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NEWS & VIEWS

38th Issue | January 2024

WORLD MALARIA REPORT 2023

Interview

Dr Rajpal Singh Yadav,
President, Academy of Public Health Entomology
Chairman, ICMR Expert Group on Evaluation of Vector Control Products

Editorial

Dear Readers,

New Year greetings from the MERA-India team. We are happy to share the thirty-eighth issue of the newsletter, "News & Views".

Our achievements in the past year in support of India's goal of eliminating malaria and connecting with the research community have culminated in new findings from the completed projects. Under the MERA-India previous call for proposals, we received projects related to artificial intelligence (AI)-powered malaria surveillance, diagnostics, vector control, and a special call for young malaria researchers. The projects funded during the first call are nearing completion and the outcomes of these studies will be published soon. To facilitate an exchange of ideas, avenues for networking among researchers, and skill enhancement for field staff, several lectures and training sessions were organized last year. We hope to continue with the same enthusiasm in the coming year.

The World Health Organization (WHO) has released the long-awaited World Malaria Report 2023, which provides a detailed account of global malaria incidence and deaths. This year's report includes a WHO recommendation for improved insecticide-treated nets (ITNs) due to increasing pyrethroid resistance. Two vaccines (RTS,S/AS01 and R21/Matrix-M) were recently recommended by WHO to prevent malaria in individuals living in high-risk areas. For the first time, a dedicated chapter focuses on the intersection between climate change and malaria in this report. Climate change is one of many threats to the global response to malaria, as millions of people continue to miss out on the services they need to prevent, detect, and treat the disease.

In the last month’s lecture series, Dr Sunil Parikh from Yale School of Public Health, USA gave a talk on ‘Optimizing antimalarial regimens to maximize efficacy and limit resistance in Africa’, with a focus on the existing drugs and addressing the bottlenecks in the treatment of malaria. The highlights from the informational lecture have been enclosed in this newsletter as a summary.

The “Malaria Scientists to Watch” section encompasses an insightful and enriching interview with an eminent malariologist, Dr Rajpal Singh Yadav, President of the Academy of Public Health Entomology, Chairman, ICMR Expert Group on Evaluation of Vector Control Products, and Retired Scientist, Department of Control of Neglected Tropical Diseases, World Health Organization, Geneva.

The "Research in Spotlight" section summarizes three cutting-edge research articles relevant to malaria. The first article by Garg *et al.* assessed afebrile malaria through mass

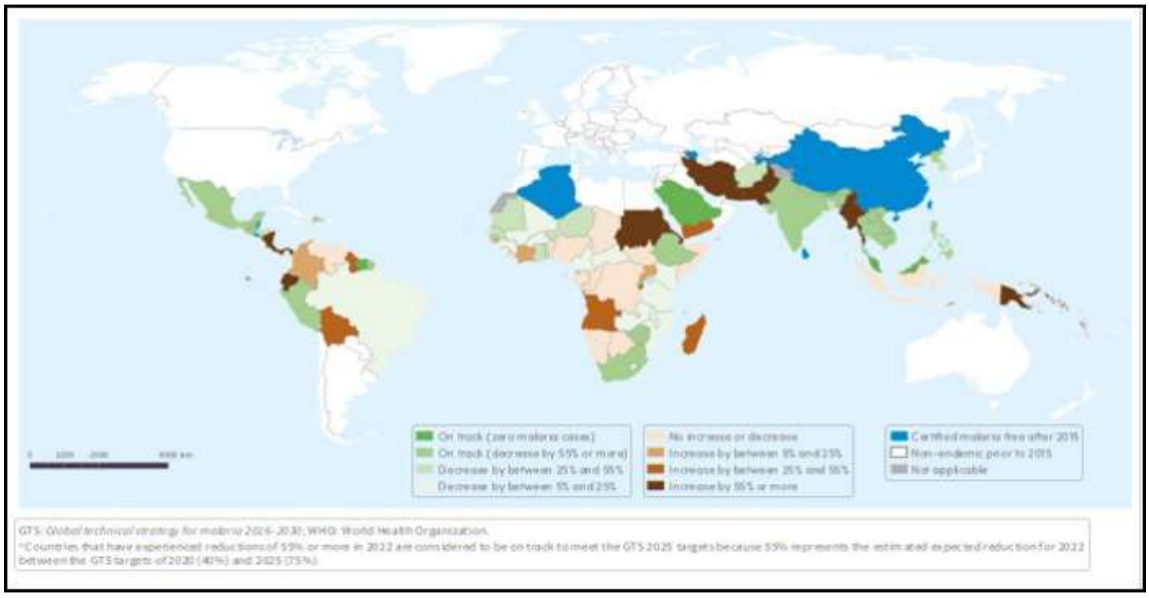
screening in the high-malaria-burden region of Chhattisgarh, India. In the second article, Pourhashem *et al.* evaluated a new synthetic fusion antigen containing cd loop and HAP2-GCS1 domain (cd-HAP) of *Plasmodium falciparum* Generative Cell Specific 1 (PfGCS1) antigen as a transmission-blocking vaccine candidate. In the third article, Mihreteab *et al.* reviewed 3-day courses of artemisinin-based combination therapy for uncomplicated malaria and the prevalence of artemisinin-resistant HRP2-negative malaria in Eritrea.

