

MERA-India brings you...

NEWS & VIEWS

Issue 31
May 2023

INTERVIEW



Prof Rajib Dasgupta,
Centre of Social Medicine &
Community Health,
Jawaharlal Nehru University,
New Delhi

Highlights

- | EDITORIAL
- | NIMR & MERA-INDIA ACTIVITIES
- | INTERVIEW
- | MALARIA THROUGH THE
LENS OF RESEARCHERS
- | RESEARCH IN SPOTLIGHT
- | UPCOMING EVENT

UPCOMING

Lecture series on Infectious Diseases 2.0



Lecture 06 by **Dr Alison Krentel,**
School of Epidemiology and Public Health,
University of Ottawa, Canada

4 Years of
MERA-India

Editorial

Dear Readers,

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

We are delighted to inform you that, since its launch, the MERA-India has successfully completed four years as of April 24, 2023.

The month of April marks an imperative occasion for the international malaria community. World Malaria Day is observed on April 25 every year. It is an opportunity to raise awareness of the ongoing fight against malaria and mobilize support for malaria control and prevention efforts around the world. This year's theme "Time to Deliver Zero Malaria: Invest, Innovate, Implement" emphasizes the critical need to invest funds, develop innovative plans of action, and put those plans into action in order to achieve the goal of zero malaria.

The MERA-India and National Institute of Malaria Research (NIMR) organized a keynote lecture and panel discussion on 28th April 2023 at ICMR, Headquarters, New Delhi to commemorate World Malaria Day and MERA-India inception day. The event featured a thought-provoking lecture by Padma Shri awardee Dr Abhay Bang followed by a Panel discussion with eminent researchers and scientists. Dr Bang highlighted tribal malaria as the final hurdle to India's malaria elimination aspirations. The discussion was focused on the current state of malaria in India and the actions required to achieve malaria-free status. Excerpts from the event have been included in this newsletter under the section "ICMR-NIMR & MERA-India Activities".

We cover an inspiring interview of Professor Rajib Dasgupta (Jawaharlal Nehru University, Delhi) in the 'Malaria Scientists to Watch' part of this issue. The "Research in Spotlight" section features three recent research articles significant in the field of malaria, where Kehrer J. *et al.* highlighted the importance of concavin for the maintenance and integrity of *Plasmodium* sporozoite shape, and hence, efficient transmission from mosquitoes to mammals; Accrombessi M. *et al.* provided evidence for the effectiveness of chlorfenapyr-pyrethroid nets in an area with pyrethroid-resistant vectors through a cluster-randomized superiority trial. Lastly, Kobylinski KC. *et al.* demonstrated the mosquito-lethal effects of ivermectin metabolites.

Furthermore, MERA-India Image Competition 2022 nominated entry submitted by Ms Sangeeta Singh (PhD student at NIMR Delhi) is featured in the "Malaria Through the Lens of Researchers" section. The 'Upcoming Events' section includes an announcement of the sixth lecture of the "Lecture Series on Infectious Diseases 2.0", to be delivered by Dr Alison Krentel, Assistant Professor at the School of Epidemiology and Public Health, University of Ottawa, Canada.

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

World Malaria Day and MERA-India Inception Day 2023

Malaria Elimination Research Alliance (MERA)-India is an ICMR initiative that was launched on the eve of World Malaria Day 2019. The purpose of MERA-India is to provide a common platform for researchers from ICMR/non-ICMR research institutions, universities, etc. to work in a coordinated and combinatorial way for malaria elimination in India. MERA-India has successfully completed four years of its journey and has funded more than 40 projects led by malaria researchers, scientists, and clinicians.

To commemorate World Malaria Day and MERA-India's inception day, ICMR, NIMR, and MERA-India organized a keynote lecture and panel discussion on 28th April 2023, at ICMR Headquarters, New Delhi. Padma Shri awardee Dr Abhay Bang, an eminent public health specialist and social innovator who has dedicated his life to improving the health and well-being of tribal communities in rural India, was invited as a Keynote speaker. He is the director and co-founder of the Society for Education, Action, and Research in Community Health (SEARCH), an organization that works towards providing affordable and accessible healthcare to populations in a remote district, Gadchiroli, in India. He gave an enlightening lecture entitled "The Last Citadel of Malaria", where he described tribal malaria as the last milestone to achieve the malaria elimination goals of India.

