RESOURCE HUB *Correspondents*

American Society of Tropical Medicine and Hygiene (ASTMH)
Sixty-sixth Annual Meeting

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MESA Correspondents bring you cutting-edge coverage from the 66th ASTMH Annual Meeting

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The Baltimore Convention Center

Baltimore, Maryland, USA

The MESA Alliance would like to acknowledge Krystal Birungi and Krijn Paaijmans for their crucial role in the reporting of the sessions.

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Background

There are a growing number of conferences being held globally where emerging evidence is shared in the field of malaria and related topics like entomology, parasitology, and health systems. These meetings offer the opportunity to hear cutting edge science and lessons learned from peers and mentors, in both broad and niche disciplines. As calendars and budgets are limited, those who could benefit from participating are often unable to attend. On the other hand, those who do participate, sometimes miss pertinent talks due to parallel scheduling of scientific sessions and side meetings.

With the overarching objective of sharing key findings with a global audience and also providing opportunities to emerging researchers, MESA identifies relevant conferences for the malaria community and reviews the scientific program to curate lists of talks to be covered by the *MESA Correspondents program*. Summaries of the highlights and technical content of the presentations are produced and shared through MESA's communication channels and those of strategic communications partners.

Session 2: New Tools for Malaria Vector Control

Session 2 of the 66th annual meeting focused on new tools for malaria vector control. All the presentations strongly emphasized the need for new tools to combat issues of resistance to currently available methods, and presented exciting alternatives in development that could make a difference in the near future.

Sarah Rees from Innovative Vector Control Consortium (IVCC) in Liverpool, UK, presented IVCC's development pipeline. IVCC is working with partners to develop a range of sustainable vector control products including novel insecticides and attractive targeted sugar baits. She shared insight into the process and challenges involved in the formulation and manufacturing of new chemical vector control products. She also mentioned Clothianidin and Chlorfenapyr, two exciting new chemicals that "begin to give us opportunities for insecticide resistance management".

John Lucas from Sumitomo Chemical Company in Tokyo, Japan, presented Clothianidin- an exciting new vector control tool. He described the development of Clothianidin, repurposed from agricultural use for vector control. Clothianidin is a neonicotinoid, a new class of insecticide. With partners, Sumitomo developed clothianidin as an indoor residual spray (IRS) and SumiShield 50WG is now both the first vector control product to pass the new WHO prequalification for a vector control product and the "first WHO recommended new mode of action chemistry for IRS in forty years". You can read more about WHO prequalified vector control products here.

Susanne Stutz from BASF, Germany, spoke about Second generation LLINs to control resistant mosquitoes - Interceptor G2. Their work is focused on the combination of the new active ingredient Chlorfenapyr with the existing pyrethroid alphacypermethrin to create a new generation of "dual" long lasting insecticidal nets (LLINs). Chlorfenapyr is non-neurotoxic, it disrupts energy generation in the mitochondria. Suzanne also discussed some of the experimental challenges when testing novel insecticides. Hut studies have produced promising results and a WHO recommendation is currently being sought for it.

Amir Galili from Westham Co, in Tel Aviv, Israel, presented the development of a new tool for vector control: Attractive Targeted Sugar Bait (ATSB). ATSB is an "attract and kill" method for vector control. Amir's presentation focussed on the challenges in developing a novel tool, which doesn't follow the mold of other types of tools. The ATSB under development comprises a combination of fruit extract and volatile semiochemicals to first attract the mosquitoes; the active ingredient Dinotefuran to kill the mosquitoes; all delivered in a flat bait-station that can be hung on a wall. Bait stations were prototyped and tested in Mali with the University of Bamako and support from IVCC.

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Session 62: Malaria Rapid Diagnostic Testing: Understanding and Managing the Threat of PfHRP2/3-Negative *Plasmodium falciparum*

Session 62 of the 66th Annual meeting focused on understanding and managing the threat of PfHRP2/3 – negative *Plasmodium falciparum* parasites which cannot be detected using HRP-based malaria rapid diagnostic tests (RDTs). Emphasis was put on the fact that, where PfHRP2/3 deletions occur, the current and most frequently used RDT could face reduced efficacy in the near future. Therefore, there is a pressing need to develop new diagnostic tests, especially considering that such tests undergo a lengthy development process before they can be brought to market.

