To begin, could you provide an insight into your own professional background?

An undergraduate interest in parasitology led me to pursue a Master’s of Science in Public Health, during which I spent two years as a Peace Corps volunteer in Ivory Coast assisting with the national programme aimed at eradicating Guinea worm. This spurred me on to complete my medical training in paediatric infectious disease, which included a fellowship research project in malaria immunology in western Kenya.

I then joined the Military Malaria Research Program as a contractor with the Henry M Jackson Foundation, posted first at the Walter Reed Army Institute of Research, USA, and then here in Bangkok, Thailand.

How are patients with artemisinin-resistant malaria currently treated? Are there alternative treatment options to artemisinin combination therapies (ACT) and if so, how effective are they?

ACTs are without doubt the most effective weapons we currently possess in the fight against malaria. Patients with artemisinin resistance can be treated with other combination therapies to cure the infection, but in the long-term we will need a new class of antimalarial drugs. For years, the US Army was one of the leading developers of new antimalarials, and it continues to discover and evaluate novel compounds, while agencies such as Medicines for Malaria Venture are supporting the development and clinical trials of novel drugs in endemic areas, in order to accelerate roll-out.

British drug maker, GlaxoSmithKline, is currently in the process of seeking regulatory approval for the world’s first malaria vaccination, RTS.S. If successful, will this impact the Armed Forces Research Institute of Medical Sciences (AFRIMS)’s work? Could you elucidate some of the ways in which AFRIMS is working towards the development of an effective vaccine?

Army researchers were heavily involved in the testing and optimisation of the RTS,S vaccine regime in adults in the US, and the licensing of this vaccine will be a major contribution to lessening the burden of malaria. The first priority of the RTS,S vaccine will be its administration to paediatric populations in sub-Saharan Africa but there may also be a role for RTS,S in elimination campaigns in Southeast Asia, if packaged with other malaria prevention and treatment interventions. Right now, AFRIMS is collecting information on the baseline level of malaria antibodies in the Cambodian population so that when a vaccine is introduced, we can effectively measure any boost in immune response.

Do you tend to collaborate with other projects or laboratories in the course of your investigations? Who are these partners, and has a multidisciplinary approach proven important to the success of the initiative?

We currently work with an array of partners and are always looking for new collaborators. While we try to conduct most of our research ‘in-house’, we will of course take opportunities to involve other institutions and labs which have distinguished expertise in malaria, such as the University of North Carolina, University of Maryland and the Pasteur Institute. One of our ongoing clinical trials is a Department of Defense, multi-centre, harmonised study investigating artemisinin resistance in three countries across three continents – Thailand, Peru and Kenya.

Are there any forthcoming events, conferences or workshops related to AFRIMS’ work that you would like to highlight?

We recently attended the American Society of Tropical Medicine and Health conference in Washington DC, which sees over 3,000 researchers from all over the world come together in November to present their results and discuss policies specific to global health. It provides an opportunity to meet fellow scientists and students, and have vital global conversations about artemisinin resistance and other barriers to malaria elimination. This year we presented our latest findings on the worsening of resistance with dihydroartemisinin therapy in northern Cambodia, and we will continue to discuss these findings with Ministry of Health officials, in the hope of stemming the tide of this persistent disease.

Dr Michele Spring’s research into artemisinin-resistant Plasmodium falciparum has led to improved detection and monitoring of antimalarial drug failures in Southeast Asia and will work to facilitate the development of the next generation of therapies
The front line of antimalarial research

The Armed Forces Research Institute of Medical Science has over five decades of clinical research experience and expertise in the battle against malaria in Southeast Asia.

ESTIMATES OF GLOBAL mortality vary, but it is likely that the mosquito-borne disease malaria is responsible for around 627,000 human deaths annually. Advances in malaria research have brought fresh promise of a vaccine, but effective drug therapies remain the cornerstone of malaria control.

Artemisinin is a compound derived from the herbal plant Artemisia annua, or sweet wormwood, and forms the basis of our current and most effective treatments for malaria. Recent years have seen the most dangerous malarial species, Plasmodium falciparum, begin to exhibit increasing resistance to artemisinin-based antimalarial drugs in regions such as Southeast Asia – specifically along the Thai-Cambodian border. Despite the best efforts of researchers worldwide, it has not yet been possible to identify a singular definitive molecular marker for this resistance, with in vitro tests proving inconclusive and parasite-resistance phenotypes still poorly-characterised.

