acute *P. falciparum* infection, on the contrary, CD25 and CD137 levels were highly elevated in community controls. Interestingly both children with acute clinical *P. falciparum* malaria and community controls were responsive to stimulations by EBV and CMV-specific peptides. Further, analysis of cytokine profiles revealed polarization of IL-10 responses compared to IFN-γ in acute cases than in community controls. Lastly, we did see differential expression patterns of LAG-3 and PD-1 in both acute cases and controls. Interpreted together, our data imply active T cell activation during acute malaria with shifts towards immunoregulatory cytokine production. Also, we report a more global malaria-induced immune suppression rather than EBV-specific.

8364

LONG-TERM DURABILITY AND PUBLIC HEALTH IMPACT OF WMEL WOLBACHIA DEPLOYMENTS FOR AEDES-BORNE DISEASE CONTROL IN NITERÓI, BRAZIL

Katie Anders[1], Luciano Moreira[2], Gabriel Sylvestre Ribeiro[2], Thais Riback[2], Diogo Chalegre[2], Cameron P. Simmons[1], Peter A. Ryan[1], Scott L. O'Neill[1]

[1]World Mosquito Program, Monash University, Melbourne - Clayton, Australia, [2]World Mosquito Program, Fiocruz, Rio de Janeiro, Brazil

Introducing *Wolbachia* (*w*Mel strain) into *Aedes aegypti* mosquitoes reduces their capacity to transmit dengue and other viruses. Field trials in multiple countries have shown reductions in dengue incidence following releases of *w*Mel-infected *Ae. aegypti*. In Brazil, *w*Mel-*Ae. aegypti* have been deployed in 5 cities with a combined population of >3 million since 2015, and previous studies have shown significantly lower dengue, chikungunya and Zika incidence in *Wolbachia*-treated areas of Niterói and Rio de Janeiro than untreated areas, 1-2 years post-release. We present the long-term entomological and public health outcomes of city-wide *Wolbachia* coverage in Niterói, a city of 500,000 people where *Wolbachia* releases were completed in three-quarters of the city in Dec 2019 and expanded to cover the remainder by June 2023. Despite initial variability in *Wolbachia* establishment after the 2019 releases, last monitoring in late 2023 indicated *w*Mel was stably established at >90% prevalence throughout these areas, demonstrating area wide coverage and long-term stability in the *Ae. aegypti* population 4 years post-release (6y in the earliest release areas). Ovitrap monitoring indicates *w*Mel is also well-established in the more recently treated 25% of the city. In the four years 2020-23 since *Wolbachia* was deployed across the majority of Niterói, there was a sustained absence of dengue outbreaks in the city. A total of 305 dengue cases were notified in Niterói in 2020-23: a median of 65 cases per year, or 13 cases per 100,000 people [annual range 6 - 30 /100,000]. By comparison, during ten years (2007-16) prior to *Wolbachia* releases, a median of 4140 dengue cases were reported each year [range 366 - 11619] corresponding to 854 per 100,000 people [75 - 2396/100,000]. Using interrupted time series analysis to account for temporal trends and phased *Wolbachia* deployment, dengue incidence in Niterói was estimated to be 95.5% lower (95% CI: 89.8 to 98.0%) following *Wolbachia* releases, compared to pre-intervention. Preliminary evidence indicates this protective effect has continued into early 2024, during which Brazil is experiencing record high dengue incidence.

8365

INTERACTIONS BETWEEN TEMPERATURE, VIRUS STRAIN, AND DOSE INFLUENCE EXTRINSIC INCUBATION PERIOD AND COMPETENCE OF *CULEX PIPIENS* FOR WEST NILE VIRUS

Elyse M. Banker, Rachel L. Fay, Laura Munn, Anne F. Payne, Alexander T. Ciota

New York State, Wadsworth Center, Slingerlands, NY, United States

West Nile virus (WNV) is a mosquito-borne flavivirus considered to be the most prevalent arthropod-borne virus in the United States. It is maintained in an enzootic cycle between *Culex* species mosquitoes and avian hosts, with human infection resulting from spillover from this cycle. Vector competence (VC) and extrinsic incubation period (EIP) of WNV is influenced by intrinsic factors including mosquito and virus genetics, as well as extrinsic factors including temperature. Previous studies have generally demonstrated that increases in temperature are associated with increased VC and shortened EIP, yet strain-specific variation of these relationships has not been adequately assessed. Further, quantification of EIP has historically relied on estimations based on subpopulation data from individual timepoints. We assessed infection and dissemination rates of WNV in *Culex pipiens* at 20^{0}C, 24^{0}C, 28^{0}C using 4 historic WN02 genotype strains and 4 contemporary NY10 genotype strains. Our results support previous findings of increased average transmission efficiency of NY10 strains, particularly at higher temperatures, but further demonstrate significant variability resulting from distinct interactions between temperature and strain. We additionally demonstrated that EIP can be effectively tracked with individually housed mosquitoes by daily molecular testing for WNV RNA in sucrose pads. Using this methodology, we quantified temperature specific EIP at 15^{0}C, 20^{0}C, 25^{0}C and 30^{0}C following infection of *Cx. pipiens* with representative WNV02 and WNV NY10 strains. We measured differences in temperature-dependent competence and EIP between strains and found that the relationship between temperature and EIP was dose dependent. Together, these data can help inform more accurate predictive models of WNV transmission with changing temperatures.

8366

PATHOGENESIS AND TRANSMISSION OF SEVERE FEVER WITH THROMBOCYTOPENIA SYNDROME VIRUS IN EXPERIMENTALLY INFECTED ANIMALS

Jeffrey M. Marano[1], Angela Bosco-Lauth[1], Airn E. Hartwig[1], Stephanie M. Porter[2], Nicole M. Nemeth[3], Marissa Quilici[1]

[1]Colorado State, Fort Collins, CO, United States, [2]United Stated Department of Agriculture - Animal & Plant Health Inspection Service, Fort Collins, CO, United States, [3]University of Georgia, Athens, GA, United States

Severe fever with thrombocytopenia syndrome virus (SFTSV; order *Bunyavirales*, family *Phenuiviridae*, genus *Banyangvirus*) is a newly recognized arbovirus of significant human health concern. Since its discovery in 2009, there have been over 15,000 cases across Eastern Asia, with case fatalities primarily in people over the age of 50. With this evolving threat, significant gaps exist regarding the pathogenesis, serological surveillance, and transmission dynamics of SFTSV. To address these gaps, we explored the pathogenesis and serology of SFTSV in juvenile cats, as they are natural hosts for the virus and present with similar symptoms to humans. Our data demonstrate that all the directly infected cats demonstrated liver pathologies and seroconverted, and 4/8 of directly infected cats became viremic, panleukopenic, and febrile, but ultimately recovered. Serum from these cats was then used to establish serological diagnostic criteria similar to what has been previously reported for dengue virus. We demonstrated a >4-fold difference in $PRNT_{90}$ values for SFTSV and Heartland virus, an endemic bandavirus within the United States. These results provide a framework for wildlife surveillance of SFTSV to monitor its potential emergence in the United States. During our initial pathogenesis studies, we observed that one of our uninfected "contact" cats contracted SFTSV and ultimately succumbed to the disease. This is

notable, as this infection occurred without a vector. These findings align with previous reports of nosocomial infections in human and animal patients and the occupational infections of veterinarians and health care staff after encountering SFTSV-positive patients. To identify these non-canonical routes of infection, we performed intramuscular, ocular, intranasal, and oral infections using several animal models. We demonstrated that non-canonical routes of inoculation can result in infection and severe disease. These studies provide the necessary foundations for surveillance and preparedness for the United States to respond to the possible emergence of SFTSV.

8367

HIGH MOUSE PATHOGENESIS ASSOCIATED WITH A NEW YORK POWASSAN VIRUS LINEAGE II ISOLATE

Samantha J. Courtney[1], Rebekah J. McMinn[1], Chasity E. Trammell[1], Anna C. Fagre[1], Allison C. Vilander[1], Sam R. Telford[2], Gregory D. Ebel[1]

[1]Colorado State University, Fort Collins, CO, United States, [2]Tufts University, North Grafton, MA, United States

Powassan virus is an emerging tick-borne flavivirus that can cause severe neurologic disease in humans including encephalitis and meningitis. There are two genetically and ecologically distinct lineages of Powassan virus (POWV). A recent phylodynamic study of POWV lineage II in North America showed geographical structuring of Northeastern and Midwestern clades. The extent that this phylogeographic structure is associated with various phenotypes is unclear. Therefore, we sought to determine whether geographically and genetically defined isolates of POWV lineage II differ in mouse pathogenesis. C57BL/6 mice were inoculated with POWV isolates originating from various regions such as New York, Massachusetts, and Wisconsin. Two New York isolates, NY19 #12 and NY19 #32, caused mice to present early, severe neurological symptoms compared to other isolates in this study. 100% of mice succumbed to infection within seven days of inoculation. In contrast, an isolate from Nantucket, MA (NFS9601) produced only 20% mortality. We further characterized the pathogenesis of NY19 #12 and NY19 #32 by serially sacrificing infected mice over ten days. Viral loads were characterized in serum, spleen, and brain tissues using qRTPCR. Mice infected by higher pathogenesis strains had viral RNA in the serum and brain two and three days earlier than those infected with a standard POWV strain (DTV-SPO). This suggests that significant variation in pathogenic phenotype occurs within lineage II POWV. Specifically, strains that produce 100% mortality rapidly produce viremia and neuroinvade sooner than strains that produce less mortality. NY19 #12 and NY19 #32 share three amino acid mutations in the envelope, NS1, and NS5 proteins compared to other strains in our study. To further understand the observed high pathogenic phenotype in mice, we are currently engineering these mutations into an infectious clone to define viral genetic correlates and mechanisms of POWV pathogenesis and neuroinvasion.

8368

COLLABORATIVE CROSS MICE AS A NEW MODEL FOR IDENTIFYING IMMUNE CORRELATES OF PROTECTION FROM NEUROINVASIVE ST. LOUIS ENCEPHALITIS VIRUS DISEASE

Manuel Arturo Flores Rodriguez, Lark L. Coffey

University of California, Davis, Davis, CA, United States

St. Louis encephalitis virus (SLEV) is a re-emerging mosquito-borne flavivirus endemic to the United States that causes a spectrum of outcomes in humans, ranging from febrile illness to potentially fatal neuroinvasive disease. There is no specific treatment for SLEV disease, and correlates of protection against neurologic disease are unknown. Existing SLEV mouse models are limited as they rely on hyper-virulent mouse brain passaged strains or intracranial administration; both techniques restrict assessment of how peripheral infection leads to neuroinvasion. To circumvent these limitations, Collaborative Cross (CC) mice were subcutaneously administered low mammalian cell passaged SLEV. CC mice are a novel model intended to recapitulate human-like population genetic diversity. CC mice, including the CC71 genotype, have been used to study the disease spectrum and neuroinvasion for other flaviviruses, including Powassan, Zika, and West Nile (WNV) viruses, where WNV is neuroinvasive in CC71. We hypothesized that CC71 mice are susceptible to SLEV infection and neuroinvasion. We inoculated CC71 with 4 strains of SLEV representing California lineages. All strains produced infection, evidenced by viremias that peaked 3 days post inoculation (dpi). Infectious virus and viral RNA were detected in multiple tissues including the brain of all mice from 8 dpi. All mice also lost weight and showed signs of neurologic disease, achieving euthanasia criteria (loss of 20% of starting weight) by 9 dpi. Gene expression data showed interferon regulatory factor 3 is not induced in the brain during SLEV infection, likely causing reduced downstream expression of antiviral factors These data show high susceptibility of CC71 to SLEV neuroinvasive disease. Together with ongoing work using additional CC genotypes that produce less severe disease, this model will be used to characterize the SLEV disease spectrum and to identify immune correlates of protection. Continued development of this model represents a novel tool to recapitulate human SLEV outcomes that will allow studies on pathogenesis, virus-host interactions, and evaluation of countermeasures.

8369

FEASIBILITY OF TRACKING NIPAH VIRUS-INDUCED BRAIN CHANGES AND LESION DETECTION USING 0.05T MRI AND RADIOMICS

Sairam Geethanath[1], Kunal Aggarwal[2], Ivan E. Oiye[1], Yu Cong[3], Naveen Anaswara[4], Emily S. Gurley[4], Venkatesh Mani[3], Claudia Calcagno[3], Michael R. Holbrook[3]

[1]Johns Hopkins University School of Medicine, Baltimore, MD, United States, [2]Technical University Munich, Munich, Germany, [3]National Institute of Allergy and Infectious Diseases, Ft. Detrick, MD, United States, [4]Johns Hopkins University School of Public Health, Baltimore, MD, United States

High-consequence pathogens, such as Ebola, Lassa, and Nipah viruses (NiV), are associated with acute or long-term neurological manifestations that can be visualized using MRI (Capone and Scheller, Neurol Clin. 2014). However, high-field (HF) MRI scanners (3T or higher) are challenging to deploy in geographic areas where disease outbreaks naturally occur or in their immediate proximity for long-term monitoring of human survivors. This inaccessibility is due to the cost, power, weight (~ 6 tons), local expertise, and siting requirements of high-field MR systems that impede longitudinal imaging in large populations, especially those in low-resource settings (Geethanath and Vaughan, J Magn. Reson. Imaging, 2019). Portable, very low-field (VLF) MRI systems may represent the only viable strategy to characterize and monitor neurological manifestations of infectious diseases in humans, *in vivo*, non-invasively, and in low-resource settings in a scalable manner. In this work, we determined the 3T radiomic features of lesions found in NiV-exposed non-human primates that showed differences between survivors and deceased patients. We developed a low-field simulator that converted high-field MR images to lower signal-to-noise ratio (SNR) images corresponding to 0.05T and performed textural analysis. The specifications matched a portable scanner in the laboratory weighing 280 kg. Subsequently, we manually detected all 3T lesions in the simulated 0.05T images. The textural variance feature at 0.05T matched better with the 3T data than lesion areas due to the sensitivity to local MR signal intensity changes. We determined that a resolution of 1.5 x 1.5 x 2 mm^3 at 0.05T is required to detect all lesions identified at 3T MRI. We prospectively acquired an in vivo human brain image at this resolution. In conclusion, we have demonstrated the potential of structural neuroimaging with a portable scanner concerning image resolution, SNR, and image analysis. Current work involves prospective neuroimaging of NiV-exposed NHPs at 0.05T in a paired manner with 3T and performing radiomics to identify and interpret classification features.

8370

HENDRA VIRUS GENOTYPE 2 LACKS SEVERE PATHOGENIC HALLMARKS OF PROTOTYPE HENDRA VIRUS INFECTION IN AFRICAN GREEN MONKEYS

Declan Pigeaud[1], Karla Fenton[1], Courtney Woolsey[1], Robert Cross[1], Christopher Broder[2], Thomas Geisbert[1]

[1]University of Texas Medical Branch, Galveston, TX, United States, [2]Uniformed Services University of the Health Sciences, Bethesda, MD, United States

Hendra virus (HeV) emerged nearly 30 years ago and causes severe, often fatal disease in humans and livestock. Until recently, all known human and equine cases of HeV disease were attributed to isolates belonging to the prototype HeV genotype. A novel genotype of HeV, HeV-g2 was identified and retrospectively revealed to be the causative agent responsible for several fatal equine encephalitis cases with previously unknown etiology. All human cases of HeV disease have resulted from direct contact with severely ill, HeV-infected horses. Given the global public health risk of HeV, documented lethality of HeV-g2 in horses, and presently unknown pathogenicity of HeV-g2 in primate species, we performed studies to assess the pathogenicity of HeV-g2 in African green monkeys. Five adult AGMs were experimentally infected with HeV-g2 via a combined intranasal and intratracheal route, at a dose known to be uniformly lethal in AGMs infected with prototype HeV. Four of the five AGMs survived until study endpoint and developed subclinical or mild signs of disease. All four surviving subjects seroconverted and serum antibodies cross-neutralized HeV-g2, HeV-prototype, and Nipah virus (NiV) *in vitro*. Infectious virus was not identified by plaque assay in plasma or tissues of infected AGMs, however viral genomes were detected by qRT-PCR throughout the study. Gross lesions observed at necropsy were mild to moderate compared to the severe pathologic lesions produced by fatal prototype HeV infection in the AGM species. Gross lesions were restricted to prominent lymphoid tissues, particularly lymphadenomegaly of mandibular and mesenteric lymph nodes. Histologic findings included multifocal pulmonary lesions including interstitial pneumonia, vasculitis, and thickening of alveolar septa. Neurological lesions included perivascular cuffing and gliosis in the temporal lobe and brain stem. Viral antigen was not detected by IHC in any subjects. Findings from this study suggest that HeV-g2 is less pathogenic than prototype Hendra virus isolates in a nonhuman primate species known to be highly susceptible to lethal henipaviral disease.

8371

EVALUATION OF *IN SILICO SHIGELLA* SEROTYPING TOOLS USING A GLOBAL *SHIGELLA* COLLECTION

Xiaoliang Ba, Charlotte E. Chong, Fahad Khokhar, Mark A. Holmes, Kate S. Baker

University of Cambridge, Cambridge, United Kingdom

Shigella is a major public health problem and a common cause of diarrhoea globally. Accurate identification of *Shigella* serotypes is crucial for understanding its epidemiology and designing vaccination strategies which is complicated by a phenomenon known as serotype switching, where mobile genetic elements that are horizontally exchanged among *Shigella* can generate new serotypes within a given genomic background. Standardised serotyping scheme classifies *Shigella* strains into four serogroups and over 50 serotypes based on biochemical tests and O-antigen structures. Apart from the laborious, time-consuming, and expertise-requiring standardised serotyping method, several *in silico* serotyping tools for predicting *Shigella* serotypes from whole-genome sequencing data have been developed, such as Shigatyper and ShigaPass. In this work, we conducted phylogenomic analyses of the serotypes of 1074 *S. flexneri* and *sonnei* isolates from South Asia and sub-Saharan Africa collected during the Global Enteric Multicentre Study (GEMS) using ShigaPass and Shigatyper. The results showed that the ShigaPass and Shigatyper serotype predictions were 87.5% and 84% concordant (respectively) with laboratory serotype data**.** Importantly, we found 36/109 of *S. flexneri* serotype 3a were predicted to be *S. flexneri* serotype 5b by ShigaPass, and that this switch occurred on multiple occasions over the course of evolution, suggesting a higher 5b prevalence and greater frequency of serotype switching than previously understood. We also found 22 out of the 24 isolates predicted to be none-*Shigella* by ShigaPass were *Shigella* by Shigatyper. The findings highlighted the error-prone nature of the standardised serotyping method due to the high similarity between *Shigella* and Enteroinvasive *Escherichia coli* (EIEC) and cross-reactivity between serotyping antisera, and potential inconsistencies in laboratory testing. The findings also demonstrated the value of using multiple *in silico Shigella* serotyping tools to ensure a more accurate prediction.

8372

IDENTIFYING OPTIMAL ENDPOINT DEFINITIONS TO MINIMIZE OUTCOME MISCLASSIFICATION IN UPCOMING SHIGELLA VACCINE TRIALS

Maria Garcia Quesada[1], Benjamin A. Lopman[1], Patricia B. Pavlinac[2], James A. Platts-Mills[3], Lance A. Waller[1], Elizabeth T. Rogawski McQuade[1]

[1]Emory Rollins School of Public Health, Atlanta, GA, United States, [2]University of Washington, Seattle, WA, United States, [3]University of Virginia, Charlottesville, VA, United States

Shigella vaccine candidates are approaching phase III trials, but primary trial endpoints have not been evaluated. Enteropathogens frequently cause subclinical infections and can be detected during diarrhea caused by another pathogen. Therefore, when there are co-infections with Shigella during diarrhea, etiologic attribution may be biased. If a Shigella vaccine has high vaccine efficacy (VE) against moderate-to-severe diarrhea but little to no VE against infection, Shigella diarrhea cases prevented by the vaccine would likely become subclinical infections. An endpoint defined as Shigella detected at any quantity would misclassify diarrhea with subclinical Shigella as cases, thereby biasing VE estimates towards the null. In this analysis, we use a simulation to identify Shigella vaccine trial endpoints that minimize misclassification of true Shigella-attributable diarrhea episodes and therefore bias in the observed VE. We simulate a birth cohort and randomly assign vaccination to half of children. Using a time-to-event model, we assign etiology-specific mild and moderate-to-severe diarrhea episode event times among the unvaccinated children to mimic empirical age- and etiology-specific incidence rates observed in the multisite Malnutrition and Enteric Disease (MAL-ED) birth cohort study. We then use an assumed VE to similarly simulate diarrhea among vaccinated children. We evaluate the performance (e.g., sensitivity and specificity) of various endpoint definitions compared to simulated true vaccine-preventable Shigella diarrhea with the goal of minimizing misclassification of outcomes. Evaluated endpoint definitions include: Shigella detected at any quantity, Shigella detected above a certain quantity cutoff, Shigella detected with restrictions on other pathogen detections, Shigella detected and presence of certain clinical syndromes (e.g., dysentery). We generate a ranking of endpoints and estimate the magnitude and direction of the bias in the observed VE. Lastly, we perform power calculations to determine the sample size needed for a trial to observe the simulated VE when using selected endpoints.

8373

MULTIPLEX PCR DETECTION OF ENTERIC PATHOGENS IN A COMMUNITY-BASED BIRTH COHORT IN ECUADOR: COMPARISON OF XTAG-GPP AND TAQMAN ARRAY CARD ASSAYS

Stuart Torres Ayala[1], Lesly Simbaña Vivanco[1], Nikolina Eve Walas[2], Kelsey Jesser[3], Nicolette A. Zhou[3], Christine S. Fagnant-Sperati[3], Hadley Burroughs[4], Gwenyth O. Lee[5], Joseph N.S. Eisenberg[6], Karen Levy[3], Gabriel Trueba[1], Benjamin F. Arnold[4]

[1]Microbiology Institute, Universidad San Francisco de Quito, Quito, Ecuador, [2]Department of Environmental Health, School of Public Health, University of California Berkeley, Berkely, CA, United States, [3]Department of Environmental & Occupational Health Sciences, University of Washington, Seattle, WA, United States, [4]Francis I. Proctor Foundation, University of

California San Francisco, San Francisco, CA, United States, [5]Rutgers Global Health Institute, Rutgers, the State University of New Jersey, New Brunswick, NJ, United States, [6]Department of Epidemiology, School of Public Health, University of Michigan, Ann Arbor, MI, United States

Enteric pathogens are a leading cause of morbidity and mortality among children. Multiplex, nucleic acid-based assays to detect enteric pathogens are an emerging tool for surveillance and epidemiologic studies due to their high throughput and ability to detect co-infections. Little is known about comparability of multiplex assays in detection of pathogens in community-based, pediatric stool samples. We compared results from Luminex xTAG Gastrointestinal Pathogen Panel (GPP) and a custom TaqMan Array Card (TAC) based on an overlapping panel of 13 viral, bacterial, and protozoan enteric pathogen targets in a community-based birth cohort in Ecuador. We selected a stratified random sample of 156 stool samples that were positive for at least one pathogen by the TAC assay, stratified by age (6, 12, 18 months) and four levels of a rural-urban gradient. Prevalence measured by GPP or TAC ranged from 1% (*Entamoeba histolytica*) to 38% (LT-producing enterotoxigenic *Escherichia coli,* [LT-ETEC]). Agreement between assays was high, ranging from 87% (*Campylobacter*) to 98% (Norovirus GI). There was some evidence of systematic differences for three pathogens: rotavirus (1% by GPP, 8% by TAC, McNemar's P=0.001), *Campylobacter* (20% by GPP, 29% by TAC, P=0.002), and ST-ETEC (5% by GPP, 15% by TAC, P<0.001), likely due to differences in assay gene targets. Assays were not significantly different for other targets studied (Norovirus GI and GII, Adenovirus 40/41, STEC toxins 1 and 2, *Shigella*, LT-ETEC, *E. histolytica*, *Cryptosporidium, Giardia*), and both assays led to similar pathogen rank based on prevalence. GPP and TAC assays showed high levels of agreement in a community-based sample of stool specimens from children aged 6 to 18 months in Ecuador across a rural-urban gradient with a high infection burden. Consistency between assays in most prevalence estimates suggests studies using the different platforms should yield broadly comparable results.

