1409

SCHOOL-BASED ANTIMALARIA INTERVENTIONS EFFICIENTLY REDUCE COMMUNITY-LEVEL *PLASMODIUM FALCIPARUM* PREVALENCE IN A HIGH-TRANSMISSION SETTING: A MATHEMATICAL MODELING STUDY

Andrea Geri Buchwald[1], Jenna E. Coalson[2], Lauren M. Cohee[1], Mark L. Wilson[3], Laura L. Hungerford[4], Terrie E. Taylor[5], Miriam K. Laufer[1]

[1]University of Maryland Baltimore, Baltimore, MD, United States, [2]The University of Arizona, Tucson, AZ, United States, [3]University of Michigan, School of Public Health, Ann Arbor, MI, United States, [4]Virginia-Maryland College of Veterinary Medicine, Blacksburg, VA, United States, [5]Michigan State University College of Osteopathic Medicine, East Lansing, MI, United States

Global antimalaria scale-up has significantly decreased malaria morbidity and mortality in many regions of the world. However, countries with the highest *Plasmodium falciparum* transmission have seen the slowest declines in malaria disease incidence and infection prevalence. In Malawi, uptake of antimalaria interventions is high among groups with the highest burden of disease (pregnant women and under-five children). Most *P. falciparum* infections, however, occur in school-aged children (5-15 years old) and prevention efforts have not been effective at reducing infection prevalence among this group. School-aged children are also less likely to receive anti-*P. falciparum* treatment, as many school-aged children's infections are asymptomatic. By targeting this highly-infected group, school-based interventions may be a cost-effective approach to reduce population-level transmission. We used a differential equation-based, deterministic, compartmental simulation model to evaluate how school-based interventions might affect community-level *P. falciparum* prevalence compared to current strategies (targeting pregnant women and under-five children) or community-based application of mass drug administrations (MDA) and mass screen-and-treat (MST) programs. The model, which accounted for asymptomatic infections, was fit to data from cross-sectional surveillance and longitudinal cohort studies in southern Malawi. We aimed to achieve a 50% decrease in community malaria prevalence while minimizing the number, frequency, and coverage of treatment campaigns as well as minimizing the number of individuals treated. The decrease in community infection prevalence was greatest when interventions were distributed randomly throughout the community. However, school-based interventions led to greater decreases in prevalence than MDA or MST targeting under-five children and pregnant women. While school-based interventions may not produce the greatest decrease in community infection prevalence, their comparative efficiency and potential cost-effectiveness may make them a better strategy for future malaria control programs.

1410

PROBABILISTIC MODEL OF *PLASMODIUM VIVAX* RELAPSE FOR IMPROVED ESTIMATION OF TREATMENT EFFICACY USING TIME-TO-RECURRENCE DYNAMICS

James Watson[1], Aimee R. Taylor[2], Caroline O. Buckee[2], Mallika Imwong[3], Cindy S. Chu[1], Nicholas J. White[1]

[1]Oxford University, Oxford, United Kingdom, [2]Harvard University, Boston, MA, United States, [3]Mahidol University, Bangkok, Thailand

Plasmodium vivax causes most of the malaria outside Sub-Saharan Africa. Vivax malaria in South East Asia exhibits the frequent relapse phenotype, with infections recurring at short intervals (3-4 weeks). As relapses from liver stage hypnozoites cannot be distinguished genetically from reinfections the radical curative efficacy of primaquine can only be characterized properly with placebo controlled trials (i.e. randomization to no radical cure) which is not possible in many countries where the standard of care includes radical cure. Data from a three way randomized controlled trial (n=600) comparing chloroquine (a slowly eliminated blood stage drug), chloroquine and primaquine together, and artesunate monotherapy (which is rapidly eliminated) were used to fit a Bayesian hierarchical model to the times to recurrent episodes (>1300 episodes recorded) conditioned on the treatments given. The relapse hazard rate is non-constant after acute vivax malaria. Tropical frequent relapse *P. vivax* on the Thai-Myanmar border area was well described by a triple mixture model with a relapse component (exponential waiting time), a `rapid' relapse component (normally distributed), and a `slow' relapse component (exponential waiting time). Time to recurrent episode provides discriminatory information between relapse and reinfection, thus providing a probabilistic framework for adjusting radical cure efficacy.