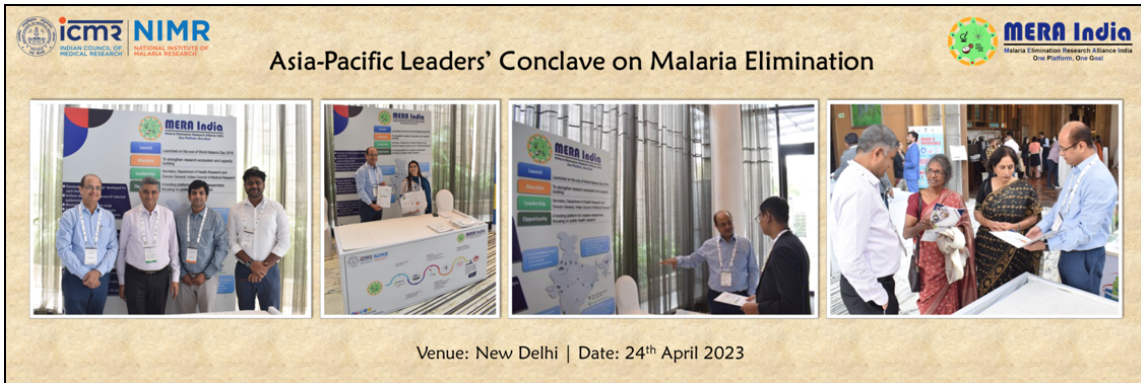


In the panel discussion, Dr Abhay Bang; Dr Tanu Jain (Director, National Control for Vector Borne Disease Control); Dr T. Sonai Rajan (Assistant Director, Entomology, Central Insecticides Board & Registration Committee); Dr Saman Habib (Chief Scientist, CSIR-Central Drug Research Institute); Dr M M Pradhan (Former State Program Officer, NCVBDC, Odisha); and Dr Tavpritesh Sethi (Associate Professor IIIT Delhi), shared their insights and experiences on the topic "Time to Deliver Zero Malaria: Invest, Innovate, Implement - Indian Context". The discussion was focused on the current state of malaria and the steps required to achieve zero malaria in India. Dr Manju Rahi, (Scientist F ICMR and Principal Investigator MERA-India) moderated the session. The panel discussion highlighted the need for the 3Cs: Commitment, Cross talk, and Consistency for achieving the goal of malaria elimination in India.



After the panel discussion, Dr Anup Anvikar (Director, ICMR-NIMR), and Dr Manju Rahi felicitated all the speakers with a token of appreciation. Dr Sachin Sharma (Chief consultant, MERA-India) concluded the session and thanked the speakers and the attendees for their presence.