Further, the "Malaria Through the Lens of Researchers" section showcases an image submitted for the MERA-India Image Competition 2022 by Ms Kripa PK, PhD scholar at ICMR-National Institute of Malaria Research, Field Unit, Chennai.

We hope that you will find this issue engaging and fascinating. Please write to us for any feedback or suggestions regarding the newsletter's content at meranewsletter@gmail.com.

With best wishes,
MERA-India team

Malaria News: WHO World Malaria Report 2023



The WHO recently released the World Malaria Report 2023, which provides an overview of global malaria control and elimination trends for the year 2022, and outlines a path forward to meet emerging challenges. According to the report, there were an estimated 249 million malaria cases in 85 malaria-endemic countries and areas (including French Guiana) in 2022, which is an increase of 5 million cases from 2021. The WHO African Region accounted for about 94% of cases worldwide, with an estimated 233 million cases in 2022. Meanwhile, the WHO South-East Asia Region accounted for about 2% of malaria cases globally. The report also highlights that the elimination of malaria has gained momentum in many countries as they approach the milestone of zero indigenous malaria cases. Between 2000 and 2022, 25 countries that were malaria-endemic in 2000 have achieved three consecutive years of zero indigenous malaria cases. Twelve of these countries were certified malaria-free by WHO.

The report covers therapeutic efficacy studies that track clinical and parasitological outcomes among people receiving antimalarial treatment. It notes that parasite resistance to antimalarial drugs has been reported in the WHO African Region and some regions of WHO Southeast Asia between 2015 and 2022. Additionally, there has been a significant increase in insecticide resistance in malaria-endemic countries. This year, the WHO issued a strong recommendation for the deployment of pyrethroid-chlorfenapyr insecticide-treated mosquito nets (ITNs) versus pyrethroid-only ITNs to prevent malaria in adults and children in areas where mosquitoes have become resistant to pyrethroids. Since 2019, Ghana, Kenya, and Malawi have been delivering the malaria vaccine RTS,S/AS01 (RTS,S) through the Malaria Vaccine Implementation Programme, and many more countries have expressed interest in receiving this vaccine. Currently, 18 countries have been approved to receive support for the malaria vaccine rollout by Gavi. Moreover, in October 2023, the R21/Matrix-M (R21)

