In rodents, the skin concentration of L-amB is 40-fold less than that in visceral organs. We hypothesize that a specific L-amB regimen targeted to skin concentrations could maximize a beneficial treatment response in CL.

Methods. SKH1 477 Elite hairless mice (Charles River), 5 per group, received intravenous L-amB at doses of (A) 3 mg/kg/day for days 1–5, 8, 9, (B) 5 mg/kg/day for 4 days, (C) 10 mg/kg load than 5 mg/kg/day for 3 days, (D)10 mg/kg/day for 2 days, (E) 15 mg/kg/day for 2 days. Serum and skin (back) punch biopsies were collected on day 0, 2, 5, 14, and 21. Nasal mucosa was biopsied on day 21. Tissue samples were homogenized and L-amB was extracted with methanol and acetonitrile. Liquid chromatography–mass spectrometry was performed using these extracted samples on an Agilent 1200 series HPLC and an AB Sciex Q-Trap 4000 mass spectrometer. Experiment conducted twice for confirmation.

Results. L-amB doses were well tolerated by the mice, except weight loss was seen in regimen E. Day 21 serum L-amB levels were 82 ± 3.2 (ng/mL) regimen A, 91 ± 4.2 in B, 89 ± 4 in C, 118 ± 3.7 in D, 98 ± 1.5 in E. Mean L-amB nasal tissue levels on day 21 were 1.33 + 3.2 (ng/mg tissue) regimen A and 6.5 ± 3 in D ($P = 0.031$). Mean L-amb skin levels on day 14 were 8.4 ± 5.6 (ng/mg tissue) in regimen A, 4.0 ± 1.7 in B, 6.2 ± 3.3 in C, 13.9 ± 7.1 in D, 33.9 ± 24.7 in E. Skin L-amB levels at day 21 were less than 5 (ng/mg tissue) except for regimen D 9.3 ± 4.2 and regimen E 7.8 ± 2.6. SKH1 477 Elite mice did not permit an adequate *Leishmania major* infection (very tiny lesions when compared with other murine species) to correlate these results clinically in this specific murine model.

Conclusion. While regimens A–D received similar total dosages of L-amB, the skin and nasal mucosal levels were significantly higher in the short, high daily dose regimens compared with the L-amB regimen that is currently used in CL patients. This suggests that better clinical results might be seen by using a L-amB dosing regimen for CL of 10 mg/kg for 2 days, a dose regularly used in the treatment of pediatric visceral leishmaniasis.

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963. Whole Blood Transcriptome Analysis Reveals Differences in Erythropoiesis and Neurologically Relevant Pathways Between Cerebral Malaria and Severe Malarial Anemia

Srinivas Nallandhighal, MS[1]; Gregory Park, PhD[2]; Yen-Yi Ho, PhD[3]; Robert Opoka, MBChB[4]; Chandy John, MD, MS[5] and Tuan Tran, MD, PhD[1,5], [1]Department of Medicine, Division of Infectious Diseases, Indiana University School of Medicine, Indianapolis, Indiana, [2]Department of Pediatrics, Division of Global Pediatrics, University of Minnesota Medical School, Minneapolis, Minnesota, [3]Department of Statistics, University of South Carolina, College of Arts and Sciences, Columbia, South Carolina, [4]Makerere University, Kampala, Uganda and [5]Ryan White Center for Pediatric Infectious Disease and Global Health, Indiana University School of Medicine, Indianapolis, Indiana

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Background. *Plasmodium falciparum* malaria can rapidly progress to severe disease that can lead to death if left untreated. Severe malaria cases commonly present as severe malarial anemia (SMA), defined in children as hemoglobin (Hb) <5 g/dL with parasitemia, or as cerebral malaria (CM), which manifests as parasitemia with acute neurological deficits and has an inpatient mortality rate of ~20%. The molecular and cellular processes that lead to CM and SMA are unclear.

