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29TH ISSUE MARCH

MERA-India brings you...

NEWS & VIEWS

INTERVIEWS

Dr Ravi Kumar

Sr Regional Director (Retd.),
NCVBDC, Karnataka

Dr Alex Eapen

Scientist E, ICMR-NIMR,
Field Unit, Chennai

UPCOMING

Lecture series on Infectious Diseases, Lecture 04 by
Professor Faith Osier
Chair Malaria Immunology & Vaccinology
Co-Director, Institute of Infection
Imperial College London

Editorial

Dear Readers,

MERA-India team brings you the twenty-ninth issue of our newsletter, “News & Views”.

Starting on a positive note MERA-India would like to congratulate and welcome Dr Anup Anvikar for his new role as Director of ICMR-National Institute of Malaria Research (NIMR), New Delhi. Dr Anvikar is a physician-scientist, who has done tremendous work on improving the diagnosis and treatment of infectious diseases. We are certain that his contribution will take NIMR to new heights.

This year month of march, marks two important occasions Holi and International Women’s Day (IWD) on the same day 08th March, Wednesday. As Holi is the celebration of colors embracing every color equally similarly IWD is celebrated to embrace every color of womanhood and give them equal opportunity in every field. MERA-India also appreciates the contribution of women in achieving milestones, especially the female mentors, experts, scientists, and colleagues working together toward the target of a malaria-free India. One great example is MERA-India fellow scientist Prof. Sarita Kumar (Delhi University, New Delhi), who has recently cracked the effective formulation of Attractive toxic sugar bait (ATSB) for restricting the mosquito population and hence controlling malaria. We encourage young women researchers to be part of MERA-India and contribute to achieving the goal of malaria elimination by 2030.

In the present issue, we have included the highlights of the second lecture in the ICMR-NIMR & MERA-India Lecture Series on Infectious Diseases 2.0. This lecture was delivered by Prof (Dr) Mitali Chatterjee who is a professor and head of the department of pharmacology, at the Institute of Post Graduate Medical Education & Research (IPGMER), Kolkata, India. We have also covered the interviews of Dr Ravi Kumar {Sr. Regional Director (Retd.), National Center for Vector Borne Diseases Control (NCVBDC), Karnataka} and Dr Alex Eapen {Scientist E/Deputy Director, ICMR-National Institute of Malaria Research (NIMR), Field Unit, Chennai, Tamil Nadu} in the “Malaria Scientists to Watch” section.

In the “Research in Spotlight” section, we have highlighted three recent findings showing an effective formulation of the Attractive toxic sugar bait (ATSB) against *Anopheles stephensi* mosquitoes by Kumar S. *et al*; the presence of non-falciparum infections in children below 15 years of age in Nigeria by Herman C. *et al*.; and impact of Durable wall lining (DWL) for malaria control in Liberia by Giesbrecht D. *et al*.

In the section “Malaria Through the Lens of Researchers”, you will find one of the shortlisted entries of the MERA-India Image Competition 2022, which was submitted by Ms Rohini Nandi, a PhD student of Dr. Satish Mishra, Molecular Microbiology and Immunology, CSIR-Central Drug Research Institute (CDRI), Lucknow. In the “Upcoming Event” section, we are announcing the fourth lecture of the Lecture Series on Infectious Diseases 2.0, to be delivered by Professor Faith Osier (Chair Malaria Immunology & Vaccinology, Co-Director, Institute of Infection, Imperial College, London).

