

**Faculty of Tropical Medicine,
Mahidol University**
Annual Report
2000

Faculty of Tropical Medicine
Annual Report 2000

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Foreword



The Year 2000 was not only the first year of the New Millennium, but also the auspicious 40th Anniversary of the Foundation of the Faculty of Tropical Medicine by co-founders Professor Emeritus Chamlong Harinasuta and Professor Emeritus Khunying Tranakchit Harinasuta in 1960.

Other milestones for the Year 2000 have included:

- Establishment of the Asian Centre of International Parasite Control (ACIPAC) under the Hashimoto Initiative for Global Parasite Control Program on 23rd March 2000. The ACIPAC project is a cooperative

Project between the Japan International Co-operation Agency (JICA), Mahidol University, the Department of Communicable Diseases Control, Ministry of Public Health, Thailand, and DTEC.

- On 9th June 2000, hosting of the very enjoyable and successful Mahidol University International Day, with entertainment and presentations by students and staff in their national costumes.

- The Faculty was highly honored to have Her Royal Highness Princess Galayani Vadhana Krom Luang Naradhivas Rajanagarindra graciously open the 12-floor Chalerm Prakiet Building on 1st December 2000. This new building houses research and hospital diagnostic and chemical laboratories, the Nutrition Unit of the Hospital for Tropical Diseases, a 300-person meeting room, an animal testing laboratory, 151-room accommodation for the Faculty's students, visitors and hospital staff, and a car-park for 150 vehicles.

- The 6th Annual Joint International Tropical Medicine Meeting (JITMM) was held concurrently with the 3rd Seminar on Food-borne Parasitic Zoonoses (FBPZ) at the Royal River Hotel between 6-8 December 2000, and was followed by the 3rd Conference in Tropical Pathology. The JITMM/FBPZ attracted a record 520 participants from 31 countries. In all, 72 invited speakers presented at the Meeting, and there were an additional 67 oral presentations and 35 poster presentations by Meeting participants. Dr. Lorenzo Savioli, Co-ordinator, Strategy Development and Monitoring for Parasitic Diseases and Vector Control (WHO) presented the Keynote 6th Chamlong-Tranakchit Harinasuta lecture entitled "Food- and Water-borne Parasitic Zoonoses in the 21st Century".

This past year has been one of major significance for the Faculty, and I wish to congratulate all staff for their exemplary efforts and achievements in teaching, learning, research, services and administration. May I also take the opportunity to express my sincere appreciation for their enthusiasm, energy, caring and creativity. It is with considerable pride and satisfaction that I note the synergistic collaboration of the Faculty with SEAMEO TROPMED, the Wellcome Unit, and more recently, the Asian Center of International Parasite Control, as well as local, national and international organizations and individuals.

I feel sure that the trend that was set by the Faculty and its partners in the Year 2000 will continue with the same or greater impetus into the Year 2001, and beyond.

It is, therefore, with great pleasure that I present the Annual Report of the Faculty of Tropical Medicine, Mahidol University, for the Year 2000.

Acknowledgements

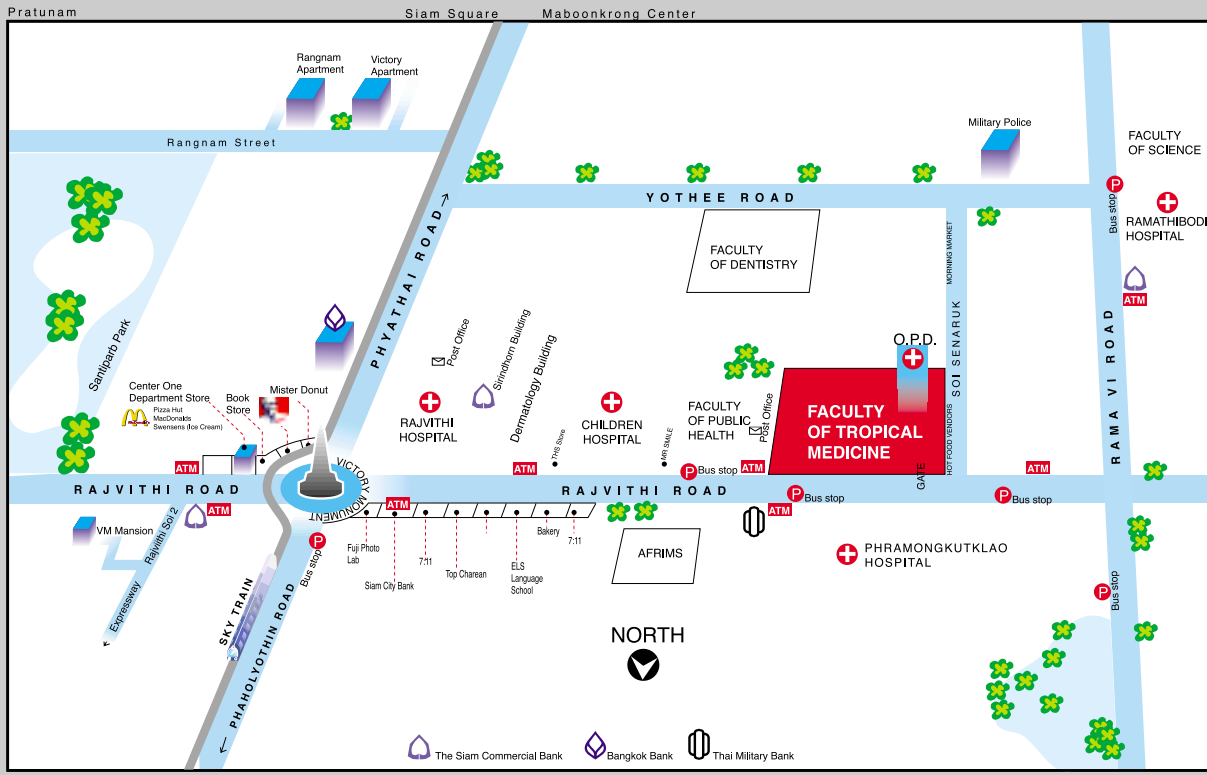
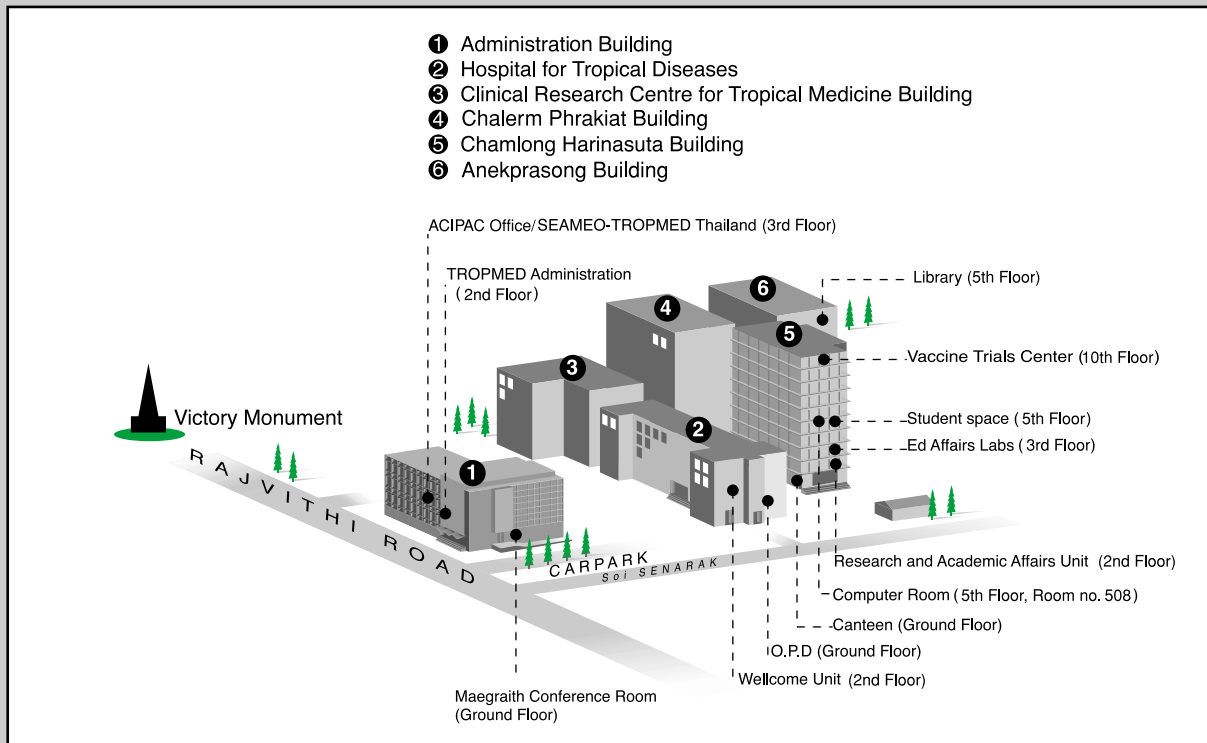
The Annual Report Committee would like to thank all contributors, Departments and Units for providing information for the preparation of this Annual Report

Editors' Note

The Faculty of Tropical Medicine, one of the leading faculties of Mahidol University, has published the Annual Report regularly in order to disseminate information on its activities. The Annual Report contains information on the Faculty's structure, including administrative executives, Faculty Board members, consultants, visiting professors, lecturers and their areas of expertise. Current research activities and abstracts, both published and unpublished, of 11 departments, the Wellcome Unit and the Vaccine Trial Centre, and also Faculty's the ongoing research projects are included, as well as the functions of the Data Management Unit. Details of courses offered by the Bangkok School of Tropical Medicine; seminars, workshops and training courses organized and held at the Faculty during the year 2000; international linkages and visitors to the Faculty are given. Medical care services provided by the Hospital for Tropical Diseases including the dates and times that each of the 9 special clinics operate are also stated. The section on Special Laboratory Services summarizes diseases/ infections for which diagnoses are provided; specific laboratory tests, and reagents that are available exclusively at the Faculty. Activities of two centres hosted by the Faculty of Tropical Medicine, namely the SEAMEO TROPMED Regional Centre for Tropical Medicine (TROPMED/Thailand), one of the four TROPMED Regional Centres; and The Asian Centre of International Parasite Control (ACIPAC), the latest project established under the cooperation of the Japan International Cooperation Agency (JICA), Mahidol University, and the Department of Communicable Diseases Control, Ministry of Public Health, Thailand, as a research and training centre for health personnel and related sectors in malaria and soil-transmitted helminthiasis control, are given in detail. The section devoted to the Office of the Dean provides information on 10 administrative and support units, their staff and budget allocations. Last but not least, TROPMED publications during the period October 1999-September 2000, and TROPMED textbooks produced by the Faculty's staff are listed.