8374

OPTIMAL AZITHROMYCIN TREATMENT RULES FOR CHILDREN WITH WATERY DIARRHEA IN THE ANTIBIOTICS FOR CHILDREN WITH SEVERE DIARRHEA (ABCD) TRIAL

Sara S. Kim[1], Allison Codi[2], James Platts-Mills[3], Patricia B. Pavlinac[4], Karim Manji[5], Christopher R. Sudfeld[6], Queen Dube[7], Naor Bar-Zeev[8], Karen Kotloff[9], Samba O. Sow[10], Sunil Sazawal[11], Benson O. Singa[12], Farah Qamar[13], Judd Walson[4], Ayesha De Costa[14], David Benkeser[2], Elizabeth T. Rogawski McQuade[1]

[1]Department of Epidemiology, Rollins School of Public Health, Emory University, Atlanta, GA, United States, [2]Department of Biostatistics, Rollins School of Public Health, Emory University, Atlanta, GA, United States, [3]Division of Infectious Diseases and International Health, Department of Medicine, University of Virginia, Charlottesville, VA, United States, [4]Department of Global Health, Department of Epidemiology, University of Washington, Seattle, WA, United States, [5]Department of Pediatrics and Child Health, Muhimbili University of Health and Allied Sciences, Dar es Salaam, Tanzania, United Republic of, [6]Department of Global Health and Population, Harvard T.H. Chan School of Public Health, Boston, MA, United States, [7]Department of Pediatrics, Queen Elizabeth Central Hospital, Blantyre, Malawi, [8]International Vaccine Access Center, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, United States, [9]Department of Pediatrics, Department of Medicine, Center for Vaccine Development and Global Health, University of Maryland School of Medicine, Baltimore, MD, United States, [10]Centre pour le Développement des Vaccins, Bamako, Mali, [11]Center for Public Health Kinetics, New Delhi, India, [12]Kenya Medical Research Institute, Nairobi, Kenya, [13]Department of Pediatrics and Child Heath, Aga Khan University, Karachi, Pakistan, [14]Department of Maternal, Child, and Adolescent Health and Aging, World Health Organization, Geneva, Switzerland

WHO diarrhea treatment guidelines that only recommend antibiotics for dysentery likely miss many episodes responsive to therapy. In a randomized trial of azithromycin for acute watery diarrhea, treatment benefit was observed among diarrheal episodes attributed to bacteria. There was residual benefit among episodes in which bacteria were detected at lower, non-attributable quantities suggesting that etiology may not fully capture who benefits from antibiotics. In the Antibiotics for Children with Severe Diarrhea trial, we used machine learning to estimate and compare optimal treatment rules for the decision to treat watery diarrhea with azithromycin. We used all available characteristics for the gold standard rule and 7 various subsets of clinical, diagnostic, and/or sociodemographic characteristics to discern the most informative variables for the treatment rule. We estimated the azithromycin effect on day 3 diarrhea and day 90 hospitalization or death via an augmented inverse probability of treatment weighted estimator in the subset of children assigned treatment under each rule. For day 3 diarrhea, the gold standard rule recommended to treat 33% of children who were predicted to benefit from antibiotics. Among the treated, 82% had ≥1 bacterial pathogen, and the risk of day 3 diarrhea was 7.3% less (95% CI: -11.5%, -3.2%) when receiving azithromycin compared to if they were not treated. For day 90 hospitalization or death, the gold standard treated 35% of children, of whom 71% had ≥1 bacterial pathogen. Among the treated, the day 90 hospitalization or death risk was 2.1% less (95% CI: -3.8%, -0.4%) than if they were untreated. For day 3 diarrhea, rules with pathogen quantities (RD: -9.2%, (95% CI: -13.4%, -5.0%)) performed similarly to the gold standard. Rules with malnutrition indicators and sociodemographics approximated the gold standard rule best (RD: -2.8%, (95% CI: -4.3%, -1.0%)) for day 90 hospitalization or death. Pathogen diagnostics are most informative for treatment decisions to improve proximal outcomes such as diarrhea duration, but targeting children based on host characteristics may suffice to prevent severe outcomes.

8375

ENTERIC PATHOGEN DETECTION AMONG CHILDREN DISCHARGED FROM OUTPATIENT TREATMENT FOR SEVERE ACUTE MALNUTRITION AND ASSOCIATIONS WITH SUBSEQUENT RELAPSE IN SOUTH SUDAN

Jackie Knee[1], Lauren D'Mello-Guyett[1], Lynn Grignard[1], Alesha Myers[1], Sarah King[2], John Agong[3], Lino Deng[3], Mesfin Gose[3], Jackson Lwate Hasan[3], Nancy Grace Lamaka[3], Anastasia Marshak[4], Dimple Save[3], Indi Trehan[5], Khamisa Ayoub[6], Heather Stobaugh[2], Oliver Cumming[1]

[1]London School of Hygiene & Tropical Medicine, London, United Kingdom, [2]Action Against Hunger USA, New York, NY, United States, [3]Action Against Hunger South Sudan, Juba, South Sudan, [4]Tufts University, Boston, MA, United States, [5]University of Washington, Seattle, WA, United States, [6]Ministry of Health for the Republic of South Sudan, Juba, South Sudan

Severe acute malnutrition (SAM) affects millions of children each year, putting them at increased risk of death and disease. Many children relapse to acute malnutrition (AM) or SAM following community-based management of acute malnutrition (CMAM) programmes. Enteric infection is hypothesized to be a risk factor for relapse. We collected rectal swabs from children recently recovered from uncomplicated SAM in South Sudan and tested them for a suite of enteric pathogens using a TaqMan Array Card. We estimated enteric pathogen prevalence and examined associations between pathogen detection and risk of relapse to AM and SAM within three and six months of recovery. One or more enteric pathogen was detected in 82% of children (389/476). Bacterial and protozoan pathogens were the most frequently detected pathogen types, with each detected in 57% of children, followed by enteric viruses (10%) and helminths (4.4%). Detection of one or more enteric pathogen, protozoan pathogen, or viral pathogen was not associated with relapse to AM or SAM at either time point. Detection ≥1 helminth was associated with increased risk of relapse to SAM, and ≥1 bacterial pathogen was associated with decreased risk of relapse to AM. Both enterotoxigenic *E. coli* and enteroaggregative *E. coli* were associated with decreased risk of relapse to SAM and/or AM at three- or six-months post-recovery. *Shigella* was the only individual pathogen associated with increased risk of relapse to AM and SAM. In this setting, most children suffering from SAM were exposed to enteric pathogens during treatment. However, we found no consistent relationship between pathogen detection at treatment discharge and risk of relapse to AM or SAM within three or six months of recovery. Despite this, limiting pathogen exposures during this vulnerable period remains important given the high risk of serious

adverse health effects. These results highlight the lack of access to safe water, sanitation, and hygiene and reinforce the potential importance of anthelmintics as part of CMAM.

8376

HIGH LEVELS OF GUT *BIFIDOBACTERIUM* ASSOCIATED WITH INTESTINAL INFLAMMATION AND FECAL METABOLITES IN CHILDREN IN RURAL BANGLADESH

Jessica A. Grembi[1], Elizabeth Costello[1], Brian C. DeFelice[2], Anna Robaczewska[1], Audrie Lin[3], Md. Ziaur Rahman[3], Shahjahan Ali[4], Md. Zahir Hussain[5], Rashidul Haque[6], Mahbubur Rahman[6], Leanne Unicomb[6], Stephen Luby[1], Susan P. Holmes[1], David Relman[1]

[1]Stanford University, Stanford, CA, United States, [2]Chan Zuckerberg BioHub, San Francisco, CA, United States, [3]University of California, Santa Cruz, Santa Cruz, CA, United States, [4]University of Colorado, Denver, CO, United States, [5]University of Pittsburgh, Pittsburgh, PA, United States, [6]International Centre for Diarrhoeal Disease Research, Bangladesh, Dhaka, Bangladesh

Childhood stunting has been associated with impaired development of the gut microbiota. However, the immune and metabolic consequences of microbiota immaturity have yet to be explored. Here, we studied 1726 rural Bangladeshi children sampled longitudinally at 3, 14, and 28 months of age and enrolled in the WASH Benefits randomized controlled trial evaluating the efficacy of water, sanitation, handwashing (WASH), and nutritional interventions. Across all ages after adjusting for covariates, the relative abundance of a single infancy-associated *Bifidobacterium* 16S rRNA gene amplicon sequence variant (ASV) was positively associated with intestinal permeability (fecal alpha-1-antitrypsin, Spearman's rho 0.13-0.22, $P<10^{-6}$) and T cell-mediated inflammation (fecal neopterin, Spearman's rho 0.24-0.26, $P<10^{-12}$), but not with inflammation from innate pathways (fecal myeloperoxidase, Spearman's rho -0.029-0.048). Metagenomic sequencing revealed that 14-month old children with high levels of the infancy-associated *Bifidobacterium* ASV harbored a diversity of species (*B. longum, B. breve, B. catenulatum,* and *B. pseudocatenulatum*) that were more abundant than in children with age-appropriate levels of *Bifidobacterium* (all $P<0.01$). To determine the metabolic effects of retaining high levels of infancy-associated *Bifidobacterium* at 14 months of age, we performed untargeted metabolomics on stool from 192 children: 96 pairs comprised of one child with high (>85th percentile) and one child with median *Bifidobacterium* relative abundance and matched on demographic variables, study arm from the trial, breastfeeding frequency, and length-for-age z-score. Tryptophan metabolites and pathways related to long-chain fatty acid metabolism and oxidative stress were elevated in children with high levels of *Bifidobacterium* for age. Our data suggest that gut microbiota immaturity affects the immune system and metabolic capabilities of the host and microbiota. Next steps include strain-level evaluation of *Bifidobacterium* genomes from this cohort to identify differential capabilities in carbohydrate and fatty acid utilization.

8377

NEONATAL ACQUISITION OF ESBL-PRODUCING ENTEROBACTERALES IN MADAGASCAR AND CAMBODIA

Anne-Lise Beaumont[1], Agathe de Lauzanne[2], Mamitiana Alain Noah Rabenandrasana[3], Norohasina Fanja Randriamanga[3], Sandrine Bernabeu[4], Alexis Criscuolo[5], Perlinot Herindrainy[3], Didier Guillemot[1], Jean-Marc Collard[5], Long Pring[2], Laurence Borand[2], Elsa Kermovant-Duchemin[6], Muriel Vray[7], Tania Crucitti[3], Bich-Tram Huynh[1]

[1]Institut Pasteur, Université de Versailles-Saint Quentin, INSERM, Paris, France, [2]Institut Pasteur du Cambodge, Phnom Penh, Cambodia, Phnom Penh, Cambodia, [3]Institut Pasteur de Madagascar, Antananarivo, Madagascar, [4]Assistance Publique - Hôpitaux de Paris, Le Kremlin-Bicêtre, France, Paris, France, [5]Institut Pasteur, Paris, France, [6]Assistance Publique - Hôpitaux de Paris, Hôpital Necker-Enfants malades, Paris, France, [7]Institut Pasteur du Sénégal, Dakar, Senegal

Bacterial infections are responsible for 23% of neonatal deaths in low- and middle-income countries (LMICs), with *Enterobacterales* being the primary cause. Of particular concern are extended-spectrum beta-lactamase-producing *Enterobacterales* (ESBL-PE), which are resistant to most first-line antibiotics. Neonatal colonization with ESBL-PE, acquired either vertically from the mother during delivery or horizontally from the environment, increases the risk of subsequent sepsis development. Maternal colonization rates with ESBL-PE are high in LMICs, suggesting a pivotal role in the transmission to the newborn. However, molecular data supporting this hypothesis are limited. This study aims to quantify rates of vertical and horizontal transmission of ESBL-PE in two LMICs and to identify associated risk factors. This work is based on data from the BIRDY study, a community cohort conducted in Cambodia and Madagascar in 2016-2022. Stool samples from mothers at delivery and from newborns < 72h were cultured on a selective ESBL medium. Each colony underwent whole-genome sequencing for characterization and comparison using phylogenetic inference techniques. Multivariate logistic regression was performed to identify risk factors associated with ESBL-PE horizontal transmission. The cohort included 496 mothers, 131 in Cambodia and 365 in Madagascar, who gave birth to 498 newborns. The prevalence of ESBL-PE colonization was 78% in mothers and 53% in newborns in Cambodia, compared to 41% and 32% in Madagascar. Preliminary findings showed 13% vertical transmission in Cambodia and 11% in Madagascar, with 87% and 89% horizontal transmission, respectively. Horizontal ESBL-PE acquisition was associated with C-section (adjusted odds ratio 3.15 [1.7-6.0]), neonatal resuscitation (2.05 [1.2-3.7]), and hospital birth (1.91 [1.1-3.4]). Vertical transmission of ESBL-PE appears to account for a small proportion of neonatal colonization cases. Medical procedures may be important risk factors for horizontal transmission. Further investigation is required to elucidate transmission routes and develop preventive strategies.

8378

EFFICACY AND SAFETY OF THERMOTHERAPY IN COMBINATION WITH MILTEFOSINE IN COMPARISON TO MILTEFOSINE MONOTHERAPY FOR THE TREATMENT OF CUTANEOUS LEISHMANIASIS IN THE AMERICAS: A PHASE III, OPEN LABEL, MULTICENTER, RANDOMIZED TRIAL

Joelle Rode[1], Juan Pascalle[2], Alejandro Llanos-Cuentas[3], Marcia Hueb[4], Jaime Soto[5], Glaucia Cota[6], Paulo Machado[7], Marina Boni[1], Bethania Blum[1], **Byron Arana**[8]

[1]Drugs for Neglected Diseases Initiative, Rio de Janeiro, Brazil, [2], Instituto Conmemorativo Gorgas de Estudios de la Salud, Panama, Panama, [3]Universidad Peruana Cayetano Heredia, Lima, Peru, [4]Julio Muller University Hospital, Cuiaba, Brazil, [5]Fundación Nacional de Dermatología, Santa Cruz de la Sierra, Bolivia, Plurinational State of, [6]Instituto René Rachou, Belo Horizonte, Brazil, [7]Federal University of Bahia, Salvador Bahia, Brazil, [8]Drugs for Neglected Diseases Initiative, Geneva, Switzerland

Oral miltefosine and injectable meglumine antimoniate continue to be the first-choice drugs for treatment of cutaneous leishmaniasis in the Americas, despite their toxicity, difficult administration, and cost. In the search for therapeutic alternatives, combining two interventions has emerged as a potential approach to reduce the toxicities of standard drugs and to increase their efficacy as compared to monotherapy. Here we report the results of a randomized, open label, multi-center, non-inferiority study conducted in Brazil, Bolivia, Panama, and Peru; aiming to assess efficacy and safety of combining thermotherapy (one application, 50^{0}C for 30 seconds) plus 3-weeks MF (2.5 mg/kg/day) with miltefosine monotherapy (2.5 mg/kg/day for 28 days orally) for uncomplicated CL cases. Primary endpoint was measured by the percentage of patients with initial clinical cure at day 90, defined as 100% re-epithelialization of lesions. The last patient follow-up visit took place in February 2024. Data analysis is ongoing with final results expected by July 2024. In total, 128 subjects were randomly assigned to either study arm (64 per arm) One patient in the combination arm withdrew consent before receiving any study intervention.

Preliminary results show positive efficacy at D90 in both study arms. Three serious adverse events were reported in the study, none related to study interventions. All adverse events reported in both study arms were similar to those previously reported for these interventions: nausea, vomiting, and diarrhea associated with miltefosine, and signs of first- and second-degree burns at the site of the thermotherapy application. Further statistical analysis will be performed and presented to assess efficacy and non-inferiority and to determine the frequency and severity of adverse events per treatment arm. Preliminary results show comparable efficacy in both

8379

FIRST-IN-HUMAN, RANDOMIZED, DOUBLE BLIND CLINICAL TRIAL OF LXE408 FOR KINETOPLASTID DISEASES

Natasha Hochberg[1], Li Ruobing[2], Amanda Nguyen[1], Christopher Breen[3], Jean Lecot[4], Andrea de Soyers[5], Linda Armstrong[3], Thierry Diagana[6], Peter Pertel[1], Megan Barton[1], Florencia Segal[1], Srinivasa Rao[6]

[1]Novartis Global Health, BioMedical Research, Cambridge, MA, United States, [2]Novartis Global Health, BioMedical Research, Shanghai, China, [3]Novartis Global Health, BioMedical Research, East Hannover, NJ, United States, [4]Novartis Global Health, Analytics-Global Medical Affairs, Basel, Switzerland, [5]Novartis Global Health, BioMedical Research, Basel, Switzerland, [6]Novartis Global Health, BioMedical Research, Emeryville, CA, United States

Existing therapies for kinetoplastid diseases are far from ideal due to toxicities, treatment length, and variable efficacy. LXE408 is a novel proteasome inhibitor with potent in vitro and in vivo activity against *Trypanosoma cruzi and* Leishmania. This study aimed to evaluate the safety and tolerability of LXE408 in humans. This open label, first in human, phase 1 clinical trial of healthy adult fasted participants included single ascending dose (SAD, 10, 30, 100, 300 and 600 mg) and multiple ascending dose (MAD, 10, 50, 150, 300 and 600 mg daily for 10 days) cohorts. Eight subjects were recruited per cohort and randomized to LXE408 or placebo in a 3 to 1 ratio. A cohort to assess glomerular filtration rate (GFR) received 300 mg of LXE408 or placebo for 10 days plus iohexol solution (intravenously at Day -1, 5 and 10). Among the 88 participants, no serious or severe adverse events (AEs) occurred. All AEs were Common Terminology Criteria for Adverse Events (CTCAE) Grade 1,2. In the SAD cohort, the most common AEs in participants on LXE408 were headache (16.7%) and nausea (10%), in the MAD cohort, 30% of those on LXE408 and 20% on placebo reported headache. Three participants discontinued the study due to AEs (constipation, headache, and nausea). One participant (LXE408 600mg MAD) experienced a grade 2 AE of asymptomatic bilirubin increase with a transient ALT increase, and one (LXE608 50mg MAD) experienced a grade 2 AE of asymptomatic lipase increase. Transient increases of ALT, amylase or lipase occurred in the SAD and MAD cohorts, but these were not considered clinically meaningful and not reported as AEs. Serum creatinine increases (grade 1 to 2) were observed, Cystatin C remained normal among those who had it measured, and the mGFR cohort data showed no significant GFR decrease. This suggests creatinine increase is not indicative of renal toxicity but rather results from altered physiology due to inhibition of renal transporters. LXE408 was safe and well tolerated. Clinical studies are planned or ongoing to assess efficacy in patients with visceral leishmaniasis, cutaneous leishmaniasis, and Chagas disease.

8380

TOPICAL APPLICATION OF AC2-26, AN ANNEXIN A1 PEPTIDOMIMETIC, REDUCES LESIONS AND IMPROVES IMMUNE RESPONSES IN A MURINE MODEL OF *LEISHMANIA AMAZONENSIS* INFECTION

Liliane M. dos Santos, Tiago Nery, Gisele Goulart, Ana Paula Fernandes

Universidade Federal de Minas Gerais, Belo Horizonte, Brazil

Cutaneous leishmaniasis is a parasitic neglected tropical disease that causes slow-healing lesions that can lead to long-lasting scars. Social and self-stigma have been known to influence the quality of life and well-being of patients, urging the search for more efficient therapies that could limit lesion development. Annexin A1 (AnxA1) is a glucocorticoid-inducible protein known for its anti-inflammatory and pro-resolving properties. AnxA1 actions can be mimicked by the administration of its N-terminal domain with 26 amino acids termed Ac2-26 peptide. Recent studies have demonstrated a therapeutic potential for Ac2-26 in infectious diseases, including cutaneous leishmaniasis. We have shown that the lack of endogenous AnxA1 is associated with susceptibility during *Leishmania amazonensis* infection. Moreover, treatment of *L. amazonensis*-infected AnxA1 KO mice with Ac2-26 increases the production of anti-inflammatory cytokines and improves pathogen clearance. Therefore, we aimed to further explore the protective effects of Ac2-26 in cutaneous leishmaniasis. Systemic treatment of WT mice with Ac2-26, by i.p injection, increases the numbers of activated T cells, improving the clearance of the parasite. To evaluate whether local treatment with Ac2-26 could potentiate these effects, we developed a topical formulation and administered it to WT mice. Mice treated topically presented diminished lesions, parasite burden and IFN-γ production when compared with i.p. treated mice. Interestingly, we found lower numbers of Th2 cells and $CD4^+$ $Arginase1^+$ T cells and increased Tregs in topically-treated mice compared to i.p.-treated mice. These results could signify that local treatment of *L. amazonensis* lesions with Ac2-26, rather than systemic administration, is a more efficient way to balance the effector responses with the regulatory responses, preventing parasite replication while controlling the damage caused by the exacerbated inflammation. Our findings suggest topical treatment with Ac2-26 may be an effective treatment approach to localized cutaneous lesions, helping reduce the social impact of the disease in patients.

8381

SEVERE ANAEMIA AND HAEMOGLOBIN TRAJECTORY FOLLOWING TREATMENT OF VISCERAL LEISHMANIASIS: AN INDIVIDUAL PATIENT DATA META-ANALYSIS USING THE INFECTIOUS DISEASES DATA OBSERVATORY DATA PLATFORM

Prabin Dahal[1], Abdalla Munir[2], Rishikesh Kumar[3], Sauman Singh-Phulgenda[1], Niyamat Ali Siddiqui[3], James Wilson[1], Gemma Buck[1], Caitlin Naylor[1], Matthew Brack[1], Manju Rahi[4], Paritosh Malaviya[5], Monique Wasunna[6], Francois Chappuis[7], Koert Ritmeijer[8], Carlos Costa[9], Gustavo Romero[10], Vassiliki Syriopoulou[11], Fabiana Alves[12], Kasia Stepniewska[1], Krishna Pandey[3], Ahmed Musa[13], Philippe J. Guerin[1]

[1]University of Oxford, Oxford, United Kingdom, [2]Infectious Diseases Data Observatory (IDDO), Oxford, United Kingdom, [3]ICMR - Rajendra Memorial Research Institute of Medical Sciences (RMRIMS), Patna, India, [4]Indian Council of Medical Research (ICMR), New Delhi, India, [5]Infectious Disease Research Laboratory, Department of Medicine, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India, [6]Drugs for Neglected Diseases initiative, Nairobi, Kenya, [7]Division of Tropical and Humanitarian Medicine, Geneva University Hospitals, Geneva, Switzerland, [8]Médecins Sans Frontières, Amsterdam, Netherlands, [9]Department of Community Medicine, Federal University of Piauí, Piauí, Brazil, [10]Center for Tropical Medicine, University of Brasilia, Brasilia, Brazil, [11]Infectious Diseases and Chemotherapy Research Laboratory, Medical School, National and

Kapodistrian University of Athens, Athens, Greece, [12]Drugs for Neglected Diseases initiative, Geneva, Switzerland, [13]Institute of Endemic Diseases, University of Khartoum, Khartoum, Sudan

In patients with visceral leishmaniasis (VL), the normalisation of haemoglobin (Hb) following treatment remains poorly understood. An individual patient data meta-analysis (IPD-MA) was undertaken to explore the Hb evolution using 29 studies (1994-2018; 7,358 patients). Anaemia and severe anaemia (SA) were classified using the WHO definitions. Risk factors of baseline SA and Hb changes during treatment and follow-up were modelled with hierarchical mixed effects regression. Of the 7,358 patients included, 4,339 (59.0%) were from the Indian subcontinent (ISC), 2,896 (39.4%) were from East Africa (EA), and 123 (1.7%) were from Greece. 447 (6.1%) patients were of <5y old, 2,904 (39.5%) were 5-15y, 4,007 (54.5%) were aged >15y. Treatment received included: miltefosine (n=1,675, 22.8%), pentavalent antimony (n=1,740, 23.6%), amphotericin B deoxycholate (n=2,068, 28.1%), liposomal amphotericin B (L-AmB) (n=338, 4.6%), paromomycin (n=712, 9.7%), a combination of these drugs (n=417, 5.7%) or other (n=408, 5.5%). At presentation, 97.8% of patients were anaemic and 47.6% had SA. In a multivariable analysis (including age, sex, and region), factors associated with increased SA risk at baseline were: age <=15y, female sex, and patients from EA (compared to the ISC). Following treatment, 21,080 follow-up Hb measurements were available from 6,585 patients. The mean Hb (unadjusted for site clustering) was 8.2 g/dL (standard deviation (SD)=2.46; n=7,358 measurements) on day 0 and 9.9 g/dL (SD=1.72, n=5,782) on day 30. The mean Hb reached 11 g/dL at around 2 months post-treatment. In multivariable analysis (including age, sex, region and drugs), male sex was associated with a higher Hb during follow-up, whereas there were no differences between region or drug. In summary, approximately half of all trial patients were severely anaemic at baseline; the true population prevalence is likely to be much higher. The marked increase of Hb during the 1st month of treatment (almost 2 g/dL) likely serves as an important surrogate of overall treatment response. Further work continues to elucidate the relationship between poor Hb response and clinical outcome.

