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NEWS & VIEWS

INTERVIEWS



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APRIL ISSUE 30

UPCOMING

Prof Isaac K Quaye

Regent University College of Science and Technology, Ghana



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MALARIA THROUGH THE LENS OF RESEARCHERS



Editorial

Dear Readers,

MERA-India team brings you the thirtieth issue of our newsletter, "News & Views'.

We begin this issue with great news which ignites a new hope for the malaria community. The World Health Organization (WHO) declared another two countries, Azerbaijan and Tajikistan, malaria free. With these new additions, the total count of malaria-free countries grows to 42 countries/territories. According to the WHO Director-General Dr Tedros Adhanom Ghebreyesus, these countries have demonstrated that malaria elimination is a realistic goal that is achievable with the necessary resources and political will. MERA-India agrees with Dr Ghebreyesus' assessment and believes that by adopting the same strategy of sustained investment, a dedicated health workforce, and early detection and treatment of every case of malaria, India can also achieve the milestone of becoming a malaria-free country.

With a focus on malaria elimination, the current issue contains excerpts from lectures presented in the ICMR-NIMR & MERA-India Lecture Series on Infectious Diseases 2.0 (LSID 2.0) and Distinguished lecture series. These lectures provide updates about the WHO-recommended new tools for malaria management and the lessons learned from the success of another malaria-free nation *viz*. Sri Lanka. The third lecture in the LSID 2.0 was delivered by Professor Sumadhya Deepika Fernando, who is a senior professor and consultant parasitologist at the Department of Parasitology, Faculty of Medicine, University of Colombo, Sri Lanka. Dr Rajpal Singh Yadav, Scientist & Chair Global Vector Control Response Action Group, Veterinary Public Health, Vector Control & Environment Unit, Department of Control of Neglected Tropical Diseases, WHO, Geneva, Switzerland, was the speaker in the distinguished lecture series. This issue also encloses the interviews of Dr Umesh Kamat, Assistant Lecturer, Goa Medical College, Goa and Dr AN Shriram, Scientist D, Division of Vector Biology and Control, ICMR-Vector Control Research Centre, Puducherry.

The "Research in Spotlight" section contains three recent research articles, where, Phang WK. *et al.* predicted the risk of *Plasmodium knowlesi* transmission in Peninsular Malaysia using machine learning-based ecological niche modeling approaches; Carucci M. *et al.* found safe drugs with high potential to block malaria transmission using spleen-mimetic screening; and Swai JK. *et al.*, compared three different techniques of mosquito collections for measuring the indoor protective efficacy (PE) of the volatile pyrethroid SR product Mosquito Shield.

Besides, this issue showcases one of the shortlisted entries of the MERA-India Image Competition 2022 in the "Malaria Through the Lens of Researchers" section, which was submitted by Mr Giridharan S from the laboratory of Professor Arun K Aggarwal, Department of Community Medicine and School of Public Health, Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh.

The 'Upcoming Events' section contains an announcement of the fifth lecture of the Lecture Series on Infectious Diseases 2.0, to be delivered by Professor Isaac K Quaye, (Regent University College of Science and Technology, Ghana).

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

ICMR-NIMR & MERA-India Activities

Lecture Series on Infectious Diseases 2.0: Lecture 03 by Professor Sumadhya Deepika Fernando



The third lecture in ICMR-NIMR and MERA-India Lecture Series on Infectious Diseases 2.0 was organized on 17th March 2023, where Professor Sumadhya Deepika Fernando, a senior professor and consultant parasitologist at the Department of Parasitology, Faculty of Medicine, University of Colombo, Sri Lanka, was invited as a speaker. Professor Fernando has been closely engaged in eliminating malaria in Sri Lanka, providing technical advice and assistance to Sri Lanka's Anti-Malaria Campaign since 2008, including making a major contribution to the preparations for WHO certification of the country for malaria elimination in 2016. She is a key member of the Technical Support Group that was established by the Ministry of Health for the elimination of malaria, and which now serves as an advisory body on the prevention of the re-establishment of malaria. Dr Anup Anvikar, Director, ICMR-National Institute of Malaria Research (NIMR) welcomed Professor Fernando and Dr Sachin Sharma, Chief Consultant, MERA-India, introduced her to the audience.