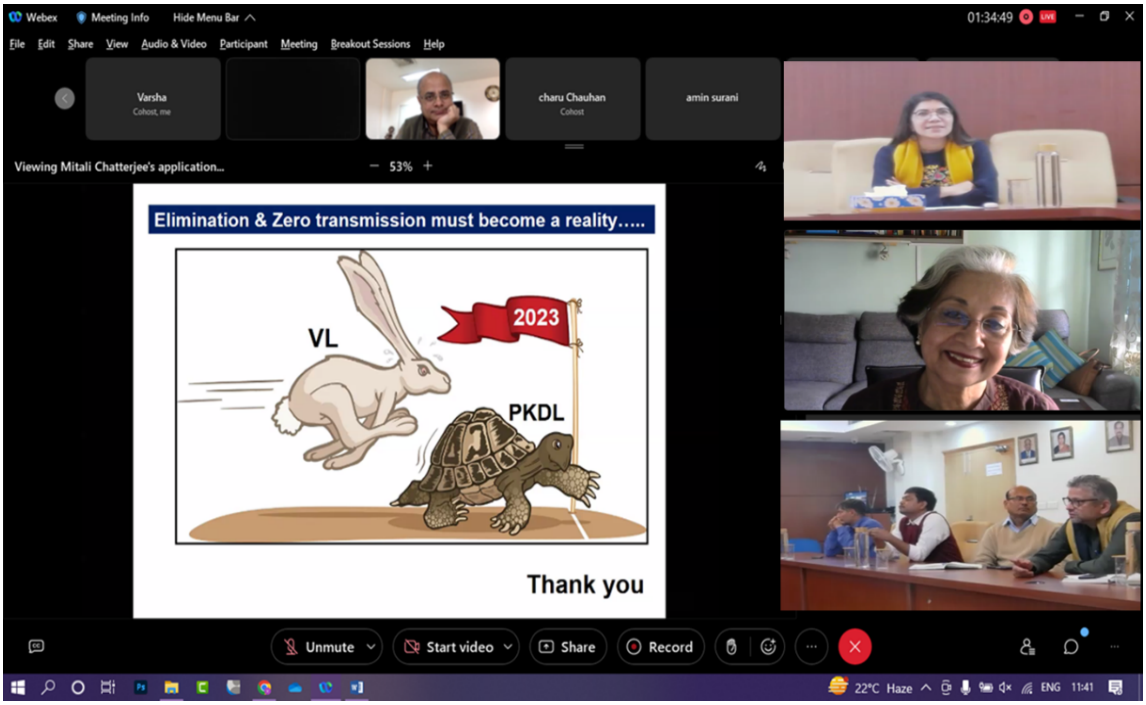
We hope that you will find this issue engaging and fascinating. Please write to us for any feedback or suggestions regarding the newsletter’s content at meranewsletter@gmail.com.

With best wishes,

MERA-India team

ICMR-NIMR & MERA-India Activity

Lecture Series on Infectious Diseases 2.0: Lecture 02 by Prof (Dr) Mitali Chatterjee



Prof (Dr) Mitali Chatterjee was the second speaker in ICMR-NIMR and MERA-India Lecture Series on Infectious Diseases 2.0. Professor Chatterjee is a professor and head of the department of pharmacology, at IPGMER, Kolkata, India. In her career, she has been honored with eminent awards like J. Ammal (Senior Category) Women Bioscientist Award, by DBT; Dr. PN Chhuttani oration, by the National Academy of Medical Sciences, and many more. Her initial scientific career was focused on visceral leishmaniasis (VL). Her research is currently focused on unraveling the immunopathology of post kala-azar dermal leishmaniasis, PKDL. Her group is also involved in active surveillance for PKDL and helping in quantifying the neglected burden of macular PKDL cases.