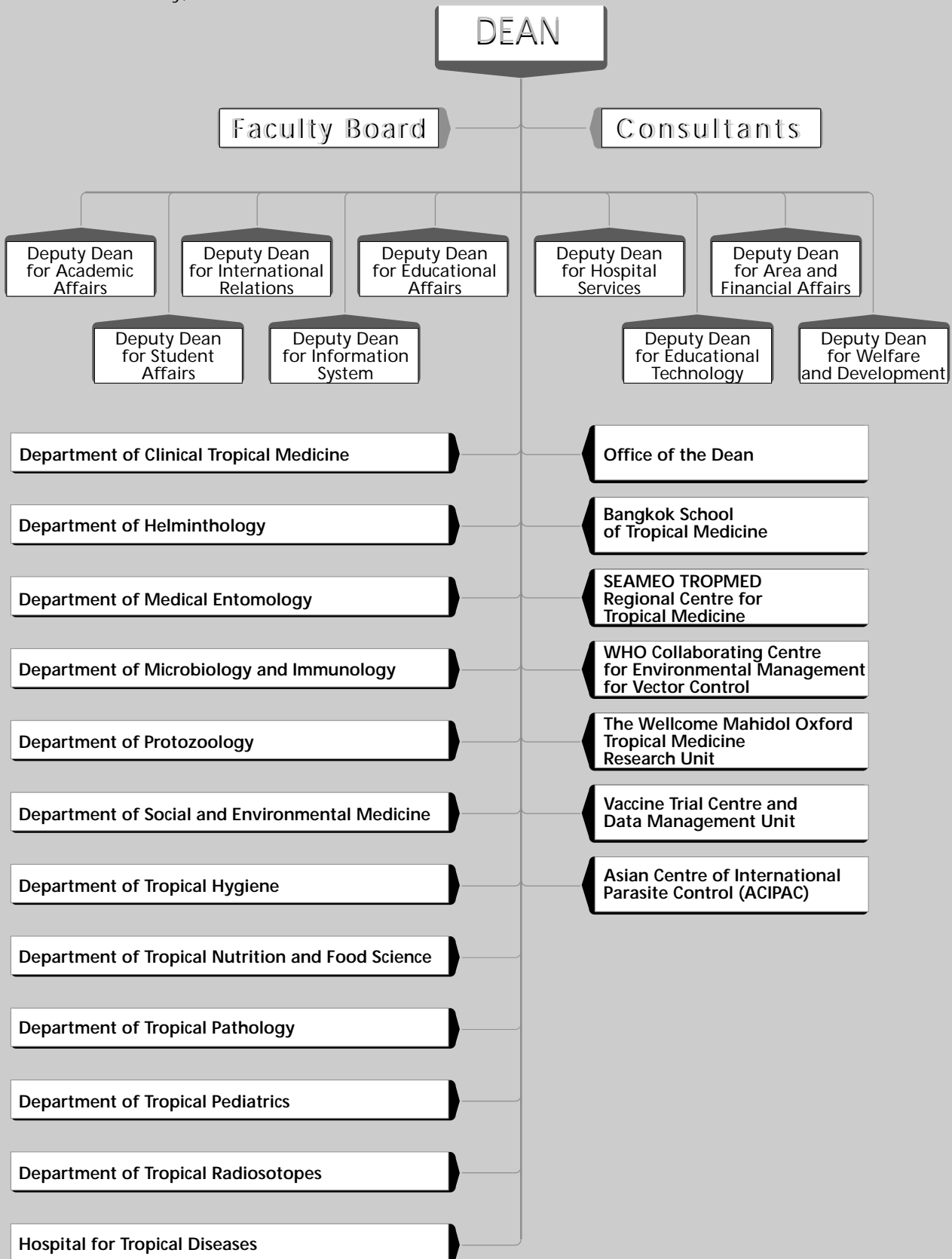
We hope that this 2000 Annual Report provides a useful and informative picture of the activities of the Faculty of Tropical Medicine in the past year.

Assoc. Prof. Jitra Waikagul
Assist. Prof. Achara Asavanich
Editors



Organization and Administration

The Faculty of Tropical Medicine,
Mahidol University, Thailand



Dean, Deputy Deans, and Assistant Deans



Prof. Sornchai Looareesuwan
Dean



Prof. Polrat Wilairatana
Deputy Dean for Hospital Services



Assoc. Prof. Suvanee Supavej
Deputy Dean for International Relations



Assoc. Prof. Jitra Waikagul
Deputy Dean for Academic Affairs



Assoc. Prof. Somjai Leemingsawat
Deputy Dean for Welfare and
Development



Assoc. Prof. Chamnarn Apiwathnasorn
Deputy Dean for Educational Technology



Assist. Prof. Thaiyooth Chintana
Deputy Dean for Area and Financial Affairs



Assist. Prof. Yaowalark Sukthana
Deputy Dean for Educational Affairs



Assist. Prof. Kasinee Buchachart
Deputy Dean for Information System



Dr. Chotechuang Panasoponkul
Deputy Dean for Student Affairs



Assoc. Prof. Kanjana Hongtong
Assistant Dean For Environment



Assist. Prof. Chalit Komalamisra
Assistant Dean for Maintenance



Mr. Chanathep Pojjaroen-anant
Assistant Dean for Internal Traffic and
Safety Service



Assist. Prof. Parnpen Viriyavejakul
Assistant Dean for International Relations



Miss Kobsiri Chalemrut
Assistant Dean for Special Activities



Mrs. Vorapan Singhsilarak
Secretary of the Faculty

CONSULTANTS

1. Prof. Emeritus Chamlong Harinasuta	6. Prof. Emeritus Prayong Radomyos
2. Prof. Emeritus Danai Bunnag	7. Assoc. Prof. Mario Riganti
3. Prof. Emeritus Arunee Sabchareon	8. Prof. Emeritus Mukda Trishnananda
4. Prof. Emeritus Swangjai Pungpak	9. Prof. Emeritus Sommaiya Vilairatna
5. Prof. Emeritus Chaisin Viravan	10. Col. Dr. Sriwatana Chitchang

VISITING PROFESSORS

Fiscal Year 1999-2000

Name	Country	Name	Country
1. Professor Walther H. Wernsdorfer	Austria	12. Professor C.P. Ramachandran	Malaysia
2. Professor Ralf Clemens	Belgium	13. Datuk Dr. Manikavasagam Jegathesan	Malaysia
3. Professor Frank P. Schelp	Germany	14. Dr. P.F. Beales	Switzerland
4. Dr. Gertrud Elise Schmidt-Ehry	Germany	15. Dr. Chev Kidson	Australia
5. Professor Gunther Wernsdorfer	Germany	16. Dr. E. B. Doberstyn	WHO/Thailand
6. Dr. Frederick Gay	France	17. Dr. David Warrell	United Kingdom
7. Professor Kenji Hirayama	Japan	18. Professor Herbert M. Gilles	United Kingdom
8. Professor Masamichi Aikawa	Japan	19. Dr. Gary M. Brittenham	USA
9. Professor Shigeyuki Kano	Japan	20. Professor John H. Cross	USA
10. Professor Somei Kojima	Japan	21. Dr. Karl A. Western	USA
11. Prof. Dr. Katsushi Tokunaga	Japan	22. Dr. Stephen L Hoffman	USA

FACULTY BOARD

(1 October 1999 – 30 September 2000)

No.	Name	Position
1.	Prof. Sornchai Looreesuwan	Dean
2.	Prof. Polrat Wilairatana	Deputy Dean for Hospital Services
3.	Assoc. Prof. Suvanee Supavej	Deputy Dean for International Relations
4.	Assoc. Prof. Jitra Waikagul	Deputy Dean for Academic Affairs
5.	Assoc. Prof. Somjai Leemingsawat	Deputy Dean for Welfare and Development
6.	Assoc. Prof. Chamnarn Apiwathnasorn	Deputy Dean for Educational Technology
7.	Assist. Prof. Thaiyooth Chintana	Deputy Dean for Area and Financial Affairs
8.	Assist. Prof. Yaowalark Sukthana	Deputy Dean for Educational Affairs
9.	Assist. Prof. Kasinee Buchachart	Deputy Dean for Information System
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11.	Assoc. Prof. Vanida Deesin	Head of Department of Medical Entomology
12.	Assoc. Prof. Pornthep Chanthavanich	Head of Department of Tropical Pediatrics
13.	Assoc. Prof. Pramuan Tapchaisri	Head of Department of Microbiology and Immunology
14.	Assoc. Prof. Malinee Thairungroj	Head of Department of Helminthology
15.	Assoc. Prof. Varaporn Suphadtanaphongs	Head of Department of Protozoology
16.	Assoc. Prof. Emsri Pongponrat	Head of Department of Tropical Pathology
17.	Assoc. Prof. Supranee Changbumrung	Head of Department of Tropical Nutrition and Food Science
18.	Assist. Prof. Channarong Sanghirum	Head of Department of Tropical Radioisotopes
19.	Assist. Prof. Pratap Singhasivanon	Head of Department of Tropical Hygiene
*20.	Assist. Prof. Piyarat Butraporn	Head of Department of Social and Environmental Medicine
**21.	Assoc. Prof. Dwip Kitayaporn	Head of Department of Social and Environmental Medicine
22.	Assoc. Prof. Wichai Supanaranond	Head of Department of Clinical Tropical Medicine
23.	Prof. Wanpen Chaicumpa	Elected Member
24.	Assoc. Prof. Surang Tantivanich	Elected Member
25.	Assist. Prof. Achara Asavanich	Elected Member
***26.	Assoc. Prof. Yupaporn Wattanagoon	Elected Member

* from 1 October 1999 – 25 January 2000

** from 25 January 2000

*** from 28 January 2000

FACULTY SENATE

No.	Name	Position
1.	Assoc. Prof. Surang Tantivanich	Chairman
2.	Assist. Prof. Achara Asavanich	Vice Chairman
3.	Prof. Wanpen Chaicumpa	Department Representative
4.	Assoc. Prof. Yupaporn Wattanagoon	Department Representative
5.	Assist. Prof. Supatra Thongrungrat	Department Representative
6.	Mr. Kriengsak Limkittikul	Department Representative
7.	Assist. Prof. Paron Dekumyoy	Department Representative
8.	Assist. Prof. Porntip Petmitr	Department Representative
9.	Assist. Prof. Yaowapa Maneerat	Department Representative
10.	Assist. Prof. Talabporn Harnroongroj	Department Representative
11.	Assist. Prof. Petcharin Yamarat	Department Representative
12.	Assist. Prof. Chantima Lohachit	Department Representative
13.	Dr. Nilarat Premmanisakul	Department Representative
14.	Dr. Udomsak Silachamroon	Department Representative
15.	Assist. Prof. Varee Wongchotigul	Secretary General



Current Research Activities and Abstracts



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Surong Prasartpan Dip. Med. Sci.Tech.

