# NEWS & VIEWS

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MERA-India

Malaria Elimination Research Alliance-India
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# MERA-INDIA Newsletter
# 'News & Views' March 2021

## El Salvador certified as malaria-free by WHO


**Figure 1**: El Salvador has become the first country in Central America to be certified as malaria-free by the World Health Organization on 25th February, 2021. The country has

now become a model for many nations striving to disrupt indigenous transmission of the disease. The official certification is a result of over 50 years of hard work and commitment put in by the Salvadorian government and its people to completely eliminate the disease despite living in a country with dense population and high susceptibility to malaria. (Click Here).

## ICMR-NIMR Activities: Mosquito Survey and Control


**Figure 2:** Demonstration of Mosquito collection and control (a-d). **A.** Different species of mosquito vectors can be collected for studying diversity and abundance using methods such as insect traps (e.g. light traps); **B.** hand collection through an aspirator andpyrethrum spray catch. **C.** Furthermore, control measures firstly involved timely survey of mosquito larva in water sources such as water tanks to determine breeding habitats in a particular area and prevent the dissemination of infectious diseases such as malaria, dengue, *etc.* **D.** Finally, endophilic mosquito vectors can be controlled by spraying walls with insecticides using spray pumps.

# Guest Commentary

## Severe Vivax Malaria And Elimination

*Plasmodium vivax* malaria imposes serious public health burden and is the most widespread of all the human malarias. The majority of the world's *P. vivax* transmission is in the South–East Asia Region. Densely populated India is nearly entirely at risk of transmission with large areas at stable risk of *P. vivax*, giving this region by far the largest population at risk. It remains a substantialhealth problem and economic burden in India with proven difficulties to control it, particularly in urban areas.Although number of malaria cases has declined in the recent years, the relative proportions of *P. vivax* cases are increasing. It is transmitted by a variety of vectors across diverse ecological habitats and shows polymorphism in the patterns of relapse. It can also be overlooked as a pathogen where a mixed infection with *P. falciparum* is present.

### Status of vivax malaria: Benign to Severe

During last two decades, there is substantial evidence that *P. vivax* is associated with all types of severe malaria syndrome including cerebral malaria and death. This may be because of improved diagnostic facilities, reporting, investigation and/ or changes in its pathogenicity. Earlier it was believed and preached that most serious and life threatening complications of malaria are caused only by *P. falciparum* infection, whereas *P. vivax* infections are relatively mild, and runs a benign course and does not require hospitalization. However, the dominant paradigm of *P. vivax* being a benign infection has been challenged recently from India. First authentic report of severe vivax malaria in world literature came in 2005 from Bikaner, India, when Kochar *et al.* reported that both sequestration and non–sequestration related complications like cerebral malaria, renal failure, circulatory collapse, convulsion, severe anemia, thrombocytopenia with or without bleeding, hemoglobinuria, abnormal bleeding, acute respiratory distress syndrome (ARDS), hepatic dysfunction, jaundice, and pregnancy-related complications including intrauterine growth restriction (IUGR) and miscarriage can be caused in patients suffering with *P. vivax* malaria. Two out of 11 patients died and one developed postmalarial psychosis. Polymerase chain reaction (PCR) test was used to confirm the diagnosis of *P. vivax* as well as to rule out P. falciparum coinfection. Since then, similar reports are coming from all over India and other parts of world. In many of these studies, the authors have used stringent test to exclude falciparum malaria and other coinfection. The occurrence, relation, and magnitude of thrombocytopenia is also more in *P. vivax* of malaria There are several possible explanations for this observation which includes possibility of a longer liver stage of *P. vivax* allowing prolonged periods for the parasite to remain in host environment, even

if transmission is interrupted and the primary infection has been treated successfully. The spectrum of severe syndromes in *P. vivax* is therefore similar to that of *P. falciparum*, while severe anaemia and acute lung injury are commonly reported manifestations in cases of severe *P. vivax*. The WHO “severe malaria syndromes” were also identified and confirmed from an autopsy study of 17 patients with *P. vivax* associated mortality from Brazil.

