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CHAPTER

Khun Niphon Chuanak and Khun Barnyen Permpanich from the Department of Immunology collect blood specimens from villagers in Sangkhlaburi (Kanchanaburi Province, near the Burmese border) as part of a 1999 study to identify causes of fever. (MFN#000017, AFRIMS photograph archives)





RTA soldiers impregnate uniforms in 1992 with permethrin, an anti-mosquito agent, as part of an AFRIMS collaborative study with Major Steve Frances of the Australian Army, to assess personal protective measures against malaria. (MFN#000300, AFRIMS photograph archives)



The 1990s

IN THE 1990s, SIX DIRECTORS GENERAL LED AFRIMS. Major General Choochat Kambhu Na Ayudhya, who directed AFRIMS from 1994 to 1998, became the first SEATO/AFRIMS director general to subsequently serve as the Royal Thai Army (RTA) surgeon general. During the decade, the US Army Medical Component (USAMC) had three commanders (as the position was now called).

During these years AFRIMS was involved in collaborative field efficacy trials of three candidate vaccines. The largest was a trial (started in 1991) of the Smith-Kline Beecham hepatitis A vaccine, carried out in partnership with the Thai Ministry of Public Health, in 40,000 school children in Kamphaeng Phet Province. The trial showed that the vaccine was safe, immunogenic, and protective, and it was a major factor in the US Food and Drug Administration's approval of the vaccine, providing a major new weapon against infectious hepatitis.

The first field trial of a malaria vaccine (R32Tox-A) in Asia was carried out by the US and RTA components in 1990–1991. The trial was conducted in Thai Rangers (Tahan Pran), immunized at their base camp in a nonmalarious area before deployment to malaria-endemic border areas of Ubon Ratchathani, where fighting was ongoing with the Laotian and Khmer militaries. The vaccine was shown to be safe and immunogenic, but it appeared to be nonefficacious, although infections did not occur until antibody titers had fallen from their peaks.

At mid-decade, WRAIR and AFRIMS collaborated with Mahidol and Oxford universities to critically evaluate a malaria vaccine (SPf66) that had shown promising but inconsistent results in South America. The vaccine was evaluated



[Left] Major General Vichai Sangkasuwan, Director General, 1990–1991. (Royal Thai Army official photograph)



[Center] Major General Kanokros Hongthong, Director General, 1991–1992. (Royal Thai Army official photograph)



[Right] Major General Pricha Singharaj, Director General, 1992–1994. (Royal Thai Army official photograph)

in a field efficacy trial among Karen children living in malaria-endemic areas of the Burmese border and was found to be nonefficacious. These two malaria sporozoite vaccine field trials inspired malaria researchers to search more intensely for new leads in vaccine development.

The 1990s also marked the start of a human immunodeficiency virus (HIV) research program at AFRIMS. Sentinel surveys showed that HIV was spreading rapidly among parenteral drug users in Bangkok, and among sex workers and their clients in the north. Colonel Donald Burke, director of WRAIR's Division of Retrovirology and former chief of AFRIMS's Department of Virology, proposed a collaboration on HIV research to Lieutenant General Phinyo Siriyaphan, the RTA surgeon general. Though such a project was politically sensitive, General Phinyo directed the RTA to screen all new recruits for HIV and share the summarized data with the Ministry of Public Health. WRAIR supported AFRIMS and the RTA Institute of Pathology in the establishment of a state-of-the-art HIV testing program to reduce the incidence of false-positive results. HIV-positive recruits were retained on active military duty and provided counseling and care.