General Affairs Officer

Chuanpit Preechawuthiwong B.A (Political Science)



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Wichai Supanaranond



Punnee Pitisuttithum



Polrat Wilairatana



Sasithon Pukrittayakamee



Sirivan Vanijanonta



Somchai Looareesuwan



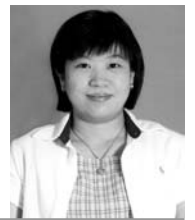
Benjaluck Phonrat



Lakana Leohirun



Yupaporn Wattanapoon



Kesine Chotivanich



Sombat treeprasertsuk



Supat Chamnachan



Thanawat Tosukhowong



Udomsak Silachamroon



Vichitra Pomkulprasit



Valai Bussaratid



Weerapong Phumratanaprapin



Wirach Maek-A-Nantawat



Wongphan Kaivpakbanyai



Apichart Nontprasert



Varanee Desakorn



Trithar Polcharoen



Sompong Mingmongkol



Vick Banmairuoy



Surong Prasartpan



Chuanpit Preechawuthiwong

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. Combinations 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.

Parasitic infestations have also been studied such as a drugs trial in gnathostomiasis, strongyloidiasis, opisthorchiasis, paragonimiasis and taeniasis.

Series of research are going on involving new antifungal drugs for AIDS with fungal disease. Traditional medicine for the treatment of HIV/AIDS is also being studied.

Research of skin diseases in HIV patients is carried out in many aspects, such as the epidemiology of cutaneous manifestations in HIV patients in Thailand, fungal infection in leukoplakia patients, superficial fungal infections in normal and HIV patients.

Titles of current research activities:

1. Emergencies of liver fluke infections during the dry season: Lam-Takong and Mae-Kwnang National Reservoirs.
2. Neurotoxicity of oral artemether in an animal model.
3. Dissolution tests for fast-release dihydroartemisinin compound tablets.
4. Comparative assessment of *in vivo* and *in vitro* sensitivity of *Plasmodium vivax* to chloroquine.
5. Investigation of the response of *Plasmodium falciparum* to a combination regimen of artesunate plus mefloquine in Mae Sot District, Tak Province.
6. Bioequivalence of mefloquine when given as Mepha and Alloquin.
7. Study on partition of an antimalaria mefloquine.
8. Bioavailability and bioequivalence of suppositories levamisole and artesunate in healthy volunteers.
9. Host factors related to severe and complicated falciparum malaria.

10. Comparative study between two tests : ELISA and immunoblot tests in gnathostomiasis patients.
11. Cutaneous manifestation in HIV patients.
12. Epidemiological study in gnathostomiasis patient.
13. Open-label, treatment protocol for the safety and efficacy of SCH 56592 (Oral Suspension form) in the treatment of invasive fungal infections.
14. Relationship of *Plasmodium* antigen and antibody profiles to therapeutic response in falciparum malaria.
15. PCR-RFLP detection of *Plasmodium vivax* dhfr mutations.
16. 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.
17. Neurotoxicity of artemether in an animal model following intermittent intramuscular injections.
18. Safety and therapeutic effects of Jin Huang Chinese medicine in uncomplicated HIV-1 patients.
6. Queensland Institute of Medical Research, University of Queensland, Brisbane, Australia.
7. Department of Medicine, University of Toronto, Canada.
8. Department of Microbiology and Infectious Diseases, Faculty of Medicine, 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.
14. The Walter and Eliza Hall Institute of Medical Research, Australia.
15. Division of Parasitology, NIMR, Mill Hill, London, England.
16. Institute of Molecular Medicine, University of Oxford, England.

Professor Sornchai Looareesuwan's Awards:

- 1999 - **Who's Who in the World** 15th ed. 1988, New Providence, NJ, USA.
- 2000 - **The Barons 500** leaders for the new century, John L Pelham (ed.), Laguna Beach, CA, USA.
- 2000 - **International Man of the Year 2000-2001** in recognition of his services to tropical medicine from International Biographical Centre, Cambridge, UK.

International institutional linkages

1. Nuffield Department of Clinical Medicine, University of Oxford, England.
2. Department of Medicine, George Washington University Medical Center, Washington DC, USA.
3. Hahnemann University, Philadelphia, USA.
4. Case Western Reserve University, USA.
5. Department of Epidemiology, University of Michigan, USA.

Abstracts

A CASE-CONTROL AUDITORY EVALUATION OF PATIENTS TREATED WITH ARTEMISININ DERIVATIVES FOR MULTIDRUG-RESISTANT *PLASMODIUM FALCIPARUM* MALARIA

van Vugt M, Angus BJ, Price RN, Mann C, Simpson JA, Poletto C, Htoo SH, Looareesuwan S, White NJ, Nosten F

Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

Shoklo Malaria Research Unit, Mae Sot, Tak Province, Thailand

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

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

Department of Clinical Neurophysiology, Institute of Neurological Sciences, Southern General Hospital, Glasgow, UK

Clinical Neurophysiology, Charing Cross Hospital, London, UK

The artemisinin derivatives are now used widely in areas with multidrug-resistant *Plasmodium falciparum* malaria such as Southeast Asia, but concerns remain over their potential for neurotoxicity. Mice, rats, dogs, and monkeys treated with high doses of intramuscular artemether or artemether develop an unusual pattern of focal damage to brain stem nuclei (particularly those involved in auditory processing). To investigate whether a similar toxic effect occurs in patients treated with these compounds, clinical neurologic evaluation, audiometry and early latency auditory evoked responses were measured in a single-blind

comparison of 79 patients who had been treated with 2 courses of oral artemether or artesunate within the previous 3 years, and 79 age- and sex-matched controls living in a malaria-endemic area on the northwestern border of Thailand. There were no consistent differences in any of these test results between the cases and controls. This study failed to detect any evidence of significant neurotoxicity in patients treated previously with oral artemether or artesunate for acute malaria. □

Published in: *Am J Trop Med Hyg.* 2000;62(1):65-9.

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

Camacho LH, Wilairatana P, Weiss G, Mercader MA, Brittenham GM, Looareesuwan S, Gordeuk VR

Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Thailand

Department of Medicine, George Washington University Medical Center, Washington DC, USA

To examine a possible relationship between the immune response and haematological recovery after acute falciparum malaria, we followed peripheral blood eosinophil counts and haemoglobin concentrations for 4 weeks after starting effective treatment in 70 adult Thai patients.

Eosinophils are induced by Th-2 cytokines as well as other stimuli. Eosinophil counts were elevated in only 8 (11%) of the subjects at presentation, but were increased in 65 (93%) by day 7. Eosinophil counts then decreased markedly by day 14, followed by a second increase until day 28. A significant positive

correlation was found between peak eosinophil counts on day 7 and the haemoglobin concentration on day 28, both in 16 subjects without stool parasites ($r = 0.65$, $P = 0.006$) and in 54 patients with stool parasites ($r=0.32$; $P=0.0019$). These results suggest that a robust eosinophilic response shortly after

completing antimalarial therapy predicts a good recovery from malaria-associated anaemia. □

Published in: *Trop Med Int Health* 1999 Jul;4(7):471-5

THE EFFECTS OF QUININE AND ARTESUNATE TREATMENT ON PLASMA TUMOR NECROSIS FACTOR LEVELS IN MALARIA-INFECTED PATIENTS

Ittarat W, Udomsangpetch R, Chotivanich KT, Looareesuwan S

Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Thailand

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Tumor necrosis factor-alpha (TNF-alpha) is an endogenous mediator of shock and inflammation including malaria. Many lines of evidence suggest that cytoadherence, the life-threatening pathology associated with complicated and cerebral malaria, results from the overproduction of TNF in response to malarial parasite. Quinine has been shown to inhibit TNF synthesis and cytoadherence *in vitro* suggesting an additional beneficial effect of quinine on its anti-TNF action. On the other hand, artesunate inhibits cytoadherence better than quinine does not suppress TNF production *in vitro*. The present

study compares the effect of artesunate and quinine on TNF levels of malaria-infected patients. Surprisingly, plasma TNF levels increased dramatically after quinine administration but did not increase after artesunate administration. This difference may be explained by previous observations showing that artesunate kills parasites *in vitro* and clears parasitemias *in vivo* far more rapidly than quinine. The rapid clearance of plasma TNF in quinine treated patients might be due to the drug's TNF-suppressive activity. □

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LOW CD8+ T LYMPHOCYTE RESPONSE TO *P. FALCIPARUM* CIRCUMSPOROZOITE PROTEIN IN NATURALLY-EXPOSED MALARIA ENDEMIC POPULATIONS IN THAILAND

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Cytotoxic T lymphocytes (CTLs) specific for epitope(s) within the circumsporozoite (CS) protein of malaria sporozoites have been shown to play an important role in protective immunity against malaria. Human CTLs against the potential epitope at the carboxy terminal region of CS protein of *Plasmodium falciparum* 7G8 strain (Pf7G8CS

368-390) were determined in thirty-six falciparum malaria patients and ten healthy controls. Four of 36 individuals and none of the healthy controls developed Pf7G8CS 368-390 specific CTL activity. The CTL activity was antigen specific and CD8+ T cell dependent. Although low CTL response has been determined, the study suggested that there

was a correlation between initial parasitemia and the specific Pf7G8CS 368-390 CTL activity. A correlation between such CTL activity and anti-R32tet32 antibody levels among individuals with previous malaria experience was found, which was in contrast to those among individuals with recent malaria infection. All these 4 CTL positive individuals had at least two episodes of clinical malaria while all 25 individuals who were exposed to malaria for the first

time did not have such a specific CTL response. These results showed that individuals with a history of natural endemic exposure to *P. falciparum* sporozoite developed low specific CTL responses to Pf7G8CS 368-390, so that previous but recent sporozoite exposure might be a prerequisite for generation of such CS protein specific CTL response. □

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HIDDEN *PLASMODIUM FALCIPARUM* INFECTIONS

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Mixed infection of *P. vivax* and *P. falciparum* malaria frequently recorded in field survey. However is mixed infection was frequently misdiagnosed as single infection due to low parasite density, difficult species identification and procedure errors in microscopic examination. Our previous report showed high rates (32-33%) of *P. vivax* infection following treatment of what was previously assumed to be only *P. falciparum* infection.