8382

EFFICACY OF SHORT-COURSE TREATMENT FOR PREVENTION OF CONGENITAL TRANSMISSION OF CHAGAS DISEASE: A RETROSPECTIVE COHORT STUDY

Moscatelli Guillermo, Samanta Moroni, Juan Carlos Ramirez, Belen Warszatska, Fernanda Lascano, Nicolas Gonzalez, Andres Rabinovich, **Jaime Altcheh**

Hospital de Niños R. Gutierrez, Buenos Aires, Argentina

In regions with controlled vector transmission of *Trypanosoma cruzi*, congenital transmission is the most frequent route of infection. Treatment with benznidazole (BZ) or nifurtimox (NF) for 60 days in girls and women of childbearing age showed to be effective in preventing mother to child transmission of this disease. Reports on short-course treatment (30 days) are scarce. Offspring of women with Chagas disease who received short course treatment (30 days) with BZ or NF, attended between 2003 and 2022, were evaluated. *T. cruzi* Parasitemia (microhaematocrit and/or PCR) was performed in infants younger than 8 months of age, and serology (ELISA and IHA) at 8 months to rule out congenital infection. A total of 27 women receiving 30 days of treatment and their children were included in this study. NF was prescribed in 17/27 (63%) women, and BZ in 10/27 (37%). The mean duration of treatment was 29.2 days. None of the women experienced serious adverse events during treatment, and no laboratory abnormalities were observed. A total of 40 infants born to these 27 treated women were included. All newborns were full term, with appropriate weight for their gestational age. No perinatal infectious diseases or complications were observed. Several studies have shown that treatment of infected girls and women of childbearing age for 60 days is an effective practice to prevent transplacental transmission of *T. cruzi*. Our study demonstrated that short-duration treatment (30 days) is effective and beneficial in preventing transplacental transmission of Chagas disease.

8383

IMPACT OF ASCARIDOLE ON METABOLIC BIOENERGETICS IN LEISHMANIASIS

Deblina Sarkar, Sritama De Sarkar, Deep Goswami, Chaitali Karmakar, Prof. Mitali Chatterjee

IPGME&R, Kolkata, Kolkata, India

Leishmania parasites, causative of Leishmaniasis, rely on a single 'mitochondrion' as their 'powerhouse' and have a compromised antioxidant defence system. Consequently, therapeutic strategies include triggering oxidative burst via mitochondrial dysfunction and subversion of host metabolic bioenergetics, but such information remains poorly defined in case of *Leishmania* infection. Thus, this study aimed to delineate the impact of an endoperoxide ascaridole on the metabolic bioenergetics of *Leishmania* parasites. The impact of ascaridole on cellular redox status, generation of mitochondrial superoxide, mitochondrial membrane potential (MMP), annexin V positivity and cell cycle arrest was evaluated by flow cytometry while extracellular acidification rate (ECAR) and oxygen consumption rate (OCR) evaluated by XF Analyzer. In *Leishmania* infected macrophages, expression of metabolic bioenergetics regulatory pathway AMPK-SIRT1-mTOR axis were assessed by ddPCR (droplet digital PCR) and immunoblotting. In *Leishmania donovani* parasites, ascaridole demonstrated strong anti-promastigote and anti-amastigote activities, IC_{50} being 2.6 and 2 μM respectively. At the respective IC_{50}-IC_{90} doses, ascaridole enhanced the generation of reactive oxygen species and caused depletion of thiols in promastigotes; however, mitochondrial superoxide remained unchanged. It failed to impact on mitochondrial respiration rather inhibited the glycolytic functions, along with diminished levels of ATP and MMP, and exhibited higher annexin V positivity, which ultimately translated into a cell cycle arrest at sub G_0/G_1 phase. Ascaridole substantially downregulated the enhanced expression of AMPK-SIRT1-mTOR axis and glycolysis regulatory enzymes in *Leishmania* infected macrophages as compared to uninfected macrophages, whereas markers of mitochondrial respiration stayed unaltered. To summarize, ascaridole selectively targeted the glycolytic bioenergetics and AMPK-SIRT1-mTOR axis suggesting that screening for compounds that mediate metabolic reprogramming could augment the limited armamentarium of anti-leishmanials.

8384

INVOLVING PATIENTS IN DRUG DEVELOPMENT FOR NEGLECTED TROPICAL DISEASES (NTDS): A QUALITATIVE STUDY EXPLORING AND INCORPORATING PREFERENCES OF PATIENTS WITH CUTANEOUS LEISHMANIASIS INTO TARGET PRODUCT PROFILE DEVELOPMENT

Maria del Mar Castro[1], **Astrid C. Erber**[2], Byron Arana[3], Glaucia Cota[4], Claudia Denkinger[5], Nicole Harrison[6], Julia Kutyi[6], Liliana López-Carvajal[7], Emma Plugge[8], Julia Walochnik[9], Piero Olliaro[10]

[1]Centro Internacional de Entrenamiento de Investigaciones Médicas (CIDEIM), Cali, Colombia, [2]Department of Epidemiology, Center for Public Health, Medical University of Vienna, Vienna, Austria, [3]Drugs for Neglected Diseases initiative (DNDi), Geneva, Switzerland, [4]Instituto René Rachou (IRR), Fundação Oswaldo Cruz (FIOCRUZ), Minas Gerais, Brazil, [5]Center of Infectious Diseases, Heidelberg University Hospital, Heidelberg, Germany, [6]Division of Infectious Diseases and Tropical Medicine, Department of Medicine I, Medical University of Vienna, Vienna, Austria, [7]Programa de Estudio y Control de Enfermedades Tropicales (PECET), Universidad de Antioquia, Medellin, Colombia, [8]Primary Care, Population Sciences and Medical Education, University of Southampton, Southampton, United Kingdom, [9]Institute of Specific Prophylaxis and Tropical Medicine, Center for Pathophysiology, Infectiology and Immunology, Medical University of Vienna, Vienna, Austria, [10]International Severe Acute Respiratory and Emerging Infection Consortium, Pandemic Sciences Institute, University of Oxford, Oxford, United Kingdom

Target Product Profiles (TPPs) are instrumental to help optimise the design and development of therapeutics, vaccines, and diagnostics. These products, in order to achieve the intended impact, should be aligned with users' preferences and needs. However, patients are rarely involved

as key stakeholders in building a TPP. Our study focuses on cutaneous leishmaniasis (CL), a parasitic NTD. At present, there is no treatment which is effective, safe and easy to administer. Thirty-three CL patients from Brazil, Colombia, and Austria, infected with New-World Leishmania species, were recruited using a maximum variation approach along geographic, sociodemographic and clinical criteria. Semi-structured in-depth interviews were conducted in the respective patient's mother tongue. Transcripts, translated into English, were analysed using a framework approach. We matched disease experiences, preferences, and expectations of CL patients to a TPP developed by DNDi (Drugs for Neglected Diseases initiative) for CL treatment. Patients' preferences regarding treatments ranged from specific efficacy and safety endpoints to direct and significant indirect costs. Respondents expressed views about trade-offs between efficacy and experienced discomfort/adverse events caused by treatment. Reasons for non-compliance, such as adverse events or geographical and availability barriers, were discussed. Considerations related to accessibility and affordability were relevant from the patients' perspective. NTDs affect disadvantaged populations, often with little access to health systems. Engaging patients in designing adapted therapies could significantly contribute to the suitability of an intervention to a specific context and to compliance, by tailoring the product to the end-users' needs. This exploratory study identified preferences in a broad international patient spectrum. It provides methodological guidance on how patients can be meaningfully involved as stakeholders in the construction of a TPP of therapeutics for NTDs. CL is used as an exemplar, but the approach can be adapted for other NTDs.

8385

DEVELOPMENT OF NOVEL HOOKWORM MRNA VACCINE CANDIDATES BY ALTERING THE INTRACELLULAR TRAFFICKING OF *NECATOR AMERICANUS* GST-1 ANTIGEN

Athos Silva de Oliveira[1], Leroy Versteeg[1], Neima Briggs[2], Rakesh Adhikari[1], Maria Jose Villar[1], Peter Hotez[1], Maria Elena Bottazzi[1], Jeroen Pollet[1]

[1]Texas Children's Hospital Center for Vaccine Development & Department of Pediatrics, National School of Tropical Medicine, Baylor College of Medicine, Houston, TX, United States, [2]Departments of Immunobiology and Internal Medicine, Yale University, New Haven, CT, United States

RNA platforms offer rapid adaptability for modifying and optimizing vaccine antigens. By adding and editing signal sequences within mRNAs, antigens can be translated more efficiently and guided to diverse locations in recipient cells. Here, we present the production of three versions of an mRNA vaccine encoding *Necator americanus* (*Na*) GST-1 protein, a previously identified hookworm antigen. The mRNA candidates, differing only in their signal sequences, code for either wild-type *Na*-GST-1 (wt), secretory *Na*-GST-1 (SS), or plasma membrane(PM)-anchored *Na*-GST-1 proteins. Translation efficiency of the mRNA candidates was tested *in-vitro* via transfection of DC 2.4 cells and quantified by immunostaining and flow cytometry. The localization of *Na*-GST-1 (intracellular, secreted, or membrane-bound) was determined by immunocytochemistry and Western blot. Forty BALB/C mice were divided into five groups and immunized intramuscularly twice. In addition to the three mRNA groups, mice were also vaccinated with either placebo LNPs or recombinant *Na*-GST-1 protein expressed in *Pichia pastoris*. ELISA analysis of the mouse sera showed higher titers of antigen-specific IgG in groups vaccinated with mRNAs than with recombinant *Na*-GST-1. While all groups induced similar levels of IgG1, IgG2a was only elicited in the mRNA groups. Furthermore, an increase in cytokine production and memory T cells using certain mRNA vaccine candidates was also observed after stimulation of splenocytes with recombinant *Na*-GST-1. Significant differences in immune response were also seen among the mRNA vaccines, reflecting the exposition of *Na*-GST-1 as an antigen. Finally, all vaccinated mice generated neutralizing antibodies capable of inhibiting the glutathione-transferase activity of *Na*-GST-1 *in-vitro*. Combined, our data illustrates the potential of the mRNA platform for better tailoring the immune response. While ongoing challenge studies in a mouse model infected with *Nippostrongylus brasiliensis* will further elucidate efficacy, we found that when using optimized signal sequences, Na-GST-1 mRNA vaccines can induce a strong immune response in mice.

8386

CONTROL OF HOOKWORMS USING *BACILLUS THURINGIENSIS* CRY PROTEINS AND VACCINES

Qian Ding[1], Hanchen Li[1], Kelly A. Flanagan[1], Duy Hoang[1], Nicholas R. Cazeault[1], Florentina Rus[1], Ernesto Soto[1], Erich M. Schwartz[2], Jane Homan[3], Wenbin Tuo[4], Gary R. Ostroff[1], Raffi V. Aroian[1]

[1]Umass Chan Medical School, worcester, MA, United States, [2]Cornell University, Ithaca, NY, United States, [3]ioGenetics LLC, Madison, WI, United States, [4]United States Department of Agriculture, Beltsville, MD, United States

Human hookworms—*Necator americanus, Ancylostoma duodenale, and Ancylostoma ceylanicum*—are intestinal parasites that siphon blood and afflict approximately 500 million people globally. These parasites are primary contributors to iron-deficiency anemia in the developing world. Alarmingly, nearly 90 million children suffer chronic infections, experiencing stunted growth and delayed cognitive and intellectual development. Additionally, millions of pregnant women are affected, which results in adverse birth outcomes. Historically, infections by soil-transmitted helminths (STHs) have been managed with small-molecule anthelmintic drugs. However, prolonged usage of these drugs has frequently led to the development of drug resistance. In response to these challenges, our objective is to develop a new therapeutic intervention and a vaccine to combat hookworm infections. To achieve this, we have pursued two innovative approaches. Firstly, we have utilized *Bacillus thuringiensis* crystal (Cry) proteins, the world's most extensively deployed biological insecticides, which are non-toxic to vertebrates. Our research has demonstrated that Cry proteins, especially Cry5Ba, are highly effective against a wide array of both free-living and parasitic nematodes that affect plants, animals, and humans. Secondly, we have employed transcriptomics, proteomics, and immunoinformatics to screen the *Ancylostoma ceylanicum* genome for potential pan-hookworm vaccine candidates and developed vaccines with excretory/secretory (ES) products from *Ancylostoma ceylanicum*. We are excited to discuss several promising new Cry proteins—CryH18, CryH1, and CryH13—as well as novel validated antigens identified through omic approaches and ES products as potential vaccine candidates against hookworm infections.

8387

OPISTHORCHIS VIVERRINI ANTI-CANCER VACCINE TARGETING THE LIVER FLUKE HOST-PARASITE INTERFACE

Michael J. Smout[1], Sujittra Chaiyadet[2], Wannaporn Ittiprasert[3], Sutas Suttiprapa[2], Paul J. Brindley[3], Thewarach Laha[2], Alex Loukas[1]

[1]James Cook University, Cairns, Australia, [2]Khon Kaen University, Khon Kaen, Thailand, [3]George Washington University, Washington DC, DC, United States

Infection with the food-borne liver fluke *Opisthorchis viverrini* is the principal risk factor for bile duct liver cancer (cholangiocarcinoma, CCA) in SE-Asia, and a vaccine is needed to reduce future infections and the many thousands of annual deaths. We explored the role of the parasite growth factor *Ov*-GRN-1 in malignancy using a novel model of liver fluke infection induced hamster CCA. We produced CRISPR/Cas9 gene knockout flukes (*ΔOv-grn-1)* and confirmed depletion of transcripts and protein. *ΔOv-grn-1* parasites colonized the hamster biliary tract and developed into adult flukes, but less hepatobiliary tract disease and high-grade CCA manifested during chronic infection with *ΔOv-grn-1* flukes compared to control flukes. The reduced liver disease was marked by less local and global fibrosis, reduced cholangiocyte proliferation, and fewer *p53* tumor suppressor gene mutations. This clinically-relevant phenotype of reduced pathology and malignancy confirmed a role for this secreted virulence factor and supports pursuit of *Ov*-GRN-1 as an anti-pathogenesis vaccine candidate. But flukes are difficult foes, and an effective vaccine will need to target a number

of key parasitism pathways to be sufficiently efficacious. To this end we are targeting *Ov*-TSP-2 alongside *Ov*-GRN-1 in a multivalent approach. *Ov*-TSP-2 is abundant on the surface of *O. viverrini* secreted extracellular vesicles (EVs), and antibodies raised to recombinant *Ov*-TSP-2 interrupt host-parasite communication by blocking the uptake of fluke EVs by host cholangiocytes. Moreover, *Ov-tsp-2* gene knockout is lethal for flukes *in vivo*. We are currently exploring the efficacy of *Ov*-GRN-1, *Ov*-TSP-2, and other nutrient acquisition antigen combinations as both protein and mRNA vaccines in the hamster model of fluke infection and CCA. We believe that targeting fluke-host communication in combination with nutrient acquisition pathways will ultimately combat this liver fluke infection associated malignancy in the form of a novel anti-fluke/anti-cancer vaccine, a public health development with the potential to benefit millions of impoverished residents of endemic regions.

8388

A LIVE-ATTENUATED *LEISHMANIA* VACCINE SHAPES THE CELLULAR RESPONSE IN THE BONE MARROW

Thalia Pacheco-Fernandez, Nazli Azodi, Spyros Karaiskos, Laura Klenow, Hannah Markle, Lais DaSilva-Pereira, Luis Santana-Quintero, Alexander Murray, Hira Nakhasi, Sreenivas Gannavaram
Food and Drug Administration, Silver Spring, MD, United States

Leishmaniasis is a neglected tropical disease for which no vaccine is available. We developed a live-attenuated *Leishmania major* lacking the *Centrin* gene (*LmCen*$^{-/-}$) as vaccine, which showed safety and immunogenicity in pre-clinical studies. Immunization with *LmCen*$^{-/-}$ induced protection against homologous and heterologous challenge infections in murine models; protection mediated by IFN-γ secreting T effector cells. Studies in leishmanization (virulent *L. major*; *Lm*WT) models showed that persistent infection is necessary for maintaining protective immunity, in addition to central and skin resident memory T cells. Similar studies with live attenuated vaccine strains regarding persistence and durability of protection have not been undertaken. Here, we evaluated the presence of latent parasites in cells from the bone marrow (BM) that could define the immune landscape. We used dual-scRNAseq to identify cells harboring parasites within the BM 28 days post-infection. We identified that about 1% cells from mice infected with virulent *LmWT* or vaccinated with *LmCen*$^{-/-}$ harbored leishmania transcripts suggesting parasitization. We investigated the effect of parasitized cells on the immune landscape in the BM. Using scRNAseq, identification of different cell populations within the BM after intradermal inoculation of both parasites showed that *LmCen*$^{-/-}$ infection led to differential expansion of neutrophil and megakaryocyte populations, compared to *Lm*WT infection. Validation via flow cytometry confirmed that vaccination with *LmCen*$^{-/-}$ leads to the expansion of myeloid progenitors of megakaryocytes (MPPII), while this change was not observed in *Lm*WT infection. In conclusion, vaccination with a live-attenuated *LmCen*$^{-/-}$ vaccine elicits neutrophils and megakaryocyte expansion in the BM, which could be responsible for strong protection against leishmaniasis. Further studies will determine the mechanisms by which the persistent presence of latent parasites within the bone marrow induce protection.

8389

SEROLOGICAL, CELLULAR, AND BLOOD TRANSCRIPTOMIC RESPONSES TO A RECOMBINANT ONCHOCERCIASIS VACCINE IN CATTLE NATURALLY EXPOSED TO *ONCHOCERCA OCHENGI*

Ben Makepeace[1], John Graham-Brown[1], Tessa R. Walsh[1], Lisa Luu[1], Germanus Soh Bah[2], Ndode Herman Okah-Nnane[2], David D. Ekale[2], Rene B. Ayiseh[3], David Abraham[4], Darrick Carter[5], Sean Gray[5], Godwin Nchinda[6], Vincent Tanya[2], Sara Lustigman[7]
[1]University of Liverpool, Liverpool, United Kingdom, [2]L'Institut de Recherche Agricole Pour le Développement, Ngaoundéré, Cameroon, [3]University of Buea, Buea, Cameroon, [4]Thomas Jefferson University, Philadelphia, PA, United States, [5]PAI Life Sciences, Seattle, WA, United States, [6]Centre International de Reference "Chantal Biya", Yaounde, Cameroon, [7]New York Blood Center, New York, NY, United States

Human onchocerciasis is a neglected tropical disease affecting 21 million people in sub-Saharan Africa caused by the filarial nematode *Onchocerca volvulus*. Disease elimination via mass administration of the microfilaricidal drug ivermectin has achieved marked but qualified success, indicating a need for additional tools. Here, we use the bovine *O. ochengi* natural infection system to assess the efficacy and immunogenicity of a recombinant onchocerciasis vaccine. Immunologically naïve calves were recruited for a trial of a recombinant fusion protein (Fus1) composed of antigen candidates *Ov*-103 and *Ov*-RAL-2 and formulated in Montanide ISA 201 VG (n = 15). The control group received adjuvant only (n =1 5); primary and booster immunisations were administered at an interval of four weeks in both groups. Four weeks post-immunisation, animals were transferred to a site of natural *O. ochengi* transmission for 24 months, receiving a further booster immunisation 6 months after turnout. All animals were sampled routinely to measure serum and peripheral blood leucocyte (PBL) responses, as well as parasite load (nodules and microfilaridermia). Immunological investigations to determine T- and B-cell responses included antigen-specific serum antibody ELISAs and peripheral blood leucocyte cultures with subsequent analyses via flow cytometry and transcriptomics. All immunised calves showed strong antigen-specific serum IgG isotype responses to immunisation, which progressively waned over the subsequent exposure period. Network analysis of RNA-Seq data from PBLs indicated differential expression of a number of pathways relating to immune function in immunised calves, including upregulation of interleukin-10, negative regulation of macrophage function, complement activation, and induction of nitric oxide synthase. However, flow cytometry demonstrated no evidence of memory T-cell responses and vaccination was not significantly associated with reductions in either adult or microfilarial worm burdens. These results underline the challenges of inducing strong immune memory when vaccinating against helminth infections.

8390

A PHASE I/II STUDY OF THE SAFETY, IMMUNOGENICITY, AND EFFICACY OF *SM*-TSP-2/ALHYDROGEL WITH OR WITHOUT AP 10-701 FOR INTESTINAL SCHISTOSOMIASIS IN HEALTHY UGANDAN ADULTS

Chrispus M. Bakunda[1], Betty Mwesigwa[1], Grace Mirembe[1], Jacqueline Namugabo[1], Hilda Mutebe[1], Immaculate Nakabuye[1], Douglas Makumbi[1], Amir Wamala[1], Allan Tindikahwa[1], Lara Hoeweler[2], Proscovia Naluyima[1], Laura Vasquez[2], Maria Elena Bottazzi[3], Peter J. Hotez[3], Elissa Malkin[2], Jeffrey M. Bethony[2], David J. Diemert[2], Hannah Kibuuka[1]
[1]Makerere University Walter Reed Project, Kampala, Uganda, [2]George Washington University, Washington, DC, United States, [3]Baylor College of Medicine, Houston, TX, United States

Tetraspanins (TSPs) are membrane spanning proteins on the schistosome's outer syncytial surface that function in tegument formation and host-parasite interface and are targets of vaccine development. Studies in schistosomiasis endemic areas showed that putatively resistant individuals express antibodies against these antigens, leading to selection of the TSP-2 antigen as a lead candidate targeting disease caused by *Schistosoma mansoni*. Recombinant *Sm*-TSP-2 expressed in *Pichia pastoris* was purified by a series of chromatography steps and adsorbed to Alhydrogel (Al: aluminum hydroxide adjuvant). Two Phase I trials conducted in the USA and Brazil of *Sm*-TSP-2/Al with or without AP 10-701, a synthetic Toll-like receptor-4 agonist, showed the vaccine to be safe, well tolerated and induced anti-*Sm*-TSP-2 IgG antibodies. A Phase I/II study is being conducted in healthy Ugandan adults aged 18-45 years. Ninety subjects were enrolled in 3 groups of 30 in the Phase I stage, a randomized, double-blind, dose escalation trial with progression to the next dose determined by review of predefined criteria, done 7 days after all subjects in the active cohort received the first vaccination. Two formulations of *Sm*-TSP-2 were tested: one using Al only, and one using Al plus AP 10-701, with Hepatitis B vaccine (HBV) as a comparator (12 subjects per study vaccine group

and 6 subjects in the HBV group), each at 3 different antigen doses: 10, 30 and 100mcg. Vaccinations were administered by intramuscular injection in the deltoid at 0, 2, and 4 months. Common adverse events (AEs) included mild to moderate injection site pain and tenderness, headache, malaise, fatigue, and dizziness. Solicited AEs were well tolerated and short-lived. No significant differences were observed in AEs between dose groups. There were no vaccine-related serious AEs. The highest IgG antibody response, as determined by ELISA, was detected among participants who received 100mcg *Sm*-TSP-2/Al with AP 10-701, which was thus chosen as the optimal dose for the Phase II stage of the study that is currently underway. Addition of AP 10-701 to *Sm*-TSP-2/Al improved IgG responses but did not compromise safety.

8391

THE ANTI-CIRCUMSPOROZOITE ANTIBODY RESPONSE OF CHILDREN TO SEASONAL VACCINATION WITH THE RTS,S/AS01$_E$ MALARIA VACCINE OVER FIVE YEARS OF FOLLOW-UP (4 BOOSTER DOSES)

M Sanni Ali[1], Lisa Stockdale[2], Issaka Sagara[3], Issaka Zongo[4], Rakiswendé Serge Yerbanga[4], Almahamoudou Mahamar[3], Frédéric Nikièma[4], Amadou Tapily[3], Frédéric Sompougdou[4], Modibo Diarra[3], Duncan Bellamy[2], Katie Ewer[2], Charles Zoungrana[4], Djibrilla Issiaka[3], Alassane Haro[4], Koualy Sanogo[3], Abdoul-Aziz Sienou[4], Mahamadou Kaya[3], Seydou Traore[3], Ismaila Thera[3], Kalifa Diarra[3], Amagana Dolo[3], Paul Snell[1], Opokua Ofori-Anyinam[5], Chris Ockenhouse[6], Cynthia Lee[6], Halidou Tinto[4], Abdoulaye Djimde[3], Jean-Bosco Ouedraogo[4], Alassane Dicko[3], Daniel Chandramohan[1], Brian Greenwood[1]

[1]London School of Hygiene & Tropical Medicine, London, United Kingdom, [2]Jenner Institute, University of Oxford, Oxford, United Kingdom, [3]The Malaria Research and Training Center, University of Sciences, Techniques and Technologies, Bamako, Mali, [4]Institut de Recherche en Sciences de la Santé, Bobo-Dioulasso, Burkina Faso, [5]GSK, Wavre, Belgium, [6]PATH, Seattle, WA, United States

Combining seasonal vaccination with RTS,S/AS01$_E$ vaccine with seasonal malaria chemoprevention (SMC) has reduced the incidence of uncomplicated and severe malaria compared to either intervention given alone, at 3 and 5 years of follow-up. This study reports the anti-CSP antibody response and potential correlates of protection during the 5 years. Sera from randomly selected subset of children (N=1634) collected before 1 month and after 3 priming doses and 4 annual booster doses were tested for *P. falciparum* anti-CSP (NANP repeat) antibodies using GSK enzyme-linked immunosorbent assay (ELISA) protocol. A subset of these samples was also tested using the Oxford MSD multiplex ELISA protocol (NANP repeat), to explore correlation between the two ELISA protocols. The rise in titers were compared using geometric mean ratios. In addition, the association between post vaccination antibody titer and incidence of malaria. The 3 priming doses induced strong anti-CSP antibody response (Geometric mean titer 368.9 IU/mL), subsequent annual, pre-malaria transmission season booster doses also induced a strong antibody response but a lower than the primary vaccination series (geometric mean titer of the fourth booster was 128.5IU/mL) and previous boosters. The rise after the first booster was higher than subsequent boosters. Children whose antibody response was in the upper and middle terciles post vaccination had lower incidences of malaria during the following year than children in the lowest tercile (hazard ratio, 0.53; 95% CI, 0.39-0.72 and 0.75 95%CI, 0.56 to 0.99, for upper and middle terciles, respectively). The two ELISA protocols were strongly correlated (Pearson's correlation coefficient, r = 0.92; 95%CI, 0.91-0.93). Seasonal vaccination with RTS,S/AS01$_E$ induced strong booster antibody response that was lower after the subsequent boosters than the first booster. The diminished antibody response was not associated with diminished protection/efficacy. Measurements of anti-CSP antibody titers from the two ELISA protocols were strongly correlated.