Relatively low parasite densities in blood (arising from its strict preference for reticulocytes) may lead to high rates of false negative diagnoses by microscopy or rapid diagnostic tests (RDTs). Microscopic diagnoses very often underestimate the true prevalence of *P. vivax* in blood in both high and low transmission settings. The lower densities of *P. vivax* in peripheral blood of mixed infection often translate into *P. falciparum* being diagnosed before *P. vivax* is spotted by the examining microscopist. Another consideration with regard to true versus estimated prevalence is the complete invisibility of the dormant liver stages to any means of mass survey. These forms are probably highly prevalent in many endemic settings. In spite of low parasitaemia in vivax than falciparum infections, the absolute number of red blood cells removed from circulation, and hence the degree of anaemia, is often similar. Further, the relapsing nature of *P. vivax* infections also contributes to anaemia. The combined presence of ARDS and anemia significantly increase the risk. How low parasitemia causes severe malaria is still not very clear. Co–infections with other pathogens (bacteraemia, HIV infection and dengue) are also important contributors to severe complications and increased risk of death, as observed with P. falciparum.

The risk of severe disease and case fatality rates are not firmly established for *P. vivax*. Amonghospitalised patients, some studies have reported similar risks of death as for *P. falciparum*. A study of hospitalized children in northwest India found case fatality rates of 3.9% for PCR confirmed *P. vivax* mono-infections and 3.2% for *P. falciparum* infections. Among non-hospitalised patients presenting at rural health facilities in PNG, the proportion of severe malaria cases among presumptive malaria patients with confirmed parasitaemia was similar for both parasites. A clearer picture of severe vivax malaria is emerging, as we may confidently express that infection by *P. vivax* is certainly not intrinsically “benign” in any sense. The communities of medicine and public health must reject the dangerous notion of *P. vivax* as generally harmless.

**Public health implications of severe and lethal *P. vivax***

The global clinical burden of *P. vivax* morbidity is poorly enumerated and difficult to assess, and estimates of severe cases and mortality do not exist. Nevertheless, the sheer population size at risk of infection (35% of the global population) and the potential clinical severity of acute cases make *P. vivax* an undeniable major global public health issue. Reliable burden estimates require improved surveillance systems. This entails the expanded use of species specific diagnostics, together with reporting systems which distinguish different *Plasmodium* species. It is likely that *P. vivax* mortality routinely passes undiagnosed which was also documented from the postmortem study in Brazil. Finally, the spread of drug resistance to the first line therapy is an increasing concern. Resistance to

chloroquine, still widely recommended as first line therapy against acute blood stage infection, is spreading in many regions of world. The uncertain repercussions of this for *P. vivax* therapy further add to its public heath significance. In spite of the fact that there is no evidence of resistance to primaquine, its long course with poor compliance requires urgent need of shifting to Tafenoquine single dose.

In summary, recognition of the potential for *P. vivax* to cause severe disease and mortality, combined with the sheer scale of the population at risk of infection and the imperfect toolkit available to fight *P. vivax*, culminate in a widely resonating public health problem. The momentum being galvanized in the fight against P. vivax must be sustained and extended to address the manifold issues associated with its public health significance and requires rethinking on present strategies for *P. vivax*, elimination challenges.

*(Professor Dhanpat Kochar, Chairman, Research Advisory Committee, Multidisciplinary Research Unit, Former Professor and Head, Incharge: Cerebral Malaria Research Centre S.P. Medical College, Bikaner - 334003, Rajasthan, India)*

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## Scientific contributions by dedicated Scientists/Researchers in the field of Malaria Research

*Am. J. Trop. Med. Hyg.*, 99(1), 2018, pp. 1–2
doi:10.4269/ajtmh.18-0390


**Editorial**

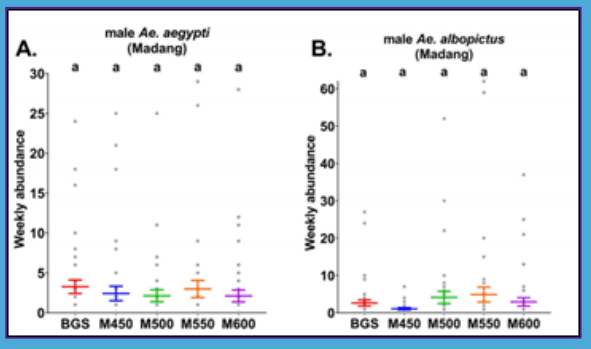
Malaria Elimination: Lessons from El Salvador