Methods. In a cross-sectional study, we compared genome-wide transcription profiles of whole blood obtained from Ugandan children with acute CM ($n = 17$) or SMA ($n = 17$) and community children without *P. falciparum* infection ($n = 12$) who were enrolled in a parent cohort study of severe malaria. We determined the relationships between gene expression, hematological indices, and plasma biomarkers, including inflammatory cytokines.

Results. Both CM and SMA demonstrated enrichment of dendritic cell activation, inflammatory/TLR/chemokines, monocyte, and neutrophil modules but depletion of lymphocyte modules. Neurodegenerative disease and neuroinflammation pathways were enriched in CM. Increased Nrf2 pathway gene expression corresponded with increased plasma heme oxygenase-1 and the heme catabolite bilirubin in a manner specific to children with both SMA and sickle cell disease. Reticulocyte-specific gene expression was markedly decreased in CM relative to SMA despite higher Hb levels and appropriate increases in plasma erythropoietin. Viral sensing/interferon regulatory factor (IRF) 2 module (M111) expression and plasma IP-10 levels both negatively correlated with reticulocyte-specific signatures, but only M111 expression independently predicted decreased reticulocyte-specific gene expression after controlling for leukocyte count, Hb level, parasitemia, and clinical syndrome by multiple regression.

Conclusion. Differences in the blood transcriptome of CM and SMA relate to neurologically relevant pathways and erythropoiesis. Erythropoietic suppression during severe malaria is more pronounced during CM versus SMA and is positively associated with IRF2 blood signatures. Future studies are needed to validate these findings.

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

964. Impact of Doxycycline as Malaria Prophylaxis on Risk of Influenza Like Illness Among International Travelers

Kathryn Lago, DO[1]; Kalyani Telu, MS[2]; David R. Tribble, MD, DrPH[3]; Anuradha Ganesan, MD, MPH[4]; Anjali Kunz, MD[5]; Charla Geist, DO[6]; Jamie Fraser, MPH[2]; Indrani Mitra, MS[2] and Heather Yun, MD, FIDSA[7], [1]San Antonio Military Medical Center, Fort Sam Houston, Texas, [2]Infectious Disease Clinical Research Program, Department of Preventive Medicine and Biostatistics, Uniformed Services University of the Health Sciences, Bethesda, Maryland, [3]Infectious Disease Clinical Research Program, Uniformed Services University, Bethesda, Maryland, [4]Preventive Medicine and Biostatistics, Infectious Disease Clinical Research Program, Uniformed Services University of the Health Sciences, Bethesda, Maryland, [5]Madigan Army Medical Center, Tacoma, Washington, [6]Landstuhl Regional Medical Center, Landsthul, Germany and [7]Brooke Army Medical Center, JBSA Fort Sam Houston, Texas

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Background. International travelers are often at risk for both influenza like illness (ILI) and malaria. Doxycycline is active against many pathogens causing ILI and is routinely used for malaria prophylaxis. We evaluated the incidence of and risk factors for ILI, and whether the choice of malaria prophylaxis was associated with ILI.

Methods. TravMil is a prospective observational study enrolling subjects presenting to 6 military travel clinics. We analyzed pre- and post-travel surveys from travelers to regions outside of the continental United States, Western or Northern Europe, Canada, or New Zealand between July 2010 and August 2018. ILI was defined as subjective fever associated with either a sore throat or cough. Characteristics of trip and traveler and the use of malaria prophylaxis were analyzed to determine association with development of ILI. Poisson regression models with robust error variance were used to estimate relative risk of ILI.