8392

EFFECTS OF HUMIDITY AND TEMPERATURE VARIATIONS ON *ANOPHELES* GENETIC TARGET CANDIDATES FOR MALARIA CONTROL

Thais Lemos-Silva, **Maria Luisa Simoes**

Institute of Tropical Medicine Antwerp, Antwerp, Belgium

The malaria mosquito innate immune system is the first line of defense against pathogens and a major regulator of vector competence and malaria transmission. Mosquitoes are influenced by environmental factors that shape their physiology and behaviour. However, the extent to which climatic factors affect the malaria vector immunity with repercussions to malaria transmission remains mostly unexplored. A limited number of studies has investigated temperature and mosquito immunity interactions. However, the role of humidity on *Anopheles* immune responses has been largely ignored. In this study, we aim at understanding how climate change will affect mosquito immune responses to *Plasmodium* infection with consequences for malaria transmission. The experimental approach we employ challenges standard methods used in vector studies that rely on static humidity/temperature parameters; instead, we incorporate ecological realism (i.e. variable humidity/temperature) into research by mimicking current and potential future climatic scenarios in nature. Using RNA-seq transcriptomic analysis and qRT-PCR, we discovered *Anopheles* genes with immunity and/or *Plasmodium* infection modulating functions that are differentially expressed in mosquitoes exposed to current climate or future climate according to climate change predictions. In addition, we observed that humidity and temperature variations selectively affect the fitness of *An. stephensi* mosquitoes at different developmental stages, impacting vector competence. Using CRISPR/Cas9-mediated gene knockout, or knockin, of *Plasmodium* host/restriction factors (that facilitate/block *Plasmodium* replication in the mosquito, respectively) as in previous studies (Simões *et al.* 2017, 2022), the novel genetic targets identified here can be exploited for the engineering of fit-for-purpose transgenic vectors for malaria transmission reduction in climate change-affected regions.

8393

TNF SIGNALING ACTIVATES CELLULAR IMMUNITY TO PROMOTE MALARIA PARASITE KILLING IN *ANOPHELES GAMBIAE*

George-Rafael Samantsidis, Hyeogsun Kwon, Megan Rogers, Catherine Fonder, **Ryan C. Smith**

Iowa State University, Ames, IA, United States

Tumor Necrosis Factor-α (TNF-α) is a proinflammatory cytokine and a master regulator of immune cell function in vertebrates. While previous studies have implicated TNF signaling in invertebrate immunity, the roles of TNF in mosquito innate immunity and vector competence have yet to be explored. Herein, we confirm the identification of a conserved TNF-α pathway in *Anopheles gambiae* consisting of the TNF-α ligand, Eiger, and its cognate receptors Wengen (Wgn) and Grindelwald (Grnd). Through gene expression analysis, RNAi, and *in vivo* injection of recombinant TNF-α, we provide direct evidence for the requirement of TNF signaling in regulating mosquito immune cell function by promoting granulocyte midgut attachment, increased granulocyte abundance, and oenocytoid rupture. Moreover, our data demonstrate that TNF signaling is an integral component of anti-*Plasmodium* immunity that limits malaria parasite survival. Together, our data support the existence of a highly conserved TNF signaling pathway in mosquitoes that mediates cellular immunity and influences *Plasmodium* infection outcomes, offering potential new approaches to interfere with malaria transmission by targeting the mosquito host.

8394

PIXEL INTENSITY OF WING PHOTOS USED TO PREDICT AGE OF *ANOPHELES GAMBIAE* SENSU LATO CAUGHT DURING THE RIMDAMAL II CLINICAL TRIAL

Greg Pugh[1], Emmanuel Sougué[2], Ryan Yoe[1], Lyndsey I. Gray[1], Blue Hephaestus[3], Anthony Somé[2], A. Fabrice Somé[2], Bryce Asay[3], Roch K. Dabiré[2], Sunil Parikh[4], Brian D. Foy[1]

[1]Colorado State University, Fort Collins, CO, United States, [2]Institute de Recherche en Sciences de la Santé, Bobo-Dioulasso, Burkina Faso, [3]Viden Technologies, Laramie, WY, United States, [4]Yale School of Public Health, New Haven, CT, United States

Mosquito age-grading is pivotal for understanding population structures, evaluating mosquito control efforts, and allows for estimates of pathogen transmission risk from the mosquito population. While traditional age-grading techniques can be burdensome and inexact, recent age-grading methods can require costly supplies or machines, and the destruction of samples for precise results. We previously developed a simple, low-cost, nondestructive, and high throughput method to quantitatively age-grade mosquitoes by computing the pixel intensity (PI) of wing photos, evaluating wing scale loss over time. Here the technique is refined by measuring mean rather that the total PI per wing image. Additionally, we developed and applied an age model to wild *Anopheles gambiae* s.l. captured during the RIMDAMAL II cluster-randomized clinical trial, evaluating the use of ivermectin for malaria control. Wing photos from newly eclosed lab-reared *An. gambiae* had a PI of 128.45 (128.35-128.62), while mosquitoes ≥ 10 days had a PI of 129.00 (128.65-129.45). Comparatively, wing photos from wild mosquitoes had a PI range of 127.85-133.08. Binned PI from wild mosquitoes exhibited a distribution reflective of traditional age-grading methods, with >80% of the population having a PI in the 3 lowest bins and <20% of mosquitoes distributed among 14 bins of the highest ranges (128.74-133.38). The distributions of mosquitoes placed in PI bins across the trial largely reflected the expected effect of ivermectin in the treatment arm. Finally, a symmetrical sigmoidal variable slope was the best fit model for lab mosquitoes of known ages, which we used to interpolate unknown ages from the field. With this model, 30% (578/1920 samples) of wild *An. gambiae* could be interpolated. These had an estimated median age of 4.96 (0.8-14.93) days and the interpolated age structures reflected the effect of the mosquito control interventions across the years of the trial. Overall, these data demonstrate how the use of wing photo PI can rapidly generate expected age distributions of wild mosquito populations and assist in evaluating the efficacy of mosquito control interventions.

8395

EXPLOITING MOSQUITO SALIVARY PROTEINS TO DEVELOP VECTOR-TARGETED VACCINES FOR MALARIA AND ARBOVIRUSES

Alexandra Francian[1], Aidan Leyba[2], Yevel Flores-Garcia[3], Robert Taylor[4], Justin Baca[4], Pavan Muttil[2], Fidel Zavala[3], Bryce Chackerian[1]

[1]University of New Mexico School of Medicine, Albuquerque, NM, United States, [2]University of New Mexico College of Pharmacy, Albuquerque, NM, United States, [3]Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, United States, [4]University of New Mexico, Albuquerque, NM, United States

Despite on-going control efforts, mosquito-borne diseases account for over 700,000 deaths annually. Two genera of mosquitoes are responsible for the majority of disease transmission; *Anopheles* species carry the parasites that cause malaria and *Aedes* species are vectors for viruses such as dengue, Zika, and Chikungunya. Factors within mosquito saliva interact with the host immune response to facilitate faster feeding and immune evasion, which is also beneficial to pathogen survival. For example, the *Anopheles* salivary protein, TRIO, influences the local inflammatory response in favor of *Plasmodium* motility and infection. Similarly, the *Aedes* salivary peptide, sialokinin (SK), increases blood vessel permeability, causing a rapid influx of virus-permissive cells. Targeting salivary proteins offers the potential for developing universal, vector-targeted vaccines, which would be especially valuable in endemic areas, providing broad protection against many diseases as they emerge. Our lab specializes in using virus-like particles (VLPs) as versatile vaccine platforms. The multivalent display of antigens on VLPs is particularly effective at eliciting high-titer and long-lasting antibody responses. This project focuses on using VLPs to develop 1) a malaria vector/pathogen combination vaccine targeting *Anopheles* TRIO and *P. falciparum* circumsporozoite protein (CSP), and 2) a pan-viral vaccine targeting *Aedes* SK. Both TRIO- and SK-VLPs resulted in high antibody titers that have not dropped up to 18 months post-immunization, essentially the lifespan of a mouse. TRIO-VLPs elicited equally high titers in interstitial fluid, a critical site for initial infection. After malaria challenge, mice vaccinated with TRIO-VLPs alone were significantly protected from infection, and the combination with CSP-VLPs further increased protection. Importantly, no cross-reactivity or sensitivity to the salivary peptides was seen in immunized mice. These preliminary data demonstrate the potential for designing interventions that target important disease vectors, as well as the promise of vector/pathogen combination vaccines.

8396

PLASMODIUM FALCIPARUM INFECTION IN THE HUMAN HOST AND THE VECTOR INFLUENCE NATURAL ANOPHELINE BITING BEHAVIOR AND PARASITE TRANSMISSION

Christine F. Markwalter[1], Zena Lapp[1], Lucy Abel[2], Emmah Kimachas[2], Evans Omollo[3], Elizabeth Freedman[1], Tabitha Chepkwony[2], Mark Amunga[2], Tyler McCormick[4], Sophie Bérubé[5], Judith N. Mangeni[6], Amy Wesolowski[5], Andrew A. Obala[6], Steve M. Taylor[1], Wendy P. O'Meara[1]

[1]Duke University, Durham, NC, United States, [2]Academic Model Providing Access to Healthcare, Eldoret, Kenya, [3]Duke Global Inc, Nairobi, Kenya, [4]University of Washington, Seattle, WA, United States, [5]Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, United States, [6]Moi University, Eldoret, Kenya

Understanding mosquito biting bias in a natural setting can help target interventions to efficiently interrupt transmission. In a 15-month longitudinal cohort study in a high transmission setting in western Kenya, we investigated human and mosquito factors associated with differential mosquito biting by matching human DNA in single- and multi-source *Anopheles* bloodmeals to the individuals they bit using short tandem repeat (STR) genotyping. We employed risk factor analyses and econometric models of probabilistic choice to assess mosquito biting behavior with respect to both human-to-mosquito transmission and mosquito-to-human transmission. Among the 1064 mosquitoes with bloodmeals that were STR typed, 777 (73%) bit a human, and 662 (85%) matched to at least one community member. Biting patterns were highly heterogeneous; 20% (118/588) of community members received 88% (631/720) of observed bites, and *Plasmodium falciparum*-infected school-age boys accounted for 50% of bites potentially leading to onward transmission to mosquitoes. *P. falciparum* sporozoites were detected in 22% (146/662) of matched mosquitoes. Using discrete choice models to explore mosquito biting preferences, infectious mosquitoes were nearly 3x more likely to bite cohort members harboring *P. falciparum* parasites compared to noninfectious mosquitoes (relative risk ratio 2.76, 95% CI 1.65-4.61). Further, this preference to feed on infected people was enhanced by the presence of higher sporozoite loads in the mosquito head-thorax. This is the first observation in a natural setting that *P. falciparum* sporozoites modify mosquito biting preferences to favor feeding on infected people. Thus, persistent *P. falciparum* transmission in this setting was characterized by disproportionate onward transmission from school-age boys and by the preference of infected mosquitoes to feed upon infected people.

8397

LANDSCAPES OF INFECTION: REDEFINING THERMAL SUITABILITY OF URBAN MALARIA TRANSMISSION BY THE INVASIVE MOSQUITO SPECIES *ANOPHELES STEPHENSI* IN THE CONTEXT OF RELATIVE HUMIDITY

Courtney Murdock[1], Joel Brown[1], Britny Johnson[1], Paul Huxley[2], Leah Johnson[2], Brandon Hollingsworth[1], Michael Wimberly[3], Mercedes Pascual[4], Rajendra Baharia[5], Ajeet Mohanty[6], Rajesh Sharma[7], Sachin Sharma[8], Keshav Vaishnav[9], Vijay Kohli[7], Vikas Desai[10]

[1]Cornell University, Ithaca, NY, United States, [2]Virginia Tech, Blacksburg, VA, United States, [3]University of Oklahoma, Norma, OK, United States, [4]New York University, New York City, NY, United States, [5]National Institute for Malaria Research, Nadiad, India, [6]National Institute for Malaria Research, Goa, India, [7]Ahmedabad Municipal Corporation, Ahmedabad, India, [8]Cornell In India & National Institutes for Malaria, Delhi, India, [9]Surat Municipal Corporation, Surat, India, [10]Urban Health And Climate Resilience Centre Of Excellence, Surat, India

Vector-borne diseases cause significant financial and human loss, with billions of dollars spent on control. Arthropod vectors experience a complex suite of environmental factors that affect fitness, population growth, and species interactions across multiple spatial and temporal scales. Temperature and water availability are two of the most important abiotic variables influencing their distributions and abundances. While extensive research on temperature exists, the influence of humidity on vector and pathogen parameters affecting disease dynamics are less understood. Humidity is often underemphasized, and when considered, is often treated as independent of temperature even though desiccation likely contributes to declines in trait performance at warmer temperatures. In this study, we explore how variation in relative humidity affects the thermal performance of mosquito life history traits that are relevant for transmission (probability of larval survival, mosquito development rate, adult longevity and fecundity, and daily biting rate) in the Asian malaria vector (*Anopheles stephensi*) and human malaria (*Plasmodium falciparum*) system. We find relative humidity to significantly alter the predicted Tmin, Tmax, thermal breadth, and qualitative shape of the temperature-trait relationship in distinct and sometimes surprising ways depending on the trait being considered. These results demonstrate that if we do not account for temporal and spatial variation in relative humidity, mechanistic models used to forecast interannual and spatial variation in malaria risk will fail to accurately predict malaria incidence. This also has ramifications for making future projections with temperature-dependent models of disease risk with ongoing climate and land use change. As *Anopheles stephensi* is currently invading urban centers of Africa and poses a significant threat to ongoing malaria elimination efforts, accurately predicting its current and future distribution, abundance, and transmission potential is crucial.

8398

ANGIOGENESIS AND CHRONIC EXPOSURE TO *ANOPHELES* SALIVARY PROTEINS

Olayinka M. Olajiga[1], Arley Calle[1], Samuel B. Jameson[1], Brendan H. Carter[1], Dawn M. Wesson[1], Eric Calvo[2], Jennifer Manuzak[3], Berlin Londono-Renteria[1]

[1]Department of Tropical Medicine and Infectious Disease, School of Public Health and Tropical Medicine, New Orleans, LA, United States, [2]Laboratory of Malaria and Vector Research National Institutes of Health (NIH/NIAID), Rockville, MD, United States, [3]Department of Microbiology and Immunology, School of Medicine, Tulane University of New Orleans, New Orleans, LA, United States

Exposure to mosquito saliva can have prolonged effects on human physiology, impacting mosquito-borne diseases like malaria. Mosquito salivary proteins, acting as anticoagulants or immunomodulators, facilitate blood uptake by mosquitoes and may influence angiogenesis. However, the impact of exposure to mosquito salivary proteins on factors important in angiogenesis has not yet been described. In this study, we investigated the effects of *Anopheles quadrimaculatus* salivary gland proteins on endothelial cells. Human Umbilical Vein Endothelial Cells (HUVECs) were treated with salivary gland protein fractions from 100 pooled *An. quadrimaculatus* salivary gland pairs and cell proliferation was measured by MTT test. Based on the MTT test, we selected three fractions displaying significant differences ($p<0.05$) compared to untreated cells to further evaluate their effect on expression of angiogenesis associated factors. First, we used an ELISA-based test and observed that cells treated with fraction C2 presented higher TNFα and PDGFBB levels by 1.7-fold and 1.8-fold, respectively. We also observed that the fraction E6 upregulated IGF-1 by 1.7-fold, while fraction F9 enhanced FGFb and EDF by 1.6-fold and 2.1-fold, respectively. Further analysis via qPCR revealed that fraction F9 also induced an increase in TYMP (3.5-fold), VEGFB (2.3-fold), VEGFC (2.2-fold), ANGPTL2 (3.2-fold), NRP1 (3.2-fold), NRP2 (2.6-fold), and EDG1 (2.3-fold) while a 2-fold decrease was observed in CSF3 when compared to the level in untreated cells. Protein fractions were sent for sequencing. These findings highlight the role of mosquito saliva in angiogenesis, offering insights into potential therapeutic avenues for future research.

8399

USING ANCESTRAL SEQUENCE RECONSTRUCTION FOR GENERATION OF BROAD-SPECTRUM VACCINE PLATFORMS AGAINST TICK-BORNE FLAVIVIRUSES

Chasity E. Trammell, Brian J. Geiss, Gregory D. Ebel

Colorado State University, Fort Collins, CO, United States

Tick-borne flaviviruses (TBFs) pose a significant health threat and there is a significant need to develop more efficient countermeasures. However, most vaccines developed target a specific viral species, requiring new vaccines be developed against each pathogen. The development of vaccines that provide broad protection against a range of related viruses has the potential of reducing disease burden against known and unknown TBFs. Towards this need, we used ancestral sequence reconstruction (ASR) to design antigens of extinct ancestral viruses that might generate antibodies capable of neutralizing a broad array of related modern-day viruses. Among the flaviviruses, envelope (E) is immunodominant and antibodies targeting particular regions are strongly neutralizing. The flavivirus NS1 protein is also a determinant of pathogenesis and is highly immunogenic. Using alignments of extant human-pathogenic TBFs, we reconstructed ancestral E and NS1 sequences that possess high sequence and structural identity to several modern-day pathogens of concern. Ancestral antigens were then inserted into infectious clones (ICs) to generate chimeric vaccine candidates. Three different vaccine platforms were used, including yellow fever virus 17D, a double subgenomic Sindbis virus, and a deer tick virus IC that had been attenuated by mutagenesis of conserved residues present in other established attenuated vaccine platforms. We observed that while the yellow fever and deer tick virus ICs had reduced viral replication and antigen presentation, Sindbis virus ICs had similar viral kinetics and antigen expression, supporting further investigation in vivo. We predict that immune responses generated against ancestral antigens will provide a reasonable level of protection against multiple modern day TBFs. The results of this study contributes to the development of a much-needed vaccine that could be used in TBF-endemic areas.

8400

PRECLINICAL DEVELOPMENT OF AN ORALLY AVAILABLE NS4B INHIBITOR FOR YELLOW FEVER

Fuxuan Wang[1], Sumangala Darsandhari[1], Biplav Shrestha[1], Abbie Wight[2], Justin Julander[3], Brett Eaton[4], Michael Murphy[4], Yu Cong[4], Manu Anantpadma[4], Elena Postnikova[4], Michael Holbrook[4], Zhengyuan Jiang[1], Yusheng Wu[1], David Renner[1], Jason Clementon[1], Weihong Zhang[1], Yanming Du[1], Ju-Tao Guo[1], **Jinhong Chang**[1]

[1]Baruch S. Blumberg Institute, Doylestown, PA, United States, [2]Utah State University, logan, UT, United States, [3]Utah State University, Logan, UT, United States, [4]NIAID, Fort Detrick, MD, United States

In a high-throughput-screening, we identified a small-molecule hit compound BDAA that specifically inhibits yellow fever virus (YFV) replication through direct targeting YFV nonstructural protein 4B (NS4B). A preclinical lead BSBI-67003 has been nominated from a hit-to-lead optimization campaign with >200 analogs, which has nanomolar EC_{50} and a selectivity index of ~10,000 against the YFV vaccine strain, as well as clinical isolates, in 7 cell lines. BSBI-67003 has a favorable pharmacokinetic profile in mice with 96% oral availability with a plasma concentration maintained above EC_{90} 24 hours post a single oral dosing at 10 mg/kg. In a 5-day repeated dosing experiment in mice, the maximum tolerated dose was determined to be >100 mg/kg BID. *In vivo* efficacy was evaluated in a YFV lethal infection model in immune competent hamsters and the minimum efficacy dose was determined to be 1 mg/kg BID. Treatment initiated as late as 4 days post infection (peak of viremia) led to 100% protection of lethal infection and significant improvement in disease markers such as body weight, liver function and viremia. A significant reduction in viremia was observed as early as 6 hours post treatment indicating a rapid acting mechanism. Regarding the mode-of-action, we demonstrated that BDAA binds NS4B and disrupts the integrity of viral replication organelles (ROs) in YFV infected cells. Such action promptly inhibits nascent YFV RNA synthesis within 30 minutes of treatment. Furthermore, the treatment also causes viral replication intermediates leaking from RO leading to activation of three major cytoplasmic double-stranded RNA sensors and a broad spectrum antiviral inflammatory response within 90 minutes of treatment. Apart from the optimal druggable properties, such unprecedented multi-mode of action should contribute to the rapid-acting and potent inhibition of viral replication *in vivo*, a feature that is essential for acute hemorrhagic fever therapy with short treatment window. A chemical process has been developed for scaleup synthesis and preclinical pharmacology/toxicology studies to prepare for IND and first-in-class Phase I clinical trials.

8401

B CELL RESPONSES TO A ZIKA PURIFIED INACTIVATED VACCINE ARE SHAPED BY PREVIOUS IMMUNIZATION WITH JAPANESE ENCEPHALITIS AND YELLOW FEVER VACCINES

Samantha Townsley[1], Vincent Dussupt[1], Lauren Smith[1], Rafael De La Barrera[1], Mélanie Merbah[1], Bonnie Slike[1], Yifan Li[1], Annika Schmid[1], Hélène Fradin Kirshner[2], Lauren Yum[1], Robert Clifford[1], Letzibeth Mendez-Rivera[1], Sam Lieberman[1], Gautam Kundu[1], Aviva Geretz[1], Rasmi Thomas[1], Kevin Wiehe[2], Morgane Rolland[1], Gregory Gromowski[1], Nelson Michael[1], Natalie Collins[1], **Shelly Krebs**[1]

[1]Walter Reed Army Institute of Research, Silver Spring, MD, United States, [2]Human Vaccine Institute, Duke University, Durham, NC, United States

Flaviviruses cause widespread morbidity and mortality despite efforts towards vaccination. There are gaps in our understanding of how B cell responses are shaped in humans following sequential infections or immunizations with flaviviruses such as Zika (ZIKV), dengue (DENV), Japanese encephalitis (JEV), and Yellow fever (YFV). We evaluated antibody responses in a phase I clinical study representing 3 groups: (group a) flavivirus-naïve individuals vaccinated with a Zika purified inactivated whole virus vaccine (ZPIV), (group b) JEV (IXIARO®) followed by ZPIV, and (group c) YFV (YF-VAX®) followed by ZPIV. We found that ZIKV-neutralizing antibodies were diminished in participants primed with either JEV or YFV vaccination compared to flavivirus-naïve participants after two ZPIV vaccinations. To determine the cause of the diminished ZIKV neutralization, we characterized the longitudinal flavivirus-specific B cells. In flavivirus-naïve participants, the frequency of ZIKV-reactive B cells significantly increased following ZPIV vaccination ($p<0.05$), and these ZIKV-reactive B cells associated with the level of binding antibodies to Zika virions ($p<0.01$). Vaccination with JEV or YFV yielded high frequencies of B cells cross-reactive to ZIKV and DENV prior to ZPIV vaccination. Following two ZPIV vaccinations, the frequency of crossreactive B cells was significantly higher in JEV-vaccinated participants compared to B cells in flavivirus-naïve ZPIV vaccinees ($p<0.001$). Cross-reactive B cells had wanned by 6 months following the 2nd ZPIV vaccination and then were boosted to a higher frequency following a 3rd ZPIV vaccination ($p<0.05$). The third ZPIV vaccination coincided with the appearance of ZIKV neutralization in the YF-VAX® primed vaccinees. These studies demonstrate the elicitation of cross-reactive B cells following flavivirus vaccination, and provide insights into the memory recall B cell response upon subsequent flavivirus exposure. Characterizing these cross-reactive B cell populations and specificities is a critical step towards eliciting cross-protective responses following flavivirus vaccination.