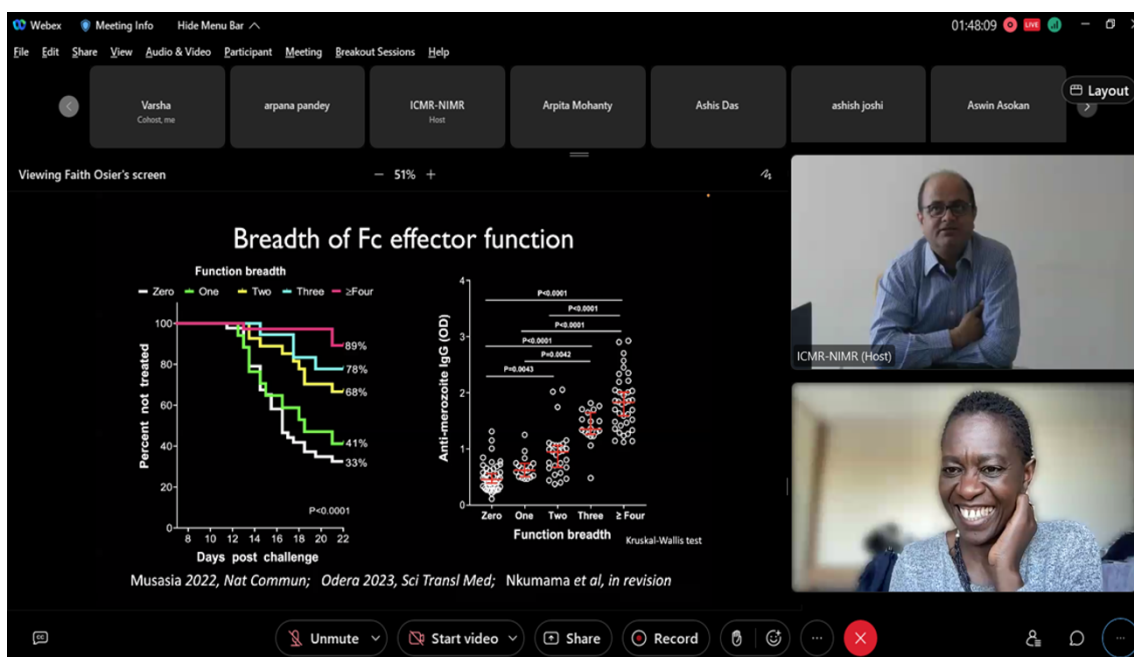
AMERA-India participation in Asia-Pacific Leaders' Conclave on Malaria Elimination



The Asia-Pacific Leaders' Conclave on Malaria Elimination was organized on 24th April 2023 in New Delhi by the Ministry of Health and Family Welfare, the Government of India in collaboration with the Asia Pacific Leaders Malaria Alliance (APLMA). The event was a great platform for the leaders from the Asia Pacific region to discuss the ongoing efforts towards malaria elimination and reinvigorate the national and regional drive towards the goal of the malaria-free Asia Pacific by 2030.

MERA-India set up a booth in the conclave and presented its journey since inception, highlighting its accomplishments and ongoing efforts towards malaria elimination, through the MERA-India booth. Dr Sachin Sharma briefed the attendees about the achievements and opportunities for malaria researchers at MERA-India. Dignitaries Dr Kamini Mendis and Dr Neena Valecha along with other attendees, appreciated the efforts of MERA-India during the event.

Lecture Series on Infectious Diseases 2.0: Lecture 04 by Professor Faith Osier



On the occasion of World Malaria Day and MERA-India inception day 2023, Professor Faith Osier, Chair of Malaria Immunology and Vaccinology, Faculty of Natural Sciences at Imperial College London, UK, was invited as a keynote speaker to deliver the fourth lecture in the ICMR-NIMR and MERA-India Lecture Series on Infectious Diseases 2.0. Dr Manju Rahi welcomed Professor Osier, and Dr Sachin Sharma introduced her to the audience.