Professor Fernando delivered the lecture entitled "Malaria elimination and challenges to the prevention of re-establishment of Malaria in Sri Lanka". She first informed the audience that Sri Lanka received the WHO certificate for malaria elimination in 2016. Yet, the threat of malaria being re-established in the country remains on account of high vector numbers and imported malaria cases. She briefed about the challenges that Sri Lanka faces in maintaining zero transmission including delayed diagnosis of imported malaria cases, introduction and spread of *Anopheles stephensi*, the urban vector of malaria, and reduced national budgets. She conveyed to the audience that the country has adopted policies and strategies to mitigate these risks and sustain an active operational research component to provide evidence for optimizing strategies. The lecture has given an insight into the challenges faced and the nature of the prevention of re-establishment program which sustains a malaria-free country.

Professor Fernando then answered the questions of the audience after the lecture. The session was concluded by Dr Anup Anvikar, Director, ICMR-National Institute of Malaria Research, with a vote of thanks to the speaker and all the attendees.

Distinguished Lecture by Dr Rajpal Singh Yadav



Dr Rajpal Singh Yadav was the speaker for the sixteenth lecture in the ICMR-NIMR and MERA-India Distinguished Lecture Series. Dr Yadav is a public health entomologist and a vector control specialist with nearly 37 years of global professional experience in the field of vector-borne diseases. He currently chairs the WHO Joint Action Group on the implementation of the Global Vector Control Response and heads the pesticide management programme in the Department of Control of Neglected Tropical Diseases at WHO, Geneva. Previously, he headed the WHO Pesticide Evaluation Scheme (2009-2017) and coordinated trials of vector control products with several research institutions and strengthened their capacity. He has facilitated the development of several WHO normative guidelines for product testing, pesticide management, and vector surveillance and control. Dr Manju Rahi Scientist F, Indian Council of Medical Research, and PI MERA-India, welcomed and introduced Dr Yadav to the audience.

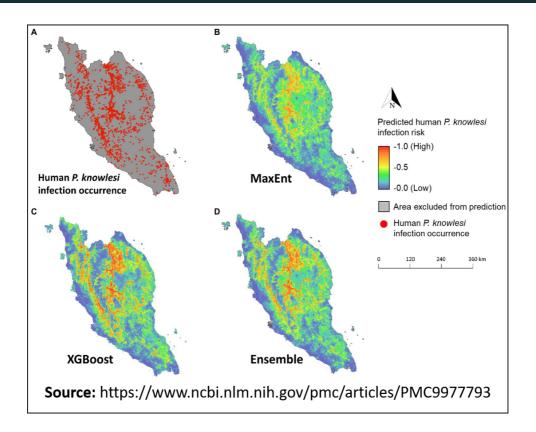
Dr Yadav delivered an illuminating lecture entitled "New Tools for Malaria Vector Surveillance and Control." He briefed the audience about the arthropod-borne diseases in the WHO region, then by showing the global distribution of major vector-borne diseases (VBDs), he highlighted that >80% of the global population is at risk of at least one VBD. He illustrated the global trend of malaria and mentioned that vector control is a core malaria intervention, reducing 60% of malaria deaths and 37% of malaria incidence. He explained the need for new tools and the WHO's position on them. He also demonstrated the pathway of the WHO Vector Control Advisory Group, for evaluating new vector control tools and introduced various new tools for Indoor Residual Spray (IRS), Insecticide-Treated Nets (ITNs), Larval control, Special repellents, Attractive Targeted Sugar Baits (ATSBs), etc. His lecture was filled with information on new malaria-focused tools, Entomological surveillance (WHO Bottle assay), Standard Operating Procedures (SOPs), WHO data collation & management, etc.

