

**Faculty of Tropical Medicine
Mahidol University**

Annual Report 1998



Faculty of Tropical Medicine Annual Report 1998

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Published by

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ISSN 0859-6824

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FOREWORD

As 1998, another successful year at the Faculty of Tropical Medicine is coming to end, it is my great pleasure to report the activities undertaken by our staff and students as well as the activities of SEAMEO TROPMED Regional Centre for Tropical Medicine. In addition to continuation of our strong tradition of research, teaching, training and health service, the year under review was highlighted by the generous donation from the Lottery Bureau to Her Royal Highness Princess Galyani Vadhana who graciously presented it to the Faculty of Tropical Medicine, Mahidol University for the establishment of the Welfare Trust Fund for Prevention and Control of Tropical Diseases under her royal patronage. The Princess recently visited our malaria field research station in Suan Phung, Ratchaburi Province. I would like to extend my sincere appreciation and congratulations to our staff for their hard work and cooperative spirit which has contributed to such a productive year of the Faculty.



Professor Sornchai Looareesuwan

Dean, Faculty of Tropical Medicine
Mahidol University, Bangkok, Thailand



EDITOR'S NOTE

The Faculty of Tropical Medicine, Mahidol University plays an important role in promoting excellence in teaching and training, research, and clinical care. The Faculty was established by the Thai Government on 5 April 1960. The Faculty has joined the SEAMEO TROPMED Project in 1967, and was designated by the Thai Government as the TROPMED National Center of Thailand. In 1994, the national status has been elevated to the regional level, thus becoming SEAMEO TROPMED Regional Center for Tropical Medicine (TROPMED/Thailand). In the fiscal year 1997/1998 (FY1997/1998), there were 378 government service staff and 314 employees affiliated in 11 departments, hospital and other supporting units, of whom 87 were academic staff comprising 11 Professors, 28 Associated Professors, 25 Assistant Professors and 23 Lecturers. Sixty two percent of the academic staff are Ph.D. holders or equivalence.

Over the years, the Faculty of Tropical Medicine has retained its strengths in tropical medicine, health science and basic science. Five international post-graduate programs are offered to doctors, researchers, medical personnel and professionals concerned with tropical medicine and public health, including 1 at the diploma level leading to Diploma of Tropical Medicine and Hygiene (D.T.M. & H.), 2 at master's degree level and 2 at doctoral level in tropical medicine and clinical tropical medicine. Overall, 1895 students from 42 countries were graduated, with the number of enrolls in FY 1997/1998 of 95 from 20 countries: Australia, Germany, Norway, Afghanistan, Japan, Singapore, Sudan, the Philippines, Indonesia, India, Sri Lanka, Nepal, Cambodia, Myanmar, Lao PDR, People Republic of China, Bangladesh, Vietnam and Thailand. The Ph.D. Program in Tropical Medicine has been revised in 1997 to include research program (plan I) and the first batch of 14 students

was enrolled. The Faculty has also conducted 3 joint courses in collaboration with other institutions within and outside Thailand including those with: the Liverpool School of Tropical Medicine, UK in teaching and training of postgraduates in both institutions registered for Master's courses in Tropical Paediatrics, but each university issues its own degree in accordance with its own degree regulations since 1993/1994 with the number of annual students enrolled between 2-8; the Austrian Society of Tropical Medicine and Parasitology in joint offering the four-month program leading to the Austrian Diploma in Tropical Medicine with annual enrolls of 9-20; and the Faculty of Public Health and the Faculty of Medicine, Ramathibodi Hospital, Mahidol University in an international program leading to the Master of Science in Medical Epidemiology. The international elective program in tropical medicine has been also offered to last year medical students since 1994/1995 with 15 attendants and continues with 15-20 students from South Africa, Australia, Austria, Germany, the Netherlands, Sweden, UK, Canada, USA and Japan.

The Faculty has ongoing collaborative activities on teaching, research and academic services with more than 24 universities and institutions from 13 countries: United Kingdom, Germany, Canada, Japan, Austria, Australia, France, People Republic of China, USA, Switzerland, Indonesia, the Philippines and Malaysia. Examples of collaboration activities are those with Freie University of Berlin in Germany; University of Calgary in Canada; Nuffield Department of Medicine, University of Oxford, Liverpool School of Tropical Medicine and the Wellcome Trust in UK; University of Innsbruck in Austria; Queensland Institute of Medical Research and James Cook University of North Queensland in Australia, Pasteur Institute and Department des Maladies Infectieuses et Médecine Tropicale, Groupe Hospitalier Pitie

Salpetriere in France; Japanese Organization for International Cooperation in Family Planning (JOICEP) in Japan, etc. To increase the international linkages, one more memorandum of understanding (MOU) was signed in FY1997/1998 between SEAMEO TROPED Network, the Faculty of Tropical Medicine as TROPED/Thailand and the Swiss Tropical Institute, Switzerland. In the year reviewed, there were 156 visitors from 25 countries and organizations who made a visit to the Faculty for collaborative research works, consultative services, specimen and information exchanges and giving seminars and conferences.

The Faculty, in conjunction with other National Centers for Tropical Medicine and Public Health in Southeast Asia and some international institutions and organizations, conducts annually the national, regional and international training courses, seminars, meetings and workshops that have directly benefited over 2,324 participants, covering various subjects on medicine, public health and medical sciences aiming to combine training in the methods of research work which contribute to the advancement of knowledge. In FY1997/1998, the Faculty organized and hosted 14 national, regional and international training courses, workshops and meetings with the participants of 488 originated both from 10 SEAMEO member countries and other 10 countries.

Beginning in August of 1997, the Faculty was engaged in organizing annually the Joint International Tropical Medicine Meeting (JITMM) with the objectives to foster a dialogue on scientific advancement in tropical medicine and to serve as a venue for approximately 500 doctors and scientists to exchange ideas leading to collaborative research and joint effort to increase awareness and to face challenges of emerging and reemerging of tropical diseases. Due to the consequences of the national economic crisis, the JITMM 1998 was held at the Faculty with the participants of 350 from various countries.

The Faculty is extensively involved in national and international programs to control tropical diseases. In FY 1997/1998, 140 research projects have been carried out by the staff of the Faculty with the total grants of 46.5 million bahts from both local and international funding agencies. These research projects are directed towards the solution of health

problems commonly encountered in Thailand and Southeast Asian countries including the followings: malaria, amoebiasis, liver fluke infections, paragonimiasis, soil transmitted helminthiasis, schistosomiasis, filariasis, dengue infection, Japanese Encephalitis, rabies, HIV/AIDS, food borne mutagens and carcinogens, nutritional problems, diarrhea and enteric fever, melioidosis, leprosy, diagnosis of tropical diseases, vaccine trials, vaccine development and vector control, etc. Results of the studies were well recognized and published mainly in international journals, with the number of 109 publications in FY1997/1998. Many staff members of the Faculty received awards in recognition to the outstanding research works from both national and international institutions and organizations.

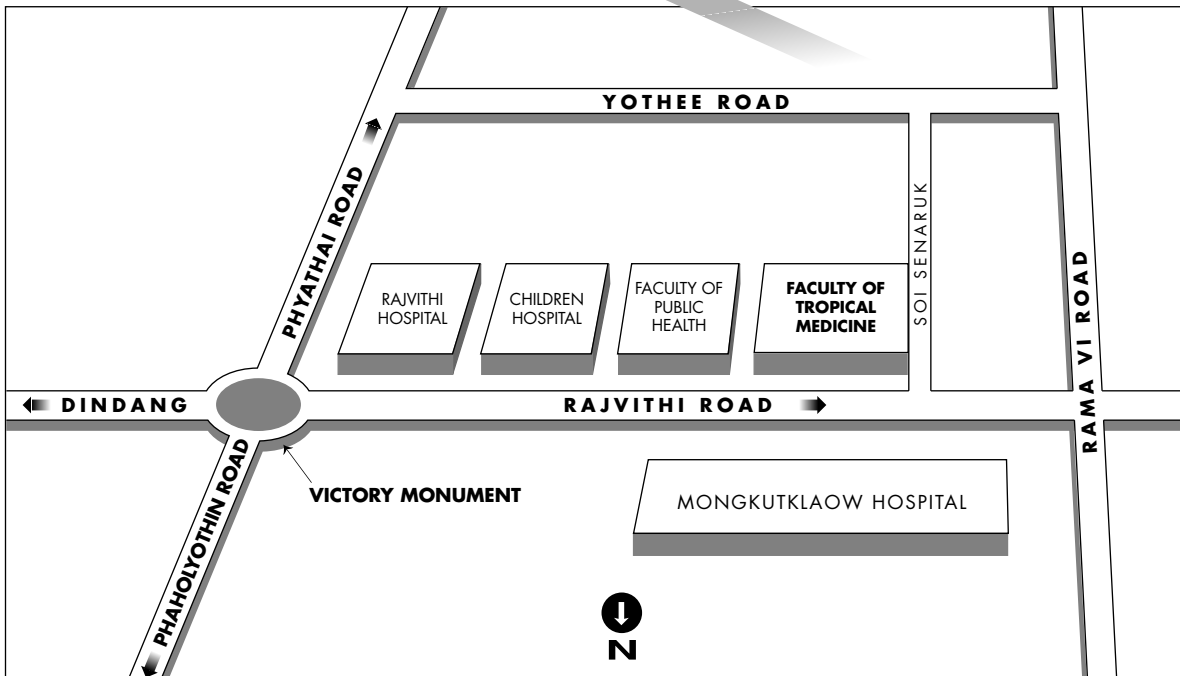
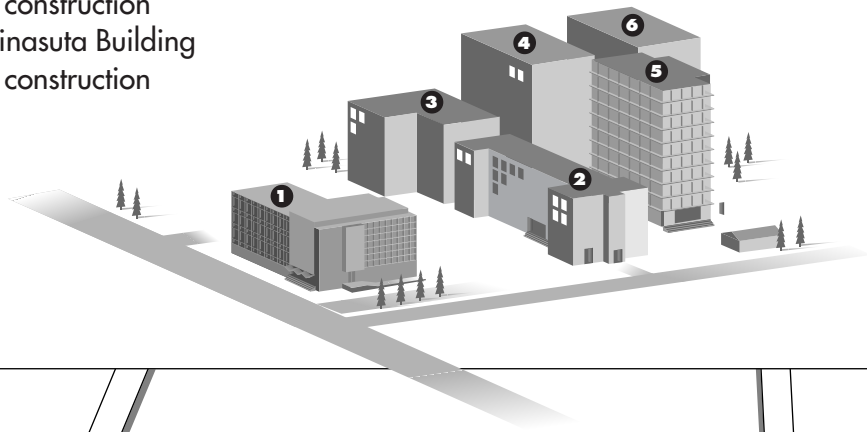
Health care services are provided by the Hospital for Tropical Diseases, a 250-bed hospital with an Intensive Care Unit, Center for Laboratory Diagnosis of Parasitic Infections, and other facilities for the management of endemic tropical diseases. The hospital is one of the world renown for the treatment of malaria.

During the consequence of the national economic crisis leading to the budget limitation and reduction since 1997 and for the year to come, the Faculty of Tropical Medicine continues to position itself in a key role to provide high quality education and training, to conduct the high quality research in the field of tropical medicine and its allied disciplines and disseminating the results of such research, as well as to provide excellent clinical care and appropriate consultancy services to the people and the society.

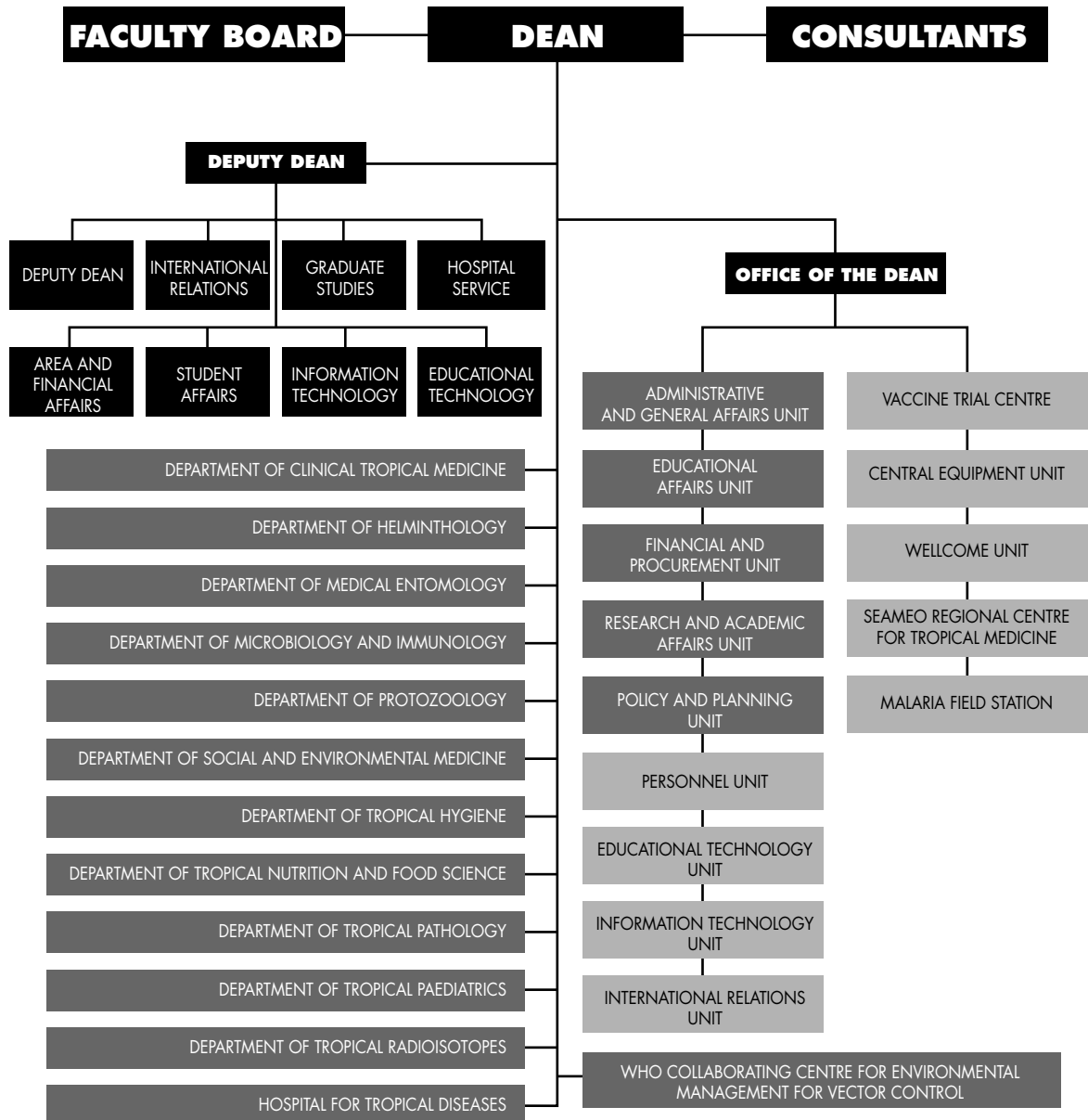


Professor Srisin Khusmith
Editor

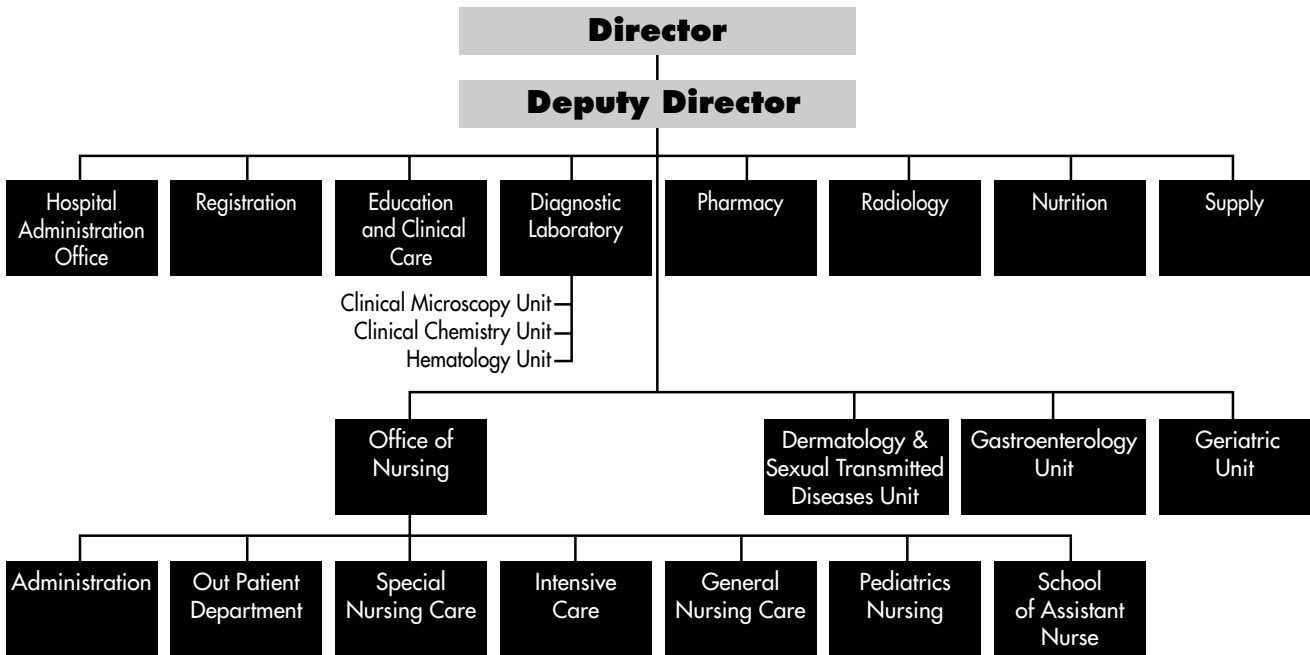
- ❶ Administrative Building
- ❷ Hospital for Tropical Diseases
- ❸ Clinical Research Centre for Tropical Medicine
- ❹ Building under construction
- ❺ Chamlong Harinasuta Building
- ❻ Building under construction



ORGANIZATION AND ADMINISTRATION OF FACULTY OF TROPICAL MEDICINE MAHIDOL UNIVERSITY THAILAND



Hospital for Tropical Diseases



Director
Hospital for Tropical Diseases
Assoc. Prof. Polrat Wilairatana



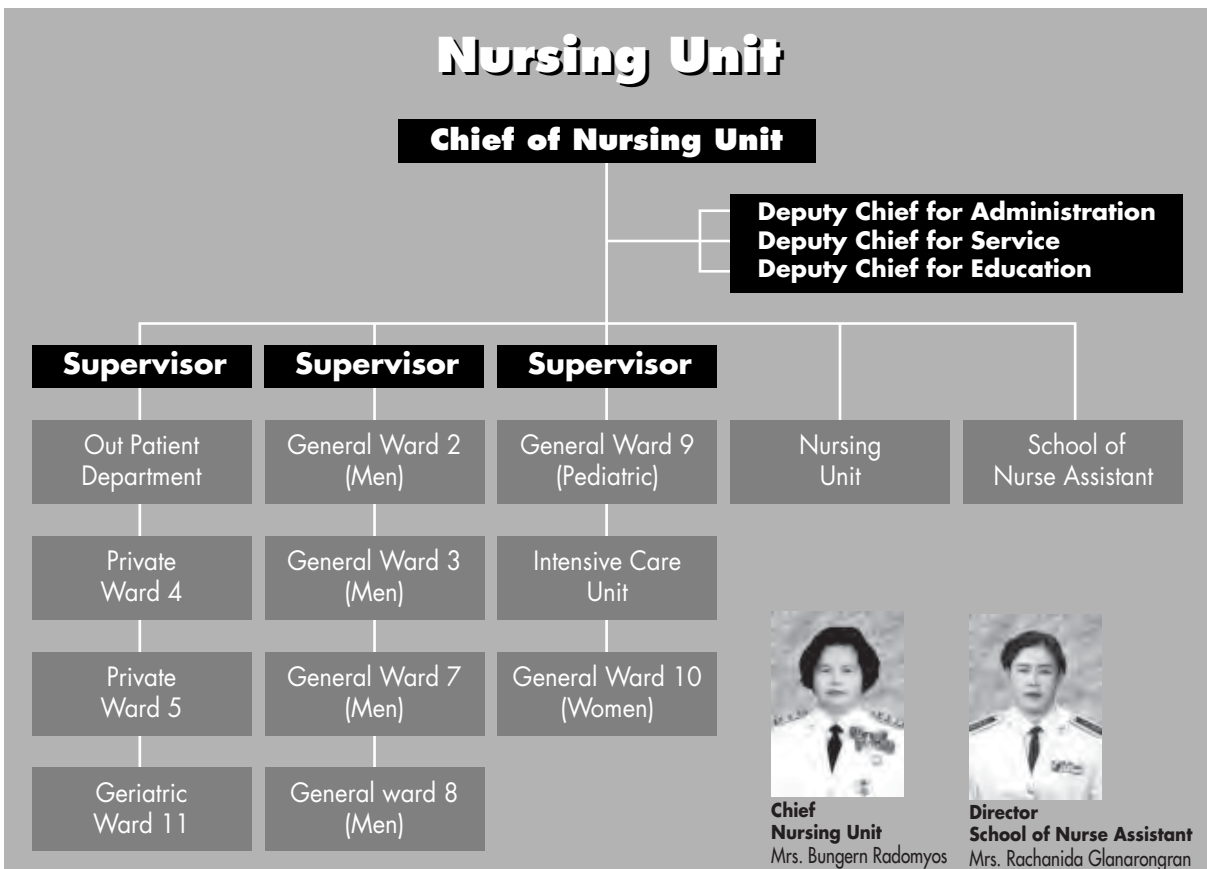
Deputy Director
Hospital for Tropical Diseases
Assist. Prof. Parnpen Viriyavejakul



Deputy Director
Hospital for Tropical Diseases
Dr. Srivicha Krudsood



Deputy Director
Hospital for Tropical Diseases
Dr. Watcharee Chokejindachai



Chief Nursing Unit
Mrs. Bungern Radomyos



Director School of Nurse Assistant
Mrs. Rachanida Glanarongran

CONSULTANTS

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Professor Emeritus Khunying Tranakchit Harinasuta
Professor Emeritus Danai Bunnag
Professor Emeritus Tan Chongsuphajaisiddhi
Professor Emeritus Sommaiya Vilairatna
Professor Emeritus Mukda Trishnananda
Colonel Sriwatana Chitchang

VISITING PROFESSORS

Professor Walther H. Wernsdorfer	Austria	Dr.Chev Kidson	Thailand
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Professor Gunther Wernsdorfer	Germany	Professor Herbert M. Gilles	United Kingdom
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Professor Masamichi Aikawa	Japan	Professor John H. Cross	USA
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Professor Somei Kojima	Japan	Dr.Stephen L. Hoffman	USA
Professor Tozo Kanda	Japan		
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FACULTY BOARD

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Assistant Professor Thaiyooth Chintana	Head of Department of Protozoology
Associate Professor Emsri Pongponrat	Head of Department of Tropical Pathology
Associate Professor Supanee Changbumrung	Head of Department of Tropical Nutrition and Food Science
Assistant Professor Channarong Sanghirun	Head of Department of Tropical Radioisotopes
Assistant Professor Pratap Singhasivanon	Head of Department of Tropical Hygiene
Assistant Professor Piyarat Butraporn	Head of Department of Social and Environmental Medicine
Professor Sirivan Vanijanonta	Head of Department of Clinical Tropical Medicine
Professor Wanpen Chaicumpa	Elected Member
Associate Professor Surang Tantivanich	Elected Member
Associate Professor Dwip Kitayaporn	Elected Member
Assistant Professor Achara Asavanich	Elected Member

DEAN AND DEPUTY DEANS



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Professor Sornchai Looareesuwan



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Prof. Prayong Radomyos



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SECRETARY OF THE FACULTY



Secretary of the Faculty
Mrs. Vorapan Singhsilarak

Current Research Activities and Abstracts

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Medical Science Associate

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General Affairs Officer

Chuanpit Preechawuthiwong B.A. (Political Science)

CURRENT RESEARCH ACTIVITIES

The Department has published more than 300 papers and has continued to pursue its mission on three major activities, teaching, research and services. The Department embarked upon clinical research on several major tropical infectious diseases.

Malaria research activities have focused on clinical trials, pathophysiology, clinical pharmacology and clinically related laboratory studies. Staff of the Department studied not less than 2500 admitted cases of this disease. It was found that 45% were falciparum malaria, 52% were vivax malaria, 2% of mixed infections of the two above, a few cases of malariae malaria and occasionally cases of ovale malaria. The major focus is on clinical trials of multidrug resistant falciparum malaria in uncomplicated and complicated

cases. Combination of various antimalarial drugs were carried out continuously; halofantrine, mefloquine, quinidine, amodiaquine, artemether and artesunate in combination with mefloquine. We found that sequential treatment with artesunate or artemether followed by mefloquine is effective, well tolerated and suitable as an alternative treatment for multidrug resistant malaria.

Besides extensive clinical studies, we also carried out interdepartmental and institutional collaborative studies of antigen in cerebral and non-cerebral malaria patients, of lymphocyte subpopulations during acute and convalescence phases of malaria, and qualitative and quantitative polymerase chain reaction to predict *Plasmodium falciparum* treatment failure.

Pathophysiologic alteration in malaria has been widely investigated. Interesting results were the dynamic alteration in splenic function during acute falciparum malaria, in erythrocyte survival following clearance of malaria parasites, defective production of and response to IL-2 in acute falciparum malaria, cytoadherence and ultrastructure of *Plasmodium falciparum* infected erythrocytes from splenectomized patients and hepatic blood flow and metabolism in severe falciparum malaria.

Studies of stage specificity of quinine, chloroquine, mefloquine, artesunate, artemether and halofantrine were carried out in vivax malaria. The antimalarial efficacy of tetracycline, doxycycline, rifampicin and azithomycin was also studied.

Other common parasitic diseases include amoebiasis, opisthorchiasis, paragonimiasis, cysticercosis, scrub typhus, salmonellosis, and the clinical manifestations of HIV/AIDS with parasitic infections have been studied in many aspects.

The Department's titles of current research activities are as follows.

1. Effects of intramuscular quinine on tetanus infection mice.
2. Clinical trial and pharmacokinetics of dihydroartemisinin in patients with acute uncomplicated falciparum malaria.
3. Pharmacokinetics and pharmacodynamics of the combination dihydroartemisinin-mefloquine in healthy subjects with uncomplicated falciparum malaria.
4. Immunogenetic analysis of uncomplicated and severe malaria defined clinically and pharmacologically.
5. Neurotoxicity effect of artemisinin derivatives in mice.
6. Gastric emptying in patients with acute falciparum malaria.
7. Pharmacokinetics and pharmacodynamics of AZT and AZT-triphosphate in healthy subjects, asymptomatic HIV-positive, and symptomatic AIDS patients.
8. SDS-PAGE analysis of whole cell protein and outer membrane protein patterns of clinical isolates of *Burkholderia pseudomallei*.
9. Study on stage development of *Plasmodium falciparum in vitro*.
10. Pharmacokinetics and dose-finding studies of the combination artemether/proguanil in healthy subject and patients with uncomplicated falciparum malaria.
11. Clinical study to fine effective regimen for the treatment of uncomplicated falciparum malaria in rural area.
12. A multicenter, randomized double-blind, Phase II study to evaluate the safety, tolerance and efficacy of multiple doses of SCH 56592 versus fluconazole in the treatment of oropharyngeal candidiasis (OPC) in HIV-positive patients.
13. A comparison treatment between topical and parenteral antifungal drugs in *Pityriasis versicolor*.

INTERNATIONAL INSTITUTION LINKAGE

1. Nuffield Department of Clinical Medicine, University of Oxford, England.
2. Department of Medicine, the George Washington University Medical Center, Washington DC, USA.
3. Hahnemann University, Philadelphia, USA.
4. Case Western Reserve University, USA.
5. Department of Epidemiology, the University of Michigan, USA.
6. Queensland Institute of Medical Research, the University of Queensland, Brisbane, Australia.
7. Department of Medicine, University of Toronto, Canada.
8. Department of Microbiology and Infectious Diseases, Faculty of Medicine, the University of Calgary, Canada.
9. Wellcome Trust Research Laboratories, Nairobi, Kenya.
10. Department of Infectious Diseases, Ullevaal Hospital, University of Oslo, Norway.
11. Department of Infectious Diseases, Faculty of Medicine, University of Vienna, Austria.
12. Department of Tropical Medicine and Specific Prophylaxis, Faculty of Medicine, University of Vienna, Austria.
13. Austrian Society of Tropical Medicine and Parasitology, Vienna, Austria.

TRAINING COURSE

Austrian Diploma Course for Tropical Medicine 1998, 5-30 January 1998

The Austrian Society of Tropical Medicine and Parasitology and the Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand have jointly offered the course leading to "the Austrian Diploma in Tropical Medicine" since 1992. This 4-month annual programme aims to enrich the Austrian medical doctors' understanding on the clinical, biological, epidemiological and social dimensions of tropical diseases particularly in Southeast Asia. Participants of the course attend lectures in Austria for 3 months followed by one month clinical practices at the Bangkok Hospital for Tropical Diseases and other hospitals in Bangkok in the second part of the programme. They also visit some hospitals in the northeast of Thailand.

ABSTRACTS

CHANGES OF LIVER FUNCTIONS AFTER ALBENDAZOLE TREATMENT IN HUMAN GNATHOSTOMIASIS

Sasithorn Inkatanuvat¹, Pravan Suntharasamai²,
Samnieng Vutikes¹, Mario Riganti³

¹Hospital for Tropical Diseases,

²Department of Clinical Tropical Medicine,

³Department of Tropical Pathology, Faculty of Tropical Medicine,
Mahidol University, Bangkok 10400, Thailand.

Ninety-eight out-patients of the Hospital for Tropical Diseases, Bangkok with clinical diagnosis of cutaneous gnathostomiasis were studied. All patients were treated with albendazole at a dosage of 400 mg (two tablets) twice daily for 14 days. They were seen periodically on day 0, day 14, day 28, day 195 and 1 year after treatment with laboratory investigations for

any side effects of the treatment. There was a statistically significant increase of total protein, albumin, alkaline phosphatase (ALP), aspartate aminotransferase (AST) and alanine aminotransferase (ALT) values when comparing the different periods. The abnormal results are clearly indicated in AST and ALT values (liver enzyme) especially on day 14 both male and female patients had highest levels. No significant association with time was found in ALP value.

Published in : J Med Assoc Thai 1998;81(10).

RESEARCH ON NEW ANTIMALARIAL DRUGS IN BANGKOK HOSPITAL FOR TROPICAL DISEASES

Polrat Wilairatana¹, Srivicha Krudsood², Kasinee Buchachart²,
Parnpen Viriyavejakul³, Sombat Treeprasertsuk²,
Valai Bussaratid⁴, Sornchai Loareesuwan¹

¹Department of Clinical Tropical Medicine,

²Department of Tropical Hygiene,

³Department of Tropical Pathology,

⁴Department of Tropical Pediatrics, Faculty of Tropical Medicine,
Mahidol University.

Clinical trials of new antimalarial drugs (atovaquone, artesunate, artemether, dihydroartemisinin, CGP 56697, pyronaridine, and biguanidedapsone combinations) for treatment of uncomplicated malaria have been studied in the Bangkok Hospital for Tropical Diseases.

Studies in artesunate and artemether have confirmed the earlier Chinese work. Patients with malaria improved faster following treatment with these

artemisinin derivatives compared with other antimalarial drugs. The artemisinin derivatives were all well tolerated and had insignificant side effects.

A clinical trial of oral dihydroartemisinin for the treatment of acute, uncomplicated, falciparum malaria involved 53 adult patients. Each received a total dose of 480 mg over 7 days (120 mg given immediately, followed by 60 mg/day) after being admitted to the Hospital for Tropical Diseases in Bangkok for 28 days. Most (92%) completed the 28-day follow-up but four patients left the hospital early, for reasons unrelated to their treatment. Most patients showed clinical improvement 1-3 days after starting treatment and none suffered from serious adverse reactions. The cure rate was 90% (44/49). The mean (S.D.) parasite-

clearance time was 40.4 (14.1) h. and the mean fever clearance time was 37.0 (30.2) h. Seven patients had a brief increase in parasitaemia after initiation of treatment but subsequent counts declined dramatically. Five patients who failed treatment (RI response) were successfully treated with quinine plus tetracycline for 7 days. No RII or RIII responses were observed. These findings indicate that treatment with oral

dihydroartemisinin is effective and well tolerated, and that dihydroartemisinin may be suitable as an alternative treatment for acute, uncomplicated, falciparum malaria.

Presented at : Joint International Tropical Medicine Meeting 1998 and The Fourth Chamlong-Tranakchit Harinasuta Lecture.

ASSESSMENT OF THE NEUROTOXICITY OF PARENTERAL ARTEMISININ DERIVATIVES IN MICE

Apichart Nontprasert¹, Marika Nosten-Bertrand²,
Sasithon Pukrittayakamee¹, Sirivan Vanijanonta¹,
Brian J Angus^{1,3}, Nicholas J White^{1,3}

¹Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand,

²Laboratoire de Génétique Moléculaire de la Neurotransmission et des Processus Neurodégénératifs, Hôpital de la Pitié Salpêtrière, Paris, France,

³Centre for Tropical Medicine, Nuffield Department of Clinical Medicine, John Radcliffe Hospital, Oxford, UK

In all experimental mammals tested (rats, dogs, primates) intramuscular injections of the oil soluble antimalarial artemisinin derivatives artemether and arteether have produced an unusual pattern of selective damage to brain stem centres predominantly involved in auditory processing and vestibular reflexes. Artesunate, the most widely of these compounds, is a water soluble hemisuccinate derivative given parenterally either by intravenous or intramuscular injection. The neurotoxic potential of parenteral artesunate and artemether was compared in a murine model. Adult Swiss albino mice were assigned

randomly to 28-day regimens of intramuscular artemether or artesunate in doses ranging from 30 to 100 mg/kg/day. At 30 mg/kg/day no abnormalities were observed in 6/12 artemether recipients and 2/12 artesunate recipients. These were reversible in all but one (artemether) mouse. At 100 mg/kg/day 8/36 artemether recipients, 2/36 artesunate recipients, and 1/18 control mice died. All but 4 surviving mice in the artemether group (86%) showed obvious and usually irreversible abnormalities of balance and equilibrium, whereas only 4 artesunate recipients (11%) exhibited abnormalities, and these were reversible in each case ($P < 0.001$). At this dose the relative risk (95% confidence interval) for death or disability was 5.3 (2.6 to 11.2) for artemether recipients. Intramuscular artemether is significantly more neurotoxic than intramuscular artesunate in this murine model.

Published in : Am J Trop Med Hyg 1998;59(4) : 519-22.

INTESTINAL FLUKE AND OPISTHORCHIS INFECTIONS IN NORTHERN THAILAND

Swangjai Pungpak¹, Prayong Radomyos²,
Bang-ern Radomyos², Thitima Wongsaroj³,
Polrat Wilairatana¹, Rangsan Praevanich²,
Vara Meesomboon³, Prapasri Jongsuksantikul³, F P Schelp⁴,
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³Division of General Communicable Diseases, Department of Communicable Diseases Control, Ministry of Public Health, Nonthaburi, Thailand

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In Thailand, national control programme of opisthorchiasis using large scale chemotherapy to treat infected individuals with praziquantel has been launched since 1988. Opisthorchiasis prevalence in the northeast has dropped in the past decade, but

Opisthorchis infection in the north has gradually increased. A preliminary study was conducted in Phrae Province, northern Thailand during September to November 1997 to reevaluate the efficacy of praziquantel against *O. viverrini*. A total of 95 adult patients with *O. viverrini* or *O. viverrini*-like ova in their stools were randomly treated with two different manufactured praziquantels at a single dose of 40 mg per kg. *Haplorchis taichui*, *H. yokogawai*, *Echinostome* spp., *O. viverrini*, *Taenia saginata* and *Enterobius vermicularis* were retrieved in the stools after treatment. Minute intestinal flukes were detected in 64% of patients. *O. viverrini* was found in lower proportions of 17%. The cure rate in both groups on the 30th day of treatment was 100%.

Further study to clarify the situation of opisthorchiasis was extended in 431 residents from 16 provinces in north Thailand who had previously been found positive for *O. viverrini* or *O. viverrini*-like ova in their stools. They were given praziquantel 40 mg. per kg. After treatment, 4 to 6 stool samples were collected from each individual and examined for adult worms. The prevalence of *O. viverrini* was 11.6%. Intestinal flukes, *H. taichui* and *H. yokogawai* were predominantly found in 63.1% and 10.4% respectively. *Echinostoma malayanum*, *H. pumilio*, *Phaneropsolus bunnei*, *Plagiorchid flukes*, *Prosthodendium molenkampi*, *Stellanchasmus falcatus*

and *Centrocestus caninus* were found in small numbers.

In conclusion, minute intestinal flukes (*H. taichui*, *H. yokogawai* and others) were commonly found in the same opisthorchiasis endemic areas in northern Thailand. Minute intestinal fluke infections were predominant. Opisthorchiasis occurred in lower proportions. Praziquantel was effective as treatment against liver and intestinal flukes.

Presented at : Joint International Tropical Medicine Meeting 1998 and The Fourth Chamlong-Tranakchit Harinasuta Lecture.

DIAGNOSIS OF *PENICILLIUM MARNEFFI* INFECTION BY QUANTITATION OF URINARY ANTIGEN USING AN ENZYME IMMUNOASSAY

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Penicillium marneffei is a major cause of opportunistic infection in patients with AIDS in north and north eastern Thailand. A method for the quantitation of *P.marneffei* antigen in urine was developed using FITC-labelled purified rabbit hyperimmune IgG in an enzyme-linked immunosorbent assay. This was evaluated in 33 patients with culture proven penicilliosis and 300 controls (52 healthy subjects, 248 hospitalised patients without penicilliosis) from the

same endemic area. Urinary antigen was found in all 33 (100%) patients with penicilliosis, with a median titer of 1:20,480. Using undiluted samples, 67 (27%) of 248 hospital patients and 3 (6%) of 52 healthy controls were reactive. At a cut-off titer of 1:40, the urine antigen detection assay had a diagnostic sensitivity of 97% and specificity of 98% (positive predictive value 84%, negative predictive value 99.7%). This test offers a valuable and rapid method for the diagnosis of penicilliosis in patients with AIDS, and could be a useful addition to conventional diagnostic methods in endemic areas.

Presented at : Joint International Tropical Medicine Meeting 1998 and The Fourth Chamlong-Tranakchit Harinasuta Lecture.

MULTIDRUG-RESISTANT FALCIPARUM MALARIA: USE OF DRUG COMBINATIONS

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Multidrug-resistant falciparum malaria is a serious problem in Thailand and therapeutic failures to all existing antimalarials are well documented. New drug development takes years before the drug can be registered for use in man. Therefore studies of currently available drugs with appropriate rationales for use could be beneficial to combat this infection. Two measures have been advocated, modification in dosage¹ and the use of drug combinations.

Until recently when synthetic drugs have been available, a single component has been widely used for treating most infections. The use of a single drug has been generally accepted because the dose can be controlled easily and drug interactions can be avoided. However, with problems of multidrug-resistant falciparum malaria, the rationale for using a single compound warrants change. The mechanism of action of different drugs varies, and they can act in different biosynthetic pathways of the plasmodium parasite. Drug combinations can act additively or in a synergistic way to kill the pathogen. They may also prevent the development of resistance. Some diseases,

such as tuberculosis and leprosy, have been successfully treated with drug combinations. In the treatment of malaria, mixtures of active components have been used for centuries. In China for more than 2000 years, an oriental remedy extracted from the Qinghao plant (*Artemisia annual L.*) has been used for treatment of chills and fever, presumed to be malaria infections. In South America more than 400 years ago, a mixture of cinchona alkaloid extracted from the barks of the cinchona tree (known as Peruvian bark extract) was introduced for treating malaria symptoms. During the Second World War, a mixture of cinchona alkaloids was manufactured as a

tablet (Totaquine) containing mainly quinine, quinidine and cinchonidine, and used successfully in the treatment of malaria. With the deteriorating situation of multidrug-resistant falciparum malaria in Thailand, attempts have been made to delay the development of resistance by the use of certain drug combinations. Some suitable combinations have proved effective *in vitro*, in animal malaria and in man.

Published in: Drug Resistance: Mechanisms and Management Singhal RL & Sood OP (eds), In: Proceedings of the Fourth Annual, Ranbaxy Science Foundation, Symposium. New Delhi, India, 1997:59-66.

CLINICAL TRIAL OF PENTOXIFYLLINE AS AN ANCILLARY TREATMENT FOR SEVERE FALCIPARUM MALARIA IN THAILAND

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Pentoxifylline, an inhibitor of tumor-necrosis factor, has been evaluated as an antimalarial agent in combination with artesunate in 45 patients with severe falciparum malaria. Patients were admitted to the intensive care unit at the Hospital for Tropical Diseases in Bangkok, Thailand, and randomly assigned to treatment for 72 hr with a combination of intravenously administered artesunate and 1) placebo, 2) low-dose pentoxifylline (0.83 mg/kg/hr), or 3) high-dose pentoxifylline (1.67 mg/kg/hr). All 45 patients had one or more manifestations of severe

malaria such as cerebral malaria (n = 18), renal failure requiring hemodialysis (n = 9), azotemia (n = 8), jaundice (n = 25), or hyperparasitemia (n = 30). The overall severity was comparable in the three groups. Clinical outcome was assessed with respect to the parasite clearance time and the fever clearance time in all patients. In addition, a number of subsidiary outcome variables were examined in specific sub-groups, including the recovery time from coma I-or patients with cerebral malaria, the duration of intubation in patients with respiratory distress, the number of hemodialysis treatments needed for patients with acute renal failure, and the number of units of blood administered to patients requiring transfusion. Concentrations of tumor necrosis factor were reduced in all three groups at 48 hr, after treatment. No significant differences among the three treatment groups were found for any of the outcome variables examined. We conclude that the addition of pentoxifylline to artesunate therapy for severe malaria produced no evident clinical benefit.

Published in: Am J Trop Med Hyg 1998;58(3):348-53.

MALARONE™ (ATOVAQUONE AND PROGUANIL HYDROCHLORIDE): A REVIEW OF ITS CLINICAL DEVELOPMENT FOR TREATMENT OF MALARIA

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The continuing spread of drug-resistant malaria emphasizes the need for new antimalarial drugs. Atovaquone is a broad-spectrum antiprotozoal drug with a novel mechanism of action, via inhibition of parasite mitochondrial electron transport, and a favorable safety profile. Early studies with atovaquone alone for treatment of malaria demonstrated good

initial control of parasitemia but an unacceptable rate of recrudescence after treatment with atovaquone alone were resistant to atovaquone *in vitro*. The combination of atovaquone and proguanil is synergistic *in vitro*, and clinical studies demonstrated enhanced efficacy of the combination compared to either drug alone for treatment of malaria. MALARONE, a fixed-dose combination of 250 mg atovaquone and 100 mg proguanil hydrochloride, is available in many countries for treatment of acute, uncomplicated malaria caused by *Plasmodium falciparum*. At the recommended dose (in adults, four tablets once daily for 3 days), the overall cure rate was >98% in more than 500 patients with falciparum malaria. In four randomized, controlled clinical trials, treatment with atovaquone and proguanil hydrochloride was

significantly more effective than mefloquine (Thailand), amodiaquine (Gabon), chloroquine (Peru and the Philippines) or chloroquine plus pyrimethamine/sulfadoxine (Philippines). In clinical trials where the comparator drug was highly effective, treatment with atovaquone and proguanil hydrochloride was equally effective. Parasites isolated during recrudescence after treatment with the combination of atovaquone and proguanil are generally not resistant to atovaquone *in vitro*. The most commonly reported adverse events in clinical trials (abdominal pain, anorexia, nausea, vomiting, diarrhea and coughing) occurred with similar frequency in patients treated with a comparator drug. MALARONE is a safe and effective new agent for treatment of malaria.

Published in: Am J Trop Med Hyg 1998 (in press).

CHLOROQUINE SENSITIVITY OF *PLASMODIUM VIVAX* IN THAILAND

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Chloroquine has been the standard treatment for *Plasmodium vivax* malaria for more than 40 years. Recently chloroquine-resistant *P. vivax* has been reported from Oceania and several parts of Asia. In order to assess the situation in Thailand, we studied prospectively 1181 patients, mean (SD) age of 24.6 (8.6) years, admitted to the Bangkok Hospital for Tropical Diseases with vivax malaria. They were

randomized to treat with oral chloroquine (25 mg base/kg body weight over 3 days) with or without primaquine 15 mg/day for 14 days. Most of studied cases (64.7%) contracted the malaria infection on the western border of Thailand. All patients responded initially to treatment, and there was no significant difference in the clinical or parasitological responses between those treated with or without primaquine. The mean parasite (PCT) and fever clearance times (FCT) were 60.2 (18.7) hrs and 29.5 (24.5) hours respectively. During the follow up period of 28 days in hospital 295 cases (25%) developed *P. falciparum*. Only four patients (0.3%) had reappearance of asexual forms of *P. vivax* in peripheral blood smears between the 14th and 28th day after treatment. These cases were retreated with the same regimen of chloroquine and responded well. These data provide no evidence for significant chloroquine-resistance in *P. vivax* in Thailand.

Submitted to Acta Tropica (1998).

EFFICACY OF ARTEMETHER-LUMEFANTRINE (CO-ARTEM™) IN MDR SETTINGS

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Three randomized, clinical trials, to compare the efficacy and tolerability of a new oral fixed combination of artemether and lumefantrine (benflumetol)

(CGP 56697; CO-ARTEM™ Novartis) were conducted in Thailand between 1995 and 1997. In the first study in Bangkok Hospital for Tropical Diseases (BHTD) the combination was compared with mefloquine in a double blind trial in 252 adult patients. Two for the clinical trials were an open, randomized comparison of the CO-ARTEM™. *vs.* artesunate-mefloquine in 617 patients in the Shoklo Malaria Research Unit (SMRU), Mae Sot, Tak Province, Thailand and a dose finding study in 359 patients with uncomplicated multi-drug resistant falciparum malaria conducted in both BHTD & SMRU centers. All three clinical trials were approved by the Ethical Review Committee. In the first study, adult patients with uncomplicated malaria aged over 12 years, with parasitemias of between 1,000-200,000/ml, who gave written informed consent to trial, were not pregnant or in lactation period, and had not been treated for malaria in the proceeding 2 weeks were randomized treated either with CO-ARTEM™. (4x4 tablets each containing 20 mg artemether and 120 mg benflumetol, given at 0, 8, 24 and 48 hours), or to mefloquine (3 tablets of 250 mg at initial diagnosis, followed by 2 tablets of 250 mg at 8 hours). All patients were admitted in the Hospital for 28-days to exclude reinfection and for careful monitoring of side effects. The 28-days cure rate with CO-ARTEM™. was lower than with mefloquine (69.3% *vs.* 84.2%, $p = 0.02$). However, CO-ARTEM™ was more effective than mefloquine in parasite clearance time (PCT; 43 hours *vs.* 66 hours, $p < 0.001$), fever clearance time (FCT; 32 hours *vs.* 54 hours, $p < 0.005$), and gametocyte clearance time (152 hours *vs.* 331 hours, $p < 0.001$). The first study revealed that CO-ARTEM™ is effective against multi-drug resistant falciparum malaria in Thailand, but higher doses were probably needed to improve the cure rate.

The second trial to study the efficacy and safety of CO-ARTEM™ in a large randomized trial in both children and adults with uncomplicated falciparum malaria along the western border of Thailand. The comparator was artesunate plus mefloquine as it is the current standard therapy at the area. This study was an open, randomized comparison of CO-ARTEM™ with artesunate-mefloquine conducted in 617 patients with acute uncomplicated multidrug-resistant falciparum malaria. Patients who fulfilled the inclusion criteria (aged over 5 years, with uncomplicated falciparum malaria, and not pregnant) and gave informed consent were randomized to treat either CO-ARTEM™, in the same dose as the first trial

(total dose was 1-2 mg of artemether per kg of body weight plus 6 to 12 mg of benflumetol per kg. The minimum dose for patients weighing less than 20 kg was one tablet. For patients weighing between 21 and 30 kg a dose of two tablets was given; for patients weighing between 31 and 40 kg, a dose of three tablets was given; and for patients weighing more than 40 kg, the usual adult dose of four tablets was given. Each dose was given at 0, 8, 24, and 48 hours) or artesunate in a single daily dose of 4 mg/kg for 3 days plus mefloquine (25 mg/kg) in a split dose, i.e. 15 mg/kg on day 2 and 10 mg/kg on day 3. Both treatments rapidly and reliably cleared fever and parasitemia, and there was no significant difference in the initial therapeutic response parameters. Parasite genotyping was used to distinguish recrudescences from new infections. The 63-day cure rate for artesunate-mefloquine (94%) was significantly higher than the cure rate for CO-ARTEM™ (81%) ($p < 0.001$). Both regimens were well tolerated. Nausea, vomiting, dizziness, sleep disorders, and other neurological side effects were between two and four times more common in the artesunate-mefloquine group than in the CO-ARTEM™ group ($p < 0.001$). It was concluded that CO-ARTEM™ is effective and very well tolerated in the treatment of multi-drug resistant falciparum malaria but that a higher dose may improve efficacy further.