In a study of 992 patients with initial presentation with *P. falciparum*, we found that 104 (10.5%) patients had *P. falciparum* appearing during 28 days in the hospital (ranged 1-28 days) following chloroquine treatment for *P. vivax*. The potential for *P. falciparum* appearing following elimination of *P. vivax* must be considered in malaria treatment. □

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A RANDOMIZED, DOUBLE-BLIND, COMPARATIVE TRIAL OF A NEW ORAL COMBINATION OF ARTEMETHER AND BENFLUMETOL (CGP 56697) WITH MEFLUQUINE IN THE TREATMENT OF ACUTE *PLASMODIUM FALCIPARUM* MALARIA IN THAILAND

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CGP 56697, a new oral fixed combination of artemether and benflumetol, was tested in a double-blinded, randomized trial in 252 adult patients treated either with CGP 56697 (4 x 4 tablets each containing 20 mg of artemether and 120 mg of benflumetol, given at 0, 8, 24, and 48 hr), or with mefloquine (three tablets of 250 mg at initial diagnosis, followed by two tablets of 250 mg at 8

hr). Baseline data of the two groups were comparable. The 28-day cure rate with CGP 56697 was lower than with mefloquine (69.3% versus 82.4%; $P = 0.002$). However, CGP 56697 was more effective than mefloquine in parasite clearance time (43 hr versus 66 hr; $P < 0.001$) fever clearance time (32 hr versus 54 hr; $P < 0.005$), and gametocyte clearance time (152 hr versus 331 hr; $P < 0.001$).

This study revealed that CGP 56697 is effective against multidrug-resistant *Plasmodium falciparum* malaria in Thailand, but higher doses will probably be needed to improve the cure rate. □

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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 in most regions of the world. Recently, however, chloroquine-resistant *P. vivax* has been reported from Oceania, several parts of Asia, and South America. In order to assess the situation in Thailand, 886 patients with vivax malaria who were admitted to the Bangkok Hospital for Tropical Diseases from 1992 to 1997 were followed prospectively. Most of the patients had been infected on the western border of Thailand and were experiencing their first malarial infection when admitted. All received oral chloroquine (approximately 25 mg base/kg body weight, administered over 3 days) and then were randomized to receive primaquine (15 mg daily for 14 days) or no further treatment. All the patients

were initially responsive to chloroquine, clearing their parasitaemias within 7 days, and there were no significant differences in the clinical or parasitological responses between those treated with primaquine and those given no further treatment. *Plasmodium vivax* parasitaemias re-appeared within 28 days of chloroquine treatment in just four patients. In each of these four cases, re-treatment with the same regimen of chloroquine resulted in eradication of the parasitaemia, with no further appearance of parasitaemia during the next, 28-day follow-up period. These data indicate that virtually all acute (i.e. blood-stage) *P. vivax* infections acquired in Thailand can still be successfully treated with chloroquine. □

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ATOVAQUONE AND PROGUANIL HYDROCHLORIDE FOLLOWED BY PRIMAQUINE FOR TREATMENT OF *PLASMODIUM VIVAX* MALARIA IN THAILAND

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Chloroquine-resistant *Plasmodium vivax* malaria has been reported in several geographical areas. The *P. vivax* life-cycle includes dormant hepatic parasites (hypnozoites) that cause relapsing malaria weeks to years after initial infection. Curative therapy must therefore target both the erythrocytic and hepatic stages of infection.

Between July 1997 and June 1998, we conducted an open-label study in Thailand to evaluate the efficacy and tolerability of a sequential regimen of combination atovaquone (1000 mg) and proguanil hydrochloride (400 mg), once daily for 3 days, followed by primaquine (30 mg daily for 14 days) for treatment of vivax malaria. All 46 patients who

completed the 3-day course of atovaquone-proguanil cleared their parasitaemia within 2-6 days. During a 12-week follow-up period in 35 patients, recurrent parasitaemia occurred in 2 patients. Both recurrent episodes occurred 8 weeks after the start of therapy, consistent with relapse from persistent hypnozoites rather than recrudescence of

persistent blood-stage parasites. The dosing regimen was well tolerated. Results of this trial indicate that atovaquone-proguanil followed by primaquine is safe and effective for treatment of vivax malaria. □

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TREATMENT OF VIVAX MALARIA ON THE WESTERN BORDER OF THAILAND

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The efficacy of chloroquine (25 mg base/kg over 3 days) in *Plasmodium vivax* malaria was evaluated in 1995/96 in 342 patients living in an endemic area on the western border of Thailand. Clearance of fever and parasites was obtained within 2 days in > 95% of the patients, and all were aparasitaemic by day 4. Reappearance of *P. vivax* occurred in 1 patient on day 21 and in 8 by day 28, giving a 28-day cure rate of 97% [95% confidence interval (CI) 95-99%]. By day 63, the relapse/re-infection rate was 63% (95% CI 57-69%). Most reappearances of parasitaemia (85%; 121/143) were symptomatic. These patients were retreated either with chloroquine alone (n = 70) or with chloroquine and primaquine (0.25 mg/kg daily for 14 days) (n = 43). Only 1 patient (in the chloroquine-only group) had prolonged parasite clearance (D8) and he developed recurrent *P. vivax*

by day 21 suggesting possible recrudescence. The addition of primaquine to chloroquine reduced the risk of having a third vivax episode within 2 months by 96% (95% CI 83-99%). This resulted in a significantly higher haematocrit at day 42 despite a greater decrease in haematocrit during the first week of treatment with chloroquine-primaquine (P = 0.04). Chloroquine remains highly effective on the western border of Thailand and the use of strictly supervised primaquine effectively prevents relapse. The introduction of primaquine on a large scale in an endemic area still requires a long-term risk-benefit assessment which must take into account potential toxicity, low compliance and reductions in the incidence and severity of *P. falciparum* infections by co-existent *P. vivax*. □

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POPULATION PHARMACOKINETICS OF MEFLOQUINE IN PATIENTS WITH ACUTE FALCIPARUM MALARIA

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OBJECTIVE: To construct a population pharmacokinetic model for mefloquine in the treatment of falciparum malaria.

BACKGROUND: Mefloquine is the treatment of choice for multidrug-resistant falciparum malaria. The factors that influence the pharmacokinetic properties of mefloquine in acute malaria are not well characterized.

METHODS: The pharmacokinetic properties of mefloquine were evaluated in 257 patients with acute falciparum malaria by use of nonlinear mixed-effects modeling. Two different oral dose regimens were used: (1) a split dose of 15 mg base/kg initially followed by 10 mg/kg 24 hours later (n = 159) and (2) a single dose of 25 mg/kg (n = 98). Mefloquine was combined with artesunate in 105 (41%) patients (74 received a split dose and 31 received a single dose).

RESULTS: Splitting the mefloquine dose increased the area under the concentration-time curve [AUC(0-infinity)] by 50% (95% confidence interval [CI], 36% to 65%) for monotherapy and by 20% (95% CI, 3% to 40%) for combined therapy. The apparent volume of distribution (V/F) was

significantly lower in patients receiving split doses of mefloquine monotherapy (mean, 8.14 L/kg; 95% CI, 7.49 to 8.86 L/kg) compared with a single dose (mean, 20.37 L/kg; 95% CI, 16.26 to 25.51 L/kg). Patients who received mefloquine monotherapy and cleared parasitemia in less than 48 hours had a significantly higher AUC(0-infinity) independent of any confounders, compared with patients with slower parasite clearance (geometric mean [95% CI], 50,373 ng/mL x day [46,121 to 55,017 ng/mL x day] versus 45,583 ng/mL x day [42,306 to 49,125 ng/mL x day]).

CONCLUSIONS: The pharmacokinetic properties of mefloquine in malaria were relatively unaffected by demographic variables (other than body weight) or disease severity. If it is assumed that apparent clearance and volume of distribution are unaffected by dose regimen, then splitting the 25 mg/kg mefloquine dose improves oral bioavailability and the therapeutic response in the treatment of acute falciparum malaria. □

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ABSENCE OF AN INTERACTION BETWEEN ARTESUNATE AND ATOVAQUONE-PROGUANIL

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OBJECTIVE: Atovaquone plus proguanil is a new, well-tolerated and highly effective antimalarial drug. In order to protect it from the development of resistance, it may be deployed in combination with an artemisinin derivative. To investigate whether artesunate affects the pharmacokinetics of atovaquone plus proguanil, and to provide preliminary information regarding the tolerability of the triple drug combination (artesunate plus atovaquone plus proguanil), a cross over study was conducted in adult volunteers.

METHODS: Twelve healthy Karen adults were randomised to receive atovaquone-proguanil (1000/400 mg) with or without artesunate (250 mg) and, at least 90 days later, the study was repeated. Blood was sampled over a 10-day period.

RESULTS: The three-drug combination was well tolerated. Artesunate did not alter the

pharmacokinetic properties of atovaquone and proguanil (maximum plasma concentrations: 13.02 microg/ml and 742 ng/ml; elimination half-lives: 42.2 h and 14.4 h; oral plasma clearance estimates: 90 ml/h/kg and 710 ml/h/kg; and apparent volumes of distribution: 4.9 l/kg and 14.5 l/kg, respectively). There was also no effect of artesunate on the biotransformation of proguanil to cycloguanil. The pharmacokinetic variables were similar to those reported previously for the individual drugs.