Results. A total of 3,227 travelers were enrolled: 62.1% male, median age of 39 (IQR 27, 59), median travel duration 19 days (IQR 12, 49). 32% traveled to Africa, 40% to Asia, and 27% to the Caribbean, Mexico, and Central or South America. Military travel (46%) and vacation (40%) were most common reasons for travel. Twenty percent took doxycycline for malaria prophylaxis, 50% other prophylaxis (89% atovaquone–proguanil), and 30% took none. 8.7% developed ILI. Compared with those on no or other prophylaxis, doxycycline was associated with decreased risk of ILI [RR 0.65 (0.43–0.99), $P = 0.046$], as was military travel [RR 0.30 (0.21–0.43), $P < 0.01$]. Increased risk of ILI was associated with female gender [RR 1.57 (1.24–1.98), $P < 0.01$], travel to Asia [RR 1.37 (1.08–1.75), $P = 0.01$], cruises [RR 2.21 (1.73–2.83), $P < 0.01$], and longer duration of travel [RR 1.01 (1.00–1.01, $P < 0.01$].

Conclusion. The use of doxycycline is associated with a decreased risk of ILI compared with taking no or other malaria prophylaxis. The reasons for this are unclear but may be related to anti-inflammatory effects, activity against bacterial respiratory pathogens, effects on disease transmission in closed populations (e.g., military deploying groups), or other unmeasured factors. With few proven strategies for decreasing ILI risk in travelers, these findings bear further investigation.

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965. Applying Clinical Prediction Tools to Patients with Lassa Fever

John Chiosi, MD[1], Jeffrey Shaffer, PhD[2] and John Schieffelin, MD, [1]Internal Medicine/Pediatrics, Tulane University School of Medicine, New Orleans, Louisiana, [2]Tulane School of Public Health and Tropical Medicine, New Orleans, Louisiana and [1]Tulane University Health Sciences Center, New Orleans, Louisiana

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Background. Clinical prediction tools such as the Quick Sequential Organ Failure Assessment (qSOFA) and the Modified Early Warning Score (MEWS) have been used to predict mortality from sepsis in high-income countries, but their application to low- and middle-income countries have been limited. Lassa fever is a viral hemorrhagic fever endemic to West Africa with a case fatality ratio for hospitalized patients of up to 69%. The purpose of this study was to evaluate existing clinical prediction tools for critical illness in predicting adverse outcomes in patients with Lassa fever.

Methods. We conducted a retrospective cohort study of patients admitted to the Kenema Government Hospital Lassa ward in Sierra Leone between 2012 and 2017. Patients were required to meet the World Health Organization case definition for suspected Lassa Fever to be admitted to the ward. We included patients who had laboratory-confirmed Lassa fever via ELISA tests for Lassa Ag or IgM. Control samples were included with negative ELISA tests for Lassa Ag and IgM. We compared criteria for qSOFA, MEWS, Systemic Inflammatory Response Syndrome (SIRS), and Universal Vital Assessment (UVA) among the Lassa Ag+ (patients with acute viremia), Ag-/IgM+ (patients who cleared the virus and developed an immune response), and Ag–/IgM– (control) groups.

Results. There were 157 patients included in this preliminary analysis. Of patients in the Ag+ group, the mean age was 20.2 years and 40.8% were female. Patient demographics were similar among all groups. Clinical outcomes significantly differed among the groups, with the highest in-hospital mortality at 62.5% in the Ag+ group. For each clinical prediction tool, mean scores significantly differed among groups ($P < 0.05$; see table). The highest scores were consistently seen in the Ag+ group.

Conclusion. Patients with acute viremia for Lassa fever had higher scores for clinical prediction tools compared with controls, which imply a higher risk of mortality. Additional research is needed on the sensitivity and specificity of these tools for mortality due to Lassa fever.

Table: Mean Score of Clinical Prediction Tools in Patients With Lassa Fever and Controls

	Ag+	Ag–/IgM+	Ag–/IgM–
qSOFA (out of 3)	2.0	1.7	1.6
SIRS (out of 4)	3.0	2.1	1.9
MEWS (out of 11)	7.6	6.8	6.6
UVA (out of 9)	3.8	2.1	1.4

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