The third trial was a dose-optimization study with two six-dose schedules (total adult dose 480 mg artemether and 2,880 mg of benflumetol) were compared with the previously used four-dose regimen (320 mg artemether and 1,920 mg of benflumetol as used in the first and second trial) in a double-blind trial involving 359 patients with uncomplicated multi-drug resistant falciparum malaria. The third trial was conducted in two places (BHTD with the same entry criteria as the first trial, and SMRU with the same entry criteria as the second trial). There were no differences between the three treatment groups in parasite and fever clearance times, and reported adverse effects. The two six-dose regimens gave 96.9% and 99.1% adjusted 28 days cure rates respectively, compared to 83.3% for the four-dose regimen ($p < 0.001$). These six dose regimens of artemether-benflumetol provide a highly effective and very well tolerated treatment for multi-drug resistant falciparum malaria.

Presented at: The 2nd European Congress on Tropical Medicine, Liverpool, UK. 14-16 September 1998, Abstract No. 464 page 117.

PATHOGENESIS AND CASE-MANAGEMENT OF SEVERE MALARIA

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The pathogenesis of severe malaria remains unclear. Studies in human patients and the laboratory have provided evidence for the roles of both mechanical and toxic-cytokine production in the pathogenesis of this condition. The sequestration of mature forms of *Plasmodium falciparum* parasites to microvascular endothelium called, "cytoadherence", leads to inadequate oxygen supply to vital organs. Sequestration, with or without rosetting, leads to microcirculatory obstruction in falciparum malaria and as a consequence increases anaerobic glycolysis and lactate production. Sequestration occurs most in brain, and might be the cause of coma in cerebral malaria, and also occurs in other vital organs such as the heart, liver, kidneys, intestines and subcutaneous tissues. The cytoadherence phenomenon requires two factors; (1) candidate ligands of the surface of parasitised erythrocytes such as *P. falciparum* erythrocyte membrane protein 1 (PfEMP-1), erythrocyte band 3 anion transporter and sequestrin and (2) endothelial receptors such as thrombospondin, and candidate endothelial receptors (ICAM-1, CD36, VCAM-1, ELAM, E-selectin, chondroitin sulphate A).

Toxic cytokines such as tumour necrosis factor alpha (TNF α) and some other cytokines were elevated and correlated with clinical and complications. Studies in African children with cerebral malaria have provided convincing evidence of an association between high circulating levels of TNF α and other cytokines with the severity, case fatality and frequency of neurological sequelae. In addition, children with a variant allele of the TNF α promoter region gene had a five times greater risk of developing cerebral malaria, and a ten times greater risk of dying of this complication. Results of two studies using monoclonal antibody to TNF α were quite interesting. In the Gambian study of 41 children with cerebral malaria treated with three different doses of a murine monoclonal antibody directed against TNF α , there was a dose dependent reduction in fever suggesting that the monoclonal antibody might be holding TNF α in circulation. Another study using a monoclonal antibody to TNF α in 610 Gambian children with cerebral malaria also

showed an antipyretic effect with the antibody but did not affect mortality. Studies using a polyclonal anti-TNF α treating cerebral malaria have been continued for several reasons. A polyclonal anti-TNF α Fab might be expected to be more effective than a monoclonal antibody since its smaller size allows greater and more rapid penetration into tissue fluid and its neutralisation of many epitopes and higher binding affinities should inhibit the biological activity of TNF α more effectively. At present, a randomised, double blind, placebo controlled study of this adjuvant is being trialed in Thailand. Tissues from patients who died from cerebral malaria do show evidence of cytokine production whether this is a result of the disease severity, or relates to the primary pathogenesis of cerebral malaria needs further investigation.

Two clinical trials using pentoxifylline (a drug believed to suppress overproduction of TNF α which also may improve impaired capillary blood flow) have showed no clinical benefit. The role of increased nitric oxide production in cerebral malaria remains uncertain. Recent studies have not correlated nitrate or nitrite levels in plasma with disease severity.

Mechanical obstruction (sequestration) is still believed to play an important role of the pathophysiology of severe malaria. Cytoadherence was demonstrated *in vitro* and sequestration was demonstrated *in vivo*. The capillaries in vital organs are packed with mature infected erythrocytes leading to hypoxia. Direct evidence of retinal haemorrhages and increased permeability of the retinal capillary network by direct examination of eye and fluorescein angiography all indicate marked microcirculatory dysfunction in severe malaria.

Case-management of severe malaria bases on the early diagnosis and early treatment with a potent antimalarial drug. Early detection and treatment of complications (convulsions, acute renal failure, pulmonary oedema, acidosis, hypoglycaemia, hyperthermia) are essential. The aim of management is to save the patient's life. The choice of antimalarial chemotherapy depends on the clinical severity, the drug sensitivity of the parasites and the availability and preparation of the drug. Chloroquine is still the drug of choice for chloroquine-sensitive parasites but there are now rare. Quinine and quinidine are the only widely available drugs which are effective against chloroquine-resistant strains. Ideally, in serious ill patients, intravenous treatment should be initiated

with a loading dose and patients should be monitored for hypoglycaemia, a most important side-effect of cinchona alkaloids. There is some evidence of increasing resistance to quinine therapy especially in Thailand and Vietnam. The difficulty in administration of intravenous infusion in rural areas and greater chance of hypoglycaemia favour use of artemisinin and its derivatives. Qinghaosu (artemisinin - an ancient Chinese herbal medicine) and its derivatives have been used successfully in treating of severe falciparum malaria. Their rapid effectiveness in eliminating parasites has been extensively documented. Large, randomised comparisons of artemether with quinine in African children (Gambian and Kenyan children) with cerebral malaria and Vietnamese adults with severe falciparum malaria have confirmed that artemether is as effective as quinine in reducing case fatality. Coma was significantly prolonged in the artemether-treated groups in two of these studies.

There were more convulsions, more children with metabolic acidosis and lower survival in children treated with artemether in the Kenyan study. However, artemether may be preferred to quinine in case of sensitivity to quinine, suspected quinine resistance, recurrent quinine - induced hypoglycaemia, and also at the peripheral levels where facilities limited (one intramuscular injection or suppositories have proved effective and easy to administer). Other symptomatic and supportive treatment included careful monitoring of fluid input and urine output, frequent observations for complications with appropriate treatment, and good nursing care are essential to reduce the high mortality rate of severe malaria.

Presented as keynote speech at the 2nd European Congress on Tropical Medicine, Liverpool, U.K. 14-18 September 1998. Abstract No. 256 page 65.

THE COURSE OF ANAEMIA AFTER THE TREATMENT OF ACUTE, FALCIPARUM MALARIA.

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To determine the course of anaemia following treatment for acute falciparum malaria, 72 adult Thai patients were followed for 4 weeks after starting effective therapy. Using the criteria of haemoglobin concentrations of < 13 g/dl in males and < 12 g/dl in females to define anaemia, all but two (97%) of the patients were anaemic at some point during the study period. At weekly observations, the erythropoietic response of each patient with anaemia was categorized clinically, on the basis of absolute reticulocyte counts (ARC) and indirect bilirubin concentrations (IBC). At 4 weeks, 40 (56%) of the patients were still anaemic. The results of tests on samples of peripheral blood from these 40 patients were consistent with hypoproliferative erythropoiesis (low normal ARC and

IBC; 33 patients), ineffective erythropoiesis (low normal ARC but elevated IBC; five patients) or an appropriate response (elevated ARC and normal IBC; two patients). Of the variables measured at the time of enrolment into the study, only low serum albumin (P = 0.002) and elevated direct bilirubin (P = 0.009) were independently associated with persisting anaemia at 4 weeks. Anaemia may therefore persist in about one in every two Thai patients for up to 28 days after beginning effective treatment for acute *Plasmodium falciparum* malaria, hypoproliferative erythropoiesis appearing to be the most common mechanism of this anaemia. While it is likely that the malarial episode itself is somehow responsible for these persistent haematological changes, other, underlying, chronic processes might have a contributory role. Whatever the cause, the continuing anaemia appears to be related to the degree of hepatic dysfunction on admission.

Published in: Ann Trop Med Parasitol 1998;92(5):525-37.

A COMPARISON OF THREE DIFFERENT DIHYDROARTEMISININ FORMULATIONS FOR THE TREATMENT OF ACUTE UNCOMPLICATED FALCIPARUM MALARIA IN THAILAND.

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We compared the safety and efficacy of three formulations of dihydroartemisinin for the treatment of acute uncomplicated falciparum malaria in patients who received a total dose of 600 mg dihydroartemisinin over 5 days. The first group was treated by dihydroartemisinin produced and formulated in the People's Republic of China, the second group was treated by dihydroartemisinin produced in Vietnam but formulated by the Government Pharmaceutical Organization of Thailand and the third group was treated by dihydroartemisinin produced and formulated by the Government Pharmaceutical Organization of Thailand. All patients

were admitted to hospital to evaluate safety and efficacy for a total of 28 days. By the third day of treatment, most patients were blood-smear negative for parasites and none had serious adverse effects. Minor symptoms such as nausea, dizziness and headache were similar in the three groups and disappeared after 3 days of treatment, One-hundred and thirty-three patients completed the 28-day follow up period. The cure rates of groups I, II and III were 80%, 85% and 92% respectively ($p > 0.02$). There were no significant differences in fever clearance or parasite clearance among the three groups. We conclude that the three formulations of dihydroartemisinin produced and formulated in different countries were safe and effective in treating uncomplicated falciparum malaria acquired in Thailand.

Published in: Internat J Parasitol 1998;28(8): 1213-8.

CHARACTERIZATION OF PLASMODIUM FALCIPARUM-INFECTED ERYTHROCYTE AND P-SELECTIN INTERACTION UNDER FLOW CONDITIONS

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Plasmodium falciparum-infected erythrocytes (IRBC) roll on the adhesion molecule P-selectin *in vitro* under flow conditions that approximate the shear stress in capillary and postcapillary venules in which cytoadherence occurs *in vivo*. The pathological significance of this adhesive interaction is currently unknown. In this study, we further investigated the molecular interactions between IRBC and P-selectin by using a laminar flow system that allowed for the direct visualization of IRBC-substratum interactions. The results showed that the IRBC-P-selectin interaction was Ca²⁺-dependent and involved the lectin domain of P-selectin and a sialic acid residue on IRBC.

The sialylated P-selectin ligand was trypsin-sensitive, which suggests that it could be part of the parasite antigen PfEMP1 that interacts with CD36 and intercellular adhesion molecule-1 (ICAM-1), but different from a trypsin-resistant IRBC ligand that adheres selectively to chondroitin sulfate A. Studies on the rolling and adhesion of IRBC on activated platelets that express both CD36 and P-selectin showed that inhibition of rolling on P-selectin reduced the adhesion of some clinical parasite isolates to CD36, whereas other parasite isolates appeared to interact directly with CD36. Thus, cytoadherence under physiological flow conditions may be mediated by multiple IRBC ligands that interact with different adhesion molecules in a cooperative fashion. These findings underscore the complexity of the interactions between IRBC and vascular endothelium.

Published in: Blood, 1998;91(12):4803-9.

ENDOGENOUS INTERLEUKIN-10 MODULATES PROINFLAMMATORY RESPONSE IN *PLASMODIUM FALCIPARUM* MALARIA.

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Tumor necrosis factors- α (TNF- α), interleukin (IL)-1b, and IL-6 are implicated in the pathogenesis of severe *Plasmodium falciparum* malaria. In this study, the effect of IL-10 on their production by peripheral blood mononuclear cells (PBMC) from acutely infected patients was examined. Exogenous IL-10 inhibited malarial antigen-induced cytokine production by reducing mRNA accumulation. Maximal

inhibition occurred when IL-10 was added in the first 2 h of stimulation. Conversely, the addition of anti-IL-10 markedly enhanced TNF- α , IL-1p, and IL-6 production. The effect was significantly greater on PBMC from patients with uncomplicated infection than PBMC from patients with severe disease. Kinetics studies showed that TNF- α , IL-6, and IL-1/3 were produced within 2-4 h of stimulation, while IL-10 was first detectable after 8 h. These findings suggest that IL-10 counter-regulates the proinflammatory response to *P. falciparum*. Severe falciparum malaria may be associated with an inadequate negative feedback response by IL-10.

Published in: J Infect Dis 1998;178:520-5.

EFFECTS OF α -THALASSEMIA ON PHARMACOKINETICS OF THE ANTIMALARIAL AGENT ARTESUNATE

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Thalassemia is common in Southeast Asia, where artemisinin derivatives are frequently used in the treatment of malaria. It has been previously reported that artemisinin derivatives can be concentrated by uninfected thalassemic erythrocytes *in vitro* but not by normal erythrocytes. As a follow-up to this report, we studied the antimalarial kinetics of intravascular artesunate (2.4 mg/kg of body weight) in 10 persons with normal hemoglobins and in 10 patients with thalassemia (2 with α -thalassemia type 1-hemoglobin Constant Spring and 8 with α -thalassemia type 1-a-thalassemia type 2). Concentrations of artesunate and its active metabolites in plasma were measured

by bioassay and expressed relative to those of dihydroartemisinin, the major biologically active metabolite. Concentrations of intravascular artesunate in plasma peaked in both the normal individuals and the thalassemic individuals 15 min after injection (the first time point). Plasma drug concentrations at all time intervals, except that at 1 h, were significantly higher in thalassemic subjects than in normal subjects ($P < 0.05$). The area under the concentration-time curve was 9-fold higher ($P < 0.001$) and the volume of distribution at steady state was 15-fold lower ($P < 0.001$) in thalassemic than in normal subjects. In light of the potential neurotoxicity of artemisinin derivatives, these results suggest that thalassemic subjects may need a drug administration regimen different from that of normal patients.

Published in: Antimicrob Agents Chemotherapy 1998; 9(42):2332-5.

MEASUREMENT OF SERUM NITRITE/NITRATE CONCENTRATIONS USING HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY

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Previous studies have reported increased serum concentrations of nitrite/nitrate the degradation products of nitric oxide in *Plasmodium vivax* malaria. In all these studies, however, nitrite/nitrate has been measure spectrometrically using Griess reagent which carries major disadvantages in the determination of serum nitrite/nitrate. The method does not allow an exact differentiation of nitrite and biogenic amines that

are physiologically present in plasma. In the present study we introduce high-performance liquid chromatography as a new, accurate and cost effective method for determination of serum nitrite/nitrate levels. Significantly increased nitrate concentrations were found in malaria patients and serum values remained above normal levels for at least 21 days. It could be shown that our HPLC method is a sensitive and cost-effective method for direct determination of nitrite/nitrate in serum samples, which is not influenced by the presence of biogenic amines.

Published in: J Chromato 1998;706:347-51.

LACK OF SIGNIFICANT ASSOCIATE BETWEEN ROSETTE FORMATION AND PARASITIZED ERYTHROCYTE ADHERENCE TO PURIFIED CD36

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The ability of *Plasmodium falciparum* infected erythrocytes from 162 Thai patients with uncomplicated malaria, 82 patients with severe malaria and 19 patients with cerebral malaria to form rosettes *in vitro* was studied. Of 263 isolates, 62 were evaluated for their adherence to different target molecules. We found that wide variation occurred in isolates from all groups in the level of rosette formation and adherence to CD36, intracellular adhesion molecule-

1, thrombospondin and chondroitin sulfate A. No statistically significant correlation between the magnitude of rosette formation and disease severity was found ($p > 0.05$). In addition, our results from the use of purified CD36 as an adherence receptor showed no association between the degree rosetting and level of cytoadherence ($p > 0.05$, $r = -0.04$). Our data provide evidence that rosette formation and cytoadherence involve different molecular mechanisms and both phenomena can occur in all manifestations of the disease.

Published in: Southeast Asian J Trop Med Public Health 1998;29(1):41-5.

EFFECT OF PENTOXIFYLLINE ON CYTOKINE PATTERNS IN THE THERAPY OF COMPLICATED PLASMODIUM FALCIPARUM MALARIA

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The effect of pentoxifylline (PTX) was tested for its capacity to modulate cytokine responses during

therapy of severe *Plasmodium falciparum* malaria in a placebo-controlled, randomized study in 45 adult patients in Bangkok, Thailand. The patients received standard antimalarial treatment with artesunate (120 mg intravenously given immediately, then 60 mg every 12 hr for a total dose of 600 mg). The patients received either low-dose PTX (20 mg/kg/day, n=15), high-dose PTX (40 mg/kg/day, n=15), or placebo (n=15) as continuous infusion for the first three days of antimalarial treatment. Tumor necrosis factor (TNF)

and interleukin-6 (IL-6) plasma levels were markedly elevated in all patients prior to treatment. After 6 hr of high-dose PTX treatment, TNF and IL-6 level significantly decreased while and increase in TNF and IL-6 levels was seen after 6 hr of low-dose PTX or placebo treatment ($p < 0.01$). After 12 and 24 hr of high-dose PTX infusion, TNF-receptor plasma concentrations were lower than in low-dose PTX- or placebo-treated patients ($p < 0.01$), whereas no

differences between the groups with regard to IL-6 receptor levels were observed. We conclude that 40 mg/kg/day of PTX reduces plasma levels of TNF, IL-6, and TNF-receptor in patients with severe malaria. Whether this reduction improved clinical outcome remains to be determined.

Published in: Am J Trop Med Hyg 1998; 58(3):343-7.

FUNCTIONS OF IgG AND IgE ANTI-MALARIA ANTIBODIES IN UNCOMPLICATED OR SEVERE *P. FALCIPARUM* MALARIA

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Plasmodial infection results in a significant elevation of the blood concentrations of immunoglobulins including IgE. To elucidate the role of the latter in malaria, two well characterized groups of adult Thai patients with either uncomplicated or severe *P. falciparum* malaria were studied during four weeks. At admission the mean parasitemias were approximately 3x higher in patients with severe than in those with uncomplicated disease. While almost 70% of the patients had IgG anti-plasmodial antibodies at admission, this incidence increased to 100% within a few days. The concentration of these antibodies as

well as that of total IgG was higher in the patients with uncomplicated disease than in those with severe disease for at least 3 weeks. IgE anti-plasmodial antibodies were present in approximately 65% of the patients and their concentrations were positively correlated to parasitemia, suggesting that the number of infecting parasites may be instrumental in the switch to an enhanced production of IgE. In the patients with severe disease IgE antibodies were present at higher concentrations than in the patients with uncomplicated disease. Taken together, the results confirm that IgG anti-plasmodial antibodies are protective in *P. falciparum* malaria and contribute to reduce disease severity. The different distribution of IgE antibodies together with their capacity to induce local overproduction of TNF suggests that they contribute to the pathogenesis of this infection.

Published in: Infect Immun 1998 (in press).

PULMONARY EDEMA AND ARDS IN CEREBRAL MALARIA PATIENTS IN THAILAND

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Pulmonary edema (PE) is considered a serious complication of falciparum malaria. Usually, it occurs with cerebral malaria (CM), acute renal failure, high parasitemias, or delayed antimalarial treatment. From

1993 to 1996, 120 patients with CM admitted to the intensive care unit of the Bangkok Hospital for Tropical Diseases were enrolled in a prospective treatment study using artesunate and mefloquine, in combination. A majority of patients developed complications in other organs, especially acute renal failure. Twenty-five patients (21%) developed PE. All were treated supplemental oxygen and for ARDS, positive end-expiratory pressure (PEEP). In most patients (19 of 25), PE was noted on the first day of admission and was associated with higher parasitemias and levels of acidemia, in comparison with non-PE patients. Ten of the 25 patients diagnosed with PE developed an

ARDS-like syndrome: 7 died, 5 within 24 hours of admission. There were no deaths in PE patients without ARDS. The mean CVP when PE was diagnosed was markedly lower in ARDS than non-ARDS, supporting the argument that fluid imbalance is not essential for malaria-induced lung injury. Early diagnosis and prompt treatment remain important principles to reduce the morbidity and mortality associ-

ated with complicated falciparum malaria. This report emphasizes the importance of pulmonary monitoring in adults with CM and that ARDS, as in other diseases, is an especially poor prognostic indicator.

Published in: Southeast Asian J Trop Med Public Health 1998 (in press).

INCIDENCE OF FILARIASIS AS A CO-INFECTION IN MALARIA PATIENTS COMING FROM THAI-MYANMAR BORDER BETWEEN 1995-1997

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Concomitant infection with malaria and filariasis is known to occur in animals and the co-infection appears to lessen the severity of malaria. We report here the incidence of co-infection with filariasis among 4,201 malaria patients admitted to the Bangkok Hospital for Tropical Diseases, Mahidol University, Thailand, between 1995 and 1997. There were eight patients (0.2%) with microfilariae (all *Wuchereria bancrofti*) in the peripheral blood smear. Four of the 8 patients had falciparum malaria and two patients among this group had cerebral malaria which

responded to treatment without any long term sequelae. The rest four patients, three had vivax malaria while the last one had uncomplicated mixed infection of falciparum and vivax malaria. Filariasis was asymptomatic in all patients and cured with diethylcarbamazine. The eight patients resided along the Thai-Myanmar border, which is known to be endemic for both diseases. Our findings indicate the existence of co-infection of malaria and filariasis in Thailand, especially among patients from the Thai-Myanmar border. From this small number of patients, it is difficult to conclude that filariasis affects the severity of malaria. However, the data does emphasize the importance of instituting early diagnosis and early treatment of both infections.

Published in Japanese J Parasitol 1998 (in press).

A CLINICAL TRIAL OF COMBINATION OF ARTESUNATE AND MEFLOQUINE IN THE TREATMENT OF ACUTE UNCOMPLICATED FALCIPARUM MALARIA: A SHORT AND PRACTICAL REGIMEN

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The difficulties in treating drug-resistant falciparum malaria in Thailand are compounded by the necessity of giving antimalarials over long periods of time. The resultant fall in patient compliance not only lowers cure rates but also predisposes to the further spread of drug-resistance. Sequential treatment with artesunate given over 5 days followed by mefloquine produced 100% cure rates in previous

study, but might not be a suitable regimen for field treatment. We conducted a clinical trial of a combination of artesunate and mefloquine given twice daily for 2 days in 150 patient with acute uncomplicated falciparum malaria. The dose of artesunate (200 mg) and mefloquine (312.5 mg) were given simultaneously in a separate package. All patients were admitted to hospital in Bangkok for 28 days to exclude re-infection and monitor the possible adverse effects. One hundred and thirty patients completed the study 28 days follow up. Twenty patients (13%) left the hospital prior to completion of follow-up for reasons unrelated to their treatment. Cure rate was 97% (126/130). There was no RII or RIII failures and all four patients of the treatment failures were at the RI type. The mean parasite clearance time and fever clearance

time were 46.4 and 42.5 hours respectively. All patients tolerated the combination drugs well and there were no serious toxic adverse reactions. The results indicate that combination of artesunate and mefloquine given twice daily for 2 days is effective and well tolerated in patients with acute, uncompli-

cated falciparum malaria and suitable as an alternative treatment for multidrug resistant falciparum malaria.

Published in: Southeast Asian J Trop Med Public Health 1998 (in press).

PREDICTING MORTALITY IN PATIENTS WITH MALARIAL ACUTE RENAL FAILURE

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APACHE III scores, calculated within the first 24 hours of admission, were analyzed in 108 patients with acute renal failure due to falciparum malaria who were admitted to Bangkok Hospital for Tropical Diseases, Thailand. Twelve (11.1%) patients died. The mean APACHE III score was 82.0 ± 25.5 (range, 45-171). There was a close relation between the APACHE III score and the hospital mortality rate. The nonsurvivors had significantly higher APACHE III scores than the survivors, 109.8 ± 36.7 and 75.7 ± 21.6 respectively ($p < 0.001$). Patients with APACHE III score 82 had a 4.2-fold higher risk of dying compared with patients with a lower score (95% CI

1.2-14.7; $p = 0.013$).

Hemodialysis treatment was performed in 97 (89.8%) of the patients. Although the mean APACHE III score for patients who were not treated with hemodialysis (95.9 ± 38.0) was not significantly higher than for patients who received hemodialysis (80.4 ± 23.5 ; $p > 0.05$), the former had a 4.4 times higher risk of dying compared with patients who received hemodialysis (95% CI 1.6-12.3; $p = 0.019$).

Using the APACHE III score and its ability to predict death, we calculated its sensitivity, specificity and accuracy to be 0.92, 0.31 and 0.41 respectively at a cutoff score of 67 points. The area under the receiver operating characteristic (ROC) curve was 0.75.

The APACHE III scoring system correlated well with the mortality of critically ill malaria patients with acute renal failure, although it was not possible to identify individual survivors or nonsurvivors. APACHE III should not be used for individual prognosis or treatment decisions.

Published in: Kidney International 1998 (in press).

TREATMENT OF MALARIAL ACUTE RENAL FAILURE BY HEMODIALYSIS

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We studied 112 patients with malarial acute renal failure (ARF) during the years of 1991 to 1997 at Bangkok Hospital for Tropical Diseases, Mahidol University in Bangkok, Thailand. Hemodialysis was performed in 101 (90.2%) of these patients. The mean

number of times the patients were hemodialysed was 6.5 (range, 1-27). Ninety-three (83.0%) patients were oliguric and the remainder were nonoliguric. Patients who had oliguric renal failure required more hemodialyses and had more complications than the nonoliguric patients. The oliguric patients had an eight-fold higher risk of requiring six or more hemodialyses (95% CI of 1.2-53.9; $p = 0.0008$). The overall mortality rate was 10.7% (12 of 112). Eleven of the patients who died were jaundiced and eight of them had cerebral malaria with $GCS \leq 8$. We conclude that hemodialysis is a useful treatment for oliguric and nonoliguric ARF from severe malaria, particularly when initiated early in the course of illness.

Published in: Am J Trop Med Hyg 1998 (in press).

INFLUENCE OF HEMOGLOBIN E TRAIT ON THE ANTI-MALARIAL EFFECT OF ARTEMISININ DERIVATIVES

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To determine if hemoglobin E trait influences the course of acute malaria, adult patients hospitalized for the treatment of symptomatic infection with *Plasmodium falciparum* were studied retrospectively. Forty-two patients with hemoglobin E trait were compared to 175 reference subjects who did not have hemoglobin E, β -thalassemia, glucose-6-phosphate dehydrogenase deficiency, or a-

thalassemia. One patient with hemoglobin E trait (2.4%) had a severe complication of malaria by World Health Organization criteria (cerebral malaria) while 32 subjects in the reference group (18.3%) had one or more severe complications: cerebral malaria (n=18), hyperparasitemia (n=16), renal failure (n=10), severe anemia (n=1) (p=0.044 after adjustment for ethnic categories). The estimated odds of severe complications in the reference subjects were 6.9 times the odds in patients with hemoglobin E trait (95% confidence interval of 1.2 to 146.4). These results suggest that hemoglobin E trait may ameliorate the course of acute falciparum malaria.

Published in: J Infect Dis 1999;179 (in press).

PLASMA LEVELS OF THE IL-6 CYTOKINE FAMILY IN PATIENTS WITH SEVERE PLASMODIUM FALCIPARUM MALARIA

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Plasma levels of members of the interleukin-6 (IL-6) family (IL-6, soluble IL-6 receptor, soluble gp130, leukemia inhibitory factor (LIF), and ciliary neutrophilic factor (CNTF)) were analyzed in 32 patients with severe malaria. 10 patients had renal failure, 8 patients had cerebral, and 14 patients had other causes of severity. Prior to treatment plasma IL-6, and soluble IL-6 receptor were significantly higher in cerebral and/or renal malaria compared to the other group (<0.05 for both). The highest levels were seen

in cerebral malaria (p< 0.05 compared to renal malaria or other forms of severe malaria). 24 hr. after initiation of therapy IL-6 levels dropped but soluble IL-6 receptor levels increased further in all groups. CNTF levels were significantly reduced in cerebral malaria and renal failure compared to moderate severe malaria or healthy controls, and normalized 24 hr. after start of treatment. Plasma concentration of gp130 and LIF were not different between malaria patients, and healthy controls. We conclude that i. excessive levels of IL-6 could be controlled by a subsequent shedding of the soluble IL-6 receptor, ii. in contrast of septicemia LIF levels are not elevated in severe malaria, and iii. low level CNTF expression could contribute to cerebral malaria and/or renal failure.

Submitted for publication (1998).

SERUM CONCENTRATIONS OF G-CSF IN COMPLICATED *PLASMODIUM FALCIPARUM* MALARIA

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It was the aim of the present study to investigate the time course of G-CSF serum concentrations in patients with complicated *P. falciparum* malaria in comparison with other immunological parameters.

26 patients suffering from complicated *P. falciparum* malaria were included into the study, 20 age and sex matched healthy volunteers were used as negative control group. Serum samples for determination of G-CSF were taken on day 0, 7 and 14. A commercially available ELISA was used for analysis.

Serum concentrations of G-CSF were increased in patients with complicated *P. falciparum* malaria on admission (583 740 pg/ml). Values had decreased to within the normal range by day 7 (13.3 8.4 pg/ml; control group: 16 13.5 pg/ml). A significant correlation was found between G-CSF (do) and procalcitonin, the parasite count, erythropoietin and macrophage inflammatory protein-1 alpha serum concentrations.

In conclusion elevated serum concentrations of G-CSF were found in patients with complicated *P. falciparum* malaria on the day of admission. This might indicate a role of G-CSF in the acute defense mechanism against these parasites.

Submitted for publication (1998).

THE OCCURRENCE OF POINT MUTATIONS IN THE DIHYDROFOLATE REDUCTASE- THYMIDYLATE SYNTHASE (DHFR) GENE IN THAI ISOLATES OF *PLASMODIUM FALCIPARUM*

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The decreased susceptibility of malaria parasites to the drugs currently used for treatment of malaria is one of the main reasons for failure to control this disease in many endemic areas in Thailand. Several groups have reported that many of the *Plasmodium falciparum* isolates from Thailand have resisted antimalarials other than chloroquine which include cycloguanils, pyrimethamine and sulfadoxine (Edstein *et al.*, 1996; 1997; Wilairatana *et al.*, 1997). Resistance to chloroquine and pyrimethamine is widespread in Thailand and it has been reported that pyrimethamine resistance is still rising (Thaithong *et al.*, 1990). Genetic analysis has demonstrated associations between point mutations in codon 108 of the DHFR gene and resistance to pyrimethamine and cycloguanil. A serine at position 108 is linked to sensitivity to both these drugs while a mutation to asparagine (Asn-108)

or threonine (Thr-108) at this position confers resistance to pyrimethamine and cycloguanil respectively ((Foote *et al.*, 1990; Peterson *et al.*, 1990). Polymerase chain reaction (PCR) using specific primers has been used successfully to detect these mutations in *P. falciparum* isolates from other geographical areas such as Africa (Plowe *et al.*, 1995) and the Brazilian Amazon (Peterson *et al.*, 1991). However, in a study with Malaysian *P. falciparum* isolates, there was no clear association found between the presence of Asn-108 and pyrimethamine resistance (Lim *et al.*, 1998). In addition, there was considerable heterogeneity found in a large number of these isolates with both Ser-108 and Asn-108 found in the same individual. Therefore we would like to determine whether these mutations occur frequently in *P. falciparum* isolates from Thailand and whether any heterogeneity of these markers exists.

Published in : Southeast Asian J Trop Public Health 1998 (in press).

CIRCULATING RECEPTORS ICAM-1, VCAM-1, E-SELECTIN AND CHONDROITIN-4-SULFATE A IMPLICATED IN CYTOADHERENCE IN THE COURSE OF SEVERE *PLASMODIUM FALIPARUM* MALARIA IN THAILAND

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The kinetic profiles of the circulating receptors was compared in a case control study to determine if they could be considered as predictive markers for the severity of *P. falciparum* malaria. We observed a significant difference between ICAM-1 concentrations in severe malaria cases compared to the uncomplicated cases ($p=0.01$). However, there was a significant

increase in CSA concentrations in both groups compared to a control group ($p= 10^{-5}$), without correlation between the plasma level of CSA and the severity of malaria infection. Plasma levels of E-selectin and VCAM-1 were increased in the two groups compared to the corresponding control groups. Our results suggest that the plasma concentration of ICAM-1 may be considered as a marker for the severity of malaria.

Published in : Southeast Asian J Trop Med Public Health 1998 (in press).

THE EOSINOPHILIC RESPONSE AND HEMATOLOGIC RECOVERY AFTER TREATMENT FOR *PLASMODIUM FALCIPARUM* MALARIA

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To examine a possible relationship between the T-helper cell type 2 (Th-2) immune response and hematologic recovery after acute falciparum malaria, we followed peripheral blood eosinophil counts and hemoglobin concentrations for four weeks after starting effective treatment in 16 adult Thai patients whose stools were negative for ova and parasites. Eosinophils are induced by Th-2 cytokines and reflect

the activity of this arm of the immune response. Eosinophil counts were normal in all but one subject at presentation, probably reflecting predominance of the Th-1 response over the Th-2 response early in the infection, but were elevated in all but one subject by day 7. Eosinophil counts then decreased markedly by day 14 and did not change significantly thereafter. A significant positive correlation was found between peak eosinophil counts on day 7 and the hemoglobin concentration on day 28 ($r = 0.65$, $p = 0.006$). These results suggest that a robust Th-2 immune response shortly after completing antimalarial therapy predicts for a good recovery from malaria-associated anemia.

Submitted for publication (1998).

RANDOMIZED DOSE-RANGING STUDY OF THE SAFETY AND EFFICACY OF WR 238605 IN THE PREVENTION OF RELAPSE OF *PLASMODIUM VIVAX* MALARIA IN THAILAND

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Primaquine, an 8-aminoquinoline, is the only antimalarial drug available for eradication ("radical cure") of the dormant hepatic stages of *Plasmodium vivax* malaria. However, primaquine has a narrow therapeutic index and a short half-life that requires daily administration for up to 2 weeks, resulting in poor compliance. WR 238605, a synthetic primaquine analog, was developed by the U.S. Army as a safer, more effective, and longer acting primaquine replace-

ment. Pre-clinical studies in vivax or vivax-like malaria animal models indicate that WR 238605 is significantly more active than primaquine against both the exoerythrocytic (tissue) and erythrocytic stages. In Phase I and II clinical studies, the drug was safe and well tolerated.

WR 238605 was expected to be well tolerated in *P. vivax* infected patients. However, dose-ranging studies are required to identify the safest and most effective dosing regimens. The purpose of this study was to obtain safety and tolerability profiles for three dosing regimens of WR 238605 in *P. vivax* infected patients first treated with a standard blood schizonticidal dose of chloroquine. WR 238605 was safe, well tolerated, and effective in preventing vivax malaria relapse. Expanded testing is now warranted to determine the most effective and most practical WR 238605 regimens for *P. vivax* radical cure.

Submitted for publication (1998).

RESEARCH ON NEW ANTIMALARIAL DRUGS IN BANGKOK HOSPITAL FOR TROPICAL DISEASES

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Multi-drug resistant falciparum malaria is a serious problem in Thailand. Therapeutic failures with all available antimalarial drugs are well documented. With this deteriorating situation, new drugs are urgently needed. The new drugs including atovaquone, artemisinin derivatives (artesunate, artemether, dihydroartemisinin), CGP 56697, pyronaridine and gibanide-dapsone have been studied in clinical trials in Bangkok Hospital for

Tropical Diseases since 1988. This paper is an overview of these clinical studies on new antimalarial drugs in patients with uncomplicated falciparum malaria.

Clinical trials of new antimalarial drugs (atovaquone, artesunate, artemether, dihydroartemisinin, CGP 56697, pyronaridine, and biguanide-dapsone combinations) for treatment of uncomplicated malaria have been studied in Bangkok Hospital for Tropical Diseases. Atovaquone, artemisinin derivatives, and CGP 56697 have proved effective and safe.

Presented at: IX International Congress of Parasitology (ICOPA IX) Makuhari Messe, Chiba, Japan 24-28 August 1998.

POLYCLONAL ANTI-TUMOUR NECROSIS FACTOR- α FAB USED AS AN ANCILLARY TREATMENT IN SEVERE MALARIA.

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Single doses (250, 500, 1000 or 2000 units/kg) of an ovine polyclonal specific Fab fragment directed against tumor necrosis factor- α were given to 17 adult patients with severe falciparum malaria immediately before treatment with artesunate in a pilot study to assess safety and optimal dosage with a view to future studies. Clinical and laboratory variables were compared with 11 controls. In the groups given Fab there was a tendency for a faster resolution of clinical manifestations and reduction of fever but also a tendency towards longer parasite clearance times. Adverse events were more common in the control group and no early anaphylactoid or late serum sickness reactions occurred in the Fab treated patients. On admission all patients

had markedly elevated TNF α (85-1,532 ng/L) and IL-6 concentrations (30-27,500 ng/L), most had elevated IFN γ values and a few had raised IL-2, IL-8 and IL-18 levels. Antibody treatment reduced IFN γ concentrations in a dose-related manner, but had no obvious effects on levels of other cytokines in this small study, although unbound TNF α was undetectable after Fab treatment. Circulating concentrations of soluble E-selectin, ICAM-1 and VCAM-1 were not affected by Fab treatment. The Fab exhibited a two compartment, dose proportional kinetics with an average elimination half-life of 12.0 hr and with about 20% being excreted renally. These results encourage a randomized, placebo-controlled trial in patients with cerebral malaria and provide some guidance about dosage.

Published in : Am J Trop Med Hyg 1998 (in press).

DETERMINATION OF MYCOPHENOLIC ACID IN PLASMA BY HIGH PERFORMANCE LIQUID CHROMATOGRAPHY

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A rapid selective, sensitive, and reproducible reversed-phase HPLC procedure for the quantitative determination of the active metabolite of an immunosuppressant - mycophenolate mofetil i.e., mycophenolic acid (MPA) in plasma is described. The procedure involved a single step extraction of MPA and the internal standard, carboxy butoxy ether mycophenolic acid (MPA) with dichloromethane (6 ml) at acidic pH. Chromatographic separation consisted of the mobile phase (acetonitrile: 0.05 M phosphate buffer pH 3.2 = 50:50 v/v) running

through the column (Techopak-10 C₁₈: 10 cm x 4.6 mm i.d., 10 μ m particle size) at flow rate of 0.8 ml/min. Detection was at uv wavelength of 254 nm. The mean recoveries of MPA and the internal standard at concentration range of 1 and 200 μ g/ml were 98.9 vs 89%, and 94.7% vs 96% for MPA vs CMPA. The within-day coefficients of variation were 2.47-9.02% for MPA, and 5.9-8.4% for CMPA. The day-to-day coefficients of variation were 2.1-4.1% for MPA and 5% for CMPA. The minimum detectable concentrations for MPA and CMPA in plasma were 5 and 10 ng/ml. The method was found to be suitable for use in clinical pharmacokinetic study.

Submitted for publication.

PHARMACOKINETICS OF A SINGLE ORAL DOSE OF DIHYDROARTEMISININ IN VIETNAMESE HEALTHY VOLUNTEERS

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Pharmacokinetics of a 240 mg single dose of oral dihydroartemisinin (DHA) was investigated in 8 healthy (5 males, 3 females) Vietnamese volunteers. Plasma concentrations were measured by high-performance liquid chromatography with electrochemical detection in the reductive mode. The concentration time profile of DHA was fitted with one-compartment model with a lag time. Pharmacokinetics of DHA is comparable between males and females even when adjusting with dosage. The median (range) values of pooled pharmacokinetics of oral DHA were: t_{lag} 0.41 (0.09-0.78) hours, $t_{1/2a}$

0.58 (0.17-1.43) hours, t_{max} 1.6 (1.1-2.2) hours, C_{max} 466 (128-787) ng/ml, $C_{max}/dosage$ 97.7 (27.2-124.6) ng/ml, $t_{1/2z}$ 2.0 (1.5-3.4) hours, AUC 1867 (420-3535) ng.h/ml, AUC/dosage 364.3 (89.3-559.7) ng.h/ml/dosage, Cl/f 45.8 (30.0-190.0) ml/min/kg, V_z/f 8.0 (5.5-29.9) l/kg. Interindividual variation was large, the coefficients of variation (CV) were 47.8% and 45.3% respectively to AUC and C_{max} . The t_{max} of DHA formulation was comparable with that of DHA metabolite of artemisinin derivatives. The $t_{1/2z}$ was longer and shorter than that of DHA metabolites of oral formulations of artesunate and artemether respectively. DHA is suggested to combined with another long acting blood schizontocidal drugs in malaria treatment.

Submitted for publication.

PHARMACOKINETICS OF A SINGLE ORAL DOSE OF DIHYDROARTEMISININ IN VIETNAMESE PATIENTS WITH UNCOMPLICATED FALCIPARUM MALARIA

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Pharmacokinetics of 240 mg single oral dose of dihydroartemisinin (DHA) was studied in 26 (21 males, 5 females) adult Vietnamese patients with uncomplicated falciparum malaria. There was no difference in DHA pharmacokinetics between male and female patients. Pharmacokinetic parameters in patients were significantly different from those corresponding in Vietnamese healthy subjects in previous study except the half-lives of absorption ($t_{1/2a}$) and elimination ($t_{1/2z}$). In patients, the median [range] of t_{lag} was longer (0.82 [0-1.48] vs 0.41 [0.09-0.78] h), t_{max} was later (2.2 [1.1-3.84] vs 1.6 [1.1-2.1] h), C_{max} and $C_{max}/dosage$ were higher (845 [345-2280] vs [128-787] ng/ml and 161.1 [27.2-124.6] ng/ml/dose/body weight), but V_d/f and total systemic

clearance CL/F were lower (3.3 [1.4-11.07] vs 8.0 [5.5-29.91] l/kg and 24 [7.1-43.03] vs 45.8 [29.9-101.1] ml/min/kg, respectively), compared to healthy subjects. These data suggested the increase of plasma protein binding and the reduction in systemic clearance of DHA in acute phase of malaria illness.

The mean [SD] of lag time for observed DHA concentration to be up to the maximum MIC of DHA (7.47 ng/ml) previously reported in Vietnamese *P.falciparum* isolates was 0.8 [0.4] h. The latest time for observed DHA concentrations to be down to the MIC_{max} of DHA was 15.0 [3.7] h, thus the duration time to be above the MIC_{max} was 14.2 [3.6] h. Therefore, the treatment dose for oral DHA is suggested to be at least 240 mg (equal 5.04 [0.9] mg/kg) per day for 5 days, no reduced dose after the first treatment dose if suggested for DHA monotherapy.

Submitted for publication.

THE COMPARISON BETWEEN TWO METHODS OF THE *IN VITRO* SENSITIVITY TEST OF *PLASMODIUM FALCIPARUM* ISOLATES

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Two different methods for the *in vitro* sensitivity testing of *Plasmodium falciparum* based on the *in vitro* micro-technique of Rieckmann *et al.*, (1978) were applied for the assessment of the susceptibility of the parasites to the antimalarial—mefloquine. Method-I involved direct application of the fresh isolates obtained from patients' blood without pre-cultivation, while method-II involved the pre-cultivation of the parasites for 1 cycle (48 h) prior to assay. Of the 60 isolates tested, 37 (61.6%) exhibited successful growth [14(23.3%), 22 (36.67%), and 1(1.67%) for growth in either method-I or method-II, method-I alone, and method-II alone, respectively], whereas 23(38.33%) were unable to demonstrate significant growth

following a successive incubation period of 24-36h of sensitivity testing. No significant association was observed between the initial parasitaemia and the success growth rate in method-I [median (range) 0.5 (0.1-2%) and 0.2 (0.1-1%), respectively for the isolates with and without successful growth]. The *in vitro* assays were eventually successful evaluated from 21 isolates out of the 37 isolates with successful growth (21.19 and 9 isolates from either method-I or method-II, method-I alone, and method-II alone, respectively). The final success rate of *in vitro* sensitivity testing was found to be significantly higher for method-I compared with that of method-II ($p < 0.0001$, 95% C.I. 2.18-10.66). Both methods however, revealed similar susceptibility pattern of the parasites to mefloquine. Method-I is considered more preferable for the assessment of the susceptibility of *P. falciparum* isolates obtained from patients' blood.

Submitted for publication.

INVESTIGATIONS OF INCIDENCE OF PYR PRETREATMENT, DRUG SENSITIVITY *IN VITRO* AND PLASMA LEVELS OF PYRIMETHAMINE IN PATIENTS WITH MULTIDRUG RESISTANCE *FALCIPARUM* MALARIA FOLLOWING THE THREE COMBINATION REGIMENS OF ARTEMETHER/PYRIMETHAMINE

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The study was carried out to investigate the status of *in vitro* susceptibility of *Plasmodium falciparum* to pyrimethamine (PYR) in multidrug resistance area of Thai-Myanmar border, the incidence of unregulated use of PYR (as Fansidar[®]) in this area and the relevance of pharmacodynamic and pharmacokinetic factors in determining the treatment outcome from the three combination regimens of ART/PYR (1-, 2- and 3-day regimens), in patients

with acute uncomplicated falciparum malaria. The majority of patients had baseline concentrations between 1- 100 (50.6%) and more than 100-500 (34.8%) ng/ml while concentrations of more than 500 ng/ml were found in only 1.1%. All of the isolates exhibited high grade resistance to PYR with the minimum inhibition concentration (MIC) of as high as 10⁻⁵ M. No association was observed between treatment outcome and the presence of baseline plasma PYR concentrations. In addition, lack of association between plasma concentrations during the acute phase (day -1 and -2) and treatment outcome was found.

Submitted for publication.

MEFLOQUINE CONCENTRATIONS DURING MALARIA CHEMOPROPHYLAXIS

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A pharmacokinetic study with prophylactic doses of mefloquine hydrochloride was conducted in 12 healthy adult subjects (Caucasian), 6 males and 6 females, mean age 29.2 ± 6.4 years, mean weight 70.6 ± 13.4 kg. Doses of 250 mg mefloquine were administered on days 0 and 1, 7, 14, 21 and 28. Six subjects received 5 more weekly doses of 250 mg mefloquine, the others 5 more weekly doses of 125

mg. After the third dose the protective threshold concentration was reached in all subjects. In female subjects mean $C_{\min SS}$, $C_{\max SS}$, and AUC_{d0-35} were significantly higher, and the weight-adjusted V_{ss} values significantly lower, than in males. After the fifth dose mean $C_{\max SS}$ in females reached 1692 ng/ml (4.48 mmol/l), equivalent to a high therapeutic concentration. This may be explained by gender-associated with excessive drug concentrations. This calls for an appropriate adjustment of the prophylactic dose regimen of mefloquine in females.

Submitted for publication.

PHARMACOKINETIC AND PHARMACODYNAMIC INTERACTIONS BETWEEN MEFLOQUINE AND QUININE IN HEALTHY MALE THAIS

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The study was carried out to investigate the pharmacokinetic and pharmacodynamic interactions between the two antimalarials, mefloquine and quinine. A randomized comparative, three way cross-over design was performed in seven healthy male Thais following the administrations of three drug regimens on three occasions, i.e., a single oral dose of QN sulfate (600 mg), or MQ (750 mg) alone, or the combination of MQ (750 mg) and QN (600 mg given 24 h after MQ). Longer period of significant prolongation of QTc interval was observed following the combination regimen (at 2.5, 3, 4, 6, 8, 12, 18, 24 hours post QN dose), but no abnormal clinical signs or symptoms were found. There were no significant changes in vital signs, routine laboratory parameters in any of the subjects. The pharmacokinetics of MQ was influenced by the presence of QN. Total clearance (CL/f) was faster [0.52

(0.35-0.83) vs 0.41 (0.31-1.64) ml min⁻¹kg⁻¹], with reduced terminal elimination half-life [$t_{1/2Z}$; 13.8 (9.5-20.4) vs 22.6 (14.3-63) h]. In contrast, the presence of MQ had no effect on the pharmacokinetics of QN. The study also demonstrated the synergism of blood schizontocidal activities of the sera collected after the combination regimen over that of QN or MQ alone regimen. The minimum inhibitory concentrations of the equivalent concentrations of QN or MQ which completely inhibited the growth of K1 strain *P. falciparum in vitro* (MICs of QNEq and MQEq) were significantly lower in the sera collected after the combination regimens, comparing to each individual drug alone [MICs of QNEq: 41.2 (21.25-73.5) vs 135 (118-150) mg ml⁻¹; MICs of MQEq: 18.2 (17-19.2) vs 25.2 (24.4-26.8) ng ml⁻¹]. Caution should be taken when multiple dose regimen of QN is to be given in patients who have been taking mefloquine within 72 h. Close monitoring with ECGs is necessary.

Submitted for publication.