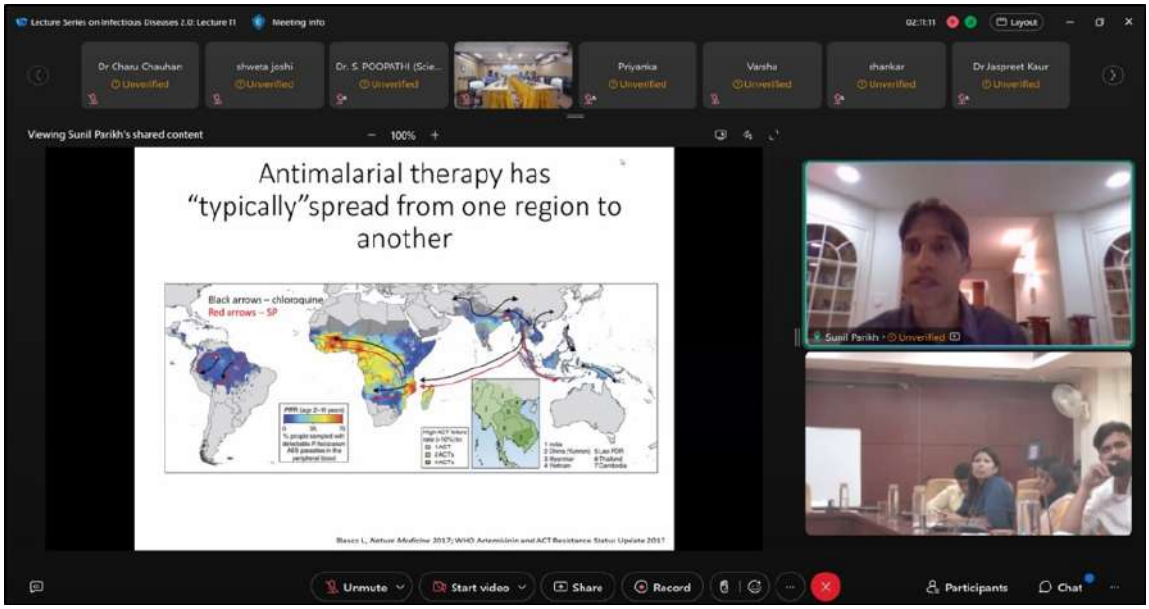
malaria vaccine became the second vaccine recommended by WHO to prevent malaria in children living in areas of risk.

The report also highlights that climate change is the single biggest health threat facing humanity. It threatens to derail progress in global health by affecting livelihoods, increasing the risks of harmful exposures to particulates, pathogens, and disease, overburdening health systems, and widening existing inequalities. Climate change is not just a singular threat but a major multiplier of other threats. Despite progress in the fight against malaria, conflict, and humanitarian crises, resource constraints, and biological challenges such as drug and insecticide resistance continue to hamper progress. The report emphasizes the need for sustained and collective efforts to make interventions accessible to the most vulnerable populations and in hard-to-reach areas. It also highlights the importance of continued investments in research and development to build new tools to mitigate the risk of vector-borne diseases.

The full report is available at: https://www.who.int/publications/i/item/9789240086173

ICMR-NIMR & MERA-India Activity

Lecture Series on Infectious Diseases 2.0: Lecture 11 by Dr Sunil Parikh



The eleventh speaker featured in the Lecture Series on Infectious Diseases 2.0 was Dr Sunil Parikh. Holding an MD degree from Johns Hopkins University School of Medicine, Dr Parikh completed his residency training at Beth Israel Deaconess Medical Center and has been affiliated with the Department of Epidemiology of Microbial Diseases at the Yale School of Public Health since 2012. His research primarily focuses on malaria in sub-Saharan Africa, where he has been involved in various projects across countries like Uganda, Burkina Faso, and Nigeria, exploring early host immune responses, human genetics, and treatment.