WRAIR and AFRIMS's RTA and US components began to build human, laboratory, and field capacity to evaluate candidate HIV vaccines. The



[Left] Major General Choochat Kambhu Na Ayudhya, Director General, 1994–1998. (Royal Thai Army official photograph)

[Right] Major General Gobchoke Puavilai, Director General, 1998–2001. (Royal Thai Army official photograph)

Department of Retrovirology was established in the US component (1993), and several vaccine manufacturers agreed to reformulate their candidate HIV vaccines to match the subtype of the virus circulating in Thailand. In the late 1990s a number of these candidate vaccines were assessed in clinical studies, and one “prime-boost” combination was advanced to phase III testing, which was implemented in the next decade. To prepare for the phase III trial, cohort development studies were done in Chiang Mai in collaboration with the Research Institute for Health Sciences, Chiang Mai University, and in Chonburi and Rayong provinces, working with the RTA and the Ministry of Public Health. Over 5,000 volunteers were followed in multiple sites for various time periods to inform the cohort selection.

The departments of Virology and Bacteriology both developed collaborations in Nepal. The former focused on hepatitis E infections and the latter on travelers’ diarrhea. Dr. Mrigendra Shresthra led local investigations of hepatitis E virus, laying the foundation for a clinical trial of a promising candidate vaccine. Because of similarities in vulnerability to diarrhea among Western travelers and military personnel, AFRIMS worked with Kathmandu travel clinics to show that infecting organisms varied with time abroad and duration of symptoms. The researchers showed that a protozoan parasite, *Cyclospora*, was a cause of diarrhea, and demonstrated how to treat it.



[Left] Colonel John Boslego, USAMC Director, 1989–1992. (US Army official photograph)



[Center] Lieutenant Colonel Daniel Jarboe, USAMC Director, 1992–1995. (US Army official photograph)



[Right] Colonel Thomas Brewer, USAMC Commander, 1995–2000. (US Army official photograph)

Over time, these collaborative studies led to the establishment of the Walter Reed-AFRIMS Research Unit–Nepal (WARUN).

A new cooperative relationship was built with Vietnam during the 1990s. The Department of Bacteriology began collaborating with the Vietnamese National Institute of Hygiene and Epidemiology. Under Dr. Phung Dac Cam, chief of the institute's Division of Enteric Pathogens, joint research has continued to the present.

Both components of AFRIMS provided direct support to their respective militaries during the decade. The RTA component established a program to screen Thai peace-keeping forces before and after deployment so that infections acquired abroad could be treated and their potential spread controlled. The US component supported the annual Cobra Gold joint training exercises, usually focusing on diagnosis and treatment of diarrheal diseases, and determination of evolving levels of drug resistance in these infections.

During the 1990s, insightful observations by WRAIR/AFRIMS entomologists Lieutenant Colonel Ronald Rosenberg and Lieutenant Colonel Richard Andre showed that falciparum malaria had returned as a public health threat in



[Top] Colonel Pricha Singharaj, principal investigator (and future AFRIMS director general), interviews a Thai Ranger (Tahan Pran) as a potential subject in a malaria vaccine trial. The 1990–1991 study, a collaboration between the Royal Thai and US armies, and the Swiss Serum and Vaccine Institute, was the first field trial of a malaria vaccine in Asia. (MFN#000375, AFRIMS photograph archives)



[Bottom] Major Arthur Brown and Colonel Boslego assess reactogenicity of candidate malaria vaccine in two Ranger volunteers at Camp Pakthongchai in Nakhon Ratchasima (Korat), in 1990. (MFN#000382, AFRIMS photograph archives)

deforested areas recently replanted as orchards, creating a favorable environment for the breeding of vector mosquitoes. They also reported that the surface protein of *Plasmodium falciparum* sporozoites had two variants, allowing a new level of epidemiologic specificity. In 1999 the Veterinary Medicine Department became the first laboratory animal facility in Thailand to achieve international accreditation.