IN VITRO SENSITIVITY OF PLASMODIUM FALCIPARUM AND CLINICAL RESPONSE TO BENFLUMETOL AND ARTEMETHER

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In vitro sensitivity tests with 103 *Plasmodium falciparum* isolates were conducted in Thailand in the framework of a clinical dose finding trial with combination of artemether and benflumetol (CGP 56697) for the treatment of uncomplicated falciparum malaria in an area affected by multi-drug resistance. The CGP 56697 tablets contain 20 mg artemether and 120 mg benflumetol. In the trial standard dose regimen, namely 4 doses of 4 tablets over 48 hours, was compared with two lower dose regimens (4 x 2

tablets and 3 x 4 tablets). The parasites showed high resistance to chloroquine, fairly advanced resistance to mefloquine and compromised sensitivity to quinine. Sensitivity to artemisinin and benflumetol prior to treatment was similar in all treatment groups. The 4 x 4 tablet regimen was more effective than the other regimens in coping with infections with relatively low sensitivity to artemisinin and/or benflumetol. Parasite density at the start of treatment was identified as the critical predictor of treatment outcome, indicating that parasite exposure to the drugs may have been too short in the cases of treatment failure, particularly, marked in the lower dose regimens. This could be remedied by an improved drug regimen.

Submitted for publication.

PHARMACOKINETICS OF MEFLOQUINE IN VIETNAMESE HEALTHY VOLUNTEERS

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The pharmacokinetics of mefloquine was investigated in eight (5 males, 3 females) Vietnamese healthy subjects following the administration of a single oral of 750 mg of mefloquine (Mephaquine®; 250 mg per tablet; Mepha Pharmaceuticals, Switzerland). The pharmacokinetics of mefloquine in both female and male Vietnamese subjects were comparable to those reported in Thai subjects in previous studies. Pharmacokinetic parameters of a fixed 750 mg dose

were similar between males and females except C_{max} and AUC which were significantly higher and VSS/F which was lower in females than in males ($p = 0.025$). When normalising for dosage, $C_{max}/dosage$ and VSS/F of both groups, but not $AUC/dosage$ were still significantly different ($p = 0.025$). Difference in volume of distribution could have contributed in part, to the observed higher whole blood concentration of mefloquine in females. Therapeutic or prophylactic regimens of mefloquine based on dosage per kilogram body weight are suggested in Vietnamese.

Submitted for publication.

PHARMACOKINETICS OF INTRAMUSCULAR ARTEMETHER IN PATIENTS WITH SEVERE FALCIPARUM MALARIA PATIENTS WITH ACUTE RENAL FAILURE

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The pharmacokinetics of intramuscular artemether and its major plasma metabolite-dihydroartemisinin, were investigated in patients with

severe manifestations of falciparum malaria. Six severe falciparum malaria patients with acute renal failure (ARF) and 11 without ARF were recruited into the study. They were treated with intramuscular artemether at a loading dose of 160 mg, followed by daily doses of 80 mg for another 6 days (total dose 640 mg). Patients with and without ARF showed a good initial response to treatment; the parasite and

fever clearance time were 66(30-164) and 76(36-140) h [median(range)], respectively. None had reappearance of parasitaemia in their peripheral blood smear within 7 days after the initiation of treatment. In comatose patients, the time to recovery of consciousness was 51.6(22-144) h. Artemether was detected in plasma as early as 1 h of 160 mg dose, and declined to undetectable level within 24 h in most cases. Patients with ARF had significantly higher C_{max} , AUC, and lower V_z/F and CL/F when compared with those without ARF. In addition, $t_{1/2,z}$ was significantly longer

in the first group. The pharmacokinetics of dihydroartemisinin in these two groups of patients was comparable. Malaria and ARF conditions significantly modified the pharmacokinetics of intramuscular artemether. The changes could be attributed to either improved absorption/bioavailability, or reduction of systemic clearance, or change in plasma protein binding

Published in : Br Clin Pharmacol 1998;45:597-600.

INITIAL EVALUATION OF LOW-DOSE PHENOBARBITAL AS AN INDICATOR OF COMPLIANCE WITH ANTIMALARIAL DRUG TREATMENT

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Since poor compliance with antimalarial therapy is often suspected but difficult to prove, this study attempted to establish a model for predicting the plasma concentration of phenobarbital (given in low doses in conjunction with the drug) as an indicator of compliance. Phenobarbital was chosen because its value had been demonstrated as a marker of compliance in long-course therapies, any significant departure from steady-state concentrations (achieved with full compliance) indication one or more missed doses. Therapy for uncomplicated malaria varies from 5 days with artesunate to 7 days with quinine + tetracycline. Volunteers with confirmed falciparum malaria were randomized into 5 groups and given malaria therapy as well as phenobarbital daily for 3-7 days. Plasma samples for determination of phenobarbital concentrations were taken just prior to the daily dose of phenobarbital. Although there was a clear and predictable individual pattern of blood concentrations following each dose of phenobarbital, inter-individual variation in blood levels was significant and reduced their predictive value beyond the second day's dose. The cause of the variations is not clear; it could be attributable to different sources of the drug, previous intake of phenobarbital by the patient, or differences in drug absorption and disposition in malaria patients.

Results for the 5-day artesunate regimen suggest that phenobarbital may be useful as a marker of compliance if the patient stops medication after 3 days; clear differences were evident at the end of the course of treatment between plasma phenobarbital concentrations in individuals completing the 5-day course and those who stopped after 3 days. For the quinine-tetracycline regimen, results suggest that it may be possible to discriminate between subjects where there is a 3-day difference in treatment. Phenobarbital is a better discriminant when dosing is every 24 hours as with artesunate, rather than the 8-hourly regimen for quinine-tetracycline. When measuring compliance for malaria treatment, if it is important to know what proportion of patients reach 3, 5 or 7 days of compliance, then phenobarbital might have a role to play in this assessment, but further investigations in more patients would be required. Alternatively, different markers could be used for the doses to be given on these days and, as long as the patient does not mix the doses for the different days, sequential doses and determination of compliance could be based on an all or none detection of the marker rather than on drug levels.

This study was supported by the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases

Published in : Bull WHO 1998 ;76 (Suppl.1): 67-73.



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CURRENT RESEARCH ACTIVITIES

1. Monoclonal antibody-based competitive ELISA and indirect ELISA for immunodiagnosis of trichinosis
2. The effects of *Trichinella spiralis* infection on renal functions in rats
3. Comparison of biochemical extract preparations of *Cysticercus cellulosae* by SDS-polyacrylamide gel electrophoresis and immunoblot technique
4. IgG-ELISA for detection of bancroftian filariasis by using antigenic molecules of partial surface and excretory-secretory of *Dirofilaria immitis* adult worms.
5. Densitometric appearance of 24 kDa of albendazole-treated patients for gnathostomiasis, relationship between infectivity and eosinophilia
6. Ivermectin and albendazole in treatment of gnathostomiasis
7. Seasonal variation in the intensity of *Gnathostoma* larvae in swamp eels (*Fluta alba*) sold in local market of Bangkok
8. *Toxocara canis* antigens (excretory-secretory, crude extract, fractionate) for serodiagnosis of human toxocarosis
9. *Angiostrongylus cantonensis* antigens for serodiagnosis of angiostrongyliasis
: improvement of crude antigens
: fractionated antigens
10. Comparative protein patterns of developmental stage of *Angiostrongylus cantonensis* by SDS-polyacrylamide gel electrophoresis and immunoblot
11. Experimental infection of freshwater fish in Thailand with infective stage of *Angiostrongylus* sp.
12. Thermal effect on opisthorchid metacercariae in fish
13. Utilizing cystic fluid of *Taenia solium* metacestodes for IgG-ELISA in the detection of neurocysticercosis

TRAINING COURSE

The APCO Training Course for Senior Administrators and Leaders of Parasite Control Project for Community Health Development

ABSTRACTS

SEASONAL VARIATION IN THE INTENSITY OF GNATHOSTOMA LARVAE IN SWAMP EELS (FLUTA ALBA) SOLD IN A LOCAL MARKET IN BANGKOK

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The viscera of swamp eels were obtained from a local market in Bangkok twice a month from June 1996 to May 1997. The livers were separated, weighed and counted. *Gnathostome* larvae were recovered from the livers by the digestion technic, examined, identified, and counted. A total of 12,278 *Gnathostoma* larvae were obtained from 18,561.1 g (15,264 pieces) of eel livers. The overall average number of larvae/g liver and the overall average number of larvae/liver are 0.91 and 0.94, respectively. The greatest number of larvae/g liver (on average) was December (high levels of infection during the months of October to December) whereas the lowest was in April (lowest levels of infection during the months of March to April). Thus there was a marked decrease in the

average number of larvae/g liver during January to April, which then started to rise in May. The finding suggests that the level of infection abruptly decreases soon after the completion of the rainy season, starts to rise when the rain has come, and reaches its peak when the amount of rainfall is highest. More than 99% of the total gnathostome larvae recovered were identified to be *G. spinigerum*, and 25.4% of the entire larvae recovered bore variant of abnormal cephalic hooklets. The most common unusual feature was that there were extra rudimentary hooklets above row one, below row four and in between the four rows of hooklets which comprised 21.4%. In addition, the body size and the number of cephalic hooklets of *G. spinigerum* are also discussed.

Published in : *Southeast Asian J Trop Med Public Health* 1998; 29 (1): 148-53.

HUMAN LUNG FLUKE PARAGONIMUS HETEROTREMUS: DIFFERENTIAL DIAGNOSIS BETWEEN PARAGONIMUS HETEROTREMUS AND PARAGONIMUS WESTERMANI INFECTIONS BY EITB

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The specificity of three major polypeptides (35, 33 and 32.5 kD) from *Paragonimus heterotremus* antigens prepared from ether-extracted adult worms was tested against sera from heterologous infections as well as against *P. westermani*-infected sera. Only the 35 kD polypeptide was not present, its antigenic determinant being bound to the antibodies from all

P. westermani-infected cases. Its cross-reactivity against various sera from heterologous helminthiases and other lung infections showed that it is not bound to these antigenic polypeptides. These major bands cannot be detected by Concanavalin A detector. Our research encourages the pattern (35,33 and 32.5 kD) of immunoblot reactions for the diagnosis of *P. heterotremus* infections; the 35 kD antigen is specific for corresponding species and able to differentiate infections between both species of *Paragonimus*.

Published in : *Trop Med Internat Health* 1998; 3(1): 52-6.

APPLICATION OF THE GELATIN PARTICLE INDIRECT AGGLUTINATION TEST IN THE SERODIAGNOSIS OF HUMAN OPISTHORCHIOSIS

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Bithynia funiculata snail antigens were partially purified by Sephacryl S-200 gel filtration chromatog-

raphy. Four fractions of *B. funiculata* snail antigens were obtained-fraction 1 (F1), fraction 2 (F2), fraction 3 (F3) and fraction 4 (F4), which F1 was chosen for the study since this is the most abundant and most reactive fraction. Levels of antibodies in sera of 85 patients with opisthorchiosis, 15 normal healthy

individuals and 72 patients with other helminthic infections were assayed against crude antigens from *O. viverrini* adult worms and the F1 fraction using the gelatin particle indirect agglutination test (GPAT). For both antigens, the mean reciprocal titer in the sera of opisthorchiasis patients was significantly higher than sera from patients with other helminthic infections and normal healthy individuals ($p < 0.0001$). In an attempt to search for another antigen in place of *O. viverrini* antigens for the serodiagnosis of opisthorchiasis, the sensitivity and specificity of the two antigens were compared. It was shown that

differences in the sensitivity and specificity were not evident. This study indicates that antigens from *O. viverrini* adult worms were the most suitable antigens for serodiagnosis of opisthorchiasis by GPAT despite being crude antigens. However, antigens from partially purified *B. funiculata* snails (F1) should prove to be useful for serodiagnosis of this disease since large amounts of antigens can be obtained with relative ease.

Published in: Japanese J Trop Med Hyg 1998; 26(1): 5-10.

PREVALENCE AND INTENSITY OF HELMINTHIASES IN PRIMARY SCHOOL CHILDREN IN AMPHOE MUANG, PRACHIN BURI

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A total of 761 stool samples from children of six primary schools in Amphoe Muang, Prachin Buri were examined for intestinal helminths using cellophane-covered thick smear technique. Two-

hundred and twenty of the 761 children (28.9%) were found to be infected with the parasites. Hookworm infection is the most prevalent (28.4%), followed by opisthorchiasis (1.0%), strongyloidiasis (0.9%), trichuriasis (0.5%), and enterobiasis (0.4%), all being light infections.

Published in: Mahidol J 1998; 5(1): 17-8.

EVALUATION OF LATRINE CONTAMINATION IN ASSOCIATION WITH SOIL-TRANSMITTED HELMINTHIC INFECTION IN THE ENDEMIC COMMUNITY OF SOUTH THAILAND

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This study was conducted in Muang District Nakhon Si Thammarat Province from June 1996 to June 1997 for the purpose of evaluating the association between latrine contamination and soil-transmitted helminthic (STH) infections among household inhabitants. Utilizing the floatation methods, soil samples collected around latrines of 115 households were examined. One hundred and twenty-nine persons from 23 latrine negative households were examined for the presence of STH eggs in their feces by Kato-Katz method. Fecal examination was performed every three months and all infected persons were treated with mebendazole 100 mg twice daily for 3 consecutive days following each examination. The prevalence of STH in the latrine-positive

households was 73.7% at the beginning and 18.6% at the end of the study; in the latrine-negative households, it was 37.3% and 9.6% respectively. The infection rates in the latrine-positive group were about double the rates in the latrine-negative group; the difference was significant during the periods June and September 1996 and June 1997, but there was no difference during December 1996 and March 1997 which is the heavy rain season in this region. The study revealed that the hookworm infection rate reaches its peak during the heavy rain period among both latrine-negative and latrine-positive household members. These results suggest that during the dry season, contaminated latrines are the main source of infection, but the latrine content were disseminated by rain water throughout the community and the whole population became equally susceptible to the parasites infective stages.

Published in: J Trop Med Parasitol 1998; 21(1): 1-7.

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CURRENT RESEARCH ACTIVITIES

The research conducted in the Department of Medical Entomology involves both basic and applied knowledge applicable in controlling vectors of tropical diseases especially mosquito-borne diseases. Other insects and arthropods of medical importance such as house flies, sand flies, cockroaches, ticks and mites are also studied in various aspects.

Laboratory colonies of different strains of mosquito vector species of *Anopheles*, *Aedes*, *Culex*, and *Mansonia* are continuously maintained in the



insectarium for further uses. The filarial parasite, *Brugia pahangi*, is also maintained in the reservoir host.

The study on biology and ecology of mosquito vectors of malaria at Am Phur Suan Pung, Ratchaburi Province, i.e. *Anopheles minimus*, *An. maculatus*, *An. dirus*, and *An. aconitus* are conducted. The infection rate of malaria parasites, vector capability, and susceptibility to insecticides are also studied in each mosquito species. The baseline data obtained from this study will be used in the



study on their species complex and malaria control in the study area.

The vectors of Japanese encephalitis, *Culex tritaeniorhynchus*, *Cx. gelidus*, *Cx. fuscocephala*, and that of dengue haemorrhagic fever, *Aedes aegypti* and *Ae. albopictus*, are studied for their ecology and vector potential. The species complex of these mosquitoes from various locations in Thailand are also investigated by enzymatic studies.

Effective controls on mosquito vectors are directed both in laboratory and field trials. The efficacy of chemical insecticides, insect growth regulator and chemosterilant are evaluated against the

vectors. The studies on the development of insect resistance to these chemicals are also conducted. Non-polluted control methods such as the use of biological insecticides, and medicinal plants are tested.



The use of insecticide impregnated bed nets and blankets (permethrin, etofenprox), especially for malaria control, has been introduced. The selection of mosquito resistance to

permethrin-and etofenprox-impregnated bed nets is conducting in the laboratory to study the impact on mosquito vectors.

Moreover, the Department of Medical Entomology acts as a reference center on mosquito vectors in Thailand through the establishment of the Mosquito Museum Annex and a project on computer aided management and service of biological museums. The Department also provides academic consultation especially on mosquito-borne diseases and their control measures, and also services on detection of filarial parasites, identification of mosquitoes and other medically important insects and arthropods.

AWARD

The research project on "*Anopheles minimus* Species A complex in Thailand and their impact on malaria control" by Sucharit S, Komalamisra N, Surathinth K, Apiwathnasorn C (*J Trop Med Parasitol* 1997;20(2):57-67) was awarded as the Best Research Work 1998 by the National Research Council of Thailand.



ABSTRACTS

THANAKA (*LIMONIA ACIDISSIMA*) AND DEET (DI-METHYL BENZAMIDE) MIXTURE AS A MOSQUITO REPELLENT FOR USE BY KAREN WOMEN

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The prevention and treatment of drug-resistant malaria is becoming increasingly difficult. On the Thai-Myanmar border multi-drug resistant strains of falciparum malaria are increasing and, because the malaria vector *Anopheles* bite outdoors during early evening, insecticide house-spraying or impregnated bednets provide only limited protection. Therefore, the protective efficacy of repellent formulations containing di-methyl benzamide (deet) and permethrin against local vectors was estimated, when applied to the skin, and their acceptability amongst pregnant Karen women who are at relatively high risk from malaria was assessed. Human landing catches of mosquitoes showed that almost complete protection was achieved using different formulations of 20% deet and 0.5% permethrin for up to 6 h. All-night

collections from human subjects indicated that this repellent combination reduced exposure to malaria parasites by at least 65 and 85% for those transmitted by *Anopheles minimus* and *An. maculatus*, respectively, the two principal vectors in this area. Pregnant women in the camps preferred repellents which were mixed with thanaka, a root paste made from pulp of the wood apple tree, *Limonium acidissimum*, used locally as a cosmetic. Apart from a temporary warming sensation where repellent thanaka was applied to the skin, the repellents were well tolerated. An intervention trial is currently in progress to determine whether deet mixed with thanaka can protect pregnant women against malaria in this part of the world. Bioassays using a laboratory strain of *Aedes aegypti* demonstrated that thanaka is itself slightly repellent at high dosages and the mixture with deet provides protection for over 10 h. This treatment would therefore also provide some personal protection against dengue, which is increasing locally, transmitted by *Ae. aegypti* and *Ae. albopictus* biting during the daytime.

Published in: *Med Vet Entomol* 1998;12:295-301.

COMPARATIVE SUSCEPTIBILITY OF TWO FORMS OF *ANOPHELES SINENSIS* WIEDEMANN 1828 (DIPTERA : CULICIDAE) TO INFECTION WITH *PLASMODIUM FALCIPARUM*, *P. VIVAX*, *P. YOELII* AND THE DETERMINATION OF MISLEADING FACTOR FOR SPOOROZOITE IDENTIFICATION

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Two karyotypic forms of laboratory raised *Anopheles sinensis*, i.e. Form A (XY1) and Form B (XY2), were experimentally infected with various indigenous strains of *Plasmodium falciparum* and *P. vivax* using an artificial membrane feeding technique, and a rodent malaria, *P. yoelii*, using a direct feeding technic and dissected 7-9 days and 10-15 days after

feeding for oocyst and sporozoite rates, respectively. The results revealed that two forms of *An. sinensis* were refractory vectors for *P. falciparum* and *P. yoelii* since 0% of oocyst and sporozoite rates were obtained, but poor vectors for *P. vivax* since 0.00-85.71% and 0.00-5.88% of oocyst and sporozoite rates were recovered. The sporozoite-like crystal found in the median lobe of the salivary gland of *An. sinensis* which could be a misleading factor in identification of true sporozoites in the salivary glands is reported for the first time.

Published in : *Southeast Asian J Trop Med Public Health* 1998;29:159-67.

IMPACTS OF PERMETHRIN-IMPREGNATED BEDNETS ON ANOPHELES DIRUS

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According to the introduction of permethrin-impregnated bednets for malaria vector control, it is of interest to study vector resistance to permethrin since the selection of mosquito with the insecticide may occur in the nature. It is possible that the selection can affect vectors susceptibility to permethrin, feeding activity, fecundity, longevity and some morphological character. The permethrin susceptibility was studied in *Anopheles dirus* in laboratory by exposing the mosquitoes to the impregnated bednet. It showed a LC50 of 0.011 gm/m² for the P generation. Then a dose of 0.00625 gm/m² was used for selection in consecutive generations. With this concentration, 42.6% mortality was obtained and the number of survivors was sufficient for further study. However, the changes in insecticide susceptibility, morphology and other activities were not found in the F2 generation. The selection are in progress.



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CURRENT RESEARCH ACTIVITIES

The current research activities of the Department involve studies on biology, molecular biology and immunology of infectious agents/diseases particularly those causing problems in tropical areas with the ultimate aims at 1) development of the simple, rapid, specific, sensitive, cost-effective and practical diagnostic methods for use in the remote areas and for self-reliance of the country; 2) identification of potential protective antigens for the vaccine development; 3) understanding of the host responses and immunity and 4) acquisition and acquaintance to modern technology, eg. genetic engineering. Further details are given below:

Sodium dodecyl sulphate-polyacrylamide gel electrophoresis and immunoblotting have been used for identification of the specific antigens of various pathogens including *Opisthorchis viverrini*, *Paragonimus heterotremus*, *Trichinella spiralis*, *Strongyloides stercoralis*, *Gnathostoma spinigerum*, *Entamoeba histolytica*, *Plasmodium falciparum* and *P. vivax*, *Leptospira*, etc. Successful identifications of the specific antigens of these pathogens lead to the development of a more simple, rapid, sensitive and

specific immunodiagnostic methods for patients suffering from the diseases. For example, in human gnathostomiasis, a 24 kDa specific diagnostic component of *G. spinigerum* was further purified from the crude extract by column chromatography, anion exchange chromatography and isoelectric focussing and used in the enzyme-linked immunosorbent assay (ELISA) which gave 100% sensitivity and specificity for the disease. Attempts to produce the antigen either by affinity chromatographies, recombinant DNA technology or anti-idiotypic antibodies are underway.

Specific polyclonal and/or monoclonal antibodies against various parasitic helminths, protozoa, bacteria and their toxins and viruses including *Opisthorchis viverrini*, *Paragonimus heterotremus*, *Schistosoma mekongi*, *Trichinella spiralis*, *Gnathostoma spinigerum*, *Entamoeba histolytica*, *Plasmodium falciparum* and *P. vivax*; bacteria or their toxins including *Bordetella pertussis*, *Vibrio cholerae* O:1 and O:139, *Salmonella*, enterotoxigenic *E. coli*, enterohaemorrhagic *E. coli*, Verocytotoxins (VT-I and VT-II), *Listeria*, *Shigella*, *Rickettsia*, Japanese encephalitis

litis virus and respiratory syncytial virus have been produced in our laboratory for detection of the pathogens/diagnosis of diseases caused by them in clinical specimens and/or contaminated food and environmental samples. The monoclonal antibodies produced against the whole cells, somatic and/or excretory-secretory antigens of these pathogens have been tested for their analytical as well as diagnostic sensitivities and specificities. Development of the simple, specific, sensitive, rapid and cost-effective methods which are practical for use in the remote areas such as the conventional or dot-blot ELISA, immuno-colloidal gold and/or the dip-stick techniques as well as the use of immunomagnetic separation for higher sensitivity of detection of the pathogens are being carried out.

Additional work includes the application of DNA technology, *e.g.* development of DNA probes, PCR technology as well as other modern technology for the detections of several pathogens, *e.g.* *Paragonimus*, *Entamoeba*, *Plasmodium*, *Salmonella*, *Vibrio cholerae*, *Bordetella pertussis*, dengue and respiratory syncytial viruses, etc. from the clinical specimens and/or foods. DNA manipulations have been used for genetical analyses of various pathogens, *eg.* *Trichinella*, *Vibrio cholerae*.

Protective activities of various antigens such as fimbriae, hemagglutinin, procholeraenoid and lipopolysaccharide of a bacterial pathogen, *Vibrio cholerae*, associated with liposome adjuvant are also studied. It was shown that the oral immunization by the combination of these components provide strong local immunity against the bacterium. Trials of the oral cholera vaccines both against *V. cholerae* O:1 and O:139 infections for tolerability, immunogenicity and protection have been carried out in volunteers.

Studies on *E. histolytica* revealed that its genome organization consisted of at least a circular supercoiled-like and a linear DNA molecules that behaved like the yeast chromosomes. There was no evidence of chromosome rearrangement in association with drug resistance. The mechanism of metronidazole resistance in *E. histolytica* involved a marked increase in superoxide dismutase, whereas pyruvate:ferredoxin oxidoreductase was not decreased. A monoclonal antibody specific against *E. histolytica* conjugated with red phycoerythrin (R-PE) was used successfully for the detection of the trophozoites in human fecal samples. An immunotoxin (IT) consisting of a monoclonal antibody against pyruvate ferredoxin oxidoreductase of *E. histolytica* (EhPFORMAb) and

the toxic moiety of the plant toxin ricin A (RA) is potent in inhibiting proliferation of the organism, therefore, the IT would be one approach for future immunotherapy for invasive amoebiasis.

Other areas of research activities on bacterial infections include diarrhea caused by *Campylobacter jejuni* and *C. coli*, anaerobic bacterial infections, non-gonococcal urethritis and heparinase detection in facultative and anaerobic bacteria. Development of better diagnostic methods have also been carried out. Short cut for biochemical tests of non-fermenting gram negative bacteria has been studied for a simple and reliable diagnosis of bacterial pathogens found in the patients. Antimicrobial susceptibility test was done by modified Kirby-Bauer's method to suit the small number of pathogens isolated each day. Surveillance of nosocomial infections for the control of hospital infections is also being investigated.

Resistance to methicillin among the staphylococci and penicillin resistance of the pneumococci are being studied using E-TEST. The test is also used for study of some antifungal susceptibility of yeasts isolated from the patients. This should be useful for the hospital's patient management in the future.

Parts of these research works are being carried out in collaborations with various international institutions, *i.e.* the Department of Microbiology, Institute of Basic Medical Science, University of Tsukuba, Tsukuba, Japan; the Department of Microbiology and Immunology, Faculty of Medicine, Monash Australian University, Melbourne, the Department of Microbiology and Immunology, Faculty of Medicine, the University of Adelaide, Adelaide, Australia; Institute for Clinical Research in Tropical Medicine, Hanoi, Vietnam, the Research Institute, International Medical Center of Japan, Tokyo, Queensland Institute of Medical Research, the University of Queensland, Australia, the University of Vienna and the University of Innsbruck, Austria, etc.

ABSTRACTS

DETECTION OF *PARAGONIMUS HETEROTREMUS* IN EXPERIMENTALLY INFECTED CAT FECES BY ANTIGEN CAPTURE-ELISA AND BY DNA HYBRIDIZATION

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An antigen capture enzyme-linked immunosorbent assay (antigen capture-ELISA) and DNA hybridization technique were developed and evaluated for their application in the detection of *Paragonimus heterotremus* infection in experimentally infected cats. An IgG fraction prepared from serum of a rabbit immunized with *P. heterotremus* excretory-secretory (ES) products was used as the capture antibody. An IgG1 monoclonal antibody specific to the 22- and

31.5-kDa ES products of *P. heterotremus* was used as the antigen probe. As little as 0.24 ng of the ES products could be detected by this technique. A specific *P. heterotremus* DNA probe derived from the *P. heterotremus* genomic DNA library containing 1,500 base pairs was used in a dot-blot hybridization assay for the detection of parasite DNA. The radioactively labeled probe could detect DNA released from as few as 2 *P. heterotremus* eggs. Both ELISA and DNA hybridization were found to have 100% specificity, with sensitivities of 73.7% and 100%, respectively.

This study was supported by the National Research Council of Thailand.

Published in : J Parasitol 1997; 83: 1075-8.

A DOT-ELISA TEST USING MONOCLONAL ANTIBODY-PURIFIED ANTIGENS FOR THE DIAGNOSIS OF PARAGONIMIASIS CAUSED BY *PARAGONIMUS HETEROTREMUS*

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A dot enzyme-linked immunosorbent assay (Dot-ELISA) using antigens purified by monoclonal antibody-affinity chromatography was developed for detecting antibodies to *Paragonimus heterotremus* in

four groups of subjects. They consisted of 30 patients with *P. heterotremus* infection, 93 patients with other parasite infections, 18 patients with pulmonary tuberculosis and 30 normal, healthy controls. Sensitivity, specificity, as well as positive and negative predictive values of the test were 100, 97, 88, and 100%, respectively.

This study was supported by the National Research Council of Thailand.

Published in : Southeast Asian J Trop Med Public Health 1997; 28: 621-3.

MONOCLONAL ANTIBODIES TO *PARAGONIMUS HETEROTREMUS* AND THEIR POTENTIAL FOR DIAGNOSIS OF PARAGONIMIASIS

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Monoclonal antibodies (Mabs) specific to the lung fluke (*Paragonimus heterotremus*) were produced against the soluble metabolic products (excretory-secretory antigen). Three hybrids secreting Mabs specific for *P. heterotremus* antigens were identified by an indirect enzyme-linked immunosorbent assay (ELISA) against a panel of homologous and 24 heterologous parasite antigens and *Mycobacterium tuberculosis*. Of the three specific clones, clone 10F2, which was IgG1 producing and which gave immune

complex bands with 31.5-kDa and 22-kDa polypeptides by gel electrophoresis and immunoblotting, was selected for further characterization and evaluation of its possible diagnostic potential. The result obtained from an indirect immunofluorescent antibody test suggested that MAb 10F2 reacted with mucosa and contents of the worm's intestine. The antibody could be readily used to prepare an affinity-purified antigen for use in an indirect ELISA that was highly sensitive and specific for the detection of circulating antibody in sera of paragonimiasis patients.

This study was supported by the National Research Council of Thailand.

Published in : Am J Trop Med Hyg 1997; 56: 413-7.

IMMUNODIAGNOSIS OF SOME HELMINTHIC INFECTIONS: FROM RESEARCH EXPERIENCE TO PRACTICAL APPLICATION

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Advantages and disadvantages of several means for diagnosis of parasitic infection are reviewed. Experiences in carrying out a research aiming at the development of a specific immunodiagnostic method are given.

Published in : J Trop Med Parasitol 1997; 20: 1-10.

SIMPLIFIED, RAPID DIAGNOSIS OF RESPIRATORY SYNCYTIAL VIRUS FROM CLINICAL SPECIMENS

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DOT-ELISA was compared with RT-PCR and tissue culture to detect RSV from nasopharyngeal aspirates. DOT-ELISA had diagnostic sensitivity and specificity of 65.62% and 93.92%, respectively. The

results indicate that DOT-ELISA can be used for screening detection of RSV from clinical specimens and is suitable for small laboratories in the provincial areas of developing countries.

Published in : Asian Pac J Allergy Immunol 1997; 15:99-103.

PARASITES ELICITED CROSS-REACTING ANTIBODIES TO *OPISTHORCHIS VIVERRINI*

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Two batches of crude antigens extracted from adult *Opisthorchis viverrini* worms were compared. One was derived from adult worms harvested from the livers of laboratory infected hamsters and another was obtained from worms sedimented from the faeces of opisthorchiasis patients following treatment with Praziquantel. SDS-PAGE and Coomassie brilliant blue staining revealed that the two preparations had similar protein components of which the predominant ones were the 17-18 kDa doublet. The antigens were used in an indirect ELISA for the detection of antibodies against *O. viverrini* in the sera of four groups of patients, ie. patients with opisthorchiasis (group 1), patients with mixed infections of *O. viverrini* and other parasites (group 2), patients with other parasitic

infections (group 3), and normal-healthy, parasite-free individuals (group 4). The sensitivity of the test was high (91-92%), regardless of the batch of the antigen used. However, its specificity was relatively low (70-80%). Cross-reaction was observed with patients infected with *Paragonimus heterotremus*, *Schistosoma* spp.; *Taenia* spp.; *Trichinella spiralis*; *Strongyloides stercoralis*; hookworms; *Plasmodium* spp.; hookworms and *Plasmodium* spp.; *S. stercoralis*, *Blastocystis hominis* and yeast; and hookworms, *Ascaris lumbricoides*, *Trichuris trichiura* and *P. falciparum*. Western blot analysis revealed that sera of patients infected with these heterologous organisms contained antibodies reactive to *O. viverrini* antigenic components ranging from Mr. 15.5 to 144.

Published in : *Asian Pac J Allergy Immunol* 1997; 15:115-22.

INDIRECT HAEMAGGLUTINATION TEST USING MONOCLONAL ANTIBODY-AFFINITY PURIFIED ANTIGENS FOR DIAGNOSIS OF HUMAN PARAGONIMIASIS DUE TO *PARAGONIMUS HETEROTREMUS*

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An indirect haemagglutination test (IHA) using antigens purified by monoclonal antibody-affinity chromatography was developed for the diagnosis of

human paragonimiasis caused by *Paragonimus heterotremus*. Sera from patients with paragonimiasis (n = 30) were evaluated, along with sera from other parasitic infections (n = 92), pulmonary tuberculosis (n = 18) and healthy controls (n = 30). The sensitivity, specificity as well as positive and negative predictive values of the IHA, calculated at the prevalence of disease at 17.6%, were all 100%.

This study was supported by the National Research Council of Thailand.

Published in : *Trop Med Internat Health* 1998;3:57-9.

RAPID DETECTION OF CHOLERA CAUSED BY *VIBRIO CHOLERAE* O139

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Hybridomas secreting specific monoclonal antibodies (MAbs) to *Vibrio cholerae* serogroup O139 were produced. Six monoclonal (hybridomas) secreting MAbs specific only to lipopolysaccharide of *V. cholerae* O139 strains and which did not cross-react to 137 strains of other enteric microorganisms were obtained. These clones were designated 12F5-G11, 12F5-G2, 15F5-H5, 5B9-F8, 14C9-D2, and 6D2-

D8. The immunoglobulin (Ig) heavy chain isotypes secreted by these clones were IgG2b, IgG2b, IgG2b, IgM, IgG2b, and IgG3, respectively. Clone 12F5-G11 was selected for mass production of MAb, which was used as a detection reagent in the antigen detection assay for diagnosis of cholera caused by *V. cholerae* O139, and this assay was compared to the conventional bacterial isolation method. Five batches of rectal swab cultures in alkaline-peptone water were collected from 6,497 patients with watery diarrhea. These were 6,310 patients admitted to Bamrasnarasura Infectious Diseases Hospital, 16 patients from Krung Thon Hospital, 78 patients from Bangkok Children's Hospital, 19 patients from Karen refugee camps, and 74 Indian patients from the National Institute of Cholera and Enteric Diseases, Calcutta, India. The *V. cholerae* O139 isolations from the rectal swab cultures and the antigen detection assay (i.e., the MAb-based dot-blot ELISA) were performed by different persons

of different laboratories, and the results were revealed after all specimens had been tested. Of the 6,497 samples tested, the dot-blot ELISA correctly identified 42 of 42 *V. cholerae* O139-positive samples and gave a result of positive for three samples which were culture negative for *V. cholerae* O139. The diagnostic sensitivity, specificity, and efficacy of the dot-blot ELISA were 100, 99.95, and 99.26%, respectively. The ELISA is easy to perform and relatively inexpensive. It can test multiple samples at a single time, does not require special equipment, and does not produce great quantities of contaminated waste. Most of all, it reduces the diagnostic time from at least 2 days for the bacterial isolation to less than 90 min. The assay is recommended as a rapid screening test of cholera cases caused by *V. cholerae* O139.

Published in : J Clin Microbiol 1998 (in press).

IMMUNOGENICITY OF LIPOSOME-ASSOCIATED AND REFINED ANTIGEN ORAL CHOLERA VACCINES IN THAI VOLUNTEERS

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A mixture of *Vibrio cholerae* antigens made up of crude fimbrial extract, lipopolysaccharide and procholeraenoid was administered orally to Thai volunteers either as free antigen or associated with liposomes. All vaccinees and controls were administered in three doses given at 14 day intervals. Nine volunteers received liposome-associated vaccine and seven received free vaccine. Liposomes without

antigens were given to eight volunteers and seven volunteers received 5% NaHCO₃ solution alone. Both vaccines had 100% immunogenicity as determined by serum vibriocidal antibody responses. Liposomes were shown by indirect ELISA to localize the immune response against lipopolysaccharide and fimbriae to the intestinal mucosa. Vaccinees given liposome-associated antigens had a higher rate of antigen-specific response than did individuals who had received free antigens. The vaccines induced intestinal antibodies of IgM and/or IgA isotypes, but not IgG antibody.

Published in : Vaccine 1998;16:678-84.

PCR DETECTION OF VIBRIO CHOLERAЕ SEROGROUPS O:1 AND O:139

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Cholera is a serious epidemic disease that has killed millions of people all over the world. In the past, the cause of cholera was the bacterium named

Vibrio cholerae strain O1, while *V. cholerae* non-O1 are associated with sporadic cases of diarrhea and extraintestinal infections. Recently, there was an emergence of cholera caused by *V. cholerae* non-O1 strain O139 synonym Bengal which is similar to *V. cholerae* O1 biotype El Tor. The clinical features of cholera produced by both strains are essentially identical. The conventional method for detection of

V. cholerae is by culture method and further identification with O1 and O139 specific antisera. This method is time consuming, expensive and lacks the necessary sensitivity.

In this study a sensitive and specific method to identify *V. cholerae* O1 and O139 by using the multiplex polymerase chain reaction was developed. The primers were designed from the cholera toxin and the O-antigen genes of *V. cholerae* O139. The optimum condition for multiplex PCR was 200 μ M of each dNTP, 15 mM MgCl₂ in PCR buffer pH 8.3, 0.05 μ M of each primer from *rfbQRS*, 0.5 μ M of each primer from *ctxAB*, and 1 U of Taq DNA polymerase. The amplification reaction was carried out for 40 cycles, each cycle consisted of denaturation at 90°C for 1 min, annealing at 50°C for 1 min and extension at 72°C for 1 min. The sensitivity of this PCR protocol was 10 pg of purified DNA, 10³ bacterial cells from pure culture and 2.5 x 10³ cells from artificially contaminated stool. The specificity of the multiplex PCR was also examined and no cross reaction was found with other 22 gram negative bacteria. However,

this method cannot distinguish *V. cholerae* O1 and O139 in mixed infection. It is suggested that this problem may be solved by designing the third set of primers of the specific gene that encodes O139 LPS or *V. cholerae* non-O1 capsule.

The multiplex PCR has also been used to detect *V. cholerae* in watery stool samples in comparison with the conventional culture method. All positive cases by PCR were *V. cholerae* O1. Comparative study on the detection of *V. cholerae* by microbiological method and multiplex PCR were performed using neat stools and Chelex R100 treated stools of 115 diarrheic patients as templates. It was found that the diagnostic sensitivity, specificity, efficacy, positive and negative predictive values of detection of the multiplex PCR were 64.28, 99.01, 94.78, 90.0 and 95.24%, respectively. The values were 100, 97.03, 97.39, 82.35 and 100%, respectively when APW enriched stools were used as templates. The study suggests that enriched stool with APW is the best template to detect *V. cholerae* by multiplex PCR.

ANTIFUNGAL SUSCEPTIBILITY TESTING OF PATHOGENIC YEAST WITH THE E-TEST

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The E-Test for 5 antifungal agents were used for detecting the minimum inhibitory concentrations (MIC) of pathogenic yeasts isolated from the patients in the Bangkok Hospital for Tropical Medicine. Fifty-five strains of yeasts including 29 *Cryptococcus neoformans*, 10 *Candida albicans* and 16 other yeasts were collected during 1995-1998.

All 29 *Cryptococcus neoformans* were sensitive to Amphotericin (MIC between 0.05-1 microgram/ml), Ketoconazole (MIC < 0.5 microgram/ml) and Itraconazole (MIC < 0.5-2 microgram/ml). Ten strains were resistant to Fluconazole with 2 of them were highly resistant (MIC > 256 microgram/ml) and 8 were resistant with the MIC > 8 - 32 microgram/ml. The susceptible strains were among the 3 strains that were inhibited by the concentration below 0.5 microgram/ml and 6 of which the MIC between 2 and 4 microgram/ml. The rest were 10 strains that the MIC were above 4 but not more than 8 microgram/ml.

No resistant *Candida albicans* for Amphotericin B but 40% resisted Ketoconazole and 70% resisted Fluconazole as well as Itraconazole.

Other yeasts found to have resistance to Amphotericin B (1/16) and the azole group (Ketoconazole and Itraconazole 3/16, Fluconazole 4/16).

The MIC of Flucytosine for all but one yeast tested were > 32 microgram/ml, possibly because the medium used was not suitable for testing this drug. The control strains were also read > 32 microgram/ml for Flucytosine (while the expected control range was only 0.125-0.5 for *C. parapsilosis* and > 32 for *C. kruezi*).

This study was supported by a research grant from Mahidol University.

PRODUCTION AND CHARACTERIZATION OF MONOCLONAL ANTIBODIES SPECIFIC TO VITELLIN AND VITELLOGENIN OF THE TIGER PRAWN, *PENAEUS MONODON*

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Monoclonal antibodies (MAbs) specific to vitellin and vitellogenin of *Penaeus monodon* were produced by immunization of Balb/C mice with a crude extract from the mature ovary. After fusion of the spleen cells from an immunized mouse with P3x myeloma, the hybridomas were selected by indirect immunoperoxidase ELISA against the ovarian extract, followed by dot-blotting against native and denatured proteins from ovarian extract, female haemolymph

and male haemolymph. Four hybridoma clones producing antibodies (PMV-11, 15, 22 and 64) were identified, They can bind to the protein in the ovarian extract and in the female haemolymph but not in the male haemolymph. One of them (PMV-64) can bind to both native and denatured proteins. Western blot analysis of ovarian extract separated by PAGE, all four monoclonal antibodies bind to the same lipoglycoprotein band. Western blot analysis of proteins separated by SDS-PAGE, PMV-64 binds to 80 and 83 kDa proteins in ovarian extract and 83 and 170 kDa proteins on the female haemolymph, respectively. All four monoclonal antibodies belong to IgG1 sub-isotype.

Published in : Invertebrate Reproduction and Development 1998 (in press).

ACANTHAMOEBA PLEUROPNEUMONITIS: THE FIRST TWO REPORTED CASES FROM THAILAND

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Acanthamoeba pleuropneumonitis is rare. Early reports of this entity were only as a part of the hematogenous dissemination of granulomatous amoebic encephalitis/meningoencephalitis (GAE/GAM). It is postulated that the portal of entry of the organism is the lung wherefrom the infection spreads to the central nervous system. However, primary lung involvement alone by this organism has never been reported. The purpose of this study is to present two cases of primary *Acanthamoeba* pleuropneumonitis in previously healthy Thai patients without any other organs involvement. Both patients acquired their infections by aspirating contaminated warm freshwater while intoxicated and fallen into a canal in one and swimming in a pond in the other. *Acanthamoeba* pleuropneumonitis starts as an acute bilateral lower

lobes airspace disease which directly extends to the pleurae. The incubation period is approximately 6-8 weeks after contact with the contaminated warm freshwater. It tends to produce pleural effusions bilaterally and rapidly. The pleural fluid is an exudate with a high number of leukocytes, predominantly polymorphonuclear type. It has an elevated protein but normal glucose and a very high LDH5 level. The fluid tends to loculate if left untreated. The organisms trophozoites can be easily identified in the pleural fluid and sputum, making the diagnosis rather simple when the disease is suspected. The response to treatment with intravenous amphotericin B is rather dramatic. Maintenance is not needed like in HIV patients. To our knowledge, this is the first two cases of isolated *Acanthamoeba* pleuropneumonitis in apparently healthy patients. This makes the hypothesis of the lung being the portal of entry of the organism more credible.

Presented at : the Joint International Tropical Medicine Meeting, 22 August 1998, Faculty of Tropical Medicine, Mahidol University and 29th World Conference of IUATLD/UICTMR Global Congress on Lung Health, 23-26 November 1998, Shangri-La Hotel, Bangkok, Thailand.

RESEARCH ON AMOEBOSIS: EXPERIENCES FROM THE THAI-AUSTRIAN AND AUSTRALIAN COLLABORATION

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During the past few years, Faculty of Tropical Medicine, Mahidol University has been collaborating with the University of Vienna, the University of Innsbruck and Queensland Institute of Medical Research (QIMR) in the fields of immunology and molecular biology of *Entamoeba histolytica* and amoebosis it causes. Collaboration between Mahidol University and the University of Vienna together with QIMR involved cloning and expression of genes encoding for the antigens of *E. histolytica*. A mouse monoclonal antibody, Eh208C2-2 MAb, raised against whole cell antigens of *E. histolytica* trophozoites of the pathogenic strain HM-1:IMSS and polyclonal antisera (PABs) against membrane antigens of *E. histolytica* trophozoites of strain HTH-56:MUTM were screened against a cDNA library of the pathogenic strain, SFL3. The MAb detected many phage plaques expressing an *E. histolytica* protein. The DNA sequence encoding the protein was approximately 55% identical, over 1,100bp, to other organisms in GenBank such as *Trichomonas vaginalis* pyruvate: ferredoxin oxidoreductase (PFOR) and pyruvate: flavodoxin oxidoreductase from *Klebsiella pneumoniae*, *Anabaena variabilis* and *Enterobacter agglomerans*. Two of seven clones detected by mouse PABs also encoded this protein. Two others encoded *Entamoeba* Hsp70, another encoded *Entamoeba* alkyl-hydroperoxide reductase and the remaining two were unidentified sequences. There is only minor variation from strain to strain of *E. histolytica* since differences at the DNA level between our sequence (*E. histolytica* PFOR GenBank accession number L46793) and other two known sequences vary by only

2% (U30149) and 7% (Z50193) over approximately 1 kb, respectively. From our previous study of IT consisting of the IgG fraction of Eh208C2-2 MAb and the toxic moiety of the plant toxin ricin, Ricin A (RA), we showed that the heterobifunctionally cross-SPDP-linked IT was potent at inhibiting proliferation of *E. histolytica* trophozoites *in vitro*. Since Eh208C2-2 MAb recognized an epitope on *E. histolytica* pyruvate: ferredoxin oxidoreductase (PFOR), therefore, our IT would be one approach for future immunotherapeutic targets for invasive amoebosis.

Research on the role of complement in the pathogenesis of amoebosis was undertaken at the Institute of Hygiene, the University of Innsbruck. It was shown that *E. histolytica* induced marked *in vivo* activation of complement. Levels of fluid phase of terminal complement component (TCC) were significantly increased in sera from patients with amoebic liver abscesses than those infected with parasites other than *E. histolytica* and normal healthy controls. Collaboration is now extended to Harvard School of Public Health, Harvard University, Boston, USA for studying in the new trend of cell biology of *E. histolytica* by using anti-PFOR monoclonal antibody. More extensive collaboration between universities and/or institutes would contribute to the progress and development for global parasitic diseases control in the future.

Presented at : IXth International Congress of Parasitology during 24-28 August 1998, Makuhari Messe, Chiba, Japan and at the Workshop on International Research Collaboration for Parasitic Diseases Control: Voices from the Pacific Rim, The 33th US-Japan Joint Conference on Parasitic Diseases.

PRODUCTION OF MONOCLONAL ANTIBODIES SPECIFIC TO NATIVE AND DENATURED VITELLIN OF THE TIGER PRAWN *PENAEUS MONODON*

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Monoclonal antibodies (MAbs) specific to native and denatured vitellin of *Penaeus monodon* were generated by immunization Balb/C mice with a crude extract from mature ovary. After fusion of the spleen cells from an immunized mouse with P3x-63-Ag8 myeloma, the hybridomas were selected by indirect immunoperoxidase ELISA against the ovarian extract,

followed by dot-Blotting against native and denatured proteins from ovarian extract, female haemolymph and male haemolymph. Four hybridoma clones producing antibodies (PMV-11, 15, 22 and 64) were identified. They can bind to the protein in the ovarian extract and in the female haemolymph but not in the male haemolymph. One of them (PMV- 64) can bind to both native and denatured proteins. Western Blot analysis of ovarian extract separated by PAGE, all four monoclonal antibodies bind to the same

lipoglycoprotein band. Western Blot analysis of proteins separated by SDS-PAGE, PMV-64 binds to 80 and 83 Kd proteins in ovarian extract and 83 and 170 Kd protein on the female haemolymph, respectively. All four monoclonal antibodies belong to IgG1 sub-isotype.

Presented at : the 24th Conference of the Science Society of Thailand, Queen Sirikit Convention Hall, Bangkok, 18-21 October 1998.

DNA VACCINES AGAINST MALARIA : STRATEGY AND PROGRESS

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The magnitude of the mortality and morbidity produced by malaria and the problems associated with the current methods of malaria control have led to renewed interest in malaria vaccine development. Vaccines are aimed at inducing immune responses that disrupt the complex life cycle of malaria parasite at one or more stages. From previous studies, it is believed that complete protection against malaria requires a multivalent vaccine that induces protective CD4⁺ T cell-dependent antibody responses and CD8⁺ cytotoxic T lymphocyte responses. In a variety of experimental systems, DNA vaccines offer one of the promising approaches since DNA vaccines have been

shown not only to induce such potent immune responses, but also to offer many advantages in terms of ease of construction, testing, production and providing long term immunity after a single immunization. In malaria, initial studies on the protective efficacy of an anti-malarial DNA vaccine have been demonstrated in the rodent malaria parasite, *Plasmodium yoelii*. Malaria DNA vaccine against *P. falciparum* is being designed to induce immune responses against hepatic stage antigens. In parallel, a multi-gene vaccine designed to induce protective antibody and CD4⁺ T lymphocyte response against the erythrocytic stages of the parasite is also under evaluation.