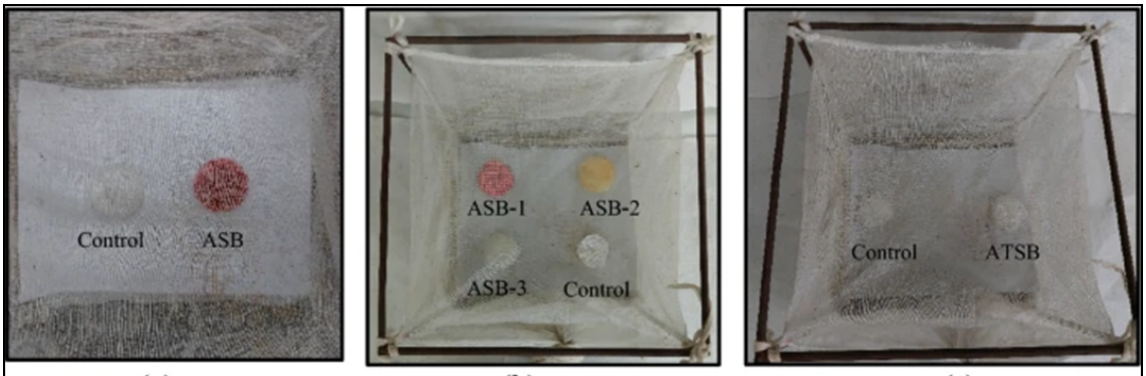
Professor Chatterjee's lecture entitled "Post Kala-azar Dermal Leishmaniasis: a neglected tropical disease that must not remain neglected". She first briefed the audience about the Kala-azar, from its beginning to its journey to efforts for its elimination. Then she highlighted the PKDL as the last mile challenge of the kala-azar elimination program. She showed that PKDL only occurs in two pockets of the world *i.e.*, South Asia (India, Bangladesh, Nepal) and East Africa (Sudan), but despite being caused by the same parasite, *Leishmania donovani*, the symptoms vary significantly in both areas. She also highlighted the importance of active surveillance to clarify myths about the disease such as, earlier it was a perception that PKDL is a male-dominant disease, but later proved that it's not gender bias, there are equal chances of getting the infection whether male or female. Professor Chatterjee mentioned the need for molecular diagnosis as the gold standard is antibody-based detection (ELISA and rk39 strip test), but for macular cases, there are chances for false positive results because of Kala-azar's past history. She also talked about the treatment and the problems associated with the treatment of PKDL. At last, she briefed the audience about future directions to improve PKDL case management.

Professor Chatterjee answered the questions of the audience after the lecture. The session was concluded by Dr Rahi 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

Kumar S. *et al.*, *Malar J.* 2023: Laboratory evaluation of the efficacy of deltamethrin-laced attractive toxic sugar bait formulation on *Anopheles stephensi*.



Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10007731

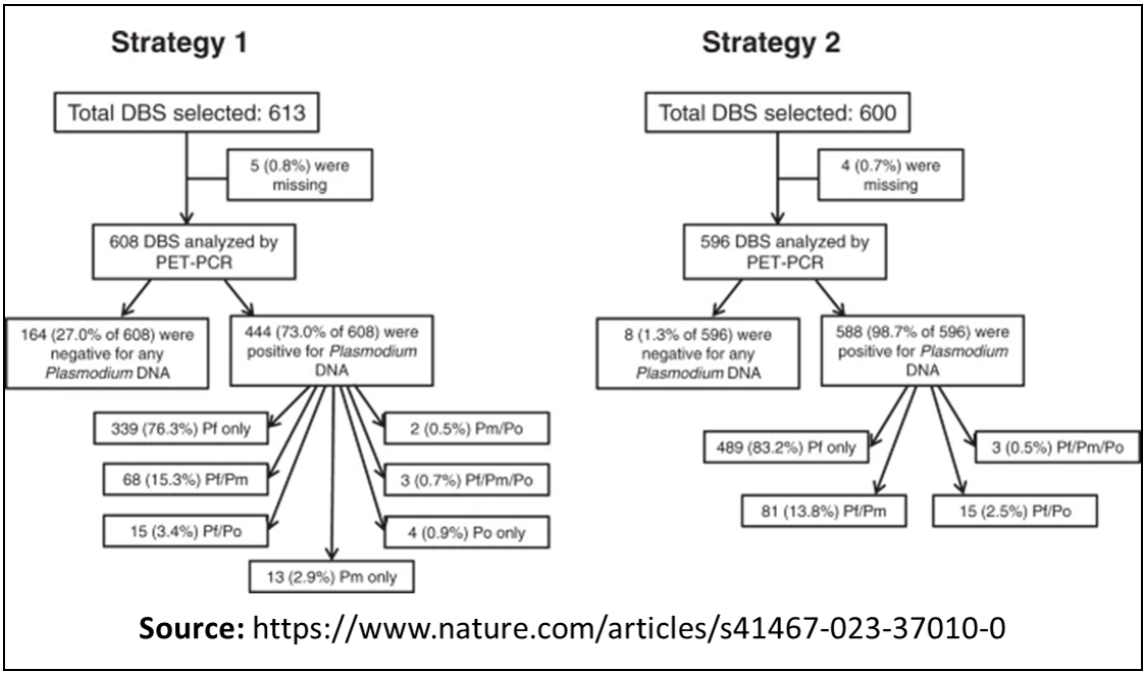
The Attractive toxic sugar bait (ATSB) is a method of killing mosquitoes by using the phenomenon of “Attract and Kill”. In this method, a formulation is prepared with the effective concentrations of flower nectar/fruit juice (attractant), sugar solution (feeding stimulator), and a toxicant.