8402

DEVELOPMENT OF A CONTROLLED ZIKA HUMAN INFECTION MODEL (CHIM)

Anna P. Durbin[1], Ruby Pritchett[1], Rachel Hampton[1], Beulah Sabundayo[1], Megan McKnight[1], Lina Moscarella[1], Xi Fang[1], Jeff Mayfield[1], Helen He[1], Cendy Alacantara[1], Will Stone[2], Elaine Lamirande[2], Stephen S. Whitehead[2]

[1]Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, United States, [2]National Institutes of Allergy & Infectious Diseases, National Institutes of Health, Bethesda, MD, United States

Zika virus (ZIKV) is a mosquito-borne flavivirus that was first isolated from the blood of a sentinel rhesus macaque in the Zika forest of Uganda in 1947. A large outbreak occurred in Latin America in 2015-16 resulting in the identification of congenital Zika syndrome (CZS) cases. Despite the development of numerous candidate vaccines for Zika, Phase 3 clinical trials have not been successfully performed due to the rapid resolution of the outbreak and the sporadic report of Zika cases. A ZIKV CHIM could play a critical role in the licensure pathway of potential Zika vaccines and therapeutics as a tool to down-select candidates and provide proof-of-concept for effectiveness. Two different ZIKV human isolates were obtained and expanded under cGMP (ZIKV-SJRP/2016-184 and ZIKV-Nicaragua/2016). Normal, healthy men and non-pregnant and non-lactating women ages 18 - 40 who were DENV and ZIKV-naïve were recruited from the Baltimore area. Twenty-eight women and 28 men were enrolled. Volunteers were block randomized to receive either ZIKV or placebo (5:2) in 4 cohorts of 14 volunteers. Volunteers were admitted to an inpatient unit and administered 100 PFU of ZIKV (or placebo) subcutaneously. Blood, cervico-vaginal secretions (CVS), semen, urine and saliva were collected and assayed for ZIKV. *Aedes albopictus* mosquitoes were fed on 7 volunteers from cohort 3 (ZIKV-SJRP, men) and 7 volunteers from cohort 4 (ZIKV-Nica, men) on days of peak viremia (days 5, 6, and 7 post-infection). Infectious ZIKV was recovered from serum in all volunteers who received ZIKV. ZIKV was recovered by culture and quantitative RT-PCR from multiple specimen types. Ninety - 100% of infected volunteers within each cohort developed a characteristic ZIKV rash. The clinical presentation and viral kinetics for both ZIKV-Nicaragua/2016 and ZIKV-SJRP/2016-184 in men and women will be presented. Both ZIKV strains were poorly transmissible to mosquitoes via feeding with only 1.8 - 2.4% of mosquitoes having ZIKV-Nica or ZIKV-SJRP detectable in the head (salivary glands), respectively.

8403

IMOJEV LIVE, ATTENUATED CHIMERIC VACCINE AGAINST JAPANESE ENCEPHALITIS: AN UPDATE AFTER 25 YEARS IN USE

Thomas P. Monath[1], Gray Heppner[1], Tracy Kemp[1], Bertrand Lepine[2], Marc Vouillamoz[2], Fabrice Baschiera[2]

[1]Quigley BioPharma LLC, Leominster, MA, United States, [2]Substipharm Biologics SA, Geneva, Switzerland

Japanese encephalitis (JE) is a mosquito-borne Flavivirus disease and a leading cause of encephalitis in Asia where ~5 billion live in 24 endemic countries. JE is characterized by high lethality and neurological sequelae in 30-50% of survivors. As for other zoonotic flaviviruses (e.g. West Nile, and Zika), there is a risk that JEV will invade the US. JE vaccines have been widely deployed in Asia, including inactivated vaccines; a live attenuated vaccine (SA-14-14-2); and a recombinant live vector vaccine (ChimeriVax-JE marketed under the trade name IMOJEV) . IMOJEV was engineered by replacing the prM-E genes of yellow fever 17D vaccine virus with the corresponding genes of the JEV SA14-14-2 virus, which contain 10 attenuating mutations that contribute to loss of neurotropism. Compared to YF-Vax®, IMOJEV was less neurovirulent in mice and non-human primates. Monkeys given a single SC dose rapidly developed high titers of neutralizing antibody and were protected against lethal IC JEV challenge. A total of 18 clinical trials in over 15,000 subjects, including 9,000 infants 9-24 months) showed the vaccine to be safe and highly immunogenic after a single SC inoculation of 4-5 logs. In adults , neutralizing antibodies are elicited rapidly, with 99% of subjects seroprotected by 30 days, with GMTs greater than 1000. The vaccine induced a durable response with 87% seroprotected 5 years after vaccination. There is no interference by anti-vector (yellow fever) immunity. First approved for persons 9 months of age or greater in Australia in 2010, and subsequently in 13 other countries in Asia, IMOJEV has enjoyed an excellent safety record, with over 11 million doses sold. IMOJEV's product profile, single-dose administration, rapid onset and durable protection, age limits, precautions and contraindications (pregnancy, breastfeeding, immune deficiency) are similar to the highly successful YF 17D vaccine from which it was derived, but with a better safety record. IMOJEV manufacturing in Vero cells is exceptionally robust and could meet unexpected demands resulting from an introduction of JEV into Europe or the Americas.

8404

SIMULTANEOUS INHIBITION OF DENGUE VIRUS INFECTION AND NS1-MEDIATED ENDOTHELIAL HYPERPERMEABILITY WITH A NATURAL STEROIDAL SAPOGENIN

E. Vanessa Jimenez Posada, Pedro H. Carneiro, Robert Beatty, Scott B. Biering, Eva Harris

Division of Infectious Diseases and Vaccinology, School of Public Health, University of California, Berkeley, Berkeley, CA, United States

The four dengue virus serotypes (DENV1-4) cause the most prevalent mosquito-borne viral disease in humans. While most cases are mild or asymptomatic, some progress to severe disease characterized by endothelial barrier dysfunction that is mediated by vasoactive cytokines and by the DENV non-structural protein 1 (NS1). Despite the urgent need for therapeutics, there is currently no specific antiviral treatment for dengue. However, spirostane-type compounds isolated from plant extracts exhibit antiviral effects against DENV and ZIKV in vitro. Based on structural similarities, we found in the Drug Bank database the spirostane compound smilagenin (SMI), a natural product, previously studied for its role in modulating inflammatory processes due its steroidal structure. We evaluated the antiviral effect of SMI in vitro by measuring the reduction of focus forming units (FFU) in the supernatants of Vero cells treated with SMI before and after DENV2 infection. We observed a significant reduction of 47% and 44% FFU/mL when cells were treated with SMI before and after DENV2 infection, respectively. Additionally, we investigated the ability of SMI to inhibit DENV NS1-induced endothelial hyperpermeability in Human Pulmonary Microvascular Endothelial Cells (HPMEC) using a trans-endothelial electrical resistance (TEER) assay, and we observed that SMI completely inhibited DENV NS1-induced hyperpermeability. We also evaluated the in vivo therapeutic efficacy of SMI in C57BL/6 mice deficient for the interferon α/β receptor infected with a lethal dose of DENV2 (strain D220) that were treated with 2mg/kg of SMI daily for 5 days starting on the day of infection. Treatment with SMI significantly reduced morbidity in mice compared to the vehicle control group, resulting in 100% survival. Our study demonstrates that SMI is a promising therapeutic for dengue, exhibiting potent antiviral effect in vitro and in vivo and protecting against NS1-induced endothelial barrier dysfunction. Further research is needed to elucidate the antiviral mechanisms of SMI and its impact on NS1-induced vascular leakage in vivo.

8405

ANTIBODY RESPONSE PROFILE ELICITED BY A LIVE-ATTENUATED TETRAVALENT DENGUE VACCINE IN CHILDREN AND ADOLESCENTS FROM ENDEMIC AREAS

Eduardo J.M. Nascimento[1], Isadora Lape[1], Brooke Norwood[1], Jesuina Fernandes[1], Huahua Wan[1], Apurva Kulkarni[1], Vianney Tricou[2], Eloi Kpamegan[1], Mayuri Sharma[1]

[1]Takeda Vaccines Inc., Cambridge, MA, United States, [2]Takeda Pharmaceuticals International AG, Zürich, Switzerland

Immunoglobulin (Ig) M, IgG1, and IgA have been implicated in protective responses against dengue virus (DENV) by promoting neutralization, clearance, and destruction of infected cells and virus by innate immune effector cells and/or the complement system (CS). TAK-003, a live-attenuated tetravalent dengue vaccine, was efficacious in preventing dengue disease and hospitalization in the phase 3 DEN-301 (NCT02747927) trial. Anti-DENV neutralizing antibodies (NAb) were quantified as part of immunogenicity endpoints of the trial. In exploratory assessments, we also investigated antibody isotype and subclasses (IgM, IgG1, and IgA), as well as complement-fixing antibody (CFA) effector function elicited by TAK-003 in randomly selected baseline (BL) seronegative (SN; n=48) and seropositive (SP; n=48) children/adolescents (4-16 years old). Antibody responses were assessed in samples collected before (day 1) and after (days 120, 270, and 450) two doses of TAK-003, administered subcutaneously 3 months apart, using Luminex-based multiplex assays. TAK-003 stimulated a multi-pronged humoral response profile in both groups. IgG1 and CFA were among the predominant responses, detected in 80-100% of the study participants. Both IgG1 and CFA targeted mostly all four DENV serotypes, often with comparable concentrations. The impact of TAK-003 on IgA and IgM responses was observed mainly in BL SN participants, with IgA detected at higher rates over time, targeting >3 DENV serotypes. Correlation analysis indicated the presence of heterogeneous relationships between function (NAb or CFA) and binding (IgG1, IgA, and IgM) antibody features, underscoring a cooperative and complex role for vaccine-driven virus neutralization and CS activation. In summary, this is the first report on a dengue vaccine-driven IgM, IgG1, IgA, and CFA response where study participants presented diverse humoral responses targeting multiple DENV serotypes for at least 1-year post-vaccination, confirming broader and long-lasting TAK-003-mediated immunity coverage, potentially allowing a sustained efficacy against infection and severe disease.

8406

COMBINING WEARABLE GPS LOGGERS WITH ENVIRONMENTAL AND SNAIL DATA TO UNCOVER FINE-SCALE *SCHISTOSOMA MANSONI* TRANSMISSION DYNAMICS IN UGANDA

Fabian Reitzug[1], Narcis B. Kabatereine[2], Betty Nabette[2], Goylette F. Chami[1]

[1]University of Oxford, Oxford, United Kingdom, [2]Vector Control Division, Ministry of Health, Kampala, Uganda

The complex and locally specific environmental interactions between humans and intermediate snail hosts give rise to highly focal schistosome

transmission patterns. To approximate these complex interactions, empirical studies have typically used proxy measures such as self-reported water contact for exposure and snail abundance or infectivity for environmental risk to predict infection outcomes. Yet, it has been difficult to empirically capture and validate which proxy variables are relevant for infection. Here, we demonstrate how granular human water contact data from wearable GPS loggers, combined with site-level snail data and remote sensing indicators, can be used to identify relevant drivers of *Schistosoma mansoni* infection at fine spatial scales. To achieve this, we draw upon a subsample of 450 participants from the SchistoTrack Cohort in Eastern and Western Uganda. All participants wore wearable GPS loggers for ten days. Using geolocated data on 144 water sites mapped by the field study team as well as remote sensing data on waterbodies, we derive water contact measures from GPS data and construct site-level and individual-level water contact networks (i.e., bipartite networks connecting all sites that are visited by the same individuals). We then use simple metrics such as degree centrality to identify key sites and individuals within these water site networks. By repeating the network construction, but instead of considering all water sites using only water sites with snails, sites with infected snails, and sites with observed faecal contamination, we describe how the topology of water contact networks that incorporate environmental risk differs from networks without consideration of environmental risk. Using the individual-level water contact networks, we apply network regression techniques to predict either infection status or one-year reinfection as the outcome. Our results identify key drivers of local infection patterns and clarify the relevance of human behavioral versus environmental drivers for explaining transmission hotspots.

8407

ACCEPTABILITY AND FEASIBILITY OF A ONE-STOP HOME-BASED GENITAL SELF-SAMPLING FOR FEMALE GENITAL SCHISTOSOMIASIS, HUMAN PAPILLOMA VIRUS AND TRICHOMONAS AND HIV SELF-TESTING: BASELINE DATA FROM A LONGITUDINAL COHORT STUDY IN ZAMBIA

Rhoda Ndubani[1], Kwame Shanaube[1], Olimpia Lamberti[2], Nkatya Kasese[1], Jennifer Fitzpatrick[1], Maina Cheeba[1], Beatrice Nyondo[1], Bronwyn Neufeld[2], Barry Kosloff[3], Bonnie Webster[4], Helen Kelly[2], Amaya L. Bustinduy[2]

[1]Zambart, Lusaka, Zambia, [2]London School of Hygiene and Tropical Medicine, London, United Kingdom, [3]Longhorn Vaccines and Diagnostics LLC, Bethesda, MD, United States, [4]Natural History Museum, London, United Kingdom

Female genital schistosomiasis (FGS) is a gynecological complication of *Schistosoma haematobium* infection affecting millions of women in sub-Saharan Africa. FGS is associated with sexual dysfunction, reproductive tract morbidity and increase prevalence of HIV and cervical precancer lesions. Diagnosis is poor, but studies have shown acceptability of genital self-sampling, for STI, FGS and HPV. We aim to determine the acceptability and feasibility of a multi-pathogen genital self-sampling method in a large cohort in Zambia. The Zipime Weka Schista study is a longitudinal cohort (2021- 2025) integrating home-based genital self-sampling for *S. haematobium* and HPV and self-testing for HIV and *Trichomonas vaginalis* (Tv) in three communities in Zambia. Sexually active women aged 15-50 years were randomly selected by community health workers. During a home visit two cervicovaginal self-swabs and a urine sample were obtained and HIV and Tv self-test were provided. Information was collected on the acceptability and feasibility of the methods for multi-pathogen genital self-sampling. From January 2022 to March 2023, 2,531 (93.7%) were enrolled. A total of 2,389 (94.3%) had self-swabs for Tv and 1,404 (55.4%) self-tested for HIV. High acceptability was found for the home self-administered procedures (2,208/2531; 87.2%). Women preferred to be seen at home than in clinic. Some reasons stated were convenience (n=1585 (71.8%)); more privacy at home (n=1215 (55.0%)); inconvenience of going to the clinic (n=264 (12.0%)); lack of transport to go to the clinic (n=208 (9.4%)); unavailability due to work commitments (n=118 (5.3%)) and lack of childcare options, (n=69 (3.1%)). A home-based multi-pathogen self-sampling and testing approach is highly acceptable and feasible in three communities in Zambia and has a high potential to increase access to diagnosis of HIV and other genital infections in women of childbearing age. This strategy shows promise as an evidence-based novel approach which could be scaled up both in Zambia and other similar contextual settings.

8408

SCHISTOSOMA MANSONI AND *HELICOBACTER PYLORI* CO-INFECTIONS AMONG SCHOOL-AGED POPULATIONS: A STUDY IN NIGERIAN COMMUNITIES

Babatunde Adewale[1], Muinah Fowora[1], Hammed Mogaji[1], Omolola Omolopo[1], Nurudeen Rahman[1], Ayorinde James[1], Herbert De'Broski[2]

[1]Nigerian Institute of Medical Research, Lagos, Nigeria, [2]University of Pennsylvania, Philadelphia, PA, United States

Helicobacter pylori is strongly associated with stomach ulcers, and gastric cancer. There are established evidence of altered pathology among persons co-infected with *Schistosoma mansoni*, a water borne trematode infection that also colonizes the intestine. For the correct clinical management of *H. pylori* disease, obtaining thorough information on the other concurrent infections is essential. Information regarding the prevalence of co-infections and associated risk factors among coinfected persons are lacking but emerging in Nigeria. This study therefore reports the epidemiological findings from school-aged population across five study communities around Kainji lake in Nigeria using the PCR technique. Of the 299 participants, an overall prevalence of 19.7% was recorded for *H. pylori*, and 34.4% for *S. mansoni*, while co-infection of both was *7.0%.* Infections were significantly different across the study communities for *S. mansoni* ($p<0.05$) when compared to *H. pylori* ($p > 0.38$). There were however no significant association between infection and gender ($p > 0.05$), with the following odd of infection for *S. mansoni* (OR=0.69 (95% CI: 0.42, 1.12)), *H. pylori* (OR=1.33 (95% CI: 0.75, 2.36)), and combination of both infection (OR=1.31 (95% CI: 0.83, 2.09)). By age category, children below 14years were twice likely to be exposed to the combination of both infections; age 12-14 years ((OR=1.9 (95% CI: 1.06, 3.44)), and age 9-11 years ((OR=1.96 (95% CI: 1.11, 3.48)). But they were also less likely to be exposed to *S. mansoni*; age 12-14 years ((OR=0.52 (95% CI: 0.27, 0.97)), and age 9-11 years ((OR=0.43 (95% CI: 0.23, 0.79)). These findings highlight about 7% of the studied population are co-infected with both pathogens, and majority were only with *S. mansoni* infection. Complementary interventions alongside treatment campaigns for *S. mansoni*, may be necessary to address *H. pylori* co-morbidity.

8409

MAIN RESULTS FROM A PHASE II RANDOMISED PLACEBO-CONTROLLED TRIAL OF PRAZIQUANTEL IN PRESCHOOL CHILDREN WITH INTESTINAL SCHISTOSOMIASIS

Amaya Lopez Bustinduy[1], Andrew Edielu[2], Gloria Kakoba[2], Jacent Nassuuna[2], Racheal Nakyesige[2], Victor Anguajibi[2], Simon Mpooya[2], Moses Adriko[3], Govert Van Damm[4], Paul Corstjens[4], Sophie Pach[1], Hannah Wu[5], Susannah Colt[5], Patrice Mawa[2], Edridah Muheki[3], Narcis Kabatereine[3], Emily Webb[1], Jennifer F. Friedman[5]

[1]London School of Hygiene &Tropical Medicine, London, United Kingdom, [2]MRC-LSHTM Research Unit, Entebbe, Uganda, [3]Vector Control Division, Kampala, Uganda, [4]Leiden University Medical Centre, Leiden, Netherlands, [5]Rhode Island Hospital, Providence, RI, United States

Praziquantel (PZQ) is an effective drug against the parasitic disease schistosomiasis, delivered annually through control programs. However, the optimal dose for parasitic cure in preschool age children is not known. We conducted a Phase II randomized placebo-controlled trial in Uganda, testing PZQ at single standard (40 mg/kg) versus repeated standard dosing (80 mg/kg delivered as two doses of 40 mg/kg three hours apart) at baseline and same or placebo at six months, in children 12-47 months infected with the parasite *Schistosoma mansoni.* Co-primary outcomes were parasitological cure and egg reduction rate at 4 weeks. Secondary outcomes included antigenic cure at 4 weeks, adverse

events, toxicity 12 h post-treatment, morbidity and nutritional outcomes, biomarkers of inflammation and enteropathy at 6 and 12 months and PZQ pharmacokinetic/dynamic parameters. A total of 354 children (median age 36 months, 49% female) were randomised (1:1:1:1). For the primary outcomes, cure rates were 90% and 67% in the 80 mg/kg and 40 mg/kg groups, respectively (absolute difference 23%, 95% CI: 14-31%, p<0.001). Egg reduction rates were higher in the 80 mg/kg versus 40 mg/kg/ group (absolute difference 2% (1-3%), p<0.001) and 22% (5-59%, p<0.001) respectively). There were no differences in adverse events or toxicity comparing the two doses. At 12 months, no difference was found in anemia or nutritional status by PZQ dose arm. A repeated 40 mg/kg dose 3 hours apart is safe and significantly more effective in achieving parasitic cure than the current proposed single 40 mg/kg dose and can be recommended for young children living in *S.mansoni* endemic areas.

8410

THE USE OF WATER EDNA IN SNAIL IDENTIFICATION FOR THE UNDERSTANDING OF *FASCIOLA* ENVIRONMENTAL BURDEN AND SNAIL DIVERSITY IN THE HIGHLANDS OF PERU

Melinda B. Tanabe[1], Martha Vanessa Fernandez-Baca[2], Rodrigo A. Ore Velarde[2], Alejandro Castellanos-Gonzalez[1], Miguel M. Cabada[1], Fasciola Peru TMRC Research Group --[3]

[1]UTMB, Galveston, TX, United States, [2]UPCH – UTMB Collaborative Research Center - Cusco, Universidad Peruana Cayetano, Cusco, Peru, [3]

Fascioliasis is a snail borne infection of the *Lymnaeidae* family. The impact of the interplays between snail species on *Fasciola* transmission has not been studied. We aimed to evaluate the seasonal variations of snail abundance and species diversity in highly endemic regions of Peru and their association with the burden of *Fasciola* in the environment using eDNA analysis of water sources. We developed a real time single and multiplex PCR tests targeting mitochondrial and nucleic genes to differentiate snails to the genus and species levels. We focused on genera level identification of aquatic snails known to occur in Peru (*Lymnaea, Biomphalaria*, and *Physa*). Species level identification and phylogenetic analysis were performed for snails of the *Lymnaeidae* family. We tested water and extracted eDNA from water samples collected every 3 months during 12 months. The association of snail abundance and diversity with the variations in quantitative *Fasciola* eDNA in environmental waters will be evaluated accounting for spatial and temporal distributions. The relationship between snail abundance and diversity with livestock fascioliasis incidence will be explored. Statistical analysis will be done for clustering by province and community subdivisions and adjusting for water quality and weather conditions throughout the year. We collected 558 water samples corresponding to 304 households, 15.6% (n=87) had snails, and of those 12.6% (n=11) tested positive for *Fasciola*. Our results determined a good reliability of eDNA for identification of snail genera and *Lymnea* subspecies as compared to PCR as the gold standard. This innovative approach will increase our understanding of snail host factors associated with infection. We hope to validate these findings in a larger sample for its ultimate use as a surveillance tool in areas of increased transmission for environmentally sound snail control.

8411

INFLAMMATION-ADJUSTED VITAMIN A DEFICIENCY IS ASSOCIATED WITH HEAVY *SCHISTOSOMA MANSONI* INFECTION INTENSITY AMONG PRESCHOOL-AGED CHILDREN IN UGANDA

Susannah Colt[1], Hannah W. Wu[1], Andrew Edielu[2], Emily L. Webb[3], Racheal Nakyesige[4], Patrice A. Mawa[2], Christopher P. Duggan[5], Jonathan D. Kurtis[6], Amaya L. Bustinduy[3], Jennifer F. Friedman[1]

[1]Rhode Island Hospital, Providence, RI, United States, [2]London School of Hygiene and Tropical Medicine Uganda Research Unit, Entebbe, Uganda, [3]London School of Hygiene and Tropical Medicine, London, United Kingdom, [4]Uganda Virus Research Institute, Entebbe, Uganda, [5]Boston Children's Hospital, Boston, MA, United States, [6]Warren Alpert Medical School of Brown University, Providence, RI, United States

Vitamin A deficiency impairs immune function against parasitic pathogens. In rodents, dietary-induced vitamin A deficiency causes higher schistosome burden, higher mortality, and a reduced immune response compared to animals who are vitamin A replete. This cross-sectional analysis examines pre-treatment relationships between inflammation-adjusted vitamin A status, *S. mansoni* burden, and a panel of immunologic markers among preschool-aged children (PSAC) enrolled to the praziquantel in preschoolers (PIP) trial. PSAC age 12-47 months with *S. mansoni* infection, diagnosed by Kato Katz eggs per gram of stool (EPG), were enrolled from the Lake Albert region in Uganda. The Thurnham Correction Factor inflammation-adjustment method was applied to measures of retinol-binding protein (RBP). Vitamin A deficiency was defined as adjusted RBP ≤0.7 µmol/L. Multivariate polytomous logistic regression and linear regression were applied for outcomes of categorical infection burden and continuous immunologic markers, respectively. A bivariate threshold of p<0.1 was used to select covariates and considered age, sex, socio-economic status, and coinfections of hookworm, malaria, and HIV for inclusion in models. In 339 PSAC, 36.0% were vitamin A deficient and the distribution of *S. mansoni* burden was 56.6% light (1-99 EPG), 24.2% moderate (100-399 EPG), and 19.2% heavy (≥400 EPG). Vitamin A deficiency was associated with a higher odds of heavy *S. mansoni* intensity compared to light intensity after adjusting for age (OR 1.96, 95% CI 1.07-3.56, p=0.03). We did not find significant associations between vitamin A deficiency and any of the measured immunologic markers in fully adjusted regression models. The associations between vitamin A status and infection burden agree with findings reported from animal studies, representing an important translational advance for our understanding of vitamin A metabolism. Future research is needed to determine if nutritional interventions improving vitamin A status in combination with preventive chemotherapy for schistosomiasis reduces morbidity for PSAC living in endemic areas.