CONCLUSION: Artesunate does not influence atovaquone or proguanil pharmacokinetics. The triple-drug combination of atovaquone and proguanil and artesunate was well tolerated. □

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NO EVIDENCE OF CARDIOTOXICITY DURING ANTIMALARIAL TREATMENT WITH ARTEMETHER-LUMEFANTRINE

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Artemether-lumefantrine is a new fixed antimalarial combination effective against multidrug-resistant falciparum malaria. A prospective electrocardiographic study was conducted in 150 patients receiving artemether-lumefantrine and 50 treated with artesunate-mefloquine. There was no evidence for clinically significant changes in the electrocardiographic

intervals and in particular no relationship between plasma concentrations of lumefantrine and QTc prolongation. Artemether-lumefantrine does not have significant cardiac effects at therapeutic doses. □

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EFFICACY OF SIX DOSES OF ARTEMETHER-LUMEFANTRINE (BENFLUMETOL) IN MULTIDRUG-RESISTANT *PLASMODIUM FALCIPARUM* MALARIA

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The new oral fixed combination artemether-lumefantrine (CGP 56697) has proved to be an effective and well-tolerated treatment of multidrug resistant *Plasmodium falciparum* malaria, although cure rates using the four-dose regimen have been lower than with the currently recommended alternative of artesunate-mefloquine. Two six-dose schedules (total adult dose = 480 mg of artemether and 2,880 mg of lumefantrine) were therefore compared with the previously used four-dose regimen (320 mg of artemether and 1,920 mg of lumefantrine) in a double-blind trial involving 359 patients with

uncomplicated multidrug-resistant falciparum malaria. 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 adjusted 28-day cure rates of 96.9% and 99.12%, respectively, compared with 83.3% for the four-dose regimen ($P < 0.001$). These six-dose regimens of artemether-lumefantrine provide a highly effective and very well-tolerated treatment for multidrug-resistant falciparum malaria. □

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EFFICACY OF PRIMAQUINE REGIMENS FOR PRIMAQUINE-RESISTANT *PLASMODIUM VIVAX* MALARIA IN THAILAND

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To define the current efficacy of Fansidar (pyrimethamine and sulfadoxine), primaquine in high dose, and artesunate for treating acute vivax malaria, we conducted a comparative clinical trial of these three drugs in an open label study. Patients (age 15-65 years) were assigned to one of four treatments regimens in a serial order. Ninety percent of the patients were infected at the Thai-Myanmar border. Patients in group I (n=23) received Fansidar 3 tablets (pyrimethamine 75 mg and sulfadoxine 1,500 mg) single dose on the first day, group II (n=23) received Fansidar 3 tablets (pyrimethamine 75 mg

and sulfadoxine 1,500 mg) single dose on the first day and then received primaquine 30 mg once daily for the following 14 days, group III (n=23) received primaquine 30 mg once daily for the following 14 days, and group IV (n=23) received artesunate 200 mg once daily for 3 days and then primaquine 30 mg once daily for 14 days. Cure rates on 28 day follow-up were 40%, 100%, 100% and 100% in groups I, II, III and IV respectively. There were 4 and 5 patients in group I showing post-treatment reappearance of parasitemia at ≤ 16 days and between 17-28 days respectively. Patients in the other three groups

showed negative parasitemia within 7 days after treatment. Artesunate plus primaquine (group IV) cleared parasitemia faster than the other three regimens. There is a high proportion of ineffectiveness of Fansidar to *P. vivax* and it should be no longer used in vivax malaria acquired at the

Thai-Myanmar border. A high dose of primaquine is safe and effective in treatment of vivax malaria at the 28 day follow-up period. □

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GENETIC ANALYSIS OF *PLASMODIUM FALCIPARUM* INFECTIONS ON THE NORTH-WESTERN BORDER OF THAILAND

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Genetic characterization of *Plasmodium falciparum* infections in north-western Thailand, a region of low transmission intensity (1 infection/person each year), has found a comparable number of parasite genotypes per infected person to regions with hyperendemic malaria. Clone multiplicity and parasite diversity were found to be homogeneous across 129 infected individuals comprising a range of age-groups (1.32 parasite genotypes; n = 98), patients (aged 2-16 years) with recrudescence infections (1.54; n = 13), and pregnant women (1.61; n = 18). Individuals belonging to groups with a high risk of infection, as deduced by clinical epidemiology, did not

harbour a higher number of clones per infection, nor greater parasite diversity than low-risk groups. In fact, multiple genotype infections were as common in low-risk groups, suggesting that there is frequent transmission of polyclonal infections from a single inoculum, rather than superinfection. Such a polyclonal transmission system would enable generation of extensive parasite diversity by recombination, despite the low level of transmission. However, co-infection with *P. vivax* was associated with fewer *P. falciparum* genotypes per infection. □

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FREQUENCY OF PRURITUS IN *PLASMODIUM VIVAX* MALARIA PATIENTS TREATED WITH CHLOROQUINE IN THAILAND

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Chloroquine-induced itch in black-skinned African malaria patients is common and frequently leads to poor compliance or treatment defaulting. To assess the frequency and severity of chloroquine-induced pruritus in an Asian population, we reviewed case records of 1189 *Plasmodium vivax* malaria patients treated with chloroquine (25 mg/kg over 3 days) at the Bangkok Hospital for Tropical Diseases from 1992 through 1997. The majority of patients were Thais or ethnic Burmese (light brown skin), referred from the western border of Thailand. Overall, there were 23 patients (1.9%) with complaints of pruritus during chloroquine therapy. Of these, 12 (52%) had palm and sole involvement, eight (35%) had generalized pruritus including the palms and soles, and three (13%) had palm itching only. One patient developed pruritus on the palms and soles on two

consecutive admissions. The pruritus did not interfere with daily activity, was reduced in intensity by anti-histamine therapy, and did not affect the patient's willingness to complete the chloroquine regimen. Therapeutic responses in the 23 patients with chloroquine itch was similar to those without itch. Among the itch patients, there was no association with gender or level of parasitaemias. Our findings indicate that the frequency of chloroquine-induced pruritus in Asian patients treated with chloroquine for *P. vivax* malaria is low in comparison with black-skinned Africans. This may be related to pharmacogenetic factors, the infective *Plasmodium* species, drug metabolism or drug-parasite interactions, or a lower affinity of chloroquine for less pigmented skin. □

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PARASITE MULTIPLICATION POTENTIAL AND THE SEVERITY OF FALCIPARUM MALARIA

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The multiplication rates and invasiveness of *Plasmodium falciparum* parasites isolated from adult Thai patients hospitalized with uncomplicated malaria ($n = 34$) were compared with those from persons with severe malaria ($n = 42$). To simulate severe malaria and control for host effects, the *in vitro* cultures were adjusted to 1% parasitemia and used the same red blood cell donor. *P. falciparum* isolates from persons with severe malaria had initial cycle multiplication rates *in vitro* that were 3-fold higher than those from uncomplicated malaria (median [95%

confidence interval], 8.3 [7.1 – 10.5] vs. 2.8 [1.7 – 3.9]; $P = .001$). Parasites causing severe malaria exhibited unrestricted red blood cell invasion, whereas those from uncomplicated malaria were restricted to a geometric mean of 40 (31% - 53%) of red blood cells. *P. falciparum* parasites causing severe malaria were less selective and multiplied more at high parasitemias than those causing uncomplicated malaria. □

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THE MECHANISMS OF PARASITE CLEARANCE AFTER ANTIMALARIAL TREATMENT OF *PLASMODIUM FALCIPARUM* MALARIA

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Studies were conducted to determine how malaria parasites are cleared from the blood after antimalarial treatment. Neither artesunate nor quinine decreased parasitized red cell deformability or increased antibody binding. In acute falciparum malaria, ring-infected erythrocyte surface antigen (RESA) was observed in erythrocytes without malaria parasites (RESA-red blood cell [RBC]), indicating prior parasitization. In uncomplicated malaria, RESA-RBC numbers increased significantly ($P = .002$) within 24 h of starting artesunate but rose much more slowly (7 days) after quinine treatment. In severe malaria, RESA-RBC increased

significantly ($P = .001$) within hours of starting artesunate but not with quinine treatment ($P = .43$). RESA-RBCs were not produced after drug treatment of malaria parasite cultures *in vitro*. Rapid malaria parasite clearance after treatment with artemisinin derivatives results mainly from the extraction of drug-affected parasites from host erythrocytes—presumably by the spleen. This explains why the fall in hematocrit after treatment of hyperparasitemia is often less than that predicted from loss of parasitized cells. □

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PHARMACOKINETICS AND PHARMACODYNAMICS OF LUMEFANTRINE (BENFLUMETOL) IN ACUTE FALCIPARUM MALARIA

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The objective of this study was to conduct a prospective population pharmacokinetic and pharmacodynamic evaluation of lumefantrine during blinded comparisons of artemether-lumefantrine treatment regimens in uncomplicated multidrug-resistant falciparum malaria. Three combination regimens containing an average adult lumefantrine dose of 1,920 mg over 3 days (four doses) (regimen A) or 2,780 mg over 3 or 5 days (six doses) (regimen B or C, respectively) were given to 266 Thai patients. Detailed observations

were obtained for 51 hospitalized adults, and sparse data were collected for 215 patients of all ages in a community setting. The population absorption half-life of lumefantrine was 4.5 h. The model-based median (5th and 95th percentiles) peak plasma lumefantrine concentrations were 6.2 (0.25 and 14.8) microgram/ml after regimen A, 9.0 (1.1 and 19.8) microgram/ml after regimen B, and 8 (1.4 and 17.4) microgram/ml after regimen C. During acute malaria, there was marked variability in the fraction of drug absorbed by patients (coefficient

of variation, 150%). The fraction increased considerably and variability fell with clinical recovery, largely because food intake was resumed; taking a normal meal close to drug administration increased oral bioavailability by 108% (90% confidence interval, 64 to 164) (P, 0.0001). The higher-dose regimens (B and C) gave 60 and 100% higher areas under the concentration-time curves (AUC), respectively, and thus longer durations for which plasma lumefantrine concentrations exceeded the putative in vivo MIC of 280

microgram/ml (median for regimen B, 252 h; that for regimen C, 298 h; that for regimen A, 204 h [P, 0.0001]) and higher cure rates. Lumefantrine oral bioavailability is very dependent on food and is consequently poor in acute malaria but improves markedly with recovery. The high cure rates with the two six-dose regimens resulted from increased AUC and increased time at which lumefantrine concentrations were above the in vivo MIC. □

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COMPLICATED MALARIA IS ASSOCIATED WITH DIFFERENTIAL ELEVATIONS IN SERUM LEVELS OF INTERLEUKINS 10, 12, AND 15

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Complicated malaria, caused by *Plasmodium falciparum*, is characterized by multiple organ dysfunction. The pathogenesis of complicated malaria involves complex host-parasite interactions that include polarized cytokine responses. Recently, correlates between Th1-like and Th2-like cytokines, especially interleukin-10 (IL), IL-12, and TNF-, and specific types of organ dysfunction have been noted. Here, we measured IL-10, IL-12, and for the first time, IL-15, in 19 patients aged 16-55 years old with complicated malaria on days 0 (admission), 3, 7, and 14. For analysis, patients were grouped together or subcategorized into hyperparasitemias or cerebral malaria (CM). For IL-10, a dramatic increase was noted on admission,

followed by a reduction toward control values that closely paralleled parasite clearance. For IL-12, modest but persistent increases were noted over the entire 14-day period that did not correlate with parasitemia. In general, especially on days 0 and 3, hyperparasitemic patients had, in comparison with CM patients, higher IL-10 and IL-12 levels. In contrast, IL-15 was generally below detection in most samples. These results provide further insight into the pathogenesis of complicated malaria by strengthening the contention that cytokines such as IL-10 and IL-12 are involved in modulating the immune response to *P. falciparum*. □