[Left] Major General Kanokros and Colonel Boslego give certificates of appreciation to Thai Ranger volunteers at the completion of the malaria vaccine trial (Camp Pakthongchai, 1991). Major Brown and RTA component staff assist. (MFN#001037, AFRIMS photograph archives)

[Right] A Thai Ranger medic on the malaria vaccine research team collects blood from a Ranger in the deployment area along the eastern border of Thailand. Khun Prasit Sookto from the Department of Immunology oversees the management of specimens. (MFN#000262, AFRIMS photograph archives)









[Left] Dr. Vallop Thaineau, chief medical officer (and later permanent secretary) of the Department of Health, Ministry of Public Health, visits Major Ronald Rosenberg and a Department of Entomology team at the malaria research field site in Chachoengsao Province (1991). (MFN#001607, AFRIMS photograph archives)

[Top Right] Colonel Chirapa Eamsila and Lieutenant Colonel Prangchai Settachan lead a team from the RTA component doing malaria surveillance among soldiers deployed to Narathiwat and Pattani provinces in 1991. (Photograph courtesy of Major General Chirapa Eamsila)



[Bottom Right] Lieutenant General Phinyo Siriyaphan, RTA surgeon general, and Colonel Donald Burke, director of WRAIR's Division of Retrovirology, meet in 1991 and discuss the initiation of a joint HIV research program. The collaboration led to a strengthening of the RTA's HIV testing program, including epidemiologic analyses that documented Thailand's control of the HIV epidemic and laid the foundation for joint vaccine development. (MFN#002884, AFRIMS photograph archives)

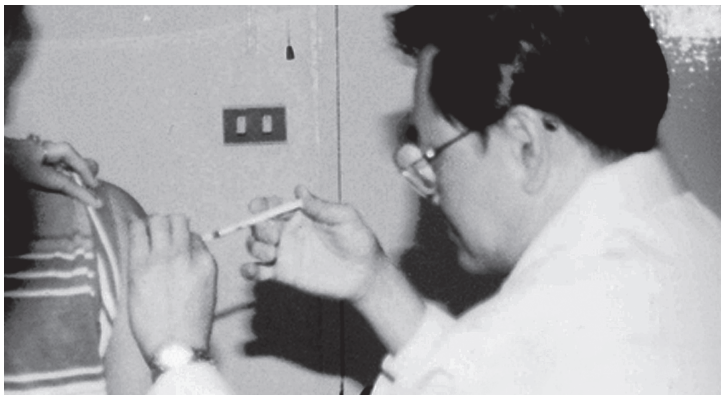


[Left] Dr. Chansuda Wongsrichanalai and Khun Theera Wimonwattrawatee from the Department of Immunology screen for malaria parasites in Sangkhlaburi near the Burmese border in 1995. (MFN#000864, AFRIMS photograph archives)

[Right] Major Dennis Shanks, chief of the Department of Medicine (later USAMC commander), Major Michael Edstein of the Department of Immunology (on assignment from the Australian Army Malaria Institute), and Major Catherine Smith, chief of the Department of Veterinary Medicine, team up to administer an antimalarial drug to a monkey in a pharmacokinetic study. (MFN#000795, AFRIMS photograph archives)







[Top Left] Professor Ted Woodward from the University of Maryland joins doctors Pacharee Kantipong and Charoen Chouriyagune and Lieutenant Colonel George Watt at Chiang Rai Provincial Hospital in 1995. They are discussing a patient with scrub typhus, which had become a subject of this research team after Dr. Charoen noted that some of his patients seemed less responsive to drug treatment than expected. (Photograph courtesy of Dr. George Watt)

[Bottom Left] Colonel Sorachai Nitayaphan, principal investigator of the AFRIMS study site, administers an experimental vaccine at the beginning of the HIV vaccine trial, which was also carried out at Chiang Mai University in 1995. This initial study assessed the safety and immunogenicity of a subtype B envelop product from Chiron-Biocrine. (MFN#003352, AFRIMS photograph archives)





In preparation for the first HIV vaccine trial at AFRIMS, Lieutenant Colonel Thippawan Chuenchitra studies the cytopathic effect of HIV in cell culture at Chiron Corporation's research laboratory in California in 1995. (Photograph courtesy of Colonel Thippawan Chuenchitra)