After the lecture, Dr Yadav addressed all the queries of the audience. The session concluded with Dr Anup Anvikar, Director, ICMR-NIMR, thanking the speaker and presenting him with a token of appreciation.

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

Research in Spotlight

Phang WK. et al., Front in Microbiol. 2023: Predicting Plasmodium knowlesi transmission risk across Peninsular Malaysia using machine learning-based ecological niche modeling approaches.



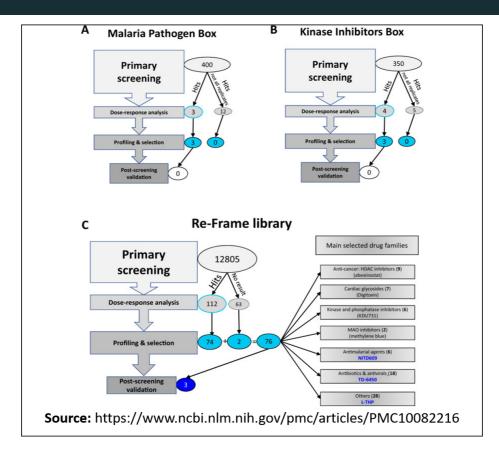
The emergence of potentially life-threatening zoonotic malaria caused by *Plasmodium knowlesi* has grown significantly over the last two decades, threatening malaria elimination efforts in Malaysia and other Southeast Asian countries. With a steady increase in *P. knowlesi* infection cases from 376 in 2008 to 2,609 cases in 2020, the transmission of the simian malaria species *P. knowlesi* has continued to challenge Malaysia's healthcare. These are attributed to several environmental changes affecting the proximity between people, macaque reservoirs, and mosquito vectors. Despite numerous studies from Malaysian Borneo to determine the association between environmental factors and *P. knowlesi* malaria transmission, the environmental influence on *P. knowlesi* malaria transmission in Peninsular Malaysia remains poorly understood.

The emerging role of machine learning approaches in healthcare and spatial epidemiology is instrumental, especially in modeling the covariate contribution to disease transmission as well as predicting the spatial distribution of the disease. In the present study, Phang WK. et al. investigated the impacts of diverse environmental variations on human P. knowlesi malaria occurrence as well as predicted the potential high-risk areas for human P. knowlesi malaria across Peninsular Malaysia using three machine learning-based models: maximum entropy (MaxEnt), extreme gradient boosting (XGBoost), and ensemble modeling. Multiple environmental parameters, including climate factors, landscape characteristics, and anthropogenic factors, were included as predictors. The comparison between models indicated that the XGBoost had a higher performance as compared to the MaxEnt and ensemble models. The key environmental covariates affecting human P. knowlesi occurrence were distance to the coastline, elevation level, tree cover, annual precipitation, tree loss, and distance to the forest. The models indicated that the disease risk areas were

mainly distributed in low-elevation areas along the Titiwangsa mountain range and in the inland central-northern region of Peninsular Malaysia.

Overall, these predictive risk maps will be beneficial in identifying high-risk areas of *P. knowlesi* malaria transmission, thereby facilitating decision-making for vector or reservoir surveillance and disease control, especially in cases of limited prevention resources.

Carucci M. et al., Nat Commun. 2023: Safe drugs with high potential to block malaria transmission revealed by a spleen-mimetic screening.