Published in : Mahidol J 1997;4:87-91.

CHARACTERISTICS OF PLASMODIUM FALCIPARUM ISOLATES RESPONSIBLE FOR MALARIA INFECTION IN THAILAND

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The sequestration of parasitized red blood cells (PRBC) is one of the pathophysiological mechanisms that accounts for some of the effects of complicated *Plasmodium falciparum* malaria. Different host molecules such as ICAM-1, VCAM-1, E-selectin, CD36, thrombospondin and chondroitin-4-sulfate (CSA) have been identified as potential receptors of cytoadherence in different organs such as brain, lung placenta, kidney and heart.

The objective of this study was to identify different characteristics of plasmodial isolates responsible for malaria in Thai patients in order to

determine whose could be considered as markers for the severity of malaria infection.

69 Thai isolates (27 complicated and 42 uncomplicated malaria cases) were used. Rosetting, cytoadherence inhibition assays using human lung endothelial cells lines (HLEC) and *P. falciparum* chemosensitivity tests against 8 antimalarial drugs were performed.

Although the cytoadherence was observed in the two groups, our results show an association between the cytoadherence phenotype and the infection severity (p=0.05). PRBC from complicated malaria patients bound to HLEC via ICAM-1 (88%), CSA (83%), E-selectin (58%), VCAM-1 (40%) and CD36 (17%), suggesting that ICAM-1, CSA and E-selectin are the main receptors of cytoadherence. 70% of isolates showed the rosette

phenotype in two groups and no association was observed between this profile and the malaria severity. The isolates were resistant to chloroquine in two groups and to Halofantrine in the complicated group ($p=0.04$). Cytoadherence inhibition assays using antimalarial drugs show a variable efficiency on PRBC for Artemether >>>Halofantrine>>Quinine, but no significant difference was observed in two groups.

A multivariate analysis is ongoing to determine the interactions between these different profiles and characteristics.

Presented at : The Joint International Tropical Medicine Meeting, 22 August 1998, Faculty of Tropical Medicine, Mahidol University.

IMMUNOGENICITY AND PROTECTIVE ROLE OF THREE FORMULATIONS OF ORAL CHOLERA VACCINE

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Three formulations of oral cholera vaccine were compared with respect to their immunogenicity and protective in a rat ileal loop model. Eight-week-old Wistar rats were divided into five groups. The first group received orally vaccine A consisting of liposome-associated *V. cholerae* lipopolysaccharide, fimbriae and procholeraenoid, whereas the rats of groups 2 and 3 received orally vaccines B and C consisting of heat-killed fimbriated and non-fimbriated whole cell *V. cholerae*, respectively. Rats of groups 4 and 5 were controls that received orally liposomes alone and normal saline solution, respectively. It was found that vaccine A elicited stronger immune responses to all three *V. cholerae* antigens. The antibody responses were detected in both serum and intestinal lavage samples. Vaccine B elicited only modest serum and intestinal responses to *V. cholerae* fimbriae (anti-F). No detectable immune response was found in rats of group 3 immunized

with vaccine C. Rats immunized with vaccines A and B had a similar order of magnitude of numbers of vibrios adhered to their intestinal mucosa. These numbers were less than those associated with the intestinal tissues of control rats of groups 4 and 5 by about two orders of magnitude. Although without any detectable immune response, rats of group 3 that were immunized with vaccine showed some reduction in numbers of vibrios associated with their intestinal mucosa. The numbers of vibrios recovered from the intestinal segments of rats of all treatment groups were in the order group 1 = 2 < 4 = 5. Electron micrography also revealed patches of vibrio colonization on the mucosa of rats of groups 3, 4 and 5. These features were not found in the groups vaccinated with vaccines A and B. The inhibition of vibrio colonization afforded by the vaccines was biotype- and serotype non-specific. The results suggest that the heat-killed whole cell fimbriated *V. cholerae* may be an alternative vaccine preparation to the liposome-associated refined antigen vaccine at a lower cost.

Published in : Vaccine 1998;16:201-7.

ANTIGENIC DIVERSITY OF PLASMODIUM VIVAX AND THEIR GEOGRAPHIC DISTRIBUTION IN THAILAND

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Fifty eight monoclonal antibodies (MAbs) raised against the erythrocytic stages of *Plasmodium vivax* were selected for typing of 501 *P. vivax* isolates from

different geographic locations throughout Thailand. Based on their reactivities in the indirect fluorescent antibody test, these MAbs were classified into five groups: group I MAbs showing generalized staining of all blood stages; group II MAbs reacting with merozoites and their organelles; group III MAbs reacting with the surface membrane of merozoites; group V MAbs reacting with the surface membrane

of trophozoites and schizonts; and group VII MABs reacting with internal components of the parasites. Sixteen MABs reacted with more than 95% of the isolates; the epitopes recognized by these MABs were considered as being invariant. The remaining MABs reacted with 30-90% of the isolates, and the epitopes recognized by these MABs were regarded as being variable. The variant epitopes were associated with > 200-, 135-, and 100-kilodalton (kD) molecules of all blood stages, the 95-kD molecule on merozoite organelles, the 200-kD molecule on the surface of trophozoites and schizonts, and the 85-kD molecule of the parasite internal components. Antigenic diversity occurred among the *P. vivax* population in

the endemic areas of Thailand and was shown to vary from place to place and was highest in the area with the highest rate of transmission along the Burmese border in western Thailand and along the Kumpuchean border in eastern Thailand, including Trad (48.4%), Tak (41.7%), Chantaburi (36.5%), and Maehongsorn (36.4%). Demonstration of antigenic diversity of *P. vivax* parasites signals a note of caution in the development of vaccines for vivax malaria. The vaccines should be directed against protective, conserved and not against variant epitopes.

Published in : Southeast Asian J Trop Med Public Health 1998;29(3) (in press).

ANTIGENIC DISPARITY OF *PLASMODIUM VIVAX* CAUSING INITIAL SYMPTOMS AND CAUSING RELAPSE

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Relapse infections are an important obstacle to the successful treatment and control of *Plasmodium vivax* malaria, but little is known about the nature of the relapse. To provide insight into the antigenic disparity of the parasites causing initial clinical symptoms and causing relapse, a panel of 58 monoclonal antibodies (MABs) against erythrocytic stages of *Plasmodium vivax* was tested by indirect fluorescent antibody test in five relapse cases. The initial and relapse strains from three patients (R3, R4, and R5) exhibited similar IFA reactivity with all MABs tested, whereas the isolates from two relapse cases (R1 and R2) showed different patterns of reactivity and were seen only with 15 MABs. In case R1, different IFA reactivities were observed with 12 MABs, nine of which reacted with the initial (RPV261) but not the relapse (RPV393) isolates, whereas the other three MABs reacted only with the relapse isolates. With regards to the second relapse case (R2) in whom two relapses occurred, different IFA reactivities were demonstrated with seven MABs that reacted only with the initial

isolate (RPV 182) and with the isolate from the first relapse (RPV 240) but not with the isolate from the second relapse (RPV 300). The antibody responses from patients who developed primary clinical symptom and relapse were detected by Western immunoblotting. In cases R3, R4 and R5, there was no difference in the spectrum of antigens from initial and relapse sera recognized by the antibodies. In contrast, in cases R1 and R2, the molecules recognized by antibodies in initial and relapse sera were markedly altered. In case R1, the series of molecules of *P. vivax* antigens recognized by initial (RPV 261) and relapse (RPV 393) sera were 21, 25, 31, 39, 42, 61, 95, 115, 200, > 200 kD and 21, 24, 31, 35, 57, 75, 200, > 200 kD, respectively. In case R2, the initial serum (RPV 182) recognized *P. vivax* antigens with molecular weight of 23, 30, 52, 57, 68, 75, 85, 95, 115, and 195 kD while the first relapse (RPV 240) and the second relapse sera recognized *P. vivax* antigens with molecular weights of 23, 30, 52, 85, 95, 115 kD and 30, 57, 68, 75, 85, 195 kD, respectively.

Published in: Southeast Asian J Trop Med Public Health 1998;29(3) (in press).



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CURRENT RESEARCH ACTIVITIES

Department of Protozoology is one of the eleven departments within Faculty of Tropical Medicine, Mahidol University. It was one of the first five Department created at the beginning of the Faculty of Tropical Medicine since the year 1960. Its responsibilities are teaching, training, research and service in the field of medical protozoa.

1. Study on DNA replication enzymes of *Plasmodium falciparum* as new chemotherapeutic targets against malaria.

2. *In vitro* gametocytogenesis of *Plasmodium falciparum* and gametocytocidal effect of 9-anilinoacridines.

3. Effects of DNA gyrase inhibitors on *Trichomonas vaginalis* in cultures.

4. *Trichomonas vaginalis* isolation and characterization of DNA topoisomerase II from *Trichomonas vaginalis*

5. *Toxoplasma* antibody in healthy Thai population.

6. Serological of *Toxoplasma gondii* antibody in HIV+ve and HIV-ve patients.

7. Inhibition of *Giardia intestinalis* and *Entamoeba histolytica* by medicinal plants.

8. Studies on ultrastructure of *Giardia intestinalis* trophozoites after exposure to drugs.

9. *Blastocystis hominis* in children with diarrhea in children hospitals.

10. *In vitro* cultivation for cryptosporidium spp.

11. Rapid detection of *Entamoeba histolytica* antibody.

TEACHING AND TRAINING

Regular courses

1. Diploma in Tropical Medicine and Hygiene (D.T.M.&H.)
 - 1.1 Core Subject TMPZ 501 : Protozoology 2 credits
 - 1.2 Elective subject TMID 505 : Parasitology 1 credit
2. Master of Science in Tropical Medicine (M.Sc.)(Trop. Med.) and Doctor of Philosophy in Tropical Medicine (Ph.D.)(Trop.Med.).
 - 2.1 Core Subject
 - TMID 512 : Tropical Medicine 6 credits
 - 2.2 Elective Core Subjects
 - TMID 503 : Medical Protozoology 2 credits
 - TMID 516 : Practical Parasitology 2 credits
 - 2.3 Free Elective
 - TMID 517 : Biochemistry of Parasites 2 credits
 - TMID 518 : Advanced Parasitology 2 credits
 - TMID 519 : Experimental Technique in Parasitology 2 credits
 - TMID 520 : Molecular Biology of Parasite 2 credits
 - TMID 521 : Antiparasitic Agents 2 credits

Services

1. Special techniques for diagnosis of protozoal diseases such as:
 - 1.1 Diagnosis of Toxoplasmosis by using Dye-Test technique.
 - 1.2 Diagnosis of Cryptosporidiasis, *Cyclospora* spp., Microspora by special staining techniques.
 - 1.3 Identifying intestinal protozoa by nuclear staining.
2. Provide protozoal specimens for teaching to other institutes when requested.

Others

1. The Department, in conjunction with some international organizations, have provided some international training courses.
2. Provides opportunities for both local and foreign medical personnel to train special topics within the Department.
3. Teaching special topics in other universities.

ABSTRACTS

ISOLATION AND CHARACTERIZATION OF MITOCHONDRIAL DNA POLYMERASE FROM *PLASMODIUM FALCIPARUM*

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This is the first study on the purification of mitochondrial DNA polymerase from *Plasmodium falciparum* by using FPLC. The mitochondria of *P. falciparum* was isolated from mature trophozoite stage by differential centrifugation. Mitochondrial DNA

polymerase was partially purified and characterized by using various specific inhibitors. Aphidicolin-resistant and N-ethylmaleimide-sensitive DNA polymerase activity was detected from purified mitochondria of *P. falciparum*. The characteristics of mitochondrial DNA polymerase was similar to those of other eukaryotic DNA polymerase γ except for its high resistance to ddTTP ($IC_{50} > 400$ mM). In addition, mitochondrial DNA polymerase γ was also resistant

to nucleotide analogues such as (S)-1-[3-hydroxy-2-phosphonylmethoxypropyl] adenine diphosphate (HPMPApp) and 9-[2-(phosphonylmethoxy)ethyl] adenine diphosphate (PMEApp) (IC₅₀s > 1 mM) whereas g-like DNA polymerase of *P. falciparum* cellular extract was previously reported as HPMPApp-sensitive enzyme (IC₅₀ = 1 mM). The different sensitivity of these inhibitors of mitochondrial DNA polymerase from *P. falciparum* and other eukaryotic DNA polymerases indicated that mitochondrial DNA

polymerase γ can possibly act as a novel target for chemotherapy of malaria in the future.

This work was supported by The Thailand Research Fund (RSA/3/2538).

Presented at : Joint International Tropical Medicine Meeting 1998 and The Fourth Chamlong-Tranakchit Harinasuta Lecture.

GAMETOCYTOCIDAL ACTIVITY OF PYRONARIDINE AND DNA TOPOISOMERASE II INHIBITORS AGAINST MULTIDRUG-RESISTANT *PLASMODIUM FALCIPARUM* IN VITRO

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Gametocytocidal activity of pyronaridine and DNA topoisomerase II inhibitors against two isolates of multidrug-resistant *Plasmodium falciparum*, KT1 and KT3 was determined. After sorbitol treatment, pure gametocyte cultures of *Plasmodium falciparum* containing mostly young gametocytes (stage II and III) obtained on day 11 were exposed to the drugs for 48 hours. The effect of the drugs on gametocyte development was assessed by counting gametocytes on day 15 of culture. Pyronaridine, a 9-anilino-aza-acridine, was the most active gametocytocidal drug against both isolates; it had a 50% inhibitory concentration of 6 and 20 nM, respectively whereas

gametocytocidal activity of 9-anilinoacridines was observed in the concentration range of 0.6-82 mM. Moreover, a 50% inhibitory concentration of pyronaridine was lower than that of primaquine which is the only drug used to treat malaria patients harbouring gametocytes. Resistance of both isolates of *Plasmodium falciparum* to chloroquine, pyrimethamine and cycloguanil did not affect susceptibility of their asexual stages and sexual stages to pyronaridine. Prokaryotic and Eukaryotic DNA topoisomerase II inhibitors such as norfloxacin, etoposide (VP16) and amsacrine (m-AMSA) were effective only on asexual blood stages but not sexual stages of the malaria parasites. Based on the results, pyronaridine may play an important role in the interruption of malaria transmission.

This work was supported by The Thailand Research Fund (RSA/3/2538).

Submitted to Parasitology International.

SEROLOGICAL STUDY OF *T. GONDII* ANTIBODY IN HIV+VE AND HIV-VE PATIENTS

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During a period of one year, 312 serum samples were sent to Department of Protozoology, Faculty of Tropical Medicine, Mahidol University for detecting *T. gondii* antibody. Out of 312, there were 64.6% of HIV infected patients. Nineteen sera were sent from patients of eye diseases, 12 sera from CNS patients, 3 sera from neonate and the rest of sera were sent from asymptomatic patients. There was no statistica

significant difference of *T. gondii* antibody between HIV+ve and HIV-ve patients (28.8% and 21.9%, p-value 0.8). The titer of *T. gondii* were low which corresponding with reactivation of chronic toxoplasmosis in immunosuppressive patients.

Presented at : Joint International Tropical Medicine Meeting 1998 and The Fourth Chamlong-Tranakchit Harinasuta Lecture, 20 August 1998, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand



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CURRENT RESEARCH ACTIVITIES

The Department consists of 4 units, namely, Social and Economic Research Unit, Environmental Toxicology Unit, Environmental Medicine Research Unit and Applied Malacology Unit. It has achieved success in all areas within its limit.

Physical development and research, teaching and training, including service activities or functions are as follows: Besides offering courses related to environmental health, environmental toxicology, social medicine and medical malacology for M.Sc. and Ph.D. as well as D.T.M.&H. students enrolled through the Bangkok School of Tropical Medicine, the Department conducts the research in various aspects depending upon the functions of each unit

listed above. Its research activities comprise both field research and laboratory investigation. Most of the Department's efforts are concentrated on disease oriented problems and urgent problem solving. Investigations in the field are mainly restricted to, firstly, operational research to test various disease control models and, secondly, field surveys to collect baseline data or information on health impacts due to water resources and industrial development. Such data could be used for monitoring and surveillance in disease prevention and control programs.

FIELD SURVEYS

The main focus of the survey is largely due to the impact of the water resource and industrial developments on public health, specifically the spread of vector borne viral and parasitic diseases, such as DHF and malaria, and adverse health effects of water pollution as well as the socio-economic study regarding tropical diseases and public health problems. The studies form part of a series, keeping a surveillance of snails intermediate host of schistosomiasis in Pak Mun River basin in Ubon Ratchathani Province. The results of epidemiological studies of adverse health effects, using mainly cross sectional surveys, indicated that the problems related to the physical, social and environmental had the main impact on public health.

Additional studies included (1) the environmental health impact study of Kaeng Sue Ten Dam Project,



Phrae Province; (2) a surveillance and prevention of schistosomiasis in the area of Pak Mun Dam Project; (3) the impact of water resource development of Rasri-Salai Project; (4) a longitudinal comparative study on insecticide impregnated bednet and DDT spraying to control malaria along the western border; (5) a social and economic impact of dengue haemorrhagic fever (DHF) in Thailand; and (6) liver fluke control model.

CLINICAL RESEARCH

In relations to HIV-1 vaccine trial and baseline data for a possible vaccine efficacy trial, there were several studies of prospective cohort of injecting drug users (IDUS) to determine rates of successful follow-up, HIV-1 incidence, and risk factors for seroconversion and to characterize infecting HIV-1 strains.

The related studies containing the following titles.

1) HIV-1 incidence, subtypes, and follow up in a prospective cohort of injecting drug users (IDUS) in Bangkok, Thailand.

2) Genetic characterization of incident HIV-1 subtype B and E strains from injecting drug users (IDUS) in Bangkok, Thailand.

3) Similar risk factors for new infection with HIV-1 subtypes B and E among injecting Drug User (IDUS) in Bangkok, Thailand.

4) Viral load and CD4 cell count in injecting drug users (IDUS) newly infected with HIV-1 subtypes B and E, Bangkok.

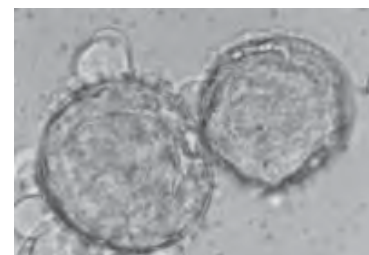
5) Incarceration as a continuing HIV risk factor among injecting drug user (IDUS) in Bangkok.

6) AIDSVAX B/B and AIDSVAX B/E likely to protect. But how well and for how long must await results of planned efficacy trials.

7) Willingness to participate in an HIV vaccine efficacy trial among injecting drug users (IDUS) in Bangkok, Thailand.

8) Estimation of vaccine efficacy for prophylactic HIV vaccines from field trials in developing countries.

9) Clinical and immunologic spectrum of disease among 2,261 HIV-1 infected patients at a hospital in Bangkok.



10) Leaving sex work : work history in a cohort of female sex workers in Northern Thailand.

11) Impact of HIV on families of HIV-infected women who have recently given birth, Bangkok, Thailand.

12) HIV-1 seroconversion in a prospective study of female sex workers in northern Thailand: continued high incidence among brothel-based women.

13) Cost and performance of malaria sector : A case study at Malaria Sector 11, Tak Province, Thailand.

14) Cost-effectiveness analysis of lambda-cyhalothrin treated nets for malaria control : the patients' perspectives.

15) Efficiency of lambda-cyhalothrin treated nets compared with DDT spraying for malaria control in Northwestern Thailand.

16) Activity costs of Health Substation : A case study in Mae Ramard District, Tak Province, Thailand.

17) Activity costs of Health Station : A case study in Sammeun Subdistrict Health Station, Mae Ramard District, Tak Province, Thailand.

18) Activity costs of Malaria Clinic : A case study in Malaria Sector 11, Mae Ramard District, Tak Province, Thailand.

LABORATORY RESEARCH

The laboratory research comprised (1) mass production of *Opisthorchis viverrini* material for use in related opisthorchiasis research, such as the production of specific monoclonal antibodies, immunodiagnostic methods for opisthorchiasis (in collaboration with the Department of Microbiology and Immunology); (2) separation and characterization of adult worm proteins and glycoproteins from the liver fluke *Opisthorchis viverrini* (in collaboration with the Department of Microbiology and Infectious Diseases, University of Calgary, Calgary, Canada); (3) immunity of *Schistosoma mekongi* infection: preparation of antigen from cercariae, schistosomulae and adult worms (in collaboration with the Department of



Microbiology and Immunology); (4) investigation on the viability and infectivity of metacercariae of *Opisthorchis viverrini* to various doses of irradiation; (5) detection of *Mycobacterium leprae* by polymerase chain reaction (PCR) using tissue samples from fresh frozen and paraffin embedded skin biopsies; and (6) maternal lead levels detection in breast milk and cord blood in different location.

TRAINING

From time to time, the Department hosted visitors from all over the world in both visiting and short training courses regarding tropical diseases. One of the events was the short training course on schistosomiasis given to Vietnamese fellows who received the assistantship from Medisch Comite' of the Netherlands.

We also organized the Readiness Workshop for AIDS Vaccine Trials for Clinicians and Nurses hosted by Bangkok Metropolitan Administration.



ABSTRACTS

HIV-1 INCIDENCE, SUBTYPES, AND FOLLOW UP IN A PROSPECTIVE COHORT OF INJECTING DRUG USERS (IDUs) IN BANGKOK, THAILAND

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Background: Despite various interventions, HIV-1 transmission rates among Bangkok IDUs have remained high since 1988. An effective HIV-1 preventive vaccine may be needed to reduce new infections in this population. To obtain baseline data for a possible vaccine efficacy trial, a prospective cohort of IDUs was established to determine rates of successful follow-up, HIV-1 incidence, and risk factors for seroconversion and to characterize infecting HIV-1 strains. **Methods:** From 05/95-12/96, IDUs attending 15 Bangkok Metropolitan Administration drug treatment clinics were screened, and HIV-negative IDUs were offered enrollment, with informed consent, into the cohort. HIV testing and counseling and interviews on demographics, drug use, and sexual behaviors were conducted at enrollment and scheduled every 4 months. Most IDUs were treated with methadone. For HIV-1 seroconversions, infect-

ing HIV-1 subtypes were determined by direct DNA sequencing of the C2-V4 envelope region. **Results:** Of 3,614 IDUs screened, 30.2% were HIV positive. Of 1,208 HIV-negative IDUs enrolled, 70% were successfully followed-up at 12 months (809 of 1,162 due for follow up through 12/15/97). One-hundred and one IDUs had seroconverted after 1,240 person-years (PYs) of observation (incidence = 8.1/100 PYs; 95% CI = 6.6-9.7). Of 82 HIV-1 specimens available for sequencing, 67 (82%) were subtype E and 15 (18%) were subtype B' (Thai B). Factors associated with HIV seroconversion in a proportional hazard model were daily heroin injection (RR = 3.6, 95% CI = 1.9-6.9, referent: no injection); being incarcerated and injecting (RR = 4.1, 95% CI = 2.3-7.4, referent: not incarcerated); being incarcerated but not injecting (RR = 1.9, 95% CI = 1.1-3.3, referent: not incarcerated); and being female (RR = 2.0, 95% CI = 1.1-3.6). **Conclusion:** Bangkok IDUs remain at high risk for HIV despite active interventions. An HIV vaccine efficacy trial seems feasible in this setting and could evaluate protection against HIV-1 subtypes B' and E.

Presented at : 12th AIDS Conference, Geneva, June 28 - July 3, 1998.

GENETIC CHARACTERIZATION OF INCIDENT HIV-1 SUBTYPE B AND E STRAINS FROM INJECTING DRUG USERS (IDUs) IN BANGKOK, THAILAND

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⁵Centers for Disease Control & Prevention, Atlanta, GA, USA

⁶Faculty of Tropical Medicine, Mahidol University, Bangkok

Background: The initial 1988 epidemic among IDUs in Bangkok was largely due to envelope (env) subtype B' (Thai B) strains, but subtype E has increased in prevalence in recent years. Since 1995, HIV-1 seroconverting IDUs have been identified in a prospective cohort study to determine the feasibility of conducting an HIV vaccine efficacy trial in this

setting. Genetic characterization of these strains is required for the design of candidate HIV-1 vaccines. **Method:** HIV-negative IDUs (n = 1,208) were evaluated by HIV EIA testing every 4 months. Following an HIV-positive test, blood was obtained at time 0 and months 1, 4, 8, 12, etc. Samples from each seroconverter during 1995-97 were characterized for HIV-1 subtype from env region DNA amplified either from lysed PBMCs or reverse-transcribed RNA from plasma. Viral subtypes were determined by phylogenetic analysis of 345 bases in the C2-V4 region of gp-120. **Results:** Through December 1997, 101 IDUs became HIV-1 infected. Of 78 samples analyzed to date, 63 (81%) were

subtype E strains and 15 (19%) were subtype B. All subtype B strains clustered with B' (Thai B) strains. The mean intra-subtype nucleotide divergence for subtype E was 6.96% (range, 0.30-13.65) and for subtype B was 15.33% (range, 3.64-29.25). The mean divergence between the two subtypes was 28.90% (range 19.27-45.92). The GPGQ motif at the crown of the V3 loop was present in 58 (92%) of 63 subtype E strains; other motifs were GPGR (2), GPGK (2), and GPGE (1). The V3 crown displayed greater variation among subtype B strains: GPGR (6 of 15),

GQGR (4), GPGQ (3), and GLGR (2). Conclusions: HIV-1 subtype E accounted for a majority of new infections among Bangkok IDUs in 1995-97; all subtype B strains were B' (Thai B). Subtype E strains displayed limited genetic diversity in the env region; while subtype B' HIV-1 vaccine evaluated in this population would be challenged by two HIV-1 subtypes.

Presented at: 12th AIDS Conference, Geneva, June 28 - July 3, 1998.

SIMILAR RISK FACTORS FOR NEW INFECTION WITH HIV-1 SUBTYPE B' AND E AMONG INJECTING DRUG USERS (IDUs) IN BANGKOK, THAILAND

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⁴ Mahidol University, Bangkok, Thailand

⁵ CDC, Atlanta, GA, USA

⁶ UNAIDS, Geneva, Switzerland

Background: Bangkok IDUs experienced an epidemic of HIV-1 subtype B' (Thai B) in 1988. Recent cross-sectional surveys have identified an increase in subtype E. Since 05/95, in a prospective cohort of 1,208 IDUs attending 15 methadone treatment clinics of the Bangkok Metropolitan Administration, HIV-1 incidence was 8.1 per 100 person-years. We evaluated demographic and behavioral factors associated with incident infection with these two subtypes. **Methods:** Data on seroconverters were obtained from enrollment and follow-up questionnaires. Incident HIV-1 strains were characterized by direct DNA sequencing of the C2-V4 envelope region. **Results:** By 12/15/97, 101 IDUs became HIV-1 infected, and 82 were available for this analysis. Of these, 87%

still injected heroin despite treatment, and needle sharing was reported by 28%. However, reported sexual activity in the four months before seroconversion was limited: 59% had no sex, only 2.4% had sex with a non-regular partner, and none had sex with a commercial sex worker. Infection was due to subtype E for 67 (82%) and subtype B' for 15 (18%). IDUs with subtype E tended to be younger than those with B' (mean age: 30 vs. 32 years, $p = 0.2$). Yet, other demographic and behavioral factors (gender, education, marital status, age of first drug use, incarceration, needle sharing, history of casual sex, and reported STDs) were similar for those with subtypes B' and E ($p > 0.1$ for any variable). **Conclusion:** Recently infected Bangkok IDUs with subtype B' or E infection are similar with regard to demographic and behavioral factors. These data suggest a similar parenteral mode of infection for both subtypes B' and E.

Presented at: 12th AIDS Conference, Geneva, June 28 - July 3, 1998.

VIRAL LOAD AND CD4 CELL COUNT IN INJECTING DRUG USERS (IDUs) NEWLY INFECTED WITH HIV-1 SUBTYPES B' AND E, BANGKOK

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Background: The HIV-1 epidemic that started among Bangkok IDUs in 1988 was initially due to env sub-

type B' (Thai B), but since then subtype E has increased in prevalence. Since May 1995, HIV-1 seroconverters have been identified in a prospective cohort study of 1,208 HIV-negative IDUs in Bangkok. We evaluated clinical characteristics of newly infected IDUs to compare infection with subtypes B' and E. **Methods:** IDUs completed epidemiologic questionnaires and had HIV EIA testing every 4

months. Following an HIV-positive test, blood was obtained at time 0 and at months 1, 4, 8, 12, etc. Incident HIV-1 strains were characterized by direct DNA sequencing of the C2-V4 envelope region, plasma viral load was determined by Roche Amplicor Monitor v. 1.5 testing, and CD4 cell counts were determined by flow cytometry. Results: By December 1997, 101 IDUs became HIV-1 infected; specimens from 83 were available for analysis: 67 (81%) had subtype E and 16 (19%) had B'. IDUs with E and B' had similar demographic and behavioral characteristics. Geometric mean plasma viral levels (copies/mL) within 4 months of seroconversion were higher for subtype E (120,000) than B' (48,000; $P = 0.05$); however, mean viral levels were more similar

6-12 months after seroconversion for E (69,000) and B' (35,000; $P = 0.2$). Mean CD4 cell counts (cells/mL) 6 months post-seroconversion were similar for E (523) and B' (568; $P = 0.4$), as were the rates of CD4 decline during the first year ($P = 0.3$). Conclusion: The initial post-infection viral peak may be higher for subtype E than for subtype B', but the vital level set point and CD4 counts within the first year appear to be similar for IDUs infected with these two subtypes. Continued follow-up of this cohort of IDUs will further define the clinical course of infection with HIV-1 subtypes B' and E.

Presented at : 12th AIDS Conference, Geneva, June 28 - July 3, 1998.

INCARCERATION AS A CONTINUING HIV RISK FACTOR AMONG INJECTING DRUG USERS IN BANGKOK

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Background: Bangkok experienced very rapid spread of HIV among IDUs in 1988, followed by stable seroprevalence at approximately 40% and continued high incidence. Estimated incidence from a prospective cohort of IDUs attending 15 Bangkok Metropolitan Administration methadone clinics during 1995-1997 was 8.1 per 100 person-years at risk. Previous surveys have shown that having been incarcerated was significantly associated with being HIV seropositive, with odds ratios in the range of 2 to 3. We determine risk factors for incarceration among cohort enrollees. Methods: HIV-negative IDUs were offered enrollment after informed consent; data were obtained from enrollment and follow-up questionnaires. HIV testing and counseling and interviews on demographics, drug use, and sexual behaviors were conducted at enrollment and scheduled every 4 months. Results: Of 1,208 HIV-negative IDUs enrolled, 101 seroconverted as of 15/12/97.

A proportional hazard model demonstrated that, after controlling for gender and heroin injection, being incarcerated and injecting (Relative Rate [RR] = 4.1, 95% CI = 2.3-7.4, referent: not incarcerated), and being incarcerated but not injecting (RR = 1.9, 95% CI = 1.1-3.3, referent: not incarcerated) were risk factors associated with HIV-1 infection. Factors associated with being incarcerated, using logistic regression, included: age less than 25 years old (Odds ratio [OR] = 2.9, 95% CI = 2.1-4.1, referent: 40+ years); having secondary education or less (OR = 1.6, 95% CI = 1.2-2.2, referent: post secondary); any use of heroin since enrollment (OR = 1.7, 95% CI = 1.3-2.2; referent: not used); and number of incarcerations before enrollment (OR = 1.4, 95% CI = 1.2-1.6). Conclusion: Incarceration is a strong risk factor for incident HIV infection in Bangkok IDUs. History of heroin use and previous incarcerations lead to higher probability of being incarcerated. This vicious cycle needs more attention and appropriate interventions to reduce HIV transmission in this high-risk population.

Presented at : 12th AIDS Conference, Geneva, June 28 - July 3, 1998.

AIDSVAX B/B AND AIDSVAX B/E. LIKELY TO PROTECT. BUT HOW WELL AND FOR HOW LONG MUST AWAIT RESULTS OF PLANNED EFFICACY TRIALS

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² Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

³ Genentech, Inc., S. San-Francisco, CA, USA

Background: The safety and immunogenicity of AIDSVAX has been evaluated through administration of monovalent subtype B formulations (MN and IIIB) to over 1000 humans. Potential human efficacy is reflected by its ability to protect chimpanzees from high-dose challenge. To maximize the potential efficacy, geography-specific formulations to cover different HIV-1 subtypes need to be produced for efficacy testing. **Methods:** We reviewed all human and chimpanzee data regarding the safety, immunogenicity, potential efficacy of AIDSVAX. In addition, we examined viruses infecting vaccinated humans (breakthroughs). With this information, a second geography-specific antigen was selected, produced, combined with MN and administered to humans in the United States and in Thailand using bivalent formulations - B/B for the US (120 volunteers) and B/E for Thailand (90 volunteers). To test the efficacy of these bivalent vaccines we designed Phase III trials. **Results:** Minimal injection site reactions are

the only associated adverse reactions observed. Data from the bivalent studies are pending. Monovalent formulations induce humoral immune responses in 99.5% of recipients. These occur after two initial doses given at T-0 and T-1 month but the titers of anti-gp120, anti-V-3, CD4 blocking and neutralizing antibodies are increased with booster doses given at time 6 months and time 12 months. Lymphocyte transformation and positive skin tests to rgp120 are common. Results from testing sera following B/B and B/E vaccination suggest the addition of macrophage-tropic strains with neutralizing sites complementary to MN will increase the likelihood of protection. Plans for US and Thai Phase III trials have been accepted by the US FDA. **Conclusion:** Indications are that AIDSVAX is safe and will likely protect humans from HIV-1 infection. The addition of complementary macrophage-tropic strains to the monovalent MN vaccine are expected to increase the likelihood of protection - the extent of protection will await the results of planned efficacy trials.

Presented at : 12th AIDS Conference, Geneva, June 28 - July 3, 1998.

WILLINGNESS TO PARTICIPATE IN AN HIV VACCINE EFFICACY TRIAL AMONG INJECTING DRUG USERS (IDUs) IN BANGKOK, THAILAND

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Objectives: To assess willingness to participate in a gp120 bivalent B/E vaccine efficacy trial and to evaluate educational needs and positive motives for and barriers to participation. **Methods:** Between 5/95 and 12/96, 1,208 IDUs attending 15 drug treatment clinics in Bangkok were enrolled into a prospective cohort to assess the feasibility of conducting an HIV vaccine trial. In 1997, 193 cohort participants at 5 clinics attended group informational sessions describing a potential efficacy trial of a gp120 vaccine product and completed questionnaires assessing

comprehension and willingness to participate. About a week later they completed a follow-up questionnaire that again assessed comprehension and willingness to participate, as well as barriers to and positive motives for participation, who (if anyone) they talked to about the information, and whether others thought participation was a good, bad, or neutral idea. **Results:** At baseline 51% were definitely willing to participate, and at follow-up 54%; only 3% were definitely not willing at either point. Baseline comprehension was high (median score = 11 out of 13) and improved at follow-up (median score = 12). In general, participants tended to rank positive motives as very important and barriers as a small problem. Altruism was the motive most frequently cited as very important (79%), while the hypothetical possibility that the vaccine might cause disease enhancement was the barrier most frequently cited as a major problem (31%). Most

(84%) of participants talked to others about the information they received; of these, 69% reported that others generally thought participation was a good idea. Conclusions: IDUs in Bangkok are able to comprehend satisfactorily the basic issues surrounding a

vaccine efficacy trial and express a high level of willingness to participate in such a trial.

Presented at : 12th AIDS Conference, Geneva, June 28 - July 3, 1998.

ESTIMATION OF VACCINE EFFICACY FOR PROPHYLACTIC HIV VACCINES FROM FIELD TRIALS IN DEVELOPING COUNTRIES

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Background: Prophylactic HIV vaccines could reduce susceptibility to infection or disease, i.e., vaccine efficacy for susceptibility (VES). They also may reduce infectiousness of vaccinees who become infected, i.e., vaccine efficacy for infectiousness (VEI). This latter effect could produce an important indirect reduction in HIV transmission even if the vaccine does not protect well against infection. We propose an augmented design for HIV vaccine trials that allows estimation of both effects. The augmented design includes steady sexual partners of primary participants. **Methods:** A placebo-controlled phase III HIV vaccine trial is simulated according to the structure of the Bangkok Metropolitan Administration (BMA) cohort of injecting drug users. In the simulation, 1,250 primary participants are recruited per arm. Participants and their steady sexual partners are followed every six months for three years. Primary participants are assumed to be at risk of infection through needle-sharing at various frequencies. In addition, 50% of the primary participants have unprotected sexual contact with a steady partner at

various frequencies. A likelihood function based on a Markov model is used to estimate the VES and VEI. **Results:** In the simulated baseline vaccine trial, cumulative incidence in the placebo arm among primary participants is 12% for the entire trial. There are 119 total infections in the placebo arm. The secondary attack rate (SAR) among sexual partners in the placebo arm is 46%. The VES and VEI were preset to 0.4 and 0.6, respectively. The estimated 95% confidence interval (CI) on VES is [0.22, 0.56] and on VEI is [0.37, 0.74]. The power to reject H₀: VES = 0 and H₀: VEI = 0 is 1.0 for both. If the HIV incidence rate is reduced so that 92 infections occur among primary participants in the placebo arm and SAR = 32%, then the estimated 95% confidence interval on VES is [0.23, 0.54] and on VEI is [0.31, 0.78]. The power to reject H₀: VES = 0 and H₀: VEI = 0 is still 1.0 for both. **Conclusions:** It should be feasible to estimate both VES and VEI for vaccine trials in developing countries that have populations where the primary participants are exposed to infection through injecting drugs or sexual contact, and who have steady sexual partners. Several populations, in addition to the BMA cohort, with this social structure are being considered for HIV vaccine trials.

Presented at : 12th AIDS Conference, Geneva, June 28 - July 3, 1998.

DEPARTMENT OF TROPICAL HYGIENE



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General Affairs Officer

Kamornwan Chaipakdee B.Ed.(Social Study)

CURRENT RESEARCH ACTIVITIES

1. Epidemiology and control of malaria in Ratchaburi Province, Thailand.
2. Correlation between malaria incidence in Thailand and changes in vegetation cover using satellite remote sensing techniques.
3. Epidemiological study of nutritional deficiency among Karen preschool children.
4. Epidemiology and control of soil-transmitted helminthiasis in a rural community near the Thai-Burmese border.

TEACHING AND TRAINING COURSES

The Department is responsible for the Faculty's teaching and training courses as well as the international training courses in epidemiology. The Department has its own field work base at the Ratchaburi province known as **Suan Phung Research Unit** where research work and training in field epidemiology is being conducted both for the local and the foreign students.

1. Diploma in Tropical Medicine and Hygiene (D.T.M.&H.)

Core subjects :

- TMHG 501 : Tropical hygiene
- TMHG 502 : Medical statistics

ELECTIVE SUBJECTS :

- TMHG 508 : Epidemiology (elective)
- TMHG 509 : Computer utilization (elective)

2. M.Sc. and Ph.D. in Tropical Medicine

CORE SUBJECTS :

- TMID 513 : Biostatistics
- TMID 514 : Research methodology and design

ELECTIVE SUBJECTS :

- TMHG 511 : Advanced statistical analysis in biomedical research
- TMHG 512 : Modern methods in epidemiological research
- TMHG 513 : Use of advanced statistical softwares in epidemiological analysis
- TMHG 514 : Data processing by computer
- TMHG 515 : Design and analysis in experimental research

3. Master Degree in Primary Health Care Management

- ADPM 606 : Epidemiological studies in health system

4. M.Sc. (Medical Epidemiology)

- TMHG 668 : Epidemiologic methods
- TMHG 676 : Epidemiology of specific health problems

5. Ph.D. (Clinical Epidemiology)

- RACE 606 : Advanced epidemiologic methods

INTERNATIONAL LINKAGES

1. Research

- 1.1. Clinica di Malattie Infettive e Tropicali, Universit· Degli Studi Di Brescia
- 1.2. Centre de Formation et de Rechherche en Mádécine et Santé Tropicales, Hopital Felix Houphouet-Boigny, Marseille, France.
- 1.3. Department des Maladies Infectieuses et Tropicales, Hopital de la Salpetriere, Paris, France.
- 1.4. Association Santé Sud, Medical Humanitarian French Association, Marseille, France.
- 1.5. Freie Universität Berlin

2. International Training Courses

- 2.1 SEAMEO-TROPMED Network
- 2.2 Tropical Health Program, University of Queensland Medical School, Australia
- 2.3 College of Public Health, University of the Phillipines, Manila
- 2.4 Faculty of Public Health, University of Indonesia, Indonesia
- 2.5 Institute for Medical Research, Malaysia
- 2.6 Freie Universität Berlin

SERVICES

1. Short Courses

- Introductory course in epidemiology
- Advanced course in tropical epidemiology (international)
- Computer utilization
- Regional workshop on geographic information system : Disease mapping for tropical infections and vector-borne diseases

2. Medical Personnel Training Courses

Management in malaria control for malaria division personnel (international)
 Health information system for malaria division personnel (international)
 Epidemiology of malaria and malaria control for medical personnel from Nepal, Laos PDR, and Vietnam

3. Other Services

Consultant in research methodology and biostatistics
 Health surveillance for the expressways personnel
 Malaria field research station

ABSTRACTS

FACTORS INFLUENCING MALARIA ENDEMICITY IN YUNNAN PROVINCE, P.R. CHINA (Analysis of Spatial Pattern by GIS)

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This study is an initial attempt to apply disease mapping through Geographical Information System (GIS) with multiple regression analysis to determine the nature and extent of factors influencing malaria

transmission in Yunnan Province, P.R. China, particularly in border areas. Secondary county-based data covering the period of 1990 to 1996 were collected and analyzed. The malaria situation in Yunnan Province as a whole is influenced mainly by the combined effects of the physical environment, the presence of efficient vector species, and mobile population along international borders with Myanmar, Lao PDR and Vietnam.

Published in : Southeast Asian J Trop Med Public Health (in press).

DOES G6PD DEFICIENCY TRAIT CONFER RESISTANCE AGAINST MALARIA?

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A one-year prospective cohort study was carried out in rural malaria endemic community near Thai-Burmese border in Western Thailand to determine whether the incidence rates of malaria differ among the G6PD deficient individuals compared to people with normal enzymes. Determination of G6PD was done by improved single-step formazan method and fluorescent screening test among 795 subjects. Data on haemoglobinopathies are pending. Using Poisson regression, after controlling for age, mosquito net use,

sleeping time and wake-up time, the G6PD heterozygous trait provided significant protection against malaria with the incidence rate ratio (IRR) = 0.36 (95% confidence limits = 0.13,0.96). However, no difference in incidence rates was observed in hemizygous and homozygous G6PD deficient males and females compared to normal subjects with IRR = 1.17 (95% confidence limits = 0.90,1.53). This study provides strong evidence that there is substantial protective effect against malaria conferred by heterozygous G6PD trait.

Presented at : the Joint International Tropical Meeting 1998 and The Fourth Chamlong-Tranakchit Harinasuta Lecture.

HEALTH PROBLEMS IN TRAVELERS COMING TO THAILAND BETWEEN 1990-1994

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Over the past one decade, the number of tourists from temperate countries coming to Thailand had been steadily increased. This study reports the common causes of ailments and injuries among travelers in Thailand. A total of 516 patients seeking our private medical services or advice through insurance claims during the period of 1990-1994 were evaluated. Two hundred and seventy-six (53.5%) were males and 240 (46.5%) were females with a mean age of 42.5 years (7 months to 86 years). The duration of their stay in Thailand before illness was between 1

day to 2 months and most were seen in the month of August. Five of the most frequent cause of morbidity were 1) road accident (18.8%), 2) acute gastroenteritis (13.2%), 3) acute respiratory tracts infections mainly bronchitis and pneumonia (10.9%), 4) other type injuries (10.7%), and 5) cardiovascular diseases (7.4%). Fifty-five percent were treated as in - patients or out-patients were able to continue with their trips, 41% were hospitalized and repatriated and 2.6% needed only advice without medication. Five of them died (1%), of which three died from drowning, one had myocardial infarction and one with unknown cause of death. Since tourism is not only for young and healthy, and because most ailments that occurred were preventable and entailed unforeseen expenses, it is important that proper counseling should be sought before traveling.

Published in : J Travel Med (in press).

EVALUATION OF THE DIRECT AGGLUTINATION TEST (DAT) AS AN IMMUNODIAGNOSTIC TOOL FOR A DIAGNOSIS OF VISCERAL LEISHMANIASIS (VL) IN NEPAL

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The direct agglutination test (DAT) was assessed as a diagnostic tool for the field study in Nepal. By using this method, anti-leishmanial agglutination test was conducted for fifteen visceral leishmaniasis (VL) cases who had been confirmed by bone marrow aspiration. The same test was done for 120 tuberculosis, 58 leprosy, 15 malaria, 26 intestinal parasitic infection cases, 24 healthy controls from adjacent to VL endemic area, and 18 controls from Kathmandu

(who had never visited the VL endemic areas). Two of the tuberculosis cases were positive for anti-leishmanial agglutinating antibodies at 1:800. All of the confirmed cases of VL were reactive to anti-leishmanial antibody at $\geq 1:3200$. Others were negative for serology. These results showed that the sensitivity of the direct agglutination test was 100% and the specificity was 99.2%. The direct agglutination test had positive and negative predictive value of 100% and 99.2% respectively. In conclusion, the DAT was found to be adaptable for the field application in a field laboratory.

Published in : J Nepal Public Health Association, July 1998;1(1):1-3.

DEPARTMENT OF TROPICAL NUTRITION AND FOOD SCIENCE



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CURRENT RESEARCH ACTIVITIES

Operational and multidisciplinary research projects:

1. Food and health relationship in Asian population
2. Dietary pattern, lifestyle and nutritional status of health science university students in Bangkok
3. Investigation of nutritional, health and dietary patterns of Thai elderly
4. Serum leptin concentration in obese subjects
5. Micronutrients and oxidative stress in obese subjects

Basic science research projects

1. Identification of gene mutation in lung cancer cells in Thai patients
2. Molecular Biology of carcinogenesis in lung cancer
3. Development of food and medicinal plant

TRAINING COURSES

Second International Short Training Course Food Safety and Food Control 1998

14-25 September 1998

28 Participants



WORKSHOP

International Workshop on The role of University/Ministry of Public Health/SEAMEO TROPMED/WHO/ICD/etc. in the course structure of Master Degree Program in Food Safety and Food Control

22-23 September 1998

25 Participants



ABSTRACTS

RIBOFLAVIN AND NUTRITIONAL STATUS OF THAI ROAD SWEEPERS IN BANGKOK

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Anthropometric measurements, haematological parameters and riboflavin status of Thai road sweepers in Bangkok were determined. According to a physical check-up and X-rays taken, all individuals

investigated were apparently healthy. The age of the study group varied between 20 and 59 years. The median for the males was 44 years and for the females 37 years. Over- and undernutrition were found among those investigated. 25.9% (BMI \leq 20.1) of the males and 1.8% (BMI \leq 18.7) of the females were undernourished. 31.5 % of the males and 43.8 % of the females were overnourished (BMI \geq 25.0). 13.0% of the males and 10.7% of the females had α EGR \geq 1.30, or vitamin B2 insufficiency.

Published in : Intern Med 1997;13:77-80.

EVALUATION AND MONITORING OF IODINE DEFICIENCY DISORDERS (IDD) IN SCHOOL CHILDREN IN NORTHEAST, THAILAND

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In using an operational research approach the possibility of improving iodine deficiency disorder (IDD) in school children at Khon Kaen province was investigated during the period of one year. Four schools in Pupaman and Srichompu districts, namely Ban Khoa Wong, Na Fai Witaya, Ban Pa Num Tieng and Ban Non Khom school were selected for this study. Ban Non Khom school served as control. Different means were used for iodine fortification. Iodinated salt was used for the children of the Ban Khoa Wong school, in Na Fai Witaya school iodinated water and iodinated fish sauce were provided for the children in Ban Pa Num Tieng school. Iodinated salt, water and fish sauce was provided through the help of the school teachers under the supervision and the advice from the team of investigators. Urine iodine excretion,

palpation of the thyroid gland and the thyroid hormones T4, T3 and TSH were selected for monitoring and evaluating the outcome of the study.