8412

ASSOCIATION OF *SCHISTOSOMA HAEMATOBIUM* INFECTION WITH PREGNANCY IN TANZANIA

Sheridan Bowers[1], Jane K. Maganga[2], Loyce Mhango[2], Peter Shigella[2], Crispin Mukerebe[2], Humphrey D. Mazigo[3], Govert J. van Dam[4], Danielle de Jong[5], Paul L. Corstjens[5], Saidi H. Kapiga[2], W. Evan Secor[6], Myung Hee Lee[7], Jennifer A. Downs[7], John M. Changalucha[2]

[1]Weill Cornell Medicine, New York, NY, United States, [2]Mwanza Intervention Trials Unit/National Institute for Medical Research, Mwanza, Tanzania, United Republic of, [3]Department of Parasitology, Catholic University of Health and Allied Sciences, Mwanza, Tanzania, United Republic of, [4]Department of Parasitology, Leiden University Medical Center, Leiden, Netherlands, [5]Department of Cell and Chemical Biology, Leiden University Medical Center, Leiden, Netherlands, [6]Division of Parasitic Diseases for Malaria, Center for Global Health, Centers for Disease Control and Prevention, Atlanta, GA, United States, [7]Center for Global Health, Weill Cornell Medicine, New York, NY, United States

Forty million girls and women in Africa suffer from female genital schistosomiasis (FGS) caused mainly by *Schistosoma haematobium* (*Sh)*. Parasitic worms that reside in urogenital venules lay eggs that migrate through mucosal tissue, causing bleeding, pain, genital discharge, and possible infertility. Associations of active *Sh* infection with confirmed pregnancy have not been investigated.

Women of reproductive age living in a community in northwest Tanzania highly endemic for *Sh* infection were screened for enrollment into a cohort study beginning in May 2021. All participants had serum schistosome circulating anodic antigen (CAA) and urine pregnancy tested. A CAA value ≥30 pg/mL was considered positive. The non-pregnant women were enrolled and had up to six follow-up visits over the ensuing 12 months, with CAA and pregnancy tested at every visit. Participants received praziquantel if the CAA value was positive. Through March 6th, 2024, 585 participants have been screened. Of those screened, 260 (44.4%) were CAA positive

at baseline and 78 (13.3%) were either pregnant at baseline or became pregnant during follow-up. Younger age, being married, and a negative CAA were all positively associated with pregnancy. The odds of pregnancy for a woman who was CAA positive, after controlling for age and marital status, was 0.54 (95% confidence interval: [0.32-0.90]; P = 0.018). In 206 enrolled women who attended at least one follow-up visit 50 (24.2%) became pregnant. The odds of becoming pregnant among those who were CAA positive during at least one follow-up visit, after controlling for age, marriage, reported infertility, and abnormal discharge was 0.82 ([0.39-1.74]; P = 0.60). This study demonstrates that women with *Sh* infection were approximately half as likely to be or become pregnant as those without *Sh* infection. For women in the cohort for whom additional data were available, a lower risk of pregnancy in those with *Sh* infection appeared to persist when controlling for sociodemographic and clinical factors. Efforts to determine reasons underlying lower fertility in *Sh* infection, and whether it is reversible after treatment, are urgently needed.

8413

PREPARING FOR VACCINE ADVERSE EVENTS OF SPECIAL INTEREST-X (AESI-X): A STANDARDIZED APPROACH APPLIED TO NOVEL VACCINES

Eileen C. Farnon[1], *Barbara J. Law*[1], *Dale Nordenberg*[1], *Andy Stergachis*[1], *Rebecca E. Chandler*[2], *Robert T. Chen*[1], *Brighton Collaboration SPEAC AESI-X Working Group*[1]
[1]*Safety Platform for Emergency vACcines (SPEAC) Project, Brighton Collaboration, Decatur, GA, United States,* [2]*Coalition for Epidemic Preparedness Innovations, Oslo, Norway*

The Coalition for Epidemic Preparedness Innovations (CEPI) aims to make novel vaccines available within 100 days of a pandemic. To ensure preparedness for novel "adverse events of special interest-X" ("AESI-X") associated with these new vaccines, the Brighton Collaboration (BC) SPEAC Project creates tools to facilitate standardized safety assessments, including case definitions (CD). Real-time harmonization of CD created during the emergence of AESI-X can be challenging, as seen in the response to AESIs associated with COVID-19 vaccines. The ensuing heterogeneity among CDs results in lack of comparability across vaccine safety surveillance systems. SPEAC is facilitating a consensus AESI-X CD Preparedness Plan among key vaccine safety stakeholders to develop standardized CDs for AESI-X early in the response. We identified three categories of AESI-X: 1) Known-known (a recognized syndrome associated with a vaccine); 2) Known-unknown (a recognized syndrome not known to be associated with a vaccine); 3) Unknown-unknown (a novel or variant syndrome not previously associated with a vaccine). We created a checklist for CD preparation and introduced this concept in an initial meeting with a small group of vaccine safety stakeholders in regulatory agencies and health authorities in February 2024. We then convened stakeholders in several meetings to draft the AESI-X CD Preparedness Plan, consisting of the following steps: 1) Signal detection and confirmation; 2) CD Working Group formation; 3) Rapid reviews of draft CD; 4) Implementation of AESI-X CD in surveillance and studies; 5) Revise and update CD during the response; 6) Assess lessons learned from the response; 7) Update the AESI-X CD Preparedness Plan as needed. A key part of the plan is routine outreach to countries introducing new vaccines offering the availability of BC CD assistance should they encounter an AESI-X. Developing this consensus process ahead of the next AESI-X will facilitate the implementation and assessment of novel vaccines for priority pathogens and other targets, by anticipating and responding to AESI-X associated with these vaccines using harmonized CDs.

8414

ENHANCING ACCESS TO HIGHLY MULTIPLEXED DIAGNOSTICS IN LMICS: LEVERAGING OXFORD NANOPORE SEQUENCING FOR DETECTION OF RESPIRATORY VIRUSES AND EMERGING PATHOGENS

Polly S. X. Yap[1], Ryan C. Chapman[2], Nathaniel Christy[3], Sharifah Syed Hassan[1], Chin Fang Ngim[1], Lian Yih Pong[1], Jessica D. Wiley[4], Robert D. Hontz[3], Anca Selariu[3], Amreeta Dhanoa[1], Wan Fadhilah Wan Ismail[5], Andrew G. Letizia[3], Michael R. Wiley[2]
[1]*Monash University Malaysia, Subang Jaya, Malaysia,* [2]*University of Nebraska Medical Center, Omaha, NE, United States,* [3]*United States Naval Medical Research Unit- INDO PACIFIC, Singapore, Singapore,* [4]*PraesensBio LLC, Omaha, NE, United States,* [5]*Mahmoodiah Health Clinic, Johor Bahru, Malaysia*

Rapid diagnostic tests and conventional molecular testing are crucial for efficiently diagnosing diseases like dengue and SARS-CoV-2. However, these tests are often pathogen-specific and have limited ability to be multiplex. Sequencing can be used to detect and characterize a wide range of pathogens, but the availability of sequencing capabilities are often limited in low- and middle-income countries (LMICs) due to costs and/or a lack of trained personnel. The purpose of this study was to demonstrate the ability to deploy a hybrid-capture sequencing approach, adapted to Oxford Nanopore sequencing technology (ONT), for enhancing the detection of viral respiratory pathogens from a community health clinic in Johor Bahru, Malaysia. We screened 167 patients for acute respiratory infection by collecting nasopharyngeal swabs during 2023, from March to June, the hottest months, and from November to December, the seasonal flu period. In 63% of the patient samples, we detected viral sequences using the Twist Comprehensive Viral Research Panel which were confirmed with pathogen specific qRT-PCR assays. We identified viruses including SARS-CoV-2, rhinovirus, respiratory syncytial virus (RSV), influenza A/B virus (FluA/B), and an unexpected Dengue virus. By using our approach, we were able to characterize the detected viruses, revealing the predominance of JN.1 and XBB.1.9.1 (as of December 2023), which are likely linked to commutes between Singapore and Malaysia. Through international collaborations prioritizing locally-driven, capacity-building-focused development, our study enhances effective skills transfer, amplifies research impact, and aids in promptly containing emerging pathogens in South East Asia, a hotspot for outbreaks. Our hybrid-capture based ONT sequencing method provides timely epidemiological and clinical sequence data for surveillance of emerging viral pathogens in LMICs, offering added insights beyond molecular testing.

8415

INTEGRATED SEROLOGICAL SURVEILLANCE FOR INFECTIOUS DISEASES IN ZAMBEZIA PROVINCE, MOZAMBIQUE USING MULTIPLEX BEAD ASSAYS

Andrea C. Carcelen[1], Celso Monjane[2], Sophie Bérubé[1], Saki Takahashi[1], Thebora Sultane[2], Imelda Chelene[2], Gretchen Cooley[3], Brook Goodhew[3], Catriona Patterson[4], Kevin Tetteh[4], Manuel Mutambe[2], Melissa Higdon[1], George Mwinnyaa[1], Gilberto Nhapure[5], Pedro Duce[5], Diana L. Martin[3], Christopher Drakeley[4], William J. Moss[1], Ivalda Macicame[2]
[1]*Johns Hopkins University, Baltimore, MD, United States,* [2]*Instituto Nacional de Saude, Maputo, Mozambique,* [3]*Centers for Disease Control and Prevention, Atlanta, GA, United States,* [4]*London School of Hygeine and Tropical Medicine, London, United Kingdom,* [5]*Instituto Nacional de Estadistica, Maputo, Mozambique*

Multiplex immunoassays allow simultaneous measurement of antibodies to multiple antigens, potentially saving time and resources, and providing data on neglected diseases that have limited funding. They also open opportunities to examine cross-pathogen vulnerabilities in populations. We incorporated a multiplexed serosurvey for vaccine preventable diseases (VPDs), malaria, neglected tropical diseases (NTDs), and enteric pathogens as part of a Countrywide Mortality Surveillance for Action (COMSA) in Zambezia Province, Mozambique. From December 2020 to March 2021,

30 clusters in Zambezia were visited, during which dried blood spots were collected from individuals aged between 6 months to 49 years. Specimens were tested for IgG antibodies to 35 antigens from 18 pathogens using a multiplex bead assay. Weighted seroprevalence estimates by age and cluster and seroprevalence curves by age were produced. The odds of seropositivity by cluster were compared using Bayesian logistic random effects models and individual level associations were identified using multiple logistic regression. Seroprevalence ranged widely across antigens by age, sex and area of residence. Low seroprevalence (67%) to measles highlights the need for increased immunization. High seroprevalence to *Plasmodium falciparum* long-term antigen ama-1 increased from 79% in children under 5 years of age to 92% in adults demonstrating very high transmission. Rural clusters had higher odds of seropositivity for most NTDs, *Plasmodium falciparum*, and enteric pathogens but lower odds of seropositivity to SARS-CoV-2 and VPDs compared to urban clusters. At the individual level, seropositivity to an antigen was strongly associated with seropositivity to other antigens in the same disease category (enteric, malaria, NTDs and VPDs). Heterogeneities in seroprevalence identified across pathogens, age, sex, and space can inform subnational risk assessments. Understanding the co-endemicity of diseases allows for integrated strategies to target interventions to the most vulnerable communities.

8416

A SEPSIS SYNOPSIS: HETEROGENEITY OF SEPSIS PRESENTATIONS ACROSS THE ACESO NETWORK

Alyse Wheelock[1], Melissa Bradshaw[1], George Oduro[2], Hannah Kibuuka[3], Stephen Okello[3], Andrew Kambugu[4], Te Vantha[5], Nehkonti Adams[6], Subramaniam Krishnan[1], Patrick Blair[1], Joshua Chenoweth[1], Deborah Striegel[1], Qianru Wu[1], Carlyle Gollogly[7], Kristen Pettrone[1], Danielle Clark[1]

[1]ACESO, the Henry Jackson Foundation, Bethesda, MD, United States, [2]Komfo Anokye Teaching Hospital, Kumasi, Ghana, [3]Makerere University Walter Reed Project, Kampala, Uganda, [4]Infectious Diseases Institute, Kampala, Uganda, [5]Takeo Provincial Hospital, Takeo, Cambodia, [6]Naval Medical Research Command, Falls Church, VA, United States, [7]ACESO, Henry Jackson Foundation, Bethesda, MD, United States

Although most deaths due to sepsis occur in low-and-middle income countries, data regarding affected populations, pathogens, management, and outcomes remain sparse in these regions. The Austere Environments Consortium for Enhanced Sepsis Outcomes (ACESO) was established to improve outcomes of sepsis in low-resource settings through advancing knowledge and developing novel diagnostics and interventions. The ACESO prospective observational sepsis study has operated sites in Takeo Province, Cambodia, Kumasi, Ghana, Fort Portal, Uganda, Antananarivo, Madagascar, and Bong County, Liberia, with planned enrollment in Iquitos, Peru. Consenting participants with suspected infection and meeting at least two SIRS criteria are followed longitudinally, with subjective and objective data collected at standardized timepoints. Here, we report descriptive statistics of key epidemiologic features of the three largest sites within the cohort. A total of 1,974 participants have been enrolled from Cambodia (N=728, since May 2014), Ghana (N=623, since July 2016), and Uganda (N=623 since October 2017). The majority were male (1,035/1,974, 52%) and had a median age of 48 (IQR 28). HIV prevalence based on prior known history ranged from 6/728 (1%) in Cambodia to 171/623 (27%) in Uganda. Across all sites, pneumonia was reported most frequently as the likely source of sepsis (n=534), followed by genito-urinary (n=165) and intra-abdominal sources (n=137). The most frequently identified pathogenic organisms isolated from baseline blood cultures varied widely across sites, from *Burkholderia pseudomallei* (n=42) in Cambodia, *Staphylococcus aureus* in Ghana (n=25), and *Streptococci* spp. in Uganda (n=10); *Salmonella* spp. were isolated across all sites (n=42). Malaria rapid diagnostic positivity ranged from 3% in Cambodia to 21% in Uganda. Inpatient mortality was 15/728 (2%) in Cambodia, 23/623 (4%) in Uganda, and 160/623 (26%) in Ghana. This analysis emphasizes the heterogeneity of sepsis presentations across low-resource settings, underscoring the critical need to include individuals living in these settings within the field of sepsis research.

8417

SEPSIS-RELATED DEATHS AMONG CHILDREN BELOW FIVE YEARS OF AGE ENROLLED IN THE CHILD HEALTH AND MORTALITY PREVENTION SURVEILLANCE (CHAMPS) NETWORK PROGRAM IN SUB-SAHARAN AFRICA AND SOUTH ASIA BETWEEN 2017 - 2022

Harun Owuor[1], Kyu Hun Lee[2], Emily S. Gurley[3], Shams El Arifeen[4], Portia C. Mutevedzi[2], Cynthia G. Whitney[2], Jeannette Wadula[5], Mohammad Zahid Hossain[4], Inacio Mandomando[6], Nega Assefa[7], Soter Ameh[8], Ikechukwu Ogbuanu[8], Dickens Dickens Onyango[9], Joyce Akinyi Were[1], Kotloff Karen[10], Shabir madhi[5], Rosauro Varo[6], Ziyaad Dangor[5], Victor Akelo[11]

[1]KEMRI CGHR, Kisumu, Kenya, [2]Emory University, Atlanta, GA, United States, [3]John Hopkins University, Baltimore, MD, United States, [4]International Centre for Diarrheal Disease Research, Bangladesh (icddr,b),, Dhaka, Bangladesh, [5]University of the Witwatersrand, Johannesburg, South Africa, [6]Centro de Investigacao en Saude de Manhica (CISM), Maputo, Mozambique, [7]College of Health and Medical Sciences, Haramaya University,, Harar, Ethiopia, [8]Crown Agents, Freetown, Sierra Leone, [9]Kenya Ministry of Health,, Kisumu, Kenya, [10]University of Maryland School of Medicine, Baltimore, MD, United States, [11]Liverpool School of Tropical Medicine, London, United Kingdom

Despite treatment advances, sepsis remains the third leading cause of death (COD) in under-5s globally. Understanding the pathogen-specific causes of sepsis has proven challenging in developing countries, where sepsis-related deaths are often diagnosed clinically or are missing from official statistics when they occur in the community. Child Health and Mortality Prevention Surveillance (CHAMPS) is a multi-country surveillance program that systematically identifies causes of under-5 mortality from defined catchment areas in seven countries in sub-Saharan Africa and South Asia. Here, we analyzed the contribution of sepsis-related deaths and pathogen-specific causes of sepsis in children <5 years enrolled in the CHAMPS Network. CODs were determined by a panel of experts using data from post-mortem investigations conducted using minimally invasive tissue specimen testing, clinical records, and verbal autopsy. Between July 2017 to January 2024, a total of 3834 children <5 years had their COD determined. Nearly a third of cases 1391(36%) had sepsis in the causal chain leading to death. Sepsis was the most common COD among late neonates (71%) and early infants (46%), with Ethiopia (60%) and South Africa (50%) having a higher proportion of sepsis-attributed deaths. *Klebsiella pneumoniae* was the predominant cause of sepsis across all age groups. In neonates, *K. pneumoniae* (48%), *Acinetobacter baumanni* (34%) and *Escherichia coli* (14%) were the most common causes, whereas, in infants and children >1 year, *K. pneumoniae* (43%), *E. coli* (17%) and *Streptococcus pneumoniae* (18%) were the most common pathogens causing sepsis. Neonatal preterm birth complications and perinatal birth asphyxia were predominant underlying conditions in neonates while malnutrition, HIV infections, and respiratory tract infections were the most common underlying conditions in late infants and children >I year. Sepsis contributed to high mortality among CHAMPS cases in LMICs, with *K. pneumoniae* predominant cause across different age groups. This highlights the need to review empirical management guidelines for the prevention and management of sepsis cases.

8418

RICKETTSIOSIS AND SCRUB TYPHUS AMONG HOSPITALIZED PATIENTS WITH ACUTE FEBRILE ILLNESS IN RURAL NORTHEASTERN AND NORTH BORDER PROVINCES OF THAILAND, 2017-2020

Adelaide F. Green[1], Saithip Bhengsri[2], Betsy Cadwell[1], Emily Bloss[2], Nuttagarn Chuenchom[3], Supphachoke Khemla[4], Sumonmal Uttayamakul[5], Pongpun Sawatwong[2], Ornuma Sangwichian[2], Duangkamon Siludjai[2], Phanthaneeya Teepruksa[2], Beth Skaggs[2], Cecilia Y. Kato[1], Christopher J. Gregory[2], John R. Macarthur[2], James D. Heffelfinger[2], Carol Y. Rao[1]

[1]Centers for Disease Control and Prevention, Atlanta, GA, United States, [2]Centers for Disease Control and Prevention - Thailand, Nonthaburi, Thailand, [3]Mae Sot Hospital, Nakhon Phanom, Thailand, [4]Nakhon Phanom hospital, Nakhon Phanom, Thailand, [5]Bamrasnaradura Infectious Diseases Institute, Department of Disease Control, Ministry of Public Health and National Institute of Health, Department of Medical Sciences, Ministry of Public Health, Nonthaburi, Thailand

Rickettsial disease (RD) and scrub typhus (ST) are acute febrile illnesses (AFI) caused by vector-borne pathogens, *Rickettsia* species and *Orientia tsutsugamushi*, respectively. RD and ST data from 2003-2018 suggest geographic and demographic differences in Thailand. We tested RD and ST among AFI patients in the northern province of Tak, bordering Myanmar, and the northeastern province of Nakhon Phanom (NP), bordering Laos. We enrolled patients aged 2 to 80 years with documented fever ≥38.0°C or reported fever lasting ≤7 days upon admission, who were admitted to 12 hospitals in Tak and NP Provinces during April 2017-May 2020. We collected data on demographics, clinical manifestations, and proxy exposures to vectors. Blood specimens were tested for pan-Rickettsia spp. and *O. tsutsugamushi* by real-time PCR. To estimate prevalence, we weighted the sample to adjust for incomplete testing. We calculated risk ratios and 95% confidence intervals for potential risk factors for RD and ST. Of the 11,275 patients enrolled, 4,470 (39.6%) were tested for RD and ST pathogens. Prevalence estimates of RD were 1.2% (95%CI: 0.5-1.8) in Tak and 1.9% (95%CI: 1.3-2.5) in NP; for ST, they were 2.6% (95%CI: 1.6-3.5) in Tak and 0.06% (95%CI: 0.001-0.1) in NP. Of 149 patients PCR-positive for either RD (94) or ST (55), 56% were female. In addition to fever, common manifestations of RD and ST were fatigue (88.4%), headache (85.3%) and chills (75.3%). Patients who visited a forest within the past month had 9.3 times the risk of being ST PCR-positive (95%CI 4.4-19.6), and those with stray animal contact within the past month had 2.3 times the risk of being RD PCR-positive (95%CI 1.1-4.5), than those who did not. Patients presenting with AFI and reporting proxy vector exposures within the past month should be evaluated for vector-borne illnesses. Although the percentage of AFI attributable to RD or ST is relatively low, ST was more prevalent in Tak province. The provincial differences in prevalence could inform regional vector-borne disease control and prevention efforts.

8419

MICROSTRATIFICATION OF VISCERAL LEISHMANIASIS ENDEMIC AREAS TO IDENTIFY HOTSPOTS AND DISEASE SHIFTING PATTERNS IN NEPAL

Krishna Pant[1], Megha R. Banjara[1], Dharmanand Joshi[1], Govinda R. Paneru[1], Abraham Aseffa[2], Rudra Marasini[3], Gokarna Dahal[3], Anand B. Joshi[1]

[1]Public Health and Infectious Disease Research Center, Kathmandu, Nepal, [2]Special Program for Research and Training in Tropical Diseases, Geneva, Switzerland, [3]Epidemiology and Disease Control Division, Ministry of Health, Kathmandu, Nepal

Micro-stratification, dividing large areas into smaller, homogeneous units, is crucial for understanding and addressing visceral leishmaniasis (VL) risk. In Nepal, where VL poses a significant health challenge, micro-stratification has been limited. This study pioneers micro-stratifying VL risk in Nepal, aiming to comprehend its prevalence and distribution across administrative levels. The objectives were to assess VL risk across administrative levels, provide insights into VL prevalence, and generate detailed risk maps. Data from the Epidemiology and Disease Control Division served as the primary source, analyzed for ward-wise VL burden, vector presence, migration history, and housing characteristics. Questionnaires and checklists aided data collection, with all 77 districts stratified based on VL risk. Entomological surveys conducted by academic and research institutions supplemented vector distribution status in the country. Among Nepal's 6743 wards, initially VL cases were uniformly distributed from east to west; however, high-risk wards progressively clustered in specific districts over time. After 2018 a noticeable shift of high-risk wards occurred towards the western regions, predominantly affecting Karnali and Sudur Paschim provinces. Provincial analyses showed diverse trends: Koshi province reported 27 high-risk wards in 2022, compared with Bagmati province's mere 6 high-risk wards. Moreover, Madhesh province observed a decline in high-risk wards, while Lumbini province emerged as a focal area for VL. Sudurpaschim province exhibited a consistent upward path in high-risk wards since 2017. To mitigate the impact of VL, targeted interventions are essential. Strengthening healthcare facilities in high and moderate-risk areas is vital to ensuring prompt diagnosis and effective case management. Implementation of active surveillance measures is essential for timely detection and response to any surge in VL cases. Intensifying indoor residual spraying campaigns in VL risk areas, coupled with targeted health education initiatives, holds the potential to enhance VL awareness and control.