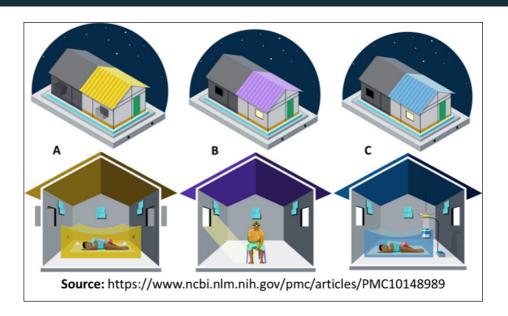
The mature sexual stages of malaria parasites are transmitted to the anopheline vectors, and their low number creates a natural bottleneck in the parasite life cycle. Blocking the transmission of these mature sexual stages is a major component of malaria eradication efforts. Drugs targeting the mature sexual stages of malaria parasites and gametocyte stages can block malaria transmission by making transmissible forms unavailable to the blood-feeding *Anopheles* mosquito vector.

The spleen serves as a primary blood filter that can remove senescent or pathologically altered erythrocytes from circulation. It retains stiff erythrocytes and clears them from circulation. The malaria parasite, *Plasmodium falciparum*, multiplies in RBCs, and only the most deformable stages, namely rings and stage V gametocytes, overcome this mechanical challenge and persist in circulation. Blocking the transmission of *P. falciparum* from its human host to its mosquito vector is envisioned as a strategy towards reducing malaria incidence and hopefully contributing towards its global eradication.

Several screening approaches to identify gametocyte-targeted compounds able to kill or inactivate the parasite have been explored. The switching from stiff immature stage V gametocytes to deformable mature gametocytes can be prevented using drugs. Druginduced stiffening of *P. falciparum*-infected RBCs, therefore, induces their elimination from the bloodstream, thus blocking malaria transmission.

Based on this mechanical approach, **Carucci M. et al.** identified safe drugs with strong potential to block malaria transmission by screening 13,555 compounds using a splenic-mimetic filtration approach called microfiltration, which quantifies the ability of erythrocytes to squeeze between microspheres. They reported identifying 82 compounds that stiffen or kill the transmission stages of *P. falciparum*. Three of the identified active drugs are safe for use in humans when administered orally. Among these, NITD609, an orally administered PfATPase inhibitor with known effects on *P. falciparum*, was found to kill and stiffen transmission stages in vitro at nanomolar concentrations. The short exposures to TD-6450, an orally administered NS5A hepatitis C virus inhibitor, were found to stiffen the transmission parasite stages and kill asexual stages in vitro. The combination of NITD609 and TD-6450 was also found to induce high *P. falciparum* gametocyte retention rates in spleen-mimetic filters. The physiologically relevant splenic-mimetic filtration approach identified multiple mechanisms of action and safe drugs with strong potential as malaria transmission-blocking agents that could be rapidly tested in clinical trials.

Swai JK. et al., Malar J. 2023: CDC light traps underestimate the protective efficacy of an indoor spatial repellent against bites from wild *Anopheles arabiensis* mosquitoes in Tanzania.



Apart from the conventional core vector control tools, new tools are essential for the efficient reduction of the malaria burden. The efficacy of new tools must be demonstrated using techniques that are appropriate both in terms of relatedness to entomological endpoints relevant to disease transmission as well as the feasibility of implementation in experimental and operational contexts. The methods for evaluating the efficacy of core malaria interventions in experimental and operational settings are well established; however, there are still gaps for spatial repellents (SR). though many other Although SR is known to have many experimental impacts against mosquitoes, such as landing inhibition, repellency, excito-repellency, knockdown, disarming, mortality, and effects on fertility and fecundity, the

key entomological endpoint impacted by SR is blood feeding. The most direct means of showing the impact of SR on blood feeding is through the collection of blood-fed mosquitoes, which may be done experimentally in huts designed to allow mosquitoes to enter and feed on the human study participants sleeping inside.

In this <u>study</u>, Swai JK. *et al.* compared three different techniques: (1) collection of blood-fed mosquitoes (feeding), (2) human landing catch (HLC), and (3) CDC light trap (CDC-LT) collections for measuring the indoor protective efficacy (PE) of the volatile pyrethroid SR product Mosquito ShieldTM. The PE of Mosquito ShieldTM measured as feeding inhibition against a wild population of pyrethroid-resistant *Anopheles arabiensis* mosquitoes was observed to be 84%; landing inhibition was 77%; and the reduction in numbers collected by CDC-LT was 30%. Although the PE measured by feeding inhibition and landing inhibition showed no statistically significant difference relative to HLC, there was a significant difference in the PE measured by CDC-LT and landing inhibition.