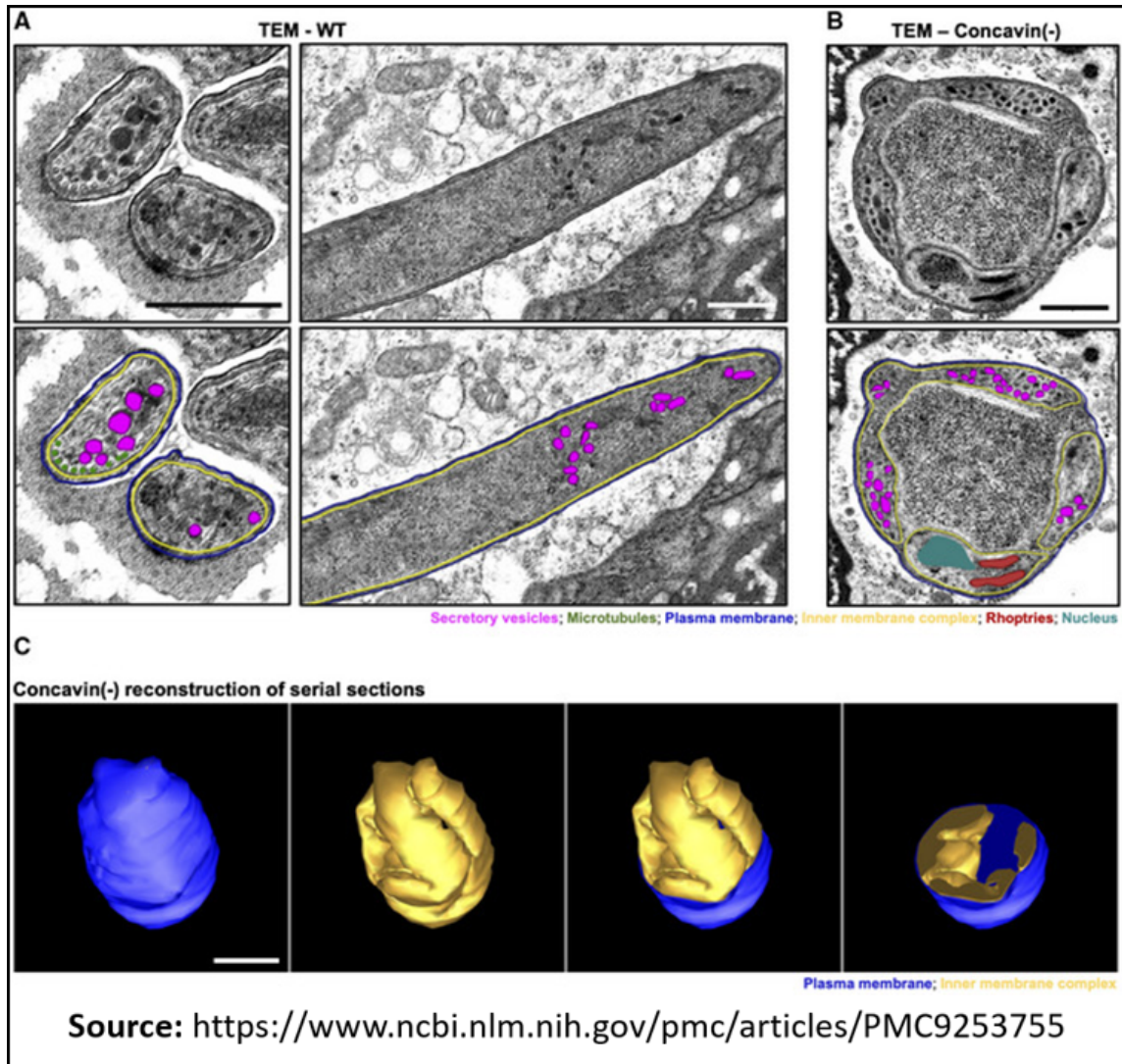
Professor Osier delivered the lecture entitled "Mechanisms of Immunity Against Malaria". She began the lecture with a description of the situation of malaria in Africa and its impact on people's health and economies. She advised on the need for a combination of new tools for disease management globally. She mentioned that although the malaria vaccine is available, there are still challenges with the immunology, implementation, manufacturing, and supply of the vaccine. She further spoke about the importance of fundamental immunology and cell biology research including new technologies like mRNA, Monoclonal Antibodies, and the human challenge platform. She shared a study showing that when given Gambian gamma globulin to malaria patients, the parasite counts along with the symptoms came down. She suggested that humans can not only acquire immunity against malaria but also can transfer it to people. Professor Osier demonstrated the power of contemporary controlled human malaria infection studies to clearly distinguish between protected and susceptible volunteers. She urged for massive investments in research and development (R & D) of malaria vaccines.

Professor Osier answered the questions of the audience after the lecture. The session was concluded by Dr Sachin Sharma with a vote of thanks to the speaker and all the attendees.

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

Research in Spotlight

Kehrer J. et al., *EMBO Rep.* 2022: *Plasmodium* sporozoite disintegration during skin passage limits malaria parasite transmission.