8420

BANGLADESHI CHILDREN HAVE IMMUNITY TO CRYPTOSPORIDIA-ASSOCIATED DIARRHEA BUT NOT TO INFECTION

Carol A. Gilchrist[1], William A. O. Petri[1], Biplob Hossain[2], Md. Mamun Kabir[2], Hannah H. So[1], G. Brett Moreau[1], Uma Nayak[1], Jennie Z. Ma[1], Zannatun Noor[2], Abu S. G Faruque[2], Md. Masud Alam[2], Rashidul Haque[2], William A. Petri[1]

[1]University of Virginia, Charlottesville, VA, United States, [2]icddrb, Dhaka, Bangladesh

Cryptosporidium is one of the top causes of diarrhea in Bangladeshi infants. The current paradigm is that humoral immunity is not important in the development of a protective anti-Cryptosporidium immune response. However, in previous work we have found that antibody responses to the *Cryptosporidium* antigens Cp23 and Cp17 in Bangladeshi infants were associated with a decrease in both the parasite burden and the probability of diarrheal disease in subsequent infections. We have followed the frequency of Cryptosporidium infections in a cohort of Bangladeshi infants living in a community, where exposure to this parasite is common. In line with previous observations, the frequency of diarrheal cryptosporidiosis significantly declined in the repeat infections (Chi-square test for trend; $p < 0.0001$) occurred in the older children. The frequency of diarrheal disease was highest in children living in this community between 1.5 and 2 years of age when there were 0.12 diarrheal episodes per child and thereafter it occurred less frequently falling to 0.01 episodes per child between 3.5-4 years [1278-1461 days]. Sub-clinical disease did not decline in frequency over the same time period (2-4 years of life) and remained at 0.33 ± 0.05 episodes per child in each 6 months (183 days) of life. Seroprevalence of the anti-Cp17 and anti-Cp23 antibodies was common in ≥1 year-olds but a general decline in the levels of anti-Cp17 and Cp23 *Cryptosporidium* antibodies occurred in older children (1-4 years). The impact of this was however offset by an increase in anti-CP17 and anti-Cp23 antibody avidity. Our results are consistent with the development of an adaptive immune response associated with protection from cryptosporidial diarrhea.

8421

MECHANISM OF INTESTINAL BARRIER REPAIR IN GIARDIASIS

Rita Taye Kosile, Vanessa Angelova, Evan Pannkuk, Steven Singer

Georgetown University, Washington, DC, United States

Giardiasis is a common diarrheal disease caused by the protozoan parasite *Giardia duodenalis*. Acute symptoms can include diarrhea, but infections are often subclinical. Disease transmission occurs by ingestion of infectious cysts in contaminated food or water. In developing countries, giardiasis is one of the leading causes of growth stunting in children under two years old. Changes in intestinal barrier integrity have been shown to contribute to impaired nutrient absorption, thereby leading to growth stunting in children. Although intestinal barrier defects have been linked to infection, there is limited understanding of barrier repair dynamics post-infection. Previous studies have demonstrated that *Giardia* infection is associated with dysbiosis in humans and animals. Because Aryl hydrocarbon receptor (AHR) signaling has been shown to promote intestinal repair in other systems, we are exploring the role of AHR in barrier repair following a *Giardia* infection. We quantified specific microbiome-derived AHR ligands in the plasma of infected C57BL/6 mice and observed a reduction of indole-3-ethanol and indole-3-pyruvic acid at 21 days post-infection. Since IL-22 signaling can also promote barrier repair, we quantified IL-22 transcripts by RT-PCR and found significantly increased levels of IL-22 mRNA in infected mice. Animals fed a diet with 20% calories from protein had elevated expression of IL-22 while animals on 2% protein did not. We also observed changes in certain barrier repair markers post-infection. This data suggests that *Giardia* can reduce barrier repair through altering levels of AHR ligands and that IL-22 may contribute to successful repair in mice fed a normal diet. Our current data can give a better understanding of possible dietary interventions to prevent growth restriction in *Giardia*-infected children.

8422

UNWINDING THE IRONY OF SEVERE ANEMIA IN ANTIMONY-RESISTANT *LEISHMANIA DONOVANI* INFECTION AT THE NEXUS OF OXIDATIVE OUTBURST AND IRON PURSUIT

Souradeepa Ghosh, Krishna Vamshi Chigicherla, Budhaditya Mukherjee

Indian Institute of Technology, Kharagpur, Kharagpur, India

Pentavalent antimonials (SbV), the mainstay for treating Visceral leishmaniasis (VL) caused by an intracellular protozoan parasite, *Leishmania donovani* (LD), have been discontinued from the Indian sub-population for decades due to rising antimony-resistance. Despite the withdrawal of SbV, recent clinical LD field isolates showed antimony resistance (LD-R) pointing towards genetic adaptation that underpins its evolutionary persister nature and superiority over drug-sensitive strains (LD-S). The highlight of this study is understanding how LD-R has tackled antimony pressure which is paramount for unveiling the underlying signaling contributing to severe anemia and chronic hepatosplenomegaly resulting from parasite overburden observed in LD-R infection. Strikingly, the common mode of action of both SbV and host-defense-arsenal includes Reactive-oxygen species (ROS) outburst which is successfully exploited by LD-R. To thrive in high ROS, LD-R is equipped with enriched reducing equivalents, also, high ROS boosts iron production, a crucial component that is critically flawed in these parasites since LD are heme-auxotrophs. To interpret the cause of severe anemia in LD-R-infection, we unveiled that LD-R has devised a strategy to produce and rapidly propel host-iron inside parasitophorous-vacuole (PV) of murine macrophages through re-orientation of macrophage surface iron exporter-Ferroportin around PV membrane. Higher iron utilization to support aggressive proliferation of LD-R leads to iron deficiency which is compensated by inflated erythrophagocytosis due to the SIRPα degradation. Cleavage of SIRPα results in loss of discriminatory signal between CD47-enriched live RBCs and CD47-deficient senescent RBCs resulting in aggravated erythrophagocytosis of both live and senescent RBCs. This poses a question of how SIRPα is degraded. Stay tuned for the epilogue of a complex diad of 2 proteases that drive SIRPα cleavage! Taken together, this study provides key insights into the emergence of drug unresponsiveness in LD and related heme-auxotrophic pathogens and offers directions for refining therapeutic strategies.

8423

UNIQUE IMMUNE AND TISSUE REPAIR MARKERS IN CONGENITAL CHAGAS

Sneider Alexander Gutierrez Guarnizo[1], Carolina Duque[1], Jill Hakim[1], Martín Obregón[2], Jessi Condori[2], Paloma Samame[3], Emily Arteaga[3], Clariza Roxana[3], Jean Karla Velarde[3], Edith Malaga[2], Andrea Diestra[2], Alejandra Pando[2], Manuela Verastegui[2], Monica Pajuelo[2], Maritza Calderon[2], Freddy Tinajeros[3], Natalie Bowman[4], Robert Gilman[1], Monica Mugnier[1]

[1]Johns Hopkins University, Baltimore, MD, United States, [2]Universidad Peruana Cayetano Heredia, Lima, Peru, [3]Hospital de La Mujer Dr. Percy Boland Rodriguez, Santa Cruz, Bolivia, Plurinational State of, [4]University of North Carolina at Chapel Hill School of Medicine, Chapel Hill, NC, United States

It remains unclear why 5% of Chagas-infected mothers transmit *Trypanosoma cruzi* to their baby (Transmitter). No molecular biomarkers are available to predict transmission risk, and the understanding of this pathogenesis is hindered by limited analyses of human-derived placenta tissue analysis. Understanding the molecular mechanisms associated with T. cruzi transmission is essential for the proper management of congenital Chagas.Here, we analyze the transcriptome of placenta tissue and peripheral blood that were collected upon delivery to detect local and systemic RNA expression changes, respectively. Differentially expressed genes (DEG) between transmitter and non-transmitter were identified using a cutoff of adjusted p-value ≤ 0.05 and absolute fold change ≥ 1.5. Placenta tissue analysis revealed a total of 298 DEG (64 decreased, 234 increased). A gene set enrichment analysis (GSEA) showed that several processes such as immune receptor activity, cellular response to IFN-γ, response to other organisms, and IgG immunoglobulin complex were implicated, probably suggesting an increased localized inflammatory response in transmitting mothers. In the peripheral blood, no DEGs were detected, but a GSEA analysis highlighted that transmission was significantly associated with distinct pathways, including increased T-cell receptor signaling and humoral immune response, higher endopeptidase activity, and decreased collagen-related protein and extracellular matrix remodeling. We highlight upstream regulators and central gene modulators that could inform the risk of transmission. Our analysis suggests that transmitting mothers exhibit unique gene expression patterns indicative of tissue damage, remodeling, and an increased inflammatory response to the parasite. We suggest that peripheral blood could be valuable for assessing congenital Chagas transmission risk. Further studies analyzing blood samples during pregnancy may be suited to validate gene-level biomarkers.

8424

CO-DELIVERY OF IL-12 AND LEISHMANIA PEPCK AS A VACCINATION STRATEGY TO INCREASE EXPRESSION OF SKIN HOMING MOLECULES AND RESIDENT MEMORY T CELL DEVELOPMENT

Anabel Zabala-Peñafiel[1], Claudia Gonzalez-Lombana[1], Anthony Phan[1], Jude Uzonna[2], Chris Hunter[1], Phil Scott[1]

[1]University of Pennsylvania, Philadelphia, PA, United States, [2]University of Manitoba, Winnipeg, MB, Canada

Cutaneous leishmaniasis is a neglected tropical disease associated with a wide spectrum of clinical presentations which are often difficult to treat. Currently, there are no vaccines for human leishmaniasis which is likely due to the inability to generate long-lived memory T cells. However, we found that *Leishmania major* infection in mice generated long-lived CD4+ dermal resident memory T cells (dTrm) and that these dTrm provide protection against rechallenge. Furthermore, we found that subcutaneous immunization with a leishmania-conserved antigen, phosphoenolpyruvate

carboxykinase (PEPCK), generated long-lived dTrm cells. Importantly, this vaccine not only induced dTrm cells that were present at the immunized (inflamed) site but were also globally seeded in the skin. However, the level of protection was not at the level induced by infection-induced immunity. Therefore, our goal is to enhance vaccine-induced immunity by increasing the generation of PEPCK-specific dTrm cells, using both tetramer staining and PEPCK TCR transgenic T cells to track the responding T cells. The first step in dTrm development is licensing T cells to enter non-inflamed skin, which is dependent upon high expression of skin home molecules, such as P and E selectin ligands (PESLs), by T cells early after activation in the lymph nodes (LNs). PESLs are induced by IL-12 signaling, and we tested if administration of IL-12 with the PEPCK vaccine would enhance PESL expression by T cells in draining LNs and lead to increased T cells entry into non-inflamed skin. We found that co-delivery of IL-12 mRNA-LNP particles with a PEPCK vaccine significantly enhanced the expression of PESLs in the draining LNs and dramatically increased the number of PEPCK-specific T cells that were present in non-inflamed skin. These results suggest that administration of IL-12 mRNA-LNP particles at the moment of immunization may enhance the generation of dTrm cells.

8425

IMMUNE SIGNATURES PREDICT TREATMENT RESPONSE IN CUTANEOUS LEISHMANIASIS PATIENTS

Rúbia Costa[1], Lucas P. Carvalho[1], Paulo Machado[2], Edgar M. Carvalho[1], **Augusto M. Carvalho**[1]

[1]Gonçalo Moniz Institute, SALVADOR, Brazil, [2]Federal University of Bahia, SALVADOR, Brazil

Cutaneous leishmaniasis (CL) caused by *Leishmania braziliensis* is characterized by an exaggerated inflammatory response that leads to parasite control, but it is also the cause of tissue damage and ulcer formation. The first-line treatment for CL in Brazil is pentavalent antimony, and we have documented that failure to therapy may occur in up to 50% of the patients. Here, we evaluated in a prospective cohort if the immune response at the lesion site can predict therapy failure with pentavalent antimony. This study was performed in Corte de Pedra, an endemic area of CL with high *L. braziliensis* transmission, located in Bahia state, Brazil. Participants were CL patients (N = 53) with classical ulcers and the diagnosis was confirmed through the detection of the DNA of *L. braziliensis* by PCR in biopsied tissues. The failure rate was 52% (N = 28) during follow-up. Cytokines production in supernatants from lesion biopsies were assessed before therapy by ELISA. Patients who fail therapy displayed higher levels of cytokines (IL-1β, TNF, IL-17, IL-10, Granzyme B, and IL-15), and chemokine (CCL2). We found a strong positive correlation between these cytokines and healing time and receiver operating characteristic (ROC) analysis showed that levels of IL-1β, Granzyme B and IL-10 can predict treatment outcome with high accuracy. Moreover, Subjects with a high IL-1β, Granzyme B, IL-10, IL-17 and CCL2 production exhibited a delayed response to therapy. Finally, clinical cure was associated with high levels of IFN-γ and CXCL9. This work identified molecules that can predict responsiveness to treatment and bring an advancement in the field as identification of patients at high risk of failing antimonial therapy, allowing earlier introduction of alternative therapy regimes such as Miltefosine or Amphotericin B.

8426

MALNUTRITION CONTRIBUTES TO VISCERAL LEISHMANIASIS SEVERITY BY EXACERBATING LIVER PATHOLOGY

Lais Amorim Sacramento[1], Claudia Lombana[1], Lisa Mattei[1], Daniel Beiting[1], Phillip Scott[2]

[1]School of Veterinary Medicine University of Pennsylvania, PHILADELPHIA, PA, United States, [2]School of Veterinary Medicine University of Pennsylvania, Philadelphia, PA, United States

Protein malnutrition is a common risk factor for developing visceral leishmaniasis (VL) since it disrupts immune mechanisms that control parasite replication in the target organs of the disease. Because malnutrition contributes to alterations in intestine function and microbiota, we hypothesized that chronic malnutrition also enhances disease severity in VL by disturbing the homeostasis of the gut-liver axis. To study the consequences of chronic malnutrition on VL pathogenesis, we used a polynutrient-deficient diet (deficient protein, energy, zinc, and iron), which mimics moderate human malnutrition for six weeks, followed by *Leishmania infantum* infection. The 16S sequencing of stool samples demonstrated that the polynutrient-deficient diet alters the intestinal microbiota composition and worsens dysbiosis over time. Also, we detected 16S DNA in the liver of polynutrient-deficient diet-fed mice by qPCR. Granuloma formation was limited in the liver and malnourished-infected mice exhibited severe liver pathology characterized by steatosis, diffuse inflammation over the parenchyma, and inflammatory cell infiltration around the veins suggestive of intestinal bacterial translocation. Kupffer cells are specialized resident liver macrophages equipped with innate immune receptors and are positioned at the sinusoids to prevent the systemic spread of microorganisms translocated from the intestine. Flow cytometric analysis revealed that the polynutrient-deficient diet-fed mice had enhanced expression of Toll-like Receptors by Kupffer cells and increased hepatic levels of IL-1beta. Collectively, our findings suggest that malnutrition contributes to VL severity by disturbing the intestinal microbiota leading to enhanced liver pathology.

8427

HUMAN FILARIAL INFECTION RESHAPES THE TRANSCRIPTIONAL AND FUNCTIONAL PROGRAMMING OF CD8 T CELLS AT HOMEOSTASIS AND IN RESPONSE TO CYTOMEGALOVIRUS (CMV) IN FILARIAL/CMV COINFECTED INDIVIDUALS

Camila Queiroz Glauss, Thomas B. Nutman

National Institutes of Health, Bethesda, MD, United States

We have previously demonstrated that filarial infection drives a distinct population signature of $CD8^+$ T cells (CD8's) at homeostasis and following antigen stimulation. To characterize the heterogeneity and function of these CD8's we performed multiparameter flow cytometry from PBMCs collected from 44 CMV- infected individuals with (Fil+; n=29) or without (Fil-; n=15) concomitant filarial infection at homeostasis and in response to CMV antigen. At baseline, CD8's from Fil+ (compared to Fil-) showed higher frequencies of $CD8^+$ cells expressing IFN-γ, TNF-α, IL2, or IL17 and increased frequencies of $CD8^+CD107a^+$ cells - known to reflect cytotoxic activity. After re-stimulation with CMV, CD8's from Fil+ subjects had diminished expression of the type 1 cytokines, TNF-α; IFN-γ, and reduced frequencies of antigen experienced ($CD137^+$) cells. $CD8^+CD137^+$ effector cells from Fil+ showed diminished frequencies of IFN-γ, TNF-α, IL2, and GrB producing cells as well as multifunctional T cells (e.g. $CD8^+CD137^+IFN^+TNF^+IL2^+$) compared to Fil- subjects. Using multidimensional profiling and clustering algorithms, the Fil+ group at homeostasis had marked expansion of several unique populations, most notably $CD8^+CD45RA^+CD57^+GrB^+Perforin^+$ - shown to be associated with high levels of differentiation. In response to CMV, Fil+ subjects showed a decrease in prevalence of $CD8^+CD45RA^+CD57^+CD137^+GrB^+Perforin^+IFN^+TNF^+$ cells compared to Fil- subjects, confirming that antigen experienced cells are diminished in Fil+ individuals. Since the population of $CD8^+CD45RA^+CD57^+$ appears to be associated with filarial infection both at baseline and after CMV re-stimulation, we performed cell sorting and mRNA sequencing to understand the transcriptionally-based nature of this population (analysis in progress). Our data suggest that filarial infection is associated with activation of CD8's; but when stimulated with CMV antigen the subpopulations fail to produce key cytokines for viral control. These findings are likely important to understand the nature of bystander suppression of viral specific responses induced by filarial infections.

8428

LATENT CYTOMEGALOVIRUS INFECTION DISRUPTS INNATE AND ADAPTIVE IMMUNITY TO *PLASMODIUM FALCIPARUM* DURING PRIMARY MALARIA INFECTION

Reena Kiran Mukhiya[1], Jessica R. Loughland[1], Jo-Anne Chan[1], Megan Soon[2], Nick Dooley[1], Luke Quigely[1], Fabian de Labastida Rivera[2], Dean Andrew[2], James Beeson[1], James McCarthy[3], Bridget E. Barber[2], Alejandro Lopez[4], Christian Engwerda[2], Michelle J. Boyle[1]

[1]Burnet Instittue, Melbourne, Australia, [2]QIMR Berghofer Medical Research Institute, Brisbane, Australia, [3]Walter and Eliza Hall Institute of Medical Research, Melbourne, Australia, [4]School of Environmental Sciences, Griffith University, Brisbane, Australia

Latent Cytomegalovirus (CMV) infection has widely reported immunomodulatory effects on the immune system, leading to altered responses to vaccination or infection within an individual. However, the impact of CMV on the immune response to the malaria parasite, *Plasmodium falciparum* is unknown. We studied the impact of latent CMV infection on immune response to *P. falciparum* malaria during Controlled Human Malaria Infection (CHMI). We assessed the influence of CMV on parasite multiplication rates and cellular and humoral immunity. Cell responses were analysed by spectral flow cytometry, and the magnitude and function of induced antibodies was quantified. We found CMV infected individuals had reduced control of parasite growth and reduced clinical symptoms compared to CMV negative individuals. Parasites control is mediated by innate cells including NK cells, monocytes and Vd2+ γδ T cells. We found, CMV infection associated differences in malaria control to be mediated by changes to NK cells. Latent CMV infection was associated with an expansion of phenotypically senescent and regulatory NK cells expressing CD57, TIGIT and PD1, and a reduced responsiveness to malaria parasites, with reduced CD107a, granzymeB and IFNγ. Additionally, latent CMV infection was associated with reduced adaptive immune responses, specific infected individuals had reduced induction of IgG1, and other functional antibodies including C1q, FcγRII, FcγRIII. In malaria, within T-helper follicular cells, only Tfh2 subsets are associated with the induction of protective antibodies. Consistent with this, latent CMV infected indivuals had a skewed Tfh compartment with expanded Tfh1 cells before and during CHMI, and the proportion of Tfh1 cells was negatively associated withantibody responses. Taken together, latent CMV infection impacts both innate and adaptive responses to malaria infection. These altered innate and adaptive immune responses may have particular importance in malaria endemic countries where CMV infection is almost universal and acquired early in life.

8429

HOST DIRECTED THERAPY TO IMPROVE ANTI-PARASITIC IMMUNITY IN VOLUNTEERS EXPERIMENTALLY INFECTED WITH BLOOD STAGE MALARIA

Bridget Barber[1], Rebecca Webster[1], Luzia Bukali[1], Damian Oyong[2], Fabian de Labastida Rivera[1], Jessica Engel[1], Dean Andrew[1], Megan Soon[1], Nick Dooley[2], Jessica Loughland[1], James McCarthy[3], Gerlinde Obermoser[4], Michael Leipold[4], Julianne Jamelink[2], Reena Mukhiya[2], Holder Maecker[4], Christian Engwerda[1], **Michelle Boyle**[2]

[1]QIMR-Berghofer, Brisbane, Australia, [2]Burnet Institute, Melbourne, Australia, [3]University of Melbourne, Melbourne, Australia, [4]Stanford University, Stanford, CA, United States

Slow immune development to malaria is linked to immunoregulatory mechanisms that are induced by infection. These regulatory responses include development of Type 1 regulatory (Tr1) CD4 T cells, which emerge early in infection after Type I IFNs signaling and JAK1/2 activation. We hypothesized that blockade of this pathway would modulate the development of malaria induced immunoregulatory responses and boost protective anti-parasitic immunity.We tested the immune boosting potential of the licensed, oral JAK1/2 inhibitor ruxolitinib, in a randomized double-blind placebo controlled human malaria infection trial. Participants were inoculated with blood-stage *Plasmodium falciparum* and randomized in a 1:1 ratio at day 8/9 to receive the anti-malarial drug artemether/lumefantrine in combination with either ruxolitinib or placebo. Participants were also re-inoculated 3 months after their first inoculation. Modulation of cell signaling was investigated by measuring phosphorylation of STAT3 following *ex vivo* stimulation of peripheral blood mononuclear cells with IFNβ. Cell phenotypes and functions were assessed by CyTOF, spectral flow cytometry and scRNAseq, and parasite specific responses measured following parasite stimulation or by quantifying parasite specific antibodies. Ruxolitinib treatment modulated cell signaling pathways during primary infection, and increased circulating IFNy/IL10 ratios, increased activation of T-follicular helper (Tfh) cells and the frequencies of malaria specific Tfh cells. Further, treated individuals had a modulated memory responses during secondary infection across multiple lymphoid subsets, including changes in T and B cell subset composition, and cytokine production. Results show that host directed therapy during infection can reduced regulatory responses associated with slow immune acquisition.

8430

DIFFERENT MICRORNA PROFILES IN THE CIRCULATING CD4+T CELLS ARE ASSOCIATED WITH DIFFERENT CLINICAL PRESENTATIONS OF *LEISHMANIA DONOVANI INFECTION*

Ritirupa Roy[1], Cinthia Hudachek[2], Shashi Bhushan Chauhan[1], Sundaram Pandey[1], Rajiv Kumar[3], Madhukar Rai[1], Mary E. Wilson[2], Shyam Sundar[1]

[1]institute Of Medical Sciences, Banaras Hindu University, VARANASI, India, [2]University of Iowa and the Iowa City VA Medical Center, Iowa, IA, United States, [3]Centre of Experimental Medicine and Surgery, Banaras Hindu University, Varanasi, India, VARANASI, India

Visceral leishmaniasis (VL) and post kala-azar dermal leishmaniasis (PKDL), caused by the intracellular protozoan *Leishmania donovani*, cause significant morbidity and mortality in the Indian subcontinent. Several microRNAs (miRNAs) associated with the outcome of leishmaniasis in murine models or human cell lines are reported, but studies of miRNAs in human VL patients are lacking. Most circulating miRNAs are found either in circulating blood cells or packaged into freely circulating microvesicles called exosomes. Because of their documented involvement in modifying immune responses, we investigated the roles of miRNAs in circulating exosomes and CD4+T cells of patients with VL or PKDL or healthy, endemic controls from Bihar, India. First, the plasma was isolated from whole blood and then PBMCs were extracted from the rest of the blood using density gradient separation followed by CD4+T cell isolation. We first screened all 827 reported human miRNAs using NanoString profiling in CD4+T cells, followed by data analysis and second, significant miRNAs were evaluated by TaqMan assays. Expression of miR-23a was decreased in CD4+T cells of VL patients compared to EC and PKDL ($p<0.05$), whereas miR-29 was decreased only in CD4+T cells of VL patients compared to EC. Nanostring profiling of miRNAs of CD4+T cells revealed many significantly upregulated and downregulated miRNAs in VL subjects compared to EC, but only few differentially regulated miRNAs in PKDL subjects compared to EC. Notably, miR-146a was significantly regulated in both plasma and CD4+T cells of VL subjects. we can infer from our study that the plasticity of T cell proliferation and differentiation in human VL is contingent upon microRNA-mediated gene regulation. Differential expression of miRNAs might provide prognostic marker to predict subjects who will develop PKDL as a complication of VL. We hypothesize these miRNAs may be critical determinants of immune response like macrophage polarization, suppression of T cell responses to *L. donovani* infection.