Adam Bennett* and Jennifer L. Smith
*Malaria Elimination Initiative, Global Health Group, University of California, San Francisco, San Francisco, California*

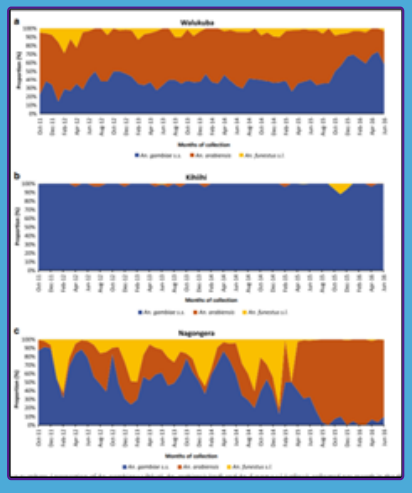
**Malaria Elimination: Lessons from El Salvador**

Adam Bennett and Jennifer L. Smith (2018), penned an editorial feature highlighting the valuable lessons that could be learnt from the measures taken by national programme of El Salvador to achieve successful elimination of malaria from El Salvador, central American country. According to the published literature by Burton et al.,2018, El Salvador could achieve elimination mainly due to three reasons, 1) Commitment in the early stages influenced by the surveillance data collected by the user friendly information systems and mobile communication, and the response made accordingly, 2) community based studies and systemic surveillance studies carried out at ground level, with provision of all essential services to accomplish the objective, 3) Finally, a firm consistent leadership by the government and constant necessary funding to ensure smooth running of the programme to achieve malaria elimination from the country.

**Outcomes from international field trials with Male *Aedes* Sound Traps: Frequency dependent effectiveness in capturing target species in relation to by catch abundance**




In an interesting study, Staunton *et al.*, 2021, demonstrate the use of sound waves with frequency similar to a female mosquito wingbeat to capture male *Aedes aegypti* mosquitoes. They have named these traps as Male *Aedes* Sound Traps (MASTs)which were field- tested in three dengue endemic countries Papua New Guinea, Mexico and Belize for capturing *Aedes* and *Culex* mosquitoes of medical importance. The mosquito capture rates of MASTs at frequencies 450, 500, 600 and 650 Hz were compared to the BG Sentinel trap, which is the gold standard surveillance trap. MAST was highly species specific and had capture rates comparable to BG Sentinel trap. The highest mosquito capture ratewas observed at 550 Hz and lowest at 450 Hz for male *Aedes* mosquitoeswhile male *Culex* mosquitoes were captured in significantly lower frequencies. Hence, according to the authors, findings from this work will help in the development of a cheap smart trap methodology to enable stringent examination of critical mosquito vector species.



**Impact of seasonality and malaria control interventions on Anopheles density and species composition from three areas of Uganda with differing malaria endemicity**

Mawejje *et al.*, 2021, described how malaria control interventions such as LLINs and IRS

could have a differential impact on species composition and diversity of *Anopheles* mosquitoes in three areas of Uganda with varying endemicity. The distribution of LLINs was linked to reductions in *An. funestus* in the lowest transmission site and *An. gambiae* in the intermediate transmission site, according to the findings. The near-collapse of *An. gambiae* and *An. funestus* was linked to a mixture of LLINs and several rounds of IRS at the highest transmission site. Following IRS, *An. arabiensis*, a behaviorally resilient vector, became the dominant species, potentially posing a threat to malaria vector control efforts. The creation of outdoor biting interventions still remains a top priority according to the authors.