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IgE DEPOSITION IN CEREBRAL MICROVESSELS AND ON PARASITIZED ERYTHROCYTE FROM CEREBRAL MALARIA PATIENTS

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Postmortem cerebral tissues of 21 cerebral malaria cases were obtained in Myanmar and Vietnam. The cerebral tissues were examined by light microscopy and by an immunohistologic method. The cerebral malaria patients were categorized into two groups based on the rate of parasitized erythrocytes (PRBC) sequestration in the cerebral tissues: group I with high (50% or more) PRBC sequestration and group II with low (less than 50%) sequestration. Deposition of immunoglobulins, IgE and IgG, and *Plasmodium falciparum* antigens were seen in the cerebral microvessels from all specimens in both groups. All specimens in group I were also positive for IgE and IgG on PRBC in the cerebral section. The

frequency of IgE and IgG deposition ranged from 42% to 51% and 100%, respectively. In group II, all specimens were negative for IgE, but positive for IgG. Thus, our data indicate that the amount of deposition of IgE in cerebral microvessels and on PRBC in the cerebral microvessels, especially PRBC from cerebral malaria patients correlated well with the degree of PRBC sequestration in that site. As IgE containing immune complexes can induce local overproduction of tumor necrosis factor (TNF), a pathogenic factor in cerebral malaria, IgE may contribute to the pathogenicity of this severe disease. □

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CYTOKINES ASSOCIATED WITH PATHOLOGY IN THE BRAIN TISSUE OF FATAL MALARIA

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Cytoadherence of *Plasmodium falciparum*-infected erythrocytes to the brain microvascular endothelial cells is believed to be an important cause of circulatory blockage in cerebral malaria. Cytokines released during acute infection may activate brain endothelial cells leading to increased binding of infected erythrocytes in the brain and reduced cerebral blood flow. This effect may be direct and more potent with the tissue-localized cytokines in the brain. In order to establish this relationship, brain

tissues of cerebral and noncerebral malaria were compared. The most prominent histopathologic changes in the brain included edema, neuronal degeneration, ring hemorrhage, and the percentage of parasitized erythrocyte sequestration was observed in cerebral malaria. Immunohistochemical staining of the brain sections demonstrated that tissue-localized TNF-alpha, IFN-gamma, IL-11B, and IL-10 were associated with the histopathology. However, IL-4 was the only cytokine present at a moderate level

in the brain tissue of noncerebral malaria, in which histopathology was the least. No tissue-localized cytokine was observed in the brain of *P. vivax* infection or of the car accident control cases. □

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CIRCULATING RECEPTORS IMPLICATED IN THE CYTO-ADHERENCE OCCURRING IN SEVERE *PLASMODIUM FALCIPARUM* MALARIA IN THAILAND

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The kinetic profiles of soluble chondroitin-sulphate A (CSA), intercellular adhesion molecule 1 (ICAM-1), vascular cell adhesion molecule 1 (VCAM-1) and E-selectin were investigated in 17 patients hospitalized with *Plasmodium falciparum* malaria. The aim was to see if these circulating adhesion molecules could be considered as markers for the severity of *P. falciparum* malaria. The levels of all the adhesion molecules were found to be higher in the sera from all the malaria cases, both severe and uncomplicated, than in those from uninfected controls. The elevation in plasma CSA, reported for the first time, was statistically very significant

($P = 0.00001$). However, when the severe cases were compared with the uncomplicated, there were no significant differences in the level of any of the receptors except ICAM-1, which was highest in those with the severe disease ($P = 0.01$). The absence of any significant correlation between the plasma concentration of CSA and malaria severity indicates that this adhesion molecule could not be used to predict the severity of malaria, although its role in sequestration of the parasites in pregnant women is well established. □

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ASCARIS LUMBRICOIDES INFECTION IS ASSOCIATED WITH PROTECTION FROM CEREBRAL MALARIA

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Following reports of increased IgE in severe malaria and hypothesizing that helminth coinfections could modify its outcome, we conducted a retrospective case-control study to establish whether helminths affect the evolution of *Plasmodium falciparum* malaria. Some 182 severe cases, 315 mild controls and 40 controls with circulating schizonts were examined for

intestinal helminths. Comparing cerebral malaria with mild controls, *Ascaris lumbricoides* was associated with a protective adjusted odds ratio (OR) of 0.58 (0.32-1.03) $P = 0.06$, for coinfection with *Ascaris* and *Necator americanus*, OR = 0.39 (0.17-0.88) $P = 0.02$. Protection followed a dose-effect trend ($P = 0.008$). When comparing cerebral malaria cases and controls with circulating schizonts

the OR was 0.25 (0.009-0.67) $P = 0.006$. We hypothesized that *Ascaris* infected patients may have had decreased cyto-adherence, possibly through endothelial cell receptor downregulation and/or decreased splenic clearance leading to the absence of selection of virulent *P. falciparum* strains. IgE-anti-IgE immune complexes resulting

from helminth preinfection may have an important role in influencing clinical presentation of severe malaria, and in establishing malaria tolerance, through the CD23/NO pathway. □

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IN VITRO ACTIVITY OF AZITHROMYCIN IN FRESH ISOLATES OF *PLASMODIUM FALCIPARUM* IN THAILAND

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The spread of multidrug resistant strains of *Plasmodium falciparum* in recent years has intensified the search for new antimalarials and antibiotics with antimalarial activities. Among the macrolide antibiotics, erythromycin was the first to be used in the treatment and prophylaxis of malaria. Azithromycin, a relatively new semisynthetic derivative of erythromycin, differs structurally from erythromycin by the addition of a methyl-substituted nitrogen atom in the lactone ring. This modification improves acid stability and tissue penetration capabilities and also broadens the antibacterial spectrum. Its antimalarial, as well as prophylactic activities, however, have only recently been described.

The study was designed as an experimental laboratory-investigation conducted at the Hospital for Tropical Diseases (Faculty of Tropical Medicine, Mahidol University) from June 1999 until March 2000. A total number of 39 fresh isolates of *P.*

falciparum obtained from patients with microscopically confirmed *P. falciparum* mono-infections, primarily from the western border regions of Thailand, were successfully tested for their azithromycin *in vitro* drug susceptibility. The *in vitro* tests for the measurement of the drug sensitivity of *P. falciparum* followed the WHO standard methodology for the assessment of the inhibition of schizont maturation with microtitre plates pre-dosed with ascending concentrations of azithromycin (0.1 to 100 mol/l blood medium mixture) (WHO, 1990). For the mathematical analysis of drug response the drug concentrations were log-transformed and the inhibition data expressed in probits (Litchfield and Wilcoxon, 1949). The transformed data were used in a quadratic regression model. □

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EFFECTS OF ARTESUNATE-MEFLOQUINE COMBINATION ON INCIDENCE OF *PLASMODIUM FALCIPARUM* MALARIA AND MEFLOQUINE RESISTANCE IN WESTERN THAILAND: A PROSPECTIVE STUDY

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Morbidity and mortality from *Plasmodium falciparum* malaria are increasing in many tropical areas. This increase results partly from the spread of drug resistance in *P. falciparum* and the absence of an effective strategy to combat it. In Thailand, increasing resistance to chloroquine and sulphadoxine-pyrimethamine led to the introduction of mefloquine in 1984. The drug was used initially in combination with sulphadoxine-pyrimethamine, later on its own at a higher dose, and finally, in certain

areas, in combination with an artemisinin derivative (artesunate).

We conducted a prospective study to assess the factors that affected the incidence of malaria among displaced Karen people over a 13-year period, and the effects of the artesunate-mefloquine combination on the evolution of mefloquine resistance. □

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CONTRASTING FUNCTIONS OF IgG AND IgE ANTIMALARIAL ANTIBODIES IN UNCOMPLICATED AND SEVERE *PLASMODIUM FALCIPARUM* MALARIA

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Plasmodial infection results in a significant elevation of the blood concentrations of immunoglobulins including IgE. Two well-characterized groups of adult Thai patients with either uncomplicated or severe *Plasmodium falciparum* malaria were studied over a period of four weeks. The mean parasitemias were approximately three-fold higher in patients with severe malaria than in those with uncomplicated disease. The mean concentrations of both total IgG and IgG antiplasmodial antibodies tended to be

highest in the group with uncomplicated disease while total IgE and IgE antibodies were higher in the group with severe disease. The IgE antibodies detected in approximately 65% of the patients were positively correlated to parasitemia. These results suggest that antiplasmodial IgG antibodies are involved in reducing the severity of *P. falciparum* malaria, while IgE antibodies may contribute to the pathogenesis of this infection. □

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THERAPEUTIC RESPONSES TO DIFFERENT ANTIMALARIAL DRUGS IN VIVAX MALARIA

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The therapeutic responses to the eight most widely used antimalarial drugs were assessed in 207 adult patients with *Plasmodium vivax* malaria. This parasite does not cause marked sequestration, so parasite clearance can be used as a direct measure of antimalarial activity. The activities of these drugs in descending order were artesunate, artemether, chloroquine, mefloquine, quinine, halofantrine, primaquine, and pyrimethamine-sulfadoxine (PS). Therapeutic responses to PS were poor; parasitemias did not clear in 5 of the 12 PS-treatment patients, whereas all the other patients made an initial recovery. Of 166 patients monitored for 28 days, 35% had

reappearance of vivax malaria 11 to 65 days later and 7% developed falciparum malaria 5 to 21 days after the start of treatment. There were no significant differences in the times taken for vivax malaria reappearance among the different groups except for those given mefloquine and chloroquine, in which all vivax malaria reappearances developed >28 days after treatment, suggesting suppression of the first relapse by these slowly eliminated drugs. There was no evidence of chloroquine resistance. The antimalarial drugs vary considerably in their intrinsic activities and stage specificities of action. □

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THERAPEUTIC RESPONSES TO ANTIBACTERIAL DRUGS IN VIVAX MALARIA

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Some antibacterial drugs have antimalarial activity that can be exploited for the prevention or treatment of malaria. Monotherapy with tetracycline, doxycycline, clindamycin or azithromycin was assessed in 92 adult patients with *Plasmodium vivax* malaria. All patients recovered following treatment and the early therapeutic responses were similar among the four groups. The overall median fever clearance time was 57 h and the mean (SD) overall time to parasite clearance was 134 (48) h. Of 66 patients who completed a 28 day follow-up, reappearances of

vivax infection occurred in 27 patients (41%) from all groups and delayed appearances of falciparum malaria occurred in 6 patients (9%), only from the azithromycin group. The overall mean (SD) time to reappearance of *P. vivax* was 23 (5) days and the time taken for detection of falciparum malaria was 13 (4) days after initiation of treatment for vivax malaria. The 28-day cumulative cure rates of clindamycin ($n = 12$), tetracycline ($n = 18$) and doxycycline ($n = 18$) groups were similar ($P 0.14$) and all were significantly higher compared to the azithromycin group ($n = 18$; $P 0.04$). The intervals

until vivax reappearance were also significantly shorter in the azithromycin group (meanSD = 216 vs. 253 days, $P < 0.05$) suggesting that some of these were recrudescences. The apparent success rates (no subsequent appearances of either vivax or falciparum) was significantly lower for the azithromycin group (11%) compared to the other

groups (34%-78%; $P < 0.01$). In current antibacterial treatment regimens, azithromycin has inferior antimalarial activity compared with clindamycin or the tetracyclines. □