The introduction to the audience was provided by Dr Sachin Sharma, Chief Consultant at MERA-India, setting the stage for Dr Parikh's insightful talk. Dr Parikh's presentation centered on "Optimizing antimalarial regimens to maximize efficacy and limit resistance in Africa." He began by providing an overview of the current global malaria situation, emphasizing the stagnation in deaths since 2015 despite global efforts. He highlighted the slow growth of the toolbox for malaria control, indicating its insufficiency. Dr Parikh pointed out that existing drugs focus on the blood stages of parasite development rather than addressing bottlenecks. Using a complex case study from high transmission areas, Dr Parikh illustrated how various factors, including co-infection, drug interactions, pharmacogenetics, malnutrition, drug concentration, drug resistance selection, and host immune responses, determine treatment success. He emphasized the need for alternate strategies in Africa, considering the limitations of existing artemisinin-based combination therapies (ACTs). Dr Parikh underscored the inevitability of drug resistance in malaria and

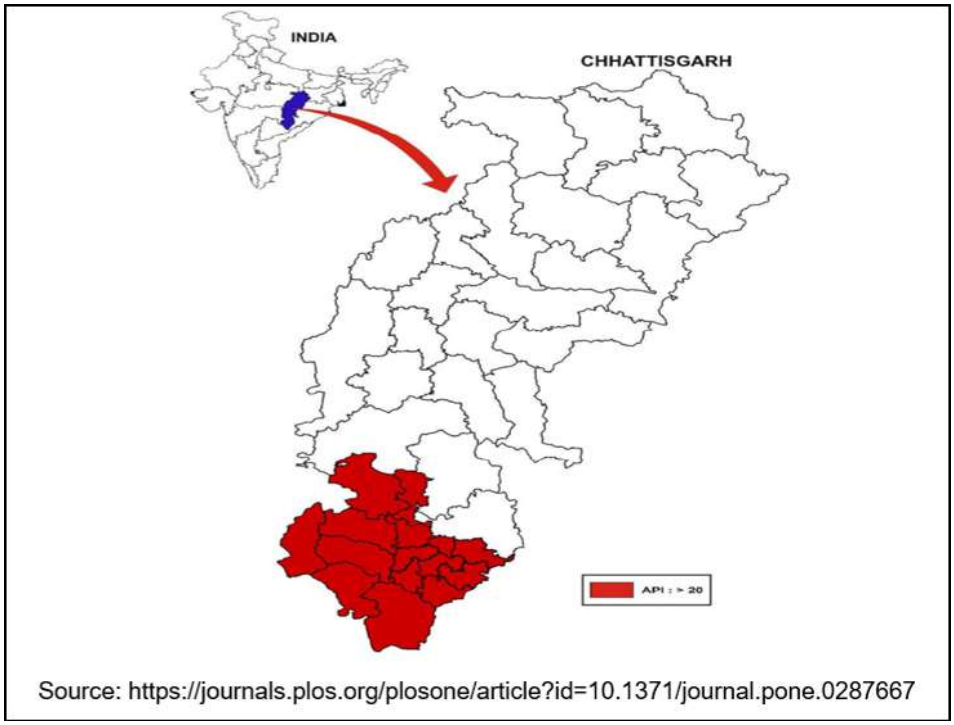
emphasized the importance of monitoring and understanding its evolution. He suggested that collaborations between clinicians, epidemiologists, pharmacologists, pharmacometricians, mathematical modelers, and bench scientists are crucial for conducting studies to design and test "optimal" dosing strategies for current and future antimalarials.

The session concluded with a question and answer session, during which Dr Parikh provided insightful responses. Dr Sachin Sharma wrapped up the session with a Q&A session and a vote of thanks to the speaker and attendees.

The recording of this lecture is available on the MERA-India website (https://www.meraindia.org.in/lecture-series).