During transmission of malaria-causing parasites from mosquitoes to mammals, *Plasmodium* sporozoites migrate rapidly in the skin to search for a blood vessel. The high migratory speed and narrow passages taken by the parasites suggest considerable strain on the sporozoites to maintain their shape. In the present [study](#), Kehrer *et al.* shows that the membrane-associated protein concavain is important for the maintenance of the *Plasmodium* sporozoite shape inside the salivary glands of mosquitoes and during migration in the skin.

The PbANKA_1422900 protein (concavain), localized at the cytosolic side of the plasma membrane, is important for the maintenance of the sporozoite shape during their salivary gland residency and is essential for efficient transmission to the vertebrate host. Functional analyses through GFP-tagging, FRAP, gene deletion, and in vivo imaging were performed, wherein it was found that the concavain (-) sporozoites progressively round-up upon entry to

the salivary glands. While these rounded or deformed sporozoites could still move, they were not ejected through the narrow salivary ducts and failed to penetrate through skin and skin-like environments, showing the importance of the slender shape for parasite transmission. Strikingly, motile concavin (-) sporozoites disintegrated while migrating through the skin, leading to parasite arrest or death and decreased transmission efficiency.

Results highlighted the importance of concavin for the maintenance and integrity of Plasmodium sporozoite shape and, hence, efficient transmission from mosquitoes to mammals. Overall, the findings imply that concavin helps maintain the shape of the cell by riveting the plasma membrane to the subtending inner membrane complex. Interfering with cell shape maintenance pathways might thus provide a new strategy to prevent malaria infection.

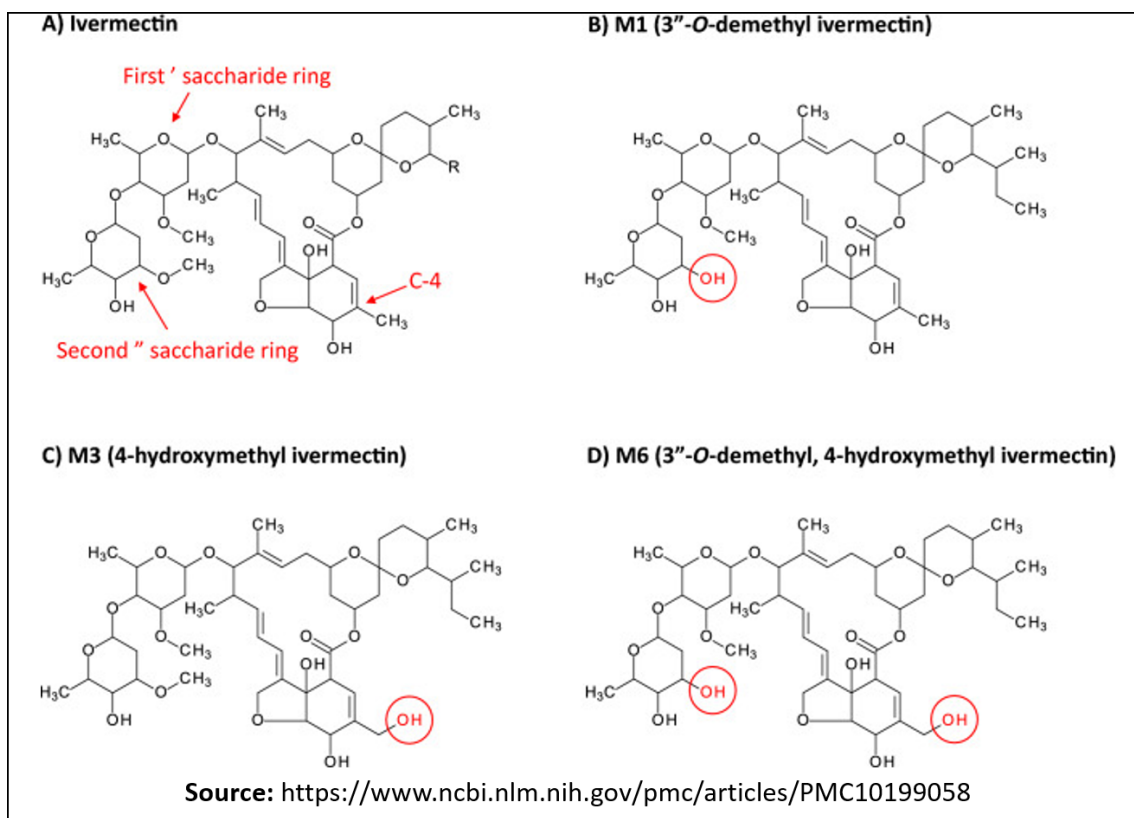
Accrombessi M. et al., Lancet. 2023: Efficacy of pyriproxyfen-pyrethroid long-lasting insecticidal nets (LLINs) and chlorfenapyr-pyrethroid LLINs compared with pyrethroid-only LLINs for malaria control in Benin: a cluster-randomised, superiority trial.