In the present study, Dr Kumar *et al.* used fruit juices as an attractant, a sugar solution, and deltamethrin, a synthetic pyrethroid as a toxicant. At first, they tried various fruit juices (Pineapple, plum, sweet lemon, orange, guava, muskmelon, papaya, mango, and watermelon) with a 10% sucrose solution (w/v) in 1:1 ratio for determining the ideal attractant for two different strains of lab-reared *Anopheles stephensi* mosquitoes [the NIMR strain (Sonepat) and the AND strain (GVD-Delhi)]. Using cage bioassay they have identified that Guava juice-ASB>Plum juice ASB>Mango juice-ASB have higher attractancy potential than the rest of the ASBs and guava juice ASB was found ideal attractant for both *An. stephensi* strains. Then they tried 10 ATSB formulations with guava juice ASB and different concentrations of deltamethrin in a 1:9 ratio and tested their toxic potential on both strains of *An. stephensi* mosquitoes. The ATSB formulations resulted in 5.1–97.9% mortality in Sonepat (NIMR strain) with calculated LC30, LC50, and LC90 values of 0.17 mg deltamethrin/10 mL, 0.61 mg deltamethrin/10 mL, and 13.84 mg deltamethrin/10 mL ATSB, respectively. Whereas, 6.12–86.12% mortality was recorded in the GVD-Delhi (AND strain) with calculated LC30, LC50, and LC90 values of 0.25 mg deltamethrin/10 mL, 0.73 mg deltamethrin/10 mL and 10.22 mg deltamethrin/10 mL ATSB, respectively.

The concentration of (0.0015625–0.8%) guava juice ASB and deltamethrin was found most

effective on both strains of *An. stephensi*. Now field trials are being conducted to test the potential of this ATSB for vector control.

Herman C. *et al.*, *Nat Commun.* 2023: Non-falciparum malaria infection and IgG seroprevalence among children under 15 years in Nigeria, 2018.



African continent contributes most to the global burden of malaria. The most fatal malaria parasite species *i.e., Plasmodium falciparum* is also most prevalent in the African continent. Nigeria is one of the countries in the African continent affected by malaria.

In the present study, authors are trying to check the prevalence of non-*P. falciparum* parasites in children <15 years of age by testing the presence of parasite DNA and serological testing of IgG antibodies against MSP1-19 antigens of *P. ovale, P.vivax*, and *P. malariae* to check past exposure. They have taken DBS samples of children under 15 years of age from the nationwide Nigeria HIV/AIDS Indicator and Impact Survey (NAIIS) household survey conducted in 2018. Although earlier *P. vivax* was reported in various studies, but the present study didn't find any *P.vivax* infection. The most prevalent non-*P. falciparum* parasite was *P. malariae* affecting 6.6% of the children tested, followed by *P. ovale* affecting 1.4% of the children. Through this study, authors have also found the effect of financial status on malaria cases. The wealthy and urban residents were found to have protection against non-*P. falciparum* malaria. In serological testing they have found the highest seroprevalence of *P. malariae* i.e., 34.2% followed by P. ovale and P.vivax. Both seroprevalence and DNA testing proved that *P. malariae* is dominating Nigerian children. This study shows that we should not neglect non-*P. falciparum* parasites, while aiming for malaria elimination.

Giesbrecht D. *et al*., *Malar J.* 2023: Durable wall lining for malaria control in Liberia: results of a cluster randomized trial.

Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9837910

Long-lasting insecticidal nets (LLINs), impregnated with pyrethroid insecticide are one of the successful vector control measures for controlling vector-borne diseases globally. But insecticide resistance is hampering the effectiveness of LLINs and hence we are in need of new intervention measures to provide extra protection against these disease-carrying vectors.