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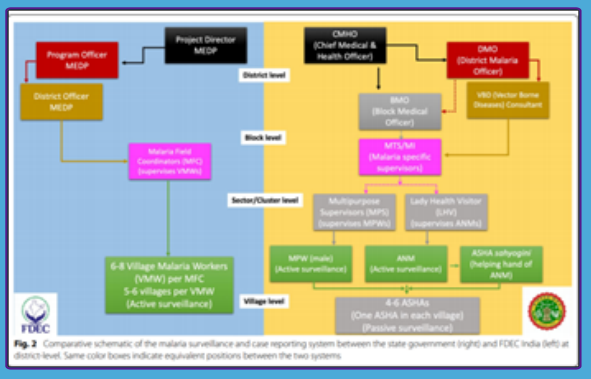
**A model for malaria elimination based on learnings from the Malaria Elimination Demonstration Project, Mandla district, Madhya Pradesh**




Rajvanshi *et al.*, 2021 worked on developing a model for malaria elimination using the protocols and knowledge acquired from the demonstration project (Malaria Elimination Demonstration Project) such as strict surveillance, vector control strategies, diagnosis and treatment, thereby showing that malaria can be eliminated from highly endemic areas along with prevention of relapse of malaria in those areas. This model can be used to eliminate malaria by 2030 not only in India, but also in other countries with similar geography, topography, climate, endemicity, health infrastructure, and socio-economic characteristics.

# Malaria Scientists to watch:
# 1. An interview with Professor B S Das

Professor B S Das, **MD, FNASc Former Advisor, Department of Biotechnology, GOI, and Emeritus Medical Scientist, ICMR**, Bhubaneswar-75101

1. ***Can you please describe your research background and scientific journey that motivated you to become a skilled malaria scientist?***

While working at SAIL, Ispat General Hospital (IGH), Rourkela, Sundergarh District, Odisha, I had gone to pursue a “certificate course in clinical nutrition”, from ICMR National Institute of Nutrition, Hyderabad, during 1984-85. Prof. David I. Thurnham, from London School of Hygiene and Tropical Medicine, was invited as a visiting faculty to take a few classes for us. Prof. Thurnham, was working on influence of nutritional antioxidants in malaria infection and suggested me to work on “nutrition and malaria”, which I did initially. Subsequently, Prof. Thurnham and asI had a few collaborative projects and have published several papers on nutrition and malaria.

But the real motivation to devote my entire research time and resources to work on clinical malaria, specifically on severe falciparum malaria was gained only after I met Dr.V.P.Sharma, the then Director, ICMR, Malaria Research Centre (current National Institute of Malarial Research). Dr.Sharma was on a visit to NIMR Field Station at Rourkela, and I was invited by the Officer-in-charge of the local field station to attend a meeting to discuss about malaria. We, at IGH, had observed that adults with cerebral malaria were far more serious with prolonged coma and higher mortality in comparison to children. The observations were quite contrary to textbook descriptions of malaria at that time, and we were not able to explain the possible mechanism. Dr.Sharma took interest to visit the hospital and saw the spectrum of severe malaria patients. His first comment was “the hospital was most ideal for clinical researches on malaria because where malaria exists, health care facilities are virtually nonexistent, and where health care facilities are excellent, malaria does not exist. Rourkela is probably the only place having a 700 bed

modern hospital, with plenty of severe malaria patients". The main problem with us at that time was a sense of isolation, internet services had not developed and we had no access to any malaria researcher in the country or abroad. Dr. Sharma brought IGH from isolation to limelight by arranging several national and international collaborations. He even convinced the local SAIL authorities about the benefits of malaria research and arranged a couple of workshops on "malaria prevention methods for construction engineers". He nominated me for Dr.MOT Iyenger Award, which was conferred in the year 1995 for my work on "severe falciparum malaria".

***2. What has been the significance of your valuable research so far that is highly inspiring for young researchers?***

We published our observations that adults were more vulnerable for multiple complications of falciparum malaria and higher incidence of death in comparison to children. Subsequently, a large number reports, mostly from South East Asia, reported similar observations. It is now universally accepted that the age dependent malarial complications are correlated with intensity of transmission.