	Malaria infection					Anaemia in children younger than 5 years				
	n/N	Prevalence	OR	95% CI	p value*	n/N	Prevalence	OR	95% CI	p value*
6 months after net distribution										
Pyrethroid-only LLIN group	412/1471	28.0 %	1 (ref)	99/241	41.1 %	1 (ref)
Pyriproxyfen-pyrethroid LLIN group	394/1463	26.9 %	0.92	0.63-1.35	0.67	117/250	46.8 %	1.24	0.71-2.18	0.45
Chlorfenapyr-pyrethroid LLIN group	231/1475	15.7 %	0.47	0.32-0.69	0.0002	82/241	34.0 %	0.71	0.40-1.26	0.24
18 months after net distribution										
Pyrethroid-only LLIN group	576/1489	38.7 %	1 (ref)	118/252	46.8 %	1 (ref)
Pyriproxyfen-pyrethroid LLIN group	564/1478	38.2 %	0.97	0.69-1.37	0.87	108/245	44.1 %	0.84	0.40-1.79	0.65
Chlorfenapyr-pyrethroid LLIN group	414/1483	27.9 %	0.60	0.43-0.85	0.0041	118/246	48.0 %	1.08	0.51-2.28	0.84
Anaemia was defined as a haemoglobin concentration of <10 g/dL. LLIN=long-lasting insecticidal net. OR=odds ratio. *A p value of <0.025 was considered significant after Bonferroni correction.										
Table 3: Malaria infection and anaemia prevalence in the study population at 6 months and 18 months after net distribution (intention-to-treat analysis)										
Source: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)02319-4/fulltext										

Long-lasting insecticidal nets (LLINs) coated with pyrethroid are the primary malaria preventive strategy used in sub-Saharan Africa. These are credited with preventing an estimated 1.5 billion cases of malaria and 7.6 million deaths during the last two decades. The regions of sub-Saharan Africa recorded an upsurge in malaria transmission during 2019 and 2020, which was most likely due to the continuous growth of pyrethroid resistance in mosquitoes that transmit malaria, which coincides with a plateau in malaria control investment, eventually leading to suboptimal coverage of interventions. Therefore, urgent actions are required for the prevention of malaria resurgences.

New classes of long-lasting insecticidal nets (LLINs) combining mixtures of insecticides with different modes of action could put malaria control back on track. In the current [study](#), Accrombessi *et al.* assessed the comparative effectiveness of pyriproxyfen-pyrethroid and chlorfenapyr-pyrethroid LLINs in preventing malaria transmission in a region of high pyrethroid resistance. A cluster-randomised superiority trial was conducted in Zou Department, Benin. Restricted randomization was used to randomly assign 60 clusters to one of three LLIN groups (1:1:1): to receive nets containing either pyriproxyfen and alpha-cypermethrin (pyrethroid), chlorfenapyr and alpha-cypermethrin, or alpha-cypermethrin only (reference). The primary outcome was malaria case incidence measured over 2 years after net distribution. It was found that chlorfenapyr-pyrethroid LLINs provided greater protection from malaria than pyrethroid-only LLINs in an area with pyrethroid-resistant mosquitoes. The mean malaria incidence over 2 years after LLIN distribution was 1.03 cases per child-year in the pyrethroid-only LLIN reference group, 0.84 cases per child-year in the pyriproxyfen-pyrethroid LLIN group, and 0.56 cases per child-year in the chlorfenapyr-pyrethroid LLIN group. This trial provides evidence for the effectiveness of chlorfenapyr-pyrethroid nets in an area with pyrethroid-resistant vectors and will therefore support a WHO policy recommendation.