The proportion of children with low urine iodine excretion, indicated by a cut-off point suggested by the WHO/ICCIDD/UNICEF working group, decreased during the course of the project in all schools receiving iodine supplementation as well as in the control school. However the decrease was less in the control school in comparison with the implementation schools. Also the goitre rate decreased in all schools under investigation. The decrease of the goitre rate for the children of the control school might be due to the activities of a village health volunteer in a nearby village who was using iodinated salt for IDD control according to the presently ongoing national programme initiated by the Ministry of Public Health. No significant difference in the level of thyroid hormones were detected before and at the end of the supplementation for the experimental schools as well as for the control school.

The results from the determination of thyroid hormones serum levels could not be used for assessing the outcome of the project. The measuring of urinary iodine excretion might be helpful in monitoring the iodine intake during the intervention phase. Long term effects of iodine fortification could be seen best by the declining proportion of children with goitre. An observation of one year might not be

enough to clearly see the outcome of the project. The other possible contributing errors in this study is due to intra observer variation of the palpation technique when the sample size is not big enough. Goitrogens in this area might be another risk factor for the high prevalence rate of the goitre. Further study in this field should be encouraged.

The results of the study indicate that iodine fortification of salt and fish sauce is more effective than fortification of drinking water. Due to the local preference to add fish sauce (nam pla) instead of salt to almost all dishes, nam pla proved to be the best

vehicle for iodine fortification. The success of the project depended heavily on the understanding and co-operation of the school teachers and the school children.

Major constraints in conducting this project had been the insufficient distribution of iodinated salt and potassium iodide solution for fortifying drinking water and the inconsistency of iodide concentration in salt after fortification.

Published in : Asia Pacific J Clin Nutr 1998;7:131-7.

EFFECTS OF STORAGE CONDITIONS ON THE STABILITY OF IODINE IN IODIZED SALT, FISH SAUCE AND DRINKING WATER

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iodinated fish sauce, and iodinated drinking water was tested under different storage conditions i.e., room temperature, 25°C and 37°C, light exposure, and duration of storage. Light exposure, temperature and duration of storage showed direct effect on the iodine concentration in fish sauce and drinking water but do not effect the iodine content in salt. However, multiple factor regression analysis revealed that only time and temperature were related to iodine stability in salt and drinking water

Stability of iodine content in iodized salt,

Published in : Food 1998;28:31-41.

NUTRITIONAL STATUS OF SCHOOL CHILDREN IN AN ENDEMIC AREA OF IODINE DEFICIENCY DISORDERS (IDD) AFTER ONE YEAR OF IODINE SUPPLEMENTATION

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ment, including hematological status, were performed. There was a significant difference in the weight and height of the children from the four schools investigated, before and after supplementation in each school. The prevalence of anemia, (as indicated by hematological measurement) and iodine deficiency (as indicated by urinary iodine concentration in the children from the four schools) were assessed and compared before and after iodine supplementation; a decrease in prevalence was found in all school children. However, serum ferritin did not change before and after supplementation in all school children.

Published in : Southeast Asian J Trop Med Public Health 1998;29:50-7.

To improve the health and nutritional status of school children in an area of iodine deficiency disorders (IDD) by means of different iodine fortifications in salt, fish sauce and drinking water, anthropometric assessment for nutritional measure-

KNOWLEDGE, ATTITUDE AND PRACTICES TOWARDS AIDS OF RURAL POPULATION IN NORTHEAST THAILAND

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Knowledge, attitude and practices of villagers in relation to AIDS and HIV infection were assessed in 3 districts of Khon Kaen province. By cluster random sampling of 350 villagers (166 males, 15 to 72 years old and 184 females, 15 to 54 years of age) from 10 villages had been selected for this study. The villagers

were asked by using a pre-prepared questionnaire by trained interviewers. The majority of them (95% C.I.: 86.9 to 91.7%) did know very well about the route of infection for HIV. However as far as the symptoms of AIDS had been concerned, they were less well informed (34.8%). Over 30% (32.6%) of villagers had the correct attitude towards prevention of HIV infection and almost 43% did not discriminate patients suffering from AIDS. From all villagers questioned only 36% confessed that they abstained from risky behaviors such as visiting prostitutes, having unprotected sex and drug injections. The information gained through this study might be used for further planning of HIV and AIDS control measures.

Published in : Thai Aids J 1998 (in press).

MANAGEMENT OF IODINE FORTIFICATION AND IODINATED SALT DISTRIBUTION IN ENDEMIC AREA OF IODINE DEFICIENCY DISORDERS IN NORTHEAST THAILAND

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The management of iodine fortifications and iodinated salt distribution on village, subdistrict and districts level in Khon Kaen province, northeast Thailand where the prevalence of iodine deficiency disorders is high, were investigated. 10 villages from 3 districts were selected at random. The information about the production, distribution and use of iodinated salt was collected from villagers, village foodstore, provincial foodstore, subdistrict and district health officers, provincial health officer, health promotion center including producers through a prepared questionnaire. Proper knowledge and attitude towards using iodized salt of villagers was found to be the range of 63.8-81.7%. The price of

salt is not the important factors for purchasing. About 48.8-60.0% of all villagers investigated did not use iodized salt. They want to buy salt from village health volunteer and health officers. The major constraints for iodized salt preparation is an inadequate and irregular supply of potassium iodate. The shortage of iodized salt supplied to the village foodstore is also a problem. The middleman preferred to sell rock salt because they can make more profit. At the subdistrict /district level, the supply of potassium iodate from the health promotion center is not enough for producing iodized salt. In addition, support and supervision from central organizations is inefficient, amount other reason because the number of man powers is limited. At the provincial and health promotion center, the revolving fund and the stock of iodized salt are inadequate. Iodized salt produced by large firm are in good quality whereas small salt producer on a cottage scale supplied low quality salt to a rather high price. Production and distribution of iodized salt should be promoted and monitored better than at present in order to reach the population at village level.

Published in : J Public Health 1998 (in press).

SEROLOGICAL AUTOANTIBODIES CHARACTERISTICS IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) PATIENTS IN INSTITUTE OF DERMATOLOGY, BANGKOK

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One hundred systemic lupus erythematosus (SLE) patients from Institute of Dermatology, Bangkok were studied for serological autoantibodies characteristics namely antinuclear antibodies (ANA), anti Sm, anti nRNP, anti nDNA, Rheumatoid factor (Rh factor), FTA-Abs and RPR. These patients aged between 10 to 71 years old in both sexes. Positive ANA, anti nDNA and anti Sm, the important

markers for SLE were found to be 79, 13 and 13 percent respectively. The others non-specifics antibody for SLE: anti nRNP, Rh factor, FTA-Abs, RPR were found to be positive 21.0, 7.0, 3.0 and 7.0 percent respectively. In cases of SLE patients with positive ANA, the percentage of anti nRNP, anti Sm and anti nDNA were found to be 32.8, 20.3 and 20.3 percent respectively. No other autoantibodies were found in SLE patients with the negative ANA in this study. Therefore, ANA might be the most important autoantibody for screening in SLE patients.

Published in : Bull Med Tech Phy Ther 1998 (in press).

NUTRITIONAL STATUS AND SERUM LIPIDS OF A RURAL POPULATION IN NORTHEAST THAILAND - AN EXAMPLE OF HEALTH TRANSITION

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An investigation was undertaken in Northeast Thailand, a country undergoing rapid health transition, to find out whether there is a likelihood that the nutritional and lipid pattern of an adult population in Northeast Thailand is related to coronary heart disease in the same way as in western countries. In a cross-sectional study, the body mass index (BMI) and the waist-hip ratio as well as the important plasma lipids were determined. The nutritional status and the lipid profile of the predominantly middle-aged population is characterised by a generally favourable nutritional status and lipid concentrations, where the distribution, indicated by

the medians, of the relevant variables over the total population is concerned. A rather high proportion of individuals was found to be overnourished and to have high triglyceride levels. Individuals with high triglyceride levels run a risk of developing coronary heart disease only when the LDL-HDL fraction is above 5. Only 3% of the total population investigated had a LDL-HDL ratio above that value. Since hypertriglyceridaemia is also linked to the insulin resistant syndrome, it is concluded that, if the mortality of coronary heart disease increases in future, then this must be accounted probably more to the after-effects of the insulin-resistant syndrome than to the direct effect of an atherogenic lipid pattern. This view is supported by a high prevalence of impaired glucose tolerance (IGT) and non-insulin dependent diabetes mellitus (NIDDM) in the population under survey. Preventive measures in the area should concentrate among others on reducing overnutrition, especially among women, and increasing physical activity and screening for NIDDM.

Published in : Internat J Vit Nutr Res 1998;68:196-202.

ALPHA 1-ANTITRYPSIN PHENOTYPE OF CHILDREN WITH LIVER DISEASES IN THAILAND

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Alpha₁-antitrypsin deficiency (PiZZ) constitutes not only the most common hereditary cause of liver diseases, but also of the most prevalent metabolic diseases in need of liver transplantation. It is a codominantly inherited disorder which predisposes to chronic liver disease, usually beginning in early infancy. The purpose of the present study has been to investigate α_1 -antitrypsin phenotype in pediatric patients with various liver diseases. Phenotypic identification of α_1 -antitrypsin variants has been carried out in 69 children with various liver diseases and 100 healthy

controls using isoelectric focusing on polyacrylamide gel slabs. PiMM represents the most common phenotype detected in both groups (92% in the group with liver diseases and 88% in normal controls). We could detect PiZZ in only one healthy child but in none of those with liver diseases. Consequently α_1 -antitrypsin deficiency does not appear to be a common cause for liver disease among children in Thailand. Further studies are necessary to elucidate the frequency of various α_1 -antitrypsin variants and the clinical relevance with respect to liver diseases in Thailand.

Published in : Asian Pacific J Allerg Immunol 1998;16:27-30.

CANCER GENES AND CHOLANGIOCARCINOMA

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Genes involved in cancer development include oncogenes and tumor suppressor genes. Ras oncogene and mutation in p53 tumor suppressor gene are commonly found in many types of cancer. In Thai

patients with cholangiocarcinoma ras oncogenes occur less frequently than in other ethnic groups and furthermore, p53 mutations also occur with lower incidence when compared with Japanese subjects. It is unclear at this time the basis for these differences.

Published in : Southeast Asian J Trop Med Public Health 1997;28 (supplement 1): 80-4.

K-ras ONCOGENE AND P53 GENE MUTATIONS IN CHOLANGIOCARCINOMA FROM THAI PATIENTS

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Paraffin embedded tissues from twenty Thai patients with intrahepatic cholangiocarcinomas were studied for *K-ras* gene mutations at codon 12, 13 and 61 and for p53 gene mutations in exon 5 to 8 using polymerase chain reaction and thermal cycle

sequencing. Results showed that point mutations at these regions in *K-ras* oncogene were not present in all the samples. One case harboured a p53 gene mutation in codon 282 in exon 8, CGG (arginine) to TGG (tryptophane), but the mutation was not found in other patient's tissues with similar histological features.

Published in : Southeast Asian J Trop Med Public Health 1998; 29: 71-5.

DETECTION OF *K-ras* GENE MUTATIONS IN LUNG CANCER BY PCR-PIRA, DOT-BLOT HYBRIDIZATION AND DIRECT SEQUENCING

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The *K-ras* gene mutations at codon 12 have been analyzed in DNA extracted from paraffin embedded lung cancer tissue from 50 patients. *K-ras* gene exon I was amplified by polymerase chain reaction and the point mutation at codon 12 was determined by primer-introduced restriction analysis (PIRA) and by mutant allele specific oligonucleotide (MASO) probe hybridization. Point mutation at codon 12 was detected in 14 cases (28%) by PCR-PIRA and 5 cases (10%) by MASO probe hybridization. The nucleotide change in these PCR products were then identified by direct sequencing. Eleven cases (22%) harboured the following mutations from the normal (GGT, glycine): TGT (cysteine) 5 cases, GTT (valine) 3 cases, GCT (alanine) 2 cases, and GAT (aspartic

acid) one case. The mutation in both cancerous and its normal counterpart tissue was found in one positive case (TGT, cysteine). Among the 17 cases, 3 (18 %) patients with squamous cell carcinoma and 8 out of 21 (38%) with adenocarcinoma exhibited the point mutation. No such mutations were found in 11 patients with the other histological types (5 cases of giant cell carcinomas, 2 carcinoid tumors, 2 bronchioalveolars, 2 undifferentiated carcinomas and one large cell carcinoma). In addition, point mutations were found in 28 % of patients (9 out of 32 cases) who had a past history of tobacco smoking and only in 11 % of non-smokers (2 out of 18 cases).

Acknowledgement : This work was supported by China Medical Board of New York, Inc. (USA).

Presented at : International Symposium Workshop on Epidemiology and Prevention of Cancer, Bangkok, November 2-5, 1998.

p53 GENE MUTATIONS IN NON-SMALL CELL LUNG CANCER FROM THAI PATIENTS

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Paraffin embedded tissues from twenty-two Thai patients with non-small cell lung cancer were studied for p53 gene mutations in exon 5 to 8 using polymerase chain reaction and thermal cycle sequencing. Results showed that point mutations in this region

of p53 gene were present in 3 cases. One harboured the base change from GAC to AAC at codon 281, changing amino acid from aspartate to asparagine, whilst the other two cases were transversion of AAA (lysine) to ACA (threonine) at codon 292. All subjects with p53 mutation had a past history of tobacco smoking.

Submitted to J Med Assoc Thai 1998.

GENETIC INSTABILITY OF MICROSATELLITES IN MOST NON-SMALL CELL LUNG CANCER CAUSED BY TOBACCO SMOKING

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Genetic alterations at 12 dinucleotide repeat loci located on human chromosomes 2, 3, 12, and 17 have been analyzed in non-small cell lung cancer from Thai patients by PCR-base assay followed by polyacrylamide gel electrophoresis and autoradiography. Twelve out of 18 cases (67%) harbored the microsatellite alterations. Single locus change was detected in 4 tumors, while eight other tumors present two or more loci changes. Among of the 18 cases, 10 (55%)

patients had a past history of tobacco smoking, of whom 9 (90%) were in the group with microsatellite alterations, whereas the non-smokers, 3 (38%) had these alterations. The result indicated that microsatellites DNA may use as biomarker for diagnosis of lung cancer.

Acknowledgement : This work was supported by The Thailand Research Fund.

Presented at : The 29th World Conference of IUATLD/ UICTMR, Bangkok, November 23-26, 1998.

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CURRENT RESEARCH ACTIVITIES

1. Malaria: Histopathologic and electronmicroscopic studies on various tissues and organs in humans
2. Pathogenic effects of cytokines and nitric oxide in cerebral malaria
3. Liver biopsy; studies of liver diseases in the tropic : Histopathologic and electronmicroscopic studies e.g. scrub typhus, salmonellosis, hepatitis, malaria
4. Liver pathology in AIDS
5. Evaluation of stool samples in HIV infected patients
6. Opportunistic infections in AIDS

ABSTRACTS

ELECTRON-MICROSCOPIC EXAMINATION OF *RICKETTSIA TSUTSUGAMUSHI* INFECTED HUMAN LIVER

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A 33 year-old Thai woman was diagnosed with scrub typhus infection according to clinical symptoms, eschar lesions compatible with the disease, and specific antibody to *Rickettsia tsutsugamushi* detected

by indirect immunoperoxidase. Percutaneous transhepatic needle biopsies were taken before and 7 days after treatment with tetracycline to study the pathology of the liver. The liver tissue was evaluated by light microscopy, using H & E and Pinkerton's stains, and by transmission electron microscopy (TEM). Before treatment it showed reactive hepatitis, *Rickettsia* organisms within the hepatocytes and sinusoids detected by Pinkerton's stain appeared as tiny bright-red organisms. By TEM, the rod-shaped

double-membrane Rickettsiae appeared intact in the cytoplasm of Kupffer's cells and hepatocytes. After tetracycline treatment, moderate levels of acidophilic and ballooning liver cells were observed. The degree of cytoplasmic organelle damage varied, including fatty metamorphosis, depletion of glycogen granules, loss of the mitochondrial cristae, dilatation of endoplasmic reticulum and cytoplasmic vacuolation. Rickettsia organisms cannot be visualized by Pinkerton's stain but were detected by TEM, in markedly vacuolated hepatocytes, in congested sinusoids and in Kupffer's cells. Intranuclear *Rickettsia* were discovered in the endothelial nucleus, showing various degrees of injury. Some were mildly degenerated, while others exhibited clumping of nucleoprotein at the cytoplasm periphery and large vacuolation centrally. Many indented organisms were found, and binary fission during Rickettsiae multiplication was always affected. Electron-microscopic examination of hepatic injury associated with scrub typhus is rare. This is the first

ultrastructural localization of Rickettsiae in the infected human liver.

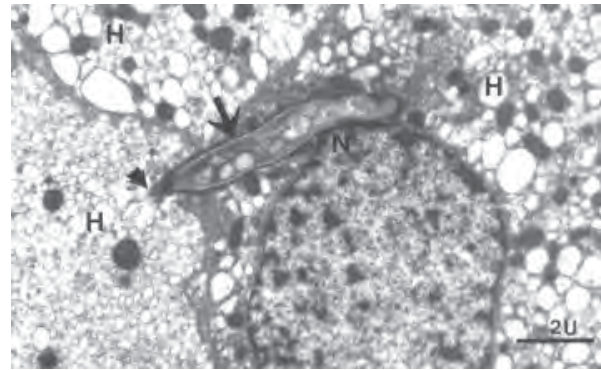


Figure 1 Electronmicrograph of three fatty metamorphosis hepatocytes(H). A perinuclear *R. tsutsugamushi* (→) in close contact to the nuclear membrane (N).

This study was supported by the Faculty of Tropical Medicine, Mahidol University.

Published in: Trop Med Inter Health 1998; 3:242-8.

INDUCIBLE NITRIC OXIDE SYNTHASE EXPRESSION IN THE BRAIN TISSUES OF CEREBRAL MALARIA

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Cerebral malaria caused by severe *Plasmodium falciparum* infection in human is still an important health problem in developing countries. The etiology of cerebral malaria is unclear. Role of cytokine induced nitric oxide (NO) in pathogenesis of severe malaria has been controversial due to the dual effects of NO in protective immunity against the malaria parasite or in enhancement of disease pathogenesis. In this study, inducible nitric oxide synthase (iNOS) was detected in the brain tissues of cerebral malaria patients, in neurons, glia cells, and endothelial cells of large and small vessels by immunohistochemical staining. Intensity of the iNOS staining and number of positive cells was associated with the severity of histopathologic changes in the brain tissues. Cerebral tissues from 2 patients, recovered from cerebral malaria but died because of renal failure and pneumonia, 1 dengue haemorrhagic fever patient, and 3 car accident victims showed only weakly or no

staining of iNOS. This study indicate proinflammatory cytokines may associate with pathogenesis of cerebral malaria via the induction of NO in the brain.

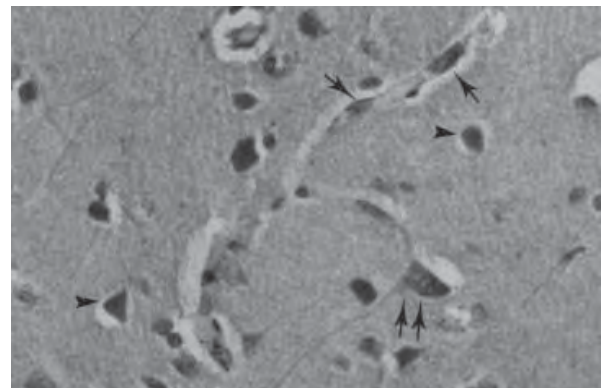


Figure 2 Brain tissue section of a cerebral malaria patient shows inducible nitric oxide synthase (iNOS) immunoreactivity in endothelial cells (arrow), neurons (double arrows) and glial cells (arrow head), (400X).

This study was supported by the Thailand Research Fund 1997-1999 and Grant from Mahidol University 1998.

Presented in: Joint International Tropical Medicine Meeting 1998 and The Fourth Chamlong-Tranakchit Harinasuta Lecture 20 - 21 Aug 1998.

INTRACEREBRAL HEMORRHAGE DUE TO NOSOCOMIAL ASPERGILLOSIS FOLLOWING NEUROSURGERY

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We document a unique case of nosocomial aspergillosis following neurosurgery in a 10 year old

girl. She presented with intracerebral hemorrhage after three weeks of operation for evacuation of craniopharyngioma. To date, this is the first case of intracerebral hemorrhage due to nosocomial aspergillosis after neurosurgery.

Submission to Pathology.

LIVER PATHOLOGY IN AIDS : A PRELIMINARY STUDY

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We attempted to study the liver pathology in people dying from AIDS. Liver necropsy was performed on 38 cases whose fatality was related to AIDS. Thirty seven cases gave good diagnostic yield while liver tissue was not obtained in one case. Infectious diseases detected were cryptococcosis which had the highest prevalence (27.0%), tuberculosis (13.5%) and penicillosis (2.7%). Among the non-infectious lesions, fatty changes were the most prevalent finding (24.3%). Other interesting findings were: one case of hepatocellular carcinoma, two cases of chronic active hepatitis, one case of reactive hepatitis, one case of severe cirrhosis, one case with increased fibrosis at the portal tract and one case of granuloma of undetermined cause. This preliminary study can be beneficial to clinicians to be aware of the opportunistic infections prevalent in Thailand.

This study was supported by the Ministry of University Affairs 1997-1998.

Presented in: Joint International Tropical Medicine Meeting 1998 and The Fourth Chamlong-Tranakchit Harinasuta Lecture, 20 -21 Aug. 1998.

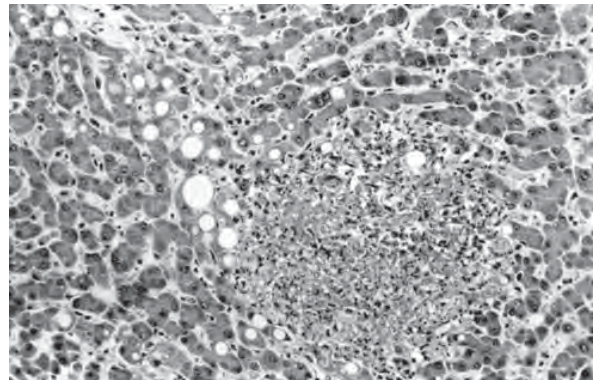


Figure 3 Liver of AIDS patients who died of Mycobacterium tuberculosis. Note spotty necrotic area. Numerous acid fast bacilli are detected in the necrotic area (400X, H&E stain)

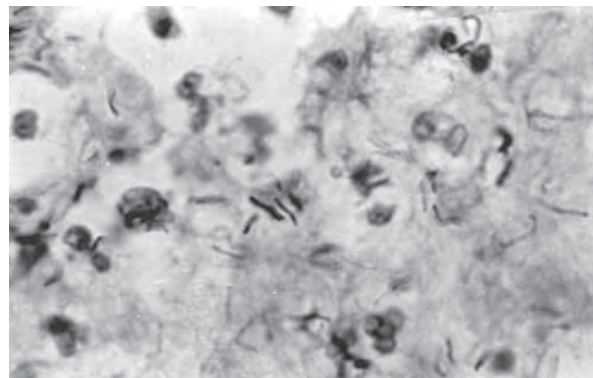


Figure 4 Acid fast bacilli in necrotic area (1,000X, Acid fast bacilli stain)

OPPORTUNISTIC PROTOZOA IN STOOL SAMPLES FROM HIV- INFECTED PATIENTS

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A retrospective study of stool samples of HIV-infected patients from January 1994 to December 1995 submitted to the Department of Tropical Pathology was analyzed. There were twenty-two cases, all of which presented with chronic diarrhea. Results showed that 50% were infected with protozoa. These include *Microsporidium* (27.27%), *Cryptosporidium* (9.09%), *Isospora belli* (4.54%) and *Giardia intestinalis* cysts (9.09%). Other infections were *Candida* sp, *Stongyloides stercoralis* larva and *Opisthorchis viverrini* ova. The data stress the importance of opportunistic protozoa in the HIV-infected patients. Awareness of their existence of the disease is an important area with increasing number of HIV infected patients for early detection and proper treatment.

Published in : Southeast Asian J Trop Med Public Health 1998; 29:31-4.

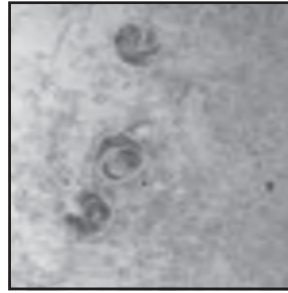


Figure 5 *Microsporidium* spore, 1-3 μm with red belt stripe (1,000X)



Figure 6 *Cryptosporidium* oocyst, 4-5 μm with 4 sporozoites (1,000X)

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CURRENT RESEARCH ACTIVITIES

The Department has undergone considerable development in research, teaching, and services. The Department's titles of current research activities are as follows.

Intestinal parasites :

(1) *Giardia lamblia* infection in an orphanage : prevalence and reinfection.

(2) Survey of intestinal parasitic infection in Cholapratan School's pupils.

(3) Efficacy of praziquantel for treatment of *Hymenolepis nana* infection in Thai children.

Dengue virus :

Prospective evaluation of seven dengue assays.

Diarrheal diseases :

Effect of milk-cereal mixtures and rice powder salt solution on acute diarrhea in young children.

Vaccine :

(1) A phase IV, observed-blind, randomized, controlled trial to evaluate safety, tolerability and immunogenicity of the Chiron acellular pertussis vaccine combined with diphtheria and tetanus toxoids (DTaP), as compared to a licensed whole-cell pertussis vaccine combined with diphtheria and

tetanus toxoids (DTwP), when administered to healthy Thai infants at 2, 4 and 6 months of age.

(2) Safety and immunogenicity of tetravalent dengue vaccine formulations in Thai adult volunteers.

Other infectious diseases :

Incidence and clinical manifestation of influenza in assistant nurse students of Faculty of Tropical Medicine, Mahidol University.

ABSTRACTS

EFFICACY AND PHARMACOKINETICS OF ATOVAQUONE AND PROGUANIL IN CHILDREN WITH MULTIDRUG-RESISTANT *PLASMODIUM FALCIPARUM* MALARIA

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A trial was conducted in 32 Thai children with uncomplicated multidrug-resistant falciparum malaria to assess the efficacy, safety and pharmacokinetics of atovaquone and proguanil; plasma concentrations of atovaquone, proguanil and its metabolite, cycloguanil, were measured in a subset of 9 children. The children received atovaquone (17 mg/kg/d for 3 d) plus proguanil (7 mg/kg/d for 3 d). Twenty-six children who had only *Plasmodium falciparum* infection and remained in hospital for 28 d were assessed for drug efficacy. The combination regimen produced a cure rate of 100%. Parasite and fever clearance times were 47 h (range 8-75) and 50 h (range 7-111), respectively. Atovaquone and proguanil were rapidly absorbed, with median time to peak concentrations of 6 h (range 6-

24) and 6 h (range 6-12), respectively. Peak concentrations of cycloguanil were achieved between 6 and 12 h (median 6) after administration of proguanil. Mean peak plasma concentration of atovaquone on day 3 was 5.1 (g/mL (SD=2.1)). The day 3 mean peak plasma concentration of proguanil was 306 ng/mL (SD=108) compared with 44.3 ng/mL (SD=27.3) for cycloguanil. Mean values for the AUC (area under plasma concentration-time curve) were 161.8 (g/mL h (SD=126.9) for atovaquone, 4646 ng/mL h (SD=1226) for proguanil, and 787 ng/mL h (SD=397) for cycloguanil. Terminal elimination half-lives of atovaquone, proguanil and cycloguanil were estimated as 31.8 h (SD=8.9), 14.9 h (SD=3.3) and 14.6 h (SD=2.6), respectively. No major adverse effect was attributable to the study drugs. Atovaquone/proguanil combination is safe and highly effective, and should be especially valuable for treatment of multidrug-resistant falciparum malaria.

Published in: Trans Roy Soc Trop Med Hyg 1998; 92: 201-6.

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CURRENT RESEARCH ACTIVITIES

The Department has had a considerable number of significant achievements in the development of research, teaching, and services during the past 10 years, particularly in the use of many radioisotopes in tropical diseases and related areas. The Department's current activities are as follows:

In research, there has been an extensive investigation of nutritional problems and associated diseases, such as the measurement of vitamin B₁₂ and folic acid levels, and vitamin B₁₂ binding proteins or transcobalamin in serum and red blood cells of patients with blood diseases, malaria, G-6-PD deficiency, typhoid fever.

In rheology, changes in blood viscosity have been studied in humans consuming garlic capsules. The investigation includes plasma trapping, ¹³¹I labelling, and filterability for an exquisite prevention of blocking of blood vessels.

In cancer patients, a study of serum glutathione-S-transferase PI (GST-II) has been established for changing pattern in progress in patients of lung cancer and cancer of the gastrointestinal tract using ELISA technique.

In *Deinococcus radiodurans*, endurance of this bacteria to UV, 60 ionizing radiation, and mitomycin C was investigated in the Japan Atomic Energy Research Institute, Takasaki, Japan after it was found

to be resistant to the nuclear power plant water cooling system and in radiated cannery food.

In teaching, the staff of the Department have provided knowledge of radioisotopes for basic nuclear technology and research for students and researchers. Furthermore, staff have lectured students in this Faculty and other faculties of Mahidol University as co-lecturers in many subjects including an enterprise with the Department of Radiological Science, Ramathibodi Hospital for Nuclear Medicine in the Tropics. The subjects which are involved in co-operation between the Department and others include Introduction to Research, Special Topics in Tropical Radioisotopes, Protozoology, Clinical Microscopy, Practical Immunology, Microbiology and Immunology, Advanced Helminthology, Basic Research Methodology, the Principles of Scientific Research, Essential Anatomy and Physiology of Tropical Diseases, and Practical Application of Atomic Energy for Peaceful Use in Environmental and Nutritional Research (SIRA609)

In services, the Department has steadily opened services to the public in the measurement of levels of (1) vitamin B₁₂ (2) folic acid (3) transcobalamin. These activities have also been provided for the staff and students of the Faculty of Tropical Medicine including other staff of the University.





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The development of vaccines against a number of infectious agents is reaching the point where evaluation of reactogenicity, immunogenicity, and protective efficacy must be evaluated in humans. These critical steps in vaccine development are best done initially in a controlled clinical facility where maximum information can be obtained from each study and where risks to study subjects or to the public can be prevented or limited.

BACKGROUND & RATIONALE OF ESTABLISHMENT

In spite of advancement in medical technology and therapeutics, infectious diseases including diarrhoeal diseases still cause health problems with high morbidity and mortality, particularly in developing tropical countries. To achieve effective control of the diseases, new and better tools for prevention including vaccines are needed. Vaccine development and implementation has been considered of vital importance.

Recognizing the urgent need of another controlled clinical facility for evaluation of reactogenicity and protective efficacy of newly developed vaccines against infectious agents in human, the World Health Organization Special Programme on Control of Diarrhoeal Diseases supported the establishment of such a facility in the tropics, where diarrhoeal diseases are endemic and the vaccines specifically needed are different from Western countries. With the initiation of Professor Dr.Natth Bhamarapavati, the former Rector of Mahidol University (MU), the Vaccine Trial Centre (VTC) was then set up at the Faculty of Tropical Medicine, Mahidol University, Bangkok in February 1984 with the approval of the Ministry of Public Health, Thailand.

The VTC is a clinical facility in the Faculty of Tropical Medicine (FTM), Mahidol University for testing newly developed vaccines which reach the step where evaluation in human volunteers is needed.

Individual scientists at any national or international institution may have their vaccines tested at this Centre. It is a joint responsibility of Mahidol University and the Ministry of Public Health (MOPH) and operated by the Faculty of Tropical Medicine on their behalf. The establishment of the Centre was started in February 1984, however, the full operation was possible around September-October 1986 and the first admission of volunteers into the ward was on the 3rd



November 1986. The VTC Bangkok, is the first and the only facility of its kind in Thailand, in the Region and perhaps also in the developing countries. The advantage of conducting vaccine trials at this Centre is that the studies will be on person residing in an area where the vaccines are going to be utilized most. The knowledge gained will benefit vaccine development and thus lead to effective control of infectious diseases in developing countries.

PHYSICAL FACILITIES

The Centre occupies the tenth and eleventh floor of the Chamlong Harinsuta Building of the Faculty of Tropical Medicine with a total area of 648 square meters:

A. Self-contained clinical facilities on the 10th floor are comprised of:

- twenty bed isolation ward
- sufficient space for recreational activities
- nursing section
- doctor's room and quarters
- laboratories

B. Outpatient unit on the 11th floor includes:

- lecture room
- recruitment and screening of volunteers
- follow-up facilities



VACCINE PROJECT

AIDSVAX

A PHASE I/II TRIAL TO EVALUATE THE SAFETY AND IMMUNOGENICITY OF AIDSVAX™ B/E VACCINE IN BANGKOK, THAILAND

To evaluate the safety and immunogenicity of three different doses of AIDSVAX™ B/E Vaccine (100,300 or 600 µg of each antigen at 0,1,6 and 12 months. It is a collaborative study between VTC and Bangkok Metropolitan Administration.

OVERVIEW

This study is an open label trial of the safety and immunogenicity of AIDSVAX™ B/E VACCINE in Thailand. A total of 90 HIV-1 uninfected individuals will receive AIDSVAX™ B/E Vaccine at 0,1,6 and 12 months : 30 subjects each will receive 100 µg, 300 µg and 600 µg of each antigen for each of the four injections. All subjects will be evaluated for safety and immunogenicity at certain timelines.

We, as a part of Bangkok Vaccine Evaluation Group, will conduct the phase III efficacy trial of AIDSVAX™ B/E VACCINE beginning in the fourth quarter of 1998.

THAI E

A PHASE I/II, DOUBLE BLIND, PLACEBO CONTROLLED STUDY OF THE CHIRON HIV THAI E GP120/MF59 VACCINE ADMINISTERED ALONE OR COMBINED WITH THE CHIRON HIV SF2 GP120 ANTIGEN IN HEALTHY HIV SERONEGATIVE THAI ADULTS

As one of the sites in Thai AIDS Vaccine Evaluation Group we are evaluating and comparing the safety and Immunogenicity of the three doses of the Thai E gp120/MF59 vaccine alone or combined with one of two doses of SF2 gp120/MF59 antigen. We are also evaluating the potential interaction between these antigens, the Thai E gp120 antigen dose groups and the SF2 gp120 antigen dose groups.

FUTURE PLANS

A Phase I/II Trial of Pasteur Merieux Connaught (PMC) Live Recombinant ALVAC-HIV (vCP1521) as a Priming vaccination and to be followed by With VaxGen gp120 B/E (AIDSVAX™B/E) in Thai HIV-Seronegative Adults as one of the four sites of Thai AIDS Vaccine Evaluation Groups (TAVEG.)

ABSTRACTS

CLINICAL RESPONSE TO HIV THAI E / MF59 VACCINE ADMINISTERED ALONE OR COMBINED WITH SF2 GP 120 ANTIGEN IN HEALTHY VOLUNTEERS

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Objective: To determine the safety of three doses of HIV Thai E gp120/MF59 vaccine alone or combined with SF2 gp 120 antigen in healthy HIV-1 seronegative Thai adults.

Design: Open-labeled, dose escalating study.

Method: Groups of three healthy HIV seronegative volunteers were sequentially blocked enrolled to one of 4 antigen/dose combination: 25 ug of Thai E gp120/MF59 (Group I), 25 ug of Thai E gp120/MF59+25 ug SF2 gp120/MF59 (Group II), 100 ug of Thai E gp120/MF59 (Group III) and 100 ug of

Thai E gp120/MF59+50 ug SF2 gp120/MF59 (Group IV). Sequential enrollment to each group was separated by 48 hrs and required that the preceding group to be free of serious reactogenic reactions. Immunizations were given at 0, 1, 6 months. All volunteers were evaluated 24-48 hours after vaccination and were required to record daily symptoms for 6 days post immunization. Up to the time of submission to abstract, only two doses of vaccination have been administered.

Results: Reported local and systemic symptoms by vaccine dose and number of vaccinations.

Conclusion: Thai E gp120/MF59 vaccine administered alone or combined with SF2 gp 120 antigen appears to be safe. No serious adverse events have been observed following two immunization.

	Group I		Group II		Group III		Group IV	
	1 st Vac	2 nd Vac	1 st Vac	2 nd Vac	1 st Vac	2 nd Vac	1 st Vac	2 nd Vac
Pain at injection site	2/3	1/3	3/3	3/3	3/3	3/3	3/3	3/3
Warmth to injection site	1/3	0/3	0/3	0/3	2/3	1/3	1/3	1/3
Malaise	0/3	0/3	1/3	2/3	0/3	1/3	1/3	0/3
Fever (> 38 OC)	0/3	0/3	0/3	1/3	0/3	0/3	0/3	0/3

Presented at: 12th World AIDS Conference Geneva June 28 - July 3, 1998.

ADVANCING AIDSVAX™ TO PHASE III. SAFETY, IMMUNOGENICITY AND PLANS FOR PHASE III.

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AIDSVAX™, a possible vaccine to protect against HIV-1 infection, is slated to begin phase III efficacy studies in 1998. It has been tested for potential efficacy in chimpanzees, tested for safety and immunogenicity in human clinical studies, and is poised to enter Phase III efficacy studies. Four candidate vaccines, each with a different envelope protein antigen or combination of antigens, have been produced in alum formulations. In both design and clinical testing, AIDSVAX™ has an excellent safety profile. Since these highly purified proteins were prepared using recombinant DNA technology, there is no possibility of these vaccines causing HIV infection.

Having been received by over 1200 people, the only side effects attributable to AIDSVAX™ have been local pain and inflammation at the injection site. After immunization, essentially all recipients developed a robust antibody response, including binding and neutralizing antibodies. The neutralizing antibodies peaked after a 12 month boost. Excellent memory is induced. Given the evidence that AIDSVAX™ is likely to protect individuals from the HIV virus, Phase III trials of two bivalent formulations are planned. One trial will use a bivalent subtype B formulation. This trial is slated for North America and will involve 500 men who have sex with men and heterosexual discordant couples. The other study will use a bivalent subtype B/subtype E formulation. This trial is slated for Thailand and will involve intravenous drug users. Both studies will be randomized, double-blinded and placebo controlled. The volunteers will be followed for three years. The endpoints of the studies are infection, as defined by seroconversion to standard diagnostic tests, and viral load, as defined by commercial PCR tests.



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The Wellcome-Mahidol University, Oxford Tropical Medicine Research Programme was initiated in 1979 to study the pathophysiological mechanisms, prevention and treatment of severe tropical infections including falciparum malaria, rabies and melioidosis.

The clinical work of the unit takes place in three up-country locations;

- in Mae Sot Provincial Hospital (studies of the pathophysiology and treatment of falciparum malaria),
- in the camps for displaced persons of the Karen ethnic minority on the north-western Thai-Myanmar border (studies of the epidemiology, prevention and treatment of malaria),
- in Sappasitprasong Hospital Ubon Ratchatani (study of melioidosis and fungal infections in patients with AIDS).

The current research activities of the unit on malaria include studies of pathophysiological mechanisms in severe malaria, descriptions of the pharmacokinetic and pharmacodynamic properties of the antimalarial drugs, and studies of the epidemiology, prevention and treatment of malaria in

the area of low or unstable transmission of the western border.

This year we conducted studies of retinal capillary blood flow in severe malaria, comparative bioactivities of different artemisinin formulations, and mechanisms of parasite clearance. The Shoklo Malaria Research Unit conducted studies with artemether-lumefantrine and atovaquone-proguanil and large scale studies of malaria in pregnancy and young children.

Studies of melioidosis include a large prospective clinical description of the disease, and a series of clinical and microbiological investigations to improve diagnosis and management of this important infection. This year we completed studies of antimicrobial maintenance treatment, and began work on phagocytosis and killing.

Studies of fungal infections include a pharmacokinetic-pharmacodynamic evaluation of different treatment strategies in cryptococcal meningitis, and the development of improved methods to diagnose penicilliosis. This year we conducted studies on the pharmacokinetics and pharmacodynamics of different amphotericin B formulations.

ABSTRACTS

FACTORS AFFECTING THE PHARMACOKINETICS OF PARENTERAL CHLORAMPHENICOL IN ENTERIC FEVER

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Chloramphenicol pharmacokinetics were studied in 29 Nepalese adults diagnosed with uncomplicated enteric fever and randomized to receive succinate ester 30 mg/kg i.v. or i.m. Serial plasma concentrations of chloramphenicol, and iothalamate (to estimate glomerular filtration rate), antipyrine (hepatocellular function) and indocyanine Green (liver blood flow) were measured by HPLC and kinetic parameters estimated by non-compartmental analysis. In culture-positive patients (n=16), mean residence times (MRTs) and steady-state volumes of distribution (Vdss) for i.v. chloramphenicol (mean (S.D.); 4.9 (0.9 h and 1.9 (0.8 L/kg; n=7) were less than after i.m. chloramphenicol (12.3 (7.3 h and 3.7 (2.5 L/kg; n=9; P < 0.05), with a higher peak plasma concentration after i.v. administration (16.2 (9.1 versus 7.8 (3.6 mg/L; P < 0.05); plasma clearance (Clp) was similar in the two groups (368 (172 and 310 (224

mL/kg/min after i.v. and i.m. respectively). In 17 patients examined during convalescence, MRT and Vdss were less than in acute illness regardless of the route chloramphenicol administration. There were similar changes in chloramphenicol kinetic parameters in culture-negative patients. Antipyrine Clp and liver blood flow correlated weakly with chloramphenicol Clp in culture-positive patients (P ≤ 0.1) and were higher in convalescence; no such associations were seen for iothalamate Clp. These data indicate that i.v. chloramphenicol produces peak plasma concentrations which are on average twice those after i.m. injection of the same dose, due principally to a smaller Vdss. Clp is uninfluenced by route of administration and is determined more by hepatic metabolism than renal excretion. Intramuscular treatment may result in sub-therapeutic chloramphenicol concentrations initially, but continued regular iv dosing is more likely to produce levels at which bone marrow toxicity occurs.

Wellcome-Mahidol University, Oxford Tropical Medicine Research Programme funded by the Wellcome Trust of Great Britain.

Published in : J Antimicrob Chemother 1996; 40: 91-8.

IN VIVO REMOVAL OF MALARIA PARASITES FROM RED BLOOD CELLS WITHOUT THEIR DESTRUCTION IN ACUTE FALCIPARUM MALARIA

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During acute falciparum malaria infection, red blood cells (RBC) containing abundant ring-infected erythrocyte surface antigen (Pf 155 or RESA), but no intracellular parasites, are present in the circulation. These RESA-positive parasite negative RBC are not seen in parasite cultures *in vitro*. This indicates that in acute falciparum malaria there is active removal of intraerythrocytic parasites by a host mechanism *in*

in vivo (probably the spleen) without destruction of the parasitized RBC. This may explain the observed disparity between the drop in hematocrit and decrease in parasite count in some hyperparasitaemic patients. The fate of these "once parasitized" RBC *in vivo* is now being investigated.

Wellcome-Mahidol University, Oxford Tropical Medicine Research Programme funded by the Wellcome Trust of Great Britain.

Published in : Blood 1997; 5: 2037-40.

ORAL FLUOROQUINOLONES FOR MAINTENANCE TREATMENT OF MELIOIDOSIS

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Ciprofloxacin (20 mg/kg/d) or ofloxacin (12 mg/kg/d) given for a median of 15 weeks (range 12-40) were used for maintenance treatment of 57 adult patients with melioidosis. The median duration of follow-up in the 45 patients who complied with treatment and were followed for at least 6 months was 28 months (range 6-65). Fluoroquinolone treatment was well tolerated. There were 13 treatment failures (5 failures to respond, 8 relapses), a failure rate of 29% (95% confidence interval 17-43%). The median time to treatment failure was 7 months (range 2-26). These results are inferior to those with courses lasting 20 weeks of amoxycillin/clavulanic acid or the combination of chloramphenicol, doxycycline and trimethoprim/sulphamethoxazole, and suggest that the fluoroquinolones should be reserved as third line agents, and not used for the maintenance treatment of melioidosis unless there is resistance to,

or intolerance of, the other available antimicrobial compounds.

Medicine and Hygiene 1997; 91: 599-601.

Wellcome-Mahidol University, Oxford Tropical Medicine Research Programme funded by the Wellcome Trust of Great Britain.

Published in : Trans Roy Soc Trop Med Hyg 1997;91:599-601.



Sappasitprasong Hospital, Ubon Ratchathani Site of Melioidosis studies

LACK OF A SIGNIFICANT ADVERSE CARDIOVASCULAR EFFECT OF COMBINED QUININE AND MEFLOQUINE THERAPY FOR UNCOMPLICATED MALARIA

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Quinine dihydrochloride (10 mg salt/kg infused over one hour) and mefloquine (15 mg base/kg) were given simultaneously to 13 adults with uncomplicated falciparum malaria. Supine and standing blood pressures were recorded and the electrocardiogram monitored. Plasma concentrations of the 2 drugs were similar to those reported previously for the 2 compounds given individually to a similar group of patients. Although postural hypotension was common (6 cases before treatment and 7 after) and the electrocardiogram QT_c interval was prolonged by a mean of 12% (SD=8) following drug treatment, there was no evidence of a clinically significant

cardiovascular pharmacodynamic interaction between these 2 structurally related antimalarial compounds.

Wellcome-Mahidol University, Oxford Tropical Medicine Research Programme funded by the Wellcome Trust of Great Britain.

Published in : Trans Roy Soc Trop Med Hyg 1997; 91: 694-6.

PROGNOSTIC SIGNIFICANCE OF REDUCED RED BLOOD CELL DEFORMABILITY IN SEVERE FALCIPARUM MALARIA

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Severe falciparum malaria is associated with microvascular obstruction resulting from sequestration of erythrocytes containing mature stages of the parasite. Since reduced red blood cell deformability (RBC-D) can contribute to impaired microcirculatory flow, RBC-D was measured in 23 patients with severe falciparum malaria (seven of whom subsequently died), 30 patients with uncomplicated malaria, and 17 healthy controls. The RBC-D, measured by ektacytometry, was significantly reduced in severe

malaria and was particularly low in all fatal cases. At a low shear stress of 1.7 Pascal (Pa), a red blood cell elongation index less than 0.21 on admission to the hospital predicted fatal outcome with a sensitivity of 100% (confidence interval [CI] = 59-100%) and a specificity of 88% (CI = 61-98%). The reduction in the RBC-D appeared to result mainly from changes in unparasitized erythrocytes. Reduced deformability of unparasitized red blood cells in severe malaria may contribute to impaired microcirculatory flow and a fatal outcome in severe falciparum malaria.

Wellcome-Mahidol University, Oxford Tropical Medicine Research Programme funded by the Wellcome Trust of Great Britain.

Published in : Am J Trop Med Hyg 1997;57(5): 507-11.

ARTESUNATE/MEFLOQUINE TREATMENT OF MULTI-DRUG RESISTANT FALCIPARUM MALARIA

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On the western border of Thailand, in an area endemic for multi-drug resistant *Plasmodium falciparum* malaria, therapeutic responses were assessed in 1967 patients with uncomplicated falciparum malaria treated with 3 d of artesunate (total dose 12 mg/kg) plus mefloquine (total dose 25 mg/kg). The regimen was well tolerated and resulted in a rapid clinical response; within 48 h, 96% of patients were aparasitaemic and 94% were afebrile. After correcting for reinfections, the cure rate by day 42 was 89% (95% confidence interval [95% CI] 87-91%). Three independent factors were found to predict recrudescence: age <14 years (adjusted hazards ratio [AHR] = 1.6, 95% CI 1.1-2.3), initial parasitaemia greater than 40,000/ μ L (AHR = 1.6,

95% CI 1.2-2.2), and pure *P. falciparum* infections (AHR = 1.8, 95% CI 1.3-2.7). These 3 factors combined accounted for 62% of all treatment failures. Patients who received mefloquine on admission with a high admission parasitaemia (>40,000/ μ L) had a three-fold (95% CI 1.3-7) risk of subsequent recrudescence compared with those who received their mefloquine on the second or third day (P=0.01). There has been no decline in the efficacy of the 3 d artesunate plus mefloquine regimen since it was introduced in 1992. This regimen is safe, well tolerated, and highly effective in the treatment of multi-drug resistant falciparum malaria.

Wellcome-Mahidol University, Oxford Tropical Medicine Research Programme funded by the Wellcome Trust of Great Britain.

Published in : Trans Roy Soc Trop Med Hyg 1997; 91: 574-7.

ARABINOSE ASSIMILATION DEFINES A NONVIRULENT BIOTYPE OF *BURKHOLDERIA PSEUDOMALLEI*

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Two distinct types of *Burkholderia pseudomallei*, differentiated by the ability to assimilate L-arabinose but with similar morphologies and antigenicities, can be isolated from soil in Thailand. Approximately 25% of soil isolates from northeast Thailand were arabinose assimilators (Ara⁺), but in 1,200 sequentially studied patients, only arabinose “nonassimilators” (Ara⁻) caused melioidosis ($P < 0.0001$). In a murine model, there was a striking difference in virulence between Ara⁻ and Ara⁺ *B. pseudomallei*. The mean (standard deviation) 50% lethal dose (LD₅₀) inoculum for Ara⁻ isolates was 182 (111) CFU/mouse compared with approximately 10⁹ CFU/mouse for Ara⁺ soil isolates. There was no significant difference between the LD₅₀s for clinical and soil Ara⁻ isolates. All attempts to convert the biochemical phenotype by selective culture failed,



Clinical discussions in Ubon Ratchathani

which suggests that the biotype is stable.

