Addressing the threat of antimalarial drug resistance to malaria elimination in Southeast Asia

Workshop report

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The Academy of Medical Sciences

TAST

BIOTEC a member of NSTDA

Executive summary

Over the past decade, the burden of malaria in the Greater Mekong Subregion has declined substantially. Between 2012 and 2018, the number of deaths from malaria fell by 95%. This progress has been underpinned by a regional commitment to malaria elimination.

Much of the progress in malaria control has come from the use of highly efficacious artemisinin-based combination therapies (ACTs), consisting of an artemisinin derivative such as artesunate and a partner antimalarial drug. Artesunate acts rapidly, clearing most of the parasites, while the longer-lasting partner drug kills any that survive.

Drug use inevitably selects for less susceptible parasite variants. Over the past decade, new parasite strains resistant to artemisinin derivatives and their partner drugs have emerged and spread widely in Southeast Asia. These new strains compromise the ability to treat malaria and undermine the drive towards elimination.

In October 2020, a joint virtual meeting organised by the UK Academy of Medical Sciences (AMS), the Thai Academy of Science and Technology (TAST) and the National Center for Genetic Engineering and Biotechnology (BIOTEC, a member of the National Science and Technology Development Agency in the Ministry of Higher Education, Science, Research and Innovation) took stock of the current state of drug resistance in the Greater Mekong Subregion and how research could address the challenges identified. Through breakout groups and discussions, the following key issues were identified:

- **Drug development:** The number of new antimalarial drugs in the pipeline is low and there is a high attrition rate. Although at least two promising new drugs – cipargamin and ganaplacide – have a realistic prospect of being licensed, their routine use is still some years away. In the meantime, the efficacy of existing drugs must be preserved through approaches such as triple combination therapy, sequential use of drugs and drug rotation.

- **Genomic epidemiology:** The characterisation of genetic markers associated with drug resistance is enabling drug-resistant infections to be identified and mapped. This provides insight into the evolution and spread of drug-resistant strains, and also provides critical information to national malaria control programmes.

- **Malaria control:** As cases of malaria have declined, community-based detection and treatment of infections, through the mobilisation of community health workers, has been shown to be highly effective at reducing the incidence of disease. However, currently recommended strategies to detect and investigate new cases may not be appropriate in remote, hard-to-reach regions. Mass drug administration and/or mass screening and treatment may be valuable alternative or complementary approaches.

- **Communities:** As malaria becomes less common, it is important to maintain community commitment to elimination, support for control measures and adherence to treatment. Elimination-based activities may be particularly challenging in geographically remote communities and among groups such as migrants who are often reluctant to engage with public healthcare systems.

- **Integration:** Malaria control has primarily been a standalone activity. As case numbers decline, it is increasingly important to integrate malaria control and other health services. This will contribute to the development of more patient-centred and sustainable services.

  Participants also identified a range of areas, in addition to current priorities such as drug development and genomic epidemiology, where additional research is needed:

- **Genetic markers of resistance:** Further research is needed to identify emerging mutations associated with drug resistance, for currently used drugs as well as newly developed drugs as they are evaluated in clinical trials.

- **'Final mile':** More research is needed to identify the most effective strategies for malaria control and elimination in areas of low transmission, particularly in environmentally challenging locations. This includes the effectiveness of mass drug administration and mass screening and treatment.

- **Integration:** With integration likely to be key to sustainability, there is a need to identify and evaluate suitable integrated models of care, potentially building upon the community health worker infrastructure established for malaria control. There may also be opportunities for synergies between COVID-19 responses and malaria control.

- **Cost-effectiveness:** For drug introductions, there is the need for additional health economic analyses that include a wider range of factors, such as the long-term benefits of maintaining the efficacy of drugs.

- **Community engagement:** It is essential to maintain public support for malaria elimination and for control measures. There needs to be an emphasis on close engagement with communities to maintain awareness of malaria as a health threat, the mobilisation of support for control activities, and gathering community input into the design of control activities.

Participants concluded that rising levels of antimalarial drug resistance needed to be dealt with as a matter of urgency. Genomic surveillance is providing the tools to understand the nature of the threat, and it was seen as vital that this information was communicated effectively to national malaria control programmes and policymakers, to inform practical control efforts and to mobilise political commitment to malaria elimination. The sharing of data and samples between research and control programmes, and across borders, was identified as essential to provide a comprehensive view of drug resistance and to identify the most effective responses.

A failure to control drug-resistant malaria in the Greater Mekong Subregion could undo years of progress, have a devastating impact on health and economic development, and increase the risk of a potentially catastrophic spread to regions such as sub-Saharan Africa.

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