The HLC testing technique provided a similar estimate of PE for Mosquito ShieldTM against *An. arabiensis* mosquitoes when compared to measuring blood feeding directly, while CDC-LT underestimated PE relative to the other techniques. The study reported that of the three techniques tested, CDC-LT could not effectively estimate the PE of the indoor spatial repellent in the given setting, thus suggesting that it is critical to first evaluate the use of CDC-LT in local settings prior to their use in entomological studies when evaluating the impact of indoor SR.

Malaria Scientists to Watch

An interview with Dr Umesh Kamat



Dr Umesh KamatAssistant Lecturer,
Goa Medical College, Goa

1. What inspired you to work in the field of malaria?

Given its size, what havoc a mosquito can play in human life- causing a variety of diseases affecting millions and killing lakhs of people- has perplexed me since my childhood. Mosquitoes, then, were synonymised with Malaria, while other diseases like Dengue, and Chikungunya were yet to become noticeable. Sir Ronald Ross had already kindled the spark of scientific investigation through a lesson in English literature. Thus, malaria was the first disease that caught my young attention, and as it goes with the first love which is never forgotten- malaria could never attract me lesser.

2. Working in the field of community behaviour, in your opinion, how achievable is the goal of malaria elimination by 2030?

The epidemiological chain in malaria comprises of the human host, the mosquito, and the parasite. Though few states in the country may achieve the elimination goal, achieving the same nationwide for the most populous country in the world with diversity in every sphere-geographical, meteorological, cultural, demographic, socio-economic- and personalized political agenda, looks like a challenging task. Given the variegated epidemiological milieu which fosters malaria and operational, technical, and financial issues which have in the past made us roll back from malaria eradication, sustaining zero malaria cases in the local population wouldn't be easy for the states where Malaria Elimination is shown to be achieved.

3. Please enlighten the readers about the on-ground gaps in the malaria intervention and suggest ways to fill these gaps.

The gaps can be put up as the 'Knowledge Gap', and the 'Knowledge-Action Gap'- the former may be called innocent about malaria, and the latter ignorant towards Malaria. Public awareness about 'Malaria Elimination' is extremely poor, thus depriving the anti-malarial movement of the momentum necessary to eliminate Malaria. In a country where 70% of the health expenditure is out of pocket, relying on the malaria statistics generated from the cases reported at the State Health Services seems bold and presumptuous. Injudicious use of antimalarials not conforming to the National Anti-Malarial Drug Policy by medical practitioners (many of whom may not even possess the requisite qualification) and insufficient surveillance of nationwide antimalarial turnover fosters antimalarial drug resistance. Research and training gaps in entomological surveillance, especially in the area of insecticide resistance, coupled with the unregulated use of chemical methods of vector control in anticipation of a quick-fix solution further complicates the arena of elimination. Lack of local political will to allot man, money, and material resources to the ongoing control activities, and political support in enforcing legal provisions under the Public Health Act which is periodically amended in tune with the changing health scenario- is a major deterrent not facilitating the behaviour conducive to Malaria Elimination.

Filling up these gaps need consorted efforts from the not only Health Department but also the Departments of Labour (to monitor work-related interstate movements), Law (to amend public health laws), Education (involving school children), Police (law enforcement); the private medical practitioners (compliance with standard treatment guidelines and notification); and the general public (Community Participation)- all, backed up by a strong political commitment to eliminate Malaria.