[Left] A 1996 recognition ceremony for volunteers at the AFRIMS HIV vaccine trial site. The ceremony was held in conjunction with AFRIMS's 35th anniversary. In the back row are Ambassador William Itoh and Colonel Thomas Brewer (USAMC commander). (MFN#003348, AFRIMS photograph archives)

[Top Right] Major Suchai Kitsiripornchai (near left) and Colonel Chirapa Eamsila (second from right) of the RTA component, and Lieutenant Colonel Gray Heppner (center), chief of the Department of Immunology, meet with an RTA unit in Umphang, Tak Province, near the Burmese border, in 1996 to discuss a malaria project. (MFN#000826, AFRIMS photograph archives)

[Bottom Right] Major Suchai, Colonel Chirapa, and Lieutenant Colonel Heppner (left to right), getting impressive support from RTA as they carry out malaria field work in remote sections of Tak Province near the Burmese border in 1996. (Photograph courtesy of Major General Chirapa Eamsila)







[Left] Colonel Peter Echeverria, chief of the Department of Bacteriology, discusses plans for a diarrhea study that was part of the 1997 Cobra Gold exercise, joint training held annually by the Thai and US militaries. This was the concluding year of Colonel Echeverria's exceptionally productive tenure at AFRIMS, which started in 1979. (Photograph courtesy of Khun Orapan Chivaratanond)

[Top Right] A helicopter used for medical evacuation participates in the 1997 Cobra Gold exercise with AFRIMS's Department of Bacteriology. (MFN#000490, AFRIMS photograph archives)

[Bottom Right] Lieutenant Colonel Pamornwan Singasawat and Lieutenant Colonel Douglas Walsh interview potential subjects in a joint malaria prophylaxis drug study among RTA soldiers in Ubon Ratchathani (1998). (MFN#000846, AFRIMS photograph archives)



[Left] Colonel Ernest Takafuji, commander of WRAIR, is accompanied by Colonel Brewer, USAMC commander, on a visit to Major General Choochat, director general of AFRIMS, in 1997. Major General Choochat subsequently became the RTA surgeon general. (MFN#002941, AFRIMS photograph archives)

[Right] The RTA component supported Thai military deployments for peace-keeping operations to Timor, Afghanistan, Iraq, and the Sudan. Here, RTA and AFRIMS staff collect blood from a returning unit in 1997, as part of pre- and post-deployment serosurveillance. This program played a key role in the response to a subsequent malaria outbreak in peacekeepers deployed to the Sudan. (MFN#003711, AFRIMS photograph archives)







[Top] The opening ceremony (1998) for the first HIV vaccine trial with a candidate vaccine specifically designed to match the subtype E epidemic in Thailand. Front row (left to right): Ambassador Ralph Boyce, Lieutenant General Supreecha Mokhavesa (RTA surgeon general), General Chetta Thanajaro (RTA commander in chief), Professor Natth Bhamarapravati (chairman, National AIDS Commission), Dr. Petchsri Sirinirund (Ministry of Public Health). Back row (left to right): Colonel Sorachai Nitayaphan (AFRIMS site principal investigator), Professor Chirasak Khamboonruang (Chiang Mai University site principal investigator), Professor Prasert Thongcharoen (Siriraj Hospital site principal investigator), Lieutenant Colonel Arthur Brown (AFRIMS), Associate Professor Punnee Pitisuttithum (Mahidol University site principal investigator), Colonel Thomas Brewer (AFRIMS), Associate Professor Srisin Khusmith (Mahidol University), Lieutenant General (Retired) Phinyo Siriyaphan, Major General Choochat Kambhu Na Ayudhya, Colonel Somprasong Supawit, Colonel Suebpong Sangkharomya. (MFN#003360, AFRIMS photograph archives)



[Bottom] Lieutenant Colonel Lorrin Pang, chief of the Department of Bacteriology, is accompanied by Khun Orapan Chivaratanond and Major Daniel Isenbarger on a visit to Dr. Phung Dac Cam in Hanoi, Vietnam, to discuss collaborative studies of enteric diseases. (Photograph courtesy of Khun Orapan Chivaratanond)