Wellcome-Mahidol University, Oxford Tropical Medicine Research Programme funded by the Wellcome Trust of Great Britain.

Published in : Infect Immun 1997; 65: 4319-21.

RIBOTYPE DIFFERENCES BETWEEN CLINICAL AND ENVIRONMENTAL ISOLATES OF *BURKHOLDERIA PSEUDOMALLEI*

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Burkholderia pseudomallei is isolated frequently from the soil in regions where the disease melioidosis occurs. However, recent surveys in Thailand have shown that the frequency of isolation of the organism from soil samples is not directly related to the incidence of melioidosis in an area. To determine whether strain populations of *B. pseudomallei* prevalent in soil are genotypically related to strains causing clinical disease, rRNA BamHI restriction fragment length polymorphisms (RFLP) of 139 soil environmental isolates and 228 human isolates were compared. Two groups of ribotype patterns were found. Group I comprised 37 different ribotype

patterns which were characterised by five to eight hybridisation bands of 2.8- > 23 kb. All of these ribotypes were identified among the clinical isolates, and 18 of them were also found in 59 environmental isolates. Group II was represented by 12 ribotypes found only in environmental strains. These ribotype patterns comprised one to five bands in the size range 9- > 23 kb. All but one of the 73 isolates in this group grew on a minimal medium supplemented with L-arabinose. In contrast, only 3% of the 66 isolates from the environment with group I ribotype patterns could utilise this sugar as their sole energy source. These findings suggest that *B. pseudomallei* strains that utilise arabinose constitute a population that is genetically distinct from other environmental and clinical strains.

Wellcome-Mahidol University, Oxford Tropical Medicine Research Programme funded by the Wellcome Trust of Great Britain.

Published in : J Med Microbiol 1997; 46: 565-670.

POOR EFFICACY OF ANTIMALARIAL BIGUANIDE-DAPSONE COMBINATIONS IN THE TREATMENT OF ACUTE, UNCOMPLICATED, FALCIPARUM MALARIA IN THAILAND

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Combinations of dapsones with proguanil or chlorproguanil have proved effective in the treatment of chloroquine-resistant falciparum malaria in Africa and for prophylaxis in Asia. These combination have not been used for treatment in areas with multi-drug-resistant parasites such as in Thailand. Combinations of dapsones (approximately 4 mg/kg) plus either proguanil (approximately 8 mg/kg; DP regimen; N=10) or chlorproguanil (approximately 1.4 mg/kg; DC regimen; N=16) were given once a day for 3 days to adult Thai patients with acute, uncomplicated, falciparum malaria. The two regimens were well tolerated and had no side-effects, but the cure rates, assessed at 28-day follow-up, were only 10% for DP

(60% with RI response and 30% with RII) and 14% for DC (29% with RI response and 57% with RII). The mean (S.D.) fever-clearance times in those patients who were cured (S) or whose infections recrudesced (RI response) were 103 (56) h for those given DP and 90 (42) h for those given DC. The corresponding parasite-clearance times were 83 (46) for DP and 53 (21) h for DC. *In vitro* susceptibility testing of isolates obtained both before treatment and at recrudescence demonstrated marked resistance to cycloguanil, dapsones, chloroquine and mefloquine. The results demonstrate that short-course treatment with dapsones plus either proguanil or chlorproguanil is ineffective for the treatment of falciparum malaria in Thailand.

Wellcome-Mahidol University, Oxford Tropical Medicine Research Programme funded by the Wellcome Trust of Great Britain.

Published in : *Ann Trop Med Parasitol* 1997; 91: 125-32.

ROSETTING CHARACTERISTICS OF UNINFECTED ERYTHROCYTES FROM HEALTHY INDIVIDUALS AND MALARIA PATIENTS

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Rosetting, defined as the binding of two or more uninfected red blood cells (RBC) to an infected RBC, occurs when malarial parasites mature, to trophozoites and schizonts, in the second half of their asexual development. Rosetting is believed to be an important factor in the development of cerebral malaria. In a series of studies to examine the characteristics of the uninfected RBC which contribute to rosetting, the ability of RBC from healthy donors to form rosettes was found to be greater in the cells of group A and B than in those of group O (P=0.05), and to decrease during storage under blood-bank conditions. Normal RBC exposed for (30 min to quinine, artesunate or artemether (each at 0.25 µg/ml) *in vitro* showed significantly decreased

rosetting. This effect could not be reversed by extensive washing followed by cultivation for another 24 h in drug-free medium. Mefloquine and pyrimethamine had no effect. Uninfected RBC from patients with uncomplicated or severe falciparum malaria exhibited a lower rosetting ability than RBC from healthy donors (P=0.01). The rosetting of uninfected RBC of all blood groups from patients with uncomplicated malaria decreased significantly within 2 h of the patients starting treatment with Qinghaosu derivatives (artesunate or artemether) and within 8 h of them starting quinine treatment. Similar effects were observed with uninfected RBC from patients with severe malaria after treatment with artesunate but not after quinine. The mechanisms underlying this potentially beneficial effect on RBC adherence are not known.

Wellcome-Mahidol University, Oxford Tropical Medicine Research Programme funded by the Wellcome Trust of Great Britain.

Published in : *Ann Trop Med Parasitol* 1998; 92: 45-6.

CHARACTERISTICS OF *PLASMODIUM VIVAX*-INFECTED ERYTHROCYTE ROSETTES

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To investigate the rosette formation properties of *Plasmodium vivax*, blood was sampled from 26 adult Thai patients admitted with acute *P. vivax* malaria and a predominance of trophozoite and schizont stages in their peripheral blood smears. In each case, *P. vivax*-infected cells formed spontaneous rosettes with two or more uninfected red blood cells. Rosette formation of *P. vivax* was dependent on the divalent cations (Ca²⁺/Mg²⁺) and was highly sensitive to trypsin and heparin, but, unlike *P. falciparum*, rosettes of *P. vivax* did not reform after removal of heparin. Plasma taken from patients with either acute

uncomplicated *P. falciparum* or *P. vivax* malaria reversed rosette formation of all *P. vivax* isolates whereas plasma from uninfected controls had no effect. There was a small but significant increase in rosette-reversing activity in plasma taken during the convalescent period ($P < 0.001$). The increment in reversal activity was significantly greater in plasma taken following recovery from *P. vivax* malaria compared with *P. falciparum* malaria. This suggests that *P. vivax* rosette reversal activity is antibody mediated and has both species-specific and cross-species components.

Wellcome-Mahidol University, Oxford Tropical Medicine Research Programme funded by the Wellcome Trust of Great Britain.

Published in : *Am J Trop Med Hyg* 1998; 59: 73-6.

ESTIMATING *PLASMODIUM VIVAX* PARASITAEMIA

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To investigate whether red blood cells infected with *P. vivax* are distributed evenly throughout the thin blood film, stained thin films were examined from 20 patients with acute *P. vivax* infections and >1% parasitaemia. The parasite counts from the tail of the films were significantly higher than those recorded in the head and middle parts of the slide; the median number of infected red blood cells per 5,000 cells ($n=20$) in the head of the slide was 81.5 (range 50-129), in the middle part it was 108 (range 57-146), and in the tail of the film it was 125 (range 67-176) ($P=0.001$). The median overestimation of the total

count defined as the tail count divided by (the sum of all 3 counts/3) was 11.4% (interquartile range [IQR] 8.4 to 22.1%, range 4 to 36%), and for the middle of the slide it was 1.2% (IQR -1.0 to 5.5%, range -17 to 11%). The counts from the head of the slide correspondingly underestimated the total by 14% (IQR 8.0 to 22.1%, range 3 to 34%). *P. vivax* counts should be made from the middle of the thin blood film, or corrected if morphology is adequately preserved only in the tail.

Wellcome-Mahidol University, Oxford Tropical Medicine Research Programme funded by the Wellcome Trust of Great Britain.

Published in : *Trans Roy Trop Med Hyg* 1998; 92: 176.

ENDOGENOUS INTERLEUKIN-10 MODULATES PROINFLAMMATORY RESPONSE IN *PLASMODIUM FALCIPARUM* MALARIA

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Tumor necrosis factor - α (TNF- α), interleukin

(IL)-1, and IL-6 are implicated in the pathogenesis of severe *Plasmodium falciparum* malaria. In this study, the effect of IL-10 on their production by peripheral blood mononuclear cells (PBMC) from acutely infected patients was examined. Exogenous IL-10 inhibited malarial antigen-induced cytokine production by reducing mRNA accumulation. Maximal inhibition occurred when IL-10 was added in the first

2 h of stimulation. Conversely, the addition of anti-IL-10 markedly enhanced TNF- α , IL-1 β , and IL-6 production. The effect was significantly greater on PBMC from patients with uncomplicated infection than PBMC from patients with severe disease. Kinetics studies showed that TNF- α , IL-6, and IL-1 β were produced within 2-4 h of stimulation, while IL-10 was first detectable after 8 h. These findings suggest that IL-10 counter-regulates the proinflammatory response to *P. falciparum*. Severe falciparum malaria

may be associated with an inadequate negative feedback response by IL-10.

Wellcome-Mahidol University, Oxford Tropical Medicine Research Programme funded by the Wellcome Trust of Great Britain.

Published in : *J Infect Dis* 1998; 178: 520-5.

CLINICAL FEATURES CANNOT PREDICT A DIAGNOSIS OF MALARIA OR DIFFERENTIATE THE INFECTING SPECIES IN CHILDREN LIVING IN AN AREA OF LOW TRANSMISSION

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The differentiation of malaria from other causes of fever in the absence of microscopy is notoriously difficult. Clinical predictors of malaria have been studied in an area of low and unstable transmission on the western border of Thailand. In 1527 children aged 2-15 years who were followed prospectively for 7 months, 82% (1254) had at least one febrile episode. Malaria caused 24% (301) of the first febrile episodes (*Plasmodium falciparum* 128, *P. vivax* 151, *P. malariae* 1, mixed infections with *P. falciparum* and *P. vivax* 21). Each malaria case was matched with the next child of similar age presenting to the dispensary with another cause of fever. Clinical symptoms or signs associated with a final diagnosis of malaria were: confirmed fever (>38°C) (odds ratio [OR] 1.6, 95% confidence interval [95% CI] 1.4-1.9), headache (OR 1.5, 95% CI 1.3-1.9), muscle and/or joint pain (OR 2.0, 95% CI 1.6-2.8), nausea (OR 1.7, 95% CI 1.4-2.3), clinical anaemia (OR 1.4, 95% CI 1.3-3.3), palpable spleen (OR 1.3, 95% CI 1.1-1.7), palpable liver (OR 1.4, 95% CI 1.1-2.1), absence of cough (OR 1.6, 95% CI 1.4-2.0), and absence of diarrhoea (OR 1.5, 95% CI 1.2-2.4). None of these signs alone or in combination proved a good predictor of malaria. The best diagnostic algorithms (history of fever and headache without cough, and history of fever with an oral temperature >38°C [sensitivity 51% for both, specificity 72 and 71%, respectively]) would result in prescription of

antimalarial drugs in 28-29% of the non-malaria febrile episodes, and only 49% of the true malaria cases. Thus half of the potentially life-threatening *P. falciparum* infections would not be treated. Although multivariate analysis identified vomiting, confirmed fever, splenomegaly and hepatomegaly as independent risk factors for a diagnosis of falciparum malaria, use of these signs to differentiate falciparum from vivax malaria, and thus to determine antimalarial treatment, was insufficiently sensitive or specific. Malaria diagnosis should be confirmed by microscopical examination of a blood slide or the use of specific dipstick tests in areas of low transmission where highly drug-resistant *P. falciparum* coexists with *P. vivax*.

Wellcome-Mahidol University, Oxford Tropical Medicine Research Programme funded by the Wellcome Trust of Great Britain.

Published in : *Trans Roy Soc Trop Med Hyg* 1998; 92: 45-9.

ARTEMISININ DERIVATIVES IN THE TREATMENT OF FALCIPARUM MALARIA IN PREGNANCY

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An artemisinin derivative (artesunate or artemether) was used for the treatment of multidrug-resistant *Plasmodium falciparum* malaria in 83 Karen pregnant women in Thailand; 55 women were treated for recrudescence following quinine or mefloquine, 12 for uncomplicated hyperparasitaemic episodes, and 16 had not declared their pregnancy when treated. The women were followed weekly until delivery. Artesunate and artemether were well tolerated and there was no drug-related adverse effect. Recrudescence within 42 d occurred in 16% of the treated episodes. Overall 73 pregnancies (88%) resulted in live births, 3 (4%) in abortions and 2 (3%) in still births, and 5 women were lost to follow-up before delivery. There was no congenital abnormality

in any of the newborn children, and the 46 children followed for more than one year all developed normally.

Wellcome-Mahidol University, Oxford Tropical Medicine Research Programme funded by the Wellcome Trust of Great Britain.

Published in : Trans Roy Soc Trop Med Hyg 1998; 92: 430-3.



A busy clinic in Mae La where studies of the epidemiology, prevention and treatment of multi-drug resistant falciparum malaria take place

QUININE AND MEFLOQUINE IN THE TREATMENT OF MULTIDRUG-RESISTANT PLASMODIUM FALCIPARUM MALARIA IN PREGNANCY

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Between 1991 and 1996, 372 pregnant women with uncomplicated multi-drug resistant *P. falciparum* malaria, living on the western border of Thailand were treated with either mefloquine (n=194), quinine (n=93) or both drugs (n=85). Antimalarial treatment was generally well tolerated; the most common side effects following quinine were dizziness (42%) and tinnitus (35%) and following mefloquine were anorexia (23%) and dizziness (36%). In the patients treated for primary infections with mefloquine, 6% failed to clear their parasitaemia by day 7 and 28% failed by day 42. The corresponding figures for quinine were 4% and 23% respectively. The failure rates in the 117 women treated for recrudescence infections were higher. This

was significant for quinine (38%, p=0.03) but not for mefloquine (37%). In this study, the percentage of pregnant women who had patent gametocytaemia on presentation ranged from 4 to 19%. Over 50% of the patients were anaemic (Ht<30%) on presentation and 52% of those not anaemic on admission developed anaemia during follow up. Mefloquine and quinine, the only antimalarials currently available for the treatment of highly drug-resistant *P. falciparum* in pregnancy, give unsatisfactory treatment responses when used as single agents. New, safe and effective regimens are needed for the treatment of pregnant women with multi-drug resistant falciparum malaria.

Wellcome-Mahidol University, Oxford Tropical Medicine Research Programme funded by the Wellcome Trust of Great Britain.

Published in : Ann Trop Med Parasitol 1998;92:643-53.

TRANSMISSION INTENSITY AND *PLASMODIUM FALCIPARUM* DIVERSITY ON THE NORTHWESTERN BORDER OF THAILAND

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Genetic analysis of the number of *Plasmodium falciparum* genotypes per infected person in regions of holoendemic and hyperendemic malaria suggest that in areas of lower transmission intensity, significantly fewer parasite genotypes per infected person should be found. A predominance of single clone infections in the human population could generate the controversial clonal population structure proposed for *P. falciparum* by Tibayrenc and others. Characterization of *P. falciparum* from individuals on the Thai-Burmese border, an area of hypoendemic transmission, revealed a higher number of genotypes per infected person than that predicted. Possible reasons for this observation are discussed, with particular attention paid to human migration and multidrug resistance.



On the western border malaria is still a major cause of morbidity and mortality in all age groups

Wellcome-Mahidol University, Oxford Tropical Medicine Research Programme funded by the Wellcome Trust of Great Britain.

Published in : *Am J Trop Med Hyg* 1998; 58 : 195-203.

ARTESUNATE AND MEFLOQUINE IN THE TREATMENT OF UNCOMPLICATED MULTIDRUG-RESISTANT HYPERPARASITAEMIC FALCIPARUM MALARIA

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Oral artesunate is the most effective treatment for uncomplicated hyperparasitaemia in falciparum malaria. To assess the contribution of mefloquine to therapeutic efficacy in an area endemic for mefloquine resistant *Plasmodium falciparum*, an open randomized comparison of a 5 d course of oral artesunate (total dose 12 mg/kg) with and without a single dose of mefloquine (25 base mg/kg) was conducted in 100 adults and children with uncomplicated hyperparasitaemia (>4% parasitized red blood cells). Both regimens were well tolerated and gave equally rapid clinical responses (84% of patients were aparasitaemic and 96% were afebrile within 48 h), but

the recrudescence rate assessed at day 42 was 6% in those receiving artesunate with mefloquine compared to 36% in those receiving artesunate alone (adjusted hazard ratio 7, 95% Confidence interval [95% CI] 2-32; $P < 0.01$). In addition, the efficacy of a 7 d course of artesunate, with and without the addition of mefloquine, was monitored in 178 patients who were not part of the randomized comparison. The failure rate was again lower in those receiving artesunate and mefloquine - 7% (95% CI 2-13) compared with 26% (95% CI 8-44) in patients treated with artesunate alone. An oral regimen of 5 d or more of artesunate, together with mefloquine (25 mg/kg) given on day 2, is an effective treatment for uncomplicated hyperparasitaemic falciparum malaria in this area of high level multidrug resistance.

Wellcome-Mahidol University, Oxford Tropical Medicine Research Programme funded by the Wellcome Trust of Great Britain.

Published in : *Trans Roy Soc Trop Med Hyg* 1998; 92: 207-11.

RANDOMIZED COMPARISON OF ARTEMETHER-BENFLUMETOL AND ARTESUNATE-MEFLOQUINE IN TREATMENT OF MULTIDRUG-RESISTANT FALCIPARUM MALARIA

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³Division of Infectious Diseases, St George's Hospital Medical School, London, UK;

⁴Division of Infectious Diseases, Tropical Medicine and AIDS, Academic Medical Centre, University of Amsterdam, The Netherlands;

⁵Centre for Tropical Medicine, Nuffield Department of Clinical Medicine, John Radcliffe Hospital, Headington, Oxford, UK.

An open, randomized comparison of artemether-benflumetol (CGP 56 697; Novartis) with artesunate-mefloquine was conducted in 617 patients with acute uncomplicated multidrug-resistant falciparum malaria on the western border of Thailand. Both treatments rapidly and reliably cleared fever and parasitemia, and there was no significant difference in the initial therapeutic response parameters. Parasite genotyping was used to distinguish recrudescences from new infections. The 63-day cure rate for artesunate-mefloquine (94%) was significantly higher than the cure rate for artemether-benflumetol (81%) ($P < 0.001$). Both regimens were well tolerated. Nausea, vomiting, dizziness, sleep disorders, and other neurological side effects were between two and four times more common in the artesunate-mefloquine

group than in the artemether-benflumetol group ($P < 0.001$). Artemether-benflumetol is effective and very well tolerated in the treatment of multidrug-resistant falciparum malaria. A higher dose than that used in the present study may improve efficacy.

Wellcome-Mahidol University, Oxford Tropical Medicine Research Programme funded by the Wellcome Trust of Great Britain.

Published in : Antimicrob Agents Chemother 1998; 42: 135-9.



Malaria treatment on the Western border: asking about side-effects

WHY IS IT THAT ANTIMALARIAL DRUG TREATMENTS DO NOT ALWAYS WORK?

NJ White

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The objective of antimalarial drug treatment in severe malaria is to save the patient's life. In uncomplicated malaria it is to reduce the parasite biomass to zero, or down to a level where host defences can deal with the remainder. Treatment regimens with rapidly eliminated drugs must generally cover four asexual life-cycles (i.e. >6 days for *Plasmodium falciparum* and *P. vivax*) to eradicate all the parasites in the blood. For slowly eliminated drugs, blood concentrations must exceed the parasites' minimum inhibitory concentration (and preferably the minimum parasitocidal concentration) until all parasites have been eradicated. Resistance means that there is a right shift in the concentration-effect relationship. This may be large and abrupt, as with the point mutations that confer pyrimethamine, sulphonamide or atovaquone

resistance, or slow and gradual, as with the processes that determine resistance to chloroquine, quinine or mefloquine. Although treatment failure in malaria usually results from poor compliance, inadequate dosing, pharmacokinetic factors or resistance, some infections will recrudescence when none of these factors operates. How parasites persist despite apparently adequate antimalarial treatment remains unresolved.

Wellcome-Mahidol University, Oxford Tropical Medicine Research Programme funded by the Wellcome Trust of Great Britain.

Published in : Ann Trop Med Parasitol 1998; 92: 449-58.

PREVENTING ANTIMALARIAL DRUG RESISTANCE THROUGH COMBINATIONS

NJ White

Faculty of Tropical Medicine, Mahidol University, 420/6 Rajvithi Road, Bangkok, Thailand; Wellcome Trust Clinical Research Unit, Centre for Tropical Diseases, Cho Quan Hospital, Ho Chi Minh City, Vietnam; Centre for Tropical Medicine, Nuffield Department of Medicine, University of Oxford, UK.

Throughout the tropical world antimalarial drug resistance is increasing, particularly in the potentially lethal malaria parasite *Plasmodium falciparum*. In some parts of Southeast Asia, parasites which are resistant to chloroquine, pyrimethamine-sulfadoxine, and mefloquine are prevalent. The characteristics of a drug that make it vulnerable to the development of resistance are a long terminal elimination half-life, a shallow concentration-effect relationship, and that one or two base-pair mutations confer a marked

reduction in susceptibility. The development of resistance can be delayed or prevented by drug combinations. The artemisinin derivatives are the most potent of all antimalarial drugs. They reduce the infecting parasite biomass by approximately 10,000-fold per asexual life cycle. There are good arguments for combining, de novo, an artemisinin derivative with all newly introduced antimalarial drugs.

Wellcome-Mahidol University, Oxford Tropical Medicine Research Programme funded by the Wellcome Trust of Great Britain.

Published in : Drug Resistance Updates 1998; 1: 3-9.

THE BANGKOK SCHOOL OF TROPICAL MEDICINE

The Bangkok School of Tropical Medicine, Faculty of Tropical Medicine, Mahidol University was established in 1960 to teach Thai medical doctors, especially those who work in rural areas in tropical medicine, parasitology and the preventive aspects of endemic diseases. The course leading to the Diploma in Tropical Medicine and Hygiene (D. T. M. & H., Bangkok) has been organized on an international basis since 1967, with the establishment of the SEAMEO Regional Tropical Medicine and Public Health Project, and the designation of the Faculty as the TROPMED National Centre of Thailand. Lectures are given in English and the courses are open to students from other countries around the world. Since its inception class sizes have steadily increased. The original curriculum was based on the D.T.M.&H. course conducted by the Liverpool School of Tropical Medicine, and has been modified to provide adequate orientation towards preventive medicine, endemic health problems of Thailand, and public health problems in other countries of Southeast Asia. The Bangkok School of Tropical Medicine has been extended to provide continuing education to doctors, research workers, medical personnel and professionals concerned with tropical medical and public health. The degree in Tropical Medicine, instituted internationally, was offered at the M.Sc. level in 1967 and at the Ph.D level in 1975. The basic intent was to provide a multidisciplinary approach to graduate training. Masters and Doctorate degree programmes in Clinical Tropical Medicine were offered to medical doctors in 1982 and 1995, respectively. The curricula of the programmes were revised and offered regularly as follows:

Regular Postgraduate Programmes

1. Graduate Diploma in Tropical Medicine and Hygiene (D.T.M.&H.)

The course provides participating medical doctors with the concepts and principles of the clinical management of tropical diseases, epidemiology, prevention and control of tropical diseases and health problems in Southeast Asia. The students gain experience with case demonstrations and field trips to hospitals in rural areas of Thailand. The duration of the course is six months, running between April and September.

2. Master of Science in Tropical Medicine (M.Sc.(Trop. Med.))

The programme provides appropriate knowledge and skills for competency in research, and the capacity to deliver technical services related to tropical medicine. Length of study is approximately two years, which includes a minimum of 24 credits for coursework and 12 credits for thesis. The programme offers 13 major fields for students to choose from according to their needs and future work as follows: Clinical Tropical Medicine, Clinical





Pharmacology, Epidemiology, Microbiology, Immunology, Biochemical Nutrition, Nutritional Epidemiology, Nutritional Toxicology, Tropical Pathology, Radiological Science, Social Medicine, Social Medicine Environmental Health, Parasitology and Medical Entomology. Applicants who are qualified to enrol in this programme are those who have graduated with a M.D. or D.D.S. or D.V.M. or B.Sc. degree.

3. Doctor of Philosophy in Tropical Medicine (Ph.D. (Trop. Med.))

The doctoral programme provides advanced knowledge and skills for competency in research, particularly in Tropical Medicine, which includes the research programme (Plan 1) and the regular programme (course work and research) (Plan 2). Students are able to choose one major field in Tropical Medicine according to their needs and future work, as follows: Clinical Tropical Medicine, Clinical Pharmacology, Epidemiology, Microbiology, Immunology, Biochemical Nutrition, Nutritional Epidemiology, Nutritional Toxicology, Tropical Pathology, Radiological Science, Social Medicine, Social Medicine Environmental Health, Parasitology and Medical Entomology. Length of study is approximately three years. Applicants who are qualified to enrol in this programme are those who have graduated with a M.D. or D.D.S. or D.V.M. or



M.Sc. or B.Sc. degree.

4. Master of Clinical Tropical Medicine (M.C.T.M.)

The M.C.T.M. programme has been established to train medical doctors to be :

a) well-versed and well-informed in tropical and endemic diseases with special reference to Southeast Asia, in relation to their causes, epidemiology, pathogenic mechanisms, prevention and control.

b) able to efficiently examine, diagnose and treat patients suffering from tropical and endemic diseases. In the major field of Clinical Tropical Medicine, students will study abnormalities mainly in adults, while in the major field of Tropical Paediatrics the student will study only the abnormalities in children.

c) able to give consultative advice, disseminate and impart knowledge of Tropical Medicine.

The programme consists of coursework and thesis. Students will conduct clinical research and gain clinical experience at a Regional Hospital of the Ministry of Public Health in a province of Thailand. The duration of the programme is one year, from April to March.

5. Doctor of Philosophy in Clinical Tropical Medicine (Ph.D. (Clin. Trop. Med.))

The Ph.D. (Clin. Trop. Med.) programme has been established for medical doctors to gain advanced knowledge and study new techniques, and apply them to areas of research which are applicable to the practice of clinical tropical medicine. Students are required to conduct an extensive research project related to clinical tropical medicine which should be an original work. The minimum length of the study is three years.

Candidates are required to have graduated with a M.C.T.M. degree or have been certified in clinical specialties by the Board of the Thai Medical Council or its equivalent and hold D.T.M.&H., or hold a licence for general medicine in their domicile country or in the country where they graduated.

The Faculty of Tropical Medicine, Mahidol University has become the SEAMEO TROPMED Regional Centre for Tropical Medicine since 1994. Much of the School's good reputation overseas derives from its education and training activities. Students enrolled in its

programmes originate from SEAMEO member countries and other countries (Thailand, Indonesia, the Philippines, Malaysia, Laos PDR, Cambodia, Myanmar, Vietnam, Singapore, Bangladesh, India, Japan, Pakistan, Afghanistan, Nepal, Iran, Sri Lanka,

Australia, the People's Republic of China, Papua New Guinea, New Zealand, Germany, Sweden, Switzerland, Norway, Austria, Spain, Denmark, Italy, Finland, France, the Netherlands, the United Kingdom, Somalia, Yemen, Tanzania, Palestine, Croatia and U.S.A.).

Collaborative Training Programmes

1. Master of Clinical Tropical Paediatrics Bangkok/Liverpool Collaboration

The Faculty of Tropical Medicine, Mahidol University and the Liverpool School of Tropical Medicine collaborate in the teaching and training of postgraduates in both institutions registered for Master's Courses in Tropical Paediatrics, but each university issues its own degree in accordance with its own degree regulations. Candidates registered for the Master's Course(s) in Liverpool commence their training in Liverpool (3-4 months) and are provided with clinical and field experience in Thailand for a period of 3 months between April and August to gain practical experience of tropical paediatrics which cannot be provided in Liverpool, in parasitic diseases (eg. malaria, hookworm infection, strongyloidiasis, giardiasis, ascariasis, liver fluke infection, gnathostomiasis, angiostrongyloidiasis, paragonimiasis, cysticercosis etc.) and other infectious diseases (eg. dengue haemorrhagic fever, Japanese encephalitis, tuberculosis, meningitis, leptospirosis, rabies, etc.). Master's candidates in Bangkok may be sent to Liverpool for clinical or field experience but this is not a pre-requisite of this agreement.



at the Hospital for Tropical Diseases and other hospitals in Bangkok and in the northeast of Thailand. This programme is directed by Professor Franz Ambrosch and the clinical part is organized by Professor Walter Wernsdorfer and Professor Tan Chongsupphajaisiddhi.

The objectives of the course are :

(1) To provide participating medical doctors with clinical experience and a better understanding of health problems at the community level in Southeast Asia and to increase their ability to cope with them.

(2) To promote a better understanding of the culture and way of life of people in Southeast Asia, leading to closer cooperation in dealing with regional health problems.

3. Master of Science in Clinical Epidemiology

The Faculty of Tropical Medicine, in collaboration with the Faculty of Public Health and the Faculty of Medicine, Ramathibodhi Hospital, Mahidol University, organizes an international programme leading to the Master of Science in Medical Epidemiology. The course focuses on the development of epidemiological skills and competency for doctors, especially in the countries of Southeast Asia, in the field of clinical or community epidemiology and also in health service research. The ultimate objective of this programme is to provide academic and health service leadership, which will facilitate effective performance of public health and medical care programmes at every level in various countries. The length of study is one year, six months for coursework and six months for the Master's thesis.

2. Austrian Diploma in Tropical Medicine

The Austrian Society of Tropical Medicine and Parasitology and the Faculty of Tropical Medicine, Mahidol University have jointly offered an annual programme leading to the Austrian Diploma in Tropical Medicine, since 1992. The 4-month programme, starting in January, focuses on tropical diseases and enables medical doctors to understand the clinical, biological, epidemiological and social dimensions of tropical diseases, particularly in Southeast Asia. After the participants have attended lectures for 3 months in Austria, they continue attending more clinical experience for 1 month in Thailand at the Faculty of Tropical Medicine, Mahidol University. Apart from lectures, participants will also have the opportunity to see many patients suffering from tropical diseases

D.T.M. & H. 1998

Dr. Kanyarat Krivichian	Thailand	Dr. Aung Myat Oo	Myanmar
Dr. Krisana Pengsaa	Thailand	Dr. Minn Minn Soe	Myanmar
Dr. Laddawan Nualchaem	Thailand	Dr. Tin Naing	Myanmar
Dr. Pechdau Tohmeena	Thailand	Dr. Achuyt Bhattarai	Nepal
Dr. Pinn Kolkijkovinda	Thailand	Dr. Eli Westerlund	Norway
Dr. Timothy John Moore	Australia	Dr. Bounmy Santisouk	Lao PDR.
Dr. Sokhon Srey	Cambodia	Dr. Somboun Bounyadeth	Lao PDR.
Dr. Moniboth Duch	Cambodia	Dr. Chong Tse David Tan	Singapore
Dr. Martin Schwazzin	Germany	Dr. Yasir Elfatih Elsanousi	Sudan

M.C.T.M. 1997-1998

Dr. Kamol Prinyanusorn	Thailand	Dr. Tripti Bala	Bangladesh
Dr. Lalita Wongpichedchai	Thailand	Dr. Winn Myint Kyi	Myanmar
Dr. Veeranoot Nissapatorn	Thailand	Dr. Thang Quoc Duong	Vietnam
Dr. Dagmara M. Poprawski	Australia	Dr. Magotra Shyam Kumar	India

M.Sc.(Trop.Med.)1998**1st year student**

Pol.Lt. Kitiyaporn Chaichana	Thailand
Miss Chuthaporn Toonboonchoo	Thailand
Miss Duangkamol Viroonudomphol	Thailand
Mrs. Tippayarat Yoonuan	Thailand
Miss Bunguorn Sermsart	Thailand
Mr. Preecha Liangpunsakul	Thailand
Mr. Pornchai Kirdsisi	Thailand
Miss Yupa Nakkinkun	Thailand
Miss Varangkana Visemanee	Thailand
Miss Waraporn Chaimchitpanid	Thailand
Miss Wacharee Tiyasuttipan	Thailand
Miss Suwaporn Anantrakulsin	Thailand
Miss Akanitt Jittmitrathap	Thailand
Mr. Apichai Supasansatorn	Thailand
Miss Umaphorn Pinyasirikul	Thailand
Mr. Ferdinand V. Satazar	Philippines

2nd year student

Mrs. Kesaree Chewachatrekasem	Thailand
Miss Napa Onvimala	Thailand
Miss Pornsawan Amarapal	Thailand
Miss Yuwadee Trongtokit	Thailand
Miss Watcharee Saisongkorh	Thailand
Miss Sunthareeya Waicharoen	Thailand
Miss Searmsap Riengrod	Thailand
Miss Saowaluk Julnimi	Thailand
Miss Siriwan Tribanyatkul	Thailand
Miss Striprai Yenyam	Thailand
Miss Oumayorn Thasanor	Thailand

Mrs. Aimmanas Attawish	Thailand
Mr. Shishis Kumar Pant	Nepal
Dr. Tran Do Hung	Vietnam

3rd year student

Miss Chutamas Koomrungrueng	Thailand
Miss Pornthip Laummaunwai	Thailand
Dr. Pearl Angeli C. Palacios	Philippines
Mr. Wick Banmairuoy	Thailand
Miss Usa Boonsathorn	Thailand

4th year student

Mrs. Montakan Vongpakorn	Thailand
Miss Ruchirat Worasing	Thailand

5th year student

Mr. Muhaimin Ramdja	Indonesia
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Ph.D.(Trop.Med.) 1998

1st year student

Miss Surangrat Srisurapanon	Thailand
Miss Kriyaporn Songmuang	Thailand
Miss Kleebkaew Pitasawad	Thailand
Miss Charinthon Ngamamonpirat	Thailand
Mrs Prapin Tharnpoophasiam	Thailand
Miss Pungasem Paeporn	Thailand
Miss Panee Chaksangchaichat	Thailand
Miss Mallika Imwong	Thailand
Mr. Mana Vatakul	Thailand
Mrs. Yupadee Sirissinsuk	Thailand
Miss Wanida Pongstaporn	Thailand
Miss Sawanee Tengrungsun	Thailand
Miss Nitchakarn Nornate	Thailand
Miss Pittayaporn Mounnoi	Thailand

2nd year student

Mrs. Kanjana Hongtong	Thailand
Mrs. Kamolrat Silamut	Thailand
Mrs. Chantima Lohachit	Thailand
Mr. Chamnarn Apiwathnasorn	Thailand
Mr. Polrat Wilairatana	Thailand
Mr. Paron Dekumyoy	Thailand
Mr. Apichart Nantprasert	Thailand
Miss Urai Chaisri	Thailand
Miss Usavadee Thavara	Thailand
Mrs. Emsri Pongpanarat	Thailand
Mrs. Patcharin Saengjaruk	Thailand
Miss Siriwan Chancharoen	Thailand
Miss Thitima Wongsaroj	Thailand
Dr. Mayfong Mayxay	Lao PDR.
Miss Wannaporn Ittiprasert	Thailand

3rd year student

Mr. Ruangyuth Chaiworaporn	Thailand
Dr. Le Thi diem Thuy	Vietnam

4th year student

Miss Roongrasamee Soisangwan	Thailand
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5th year student

Miss Pongsri Tippawangosol	Thailand
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Ph.D.(Clin.Trop.Med.) 1998

1st year student

Dr. Yoshinari Moriyama	Japan
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5th year student

Dr. Yupaporn Wattanakoon	Thailand
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THESIS TITLES

M.C.T.M. 1998

DEPARTMENT	TITLE OF THESIS	NAME	ADVISOR
Clinical Tropical Medicine	Scrub typhus and/or leptospirosis as the causes of sepsis in Maharat Nakhon Ratchasima Regional Hospital	Dr. Kamol Pinyanusorn	Prof. Juntra Laothavorn
Clinical Tropical Medicine	Clinical manifestations and outcomes in tuberculosis in HIV positive patients in Bamrasnaradura Hospital, Nonthaburi	Dr.Lalita Wongpichedchai	Prof. Sasithorn Pukrittayakamee
Clinical Tropical Medicine	Seroprevalence of toxoplasmosis in HIV infected patients in Chonburi Regional Hospital,1997	Dr.Veeranoot Nissapatorn	Assist.Prof.Yupaporn Wattanagoon
Clinical Tropical Medicine	Clinical manifestations and outcomes in tuberculosis in HIV positive patients in Bamrasnaradura Hospital, Nonthaburi	Dr.Dagmara M.Popzrawski	Assoc.Prof. Punnee Pitisuttithum
Clinical Tropical Medicine	Clinical manifestations and outcomes in tuberculosis in HIV positive patients in Bamrasnaradura Hospital, Nonthaburi	Dr.Tripti Bala	Prof. Pravan Suntharasamai
Clinical Tropical Medicine	Contribution of scrub typhus in sepsis at Maharat Nakhon Ratchasima Hospital	Dr. Winn Myint Kyi	Assoc.Prof. Polrat Wilairatana
Clinical Tropical Medicine	Seroprevalence of toxoplasmosis in HIV infected patients in Chonburi Regional Hospital, 1997	Dr.Thang Zuoc Duong	Assoc.Prof. Wichai Supanaranond
Clinical Tropical Medicine	Seroprevalence of toxoplasmosis in HIV infected patients in Chonburi Regional Hospital	Dr.Shyam Kumar Magotra	Prof. Swangjai Pungpak

M.Sc.(Trop.Med.)

DEPARTMENT	TITLE OF THESIS	NAME	ADVISOR
Clinical Tropical Medicine	<i>In vitro</i> sensitivity of <i>Plasmodium vivax</i> to chloroquine	Miss Oumaporn Trasanor	Prof.Juntra Laothavorn
Clinical Tropical Medicine	Bioequivalency of mefloquine when given as Mepha in combination with dihydroartemisinin	Dr.Pearl Angeli C. Palacios	Prof.Juntra Laothavorn
Clinical Tropical Medicine	Pharmacokinetics of mycophenotic ACID in Thai recipients of kidney transplantation	Mr.Wick Banmairuroy	Prof.Juntra Laothavorn
Helminthology	Evaluation of immune - reaction between excretory- secretory and partially purified somatic antigens of <i>Fasciola gigantica</i>	Mrs.Montakan Vongpakorn	Assoc.Prof.Jitra Waikagul
Medical Entomology	Pyrethroid resistance in association with the use of insecticides impregnated bednets	Mr.Shishir Kumar Pant	Assist.Prof. Narumon Komalamisra
Microbiology and Immunology	Prevalence of cytomegalovirus in Thai blood donors by monoclnal antibody staining of blood leukocytes	Miss Pornsrawan Amarapal	Assoc.Prof.Surang Tantivanich
Microbiology and Immunology	DND amplification for <i>Vibrio cholerae</i> O:139 detection	Miss Watcharee Saisongkorh	Assoc.Prof. Pramuan Tapchaisri
Microbiology and Immunology	Simple and rapid detection of scrub typhus	Miss Sunthareeya Waicharaen	Dr.Varee Wongchotigul
Microbiology and Immunology	A rapid direct-agent detection system for <i>Orientia tsutsuyamushi</i>	Miss Searmsap Riengrod	Dr. Varee Wongchotigul
Microbiology and Immunology	Diagnosis of pertussis using MAb-based dot-blot ELISA, indirect ELISA and DNA amplification	Miss Saowaluk Julnimi	Assoc.Prof. Manas Chongsanguan
Microbiology and Immunology	Development of dual detection of <i>Vibrio cholerae</i> O:1 and O: 139 in immunomagnetic enriched samples by MAb-based dot blot ELISA	Miss Sriprai yenyam	Dr.Yuvadee Mahakunkijcharoen
Microbiology and Immunology	Epidemiology study of B Hemolytic <i>Streptococcus</i> Group A in the pharynx of school children in Cantho Province, Vietnam	Dr.Tran Do Hung	Assist.Prof.Usanee Suthisarnsuntorn
Microbiology and Immunology	Gene cloning and expression on hepatitis B core antigen in yeast cells	Miss Usa Boonsathorn	Assoc.Prof.Surang Tantivanich
Microbiology and Immunology	Genitic analysis of <i>Tricinella spiralis</i> , Thailand isolates	Miss Pornthip Laummaunwai	Prof.Wanpen Chaicumpa

M.Sc.(Trop.Med.)

DEPARTMENT	TITLE OF THESIS	NAME	ADVISOR
Microbiology and Immunology	Monoclonal antibodies based detection of dengue virus infected cells	Miss Arceerat Srijuggravatvong	Prof.Srisin Khusmith
Microbiology and Immunology	The multistage character of immunity to <i>P. falciparum</i> , naturally occurred by endemic Thai population	Miss Kesaree Chewachatrekasem	Prof.Srisin Khusmith
Protozoology	Isolation and characterization of DNA topoisomerase II from <i>Plasmodium falciparum</i>	Miss Ruchirat Worasing	Assist.Prof.Porntip Petmitr
Protozoology	<i>In vitro</i> sensitivity of <i>Plasmodium falciparum</i> gametocytes to AT-specific minor groove binding drugs	Mr.Muhaimin Ramdja	Assist.Prof.Porntip Petmitr
Protozoology	The correlation of <i>in-vivo</i> and <i>in vitro</i> sensitivity of antimalarial drugs	Miss Chutamas Koomrungrueng	Assist.Porntip Petmitr
Tropical Nutrition and Food Science	Cytotoxic and mutagenic tests of medicinal plants	Mrs. Aimmanas Attavish	Assoc.Prof.Supranee Changbumrung
Tropical Nutrition and Food Science	Serum leptin concentration in human obese subjects	Miss Siriwan Tribanyatkul	Assoc.Prof. Rungsun Tungtrongchitr
Tropical Nutrition and Food Science	Application of polymerase chain reaction for identification of rotavirus serotypes in field study	Miss Napa Onvimala	Assoc.Prof.Supranee Changbumrung

Ph.D.(Trop.Med.)

DEPARTMENT	TITLE OF THESIS	NAME	ADVISOR
Clinical Tropical Medicine	The relationship between the morphology of <i>Plasmodium falciparum</i> parasites, antimalarial treatment and pathology in falciparum malaria	Mrs.Kamolrat Silamut	Prof.Sasithon Pukrittayakamee
Social and Environmental Medicine	Ecological studies of <i>Bithynia goniomphalos</i> a snail intermediate host of <i>Opisthorchis viverrini</i> in Northeast Thailand	Mrs.Chantima Lohachit	Assoc.Prof.Viroj Kitikoon
Tropical Nutrition and Food Science	Platelet fatty acids and serum lipoprotein A in hyperlipid anemia and related heart disease patients and healthy individuals	Mrs. Kanjana Hongtong	Assoc.Prof.Supranee Changbumrung

Ph.D.(Trop.Med.)

DEPARTMENT	TITLE OF THESIS	NAME	ADVISOR
Clinical Tropical Medicine	Isolation and characterization of mitochondrial DNA polymerase from <i>Plasmodium falciparum</i>	Mr.Polrat Wilairatana	Prof. Sornchai Looareesuwan
Clinical Tropical Medicine	Neurotoxicity of antimalarial drugs in animal model	Mr.Apichart Nontprasert	Prof. Sasithon Pukritayakamee
Clinical Tropical Medicine	Ultrastructural studies of <i>Plasmodium falciparum</i> in human organs : the interactions between the parasitized erythrocytes and the host cells	Mrs. Emsri Pongpanarat	Prof. Sornchai Looareesuwan
Clinical Tropical Medicine	Clinical pharmacology of the combination of artemether and proquanil	Dr. Le Thi Diem Thuy	Prof. Juntra Laothavorn
Clinical tropical Medicine	Pharmacokinetics and pharmacodynamics of artemisinin derivative combination in uncomplicated malaria	Miss Pongsri Tippawangosal	Assoc.Prof. Kesara Na Bangchang
Clinical Tropical Medicine	The role of clinical pharmacology in the treatment of tropical diseases	Dr.Yupaporn Wattanakoon	Prof. Juntra Laothavorn
Helminthology	Cloning of antigenic gene from female <i>Angiostrongylus cantonensis</i> adult worms	Mr.Paron Dekumyoy	Assoc.Prof. Jitra Waikagul
Medical Entomology	Some promising phytochemical plants for control of mosquito vectors	Mr.Chamnarn Apiwathnasorn	Assist.Prof. Achara Asavanich
Microbiology and Immunology	Rapid diagnosis of shigellosis	Miss Roongrasamee Soisangwan	Prof. Wanpen Chaicumpa
Microbiology and Immunology	Characterization of B cell - epitope of HIV - 1 subtype E	Miss Surangrat Srisurapannon	Prof. Srisin Khusmith
Social and Enviromental Medicine	Studies on <i>Schistosoma spindale</i> Montgomery, 1906 : The effects of antiparasitic drugs on <i>Schistosoma spindale</i> in mice and the resistance to reinfection after treatment	Mr.Ruangyuth Chaiworaporn	Assoc.Prof. Viroj Kitikoon

SEAMEO TROPMED Regional Centre for Tropical Medicine



**TROPMED/Thailand Centre
Director and Secretary General/Coordinator**
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Professor Nelia P Salazar

Executive Editor
**Southeast Asian Journal of Tropical Medicine
and Public Health**

Associate Professor Suvanee Supavej

Assistant Coordinator (Programme)
Ms. Vimolsri Panichyanon

Finance Officer
Mrs. Tubtim Potha



Professor Nelia P Salazar

Associate Professor Suvanee Supavej



Ms. Vimolsri Panichyanon



Mrs. Tubtim Potha

General information on SEAMEO and SEAMEO TROPMED Network

The Southeast Asian Ministers of Education Organization (**SEAMEO**), founded in 1965, is a chartered international organization for the promotion of regional cooperation in education, science, technology and culture.

Member countries are Brunei Darussalam, Cambodia, Indonesia, Lao People's Democratic Republic, Malaysia, the Philippines, Singapore, Thailand, and Viet Nam.

Associate Member Countries are Australia, Canada, France, Germany, New Zealand, and The Netherlands.

The Council of Ministers representing the aforementioned countries is called **SEAMEC**. SEAMEO's executory functions are performed by the Secretariat (**SEAMES**) located in Bangkok, Thailand.

SEAMEO TROPMED operates as a Network in Tropical Medicine and Public Health through four **TROPMED Regional Centres** in Indonesia, Malaysia, the Philippines, and Thailand, with a coordinating unit, the **TROPMED Central Office** in Bangkok, Thailand.

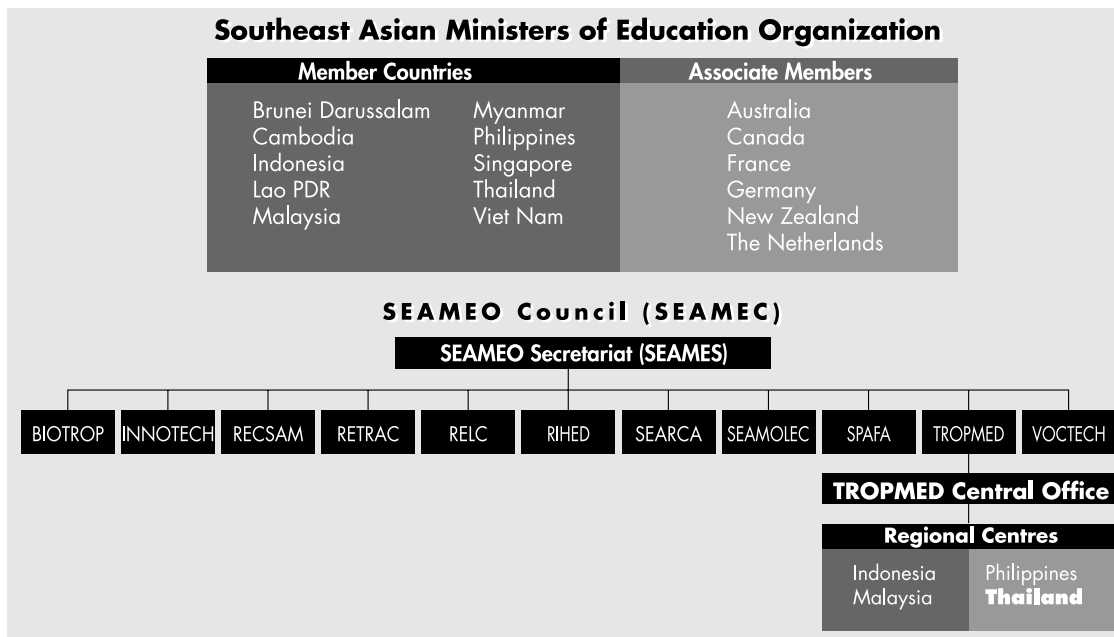
SEAMEO TROPMED serves to facilitate the strengthening of national and institutional capabilities in research and training through postgraduate academic programmes; workshops, seminars, and technical meetings; multisectoral and multidisciplinary

linkages; personnel exchanges; technical consultant services; publications and information dissemination.