8431

ISOLATION AND CHARACTERIZATION OF α-GAL-CONTAINING EXTRACELLULAR VESICLES FROM *TRYPANOSOMA CRUZI*: UNVEILING NEW BIOMARKERS FOR CHAGAS DISEASE

Priscila Silva Grijo Farani, Nasim Karimi Hosseini, Susana Portillo, Maria Tays Mendes, Brian Grajeda, Colin Knight, Cameron Ellis, Igor Almeida

The University of Texas at El Paso, El Paso, TX, United States

Chagas disease (CD), caused by the protozoan parasite *Trypanosoma cruzi*, remains a significant public health issue, predominantly affecting impoverished regions and resulting in considerable morbidity and mortality. The disease's complexity is further compounded by the parasite's sophisticated evasion mechanisms, including the secretion of extracellular vesicles (EVs) that facilitate host immune system evasion and pathogen persistence. This study aims to isolate and characterize α-Gal-containing EVs from three major *T. cruzi* genotypes: TcI (Colombiana strain), TcII (Y strain), and TcVI (CL Brener clone), highlighting their potential role as novel biomarkers for CD. EVs were purified from tissue culture cell-derived trypomastigotes (TCT-EVs) by affinity chromatography and separated into two fractions: α-Gal(-) (flow-through) and α-Gal(+) (eluate). Proteomic analysis of these fractions revealed a rich repertoire of glycosylphosphatidylinositol (GPI)-anchored proteins, including *trans*-sialidase (TS), mucin-associated surface proteins (MASP), and gp63 in the α-Gal(-) fraction. On the other hand, the α-Gal(+) TCT-EV fraction contained mainly GPI-anchored mucins of the TcMUC II family, which is abundant in TCTs and targets lytic protective anti-α-Gal antibodies. Notably, by chemiluminescent ELISA, isolated α-Gal(+) TCT-EVs demonstrated strong specific reactivity with sera from chronic CD (CCD) patients across multiple geographic regions, underscoring their potential as sensitive and specific biomarkers for diagnosis and chemotherapy follow-up. This research opens new avenues for the early diagnosis and therapeutic monitoring of CD, offering a promising strategy for tackling one of the most neglected tropical diseases.

8432

EXTRACELLULAR VESICLES FROM *TAENIA SOLIUM* DAMPENS PI3K-AKT-MTORC1 SIGNALING AND AMELIORATES DSS-COLITIS IN MICE

Suraj Singh Rawat, Amit Prasad

Indian Institute of Technology Mandi, Mandi, Himachal Pradesh, India

Neurocysticercosis (NCC) is a neurological infection caused by the larval stage of *Taenia solium*, it accounts for up to 30% of acquired epilepsy in endemic areas. *T. solium* cysticerci in viable stage modulates host immune response and induces predominant type II (anti-inflammatory) immune response. Cysticerci secretes a plethora of molecules during the infection, which interact with host immune cells and suppresses them. *T. solium* cysticerci were grown in serum free medium and extracellular vesicles (EV) were isolated via ultracentrifugation-based protocol. Here, for the first time we report that *T. solium* cysticerci release EV that are readily internalized by macrophages in a dose dependent manner. In the metabolomic analysis we identified that EVs are rich in metabolites that are associated with the negative regulation of AKT signaling. We found that the EV induced anti-inflammatory gene expression in macrophages, indicating an immunodominant role of EVs in maintaining anti-inflammatory state during viable cysticercosis infection. Further, we investigated that EV induced degradation of AKT and mTORC1 proteins via autophagy mediated pathway and increased lysosomal activity in the macrophages. To investigate the therapeutic role of EV, we developed colitis in mice via 3% DSS in drinking water. We found that EVs significantly lowered the disease severity in DSS+EV groups. In the histopathology scores, EV rescued altered colon morphology induced by DSS and protected the mice in both the pre- and post-EV stimulation groups. On further analysis, pAKT level was high in the DSS only group which was suppressed upon EV stimulation. LC3 protein expression was increased after EV stimulation, henceforth activating the autophagy. In conclusion, these findings suggested that the EV from *T. solium* parasite can suppress the PI3K-AKT-mTORC1 pathway and suppress inflammation. Our study has provided the novel aspect of *T. solium* EV as potential therapeutic agents.

8433

A SPECIALIZED RIBOSOME PROMOTES HOST-TO-VECTOR TRANSMISSION IN THE HUMAN MALARIA PARASITE

Tiziano Vignolini, Justine Couble, Grégory Doré, Sebastian Baumgarten

Pasteur Institute, Paris, France

Ribosomal RNA (rRNA) in eukaryotes is encoded by repetitive gene clusters. In contrast, genomes of Plasmodium species contain only a few individual rRNA-encoding genes that are divergent in their primary sequence and located on different chromosomes. The expression pattern of these rRNAs is tightly developmentally regulated, making Plasmodium one of the most compelling instances of ribosome heterogeneity. In addition to the two known classes of rRNAs in P. falciparum, here we report on a third, highly divergent rRNA type with a deep evolutionary origin among primate-infecting Plasmodium. This 'O-type' rRNA does not include an 18S, features a 1.5x longer 28S that is processed into three fragments, and is predominantly expressed in the early stages of parasite development in the mosquito. We used RNA-RNA interaction sequencing to reconstruct the O-type 28S secondary structure, identifying a conserved ribosome core outfitted with extensive expansion segments. We showed that O-type rRNA assembles with 18S rRNA of different ribosome types and interacts with multiple other rRNA-associated ncRNAs including tRNA and snoRNAs that guide a distinct rRNA modification pattern. Importantly, knock-out of the O-type 28S led to an arrest of parasite development in early gametocytogenesis, suggesting a specialized function that cannot be compensated for by another cytoplasmic ribosome. Moreover, comparative ribosome profiling revealed that O-type ribosomes are responsible for the efficient translation of a subset of mRNAs during gametocyte development. Altogether, we report on the structural, compositional, and functional heterogeneity of a new ribosome type with a specialized role during host-to-vector transmission of P. falciparum.

8434

HIDE AND GO SEQ: CAPTURING THE ANTIBODY-VSG ARMS RACE DURING TRYPANOSOMA BRUCEI INFECTION

Lulu M. Singer[1], Jaime E. So[2], Alexander K. Beaver[2], Monica R. Mugnier[1]

[1]Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, United States, [2]Johns Hopkins University School of Medicine, Baltimore, MD, United States

Trypanosoma brucei, the protozoan parasite that causes Human African Trypanosomiasis (HAT) and Animal African Trypanosomiasis (AAT), continues to pose significant medical and economic burdens in endemic countries. T. brucei, an entirely extracellular parasite, is able to evade clearance using a sophisticated mechanism of antigenic variation. The parasite is covered in a dense coat of the antigenically variable Variant Surface Glycoprotein (VSG) and can switch expression of its VSG to avoid elimination by antibodies. T. brucei has access to a genomic repertoire of 1000s of VSG encoding genes that can be expressed or recombined into novel VSGs, giving the parasite a massive pool of antigens to choose from. With potentially hundreds of VSGs expressed during a single infection, the anti-VSG response is impossible to capture using standard low throughput techniques, and little is known about the in vivo anti-VSG response. Here, we aimed to elucidate the dynamics of the VSG-antibody interface during T. brucei infection in mice using high throughput methods. We combined VSG-seq, a targeted mRNA sequencing approach, with phage immunoprecipitation sequencing (PhIP-seq), a high throughput epitope mapping method. Using a phage display library of over 76,000 VSG peptides, we were able to track the dynamics and specificities of the anti-VSG response. With this longitudinal approach, we were able to visualize

the isotype specific kinetics of the anti-VSG response during infection. We were also able to identify and map peptide epitopes to expressed VSGs, providing insight into binding specificities and what VSG regions are accessible to different isotypes.

8435

ESTABLISHMENT OF A LABORATORY SYSTEM TO INTERROGATE TRYPANOSOMA CRUZI DEVELOPMENT WITHIN THE KISSING BUG VECTOR RHODNIUS PROLIXUS

Ruby Harrison[1], Kevin J. Vogel[2], Drew Etheridge[1]

[1]University of Georgia Center for Tropical and Emerging Global Diseases, Athens, GA, United States, [2]University of Georgia Department of Entomology, Athens, GA, United States

The single-celled eukaryote Trypanosoma cruzi alternates between insect and vertebrate hosts including humans, in which it causes Chagas disease. Endemic to Latin America, T. cruzi is estimated to chronically infect ~7 million people. While T. cruzi interactions with its vertebrate hosts are relatively well-characterized, factors affecting vector infection and transmission are poorly understood. To address this gap in our understanding of T. cruzi's basic biology, we established a model pathogen-host system using the kissing bug Rhodnius prolixus and the genetically tractable Y strain of T. cruzi. We first adapted rearing methods for efficient and high-throughput rearing of R. prolixus using custom 3D printed materials including an artificial feeding system. We next tracked T. cruzi colonization of different regions of the insect digestive tract using quantitative PCR and found that T. cruzi transiently passes through midgut regions but stably colonizes the hindgut long-term. Comparison of movement of inert fluorescent microspheres and parasites from anterior to posterior regions of the gut indicated that both arrive at the hindgut at circa 5 days post-ingestion, suggesting T. cruzi is passively carried to its preferred tissue by the peristaltic movement of the insect gut. Finally, we developed robust methods for isolation and purification of parasites released from insect excreta or from gut homogenates towards assessment of parasite transition from replicative to infectious stages. By establishing this easily cultured parasite-host model system, we are now well-positioned to begin interrogating the molecular basis for T. cruzi's colonization and transmission in its insect vector in future studies.

8436

CIRCADIAN RHYTHMS MEDIATE MALARIA TRANSMISSION POTENTIAL

Inês Bento[1], Brianna Parrington[2], **Rushlenne Pascual**[2], Alexander Goldberg[2], Eileen Wang[3], Hani Liu[2], Mira Zelle[2], Joseph Takahashi[4], Joshua Elias[3], Maria Mota[1], Filipa Rijo-Ferreira[5]

[1]Instituto de Medicina Molecular, João Lobo Antunes, Faculdade de Medicina Universidade de Lisboa, Lisbon, Portugal, [2]Berkeley Public Health, Molecular and Cell Biology Department, University of California, Berkeley, Berkeley, CA, United States, [3]Chan Zuckerberg Biohub – San Francisco, San Francisco, CA, United States, [4]Department of Neuroscience, Peter O'Donnell Jr. Brain Institute, University of Texas Southwestern Medical Center, Howard Hughes Medical Institute, Dallas, TX, United States, [5]Berkeley Public Health, Molecular and Cell Biology Department, University of California, Berkeley, Chan Zuckerberg Biohub – San Francisco, Berkeley, CA, United States

Malaria transmission begins when infected female Anopheles mosquitos deposit Plasmodium parasites into the mammalian host's skin during a bloodmeal. The salivary gland-resident sporozoite parasites migrate to the bloodstream, subsequently invading and replicating within hepatocytes. As Anopheles mosquitos are more active at night, with a 24-hour rhythm, we investigated whether their salivary glands are under circadian control, anticipating bloodmeals and modulating sporozoite biology for host encounters. Here we show that approximately half of the mosquito salivary gland transcriptome, particularly genes essential for efficient bloodmeals such asanti-blood clotting factors, exhibits circadian rhythmic expression. Furthermore, we demonstrate that mosquitoes prefer to feed during nighttime, with the amount of blood ingested varying cyclically throughout the day. Notably, we show a substantial subset of the sporozoite transcriptome cycling throughout the day. These include genes involved in parasite motility, potentially modulating the ability to initiate infection at different times of day. Thus, although sporozoites are typically considered quiescent, our results demonstrate their transcriptional activity, revealing robust daily rhythms of gene expression. Our findings suggest a circadian evolutionary relationship between the vector, parasite and mammalian host that together modulate malaria transmission.

8437

GENE-EDITING IN STRONGYLOIDES RATTI REVEALS THE NATURE OF HELMINTH SPECIFIC T CELLS

Fungai Musaigwa[1], Olufemi Akinkuotu[1], Hannah Dobson[2], Annabel Ferguson[1], Adriana Stephenson[1], Ulrich Femoe[1], Li-Yin Hung[1], Parvathi Annamalai[1], Juan Inclan Rico[1], Heather Rossi[1], De'Broski R. Herbert[1]

[1]Department of Pathobiology, School of Veterinary Medicine, University of Pennsylvania, Philadelphia, PA, United States, [2]Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, United States

CD4+ helper 2 (TH2) cells are key in driving parasitichelminth immunity and regulation of infection induced tissue pathology.However, the importance of antigen-specific vs. non-specific "bystander" CD4+T cell populations remains unclear. Our work describes a recently generated *Strongyloidesratti* mutant line using CRISPR-CAS targeting. This mutant, termed *Atilla,*contains an insertion of two copies of the immunodominant CD4+ T cell epitope2W1S, fused with FLAG and HA peptides into the astacin-likemetalloendopeptidase gene. Data show that *Attila* infection in C57BL/6mice induces marked expansion of trackable 2W1S+ specific CD4+ T cells in multipleorgans including: lung, spleen, mesenteric lymph nodes, and peritoneum. Uponrepeat inoculation, *Attila* specific 2W1S+CD62L-CD44+CD4+ T cellsco-expressed the transcription factor GATA3, the interleukin 33 receptor ST2and the chemokine receptor CXCR6. *In vitro* re-stimulation of splenocytesand lung cells from infected mice with the 2W1S peptide following induced significantlyincreased type 2 cytokine release in comparison to vehicle -treated controls.Notably, adoptive transfer of enriched 2W1S+CD62L-CD44+CD4+ T cells into mutantmice lacking alpha beta and gamma delta T-cell populations conferred host protection upon parasitechallenge as defined by significantly reduced fecal egg output burden andimproved survival kinetics as compared to mock-treated control mice. This work supportsa hypothesis that antigen-specific T cells serve an important role in helminthimmunity and limiting host pathology anddemonstrates that *Attila* is a robust exploratory tool forunderstanding helminth-specific T cellresponses.

8438

MRGPRA3 NEURONS DRIVE CUTANEOUS IMMUNITY AGAINST HELMINTHS THROUGH SELECTIVE CONTROL OF MYELOID CYTOKINES

Juan Inclan Rico, Camila M. Napuri, Li-Yin Hung, De'Broski R. Herbert

University of Pennsylvania, Philadelphia, PA, United States

Skin employs interdependent cellular networks for barrierintegrity and host immunity, but most underlying mechanisms remain obscure. Herein, we demonstrate that the human parasitic helminth, Schistosoma mansoni,inhibits pruritus evoked by itch-sensing afferents bearing the Mas-related Gprotein-coupled receptor A3 (MrgprA3) in mice. MrgprA3 neurons control IL-17+γδ T cell expansion, epidermal hyperplasia, and host resistance against S.mansoni through shaping cytokine expression in cutaneous antigen-presentingcells (APCs). MrgprA3 neuron activation induces IL-1β and TNF in macrophagesand cDC2s partially through the neuropeptide calcitonin gene-related peptide(CGRP). Collectively, this work reveals a previously unrecognized mechanism ofintercellular communication

wherein itch-inducing MrgprA3 neurons initiate hostimmunity against skin-invasive parasites by directing cytokine expressionpatterns in myeloid APC subsets.

8439

IN VIVO SCREEN REVEALS *PLASMODIUM FALCIPARUM* TARGETS FOR MOSQUITO-BASED MALARIA INTERVENTION

Alexandra Probst[1], Douglas Paton[2], Federico Appetecchia[2], Selina Bopp[2], Tasneem Rinvee[2], Sovitj Pou[3], Rolf Winter[3], Esrah Du[2], Sabrina Yahiya[4], Charles Vidoudez[5], Naresh Singh[2], Janneth Rodrigues[6], Pablo Castañeda-Casado[6], Chiara Tammaro[2], Daisy Chen[7], Karla Godinez Macias[7], Giovanna Poce[8], Aaron Nilsen[3], Elizabeth Winzeler[7], Jake Baum[9], Jeremy Burrows[10], Michael Riscoe[3], Dyann Wirth[2], Flaminia Catteruccia[2]

AImmunology and Infectious Diseases, [1]Harvard. T. H. Chan School of Public Health, Boston, MA, United States, [2]Portland VA Medical Center, Portland, OR, United States, [3]Department of Life Sciences, Imperial College London, London, United Kingdom, [4]Harvard Center for Mass Spectrometry, Cambridge, MA, United States, [5]Tres Cantos Open Lab Foundation, GlaxoSmithKline, Tres Cantos, Spain, [6]Department of Pediatrics, School of Medicine, University of California, San Diego, San Diego, CA, United States, [7]Department of Chemistry and Pharmaceutical Technologies, Sapienza University of Rome, Rome, Italy, [8]School of Biomedical Sciences, University of New South Wales, Sydney, Australia, [9]Medicines for Malaria Ventures, Meyrin, Switzerland

Progress against malaria has plateaued in recent years,necessitating new strategies to combat this deadly disease. We recentlydemonstrated that *Plasmodium falciparum* can be directly targeted withinthe *Anopheles* vector by allowing mosquitoes to land on surfaces coatedwith the antimalarial atovaquone. To discover additional inhibitors of mosquitostage *P. falciparum* that could be incorporated into mosquito bed nets,we performed an in vivo screen of 81 antimalarials by applying them onto thethorax of *Anopheles* females. This initial screen identified 22 activecompounds with seven distinct modes of action. Most compounds, however, werenot effective when mosquitoes had to actively take them up when landing ontreated surfaces, as they would when landing on bed nets. We therefore usedmedicinal chemistry approaches to introduce compound structural changes toincrease mosquito uptake upon exposure. This led to the generation of twohighly potent endochin-like quinolones (ELQs) targeting different sites (oxidizingand reducing) of cytochrome bc1. To assess the compatibility of these compoundswith bed net-like formulations, we incorporated them into low densitypolyethylene films. Brief contact exposure to these films completely ablated *P.falciparum* infection, and films fully maintained their antiplasmodialactivity over one year later. Importantly, mutant parasites generated via bloodstage selections showed severe defects during sporogony, and the two ELQcompounds did not show cross resistance. The potent activity of ELQs againstmosquito stage *P. falciparum* and the impaired transmissibility ofresistant mutants highlights the promise of using a combination of thesecompounds for vector-targeted antiplasmodial interventions.

8440

TICK INNATE IMMUNE RESPONSE TO PATHOGEN INFECTION AT SINGLE-CELL RESOLUTION

Abdulsalam Adegoke

University of Michigan Medical School, Ann Arbor, MI, United States

Ticks rely on robust cellular and humoral immunity to control pathogen infection. However, a tick's innate immune system is a complex black box comprised of immune cells (called hemocytes), known to play a significant role in both cellular and humoral responses toward pathogens. Despite the importance of hemocytes in regulating microbial infection, understanding their basic biology and molecular mechanisms remains limited. A complete understanding of the immune factors involved in the interactions between ticks and tick-borne pathogens in hemocytes is crucial to elucidate their role in vector competence and to help identify novel targets for developing new strategies to block pathogen transmission. This study examined the tick hemocyte heterogeneity at the transcriptomic level. We used the 10X genomics single-cell RNA sequencing platform to analyze their transcriptome at a unique level in unfed, partially blood-fed, and pathogen-infected hemocytes. We were able to show the presence of seven distinct hemocyte transcriptomic populations in the tick vector. Our results revealed that clusters representing granulocyte and oenocytoids populations are increased with pathogen infection. This work opens a new field of tick innate immune biology to understand the role of hemocytes, particularly in response to prolonged blood-feeding (hematophagy) and tick-pathogen interactions.

8441

EXPANDING TOOLBOX FOR ODOR-BASED TSETSE FLY CONTROL IN EAST AFRICA

Paul O. Mireji

Arthropod Biotechnology, Kenya Agricultural and Livestock Research Organization, Kikuyu, Kenya

Tsetse fly - transmitted Human AfricanTrypanosomiasis (HAT) and Animal African Trypanosomiasis (AAT) are among mostneglected tropical diseases in sub-Sahara Africa. Tsetse fly control strategiesconstitute cornerstones efforts in suppression and eradication of HAT and AAT.Tsetse fly lures that attract the flies to traps/insecticide-treated targetsand repellents that minimize contact between infective flies and theirvertebrate hosts can augment the strategies. We formulated a Novel AttractantBlend (NAB) comprised of ε-nonalactone, nonanoic acid, 2-nonanone and acetone) and Novel Repellent Blend (NRB) (δ-nonalactone, heptanoic acid,4-methylguaiacol and geranyl acetone) based on tsetse-refractory waterbuck odorconstituents, their structural analogues and attractant buffalo odor. Using two-choice wind tunnel in the laboratory and Latin square experimentaldesign in the field, we establish that 1) NAB is 2.4 times as attractive to *Glossina pallidipes* tsetse flies as POCA (3-n-Propylphenol,1-Octen-3-ol, 4-Cresol, and Acetone) blend routinely used in tsetse control and2) NRB is two-folds more efficacious than current commercial repellent blendagainst most savannah species. We microencapsulated the optimized NRB intoβ-cyclodextrin nano particles by kneading technique, evaluated responses of *G. pallidipes* tsetse to the microencapsulated blend andestablished kinetic release rates from the microcapsules under fieldconditions. We established significantly ($p<0.05$) lower release rate(5.35mg/h) in microencapsulated blend than the un-encapsulated control (11.82mg/h) and that the micro-capsulation did not significantly affect responses ofthe tsetse flies to traps. We assessed efficacy of NRB in livestock protectionusing randomized block experimental design and established at least 95%repellence of *G. pallidipes* from oxen by NRB. We successfully masked theNRB in fragrance for odor appeal (for potential use in security and hospitalityindustries) and are developing NAB and NRB into semiochemical prototypes forintegrated push-pull deployment in areawide control of tsetse flies in EasternAfrica.8442

8442

EFFECTIVENESS OF PYRETHROID-PIPERONYL BUTOXIDE NETS *VERSUS* STANDARD PYRETHROID-ONLY NETS IN PREVENTING MALARIA IN CHILDREN UNDER 10 YEARS LIVING IN KISANTU HEALTH ZONE, DEMOCRATIC REPUBLIC OF THE CONGO: A QUASI-EXPERIMENTAL STUDY

Gillon KAOUNGA ILOMBE[1], **GRACE NYAWEZA NGUYA**[1], Joris LOSIMBA LIKWELA[2], Philippe LUKANU2, Aimée LULEBO[3], Nicole MUELA[4], Joachim MARIËN[5], Pascal LUTUMBA[6], Fiacre AGOSSA[7], Albert KALONJI[2], Jean-Pierre Van geertruyden[8], Eric MUKOMENA[9], Seth IRISH[10]

[1]National control malaria programme, Kinshasa, Congo, Democratic Republic of the, [2]SANRU asbl - Primary Health Care in Rural Areas, Kinshasa, Congo, Democratic Republic of the, [3]University of Kinshasa, Faculty of Medicine, Public Health School, Kinshasa, Democratic Republic of Congo, Kinshasa, Congo, Democratic Republic of the, [4]Programme

Elargi de Vaccination, Ministry of Public Health, Kinshasa, Democratic Republic of Congo, Kinshasa, Congo, Democratic Republic of the, [5]Evolutionary ecology group, University of Antwerp, Antwerp, Belgium, Antwerp, Belgium, [6]Departments of Tropical Medicine, University of Kinshasa, Kinshasa 01015, Democratic Republic of the Congo, Kinshasa, Congo, Democratic Republic of the, [7]PMI VectorLink Project, Abt Associates, Kinshasa, Democratic Republic of the Congo, Kinshasa, Congo, Democratic Republic of the, [8]Global Health Institute, Faculty of Medicine, University of Antwerp, Antwerp, Belgium, [9]National Malaria Control Program, Ministry of Health, Kinshasa, Democratic Republic of Congo, Kinshasa, Congo, Democratic Republic of the, [10]President's Malaria Initiative and Entomology Branch, Division of Parasitic Diseases and Malaria, Center for Global Health, Centers for Disease Control and Prevention, Atlanta, GA USA., Atlanta, GA, United States

The Democratic Republic of the Congo(DRC) is among the countries with the highest malaria incidence. Among the new generation of insecticide-treated nets(ITNs) with improved effectiveness of insecticides, ITNs treated with a combination of piperonyl butoxide(PBO)& pyrethroids appear promising for malaria control. This study evaluated the effectiveness of these ITNs under community conditions of use in DRC. A quasi-experimental study registered with ClinicalTrials.gov was carried out from January to December 2018, in Kisantu Health Zone. Thirty villages were randomly allocated as clusters(1:1) to receive one of two types of ITNs, ITNs treated with deltamethrin alone; or PBO with deltamethrin. After the intervention, the assessments were conducted monthly, quarterly&every six months for malaria infection, mosquito density&durability; respectively. The comparison of changes in different indices between the two groups was made using the ANOVA test for repeated measurements. A total of 1,790 children were included. There was a significant non-linear effect of time on the malaria infection incidence($p<0.0001$). The malaria infection incidence was higher in January–March, May-June&November. It remained higher in the control group compared to the intervention group($p<0.001$). Similarly, there was a significant non-linear effect of time on the density of both *Anophele(A) funestus* sl & *A. gambiae* sl. These densities decreased after the first month following the intervention&increased after time point 2. In cone bioassays at 12months post-distribution bio-efficacy was better in the intervention group ($p<0.001$). The nets treated with the combination of PBO&deltamethrin were found to be more effective for malaria control in the DRC.