Kobylinski KC. *et al.*, *Sci Rep.* 2023: Ivermectin metabolites reduce *Anopheles* survival.



Ivermectin mass drug administration (MDA) is a potential new tool for malaria control and elimination. Blood-feeding on ivermectin-treated humans or livestock is lethal to *Anopheles* mosquitoes. The impact of ivermectin on *Anopheles* survival when fed on blood

from a treated host *in vivo* consistently exceeds that of when mosquitoes are fed blood spiked with ivermectin *in vitro*. This discrepancy has been observed in clinical trials with *Anopheles gambiae* in Kenya and *Anopheles dirus* and *Anopheles minimus* in Thailand. One explanation for this difference is that there are active metabolites of ivermectin that possess a mosquito-lethal effect. If slowly eliminated ivermectin metabolites impart a mosquito-lethal effect, then this would result in a longer duration of mosquito mortality than previously predicted.

There are three primary metabolites produced in humans at detectable concentrations following ivermectin ingestion: M1 (3"-O-demethyl ivermectin), M3 (4-hydroxymethyl ivermectin), and M6 (3"-O-demethyl, 4-hydroxymethyl ivermectin). Using *An. dirus*, one of the most ivermectin-tolerant species, and *An. minimus*, one of the most ivermectin-vulnerable species, [Kobylinski et al.](#) evaluated the mosquito-lethal effect of the three most prevalent ivermectin metabolites produced in humans, which were produced via bacterial modification or synthesis. *Anopheles dirus* and *Anopheles minimus* mosquitoes were fed human blood diluted with ivermectin and its metabolites at varying concentrations, and mortality was tracked every day for a period of fourteen days. The concentrations of ivermectin and its metabolite were quantified by liquid chromatography linked with tandem mass spectrometry to confirm the concentrations in the blood matrix. Results revealed that neither the LC50 nor LC90 values differed between ivermectin and its major metabolites for *An. dirus* or *An. minimus*. Additionally, there were no substantial differences in the time to median mosquito mortality when comparing ivermectin and its metabolites, demonstrating

an equal rate of mosquito killing between the compounds evaluated. These results demonstrate that ivermectin metabolites have a mosquito-lethal effect equal to that of the parent compound, contributing to *Anopheles* mortality after treatment of humans.

Malaria Scientist to Watch: An interview with Professor Rajib Dasgupta



[Professor Rajib Dasgupta](#)

Centre of Social Medicine & Community Health,
Jawaharlal Nehru University, New Delhi

1. Tell us about your journey from being a medicine graduate to your current role as a professor at the Jawaharlal Nehru University and a public health expert?

After my graduation in medicine from the University of Calcutta, I obtained my MPH and PhD from the Centre of Social Medicine & Community Health, Jawaharlal Nehru University. I served in the public health services of the Municipal Corporation of Delhi (MCD) from 1993 to 2003, in the Epidemiology Division. During those formative years as a public health professional, I managed epidemics of two new infections - *Vibrio cholerae* O139 and SARS, and two re-emerging infections - Plague and Dengue. I also acquired considerable managerial skills in administrative and financial matters and worked in close collaboration with the political arm of the MCD and the media.

I joined JNU in 2003, where I am currently a professor in Community Health. I teach and research nutrition, communicable diseases, epidemiology, and research methodology. I was a Fulbright Senior Research Fellow at the Global Diseases Epidemiology and Control, Department of International Health, Johns Hopkins Bloomberg School of Public Health, USA. I was also a Visiting Fellow in 2016 at the Australian Research Centre in Complementary and Integrative Medicine, Faculty of Health, University of Technology Sydney, Australia. I am also a recipient of the Erasmus+ Global Mobility Programme at Tampere University, Finland.