The **SEAMEO TROPMED Network** is one of 11 administrative units under SEAMEO, known as **SEAMEO Centres** with specialties in tropical biology (**BIOTROP** in Indonesia); Educational Innovation and Technology (**INNOTECH** in the Philippines); Science and Mathematics (**RECSAM** in Malaysia); Language (**RELC** in Singapore); Higher Education (**RIHED** in Thailand); Regional Training Centre in Viet Nam (**RETRAC**); Open learning and Distance Education in Indonesia (**SEAMOLEC**); Graduate Study and Research in Agriculture (**SEARCA** in the Philippines); Archeology and Fine Arts (**SPAFA** in Thailand); and Vocational and Technical Education (**VOCTECH** in Brunei Darussalam).

The SEAMEO TROPMED Network and SEAMEO Centres each has a Governing Board consisting of representatives from Member Countries and which is responsible for operational policies, programme quality and evaluation of the unit.

In line with the overall mission of SEAMEO, the primary role of SEAMEO TROPMED is to promote health and to prevent and control disease thereby improving the quality of life of people in South and Southeast Asia.



Functions of SEAMEO TROPMED Network

- Coordinates regional programmes and activities of the SEAMEO TROPMED Network
- Promotes linkages and networking with national, regional and international organizations and institutions
- Organizes conferences, seminars and training courses in tropical medicine and public health
- Facilitates personnel exchanges between partner institutions
- Undertakes publication of The Southeast Asian Journal of Tropical Medicine and Public Health and proceedings of technical meetings and scientific fora
- Manages special projects under various programmes of cooperation in health research and human resources development

SEAMEO TROPMED Regional Centre for Tropical Medicine (TROPMED/Thailand)

TROPMED/Thailand is hosted by the Faculty of Tropical Medicine, Mahidol University under the Ministry of University Affairs Thailand. The Faculty was established in 1960, with specialties in tropical medicine and tropical paediatrics. Courses are conducted at the Bangkok School of Tropical Medicine.



Objectives:

- Teaching endemic tropical diseases, parasitology, community and preventive medicine, with special reference to Thailand and other countries in Southeast Asia.
- Research in the field and laboratory on tropical diseases and public health leading to innovation on alternative control measures of diseases,

and promotion of health of people in Southeast Asia.

- Clinical care of patients suffering from endemic tropical diseases, and clinical research into medical problems of Thailand and neighbouring countries, including trials of new chemotherapeutic compounds and new vaccines.

Activities

In the FY 1997/1998, the Strategic Plan of SEAMEO for the 1990s has been implemented and monitored according to the five Key Result Areas (KRAs). The accomplishments reported in accordances with the 5 KRAs are as follow:

KRA1. ENHANCED PROGRAMME QUALITY AND RELEVANCE

1.1 Post-graduate Regular Courses. TROPMED/Thailand offers 5 post-graduate courses at the Diploma, Master and PhD levels with a total of 95 students from 15 countries (Afghanistan, Australia, Austria, Cambodia, India, Indonesia, Japan, Lao PDR, Myanmar, Nepal, PR China, the Philippines, Sri Lanka, Thailand and Vietnam).

Table 1. Number of students and number of graduates in 1997/1998.

Course	No. of students	No. of nationalities	No. of graduates
DTM & H	23	11 (Afghanistan, Australia, Austria, Cambodia, Japan, India, Lao PDR, Myanmar, Sri Lanka, Thailand, Viet Nam)	23
MSc (CTM)	4	4 (Indonesia, Lao PDR, the Philippines, Viet Nam, Thailand,)	4
MSc (Trop.Med.)	40	7 (Indonesia, Lao PDR, Nepal, the Philippines, PR China, Thailand, Viet Nam)	9
PhD (Trop.Med.)	27	3 (Indonesia, Thailand, Viet Nam)	2
PhD (CTM)	1	1 (Thailand)	-
Total	95	15	37

There is a steady increase in the percentage of fee-paying students in the courses leading to MSc (CTM) and MSc (Tropmed) while the high percentage is maintained in the DTM & H course. The number of PhD students has remarkably increased since the FY 1996/97 especially those attending the off-campus PhD programme.

Table 2. Number and percentage of fee-paying students attended regular courses during 1993-1998.

Course	Number and percentage of fee-paying students in FY					
	1993/94	1994/95	1995/96	1996/97	1997/98	1998/99
DTM & H	43/56 77%	40/56 70%	17/26 65%	18/26 69%	18/23 78%	14/18 78%
MSc (CTM)	2/14 14%	5/15 24%	6/11 65%	2/4 50%	7/8 87%	
MSc (Trop.Med.)	1/15 6%	2/8 20%	2/7 23%	1/7* 41%	9/16 56%	15/16 48%
PhD (Trop.Med.)	3/4 80%	1/1 100%	0 0%	1/2 50%	13/15 87%	10/13 80%

1.2 Joint regular courses. TROPMED/Thailand conducted 3 joint courses in collaboration with other institutions within and outside Thailand.

Table 3. Joint regular courses with other institutions.

Course	Collaborative institutions	No. of students						
		1992/93	1993/94	1994/95	1995/96	1996/97	1997/98	1998/99
DTM	Austrian Society of Tropical Medicine and Parasitology, Austria	20	20	20	15	12	9	14
MSc (Trop. Paediatrics)	Liverpool School of Tropical Medicine, UK	-	8	4	-	1	2	-
MSc (Med Epidemiol)	Faculties of Public Health, and Graduate Studies, Mahidol University, Thailand	NA*	NA*	NA	NA	8	4	-

*NA = Not available

1.3 Elective programme in tropical medicine. The international elective programme in tropical medicine for last year medical students has been first offered in 1994/95 with 15 attendants. The programme continues with 15-20 students from Africa, Australia, Europe and USA as shown in Table 4.

Table 4. Number of students attended elective programme in tropical medicine.

Academic year	No. of students	Countries
1994/95	15	Australia (1), Austria (2), Canada (2), Germany (2), Japan (5), the Netherlands (2), USA (1)
1995/96	15	Australia (1), Austria (2), Canada (2), Japan (5), South Africa (5)
1996/97	20	Australia (1), Austria (4), Canada (1), Germany (1), Japan (6), Sweden (2), USA (1), South Africa (4)
1997/98	19	Austria (4), Canada (1), Germany (1), UK (1), Japan (12)
1998/99	17	Australia (1), Austria (8), USA (7), UK (1)

1.4 Research attachment programme. TROPMED/Thailand accepted 9 researchers to conduct joint research studies in tropical medicine for a period of 3 months to 2 years from the following countries :

France (4), Germany (1), Norway (1), Sweden (1), Switzerland (1), UK (1)

1.5 Training. Two workshops, 2 training courses and 3 meetings at the regional and international levels were convened with the total number of 446 participants.

1.6 Special training programmes. Special training programmes were individually arranged for 18 researchers from 8 countries : Bangladesh (2), India (3), Myanmar (1), PR China (1), Romania (2), the Republic of Maldives (1) and Viet Nam (3) These trainees were supported by WHO and the Netherlands-Viet Nam Medical Committee.

KRA2. INCREASED ACCESS TO MARKET

2.1 Marketing workshop participation. Two staff from TROPMED/Thailand participated in the Marketing Workshop organized by SEAMES held at RECSAM, Penang, Malaysia in November 1997.

2.2 Marketing through Mahidol Homepage. TROPMED/Thailand homepage can be accessed at <http://www.mahidol.ac.th/tm>. Requests for training programmes through internet have been received since the launching of the homepage.

2.3 Production of new brochures. New brochures of the regular courses were produced.

2.4 Active marketing. A marketing team has been set up to launch an active marketing by holding meetings with last year science students in various universities in Bangkok. As a result, the number of students enrolled in the Master and PhD programmes were notably increased in the FY 1997/98 and FY 1998/99.

KRA3. INCREASED LINKAGES

3.1 One more MOU was signed in FY 1997/1998 between SEAMEO Network, TROPMED/Thailand and the Swiss Tropical Institute, Switzerland.

3.2 The Institutional Linkage through SEAMEO-CIDA. The linkage with the University of Calgary has been renewed and a workshop on Laboratory Diagnosis of Diarrhoeal Diseases with 15 participants from Cambodia (5) and Lao PDR (10) was held at Mahosot Hospital, Vientiane, Lao PDR during 9-20 March 1998.

3.3 Visitors. In FY 1997/98, there were 72 visitors from 15 countries who paid a visit to TROPMED/Thailand : (Australia (6), Bangladesh (1), Canada (2), Indonesia (1), Ireland (1), Japan (34), Lao PDR (2), Netherlands (1), PR China (8), Singapore (1), Switzerland (1), Thailand (2), Taiwan (1), UK (8), USA (3).

KRA4. IMPROVED FINANCIAL STATUS THROUGH COST CONTROL AND INCREASED REVENUE

4.1 Cost control measures. Measures were implemented to reduce shortfalls with the target of 10% reduction in electricity, water, telephone and facsimile.

4.2 Increase in grants from local funding agencies. There were 140 research projects with total grants of 44.7 million Bahts (19.2 millions from local funding agencies and 25.5 millions from international agencies). It is noted that grants from local sources have been steadily increased during the past 5 years.

Table 5. Number and amount of research grants since FY 1993/94.

Fiscal year	Total no of research projects	Total grants in million Baht	Grants supported by local agencies		Grants supported by international agencies	
			No of projects	Total amount	No of project	Total amount
1993/94	109	7.1	NA*	3.1	NA	4.0
1994/95	135	33.2	62	7.1	98	26.1
1995/96	133	31.9	58	8.3	43	23.6
1996/97	145	26.6	49	11.5	24	15.1
1997/98	140	47.7	62	19.2	21	25.5

*NA = Not available

KRA5. ENHANCED QUALITY OF SEAMEO MANAGEMENT

5.1 Woman in managed or supervisory positions. TROPMED/Thailand has equitable representation of women and professional staff in managed or supervisory positions.

Table 6. Representation of female in management positions.

Position	F	M	Total
Deputy Deans	3	5	8
Heads of Departments	6	5	11
Assistant Deans	1	2	3
Deputy Directors of the Hospital	3	-	3
Total	13	12	25

5.2 Number of promotion per year.

Table 7. Number of staff promoted.

Academic post	No. (%)
Associate Professor	7
Assistant Professor	3
P.C.promotion	53
Higher degree	11
Study tour	28 (7.5%)
Attending conference/seminar	262 (71.8%)

5.3 Infrastructure development. The Centre is equipped with 150 computer terminals which are connected via fibreoptic system to the Computer Centre of Mahidol University. The intranet for in-house administration has been completed. The Clinical Data Analysis Unit is being established.

5.4 Achievements.

1. Awards.

Some staff were awarded.

Recipients	Award
1. Prof.Sornchai Looareesuwan	International Who's Who of Intellectuals, 20 th ed. International Biographical Centre, Cambridge, UK. 1997 The Dushdi Mala Medal. A Royal Decoration from HM The King on 16 September 1997 Who's Who in the World, 15 th ed. New Providence, USA. 1998 Who's Who in Science and Engineering, 4 th ed. New Providence, USA. 1998-1999 Distinguished research in the treatment of malaria from the Pharmaceutical Organization of Thailand, 1997
2. Prof. Supat Sucharit Assist. Prof. (Specialist) Kamhaeng Surathinth Assist. Prof. Narumon Komalamisra Assoc. Prof. Chamnarn Apiwathnasorn	Best research in medical science from the National Research Council of Thailand for the study on species complex of <i>An. minimus</i> , 1997
3. Assoc.Prof. Polrat Wilairatana	Fellowship in the American College of Gastroenterology

2. Published research studies. Fifty-six research studies were published in local and international journals.

Support services continue to play an important role in the smooth running of the Faculty- and School-related activities. These include the Hospital for Tropical Diseases, the research and diagnostic laboratory facilities of the eleven departments, the Central Equipment Unit, the Research and Academic Affairs Unit, the Library, the Information and Computer Unit, the Educational Technology Unit, and the International Relations Unit.

Special Laboratory Services

The Faculty of Tropical Medicine, Mahidol University, offers the following laboratory services and reagents which are not readily available anywhere else.

Immunodiagnoses of various tropical infections

The following table summarizes the diseases/infections for which diagnoses are provided, the serological tests used, the specimen(s) required, the turn around time for each test, the cost per test and the place where specimens should be sent.

Disease/Infection	Serological test used	Specimen required	Time required (hour)	Cost per test (Baht)	Place where specimen should be sent
Gnathostomiasis	1. Indirect ELISA (uses purified specific antigen) 2. Western blot analysis (uses crude extract of the infective larvae)	1. 5 ml of clot blood or 2. 1-2 ml of serum	3 1	300 (Thai) 2,000 (Foreigner)	Dept. Microbiology and Immunology via OPD Dept. Helminthology (Western blot only) via OPD
Paragonimiasis	1. Indirect ELISA 2. Western blot analysis (both assays use partially purified adult worm antigens) 3. Both (crude extract of adult worms)	1. 5 ml of clot blood or 2. 1-2 ml of serum 3. same	3 1 same	300 (Thai) 2,000 (Foreigner) same	Dept. Microbiology and Immunology via OPD Dept. Helminthology OPD
Trichinellosis	1. Indirect ELISA 2. Western blot analysis (both assays use E-S and crude somatic antigens of the infective larvae)	1. 5 ml of clot blood or 2. 1-2 ml of serum	3 1	300 (Thai) 2,000 (Foreigner)	Dept. Microbiology and Immunology via OPD
Strongyloidiasis	1. Indirect ELISA 2. Western blot analysis (uses partially purified antigens from rhabditiform larvae) 3. Indirect ELISA (crude extract of filariform larvae)	1. 5 ml of clot blood or 2. 1-2 ml of serum 3. same	3 1 same	300 (Thai) 2,000 (Foreigner) same	Dept. Microbiology and Immunology via OPD Dept. Helminthology via OPD
Toxocarasis	Indirect ELISA (crude extract of adult worms)	same	same	same	Dept. Helminthology via OPD
Leptospirosis	Microagglutination method and dark-field microscopy using living leptospire	1. 5 ml of clot blood 2. 1-2 ml of serum 3. Blood absorbed onto filter paper	3	60	Dept. Microbiology and Immunology via OPD or directly to Leptospirosis unit, Dept. Microbiology and Immunology

Disease/ Infection	Serological test used	Specimen required	Time required (hour)	Cost per test (Baht)	Place where specimen should be sent
<i>Salmonella</i> septicemia or Salmonellosis and Typhoid	Monoclonal antibody-based dot-blot ELISA using monoclonal antibodies specific to <i>Salmonella</i> core polysaccharide and antigen 9 (antigen detection)	1. Three urine samples collected at 1 hour intervals (5 ml each) 2. Retal swab, Food/water samples in buffered peptone solution	1-2	300	Dept. Microbiology and Immunology via OPD
Cholera caused by serogroup O:1	1. Monoclonal antibody- based dot-blot ELISA using specific monoclonal antibodies to antigen A of <i>V. cholerae</i> serogroup O:1 (antigen detection) (diagnostic kits are also available)	1. Rectal swab in 1% alkaline peptone solution 2. Watery stool 3. Food sample in 2% alkaline peptone solution 4. Water sample in 10% alkaline peptone solution	1-2	150	Dept. Microbiology and Immunology via OPD
Cholera caused by serogroup O:139	1. Monoclonal antibody-based dot-blot ELISA using specific monoclonal antibodies (antigen detection)	1. Rectal swab in alkaline peptone solution 2. Watery stool	3 1	150	Dept. Microbiology and Immunology via OPD

Other tests

Disease/ Infection	Serological test used	Specimen required	Time required (hour)	Cost per test (Baht)	Place where specimen should be sent
Serum folate	Microbiological test using <i>Lactobacillus casei</i>	1. 5 ml of clot blood or 2. 1-2 ml of serum	7	150	Dept. Tropical Radioisotopes
Red cell folate	Microbiological test using <i>Lactobacillus casei</i>	Heparinized blood (2 ml)	7	150	Dept. Tropical Radioisotopes
Vitamin B12 quantitation	Radiodilution assay	1. 5 ml of clot blood or 2. 1-2 ml of serum	5	150	Dept. Tropical Radioisotopes

Disease/ Infection	Serological test used	Specimen required	Time required (hour)	Cost per test (Baht)	Place where specimen should be sent
Pyrogen free testing	Rabbit test by intravenous infection of the fluid to be tested and determination of body temperatures at intervals	Fluid to be tested	7 days	2000	Dept. Microbiology & Immunology
Detection of heavy metals in blood (Lead, arsenic, cadmium, copper, selenium, chromium, aluminium)	Atomic absorption	1. Heparinized whole blood (1 ml)	2	100	Central Equipment Unit or OPD
Detection of lead in air and waste water	Atomic absorption	1. Air sample 2. Water sample	2	100	Central Equipment Unit
Detection of toluene and xylene in air	Gas chromatography mass spectrophotometre	1. Air sample	2	has not yet been set	Central Equipment Unit

Special reagents available

Reagents available at The Faculty of Tropical Medicine*

Reagent	Quality	Cost	Place where the reagent is available
Monoclonal antibodies to <i>V. cholerae</i> O:1	Monospecificity to antigen A of <i>V. cholerae</i> O:1	150 Baht/ml	Dept. Microbiology & Immunology
Monoclonal antibodies to <i>V. cholerae</i> O:139	Monospecificity to <i>V. cholerae</i> O:139 LPS	150 Baht/ml	Dept. Microbiology & Immunology
Monoclonal antibodies to <i>Salmonella</i> core-polysaccharide	Core-polysaccharide of the genus <i>Salmonella</i> (react to all salmonellae)	150 Baht/ml	Dept. Microbiology & Immunology
Monoclonal antibodies to group D <i>Salmonella</i>	Specific to <i>Salmonella</i> antigen 9	150 Baht/ml	Dept. Microbiology & Immunology
Monoclonal antibodies to <i>Pertussis</i> toxin	Specific to S1 component (active, toxic part) of pertussis toxin	150 Baht/ml	Dept. Microbiology & Immunology
Monoclonal antibodies to Verotoxins I and II of enterohaemorrhagic <i>Escherichia coli</i>		150	Dept. Microbiology & Immunology
Monoclonal antibodies to <i>E. coli</i> O157:H7		150	Dept. Microbiology & Immunology
Monoclonal antibodies to the genus <i>Leptospira</i>		150	Dept. Microbiology & Immunology
Monoclonal antibodies to E-S antigen of <i>Trichinella spiralis</i>			Dept. Microbiology & Immunology
Polyclonal antibodies specific to <i>V. cholerae</i> O:1 or O:139	Specific to O antigens of serogroup O:1 or O:139, respectively by extensive absorption with heterologous antigens	1,000 Baht/ml	Dept. Microbiology & Immunology
Endotoxin of Gram negative bacteria (<i>V. cholerae</i> , <i>Salmonella</i> spp., <i>Escherichia coli</i> , and others)	Protein free endotoxin (lipopolysaccharide) from repeated extraction with phenol-water method	200 Baht/ml	Dept. Microbiology & Immunology

* Order should be made in advance

The Central Equipment Unit

Head

Yupa Chantachum M.Eng. (Nuclear Tech.)

Scientist

Hathairad Hananantachai M.Sc. (Environment)

Medical Science Associate

Somchai Poodung Cert. Medical Science Technology

General Affairs Officer

Tuenjai Ketanon Dip. Business Administration (Computer, Secretary)

Functions of the Unit

1. To provide scientific instrumentation and laboratory supplies for research and study within the Faculty
2. To offer assistance and guidance in the operation of on-site equipment to the Faculty's staff
3. To provide a general scientific consultancy service for members of the Faculty

The Educational Affairs Unit

Head

Wanpen Puttitanun B.A.

Educational Affairs Officer

Pramool Sarapantha Ph.D.

Ghosit Chumswat B.A.(Edn.), M.A.(Hist. & Phil.)

Scientist

Chutamas Koomrungruang B.Sc.(Biology)

Medical Scientist

Wannaporn Ittiprasert B.Sc.(Med. Tech.)

General Affairs Associate

Rangson Praevanit Cert.Commercial

Nutjanat Taiwrob Cert.Commercial

Chiraporn Praevanit Voc.Cert.Commercial

Chutarat Pradabprachr B.Ed.

Aree Buaprae

Nuljun Pochana Cert.Commercial

Staff

Anurat Kalasen Cert.Commercial

Srisuchart Monchonmu Cert.Commercial



Wanpen Puttitanun



Pramool Sarapantha



Ghosit Chumswat



Chutamas
Koomrungruang



Rangson Praevanit



Nutjanat Taiwrob



Chiraporn Praevanit



Chutarat Pradabprachr



Aree Buaprae



Nuljun Pochana



Anurat Kalasen



Srisuchart Monchonmu

The Research and Academic Affairs Unit

Head

Pornpimon Adams B.Sc.(Biology), M.Sc.(Trop.Med.)

General Affairs Officer

Warissara Chaiyabhandhu B.A.(General Management)

Sivaporn Sangpan B.A.(Lib.Info.Sc.)

Illustration Officer

Ronnachai Rarerng B.Ed.(Ed.Tech.Inn.)



Sivaporn Sangpan

Warissara Chaiyabhandhu

Pornpimon Adams

Ronnachai Rarerng

The Unit provides publishing facilities such as the Annual Report, the Mosquito-Borne Diseases Bulletin, prospectus, brochures and other printed materials. The unit also maintains a research and abstract database for the Faculty. Other academic services include distribution of research funding information, and organization of the Faculty's annual Seminar and the Chamlong-Tranakchit Harinasuta Lecture, and secretariat service for ethical committee of Faculty of Tropical Medicine, Mahidol University.

The Educational Technology Unit

Head

Sompoch Thanuvathana Cert. Med. Illus., B.Sc.(Med. Illus. & A.V. Tech.), M.Ed.(Ed.Tech.)

Illustration Officer

Pluem Kidkian Dip. Fine Arts, Cert. Med. Illus., B.Sc.(Med. Illus. & A.V. Tech.)

Saranya Vongngernyuang B.Sc.(Med. Illus. & A.V. Tech.)

Staff

Tawan Wathanakul Voc. Cert.

Sanchai Meeprom

The Unit is comprised of 3 divisions :

1. Audio-Visual Division
2. Museum of Tropical Medicine
3. Computer-Assisted Instruction (CAI) Division

Functions of the Unit

1. Produce and service educational media (such as slides, videos, medical illustration, multimedia of tropical diseases) for staff of the Faculty and Hospital for Tropical Diseases, and Assistant Nurses of the Hospital School
2. Prepare and control audio-visual equipment for teaching, seminars and workshops
3. Provide instruction in making educational media to staff and others, both inside and outside the Faculty



Sompoch Thanuvathana



Pluem Kidkian



Saranya Vongngernyuang



Tawan Wathanakul



Sanchai Meeprom

The Information Technology Unit

Head

Duangjai Sahassananda B.Sc.(Med.Tech.)

Programmer

Somchai Pichaiyongvongdee B.Sc.(Public Health)

General Affairs Associate

Pramot Ketsuk B.Sc. (Computer Science)

Jetsadaporn Chantachorn B.A.(General Management)

Electronic Associate

Pongnatee Kingsawat (Electronic)

The Information Technology Unit provides information and computer services through the year 1998 for the faculty's staff, students and participants in the short training courses as :

I. Lecture

Special lecture in information technology
6 times

II. IT visiting

IT visiting other institutes
6 times

III. Training

Computer software training 12 times
for 226 participants and 38 observers
(20 terminals each time)



IV. General services

- Computer room 3,115 times
- UTP installations 26 stations
- Consulting/Program installation/Virus scan 292 times

(Not include emergency call and telephone consult)

- Computer upgrade 18 machines
- Slide making 4,869 frames
- Laser print 1,113 pages
- Color print 446 pages
- Making Certificates 500 copies
- Computer scan image and OCR 862 pages



V. Database projects

The unit has 3 projects for the information technology as :-

1. AHEAD project

This project collaborate with the IDRC to make the CD-ROM on Asian Health, Environmental and Allied Databases. The function of the Unit is to collect the information on mosquito-borne diseases and prepare in the electronic form.

2. HEED-Net project

This project will collaborate with the Ministry of Public Health; Faculty of Economics, Chulalongkorn University and Faculty of Tropical Medicine, Mahidol University to make the health and economic information in the GIS form.

3. SEAMEO-TROPMED (Virtual Library, Homepage).

VI. Application development

The unit has to develop the computer system and programming for 3 topics as :

- Hospital Database Development on a Client/Server Environment, Case study on the Hospital for Tropical Diseases.
- Database development for the service of the Information Technology Unit.
- Stock Database system for the Central Equipment Unit.
- Faculty Homepage on <http://www.mahidol.ac.th/mahidol/tm/h-tromed.htm>
- Intranet for Administrator Section.

The International Relations Unit

Head

Keeratiya Nontabutra B.A.

Staff

Wanida Onwan B.A.

Prachoom Buaprasert



Keeratiya Nontabutra



Wanida Onwan

SHORT TRAINING COURSES

From time to time the Faculty, in conjunction with other National Centres for Tropical Medicine and Public Health in Southeast Asia and some international organizations, organizes training courses and workshops on special subjects in a range of medical, public health and biomedical science areas, aiming to combine training in the methods of research with work which contributes to the advancement of knowledge. The courses that are held regularly each year are:

- 1. Regional Training Courses on the Control of Intestinal Helminthic Infections with Special Emphasis on Soil-transmitted Helminthiasis, Family Planning Practice and Integrated Programmes**, a two-week course organized by the Department of Helminthology each year in October/November with support from the Japanese Organization for International Co-operation in Family Planning (JOICFP), the Asian Parasite Control Organization (APCO) and Japan Association for Parasite Control (JAPC).
strengthen research and training capability in the field of clinical pharmacology, with special reference to the chemotherapy of malaria, and disseminate information on proper management of infections.
- 2. Asian Course in Tropical Epidemiology**, a three-week course in tropical epidemiology in collaboration with the Asian and European Tropical Epidemiology Group (GTZ), SEAMEO TROPMED and WHO-TDR conducted each year in November.
- 3. Workshop on Clinical Tropical Pharmacology in the Chemotherapy of Malaria**, a two-week to one-month international short course in clinical tropical pharmacology. The workshop is held annually from July to August, with financial support from WHO, SEAMEO TROPMED Network, and the Natural Science and Technology Development Agency of Thailand. Participants are medical doctors and research scientists who are working or plan to work in this field. The objectives of the course are to upgrade and
- 4. Workshop in Practical Clinical Parasitology**, this two-week course organized by Department of Helminthology, Department of Protozoology and Clinical Pharmacology Unit, Faculty of Tropical Medicine, Mahidol University. The course offered in October, consists of a series of lectures on the parasites, diagnosis, clinical manifestation and treatment. Hands-on laboratory sessions covering the diagnosis of parasitic infections are included.
- 5. Travel Medicine for Danish General Practitioners**, this course is specially arranged by the collaboration of Department of Infectious Diseases Aarhus University Hospital, University of Aarhus, Denmark and the Department of Clinical Tropical Medicine and Department of Tropical Paediatrics, Faculty of Tropical Medicine, Mahidol University, Bangkok. The Faculty has jointly offered this special short course for Danish General Practitioners' since 1996. This short course aims to enrich the Danish general practitioners understanding of the clinical, epidemiological and prevention of tropical diseases particularly Southeast Asia.

Workshops and Training Courses

1 October 1997 - 30 September 1998

1. Workshop on Cost-Effectiveness Analysis of Disease Vector Control

29 September - 3 October 1997

Participants from :	Bangladesh	2	Bhutan	1
	Indonesia	2	Maldives	2
	Myanmar	2	Nepal	2
	Sri Lanka	2	Switzerland	2
	Thailand	4		
	Total	19		

Workshop and Training Courses

2. The APCO Training Course for Senior Administrators and Leaders of Parasitic Control Project

10 - 19 November 1997

Participants from :	Bangladesh	2	Bhutan	2
	Cambodia	2	Indonesia	2
	Lao PDR	2	Malaysia	2
	Myanmar	2	Nepal	2
	Philippines	2	Sri Lanka	2
	Vietnam	2	Thailand	6
	Total	28		

3. Regional Workshop on Geographic Information Systems : Disease Mapping for Tropical Infections & Vector-Borne Diseases

15 - 19 December 1997

Participants from :	Cambodia	2	Lao PDR	2
	Indonesia	2	Malaysia	2
	Philippines	4	Thailand	2
	Vietnam	2	PR China	1
	Republic of Maldives	1		
	Total	18		

4. Austrian Course Diploma for Tropical Medicine

5 - 30 January 1998

Participants from :	Austria	9
	Total	9

5. Workshop on Clinical & Laboratory Diagnostic Parasitology : A Practical Approach for Better Health Services

19 - 30 January 1998

Participants from :	Cambodia	2	Indonesia	1
	Lao PDR	2	Myanmar	2
	Vietnam	3	Thailand	16
	Total	26		

6. Regional Workshop on Development of Research Protocols

16 - 18 March 1998

Participants from :	Cambodia		Lao PDR	
	PR China		Vietnam	
	Myanmar			
	Total		7	

7. Workshop on the Design, Conduct and Reporting of Clinical Trial

3 - 11 August 1998

Participants from :	Bangladesh	1	Hong Kong	2
	Lao PDR	2	Malaysia	2
	Myanmar	1	Vietnam	2
	Thailand	10		
	Total	20		

Workshop and Training Courses

8. Workshop on Diagnostic Microbiology

9-20 March 1998 at Mahosot Hospital, Lao PDR

Participants from :	Cambodia	5
	Lao PDR	15

Total	20
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9. Postgraduate Training in Epidemiology for one WHO fellow from Maldives,

14 July 1997 -14 May 1998

10. Training on Investigation of Causative Agents of Acute Respiratory Infections for one WHO fellow from Lao PDR

6 October - 28 November 1997

11. Training on Clinical and Laboratory Diagnostic Parasitology for one WHO fellow from Sri Lanka,

20 October - 7 November 1997

12. Training on Bacteriology of Diarrhoeal Diseases for one WHO fellow from Sri Lanka

3 - 28 November 1997

13. Training on Research Methodology for one WHO fellow from Bangladesh

3 November 1997 - 23 January 1998

14. Training on Vector Borne Diseases for 2 USAID fellows from Nepal

15 June - 10 September 1998

15. Training on Medical Parasitology for one WHO fellow from Sri Lanka

28 September - 16 October 1998

16. Joint International Tropical Medicine Meeting 1998

20 - 21 August 1998

Participants : 350

INTERNATIONAL LINKAGES

The Faculty of Tropical Medicine has ongoing collaborative activities on research and training with the following :

1. WHO/TDR programme
2. Freie University of Berlin, Germany, under the assistance of German Agency for Technical Cooperation
3. Liverpool School of Tropical Medicine, UK
4. Martsinovsky Institute of Medical Parasitology and Tropical Medicine, Russian Federation
5. The University of Calgary, Canada
6. Nuffield Department of Medicine, University of Oxford, UK
7. Asian Parasite Control Organization (APCO), Japan
8. The Wellcome Trust, UK
9. International Development Research Centre (IDRC), Canada
10. Japanese Organization for International Cooperation in Family Planning (JOICFP), Japan
11. SEAMEO TROPMED Regional Centres in Indonesia, Philippines and Malaysia
12. University of Innsbruck, Austria
13. Queensland Institute of Medical Research, Australia
14. James Cook University of North Queensland, Australia
15. Deutsche Gesellschaft für Technische Zusammenarbeit (GTZ), Germany
16. Department des Maladies Infecteuses et Médecin Tropicale, Groupe Hospitalier Pitie Salpêtrière, France
17. Pasteur Institute, France
18. Chinese Academy of Preventive Medicine, PR China
19. Airlangga University, Surabaya, Indonesia
20. Naval Medical Research Institute, Bethesda, Maryland, USA
21. Agreement for Academic Exchange and Cooperation between University of Tsukuba, Japan and Mahidol University, Kingdom of Thailand.
22. Memorandum of Understanding, Collaboration between the Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand, the SEAMEO TROPMED Network and the Swiss Tropical Institute, Basel, Switzerland.
23. Agreement of Co-operation between the Tropical Medicine and Public Health Network of the Southeast Asian Ministers of Education Organization (SEAMEO TROPMED) and the Australian Centre for International and Tropical Health and Nutrition (ACTTHN) of the Queensland Institute of Medical Research and the University of Queensland.
24. Memorandum of Understanding between the Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand and the Health of Animals Laboratory, Canadian Food Inspection Agency, Government of Canada, Saskatoon, Canada.

The nature of these activities are : collaborative research works; consultative services; personnel, specimen and information exchanges, joint training courses, seminars and conferences.

During October 1997 - September 1998

Name	Country/Organization	Name	Country/Organization
1. Prof. Wernsdorfer	Austria	61. Dr. Alicia P. Magos	Philippines
2. Wolfram Brunger	Belgium	62. Dr. Francisco Felizar, Jr.	Philippines
3. Dr. Nigel	Belgium	63. Chancellor Cristina Padolina	Philippines
4. Dr. Mohammad	Brunei Darussalam	64. Dr. Art Pesigan	Philippines
5. Dr. Claire Mathewson	Canada	65. Dr. Roderick Ofirin	Philippines
6. Dr. Clarence A. Guenter	Canada	66. Dr. Yang Huang	PR China
7. Mrs. Guenter	Canada	67. Dr. Cheng Hong	PR China
8. Dr. Amar Kureishi	Canada	68. Dr. Li Xue-Zhong	PR China
9. Dr. May Ho	Canada	69. Dr. Duo Lin	PR China
10. Dr. Alessio Panza	EU/Thailand	70. Zuo Jiazheng	PR China
11. Dr. Frederick Gay	France	71. Hu Junsheng	PR China
12. Dr. Adrien Six	France	72. Duan Xinwen	PR China
13. Dr. Jean Paul Gonzalez	France	73. Zhang Yanhe	PR China
14. Dr. Sylvester	German	74. Song Shunyou	PR China
15. Dr. Rudiger Kluge	German	75. He Xiaojun	PR China
16. Dr. Ridad Agoes	Indonesia	76. Wu Xiaochun	PR China
17. Dr. Rainer Gross	Indonesia	77. Zheng Ying	PR China
18. Prof. Hagai Ginsburg	Israel	78. Liao Yongxiang	PR China
19. Moshe Hoshen	Israel	79. Luo Yaoju	PR China
20. Wilfred Stein	Israel	80. Du Ying	PR China
21. Dr. Pandu Wijeyaratne	ISTI, USA	81. Jin Kuan	PR China
22. Dr. Maj. Koki Kaku	Japan	82. Jiang Qingwu	PR China
23. Prof. Toshio Nakabayashi	Japan	83. Zhang Hongru	PR China
24. Prof. Hiroshi Ohtomo	Japan	84. Qu Yanglin	PR China
25. Dr. Hisao Kurazono	Japan	85. Zhao Ruqin	PR China
26. Dr. Masamichi Aikawa	Japan	86. Li Dong	PR China
27. Prof. Kiyoshi Kita	Japan	87. Deng Tianwan	PR China
28. Mr. Norio Mogi	Japan	88. Liu Aiting	PR China
29. Mr. Yasuharu Matsumoto	Japan	89. Hu Chengfa	PR China
30. Mr. Makoto Kanie	Japan	90. Pan Yuhua	PR China
31. Mr. Makoto Iwaki	Japan	91. Shen Wenlong	PR China
32. Prof. Akihiko Yano	Japan	92. Luo Liangul	PR China
33. Mr. Masaharu Yoshida	Japan	93. Lihe	PR China
34. Mr. Kenichi Kimiya	Japan	94. Ma Shaoliang	PR China
35. Mr. Kazumi Jigami	Japan	95. Yang Yiqing	PR China
36. Mr. Shigeki Fukuda	Japan	96. Yang Changgui	PR China
37. Dr. Masaru Umeda	Japan	97. Zhao Ruixiang	PR China
38. Dr. Takaaki Hara	Japan	98. Dong Yingkuan	PR China
39. Mr. Ryuji Matsunaga	Japan	99. Li Fuan	PR China
40. Dr. Masato Kawabata	Japan	100. Fan Youde	PR China
41. Ms. Yukak Morimatsu	Japan	101. Wen Qi	PR China
42. Mr. Taro Honiyou	Japan	102. Dou Lin	PR China
43. Ms. Youko Iwasaki	Japan	103. Dr. Lugt	Switzerland
44. Ms. Satsuki Shimabukuro	Japan	104. Dr. Peter	Switzerland
45. Mr. Hirotaka Shiratori	Japan	105. Dr. Rossi Sasuni	Switzerland
46. Ms. Eriko Tomita	Japan	106. Dr. Ali	Switzerland
47. Dr. Hiroyuki Wakiyama	Japan	107. Dr. Hocard Engers	Switzerland
48. Mr. Manabu Saito	Japan	108. Dr. Farrokh Modabber	Switzerland
49. Mr. Tomonori Aoyama	Japan	109. Dr. Marie Lin	Taiwan
50. Mr. Kouta Imasimizu	Japan	110. Mrs. Ngampisa Aksornprai	Thailand
51. Mr. Shogo Ehata	Japan	111. Dr. Cathy Walton	UK
52. Mr. Takashi Doi	Japan	112. Dr. Charmaine Philips	UK
53. Mr. Mitsuyosi Suzuki	Japan	113. Prof. Michael Dexter	UK
54. Mr. Takanori Yajima	Japan	114. Dr. Bob Howells	UK
55. Ms. Seiko Suzuki	Japan	115. Prof. H.M. Gilles	UK
56. Prof. Ushijima	Japan	116. Dr. Leopoldo Villegas	UK
57. Dr. Khamphong	Lao PDR	117. Dr. Valerie Goodrich	USA
58. Dr. Chansy	Lao PDR	118. Dr. Chris Geohas	USA
59. Dr. Supachai	Lao PDR	119. Dr. Gary Brittenham	USA
60. Dr. Wolf Wagner	Mongolia	120. Dr. Patricia L. Rosenfield	USA

Name	Country/Organization	Name	Country/Organization
121. Dr. Donald Francis	USA	139. Mr. Nguyen Duc Thuc	Vietnam
122. Ms. Marlene	USA	140. Ms. Nguyen Thi Phi Thao	Vietnam
123. Ms. Diana Lee	USA	141. Mr. Le Dinh Hien	Vietnam
124. Dr. Nguyen Van Bien	Vietnam	142. Mr. Nguyen Duc Hanh	Vietnam
125. Dr. Nguyen Van Thinh	Vietnam	143. Mr. Vuong Thai Lu	Vietnam
126. Dr. Nguyen Van Toan	Vietnam	144. Mr. Nguyen Duc Thuan	Vietnam
127. Mr. Nguyen Van De	Vietnam	145. Mr. Le Ba Kieu	Vietnam
128. Mr. Doanh Baccam	Vietnam	146. Mr. Tran Buu	Vietnam
129. Mr. Bui Dac Thang	Vietnam	147. Prof. Nguyen Thi Ha	Vietnam
130. Mr. Le Xuan Hao	Vietnam	148. Dr. Le Van Khang	Vietnam
131. Mr. Le Tung	Vietnam	149. Prof. Duong Dinh Thien	Vietnam
132. Ms. Bui Thi Binh	Vietnam	150. Dr. Tran Van Dan	Vietnam
133. Mr. Nguyen Thanh Cong	Vietnam	151. Dr. Le Thi Hoan	Vietnam
134. Mr. Hoang Hong	Vietnam	152. Dr. Luu Ngoc Hoat	Vietnam
135. Mr. Le Huu Van	Vietnam	153. Dr. P.K. Das	WHO/SEARO
136. Mr. Tran Trong Hien	Vietnam	154. Dr. Chusak Prasittisuk	WHO/SEARO
136. Mr. Tran Trong Hien	Vietnam	155. Dr. P.R. Arbani	WHO/SEARO
137. Mr. Nguyen Phu Dong	Vietnam	156-163 SEAMEO-Internships 8 persons	Canada
138. Mr. Pham Thanh Toan	Vietnam		

STUDENT AND RESEARCHERS STUDENTS FROM OVERSEA ATTENDING ELECTIVE PROGRAMME OR TROPMED RESEARCH IN 1998

Name	Country	Institute	Subject	During
1. Mr.Sven-Erik Lehm	UK	Faculty of Medicine, University of Liverpool	PhD Sandwich programme in Entomology	2-23 Jan.1998
2. Ms.Charmaine Phillips	UK	Faculty of Medicine, University of Liverpool	Elective Programme in Tropical Medicine	9-15 June 1998
3. Ms.Louise Scovell	UK	Faculty of Medicine, University of Liverpool	Elective Programme in Tropical Medicine	9-15 June 1998
4. Ms.Martina Enk	Austria	Faculty of Medicine, University of Innsbruck	Elective Programme in Tropical Medicine	6-31 July 1998
5. Ms.Ines Derflinger	Austria	Faculty of Medicine, University of Innsbruck	Elective Programme in Tropical Medicine	6-31 July 1998
6. Ms.Simone Holl	Austria	Faculty of Medicine, University of Innsbruck	Elective Programme in Tropical Medicine	3-31 Aug.1998
7. Mr.Eugen Sleiter	Austria	Faculty of Medicine, University of Innsbruck	Elective Programme in Tropical Medicine	3-31 Aug.1998
8. Mr.Burger Dietmar	Austria	Faculty of Medicine, University of Innsbruck	Elective Programme in Tropical Medicine	3-31 Aug.1998
9. Mr.Rainer Gattringer	Austria	Faculty of Medicine, University of Vienna	Elective Programme in Tropical Medicine	20 July-11 Sept.1998
10. Mr.Michael Ramhartr	Austria	Faculty of Medicine, University of Vienna	Elective Programme in Tropical Medicine	20 July-11 Sept.1998
11. Mr.Gerhard Poppl	Austria	Faculty of Medicine, University of Vienna	Elective Programme in Tropical Medicine	20 July-11 Sept.1998
12. Dr.Soe Win	Myanmar		Research on Malaria	15 July 1998-14 July 1999
13. Mr.Daniel P. Mason	USA	Harvard University	Research on Malaria	7 Sept.1998 - Aug.1999

LECTURERS AND THEIR AREAS OF EXPERTISE

Lecturer	E-mail Address	Field of Specialization/Expertise
Achara Asavanich	tmaas@mahidol.ac.th	Malaria vector
Arunee Sabchareon	tmasc@mahidol.ac.th headtmpd@mahidol.ac.th	Malaria in children
Bhistsavat Pongpanluk	-	Fundamental of nursing
Chalit Komalamisra	tmckm@mahidol.ac.th	Helminthology
Chamnarn Apiwathnasorn	tmcaw@mahidol.ac.th	Mosquito taxonomist/Ecologist/Field Study
Channarong Sanghirun	rd123@mahidol.ac.th headtmrd@mahidol.ac.th	Radioisotopes in medical science and biology Monoclonal antibody for diagnosis of parasites
Chantima Lohachit	tmclh@mahidol.ac.th	Medical and freshwater malacology Limnology/Ecology/Spermatogenesis (TEM) Environmental Health
Chotechuang Panasoponkul	tmcpn@mahidol.ac.th	Vector borne diseases eg. Filariasis, Malaria and Field work
Chukiat Sirivichayakul	tmcsw@mahidol.ac.th	General pediatrics Chemotherapy of childhood malaria Parasitic infection in children Childhood diarrhea
Chutatip Siripanth	tmcsr@mahidol.ac.th	Cultivation of <i>Giardia</i> and <i>E. histolytica</i>
Dwip Kitayaporn	tmckt@mahidol.ac.th	Epidemiology of HIV/AIDS Research methodology
Emsri Pongponratn	tmep@mahidol.ac.th headtmpa@mahidol.ac.th	Electronmicroscopy : pathology of malaria
Jintana Pattarapotikul	tmjpt@mahidol.ac.th	Immunology and molecular biology of malaria
Jitra Waikagul	tmjwk@mahidol.ac.th	Taxonomy / Biology of helminths
Kasinee Buchachart	tmkbc@mahidol.ac.th	Statistical analysis & data processing of epidemiological research
Kesara Na-Bangchang	tmknb@mahidol.ac.th	Pharmacokinetics/Drug Metabolism
Krisana Pengsaa	tmkps@mahidol.ac.th	General pediatrics Chemotherapy of parasitic diseases Immunization in children/Neonatal infection
Ladda Tangbanluekal	grltb@mahidol.ac.th	Environmental and industrial toxicology Health risk assessment from toxicants
Malinee Thairungroj	-	Medical helminthology/Immunodiagnosis
Manas Chongsa-nguan	tmmcs@mahidol.ac.th	Immunology of tropical infections Bacterial identification
Mario Riganti	-	Anatomical pathology Gnathostomiasis Chemotherapy of gnathostomiasis Tropical pathology
Narumon Komalamisra	tmnkm@mahidol.ac.th	Isoenzyme of vectors/Vector genetics/ Molecular entomology
Nilarat Premmanisakul	tmnpr@mahidol.ac.th	Medical epidemiology
Nitaya Thammapalerd	tmntm@mahidol.ac.th	Immunology and molecular biology of amoebiasis
Niyomsri Vudhivai	tmnvd@mahidol.ac.th	Biochemical nutrition/Community nutrition
Panyawut Hiranyachattada	tmphr@mahidol.ac.th	Helminthology
Parnpen Viriyavejakul	tmpvr@mahidol.ac.th	Anatomical pathology / Opportunistic infections in AIDS
Paron Dekumyoy	tmpdk@mahidol.ac.th	Immunodiagnosis of helminthiasis

Lecturer	E-mail Address	Field of Specialization/Expertise
Petcharin Yamarat	tmpym@mahidol.ac.th	Rheology of malarial blood, blood of subjects digested garlic, cord blood
Phanorsri Attanath	tmpat@mahidol.ac.th	<i>In vitro</i> sensitivity test to antimalarials Pharmacokinetics of antimalarials
Piyarat Butraporn	tmpbt@mahidol.ac.th headtmse@mahidol.ac.th	Social epidemiology in tropical diseases Health impacts of water resource development
Polrat Wilairatana	tmpwl@mahidol.ac.th	Tropical gastroenterology Pathophysiology of severe malaria
Ponganant Nontasut	tmpnd@mahidol.ac.th	Chemotherapy in intestinal parasites
Pornthep Chanthavanich	tmpct@mahidol.ac.th	Chemotherapy of parasitic diseases Chemotherapy of malaria in children Vaccination in children
Porntip Petmitr	tmppm@mahidol.ac.th	Biochemistry of malaria parasites, cultivation of <i>P. falciparum</i> gametocytes and <i>T. vaginalis</i>
Pramuan Tapchaisri	tmpct@mahidol.ac.th	Immunology, molecular biology of tropical infections
Praneet Pongpaew	tmppp@mahidol.ac.th	Nutritional epidemiology/Community nutrition
Pratap Singhasivanon	tmpsh@mahidol.ac.th	Epidemiology of tropical diseases / Research methodology
Pravan Suntharasamai	tmpst@mahidol.ac.th	Clinical tropical medicine Vaccinology/Clinical epidemiology
Punnee Pitisuttithum	tmppt@mahidol.ac.th	Tropical diseases vaccine trial especially Phase I, II vaccine trial eg. Cholera vaccine, Rotavirus vaccine, AIDS vaccine, etc., Clinical studies of tropical diseases eg. cryptococcal meningitis in AIDS; chronic diarrhea in AIDS, etc. Drug trial in AIDS with opportunistic infection
Ratanaporn Kasemsuth	tmrks@mahidol.ac.th	Radioisotopes in medical science and biology RIA. (Radio Immunoassay)
Rungsunn Tungtrongchitr	tmrtg@mahidol.ac.th	Community nutrition/Nutritional epidemiology
Sasithon Pukrittayakamee	tmspk@mahidol.ac.th	Tropical medicine
Sirivan Vanijanonta	tmsvn@mahidol.ac.th	Clinical tropical medicine Parasitic lung infectious diseases CNS parasitic diseases Tropical geriatrics Amoebiasis
Somjai Leemingsawat		Tick and mite-borne diseases Filarial parasites & vectors
Songsak Petmitr	tmspm@mahidol.ac.th	Molecular biology/Cancer
Sornchai Looareesuwan	tmslr@mahidol.ac.th	Pathophysiology of severe malaria Chemotherapy of malaria
Srisin Khusmith	tmskm@mahidol.ac.th	Immunology/Molecular biology/Malaria
Srivicha Krudsood	tmsks@mahidol.ac.th	Internal medicine
Supatra Thongrunkiat	tmstr@mahidol.ac.th	Mosquito colonization/Malaria parasite & vector Dengue virus and vector/Mosquito inoculation
Supranee Changbumrung	tmscb@mahidol.ac.th headtmnu@mahidol.ac.th	Biochemical nutrition Nutritional epidemiology Nutritional toxicology