Thomas E Wellems from NIAID in Bethesda, United States, talked about the discovery of the HRP2 antigen and its journey from bench to bedside. Thomas described the process of development, dissemination, and use of the PfHRP2/3 antigens in Malaria Rapid Diagnostic Tests (RDTs), which have provided a good point of care diagnostic tool to guide the use of antimalarial drugs. However, PfHRP2/3 deletions in *P. falciparum* parasites are increasingly being reported in multiple studies in different sites, such as the Amazon Region of Peru or the Democratic Republic of the Congo. Thomas posed the following question: "*Are there alternative antigens with the desirable features of both PfHRP2 and LDH (lactate dehydrogenase, another antigen currently targeted by some RDTs) combined?*" Results are showing that using LDH antigens or *Plasmodium falciparum* insulin degrading enzyme homolog (PfIDEh) antigens in an immuno-PCR system can detect parasites with high sensitivity (less than one parasite per microliter). He concluded that using alternatives to HRP2/3 together with novel methods to improve sensing of bound antibodies would greatly improve test sensitivity of malaria RDTs.

Jane Cunningham from the World Health Organization in Geneva, Switzerland, presented Pfhrp2/3 gene deletions and asked *how big is this problem*? She presented the work that WHO has been doing to document and guide studies concerning Pfhrp2/3 gene deletions. She described the process through which the WHO created a Malaria Threats Map of Pfhrp2/3 gene deletions, an online mapping tool showing the distribution of Pfhrp2/3 gene deletions around the world. She also presented the guidelines that WHO has put in place to guide the detection and reporting of Pfhrp2/3 gene deletions, differentiating between a true negative malaria Rapid Diagnostic Test (RDT) result and a negative result due to deletion, and the steps to be taken based on the results. She discussed the need to balance the risk of missed cases of *P. falciparum* malaria due to Pfhrp2/3 deletions against the equally real risk of missing cases by using a less sensitive RDT. Jane also cautioned the longer-term risk of eroding confidence in antigen-based malaria testing until a comparable test is available.

Jonathan B Parr from the University of North Carolina, United States, presented new techniques for identifying Pfhrp2/3 deletions and understanding their evolution. The work involved a detailed comparison of six published PCR protocols to test for Pfhrp2/3 gene deletions. Results showed that all assays vary in their limits of detection, extension temperature seems to have an effect on sensitivity and amplification of the paralogous gene can cause spurious results. All of these technical challenges could lead to misclassifying Pfhrp2/3 gene deletions. He stated that accurate molecular confirmation of Pfhrp 2/3 deletions is challenging without careful laboratory protocols, but that alternative approaches such as luminex-based platforms are under development.

Rhoel D. Dinglasan from the University of Florida, United States, presented novel *P. falciparum* biomarkers: Discovery and testing results. The aim of this work was to develop a lateral flow immunoassay that does not rely on using a blood sample. Rhoel and his team set out to find a new biomarker for malaria that is present in non-blood biofluids, is expressed in both asexual and

gametocyte stages, and is conserved across the five *Plasmodium* species which infect humans. He shared the results from a prototype saliva-based malaria rapid diagnostic test that uses the *Plasmodium* secreted sexual stage protein 17 (PSSP17) as a biomarker, and is currently being tested with saliva taken from "asymptomatic" children from several schools in Cameroon. The initial results show that the test is able to identify sub-microscopic infections in schoolchildren, but it's difficult to estimate the true limit of detection with the current samples.

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Session 121: School-Based Malaria Interventions: Impact on Health and Transmission

Session 121 of the 66th Annual Meeting focused on School-Based Malaria Interventions and their impact on health and transmission. All the speakers agreed that school-age children are a demographic group most affected by malaria infections and that contribute the most to malaria transmission. They called for targeted malaria interventions within this group as a way to reduce malaria transmission in the community, and encouraged scientific discussion on how this can be advanced.