I have been part of several large collaborative projects and evaluations in nutrition, polio, tuberculosis, and One Health funded by ICMR, UK Research and Innovation, the World Health Organisation, and the Novo Nordisk Foundation.

Till date, 29 PhD and 27 M Phil degrees have been awarded under my supervision.

2. Please express your thoughts on the importance of “Public Health” in the management of vector-borne diseases like Malaria.

Public health and epidemiological approaches are key to the management of any disease including a vector-borne disease such as malaria. Great progress has been made in the knowledge of the vector as well as the clinical and laboratory dimensions of the disease.

However, successful management and elimination of malaria require a problem-oriented interdisciplinary approach to understand how health problems such as this are shaped by socio-economic factors and delineate the structural constraints that contour the scope of technical health knowledge and health interventions.

3. You have been closely engaged with the ICMR, the National Certification Committee for Polio Eradication (NCCPE), and the National Health Mission (NHM), as well as several key national health programmes. Please share your perspectives regarding the common barriers to disease management in India.

I have been engaged with aspects of designing, monitoring, and evaluating key national health programs as well as eradication and elimination initiatives. These involve not just understanding technical dimensions but also extensive interactions with beneficiary communities to understand their perspectives as well as state and district-level program personnel to enable modification in sync with local contexts. While programs are designed based on certain theoretical understandings as well as experience in other parts of the globe, each one needs to be built brick by brick to adapt to the diverse Indian settings. Inadequate appreciation and application of these lead to barriers, distortions, and delays.

4. Being a professor at Jawaharlal Nehru University and a public health professional, what advice would you give to PhD students and young researchers?

Central to any research are rigor and theorization. It is important to understand that research is not just an agglomeration of certain tools and techniques. The methods cannot and should not shape research questions. The research problem should be framed on a deep understanding of the gaps in theory and/or practice and build on the current state of knowledge. Interdisciplinary public health research should entail an interdisciplinary approach that involves disciplines such as sociology, anthropology, psychology, economics, history, politics, demography, statistics, and public administration, apart from the disciplines that are traditionally included in public health. This requires more holistic training for public health students and scholars than what most institutions currently offer.

5. You have been associated with MERA-India as a mentor for community behaviour projects. What significance do you see for MERA-India in achieving India's malaria elimination target?

Malaria control and subsequent elimination require the integration of social science knowledge and practice into malaria research and programs. These are almost as a rule weak if not totally ignored. MERA-India has initiated several key steps in this regard and needs to be congratulated. Social scientists need to be inducted into malaria elimination research at the very outset and they need to understand the requirements of the program and practice rigorous social science. The outputs of such research should be translated into program strategies. It is a good beginning and MERA-India needs to support and sustain quality social and behavioural sciences research that can significantly strengthen and sustain the elimination efforts.

Malaria Through the Lens of Researchers

In the present issue, we are highlighting one of the shortlisted entries in the MERA-India Image Competition 2022, submitted by Ms Sangeeta Singh (a PhD student at NIMR Delhi).



Image title: "Consent form filling by the pilgrims for malaria testing"

A brief description of the image is as follows:

The image is showing team of researchers taking consent from the pilgrims before malaria testing under the project "Transmission of malaria during the pilgrim walk in western Rajasthan"

Upcoming Event

Lecture Series on Infectious Diseases 2.0 Lecture 06 by Dr Alison Krentel

ICMR-NIMR and MERA-India are hosting the sixth lecture in the series “Lecture Series on Infectious Diseases 2.0” to be delivered by Dr Alison Krentel. She is an Assistant Professor in the School of Epidemiology and Public Health at the University of Ottawa, Canada. She is the current chair and one of the founding members of the Canadian Network for Neglected Tropical Diseases. The lecture will be held in June, and further details will be shared through our website (<https://meraindia.org.in>) and social media accounts.

To receive regular updates about the events being organized by MERA-India, please subscribe at https://www.meraindia.org.in/event_sub.



Copyright © 2022 MERA-INDIA, All rights reserved.

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](tel:011-25307344)

Website: <https://meraindia.org.in>