In the present study, Giesbrecht D. *et al.* performed a clustered randomized trial for testing the potential of Durable Wall Lining (DWL) in malaria control. DWL is made of a novel material treated with two non-pyrethroid insecticides, designed to be installed to cover openings, ceiling surfaces, and the surface of the inner walls of rural houses. Mosquitoes entering the household will either fail to enter due to the mechanical barrier or if enter will be exposed to the non-pyrethroid insecticides and even if still enter the house and took a bite on the resident, will take a lethal dose of insecticides while resting on the walls, post blood meal. The authors have taken children from 2-59 months as the participants. The clusters from Bomi County of Liberia were selected and randomly assigned to receive DWL in addition to the LLINs and clusters with no DWL but using LLINs were taken as controls. Then they measured the *P. falciparum* malaria in participated below 5 years children in all clusters. They have shown that DL installed clusters had decreased *P. falciparum* prevalance then the control ones. Although trial was hampered due to ebola outbreak, but this study showed the potential of DWLs in malaria control, specially in places with open gables and eaves.

Malaria Scientist to Watch

An interview with Dr Ravi Kumar

Dr Ravi Kumar
Sr. Regional Director (Retd.),
NCVBDC, Karnataka
Independent Consultant & Public Health Adviser

1. *You have been an integral part of the malaria elimination activities in the government system; what is your view on achieving the goal of malaria elimination by 2030 with ongoing interventions?*

I am optimistic about the country reaching the goal of malaria elimination by 2030. The National Framework for Elimination of Malaria 2016 has identified the roadmap indicating the activities. A thorough review of the malaria control activities has been taken up which has led to the drafting of the National Strategic Plan for Elimination of Malaria, of which I am a part. A detailed plan for certification of elimination at national and sub-national levels is being drawn up. NHM is providing requisite budgetary support. Some states, like Karnataka, have already initiated steps in preparatory activities for certification of elimination by district-level assessments.

Consistent reduction of malaria incidence has been seen in most parts of the country. This has been possible because of nationwide surveillance and vector management activities. However, the progress toward elimination requires the maintenance of high-quality surveillance activities across the country in subsequent years. There is a need to maintain requisite active and passive surveillance including in urban areas. Validation of the fever /malaria incidence, assessment of coverage, and compliance with intervention measures are required.

Challenges remain. The biggest of them is to prevent the re-introduction of malaria to any area which has not had the indigenous transmission in recent times. In this regard, mobile /migratory populations pose a significant risk. Urban areas pose a challenge with low priority being accorded by local self-governments. Private sector reporting as well as their adherence to valid treatment guidelines is a grey area. Inadequate entomological setup has been a limitation resulting in an inadequate understanding of vector bionomics and insecticide resistance.

There is a need for concerted efforts by the entire health department in capacity-building activities and rigorous supervision /monitoring. With the belief that a sufficient budget would be provided by policymakers and implementation of activities would be taken up as per the roadmap, I feel that malaria elimination is achievable.

2. *What is the significance of Roll Back Malaria (RBM) in India in your opinion?*

RBM, as a concept, gave good impetus to the intensification of prevention and control of malaria control activities in India. Pilot sites were identified in different parts of the country for initiating activities. Capacity-building activities were done across the country with

assistance from RBM.

3. *As you were involved with the Government of India in the monitoring of the implementation of the joint action plan (Bangladesh, Bhutan, India and Nepal) for control of malaria in border areas, please share the roadblocks to the implementation of the malaria control measures across borders.*

The situation around the border areas poses peculiar challenges in malaria control. The security and access issues are constraints. While systematic activities can be put in place in formal border establishments, there are numerous porous border areas that pose a challenge in screening activities. Prevention of the introduction of multi-drug resistant *P. falciparum* to north-eastern states from border countries is a challenge. Synchronization of surveillance and vector management activities is also a challenge.

There is a need to have an adequate communication channel for sharing information on malaria outbreaks or cases with neighbouring malaria-endemic countries and use it effectively. In the case of a cross-border transmission focus with a neighboring country (a focus that crosses the borders between two countries), measures are needed to ensure that transmission is eliminated throughout the focus and to mitigate the risk of re-establishment of transmission in place. At points of entry, travelers need to be provided with information on malaria, including guidance on where and when to seek care. A program to raise awareness among people traveling to malaria-endemic countries on preventing malaria (chemoprophylaxis and prevention of mosquito bites) is in place. Drugs for chemoprophylaxis are to be made available.