4. What piece of advice do you want to give to young malaria researchers?

Young Malaria researchers should not trap themselves in short-term studies undertaken with academic objectives restricted to publishing and presenting research papers. One should work with the philosophy of Action Research, Implementation Research- the Health Systems Research. Basic and Applied Research has provided us with measures for Vector Control, Malaria Diagnosis, and Treatment, measures to safeguard from Mosquito bites, and environmental sanitation measures like waste water management and solid waste disposal. Despite such measures being accessible and affordable, what are the game changers to build an enabling environment that would bring about the behaviour changenot only in the general community but also among the vulnerable populations, the health professionals, para-professionals, the bureaucrats and the politicians- is the question to be addressed.

5. What significance do you see for MERA-India in achieving India's malaria elimination target?

Malaria Elimination Research Alliance (MERA-India) is committed to fostering translational research to identify and prioritize areas that have a tangible impact on Malaria elimination from India. Research in Community Behaviour, Low-Density Parasitemia, and its significance, Artificial Intelligence to map and trace Malaria patients, Vector Biology, and innovative vector-control methods is being carried out in a multi-centric mode. With Dr Amit Sharma, Dr Manju Rahi, and Dr Sachin Sharma coordinating as a Nucleus of the activities with respective area experts mentoring these research initiatives, MERA-India will surely guide us to the elimination goal; whether through it or not, depends on how effectively the on-ground gaps are filled.

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An interview with Dr AN Shriram



Dr AN Shriram
Scientist D,
Division of Vector Biology and Control,
ICMR-Vector Control Research Centre, Puducherry

Please share the highlights of your experience working as a medical entomologist.

After obtaining my postgraduate degree in Medical Entomology (1990) from Pondicherry University, I worked as Junior Research Fellow at the ICMR-NIMR (formerly Malaria Research Centre, New Delhi) and as Technical Officer at the ICMR-NIMR field unit in Jabalpur until 1992. Subsequently, I moved to the ICMR-VCRC field unit at Mayiladuthurai, Tamil Nadu, and worked in a village-scale field trial project on the evaluation of *Bacillus sphaericus* formulations against *Culex quinquefasciatus*, vector of bancroftian filariasis until 1994. In the same year, I moved to the ICMR-Regional Medical Research Centre, Port Blair, Andaman Nicobar Islands, and worked until 2018. During this period, I had undertaken studies to understand the epidemiology of the diurnally sub-periodic form of filariasis and demonstrated the operational feasibility of DEC-fortified salt towards the elimination of this form of filariasis in the lone foci of infection in India.

I obtained my Ph.D. in Medical Entomology from Pondicherry University in 2004, for the work carried out on the transmission dynamics of the diurnally sub-periodic form of *Wuchereria bancrofti*, transmitted by a day-biting mosquito *Aedes niveus*. Besides, I undertook studies on the bio-ecology of *Ae. aegypti* and *Ae. albopictus*, spatial distribution, expression of heat shock proteins (HSPs) in response to thermal stress, and detected DENV in *Ae. albopictus* from Andaman and Nicobar Islands for the first time. I moved to ICMR-VCRC in 2018 and was involved in the creation/upgrading of facilities, SOPs that enable adherence to GLP principles and promote the quality and validity of test data, and will enable mutual acceptance of data among different test sites/countries. National GLP Compliance Monitoring Authority (NGCMA) has certified the facilities for Phase II evaluation of LLINs in experimental huts. Currently, along with my team in Odisha, we are tracking the elimination of malaria in Odisha State, which is looking at entomological-parasitological-sociological and operational components. As a faculty member of the Master's Programme in Public Health Entomology, I also teach and guide students which is an effort to enhance India's dwindling human resources in medical entomology.