Research in Spotlight

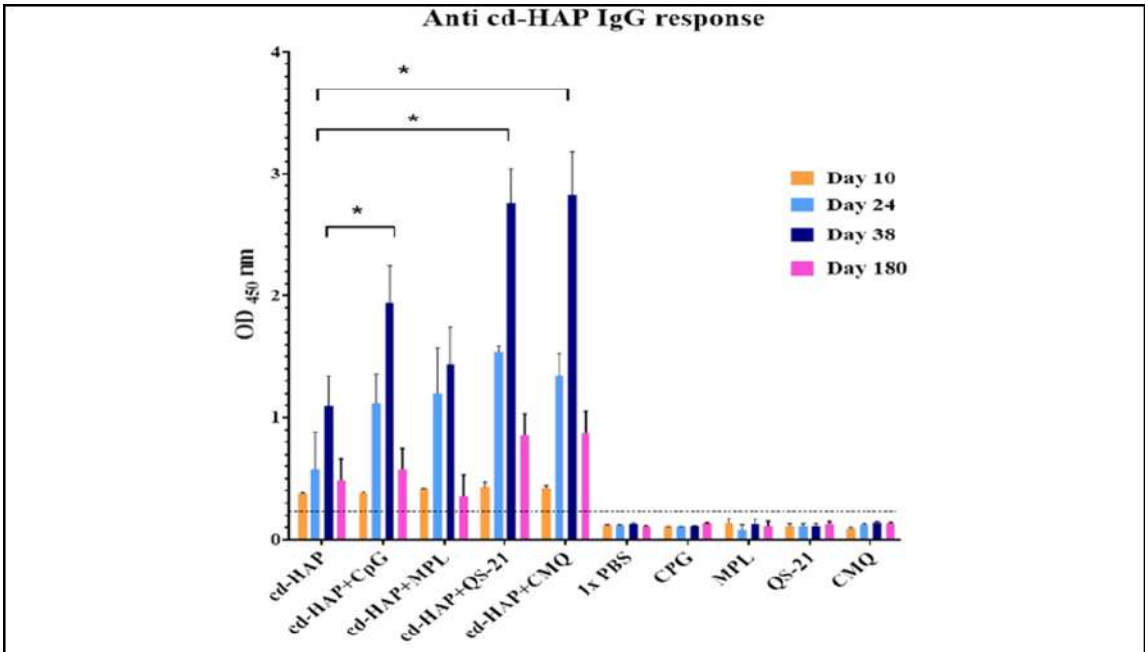
Garg *et al.*, *PLoS ONE.* (2023): Assessing afebrile malaria and bed-net use in a high-burden region of India: Findings from multiple rounds of mass screening



Source: https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0287667

The Global Technical Strategy for Malaria Elimination 2016-2030 has identified asymptomatic malaria as a significant challenge. This is because such infections are not evident to the health system and usually remain undiagnosed. Asymptomatic infections contribute significantly to the malaria transmission cycle, recurrent episodes of symptomatic parasitemia, chronic anemia, maternal and neonatal mortality, co-infection with invasive bacterial diseases, and cognitive impairment. Asymptomatic malaria is prevalent in malaria-affected regions worldwide, including India, where many cases of malaria-positive individuals were found to be asymptomatic and afebrile. This study conducted in Chhattisgarh focused on afebrile malaria, the most common type of asymptomatic malaria. The study aimed to determine the prevalence of afebrile malaria and its determinants, as well as the rate of LLIN use by individuals. Six repeated cross-sections corresponding to the six waves of the Mass Screening and Testing (MSaT) implemented in 2020, 2021, and 2022 in the high-malaria-burden region of Chhattisgarh were analyzed. A structured questionnaire was used to interview individuals. The study found that malaria prevalence in the afebrile population varied from 0.6% to 1.4% across the different waves of mass screening. In contrast, malaria positivity among febrile individuals was greater than 33% in each wave. Afebrile malaria contributed to 19.6% to 47.2% of the overall malaria burden in the region. Moreover, the indigenous communities (scheduled tribes) were more susceptible to malaria, including afebrile malaria, while individuals using LLINs were less likely to be affected by afebrile malaria.