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EFFECT OF ARTEMISININ ON LIPID PEROXIDATION AND FLUIDITY OF THE ERYTHROCYTE MEMBRANE IN MALARIA

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The effect of artemisinin on membrane fluidity of erythrocytes was investigated using spin labeling compounds, doxyl stearic acids. The membrane fluidity of erythrocytes from the *in vitro* culture and malaria patients was determined. *In vitro*, the erythrocytes in parasite culture showed an increase in membrane fluidity which was associated with the parasite counts and stage of parasites. Artemisinin caused reduction in membrane fluidity and the effect was more pronounced in the erythrocytes infected with schizont stage-parasites. *In vivo*, the elevation of plasma TBARs (thiobarbituric acid reactive substances) and reduction of membrane fluidity were evident in *Plasmodium falciparum*-infected

patients, particularly in severe cases. The levels of plasma TBARs were related to the severity of the disease. Treatment with artemisinin alone showed no effect on plasma TBARs, and did not alter the membrane fluidity. Desferrioxamine, however, reduced oxidative damage during the infection without compromising the therapeutic effect of artemisinin. These findings suggested that the infected erythrocytes were prone to the effect of artemisinin. Addition of a chelator such as desferrioxamine is beneficial and can improve the treatment of severe malarial. □

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SERUM CONCENTRATIONS OF GRANULOCYTE-COLONY STIMULATING FACTOR IN COMPLICATED *PLASMODIUM FALCIPARUM* MALARIA

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Involvement of neutrophils in the control of blood parasites in malaria has been reported. Both, mononuclear phagocytes and neutrophils are known to be stimulated by cytokines such as TNF-alpha in order to augment the defence potency against the parasites. Previously, it has been shown that serum-G-CSF concentrations are increased in patients with bacterial sepsis. In vitro studies have shown that *P. falciparum*-infected erythrocytes induce the release of G-CSF by several cells such as endothelial cells and monocytes, however, nothing is known about G-CSF serum concentrations during the clinical course of severe *P. falciparum* malaria. Thus, it was the aim of the present study to investigate the time course for G-CSF serum concentrations in patients with complicated *P. falciparum* malaria, and to correlate these values with other mediators of inflammation and hematopoiesis. Twenty-six patients suffering from complicated *P. falciparum* malaria

were included in the study, and 20, age and sex matched, healthy volunteers were used as the negative control group. Serum samples for determination of G-CSF were taken on day 0, 7 and 14, and measured by ELISA. We found significantly increased serum concentrations of G-CSF in patients with complicated *P. falciparum* malaria on day 0, values decreasing to within the normal range by day 7. A significant correlation was found between G-CSF (d0) and procalcitonin, the parasite count, erythropoietin and macrophage inflammatory protein, however no correlation could be shown for the neutrophil count. In conclusion, on the day of hospital admission, elevated serum concentrations of G-CSF were detected in patients with complicated *P. falciparum* malaria, which might indicate a role of G-CSF in the acute defence mechanism against the parasites. □

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CYTOADHERENCE CHARACTERISTICS OF *PLASMODIUM FALCIPARUM* ISOLATES IN THAILAND USING AN *IN VITRO* HUMAN LUNG ENDOTHELIAL CELLS MODEL

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Using an *in vitro* model of human lung endothelial cells, we studied different characteristics of *Plasmodium falciparum* isolates as potential factors for malaria severity in 2 Thai patient groups: 27 with complicated malaria and 42 with uncomplicated malaria. In regard to binding properties, no association existed between

cytoadherence and rosette phenotypes ($P=0.1$) and hypothermocytemia increased the cytoadherence level ($P=0.007$). Cytoadherence was significantly associated with malaria severity ($P=0.05$) in contrast to rosette formation ($P=0.9$). Intercellular adhesion molecule-1 and chondroitin-4-sulfate were major receptors of cytoadherence in those with complicated

malaria compared with those with uncomplicated malaria ($P < 10^{-4}$). Chondroitin-4-sulfate could act as a putative receptor for malaria complications in non-pregnant women. CD36 was the main receptor in patients with uncomplicated malaria ($P < 10^{-3}$). Vascular cell adhesion molecule-1 and E-selectin played a minor role in 2 groups ($P = 0.6$). Qinghaosu derivatives were more efficient than other

antimalarial drugs, but a positive correlation was observed between the 50% inhibitory concentrations of halofantrine and quinine and the number of adhesive parasitized red blood cells, suggesting their influence on cytoadherence. □

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SYNERGISM OF MULTIPLE ADHESION MOLECULES IN MEDIATING CYTOADHERENCE OF *PLASMODIUM FALCIPARUM*-INFECTED ERYTHROCYTES TO MICROVASCULAR ENDOTHELIAL CELLS UNDER FLOW

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Plasmodium falciparum-infected erythrocytes (IRBCs) have been shown to interact with a number of endothelial adhesion molecules expressed on transfectants, on cell lines, and as immobilized purified receptor proteins under flow conditions. However, the experiments were designed in such a way that maximal numbers of adhesion molecules were provided as substratum. Whether the interactive events actually occur on microvascular endothelium, where the distribution and expression of adhesion molecules may be less, remains undetermined. In this study, the cytoadherence of IRBCs on human dermal microvascular endothelial cells (HDMECs) as a model of human microvasculature was examined. IRBCs were observed to tether, roll, and adhere on resting HDMECs, which constitutively expressed CD36 and intercellular adhesion molecule-1 (ICAM-1) at an optimal shear stress of 1 dyne/cm². Stimulation of HDMECs with tumor necrosis factor-

alpha for 5 and 24 hours, which resulted in up-regulation of ICAM-1 and induction of vascular cell adhesion molecule-1 expression, significantly increased the percentage of rolling cells that adhered without affecting the rolling flux. In contrast, P-selectin expression on HDMECs induced by oncostatin M led to an increase in both rolling flux and adhesion. Inhibition studies with receptor-specific monoclonal antibodies revealed that adhesion of IRBCs on HDMECs was largely CD36 dependent, whereas rolling could be mediated by any of the adhesion molecules studied. Collectively, these findings indicate that IRBCs interact synergistically with multiple adhesion molecules on vascular endothelium. The rolling of IRBCs may be the rate-limiting step in cytoadherence, since it can be modulated by cytokines to enhance CD36-mediated IRBC adhesion. □

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THROMBOPOIETIN IN *PLASMODIUM FALCIPARUM* MALARIA

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Thrombopoietin (TPO) is the key growth factor for platelet production and is elevated in states of platelet depletion. As thrombocytopenia is a common finding in malaria, we analysed TPO regulation before, during and after antimalarial treatment. Before treatment, TPO serum levels were significantly higher in patients with severe malaria (n= 35) than in patients with uncomplicated malaria

(n= 44; P= 0.024), normalizing within 14-21 d of therapy. The rapid normalization of TPO levels and increase in low peripheral platelet counts after treatment indicate that the biosynthesis of TPO and its regulation in malaria patients are normal. □

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CLINICAL TRIAL OF SEQUENTIAL TREATMENTS OF MODERATELY SEVERE AND SEVERE MALARIA WITH DIHYDROARTEMISININ SUPPOSITORY FOLLOWED BY MEFLOQUINE IN THAILAND

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One hundred and fifty patients with severe falciparum malaria were administered a sequential combination of dihydroartemisinin suppository followed by an oral mefloquine tablet. Dihydroartemisinin suppositories (80 mg/capsule) were given rectally according to body weight. Patients with body weight of less than 30 kg, 30-40 kg, 41-50 kg, 51-60 kg, 61-70 kg, 71-80 kg, 81-90 kg, and 91-100 kg were given 1 capsule once daily for 3 days; 2 capsules once daily on the first day followed by 1 capsule once daily for 2 days; 2 capsules once daily for 2 days followed by 1 capsule once daily for 1 day; 2 capsules once daily for 3 days; 3 capsules once daily for 1 day followed by 2 capsules once daily for 2 days; 3 capsules once daily for 2 days followed by 2 capsules once daily for 1 day, 3 capsules daily for 3 days; and 4 capsules once daily on the first day followed by 3 capsules once daily for 2 days, respectively. Two doses of mefloquine, 15 mg/kg/

dose and 10 mg/kg/dose, were given at 72 hr and 84 hr, respectively. All patients were admitted for 28 days to the Bangkok Hospital for Tropical Diseases to assess efficacy, tolerability, and delayed neuropsychiatric effects. The mean [SD] parasite clearance time and fever clearance time were 46.1±15.7 hr and 82.5±59.6 hr respectively. No deaths occurred. None of the patients had major adverse drug effects. The cure rates at 28 days of follow-up in patients were 95.0% (113 of 119 patients). Dihydroartemisinin suppository followed by mefloquine was well tolerated and effective. In severe malaria, sequential treatment is a suitable alternative treatment to parenteral drugs; further studies in a larger number of patients under field conditions are required. □

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POST-GRADUATE STUDY AT THE FACULTY OF TROPICAL MEDICINE, MAHIDOL UNIVERSITY AND THE ROLE OF SEAMEO TROPMED IN EDUCATION IN SOUTHEAST ASIAN REGION