4. *What advice do you want to give to young researchers working in the field of malaria?*

The young researchers have to identify relevant areas for research in the context of elimination strategy. They should have a close interaction with NCVBDC and the state program officers as to the current requirements. There is tremendous scope for validation studies regarding various aspects of routine and reported surveillance and vector control parameters. Other suggested areas are: Digital surveillance through mobile and or other digital platforms, Artificial intelligence (AI)-enabled Drones, Use of near real time RS and GIS mapping, Molecular markers for drug/insecticide resistance genes for both parasites and vectors, Xeno-monitoring of parasites using different methods from saliva and excreta etc., Early warning system for outbreak detection in low endemic areas, Markers for relapse and liver stages of parasite, Next Generation RDTs (low parasite detection level and HRP2/3 deletion detecting RDTs), Digital microscopy for low parasite detection, Asymptomatic/Low parasitaemia detection through a sensitive tool (e.g., TrueNat, PCR, LAMP), Detection of malaria parasites other than *P. vivax* and *P. falciparum* using multi-parasite detection RDTs or multiplexing, Drug compliance research, G6PD deficiency and other host factors that correlate with drug treatment (including metabolism), Outdoor transmission research in context with changing vector's biting and resting behavior, Insecticide Resistance profiling and management (including larvicides), etc.

In my opinion, I advise the young researchers to consider therapeutic efficacy studies for recommended antimalarials, national pharmacovigilance programs, elimination models for islands, isolated tribal areas, costing studies – economic analysis of malaria elimination, social benefits/impact of malaria elimination, climate change: new malaria foci identification etc.

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

MERA-India would be very relevant if its objectives of networking are being met. It would also be very significant if it can be a part of advocacy with policy makers in generating priority in resource allocation. It can also contribute to the malaria elimination certification assessments.

An interview with Dr Alex Eapen

Dr Alex Eapen
Scientist E/Deputy Director,
ICMR-NIMR, Field Unit, Chennai,
Tamil Nadu, India

1. *Please share your journey from getting a Ph.D. to being a senior scientist.*

After my post-graduation in Aquatic Biology & Fisheries from University of Kerala, I joined ICAR-Central Marine Fisheries Research Institute as a Senior Research Fellow and had a short stint before getting an offer as Asst. Research Scientist in ICMR-NIMR (erstwhile Malaria Research Centre) in September, 1988. My PhD from University of Madras was interdisciplinary with a research topic on a native/indigenous larvivorous fish, *Aplocheilus parvus* and its operational feasibility to control immature mosquitoes thus linking my academic subject with my profession. During this period, I had been actively involved in several operational research projects, funded by national and international agencies as a site investigator/Co-PI and PI. All the field research experiences gained over the years enriched me with adequate expertise to conduct major research projects related to public health. As a scientist, I had undergone several trainings/workshops, both abroad and in India sponsored by WHO, NIH, Bill and Melinda Gates Foundation and was also a commissioner/ an expert member in the 'Lancet Commission on Malaria Eradication' hosted by Global Health Group of the University of California, San Francisco. I had also undertaken several situational analysis studies and outbreak investigations on Malaria, Dengue, and Chikungunya in Tamil Nadu, Kerala, and Odisha.

2. *Being a scientist at a dedicated institute for malaria, please mention some of your scientific outcomes translated to the program.*

I was actively involved in many translational operational projects such as Bio-environmental control of malaria in urban areas which led to the formulation of a '7 point action plan for malaria control in urban areas in India', large-scale evaluation of bio-larvicides in major waterways in Chennai and Kochi resulting in the incorporation of the bio-pesticides for vector control interventions in Tamil Nadu, Malariogenic stratification of Dindigul Municipality and development/implementation of Geographical Information System (GIS) based malaria surveillance system in Dindigul, first of its kind for the health sector in India (1999) which was followed up by the state program for the operational management of vector control programs. Besides, scientific studies on the therapeutic efficacy of antimalarials

(chloroquine) to *P. falciparum* detected a high level of chloroquine resistance in Tamil Nadu (2006) and based on the results, the treatment regimen was changed by the state program. Moreover, rainwater harvesting and methods to mitigate vector breeding resulted in an action plan with environment-friendly designs. Bionomics of *An. stephensi*, an urban malaria vector in relation to its breeding, life table characteristics, host preference, resting, and feeding behavior were also investigated in detail and the findings were published in peer-reviewed international publications of high impact factor. Environmental monitoring of vector breeding habitats identified overhead tanks as the potential breeding habitat with a strong positive correlation of fluoride influencing oviposition of *An. stephensi*. All these research studies highlight integrated environmental, vector management methods to scale down and eliminate malaria regionally. Three doctoral research programs have been completed on *An. stephensi* and a few research scholars are still working on other biological aspects of the vector.