As a component of our overarching research on clinical manifestations of severe malaria, we were looking at pathogenesis of death in cerebral malaria. The dominant concept during late eighties and early nineties was that cerebral malaria occurs due to cytoadherence of parasitized RBCs (PRBCs) to brain vasculature, and blockage of the cerebral vessels by PRBCs. Cerebral oedema is only an occasional terminal event. Margination of lymphomonocytes to brain capillaries was responsible for cerebral malaria like symptoms in mice. We did post-mortem brain biopsies from patients dying of cerebral malaria and on histopathological examination from multiple sites; we found both clogging of capillaries with Parasitized RBCs as well as margination of leukocytes to vascular endothelium and extensive cerebral edema. We proposed the role of PRBCs and lymphomonocytes in initiation and progression of cerebral malaria. Post-publication the paper drew a lot of attention from different research groups, but over a period of time the hypothesis was universally accepted as it is or with some modifications.

***3. As a senior research scientist, we would like to know, what are the research gaps that you think require urgent attention in eliminating malaria from India?***

The MRC/NIMR has been doing pioneering research on vector biology since its inception. In the recent past there have been some outstanding contributions on parasite biology by individual groups from different institutions from the country. However, enough attention has not been given to malaria epidemiology. Malaria being a local and focal disease, epidemiological mapping of the country needs adequate human as well as financial resources. A clear understanding of epidemiology at local level will help rapid elimination of malaria.

***4. Finally, other than malaria research, did/do you have any other non-scientific interests?***

I have an interest in reading books on history and philosophy; more specifically on Indian Philosophy.

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## 2. An interview with Dr. Mradul Mohan

Dr. Mradul Mohan, Ph.D., **Scientist-B, ICMR-National Institute of Malaria Research (NIMR)**, Dwarka, Delhi-110077

***1. Can you please describe your research background and career route that motivated you to become a skilled malaria scientist?***

Since my childhood, biology fascinated me as subject a lot. I wanted to be a medical doctor, but there was something else planned for me. I had started to prepare for medical entrance examinations but I could not succeed. I did my graduation from Dr. Bhim Rao Ambedkar University, Agra. After graduation I took admission under the Master of Science in Microbiology discipline from Agra University. During my post-graduation I learned various disciplines of microbiology like immunology, molecular biology, biochemistry. I did my Ph.D from CSIR-Central Drug Research Institute, Lucknow in the year 2014 under supervision of Dr. Amit Misra. My doctoral work basically addressed the negative regulation of cytokine signalling during Mycobacterium tuberculosis infection.

***2. What was the biggest motivation in your life that made you become a scientist?***

During my Masters I was the student of Dr. V. M. Katoch. He taught us molecular biology amazingly and it drove my interest in science and eventually I did my doctorate. ICMR has advertised scientist position in the year 2014. I got qualified scientist exam and lucky to get selected for scientist B post.

***3. Educate us with your line of research and what has been the significance of your***

***valuable research so far in your career?***

I have joined ICMR-NIMR during October 2018 as initially I was working as scientist B at ICMR –NIOH, Ahmedabad. At ICMR-NIOH, I was looking for heavy metal toxicity. While at ICMR-NIMR, I am currently working as a co-investigator in various research projects comprising the different aspect of malaria research. As far as my research interests are concerned, I want to explore the intricate relationship between a parasite and host especiallyhow the parasite manipulates the host's machinery for its own survival needs to be explored. Host genetic makeup may also contribute towards the disease susceptibility. I am also working to look in to the complex form of malaria cerebral/severe malaria.

***4. In the area of malaria research that served as a catalyst in your budding research career, what inspired you the most?***

It is the beginning of my career. I want to look in to the parasite's striking ability to manipulate the host's response.  As I said I am beginner in the field of Malaria research, and I am trying to understand its relationship with the host.

***5. Have/have you had any other scientific interests other than malaria research?***

Tuberculosis and COVID-19 are my research interests other than malaria research. As current COVID-19 pandemic is driving the whole scientific community to get some therapeutic solution for it.

***6. Finally, on a lighter note, do you have any hobbies other than science that keeps you going on even during challenging times during your research career?***

Since childhood, music is my hobby. I love to listen all sorts of music songs like ghazals, old and new Bollywood songs, local folk songs. Singing is also my hobby; I love to sing Ghazals, Bollywood songs. History and International Relation are my favorite subjects after science; you may consider history reading my hobby.

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