Don Mathanga from the College of Medicine of the University of Malawi in Blantyre, talked about malaria in school-age children and its impact on health and education. He highlighted that school-age children are a group that uses interventions such as long-lasting insecticidal nets (LLINs) much less compared to other age groups and have limited access to treatment. He presented the results from a cluster-randomised trial in 58 primary schools in Malawi that aimed to evaluate the impact of school-based malaria case management on absenteeism, well-being, health, and education. The intervention involved training teachers to use rapid diagnostic tests (RDTs) and treat malaria-infected children using a 'learner treatment kit'. Even though the results showed no significant impact on daily attendance or in malaria parasitaemia, anaemia, and educational performance, they showed significant differences in the primary point of access to care: In the intervention schools fewer children reported that shops and health centres were their primary point of access to care for a febrile event compared to children in schools in the control group. These results add value to the idea of improving access to treatment in this age group through schools.

Bronner Gonçalves from the London School of Hygiene and Tropical Medicine, United Kingdom, presented recent transmission studies in Burkina Faso and reviewed the evidence supporting the significant role of school-age children in malaria transmission. He presented data from a study that aimed to quantify age-specific infectiousness prevalence and mosquito exposure by using membrane feeding infectivity surveys. The results showed that school-age children (5-15 years old) had the highest infectiousness prevalence, but since adults had higher mosquito exposure, the result was that school-age children and adults contributed almost equally to onward transmission in the study area.

Catherine Maiteki-Sebuguzi from the Uganda National Malaria Control Programme presented the results from the START-IPT trial, which aimed to evaluate the impact of IPT (intermittent preventive treatment) with an ACT (artemisinin combination therapy) in schoolchildren on malaria transmission indicators at the community level. In the schoolchildren in intervention schools, there was a lower proportion of RDT positive and microscopy positive results, together with less history of fever. Parasite prevalence at the community level was not statistically significant between the control and intervention clusters, but a positive trend was seen. Catherine concluded that the results suggest that IPT for schoolchildren benefited the individual children and may reduce malaria transmission within the community. She also shared some of the challenges faced by this form of intervention, such as community sensitization and recruitment through schools; as well as some questions for future studies, such as how to achieve high coverage rates or how to integrate the intervention with other school-based programmes.

Lauren M. Cohee from the University of Maryland School of Medicine in the United States, presented the results of a systematic review of school-based malaria treatment interventions and considerations of key factors in designing future interventions. They performed pooled analyses of data from 12 randomised trials assessing the effect of antimalarial treatment to "asymptomatic" school-age

children across Africa. The evidence suggests that treating asymptomatic schoolchildren decreases the prevalence of malaria infection and anaemia, with the greatest effects seen with ACTs. The evidence also suggests some potential to decrease malaria transmission and improve educational outcomes, but more studies are needed since educational outcomes are difficult to measure. However, there are remaining questions, such as if treating “asymptomatic” school-age children is appropriate for all transmission settings or if there’s a need to tailor the treatment or age groups based on the epidemiological setting.

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Session 175: Malaria: Mosquito Transmission and Interruption

Session 175 of the 66th Annual Meeting was about Mosquito Transmission and Interruption. The talks in this symposium focused on the role of mosquitoes in malaria transmission and ways transmission can be controlled and interrupted.

Guofa Zhou from the University of California at Irvine, United States and the Kenya Medical Research Institute, Kisumu, Kenya, gave a presentation on malaria transmission at three sentinel sites in Western Kenya from 2002 to 2016: the resurgence and causality analysis. This study focused on identifying causes for sustained malaria transmission and resurgence in three villages in Kenya, which had all received three rounds of LLIN (Long Lasting Insecticide-treated Nets) distribution. Methods included modelling malaria prevalence and vector densities. The results showed that changes in malaria prevalence over time were almost entirely due to the mass distribution of new LLINs, insecticidal decay effect and loss of net physical integrity, while changes in vector density were most affected by insecticide resistance, climatic factors and mass distribution of LLINs. He concluded that the distribution of new LLINs to replace old nets remains a useful malaria control strategy in areas with moderate insecticide resistance.