In addition, I was involved in the discovery of new larvivorous fish, *Puntius sharmai* in Chennai, India(1992), new sibling species of *An. culicifacies* complex (Species E), malaria vector in Rameswaram Island, Tamil Nadu (1999), and a new mosquito species *Heizmannia rajagopalani* in Kerala, India (2019). Several public health insecticides were field tested over the years before it was approved for operational use in the program.

3. *How difficult is it to manage urban malaria than rural malaria and what are the major roadblocks to urban malaria management?*

Challenges to manage urban malaria are aplenty and the vector, *An. stephensi* has already been reported as an invasive vector by the World Health Organization (WHO) considering the spread of *An. stephensi* to be a potential threat to malaria control and elimination in Africa and Southern Asia. Even in rural areas in India where the vector was observed occasionally, has now become a common phenomenon with its presence throughout the year. The challenges in urban areas include the tolerance/ resistance of *An. stephensi* to conventional larvicide, Temephos due to recurring treatment in water storage containers unlike varied natural and stored clean water habitats in rural areas; sub-microscopic or low-density malaria parasites and asymptomatic reservoirs in the community; exponential increase in overhead tanks due to urbanization and construction of buildings, both commercial and residential apartments; temperature tolerance of the immature *An. stephensi* and its survival in synthetic/plastic overhead tanks. In addition, population movement due to migrant laborers in mega construction projects such as flyovers, metro rail projects, high rise residential and commercial buildings; behavioral change of the vectors leading to outdoor transmission; empirical treatment by private medical practitioners and hospitals with case report as malaria positive (MP +ve) instead of parasites species such as *P. vivax* or *P. falciparum* for proper treatment as per NCVBDC drug schedules are the major barriers impeding the progress towards elimination.

4. *In your opinion, how important is it to track neglected Plasmodium species to achieve the goal of malaria elimination?*

Unlike *P. falciparum*, control of *P. vivax* represents varied challenges as the parasite tolerates a wide range of environmental conditions and can be transmitted from infected human beings to vectors before the symptoms develop. So, prompt and effective treatment will have less influence on *P. vivax* transmission in contrast to other parasite species. Furthermore, *P. vivax* is difficult to detect and treat because the parasitemia is usually low compared to that of *P. falciparum*, and current diagnostic tests cannot detect dormant forms residing in the liver. As a result, there may be a large reservoir of infected people who are unaware of their condition and are only diagnosed when they relapse and report symptoms.

In addition, the elimination of *P. vivax* liver-stage parasites requires a 14-day course of primaquine, which can lead to serious side effects (hemolytic anemia) in patients who have severe forms of glucose-6-phosphate dehydrogenase (G6PD) deficiency. Compliance with 14 days of treatment with primaquine is also another issue. Hence, *P. vivax* elimination requires specific, additional interventions such as targeting outdoor-biting mosquitoes; ensuring detection of even low-density *P. vivax* infections, testing all patients for G6PD deficiency before administering primaquine wherever possible, and importantly treating both blood and liver stages of *P. vivax* malaria. Therefore, control of *P. vivax* and its elimination requires new diagnostic tools, especially against the hypnozoite reservoir that currently evades most methods of detection and treatment.

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

MERA - India is a good research platform taking the keen initiative by funding various projects to find solutions for evidence-based research. So the outcome of the synergic association between the research organization/institute/universities and the state/national program would be very useful in achieving malaria elimination at regional and sub-regional levels.

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 Ms Rohini Nandi, a PhD student of Dr. Satish Mishra, Molecular Microbiology and Immunology, CSIR-Central Drug Research Institute (CDRI), Lucknow.