1411

NEUTROPHILS INFLUENCE ANTIGEN PRESENTATION DURING IMMUNE RESPONSE TO LIVE ATTENUATED LEISHMANIAL VACCINE

Parna Bhattacharya[1], Pradeep Dagur[2], Nevien Ismail[1], Kazuyo Takeda[1], Ranadhir Dey[1], Hira Nakhasi[1]

[1]Food and Drug Administration, Silver Spring, MD, United States, [2]National Institutes of Health, Rockville, MD, United States

No vaccine exists against Visceral Leishmaniasis. We have earlier reported the protective role of live attenuated centrin gene deleted *L. donovani* (*LdCen*$^{-/-}$) parasite vaccine in animal models. *LdCen*$^{-/-}$ induces strong innate immunity leading towards protective Th1 response. Neutrophils are indispensable for first line of defense against pathogens. Additionally, role of neutrophils as antigen presenting cells (APCs) has been demonstrated in enhancing virus based vaccine induced responses and tuberculosis vaccination. Emerging evidence suggests that neutrophils should be considered as important modulators of leishmaniasis. Although studies have shown the importance of neutrophils during *Leishmania* infection, none have shown its role in development of specific response to a Leishmania vaccine. Hence, we studied the role of neutrophils as APCs in the induction of specific response to *LdCen*$^{-/-}$ intradermal vaccination. Increased neutrophil migration with heightened microbicidal attributes was observed after infection with *LdCen*$^{-/-}$ compared to *LdWT in vitro*. *LdCen*$^{-/-}$ infection induced TLR activation and *NF-KB* pathway induction in macrophages was found to be essential for higher neutrophil recruitment in response to infection . Likewise, *in vivo* study showed that intradermal injection with *LdCen*$^{-/-}$ induces higher neutrophil recruitment at the site of injection (ear) and lymph nodes compared to *LdWT* parasites. Phenotypic characterization of recruited dermal neutrophils revealed the presence of heterogeneous neutrophil population. Low density neutrophils sort selected from *LdCen*$^{-/-}$ infected mice exhibited attenuated expression of pro-parasitic molecules compared to *LdWT*. Adoptive transfer of *LdCen*$^{-/-}$ parasite bearing neutrophils were able to induce heightened Th1 differentiation in visceral organs compared to *LdWT* thereby highlighting the robust APC feature of neutrophils in *LdCen*$^{-/-}$ induced immunity. Also, the engulfment of *LdCen*$^{-/-}$ parasitized neutrophil by dendritic cells (DCs) enhanced Ag presentation capability of DCs compared to *LdWT*. Thus neutrophils play novel role in shaping early vaccine immunity.

1412

PHARMACOKINETIC-PHARMACODYNAMIC ASSESSMENT OF THE SAFETY OF FEXINIDAZOLE FOR THE TREATMENT OF HUMAN AFRICAN TRYPANOSOMIASIS

James Watson[1], Nathalie Strub-Wourgraft[2], Antoine Tarral[2], Joel Tarning[1], Nicholas J. White[1]

[1]Oxford University, Oxford, United Kingdom, [2]Drugs for Neglected Diseases initiative, Geneva, Switzerland

Fexinidazole is a new oral treatment for *Trypanosoma brucei* (*T.b. gambiense*) human African trypanosomiasis (g-HAT). Fexinidazole *in vitro* is also active against other human kinetoplastid parasites, *T. cruzi* and *Leishmania donovani,* the causative agents of Chagas disease and visceral leishmaniasis, respectively. During a dose-ranging study conducted