[Left] Her Royal Highness Princess Sirindhorn is greeted by Colonel Chirapa, Major Russell Coleman (chief, Department of Entomology), and Colonel Brewer (USAMC commander) as she visits an AFRIMS entomology field site in Tak Province in 1998. (MFN#003724, AFRIMS photograph archives)

[Right] Colonel Narongrid Sirisopana leads a community cohort study of HIV incidence in Rayong Province in 1998. To his right is Khun Chalerm Sri Tontichaivanich, a key collaborator from the Provincial Health Office. The results of this study informed the study design for the later large community trial of the HIV vaccine combination that was the first to show protection. (MFN#003347, AFRIMS photograph archives)

[Left] Soldiers participating in a double-blind study of chemoprophylaxis against falciparum malaria in 1998. Khun Nichapat Uthaimongkol of AFRIMS (left) and an RTA nurse give the study drug to volunteers near the border in Ubon Ratchathani. (MFN#000033, AFRIMS photograph archives)

[Top Right] Ambassador Itoh visits Baan Nakornchoom School, Kamphaeng Phet Province, in 1998 to observe an epidemiologic study of dengue fever. The ambassador is accompanied by Dr. Ananda Nisalak, Colonel Brewer (USAMC commander), and Lieutenant Colonel Timothy Endy (chief, Department of Virology). (MFN#002949, AFRIMS photograph archives)

[Bottom Right] Ambassador Richard Hecklinger visits the Department of Veterinary Medicine in 1999 and is briefed by Lieutenant Colonel John Parrish, department chief. (MFN#002962, AFRIMS photograph archives)









[Left] Ms. Marie Huhtala, deputy chief of mission at the US embassy, visits the insectory of the Department of Entomology, accompanied by Major Russell Coleman, department chief, in 1998. (MFN#002953, AFRIMS photograph archives)

[Right] Dr. Sanjaya Shrestha vaccinates a Nepali woman in 1999. He and his father, Dr. Mrigendra Shrestha, have led the collaborative studies at WARUN since its establishment in the 1990s. (MFN#002821, AFRIMS photograph archives)

[Inset] The AFRIMS's laboratory animal facility became accredited in 1999, the first in Thailand. Reaccreditation has occurred every 3 years since, with evaluations that place it among the top 5% of the many hundreds of facilities accredited around the globe. Dr. Montip Gettayacamin led this quality improvement effort from the first application until 2010. (MFN#003727, AFRIMS photograph archives)





[Top] Major General Nancy Adams, US Pacific Command surgeon, visits Lieutenant General Preeyaphas Nilubol, the RTA surgeon general, in 1999. They are accompanied by Major General Pravit Tanprasert, deputy surgeon general, and Colonel Brewer, USAMC commander. (MFN#002980, AFRIMS photograph archives)



[Bottom] Colonel Martin Crumrine, WRAIR commander, visits with Colonel Suebpong Sangkharomya, AFRIMS deputy director general, in 1999. (MFN#002963, AFRIMS photograph archives)



[Top Left] Dr. Robert McNair Scott and a WARUN staff member review records during the hepatitis E vaccine trial carried out with the Nepalese military (Kathmandu, 1999). Dr. Scott was an active duty officer of the USAMC in the 1970s. (MFN#002818, AFRIMS photograph archives)



[Bottom Left] Khun Ratana Sithiprasasna and Khun Suda Ratanawong of the Department of Entomology identify adult mosquitoes collected in 1999 in and around homes of a Thai village in Sangkhlaburi, Kanchanaburi Province. (MFN#002606, AFRIMS photograph archives)

[Right] Khun Sommai Promstaporn, Department of Entomology, and volunteers collect mosquito larvae from water storage containers as part of a study of dengue vectors in Ratchaburi Province in 1998. (MFN#002720, AFRIMS photograph archives)