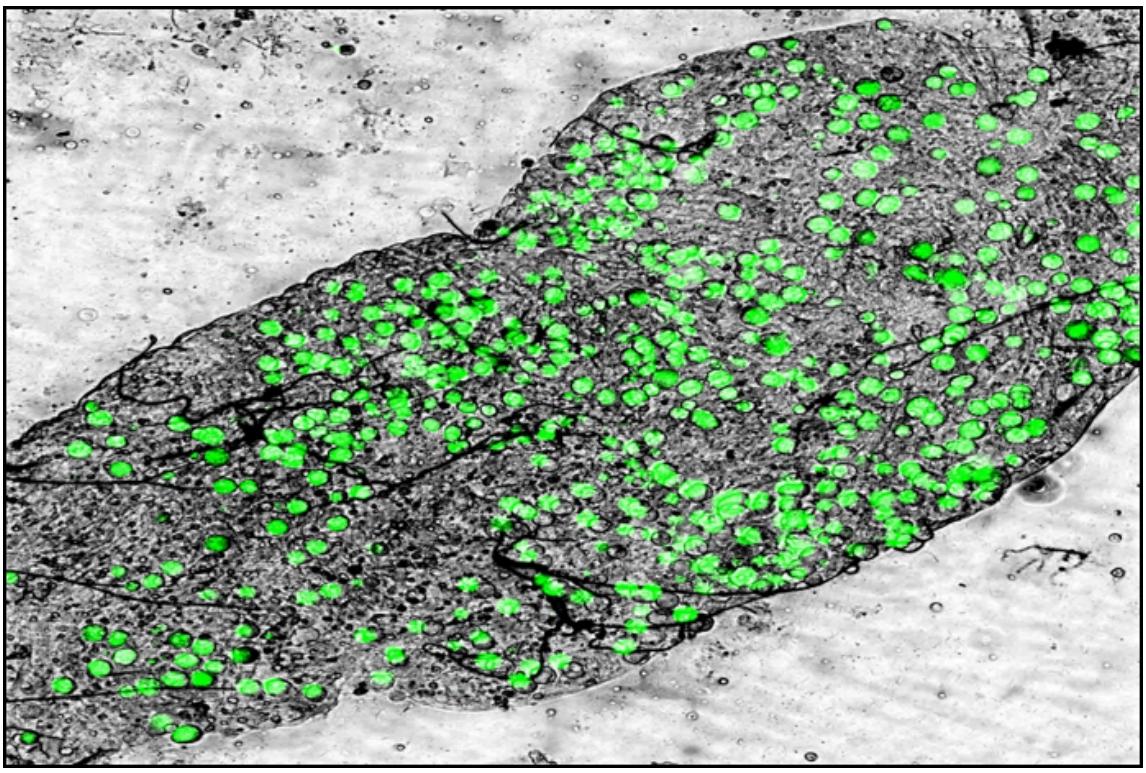


Image title: “Mosquito Midgut GFP Tag Oocysts”
A brief description of the image is as follows:

Gametocytes, the transmittable form of malarial parasite enters into its vector female Anopheles's midgut and differentiate into male and female gametes which fuse to form zygote and further develop into ookinetes. In this image of blood meal taken mosquitoes, gametocytes transform into ookinetes post-feeding of 22-24hrs. After that ookinete develops into oocysts. It takes almost 10-12 days post-meal. Here the picture shows the GFP- tagged oocyst within the midgut of the female Anopheles mosquito.

Upcoming Event

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

ICMR-NIMR and MERA-India are hosting the fourth lecture in the series “Lecture Series on Infectious Diseases 2.0”. Professor Faith Osier is the Chair of Malaria Immunology & Vaccinology and Co-Director of the Institute of Infection, Imperial College London. She is President of the International Union of Immunological Societies having > 60,000 members globally, and the first African in this role. She has won multiple prestigious prizes including the Sofja Kovalevskaja, the Royal Society Pfizer, and the UKRI-MRC/DFID African Research Leader Awards.

Professor Osier is a malaria expert, believing that we can “Make Malaria History” through vaccination. She will deliver the lecture on the occasion of World Malaria Day, 25th April 2023 at 1100 hrs IST.

Further details will be shared soon. For more details, please visit our website https://www.meraindia.org.in

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