Artemisinins clear parasitaemia quickly, but for maximum efficacy they should be administered along with a companion drug. Many are sold or administered incorrectly, or taken in isolation rather than in combination, leading to a burgeoning resistance which threatens to undermine steady progress in combating the disease. This resistance manifests through delayed parasite clearance during therapy and renewed outbreaks of malaria in the period following treatment. With factors such as the proliferation of cheap and ineffectual counterfeit drugs; a lack of access to healthcare; and the high mobility of populations all contributing, resistance is a major concern for scientists and healthcare organisations. Addressing this problem swiftly is important, not only for the wellbeing of local populations, but to prevent resistance from spreading.

A MAJOR STEP FORWARD

Containing this emerging drug resistance is challenging, not only because of the difficulty in identifying biomarkers and characterising the resistant strain of P. falciparum, but more fundamentally because questions remain as to how and why resistance first emerges, leaving those working on disease prevention ‘behind the curve’, managing the situation reactively. Both public and private local health centres need to be able to make accurate diagnoses, and administer medication judiciously and appropriately, as well as participate in continued treatment efficacy studies to monitor for resistance and pinpoint the most effective treatments.

One way that the community can begin to bridge the gap is by improving malaria diagnostics. Molecular...
INTENTIONS

AR TIFARIAL RESEARCH BY THE ARMED FORCES RESEARCH INSTITUTE OF MEDICAL SCIENCE (AFRIMS)

OBJECTIVES

AFRIMS aims to tackle antimalarial resistance in Southeast Asia and worldwide through a combination of field- and laboratory-based studies. Goals include the improvement of diagnostic tests for malaria and conducting clinical trials into new antimalarial drugs.

PARTNERS

Thai Ministry of Public Health
Royal Thai Army
Cambodian National Center for Parasitology, Entomology and Malaria Control
Royal Cambodian Armed Forces
Communicable Disease Control Department, Ministry of Health, Cambodia

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tests such as polymerase chain reaction (PCR) are sensitive, and able to detect malaria at very low serum concentrations, but not available for use in most malaria endemic areas – whereas the current line of rapid diagnostic tests for malaria are useful in remote locations. Developing point-of-care tests with the sensitivity of PCR for malaria diagnosis or identification of genetic predispositions which could affect responses to antimalarials may provide much-needed information to help direct interventions and impede the emergence of resistance. “The coming year will see AFRIMS involved in field-testing a new category of rapid tests which look for a hereditary condition called G6PD deficiency,” reveals Spring. “People deficient in this enzyme are susceptible to severe side-effects if they take certain antimalarial drugs like primaquine, so being able to identify those at risk before they are given the drug will be a major step forward.

BREADTH OF EXPERTISE

The broad array of underlying causes of artemisinin resistance necessitates a layered, multi-pronged and collaborative approach at all levels. Investment in R&D of new malaria drugs, as well as the provision of preventative measures to decrease transmission rates – such as insecticide-treated bed nets, vector control and vaccines – are also crucial. Putting all of these measures in place is a tall order, but failing to do so will facilitate the continued spread of resistance.

As an international organisation with access to a breadth of research expertise and a long history of successes in the field of tropical medicine, AFRIMS is well placed to support these efforts. “AFRIMS’ greatest strengths are its Thai and Cambodian employees; they are the backbone of the institution and provide vital continuity,” enthuses Spring. “Our teams detected the first evidence of artemisinin resistance in malaria and conducted some of the initial clinical trials evaluating the efficacy of artesunate and tafenoquine.”

LONG-TERM EFFORT

Working successfully in a cross-cultural setting is not without its challenges, but AFRIMS is a well-integrated organisation whose employees have years of experience in conducting quality research which ensures the continued production of effective drugs and vaccines against debilitating tropical diseases. Perhaps the greatest challenge lies in maintaining these efforts during times of global financial difficulty. The most important aspect of working outside of the US, according to Spring, is carrying out research alongside host country researchers toward a common goal. AFRIMS aims to perform research relevant to local Ministries of Health, with capacity building and technology transfer when needed.

The goal of eradicating malaria remains, for now, somewhere in the future, and making it happen will require a sustained and long-term effort. Spring and her colleagues know from experience that even if malaria infections are driven to a nadir, any temporary let-up in prevention and treatment efforts can lead to a resurgence of the disease or even create new resistant strains, with dire consequences for patients. The invaluable work done by AFRIMS and similar organisations must therefore be coordinated, concerted, and sustained.

AFRIMS’ successes

In the half century since its initiation, The Armed Forces Research Institute of Medical Sciences has overseen some inspiring work on tropical disease prevention

• Its virology researchers were the first to conduct clinical studies which led to the licensing of the hepatitis A and Japanese encephalitis vaccines
• AFRIMS teams have generated crucial insights into the immunology, pathology and epidemiology of dengue infections
• The Department of Retrovirology helped conduct the recent Phase 3 trial on an HIV vaccine involving 16,000 Thai participants – the only vaccine to date which has demonstrated efficacy