2. Please describe the importance of vector surveillance and share the latest tools being used in the field.

Vector surveillance is a well-organized systematic collection, analysis, and explanation of entomological data for health risk assessment, and for planning, executing, monitoring, and assessing vector control interventions. Surveillance data are crucial for evidence-based intervention and need to be combined and well-timed. To envisage strategies and interventions that are suitable, we need to know the bio-ecology of local vector mosquitoes and the epidemiology, as well as the scope of potential secondary vectors, especially in the context of the elimination of VBDs. Besides, the various conventional tools, like mouth aspirators, prokopack aspirators, CDC light, and CDC light plus CO₂ traps, animal baited traps, Citizen science (in resource-limited settings), sticky pot (sampling outdoor resting mosquitoes), human odour baited light trap and human baited double net trap (outdoor host-seeking vector mosquitoes) are some of the tools that are being currently evaluated and used for vector surveillance in the context of malaria.

3. Being an entomologist, please mention the scope for budding entomologists in India.

An entomologist could take up teaching, research, and technical jobs at colleges and universities, research centers, government organizations, and defense sectors. Besides, growing tourism, travel, and trade not only move people across at unimaginable speed but also the pathogens and vectors, resulting in new ecological niches. Many arbovirus pathogens have escaped their original locations and have found a foothold in this country. For instance, Zika, Chikungunya, Dengue, and West Nile virus offer scope to focus on research surveillance systems, vector control tools, and the development of a vaccine in the coming years. The emerging threat of tick-borne diseases in the country (e.g. KFD, CCHF, and a host of other pathogens) provides scope for systematic surveillance and control measures to the budding entomologists.

4. Please enlighten the readers about the importance of vector management.

The key method by which Malaria, Dengue, and Leishmaniasis are controlled is through vector control. Vector control has a long and illustrious history. Vector control has been responsible for decreasing the burden and dwindling of many VBDs. Emerging threat from insecticide-resistant vectors, climate change, necessitates integrating and supplementing of vector control interventions to eliminate these diseases. There is a need to return to vector control methods grounded on in-depth knowledge of the dynamics of transmission, which utilize a range of insecticide and non-insecticide-based site-specific approaches for effective and sustainable vector control.

5. What is your view on the contribution of MERA-India in achieving India's malaria elimination target?

MERA-India is highly relevant in the present scenario. It would be significant if it can play a key role in addressing the elimination of malaria among the tribal communities in India. Finally, this will hasten the elimination process and achieve the target in India.

Malaria Through the Lens of Researchers

In this issue, we are highlighting one of the shortlisted entries in the MERA-India Image Competition 2022, submitted by Mr Giridharan S from the group of Professor Arun K Aggarwal, Department of Community Medicine and School of Public Health, PGIMER, Chandigarh.



Image title: "Layers of oil, spray in the air; To begin their end, we must be well-prepared"

A brief description of the image is as follows:

The life of a mosquito begins when the egg hatches to release larvae. It resides near the water surface for up to 2 weeks, before evolving into the disease carrier we know it to be. This image shows the dreaded vector at its most vulnerable phase - the larva helplessly trapped in a pipette. They can make any collection of standing water their home. The ones in the image flourished in rainwater accumulated in flowerpots. Control at this stage is paramount to ensure they do not develop into adult mosquitoes, putting an end to the transmission of disease before it even begins.

Upcoming Event

Lecture Series on Infectious Diseases 2.0 Lecture 05 by Professor Isaac K Quaye



ICMR-NIMR and MERA-India are hosting the fifth lecture in the series "Lecture Series on Infectious Diseases 2.0" to be delivered by Professor Isaac K Quaye. He is a Professor at the Regent University College of Science and Technology, Ghana. Also, he is the founding Chair for the Pan African Vivax and Ovale Network (PAVON), which collaborates with NMPs to re-focus attention on the emergence of *P. vivax* and *P. ovale* in Africa. Following his post-doctoral training in genome science at the University of Washington under Professor Carol Sibley, Professor Quaye has more than 20 years of professional expertise in the field of malaria.

He will be delivering the lecture on the topic entitled "Current *Plasmodium* biological concepts vis-à-vis Malaria elimination" on 17th May 2023.

To join this lecture, Please click on this link: https://bit.ly/LSID23-May.











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