Anais Bompard from the Institute of Research for Development (IRD) in Montpellier, France, presented on High *Plasmodium falciparum* oocyst loads in naturally infected mosquitoes in Africa. In this study, they collected mosquitoes, parasites in mosquitoes, and parasites in the human population to better understand malaria transmission in two villages in Burkina Faso. The study found that oocyst load in naturally infected mosquitoes was higher than expected and some mosquitoes were seen with an 'extreme' oocyst load (5% had more than 50 oocysts and 2% had more than 100 oocysts). They calculated between 5 and 18 oocysts per infectious bite in the study villages. They also found an association between parasite exposure and malaria prevalence in humans, although more data are needed from different study sites.

Carlos Chaccour from the Barcelona Institute for Global Health (ISGlobal), presented results on targeting cattle for malaria elimination: marked reduction of *Anopheles arabiensis* survival for over six months using a slow-release ivermectin formulation. Ivermectin is an endectocide and its potential impact on malaria transmission is mostly driven by its permanence in the blood which mosquitoes feed on. The study demonstrated that veterinary slow-release formulations can safely deliver ivermectin concentrations for over 6 months with a significant impact on mosquito survival, thus presenting a viable option to complement personal protection in malaria elimination efforts. He cautioned that ivermectin could only be used as a complementary method used in combination with personal protective tools.

Cielo Pasay from the Clinical Tropical Medicine, QIMR Berghofer Medical Research Institute in Brisbane, Australia, talked about investigating the activity of the macrocyclic lactones ivermectin and moxidectin against malaria vectors. The aim of the study was to investigate the efficacy of ivermectin and moxidectin against *Anopheles farauti*, a partially zoophagic malaria vector. Experiments involved injecting pigs subcutaneously with 600 micrograms/kg of the drugs and testing mosquito mortality with direct feeding assays. The findings were that ivermectin was lethal to *Anopheles farauti* for up to two weeks. Moxidectin, however, was not lethal to mosquitoes *in vivo*. Cielo discussed the implications of these results, being that ivermectin could be used as a push-pull strategy "*where LLINs and IRS (indoor residual spraying) push mosquitoes away from humans, and insecticide zoo-prophylaxis pulls hungry mosquitoes to an alternative death*".

Fitsum Tadesse from the Armauer Hansen Research Institute in Addis Ababa, Ethiopia, discussed the contribution of symptomatic and asymptomatic infections to the infectious reservoir of *Plasmodium falciparum* and *Plasmodium vivax* in Ethiopia. The study showed that asymptomatic infections are highly prevalent: they are responsible for the majority of *Plasmodium vivax* infectious reservoirs in Ethiopia and they are also the major contributors to the infectious reservoir of *Plasmodium falciparum*. Fitsum discussed that early identification and treatment of asymptomatic infections could be an important factor in eliminating malaria.

Jennifer Stevenson from the Department of Molecular Microbiology and Immunology, Johns Hopkins Bloomberg School of Public Health in Baltimore, United States, presented outdoor primary and 'secondary' vectors contributing to residual transmission in Zambia. She presented data from entomological surveillance studying residual transmission in outdoor mosquitoes in Zambia in an attempt to identify their contribution to the continuing malaria prevalence. They identified some outdoors mosquito species not previously expected to act as malaria vectors, and different patterns between *Anopheles arabiensis* host-seeking behaviour indoors and their activity outdoors. She concluded by sharing some innovative ideas being tested in a semi-field system to control outdoor biting mosquitoes, including evaluating a controlled release spatial repellent and testing the acceptability and efficacy of screening outdoor cooking areas. Further studies are required to fully understand the behaviour of these outdoor species and find ways to control them if malaria elimination is to be achieved.

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