Pourhashem *et al., Malaria Journal.* (2023): Evaluation of a new fusion antigen, cd loop and HAP2-GCS1 domain (cd-HAP) of *Plasmodium falciparum* Generative Cell Specific 1 antigen formulated with various adjuvants, as a transmission blocking vaccine

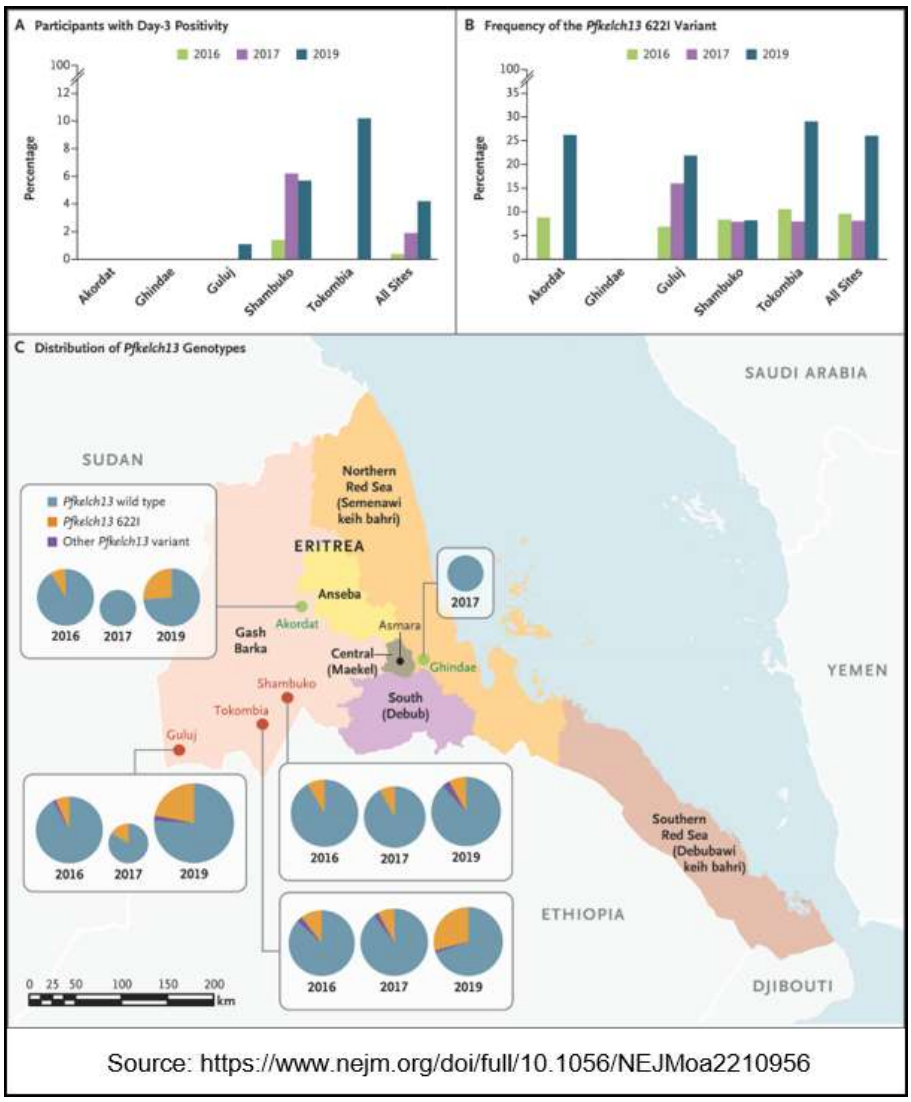


Source: https://malariajournal.biomedcentral.com/articles/10.1186/s12936-023-04798-7#Abs1

Malaria is a major global health challenge, and the development of transmission-blocking vaccines (TBVs) is a priority for its elimination and eradication. *Plasmodium falciparum* Generative Cell Specific 1 (PfGCS1) has shown promise as a TBV candidate because it is essential for gamete fertilization. The HAP2-GCS1 domain and cd loop of this antigen can induce antibodies that partially inhibit the transmission of *P. falciparum*. In this study, a new synthetic fusion antigen containing the cd loop and HAP2-GCS1 domain (cd-HAP) of PfGCS1 has been evaluated as a transmission-blocking vaccine candidate. The structure of the new fusion protein was analyzed to confirm that it contains common epitopes with the native form of PfGCS1 by examining the profile of naturally acquired IgG antibodies to the cd-HAP antigen in Iranian individuals infected with *P. falciparum*. The immunogenicity of cd-HAP was then evaluated in BALB/c mice using different adjuvant systems such as CpG, MPL, QS-21, and a combination of them (CMQ).