Lecturer	E-mail Address	Field of Specialization/Expertise
Surang Tantivanich	tmstt@mahidol.ac.th	Medical virology
Talabporn Harnroongroj	tmthr@mahidol.ac.th	Community nutrition/Biochemical nutritional
Thaiyooth Chintana	tmtct@mahidol.ac.th headtmpz@mahidol.ac.th	Amoeba, <i>Toxoplasma gondii</i>
Thongchai Deesin	-	Ecologist / Vectors borne diseases/Field study
Udomsak Silachamroon	-	Internal medicine/Pulmonary Medicine/TB
Usanee Suthisarnsuntorn	-	Clinical microbiology/Bacteriology Infections diseases pediatrics
Valai Bussaratid	tmvbs@mahidol.ac.th	Dermatology/Internal medicine
Vanida Deesin	tmvdi@mahidol.ac.th	Vector control/Vector borne diseases
Varaporn Suphadtanaphongs	tmwsp@mahidol.ac.th	Cultivation and drug sensitivity test of <i>P. falciparum</i>
Varee Wongchotigul	tmvwc@mahidol.ac.th	Rickettsiology (Scrub typhus)
Varunee Desakorn	tmvds@mahidol.ac.th	Immunodiagnosis/Biostatistics
Venus Supawan	tmvsp@mahidol.ac.th	Biochemical nutrition/Community nutrition
Vichitra Pornkulprasit	tmvpk@mahidol.ac.th	Radiology
Voranuch Wangsuphachart	tmvws@mahidol.ac.th	Environmental epidemiology Comparative risk assessment Epidemiology of internet
Wanchai Phatihatakorn	tmwpk@mahidol.ac.th	Environmental health impact assessment GRD Monitoring, evaluate and surveillance of parasitic disease
Wanpen Chaicumpa	tmwcc@mahidol.ac.th	Immunology of tropical infections
Waranya Wongwit	tmwvg@mahidol.ac.th	Biochemistry of parasites (gene therapy)
Watcharee Chocejindachai	tmwar@mahidol.ac.th	Chemotherapy of malaria in children Chemotherapy of parasitic diseases Vaccine/General pediatrics
Weerapong Phumratanaprapin	tmwpr@mahidol.ac.th	Internal medicine
Wichai Supanaranond	tmwsp@mahidol.ac.th	Dermatology / Sexual transmitted diseases
Wichit Rojekittikhun	tmwrj@mahidol.ac.th	Helminthology (esp. <i>Gnathostoma</i> & immunodiagnosis)
Wijitr Fungladda	tmvfd@mahidol.ac.th	Social epidemiology of tropical diseases (malaria, opisthorchiasis)
Wipawee Usawattanakul	tmwus@mahidol.ac.th	Immunology of parasitic infections
Yaowalark Sukthana	tmymv@mahidol.ac.th	Oto-Rhino-Laryngology/ <i>Toxoplasma gondii</i>
Yaowapa Maneerat	tmymn@mahidol.ac.th	Pathology of malaria (Cytokines & nitric oxide involvement)
Yupaporn Wattanagoon	tmywt@mahidol.ac.th	Internal medicine
Yuvadee Mahakunkijcharoen	tmymh@mahidol.ac.th	Immunology of parasitic infections and bacterial infections

ONGOING RESEARCH PROJECTS OF FACULTY OF TROPICAL MEDICINE IN 1998

No.	On going Research Projects in 1998	Grants	Principal Investigator
Department of Clinical Tropical Medicine			
1	Pharmacokinetics and pharmacodynamics of the combination dihydroartemisinin-mefloquine in healthy subjects with uncomplicated falciparum malaria	The Thailand Research Fund (TRF)	Assoc.Prof. Kesara Na-Bangchang
2	Immunogenetic analysis of uncomplicated and severe malaria defined clinically and pharmacologically	Japan Association for Tropical Medicine	Prof. Juntra Laothavorn
3	Gastric emptying in patients with acute falciparum malaria	Faculty of Tropical Medicine	Assoc.Prof. Polrat Wilairatana
4	Pharmacokinetics and pharmacodynamics of AZT and AZT-triphosphate in healthy subjects, asymptomatic HIV-positive, and symptomatic AIDS patients	SEAMEO - TROPMED and University of Liverpool, UK.	Assoc.Prof. Yupaporn Wattanagoon
5	Study on stage development of <i>Plasmodium falciparum</i> <i>in vitro</i>	Wellcome Unit	Mr. Apichart Nontprasert
6	Pharmacokinetics and dose-finding studies of the combination artemether/proguanil in healthy subjects and patients with uncomplicated falciparum malaria	Ph.D. Grant	Prof. Juntra Laothavorn
7	Clinical study to fine effective regimen for the treatment of uncomplicated falciparum malaria in rural area	Government Budget	Assoc.Prof. Polrat Wilairatana
8	Assessment of the neurotoxicity of parenteral artemisinin derivatives in mice	Wellcome Trust of Great Britain	Mr. Apichart Nontprasert
Department of Helminthology			
9	The IFAT for human gnathostomiasis	Mahidol University	Miss Wattana Pahuchon
10	Monoclonal antibody-based competitive ELISA and indirect ELISA for immunodiagnosis of trichinosis	Mahidol University	Mrs. Supaporn Nuamtanong
11	Comparison of biochemical extract preparations of <i>Cysticercus cellulosae</i> by SDS - polyacrylamide gel electrophoresis and immunoblot technique	Mahidol University	Assist.Prof. Paron Dekumyoy
12	Experimental infection of freshwater fish in Thailand with infective stage of <i>Angiostrongylus</i>	Mahidol University	Assist.Prof. Chalit Komalamisra
13	<i>Toxocara canis</i> larval antigens for serodiagnosis of human toxocarasis	Mahidol University	Assist.Prof. Wanna Maipanich

No.	On going Research Projects in 1998	Grants	Principal Investigator
Department of Helminthology			
14	Efficacy of high dose mebendazole against trichuriasis in adult patients	Mahidol University	Assoc.Prof. Jitra Waikagul
15	The effects of <i>Trichinella spiralis</i> infection on renal functions in rat	APCO, Japan	Mr. Panyawut Hiranyachattada
Department of Medical Entomology			
16	Evaluation of some certain chemical stimuli as attractants for sound trapping of <i>Culex tritaeniorhynchus</i>	Faculty of Tropical Medicine	Assoc.Prof. Vanida Deesin
17	Medicinal plants for control of mosquitoes and flies		Assoc.Prof. Yupha Rongsriyam
18	Combination effects of <i>Bacillus sphaericus</i> 2362 and the insect growth regulator for the control of Anopheline vector in small scale field trial	Faculty of Tropical Medicine	Assoc.Prof. Yupha Rongsriyam
19	Critical biology and disease transmission indices in dengue	Government Budget	Assoc.Prof. Yupha Rongsriyam
20	Enzyme study in <i>Aedes aegypti</i> vector of dengue fever, dengue haemorrhagic fever and dengue shock syndrome	National Research Council of Thailand (NRCT)	Prof. Supat Sucharit
21	Comparative susceptibility to oral infection with dengue virus among local strain of <i>Aedes aegypti</i> collected at different seasons of the year	National Research Council of Thailand (NRCT)	Assist.Prof. Supatra Thongrunkiat
22	Computer aided management and service of biological museum Faculty of Tropical Medicine	NECTEC	Assoc.Prof. Chamnarn Apiwathnasorn
23	Contamination and accumulation of some heavy metals, lead and cadmium in <i>Culex quinquefasciatus</i> and <i>Musca domestica</i>	Mahidol University	Assoc.Prof. Chamnarn Apiwathnasorn
24	Pyrethroid resistance and its significance in malaria control		Assoc.Prof. Yupha Rongsriyam
25	Specificity of the synthetic primers from sequencing DNA fragments of <i>Anopheles minimus</i>	Faculty of Tropical Medicine	Assist.Prof. Narumon Komalamisra
26	Impacts of permethrin impregnated bednets on <i>Anopheles dirus</i>	National Research Council of Thailand (NRCT)	Assoc.Prof. Vanida Deesin
Department of Microbiology and Immunology			
27	Anaerobic bacteria intraabdominal infection	Mahidol University	Assoc.Prof. Suvanee Supavej

No.	On going Research Projects in 1998	Grants	Principal Investigator
Department of Microbiology and Immunology			
28	Production of monoclonal antibodies for use in the diagnosis of scrub typhus	Faculty of Tropical Medicine	Mrs. Varee Wongchotigul
29	Production of monoclonal antibodies against cyst specific antigens of <i>Entamoeba histolytica</i>	Faculty of Tropical Medicine and National Research Council of Thailand (NRCT)	Assoc.Prof. Nitaya Thammapalerd
30	Detection of dengue virus in mosquitoes (<i>Aedes aegypti</i>) by Polymerase Chain Reaction virus-cultivation	Mahidol University	Assoc.Prof. Wipawee Usawattanakul
31	Development of Polymerase Chain Reaction for the diagnosis of vivax malaria	Mahidol University	Assoc.Prof. Pramuan Tapchaisri
32	Diagnostic mycology lab set-up for deep mycoses (Antimycotic testing for yeasts)	Mahidol University	Assist.Prof. Usanee Suthisarnsuntorn
33	Identification and characterization of T cell epitopes on <i>P. falciparum</i> sporozoite surface protien 2 recognized by human		Prof. Srisin Khusmith
34	Role of CD8+ cytotoxic T lymphocytes in HIV/AIDS		Prof. Srisin Khusmith
35	Cloning of <i>Salmonella</i> enterotoxin gene	Tsukuba University, Japan	Assoc.Prof. Manas Chongsa-nguan
36	Genetic and biologic variations of <i>T. spiralis</i> (Thai isolates)		Prof. Wanpen Chaicumpa
37	Hybridoma technology for specific monoclonal antibodies to <i>Shigella</i> spp.		Prof. Wanpen Chaicumpa
38	Penicillin E-test for Streptococcus pneumoniae	Mahidol University	Assist.Prof. Usanee Suthisarnsuntorn
39	MRSA detection by E-test	Mahidol University	Assist.Prof. Usanee Suthisarnsuntorn
40	Rapid diagnosis of Shigellosis	NSTDA	Prof. Wanpen Chaicumpa
41	Preparation of monoclonal antibodies to Shiga-like toxin of enterohaemorrhagic <i>E. coli</i>	NSTDA	Prof. Wanpen Chaicumpa
42	The use of recombinant <i>Entamoeba histolytica</i> pyruvate : ferredoxin oxidoreductase (γ PFOR) as a candidate vaccine against invasive amoebiasis		Assoc.Prof. Nitaya Thammapalerd
43	Production of recombinant pyruvate : ferredoxin oxidoreductase of <i>Entamoeba histolytica</i> (Eh γ PFOR) and its application for diagnosis of invasive amoebiasis		Assoc.Prof. Nitaya Thammapalerd
44	Development of leptospirosis diagnosis	NSTDA	Prof. Wanpen Chaicumpa

No.	On going Research Projects in 1998	Grants	Principal Investigator
Department of Microbiology and Immunology			
45	Pathology of enterohaemorrhagic <i>Escherichia coli</i> infection	The Thailand Research Fund (TRF)	Prof. Wanpen Chaicumpa
46	Monoclonal antibodies to Shiga-like toxins of enterohaemorrhagic <i>E. coli</i>	NSTDA	Prof. Wanpen Chaicumpa
47	Development of schistosomiasis diagnosis	NSTDA	Prof. Wanpen Chaicumpa
48	Development of an antigen detection assay for diagnosis of leptospirosis	BIOTEC	Prof. Wanpen Chaicumpa
49	Rapid detection of <i>Salmonella</i> in contaminated foods by immunomagnetic enrichment and enzyme immunoassay	The Thailand Research Fund (TRF)	Miss Yuvadee Mahakunkijcharoen
50	A simplify and diagnosis of cytomegalovirus	Mahidol University	Assoc.Prof. Surang Tantivanich
Department of Protozoology			
51	Isolation and characterization of DNA topoisomerase II from <i>Trichomonas vaginalis</i>	The Thailand Research Fund (TRF)	Assist.Prof. Porntip Petmitr
52	Prevalence of <i>Toxoplasma gondii</i> in Thai healthy population		Dr. Yaowalark Sukthana
Department of Social and Environmental Medicine			
53	A participatory action research on development of a school model to control liverfluke infection in Northern Thailand	Faculty of Tropical Medicine	Mr. Prasart Vorasanta
54	Early detection of Rifampicin resistant of <i>M. leprae</i> among Thai leprosy patient	National Research Council of Thailand (NRCT)	Dr. Pongrama Ramasoota
55	Tuberculosis vaccine design using T7 phage display techniques	STINT Foundation, Sweden	Dr. Pongrama Ramasoota
56	Opisthorchiasis risk foods assessment	National Council of Women of Thailand (NCWT)	Assist.Prof. Wanchai Phatihatakorn
57	Hazardous substance management and development of computerized database inventory list on major hazardous substances used at Faculty of Tropical Medicine, Mahidol University	Mahidol University	Assist.Prof. Voranuch Wangsuphachart

No.	On going Research Projects in 1998	Grants	Principal Investigator
Department of Social and Environmental Medicine			
58	Search for a model to prevent alcohol consumption among Thai students	Mahidol University	Mr. Rungwit Mas-ngammueng
Department of Tropical Hygiene			
59	Epidemiological study of nutritional deficiency among Karen preschool children	Faculty of Tropical Medicine	Mr. Surapon Yimsamran
60	Effects of health education intervention on malaria prevention and treatment behaviors, Ratchaburi, Thailand	Government Budget	Dr. Pranee Srisuriya
61	Malaria in Thai-Burmese border : Interaction between host , agent, and environment	Government Budget	Assist.Prof. Pratap Singhasivanon
62	Association between parasite species and density with disability days among Thai malarious cases in Suanpung District, Ratchaburi Province, Thailand.		Assist.Prof. Pratap Singhasivanon
Department of Tropical Nutrition and Food Science			
63	Identification of genes mutation in lung cancer cells in Thai patients	Mahidol University China Medical Board	Assist.Prof. Songsak Petmitr
64	Food and health relationship in Asian population	Palm oil Research Institute of Malaysia	Assoc.Prof. Supranee Changbumrung
65	Dietary pattern, lifestyle and nutritional status of health science university students in Bangkok	Faculty of Tropical Medicine	Assoc.Prof. Niyomsri Vudhivai
66	Molecular biology of carcinogenesis in lung cancer	The Thailand Research Fund (TRF)	Assoc.Prof. Supranee Changbumrung
67	Development of food and medicinal plants	Government Budget	Assoc.Prof. Supranee Changbumrung
68	Investigation of nutritional, health and dietary patterns of Thai elderly		Prof. Praneet Pongpaew
69	Serum leptin concentration in obese subjects	Free University, Berlin, Germany	Assoc.Prof. Rungsun Tungtrongchitr
70	Micronutrients and oxidative stress in obese subjects	Freie University, Berlin, Germany	Assoc.Prof. Rungsun Tungtrongchitr

No.	On going Research Projects in 1998	Grants	Principal Investigator
Department of Tropical Pathology			
71	Pathogenic effect of nitric oxide in sera and cerebrospinal fluid on cerebral malaria	The Thailand Research Fund (TRF) and Mahidol University	Assist.Prof. Yaowapa Maneerat
72	Liver pathology in AIDS	Ministry of University Affairs	Assist.Prof. Parnpen Viriyavejakul
73	Study of opportunistic infections in AIDS by needle biopsy	Mahidol University	Assist.Prof. Parnpen Viriyavejakul
Department of Tropical Paediatrics			
74	Comparison of the effects of milk-cereal mixtures and rice powder salt solution compare with milk-cereal mixtures and ORS and with milk and ORS on acute watery diarrhea in young children	National Research Council of Thailand (NRCT)	Prof. Arunee Sabchareon
75	A phase IV, observed-blind, randomized, controlled, trial to evaluate safety, tolerability and immunogenicity of the Chiron acellular pertussis vaccine combined with diphtheria and tetanus toxoids (DTaP), as compared to licensed whole-cell pertussis vaccine combined with diphtheria and tetanus toxoids (DTaP), when administered to healthy Thai infants at 2, 4 and 6 months of age		Prof. Arunee Subchareon
76	Safety and immunogenicity of tetravalent dengue vaccine formulations in Thai adult volunteers (DEN 04198)	Pasteur Merieux Serum and Vaccines, Lyon, France	Assoc.Prof. Pornthep Chanthavanich
Department of Tropical Radioisotopes			
77	Study of four Thai medicinal herbs as individuals and combinations for anti-snake venoms.		Assist.Prof. Channarong Sanghirun
78	Viscosity of red cell ghosts and hemoglobin of red cells from patients with <i>Plasmodium falciparum</i> malaria	Mahidol University	Assist.Prof. Petcharin Yamarat
79	Effect of garlic on blood rheology and prevention of thrombolism	National Research Council of Thailand (NRCT)	Assist.Prof. Petcharin Yamarat

No.	On going Research Projects in 1998	Grants	Principal Investigator
Vaccine Trial Centre			
80	Development of new vaccines against cholera due to <i>Vibrio cholerae</i> O139	WHO	Prof. Sricharoen Migasena
81	A phase I/II, double-blind, placebo-controlled study of the Chiron biocine HIV Thai E gp 120/MF59 vaccine administered alone or combined with the Chiron biocine HIV SF2 gp120 antigen in healthy HIV-seronegative Thai adults	WRAIR, USA	Prof. Sricharoen Migasena / Assoc.Prof. Punnee Pitisuttithum
82	A phase I/II trial to evaluation the safety and immunogenicity of AIDSVAX™ B/E vaccine in Bangkok, Thailand	VAXGEN Co, Ltd.	Assoc.Prof. Punnee Pitisuttithum
83	A multicenter, randomized, double-blind, phase II study to evaluate the safety, tolerance and efficacy of multiple doses of SCH 56592 versus fluconazole in the treatment of oropharyngeal candidiasis (OPC) in HIV-positive patients	Schering Pough Co., Ltd.	Assoc.Prof. Punnee Pitisuttithum
84	A phase III trial to determine the efficacy of AIDSVAX™ B/E Vaccine in intravenous drug users in Bangkok, Thailand	VAXGEN Co., Ltd.	Bangkok AIDS Vaccine Evaluation Group

1. Acharya GP, Davis TME, Ho M, Harris S, Chataut C, Acharya S, Tuhladar N, Kafle KE, Polhrel B, Nosten F, Dance DAB, Smith A, Weber A, White NJ. Factors affecting the pharmacokinetics of parenteral chloramphenicol in enteric fever. *J Antimicrob Chemother* 1996;40:91-8.
2. Angkasekwinai P, Looareesuwan S, Chaiyaroj SC. Lack of significant associate between rosette formation and parasitized erythrocyte adherence to purified CD36. *Southeast Asian J Trop Med Public Health* 1998;29(1):41-5.
3. Angus B, Thanikkul K, Udomsangpetch R, White NJ. *In vivo* removal of malaria parasites from red blood cells without their destruction in acute falciparum malaria. *Blood* 1997;5:2037-40.
4. Aursudkij B, Wilairatana P, Vannapan S, Walsh DS, Gordeuk V, Looareesuwan S. Pulmonary edema and ARDS in cerebral malaria patients in Thailand. *Southeast Asian J Trop Med Public Health* 1998 (in press).
5. Camacho LH, Gordeuk VR, Wilairatana P, Pootrakul P, Brittenham GM, Looareesuwan S. The course of anaemia after the treatment of acute, falciparum malaria. *Ann Trop Med Parasitol* 1998;92(5):525-37.
6. Chaicumpa W, Chongsa-nguan M, Kalambaheti T, Wilairatana P, Srimanote P, Makakunijcharoen Y, Looareesuwan S, Sakolvaree Y. Immunogenicity of liposome - associated and refined antigen oral cholera vaccines in Thai volunteers. *Vaccine* 1998;16:678-84.
7. Chaicumpa W, Srimanote P, Sakolvaree Y, Kalampaheti T, Chongsa-nguan M, Tapchaisri P, Eampokalap B, Moolasart P, Balakrish NG, Echeverria P. Rapid detection of cholera caused by *Vibrio cholerae* O139. *J Clin Microbiol* 1998 (in press).
8. Chaicumpa W. Immunodiagnosis of some helminthic infections: from research experience to practical application. *J Trop Med Parasitol* 1997;20:1-10.
9. Chaisiri K, Pongpaew P, Tungtrongchitr R, Phonrat B, Kulleap S, Suttiwong P, Intarakhao C, Mahaweerawat U, Khongdee W, Sanchaisuriya P, Saowakontha S, Merkle A, Schelp FP. Nutritional status and serum lipid of rural population in northeast Thailand - An example of health transition. *Internat J Vit Nutr Res* 1998;68:196-202.
10. Chanjanakijskul S, Tungtrongchitr R, Pongpaew P. Serological autoantibodies characteristics in systemic lupus erythematosus (SLE) patients in Institute of Dermatology, Bangkok. *Bull Med Tech Phy Ther* 1998 (in press).
11. Chaowagul W, Suputtamongkol Y, Davis TME, Pukrittayakamee S, Teja-Isavadharm P, Webster HK, White NJ. Lack of a significant adverse cardiovascular effect of combined quinine and mefloquine therapy for uncomplicated malaria. *Trans Roy Soc Trop Med Hyg* 1997;91:694-6.
12. Chaowagul W, Suputtamongkol Y, Smith MD, White NJ. Oral fluoroquinolones for maintenance treatment of melioidosis. *Trans Roy Soc Trop Med Hyg* 1997;91:599-601.
13. Chongsrisawat V, Jantaradsamee P, Vivatvakin B, Pongpaew P, Poovorawan Y. Alpha-1-antitrypsin phenotype of children with liver diseases in Thailand. *Asian Pac J Allergy Immunol* 1998;16:27-30.
14. Chotivanich K, Pukrittayakamee S, Simpson JA, White NJ, Udomsangpetch R. Characteristics of *Plasmodium vivax*-infected erythrocyte rosettes. *Am J Trop Med Hyg* 1998;59:73-6.
15. Chotivanich K, Simpson JA, White NJ. Estimating *Plasmodium vivax* parasitaemia. *Trans Roy Soc Trop Med Hyg* 1998;92:176.
16. Chotivanich K, Udomsangpetch R, Pipitaporn B, Angus B, Suputtamongkol Y, Pukrittayakamee S, White NJ. Rosetting characteristics of uninfected erythrocytes from healthy individuals and malaria patients. *Ann Trop Med Parasitol* 1998;92:45-6.
17. Dekumyoy P, Waikagul J, Eom KS. Human lung fluke *Paragonimus heterotremus*: differential diagnosis between *Paragonimus heterotremus* and *Paragonimus westermani* infections by EITB. *Trop Med Int Health* 1998;3(1):52-6.
18. Dondorp AM, Angus BJ, Hardeman MR, Chotivanich K, Silamut K, Ruangveerayuth R, Kager PA, White NJ, Vreeken J. Prognostic significance of reduced red blood cell deformability in severe falciparum malaria. *Am J Trop Med Hyg* 1997;57(5):507-11.
19. Ho M, Schollaardt T, Niu X, Looareesuwan S, Patel KD, Kubes P. Characterization of *Plasmodium falciparum*-infected erythrocyte and p-selectin interaction under flow conditions. *Blood* 1998;91(12):4803-9.
20. Ho M, Schollaardt T, Snape S, Looareesuwan S, Suntharasamai P, White NJ. Endogenous interleukin-10 modulates proinflammatory response in *Plasmodium falciparum* malaria. *J Infect Dis* 1998;178:520-5.
21. Horsawad V, Pongpaew P, Tungtrongchitr R, Phonrat B, Vudhivai N, Chanjanakitskul S, Himman-ngnan T, Supanaranond V, Chantachum Y, Schelp FP. Lead exposure, urinary aminolevulinic acid concentration and haematological parameters of road sweepers working in congested areas of Bangkok. *J Nutr Environ Med* 1998 (in press).
22. Hu H, Singhasivanon P, Salazar NP, Thimasarn K, Li X, Wu Y, Yang H, Zhu D, Supavej S, Looareesuwan S. Factors influencing malaria endemicity in Yunnan Province, P.R. China (Analysis of Spatial Pattern by GIS). *Southeast Asian J Trop Med Public Health* 1998 (in press).
23. Hutagalung R, Wilairatana P, Looareesuwan S, Brittenham G, Aikawa M, Gordeuk V. Influence of hemoglobin E trait on the severity of falciparum malaria. *J Infect Dis* 1998;179 (in press).
24. Inkatanuvat S, Suntharasamai P, Vutikes S, Riganti M. Changes of liver functions after albendazole treatment in human gnathostomiasis. *J Med Assoc Thai* 1998;81(10):735-9.
25. Ittarat W, Looareesuwan S, Pootrakul P, Sumpunsirikul P, Vattanavibool P, Meshnick SR. Effects of α thalassemia on pharmacokinetics of the antimalarial agent artesunate. *Antimicrob Agents Chemother* 1998;9(42):2332-5.
26. Joshi AB, Singhasivanon P, Jimba M, Joshi DD, Khusmith S, Shrestha M, Nandy A. Evaluation of the direct agglutination test (DAT) as an immunodiagnostic tool for a diagnosis of visceral leishmaniasis (VL) in Nepal. *J Nepal Public Health Association* 1998;1(1):1-3.

27. Kalambaheti T, Chisri U, Srimanote P, Pongponratn E, Chaicumpa W. Immunogenicity and protective role of three formulations of oral cholera vaccine. *Vaccine* 1998; 16: 201-7.
28. Karbwang J, Fungladda W, Pickard CE, Shires S, A. Hay A, Feely M. Initial evaluation of low-dose phenobarbital as an indicator of compliance with antimalarial drug treatment. *Bull World Health Organ* 1998;76(Suppl.1): 67-73.
29. Karbwang J, Na-Bangchang K, Tin T, Sukontason K, Rimchala W, Harinasuta T. Pharmacokinetics of intramuscular artemether in patients with severe falciparum malaria patients with acute renal failure. *Br Clin Pharmacol* 1998;45:597-600.
30. Kedjarune U, Migasena P, Changbumrung S, Pongpaew P, Tungtrongchitr R. Flow rate and composition of whole saliva in children from rural and urban Thailand with different caries prevalence and dietary intake. *Caries Res* 1997;31:148-54.
31. Khusmith S, Tapchaisri P, Tharavanij S, Bunnag D. Antigenic diversity of *Plasmodium vivax* and their geographic distribution in Thailand. *Southeast Asian J Trop Med Public Health* 1998;29(3)(in press).
32. Khusmith S, Tharavanij S, Bunnag D. Antigenic disparity of *Plasmodium vivax* causing initial symptoms and causing relapse. *Southeast Asian J Trop Med Public Health* 1998;29(3)(in press).
33. Kilmarx PH, Limpakarnjanarat K, Mastro TD, Saisorn S, Kaewkungwal J, Korattana S, Uthairavit W, Young NL, Weniger BG, St Louis ME. HIV-1 seroconversion in a prospective study of female sex workers in northern Thailand: continued high incidence among brothel-based women. *AIDS* 1998;12:1889-98.
34. Kitjaroenatham A, Khusmith S, Laothavorn J, Na-Bangchang K, Thammapalerd N. Monoclonal antibodies to quinine. *Southeast Asian J Trop Med Public Health* 1998;29(2):337-40.
35. Lim PKC, Looareesuwan S, Chindanonond D, Saleh AM, Tan SK. The occurrence of point mutations in the dihydrofolate reductase-thymidylate synthase (DHFR) in Thai isolate of *Plasmodium falciparum*. *Southeast Asian J Trop Med Public Health* (Submitted).
36. Lindsay SW, Ewald JA, Samung Y, Apiwathnasorn C, Nosten F. Thanaka (*Limonia acidissima*) and deet (di-methyl benzamide) mixture as a mosquito repellent for use by Karen women. *Med Vet Entomol* 1998;12:295-301.
37. Longyant S, Sithigorngul P, Thammapalerd N, Sithigorngul W, Menasveta P. Production and characterization of monoclonal antibodies specific to vitellin and vitellogenin of the tiger prawn, *Penaeus monodon*. *Invertebrate Reproduction and Development* 1998 (in press).
38. Looareesuwan S, Chulay JD, Canfield CJ, Hutchinson DB. Malarone™ (atovaquone and proguanil hydrochloride): a review of its clinical development for treatment of malaria. *Am J Trop Med Hyg* 1998 (in press).
39. Looareesuwan S, Olliaro P, White NJ, Chongsuphajaisiddhi T, Sabcharoen A, Thimasarn K, Nosten F, Singhasivanon P, Supavej S, Khusmith S, Wylings S, Kanyok T, Walsh D, Leggat PA. Consensus recommendation on the treatment of malaria in southeast Asia. *Southeast Asian J Trop Med Public Health* 1998;29(2):355-60.
40. Looareesuwan S, Wilairatana P, Chalermrut K, Rattanapong Y, Canfield C, Hutchinson D. Efficacy and safety of atovaquone/proguanil compared with mefloquine for treatment of acute *Plasmodium falciparum* malaria in Thailand. *Am J Trop Med Hyg* 1998 (in press).
41. Looareesuwan S, Wilairatana P, Chocejindachai W, Viriyavejakul P, Krudsood S, Singhasivanon P. Research on new antimalarial drugs and the use of drugs in combination at the Bangkok Hospital for Tropical Diseases. *Southeast Asian J Trop Med Public Health* 1998 (in press).
42. Looareesuwan S, Wilairatana P, Gemperli B, Gathman I, Royce C. Phase III trial in Thailand comparing a new oral combination antimalarial CGP 5669 with oral mefloquine in the treatment of *Plasmodium falciparum* malaria. *Am J Trop Med Hyg* 1998 (in press).
43. Looareesuwan S, Wilairatana P, Vannaphan S, Wanaratana V, Wenisch C, Aikawa M, Brittenham G, Graninger W, Wernsdorfer W. Clinical trial of Pentoxifylline as an ancillary treatment for severe falciparum malaria in Thailand. *Am J Trop Med Hyg* 1998;58(3):348-53.
44. Luxemburger C, Nosten F, Kyle DE, Kiricharoen L, Chongsuphajaisiddhi T, White NJ. Clinical features cannot predict a diagnosis of malaria or differentiate the infecting species in children living in an area of low transmission. *Trans Roy Soc Trop Med Hyg* 1998;92:45-9.
45. Mahaweerawat U, Intarakhao C, Pongpaew P, Tungtrongchitr R, Kitjaroenatham A, Phonrat B, Saowakontha S, Schelp FP. Knowledge, attitude and practices towards AIDS of rural population in Northeast Thailand. *Thai Aids J* 1998 (in press).
46. Maleewong W, Intapan PM, Priammuenwai M, Wongkham C, Tapchaisri P, Morakote N, Chaicumpa W. Monoclonal antibodies to *Paragonimus heterotremus* and their potential for diagnosis of paragonimiasis. *Am J Trop Med Hyg* 1997;56:413-7.
47. Maleewong W, Intapan PM, Wongkham C, Pajongthanasaris M, Morakote N, Tapchaisri P, Chaicumpa W. A Dot - ELISA test using monoclonal antibody-purified antigens for the diagnosis of paragonimiasis caused by *Paragonimus heterotremus*. *Southeast Asian J Trop Med Public Health* 1997; 28: 621-3.
48. Maleewong W, Intapan PM, Wongkham C, Pajongthanasaris MP, Morakote N, Chaicumpa W. Indirect haemagglutination test using monoclonal antibody-affinity purified antigens for diagnosis of human paragonimiasis due to *Paragonimus heterotremus*. *Trop Med Inter Health* 1998;3:57-9.
49. Maleewong W, Intapan PM, Wongkham C, Wongratanacheewin S, Tapchaisri P, Morakote N, Chaicumpa W. Detection of *Paragonimus heterotremus* in experimentally infected cat feces by antigen capture - ELISA and by DNA hybridization. *J Parasitol* 1997; 83: 1075-8.
50. Manopaiboon C, Shaffer N, Clark L, Bhadrakom C, Siriwasin W, Chearskul S, Suteewan W, Kaewkungwal J, Bennetts A, Mastro TD. Impact of HIV on families of HIV-infected women who have recently given birth, Bangkok, Thailand. *J Acq Immun Def Syn Hum Retrov* 1998;18:54-63.
51. McGready R, Cho T, Cho JJ, Simpson JA, Luxemburger

- C, Dubowitz L, Looareesuwan S, White NJ, Nosten F. Artemisinin derivatives in the treatment of falciparum malaria in pregnancy. *Trans Roy Soc Trop Med Hyg* 1998;92:430-3.
52. McGready R, Cho T, Hkirijaroen L, Simpson J, Chongsuphajaisiddhi T, White NJ, Nosten F. Quinine and mefloquine in the treatment of multidrug-resistant *Plasmodium falciparum* malaria in pregnancy. *Ann Trop Med Parasitol* 1998;92:643-53.
53. Menyawi EL I, Looareesuwan S, Knapp S, Thalhammer F, Stoiser B, Burgmann H. Measurement of serum nitrite/nitrate concentrations using high-performance liquid chromatography. *J Chromatogr* 1998;706:347-51.
54. Muanza K, Traore B, Gay F, Krudsood S, Danis M, Looareesuwan S. Circulating receptors ICAM-1, VCAM-1, E-selectin and chondroitin-4-sulfate A implicated in cytoadherence in the course of severe *Plasmodium falciparum* malaria in Thailand 1998. *Southeast Asian J Trop Med Public Health* 1998 (in press).
55. Muennoo C, Rojekkittikhun W, Waikagul J. Prevalence and intensity of helminthiasis in primary school children in Amphoe Muang, Prachin Buri. *Mahidol J* 1998;5(1):17-8.
56. Nathawut S, P Busaba, Wilairatana P, Dangdoungjai J, Udomsangpetch R, Chantharakri U, Looareesuwan S. Presentation of oxidant tissue damaged by desferrioxamine in severe falciparum malaria treated with artemisinin derivatives. *Am J Trop Med Hyg* 1998 (Submitted).
57. Nontprasert A, Nosten-Bertrand M, Pukrittayakamee S, Vanijanonta S, Angus BJ, White NJ. Assessment of the neurotoxicity of parenteral artemisinin derivatives in mice. *Am J Trop Med Hyg* 1998; 59(4):519-22.
58. Ohrt C, Mirabelli-Primdahl L, Looareesuwan S, Wilairatana P, Walsh DS, Kain CK. Determination of *Plasmodium falciparum* treatment failure using PCR-single-stand confirmation al polymorphism. *Clin Infect Dis* 1998 (in press).
59. Paul REL, Hackford I, Brockman A, Muller-Graf C, Price R, Luxemburger C, White NJ, Nosten F, Day KP. Transmission intensity and *Plasmodium falciparum* diversity on the northwestern border of Thailand. *Am J Trop Med Hyg* 1998;58:195-203.
60. Perlmann P, Perlmann H, Looareesuwan S, Krudsood S, Kano S, Matsumoto Y, Brittenham G, Troye-Blomberg M, Aikawa M. Functions of IgG and IgE anti-malaria antibodies in uncomplicated or severe *P. falciparum* malaria. *Infect Immun* 1988 (in press).
61. Petmitr P, Pongvilairat G, Auparakkitanon S, Ralph RK, Denny W, Wilairat P. Gametocytocidal activity of pyronaridine and DNA topoisomerase II inhibitors against multidrug-resistant *Plasmodium falciparum* in vitro. *Parasitol International* (Submitted).
62. Petmitr S, Makthiengtrong S, Sutinont P, Migasena P. p53 gene mutations in non-small cell lung cancer from Thai patients. *J Med Assoc Thai* 1998 (Submitted).
63. Petmitr S, Pinlaor S, Thousungnoen A, Korlak A, Migasena P. *K-ras* oncogene and p53 gene mutations in cholangiocarcinoma from Thai patients. *Southeast Asian J Trop Med Public Health* 1998;29:71-5.
64. Petmitr S. Cancer genes and cholangiocarcinoma. *Southeast Asian J Trop Med Pub Health* 1997;28(suppl. 1): 80-4.
65. Phonrat B, Pongpaew P, Tungtrongchitr R, Horsawat V, Supanaranond W, Vutikes S, Vudhivai N, Schelp FP. Risk factors for chronic diseases among road sweepers in Bangkok. *Southeast Asian J Trop Med Public Health* 1997;28:36-45.
66. Pongpaew P, Schelp FP. Elderly in a country going through epidemiological health transition: The example of Thailand. *Nutrition, Health Aging* 1997;1:45-50.
67. Pongpaew P, Schelp FP. Etiology of malnutrition: poverty or ignorance? (Part II). *The Nest* No 3., December 1997; pp 2-3.
68. Pongpaew P, Schelp FP. Elderly in a country going through epidemiological health transition: The example of Thailand. *Age Nutrition* 1997;8:30-5.
69. Pongpaew P, Supawan V, Intarakhao C, Tungtrongchitr R, Chantaranipapong Y, Phonrat B, Mahaweerawat U, Saowakontha S, Schelp FP, Intarakhao P. The investigation of iodine content in human milk from mothers residing in the endemic area of iodine deficiency disorders comparing with cow's milk and soy bean milk products. *Food* 1997;27:255-64.
70. Pongpaew P, Supawan V, Tungtrongchitr R, Phonrat B, Vudhivai N, Chantaranipapong Y, Kitjaroentham A, Jintaridhi P, Intarakhao C, Mahaweerawat U, Saowakhontha S, Schelp FP. Urinary iodine excretion as a predictor of the content iodine of breast milk. *J Med Assoc Thai* (Submitted).
71. Pongpaew P, Tungtrongchitr R, Phonrat B, Intarakhao C, Mahaweerawat U, Chantaranipapong Y, Supawan V, Vudhivai N, Tribunyatkul S, Saowakhontha S, Schelp FP. Management of iodine fortification and iodinated salt distribution in endemic area of iodine deficiency disorders in northeast Thailand. *J Public Health* 1998 (in press).
72. Pongpaew P, Tungtrongchitr R, Phonrat B, Supawan V, Schelp FP, Intarakhao C, Mahaweerawat U, Saowakhontha S. Nutritional status of school children in an endemic area of iodine deficiency disorders (IDD) after one year of iodine supplementation. *Southeast Asian J Trop Med Public Health* 1998;29:50-7.
73. Pongpaew P, Tungtrongchitr R, Supawan V, Vudhivai N, Sanchaisuriya P, Intarakhao C, Mahaweerawat U, Phonrat B, Jotking P, Kongdee W, Schelp FP, Saowakhontha S. Evaluation and monitoring of iodine deficiency disorders (IDD) in school children in northeast Thailand. *Asian Pac J Clin Nutr* 1998;7:131-7.
74. Pongponratn E, Maneerat Y, Chaisri U, Wilairatana P, Punpoowong B, Viriyavejakul P, Riganti M. Electron-microscopic examination of *Rickettsia tsutsugamushi* infected human liver. *Trop Med Inter Health* 1998;3:242-8.
75. Price R, Luxemburger C, van Vugt M, Nosten F, Kham A, Simpson J, Looareesuwan S, Chongsuphajaisiddhi T, White NJ. Artesunate and mefloquine in the treatment of uncomplicated multidrug-resistant hyperparasitaemic falciparum malaria. *Trans Roy Soc Trop Med Hyg* 1998;92:207-11.
76. Price RN, Nosten F, Luxemburger C, van Vugt M, Phaipun L, Chongsuphajaisiddhi T, White NJ. Artesunate/mefloquine treatment of multi-drug resistant falciparum

- malaria. *Trans Roy Soc Trop Med Hyg* 1997;91:574-7.
77. Punpoowong B, Viriyavejakul P, Riganti M, Pongponratn E, Chairu U, Meneerat Y. Opportunistic protozoa in stool samples from HIV- infected patients. *Southeast Asian J Trop Med Public Health* 1998;29:31-4.
 78. Rojekittikhun W, Pubampen S, Waikagul J. Seasonal variation in the intensity of *Gnathostoma* larvae in swamp eels (*Fluta alba*) sold in a local market in Bangkok. *Southeast Asian J Trop Med Public Health* 1998;29(1): 148-53.
 79. Rongsriyam T, Jitpakdi A, Choochote W, Somboon P, Tookyang B, Suwonkerd W. Comparative susceptibility of two forms of *Anopheles sinensis* Wiedemann 1828 (Diptera: Culicidae) to infection with *Plasmodium falciparum*, *P. vivax*, *P. yoelii* and the determination of misleading factor for sporozoite identification. *Southeast Asian J Trop Med Public Health* 1998;29(1):159-67.
 80. Rongsriyam Y, Baskoro T, Apiwathnasorn C, Palakul K. Phytochemical Thai plants for replacement of insecticides used in mosquito control. *Southeast Asian J Trop Med Public Health* 1998 (in press).
 81. Rongsriyam Y, Deesin V, Komalamisra N, Thongrungrat S. Secondary killing effect of chlorpyrifos bait by coprophagous uptake of *Blattella germanica*. *Southeast Asian Trop Public Health* 1998 (in press).
 82. Rongsriyam Y, Esparar DG, Apiwathnasorn C, Asavanich A. Pyrethroid impregnated blanket, a new alternative for personal protection against mosquito bites. *Southeast Asian J Trop Med Public Health* 1998 (in press).
 83. Rongsriyam Y, Purushottam G, Thongrungrat K, Leemingsawat S. Sublethal effect of pyriproxyfen and etofenprox on *Culex tritaeniorhynchus*. *Mosq Borne Dis Bull* 1998 (in press).
 84. Rongsriyam Y, Yap A, Pongponrat E, Asavanich A, Komalamisra N. Comparative studies of member species of *Anopheles maculatus* group and their vectorial status. *Southeast Asian J Trop Public Health* 1998 (in press).
 85. Sabchareon A, Attanath P, Chanthavanich P, Phanuaksook P, Prarinyanupharb V, Poonpanich Y, Mookmanee D, Teja-isavadharm P, Heppner DG, Brewer TG, Chongsuphajaisiddhi T. Comparative clinical trial of artesunate suppositories and oral artesunate in combination with mefloquine in the treatment of children with acute falciparum malaria. *Am J Trop Med Hyg* 1998;58:11-6.
 86. Sabchareon A, Attanath P, Phanuaksook P, Chanthavanich P, Poonpanich Y, Mookmanee D, Chongsuphajaisiddhi T, Sadler BM, Hussein Z, Canfield CJ, Hutchinson DBA. Efficacy and pharmacokinetics of atovaquone and proguanil in children with multidrug-resistant *Plasmodium falciparum* malaria. *Trans R Soc Trop Med Hyg* 1998;92:201-6.
 87. Sakolvaree Y, Launa Ybanez L, Chaicumpa W. Parasites elicited cross-reacting antibodies to *Opisthorchis viverrini*. *Asian Pac J Allergy Immunol* 1997;15:115-22.
 88. Sibmooh N, Pipitaporn B, Wilairatana P, Dangdounjai J, Udomsangpetch R, Looareesuwan S, Chantharaksi U. Effects of artemisinin derivatives on lipid peroxidation in the plasma and fluidity of the erythrocyte membrane in falciparum malaria. *J Infect Dis* 1998 (Submitted).
 89. Singhasivanon P, Premmanisakul N, Krudsood S, Srisuriya P, Buchachart K, Popak N, Charusabha C, Yimsamran S, Singhasivanon V. Health problems in travelers coming to Thailand between 1990-1994. *J Travel Med* (in press)
 90. Smith MD, Angus BJ, Wuthiekanun V, White NJ. Arabinose assimilation defines a nonvirulent biotype of *Burkholderia pseudomallei*. *Infect Immun* 1997;65:4319-21.
 91. Tantivanich S, Klongkamnunkarn K, Desakorn V. Simplified, rapid diagnosis of respiratory syncytial virus from clinical specimens. *Asian Pac J Allergy Immunol* 1997; 15:99-103.
 92. Trakulsomboon S, Dance DAB, Smith MD, White NJ, Pitt TL. Ribotype differences between clinical and environmental isolates of *Burkholderia pseudomallei*. *J Med Microbiol* 1997;46:565-70.
 93. Treeprasertsuk S, Chindanon D, Wilairatana P, Krudsood S, Bussaratit V, Viriyavejakul P, Glanarongran R, Srinukham S, Looareesuwan S. Incidence of filariasis as a co-infection in malaria patients coming from Thai-Myanmar border between 1995-1997. *Japanese J Parasitol* 1998 (in press).
 94. Tungtrongchitr R, Pongpaew P, Schelp FP, Phonrat B, Mahaweewat U, Paksanont S, Sanchaisuriya P, Jotking P, Intarakhao C, Saowakontha S. Vitamin B12, folic acid and haemoglobin status of rural women in child bearing age in Northeast Thailand. *J Med Assoc Thai* 1997;80:785-90.
 95. Tungtrongchitr R, Pongpaew P, Supawan V, Chantaranipapong Y, Mahaweewat U, Phonrat B, Intarakhao C, Saowakontha S, Schelp FP. Effects of storage conditions on the stability of iodine in iodized salt, fish sauce and drinking water. *Food* 1998;28:31-41.
 96. van Vugt M, Brockman A, Gemperli B, Luxemburger C, Gathman I, Royce C, Slight T, Looareesuwan S, White NJ, Nosten F. Randomised comparison of artemether-benflumetol and artesunate-mefloquine in the treatment of multidrug-resistant falciparum malaria. *Antimicrob Agents Chemother* 1998;42(1): 135-9.
 97. Viriyavejakul P, Phudhichareonrat S, Boonpasat Y, Viriyavejakul A. Intracerebral hemorrhage due to nosocomial aspergillosis following neurosurgery. *Pathology* (Submitted).
 98. Viriyavejakul P, Riganti M. Electron-microscopic examination of *Rickettsia tsutsugamushi* infected human liver. *Trop Med Inter Health* 1998;3:242-8.
 99. Vudhivai N, Pongpaew P, Tungtrongchitr R, Phonrat B, Horsawat V, Schelp FP. Riboflavin and nutritional status of Thai road sweepers in Bangkok. *Internat Med* 1997;13: 77-80.
 100. Waikagul J, Muennoo C, Sanguankiat S, Maipanich W, Pubampen S, Nontasat P, Yoonuan T. Evaluation of latrine contamination in association with soil transmitted helminthic infection in the endemic community of south Thailand. *J Trop Med Parasitol*. 1998;21(1):1-7.
 101. Watthanakulpanich D, Waikagul M, Dekumyoy P, Anantaphruti MT. Application of the gelatin particle indirect agglutination test in the serodiagnosis of human opisthorchiasis. *Japanese J Trop Med Hyg* 1998; 26(1): 5-10.
 102. Wenisch C, Linnau KF, Looareesuwan S, Rumpold H. Plasma levels of the IL-6 cytokine family in patients with severe *Plasmodium falciparum* malaria. *J Infect Dis* 1998 (in press).
 103. Wenisch C, Looareesuwan S, Wilairatana P, Parschalk B,

- Vannaphan S, Wanaratana V, Wernsdorfer W, Graninger W. Effect of pentoxifylline on cytokine patterns in the therapy of complicated *Plasmodium falciparum* malaria. *Am J Trop Med Hyg* 1998; 58(3):343-7.
104. White NJ. Preventing antimalarial drug resistance through combinations. *Drug Resistance Updates* 1998;1:3-9.
105. White NJ. Why is it that antimalarial drug treatments do not always work? *Ann Trop Med Parasitol* 1998;92:449-58.
106. Wilairatana P, Chanthavanich P, Singhasivanon P, Treeprasertsuk S, Krudsood S, Chalermrut K, Phisalaphong C, Kraisintu K, Looareesuwan S. A comparison of three different dihydroartemisinin formulations for the treatment of acute uncomplicated falciparum malaria in Thailand. *Internat J Parasitol* 1998;28(8): 1213-8.
107. Wilairatana P, Kudsood S, Chokejindachai W, Bussaratid V, Silachamroon U, Viriyavejakul P, Hendriksen C, Scheiwe MW, Looareesuwan S. A clinical trial of combination of artesunate and mefloquine in the treatment of acute uncomplicated falciparum malaria: a short and practical regimen. *Southeast Asian J Trop Med Public Health* 1998 (Submitted).
108. Wilairatana P, Kyle DE, Looareesuwan S, Chinwongprom K, Amradee S, White NJ, Watkins WM. Poor efficacy of antimalarial biguanide-dapsone combinations in the treatment of acute, uncomplicated, falciparum malaria in Thailand. *Ann Trop Med Parasitol* 1997;91:125-32.
109. Wilairatana P, Westerlund E, Aursudkij B, Vanaphan S, Krudsood S, Viriyavejakul P, Chokejindachai W, Treeprasertsuk S, Srisuriya P, Gordeuk V, Brittenham G, Neild G, Looareesuwan S. Treatment of malarial acute failure by hemodialysis. *Am J Trop Med Hyg* 1998 (Submitted)

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