The cd-HAP antigen formulated with a combination of adjuvants produced the highest levels and titers of IgG in mice that could reduce oocyst intensity and infection prevalence by 82%. This shows that the cd-HAP antigen formulated with a combination of the adjuvants (CMQ) could be a promising formulation to develop a PfGCS1-based transmission-blocking vaccine.

Mihreteab *et al.*, *N Engl J Med.* (2023): Increasing Prevalence of Artemisinin-Resistant HRP2-Negative Malaria in Eritrea



Source: https://www.nejm.org/doi/full/10.1056/NEJMoa2210956

There is now strong evidence of partial resistance to artemisinin in *P. falciparum* in Africa. This study has identified additional areas of partial resistance in the Horn of Africa. The study's most concerning finding is the emergence and spread of a novel Pfkelch13 622I variant lineage, which was accompanied by deletions in both hrp2 and hrp3 in around 16.9% of parasites, which can lead to false negative results on HRP2-based rapid diagnostic tests. This makes these parasites more likely to go undetected by HRP2-based rapid diagnostic tests. In Eritrea, the study found evidence of partial resistance to artemisinin in patients who showed positive results on day 3 after artemisinin-based combination therapy. The percentage of these patients increased from 0.4% in 2016 to 4.2% in 2019. The study also found a significant increase in the percentage of parasites carrying the Pfkelch13 R622I mutation, from 8.6% in 2016 to 21.0% in 2019. Over the last 20 years, Eritrea has made significant strides in reducing malaria-related illnesses and deaths. This has been achieved through active government involvement and the effective implementation of measures such as insecticide-treated nets, indoor residual spraying,

larvicidal activities, and malaria case management. However, the decrease in malaria prevalence may have led to the emergence and spread of partial resistance to artemisinin. This is because the reduction in parasite genetic diversity and naturally acquired immunity has created an environment that favors partial resistance. This study conducted in Eritrea has revealed the presence of partial resistance to artemisinin in *P. falciparum*, along with deletions in both hrp2 and hrp3 in parasite populations.

Malaria Scientist to Watch:
An interview with Dr Rajpal Singh Yadav

Dr Rajpal Singh Yadav,
PhD, FNASc, FRES
President, Academy of Public Health Entomology
Chairman, ICMR Expert Group on Evaluation of Vector Control Products
Chairman, Scientific Advisory Committee, ICMR-VCRC
Sr. Dy. Director, ICMR-NIMR (retired)
Scientist, WHO HQ, Geneva, Switzerland (retired)

1. Tell us about your educational background and relevant work experience in entomology and vector control.

I graduated in biology, obtained a master's degree in Zoology with specialization in Entomology with a first class first position, and a doctoral degree in insect toxicology with the Council of Scientific and Industrial Research (CSIR) and the Indian Council of Medical Research (ICMR) fellowships from the University of Rajasthan. My training includes an epidemiology course at the School of Public Health, University of Philippines, and a British Council Fellowship on health impact assessment at the Liverpool School of Tropical Medicine, UK. From 1984 to 2008, I served at the ICMR-National Institute of Malaria Research (NIMR) and headed its Gujarat and Odisha field centres. In these roles, I led research on vector biology and control of malaria, arboviral diseases, filariasis, and Japanese Encephalitis in forested, urban, industrial, and agricultural ecosystems. Additionally, I supported the national vector-borne disease control programme, and trained health personnel on vector control and disease outbreak containment. I was a short-term staff at the WHO regional offices in New Delhi and Cairo, and WHO HQ on several occasions (1991–2007). Then in 2009, I joined the UN International Civil Service at WHO, Geneva as a senior scientist where I headed the WHO Pesticide Evaluation Scheme (WHOPES), coordinated global trials of vector control products, strengthened the capacity of several research institutions including GLP trial capacity, led development of several WHO normative guidelines and standard operating procedures (SOPs) for product testing, pesticide management, and vector surveillance and control. I was the co-chairman of the WHO Joint Action Group on the implementation of the Global Vector Control Response (2017–2023).

2. Vector control strategies may need to adapt to changing circumstances, including the emergence of new vector-borne diseases or the development of insecticide resistance especially in terms of malaria. How do you approach the development of innovative solutions and adaptability in your work?

Besides heading WHOPES, I was a member of the Secretariat of the WHO Vector Control Advisory Group established in 2013 to facilitate and guide the development of innovative vector control tools. To ensure the generation of high-quality trial data, I led the Good Laboratory Practice (GLP) certification of 8 laboratories including Vector Control Research Centre (VCRC) and NIMR, and co-chaired a WHO global team to implement the Global Vector Control Response, which was adopted as a strategy by the World Health Assembly in 2017. My unit also developed or updated several guidelines and SOPs on product testing, insecticide resistance management, vector control operations, and pesticide management.

3. How would you prioritize vector control interventions in an area with limited resources and multiple vector-borne diseases? What factors would you consider?

The WHO integrated vector management approach addresses these challenges in areas with multiple diseases or by using multiple tools against a single disease in a given target area. Starting with a situation analysis, stratifying and targeting high disease burden areas, involving local communities and other health/non-health sectors, exploring local solutions, and effective communication and advocacy for political support all have the potential of offsetting operational costs and enhancing investment in public health entomology and vector control. The available tools must be deployed judiciously with universal coverage based on scientific evidence.

4. Since you worked with WHO for many years, could you please highlight how WHO approach of conducting research is different from research at institutions/Universities?

During the first few decades of WHO's inception in 1948, WHO was funding and conducting operational research through pilot trials in many countries. The WHOPES was established in 1960 to conduct product trials, as well as a Special Programme for Research and Training in Tropical Diseases (TDR) in 1974 as a global programme of scientific collaboration. In the last two decades, WHO's focus has been to strengthen the capacity of research institutions and country programmes to plan, implement and monitor research and control operations. Unlike many other countries, the involvement of universities in India in mainstream research and training for the control of vector-borne disease is far too low.

5. Capacity building of entomology plays an important role in malaria elimination, how do you see MERA-India can contribute to this?

MERA-India can contribute by advocating with health ministries and municipal corporations for enhancement of resources for recruitment of more entomologists and developing their career pathways in order to attract and retain them; train them in management of malaria elimination and IVM strategies; promote basic and operational research on vector-borne diseases at universities, and information exchange.

Malaria Through the Lens of Researchers

In the present edition, we are showcasing yet another distinguished entry from the MERA-India Image Competition 2022. This particular submission is credited to Ms Kripa PK, a PhD scholar under the guidance of Dr Alex Eapen, associated with ICMR-NIMR, Field Unit, Chennai.

Image title: "*Anopheles stephensi* blood feeding, Eggs and Egg ridges"

A brief description of the image is as follows:
Anopheles stephensi lay eggs after blood feeding. In the laboratories, blood feeding is facilitated through an artificial membrane feeding system. The egg ridge count has been done in the laboratory and it is widely used to differentiate the subspecies (type, mysorensis, and intermediate forms) of *Anopheles stephensi*.

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Our mailing address is: meraindiaicmr@gmail.com

MERA-India Secretariat, Room No. 344, ICMR-National Institute of Malaria Research, Sector 8, Dwarka, New Delhi, 110 077, India

Telephone: 011-25307344

Website: https://meraindia.org.in