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The Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand, was established by the Thai Government on 5 April 1960. Its mission is post-graduate teaching through the Bangkok School of Tropical Medicine, medical service through the Hospital for Tropical Diseases, and research. Post-graduate teaching was initially for Thai medical doctors who had obtained the degree of Bachelor of Medicine. The post-graduate course was designed especially for those doctors who worked in rural areas in tropical medicine, parasitology and the preventive aspects of endemic diseases. Since that time, the extent and impact of the Faculty's educational and research activities have extended throughout Southeast Asia and to tropical regions all over the world, and it now serves as an international institute. The Bangkok School of Tropical Medicine, Faculty of Tropical Medicine, offers 5 regular international post-graduate programs, taught in English, to doctors, researchers, medical personnel and professionals concerned with tropical medicine and public health. These are the graduate Diploma in Tropical Medicine and Hygiene and Master of Clinical Tropical Medicine (courses for qualified medical doctors only); the Master of Science in Tropical Medicine; Doctor of Philosophy in Tropical Medicine; and Doctor of Philosophy in Clinical Tropical Medicine. Overall, 2,234 students from 42 countries have graduated. Students enrolled in the Faculty's programs originate from SEAMEO member countries (Brunei Darussalam, Cambodia, Indonesia, Lao People's Democratic Republic, Malaysia, Myanmar, the Philippines, Singapore, Thailand, and Viet Nam) and

other countries (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, Romania, Russia, the U.S.A. and Venezuela). In recent years, the number of self-supporting participants has increased markedly. The Faculty of Tropical Medicine is a leader in postgraduate tropical medicine education in the Southeast Asian Region and beyond, together with its collaborative and cooperative programs and linkages in training and research, especially with the Southeast Asian Ministers of Education Organization (SEAMEO) through SEAMEO TROPMED. SEAMEO TROPMED was established in 1967 with its primary activities being teaching, research and training in tropical medicine and public health, under SEAMEO. The Faculty has been the SEAMEO TROPMED Regional Centre for Tropical Medicine since 1994. The role, activities and impact of SEAMEO TROPMED in relation to education, training and research are detailed, as well as emerging regional trends in education and research. The Faculty has ongoing collaborative activities in teaching, research and academic services with more than 25 universities and institutions from 13 countries. The Faculty recently became the Asian Centre of International Parasite Control (ACIPAC). □

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GUIDELINE IN MANAGEMENT OF SEVERE MALARIA

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Severe malaria remains a major cause of mortality in the world. Malaria can mimic many diseases and there are no absolute diagnostic clinical features. A high index of suspicion is a clue for clinical diagnosis. Previous travel history to endemic area should be elicited in all, and in particular, febrile patients. Management of severe malaria needs potent antimalarial drugs and intensive care. Artemisinin derivatives can be of alternative use to quinine. Dexamethasone and mannitol have no beneficial value in the management of cerebral malaria. In pulmonary oedema patients whose hydration

assessments are difficult to monitor, central venous pressure evaluation may be useful. Acute renal failure patients may need dialysis until their uraemic syndrome subsides or patients can void urine. Most severe malaria patients have thrombocytopenia; however, platelet concentrate transfusion is indicated only in patients with systemic bleeding. Morbidity and mortality will be reduced in severe malaria patients with early diagnosis and prompt treatment. □

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GASTRIC INTRAMUCOSAL pH AS A PROGNOSTIC INDEX OF MORTALITY IN CEREBRAL MALARIA

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To determine if measurement of gastric intramucosal pH has prognostic implications regarding ICU mortality, 42 cerebral malaria patients in ICU were studied. Gastric intramucosal pH was measured on ICU admission and again 6 hours later. A value of ≥ 7.30 was used to differentiate between normal and low gastric intramucosal pH. 32 patients had a normal gastric intramucosal pH and 10 patients had a low gastric intramucosal pH on ICU admission. The mortality rate was greater in the low gastric intramucosal pH group on admission (40% v. 0%; $P < .05$). Apart from coma, the presence of malarial complications was similar in the low and normal gastric intramucosal pH groups. Further stratification of patients according to gastric

intramucosal pH measured 6 hours after admission showed a greater mortality rate in patients with persistently low gastric intramucosal pH compared with patients with normal gastric intramucosal pH during the first 6 hours (57.14% v. 0%, $P < .05$). Measurement of gastric intramucosal pH on ICU admission, and again 6 hours later, has a high specificity for predicting survival in this ICU patient population (84.20% v. 100%). Furthermore, given that it is a relatively noninvasive procedure, measurement of gastric intramucosal pH may be a useful addition to monitoring cerebral malaria patients in the ICU. □

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ANALYSIS OF MEFLOROQUINE RESISTANCE AND AMPLIFICATION OF PFMDR1 IN MULTIDRUG-RESISTANT *PLASMODIUM FALCIPARUM* ISOLATES FROM THAILAND

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Resistance to quinoline-containing compound has been associated with the *Plasmodium falciparum* multidrug resistance 1 (pfmdr1) gene. We analyzed wild *P. falciparum* isolates with high levels of chloroquine and mefloquine resistance for their macrorestriction maps of chromosome 5 and sequence of pfmdr1. Two types of chromosome 5 amplification were found. Eleven of 62 resistant isolates displayed Bgl 1 fragments larger than 100 kb. Twenty-nine isolates possessed multiple copies of the fragments. We failed to detect any amplification of this region on chromosome 5 in 22 mefloquine-resistant isolates, suggesting that

other mechanisms can mediate the mefloquine-resistant phenotype. There was no direct association between pfmdr1 mutations and chloroquine sensitivity. Resistant lines could have Asn-86 and Tyr-184 or Phe-184, the predicted sequence of those chloroquine-sensitive isolates. No mutation at Asn-1042 and Asp-1246 was detected among these chloroquine-resistant isolates. Therefore, a few base substitutions in the pfmdr1 gene may not be sufficient to account for all chloroquine-resistant phenotypes.

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MALARIA TREATMENT WITH HERBAL MEDICINE AT THE BANGKOK HOSPITAL FOR TROPICAL DISEASES

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Even though we are approaching the 21st century, malaria is still a serious public health problem. It is estimated that about 1-2 million people die each year because of malaria, being mostly African children under 2 years of age - this figure translates into one child dying every 15 seconds. Because of the lack of an effective malaria vaccine, early diagnosis and early treatment with potent antimalarial drugs is still recommended. At present, the most effective antimalarial drugs are artemisinin and its derivatives, including artesunate, artemether, arteether, dihydroartemisinin in various formulas and preparations (such as oral tablet, powder, suppository, intramuscular and intravenous injection). Some of these preparations are now

registered for use in many countries, both as a single preparation and as a combined drug with other antimalarials. Artemisinin and its derivatives are derived from the plant *Artemisia annua* L., which is grown extensively in southern China and northern Vietnam. It has been used in China for the treatment of fever, presumably malaria, for more than 2000 years. However, the novel structure and its action and efficacy have only been elucidated during the last 30 years. It is a potent antimalarial drug, which can kill over 90% of malaria parasitemias within 24 hours of treatment. However, recrudescence rates are high (between 10-50%) depending upon dosage, duration of treatment and disease severity of patients. The lower the dose or the shorter the duration used, or

the greater the severity disease in patients, the higher is the recrudescence rate encountered. At present, the dose and duration of treatment are based on clinical trials due to complexities of pharmacokinetics and pharmacodynamics. Artemisinin can be used for the treatment of multidrug-resistant falciparum malaria and also severe and complicated malaria. The World Health Organization is interested in this compound and is now investigating the drug for use as a combination therapy in uncomplicated falciparum malaria in various countries in all continents. The suppository forms are also interesting as they can be used in children in rural areas, where facilities are limited and treatment may be administered by unskilled personnel (e.g. a sick child's mother). Early treatment by suppositories in severely ill patients in remote areas might reduce complications and also reduce morbidity and mortality rates. This hypothesis is now being tested in many parts of the world by TDR/WHO. In addition to its potency in the anti blood stage of malaria, it also has activity on the gametocyte. Many studies show gametocyte reduction after treatment with artemisinin and its derivatives. This additional effect may be good for malaria control, as further transmission is inhibited. The implications of this need further investigation to see whether the incidence of malaria could be reduced after massive use of this drug. Further studies are needed.

At our center, we have conducted many clinical trials and they showed that artemisinin and its derivatives prove safe and effective in the treatment of multidrug resistant falciparum malaria. Our studies have been running since 1987 with a single agent and with drugs in combination. Artesunate, artemether and dihydroartemisinin monotherapy with a dose of 500-600 mg given over 5-7 days reveals a cure rate of 80-95%. Their combinations with mefloquine (25 mg/kg) give a cure rate of nearly 100% with the shortest duration of treatment, 2 days. Other combinations, such as artemether combined with benflumetol and given in 6 doses for 3 days give a cure rate of over 95%. Now its combination has been registered in Switzerland under the trade name Co-artemether (Coartem). Recently, an arteether intramuscular preparation has been registered in the Netherlands under the brand name Atecef. An artesunate suppository (200 mg/capsule) has been registered in Thailand and South American countries under the brand name Plasmotrim rectocaps. All these preparations have been undergoing trials with good results and virtually no side effects. Artesunate (tablet and intravenous) has been registered in many countries such as China, Thailand, Myanmar, etc. Other derivatives are being studied. □

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Medicine at Hsu Chew University, 2-3 July 2000.

DETERMINATION OF EARLY DRUG FAILURE IN THE TREATMENT OF ACUTE FALCIPARUM MALARIA

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In general, therapeutic responses depend upon three major factors (parasite, drug and host). The parasites factor included intrinsic resistance and parasite load; the drug factor included doses used, variation in absorption (e.g. halofantrine, malarone will be effected by fatty meal); and the host factor included immunity (e.g. age & pregnancy; children

and pregnant woman are prone to treatment failure), insufficient absorption (e.g. vomiting, diarrhea), alteration in drug metabolism or disposition (genetic polymorphism), other diseases of the host (e.g. liver disorder or heart diseases). However, as clinicians, to predict treatment failure one should also pay attention to other factors such as the sensitivity of

parasites to antimalarial drugs, half-life of the drug, education of patients (which will affect patient compliance), socioeconomic of patients (cost of antimalarial drug), and whether it is a hospital treatment or field treatment. Furthermore, determination of early drug failure in the treatment of acute falciparum malaria could guess using both *in vitro* and *in vivo* responses (*in vitro*: the parasite sensitivity to antimalarial drugs, and *in vivo*: the factors discussed earlier). These could guide clinicians on the determination of early drug

treatment failure. The reduction rate of parasites after treatment is also give for a clue treatment failure in long acting malarial drugs (such as mefloquine, malarone, halofantrine, sulfadoxine/pyrimethamine). These factors could help and alert physicians to watch out for early drug treatment failure. □

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CLINICAL TRIAL AND GOOD CLINICAL PRACTICE

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The aim of clinical trial is to study for an answer of safety and efficacy of the drugs. Therefore, a prospective and control arm is needed. Firstly, a proposal, which defines a purpose of the trial, design, conduction, analysis and conclusion, has to be written. It is a general rule that one must review basic biological data as well as data in animal studies before performing a clinical trial.

In general, clinical trial is divided into 4 phases. Phase I (clinical/pharmacological study in healthy volunteers) is usually non-blind performed in a clinical research center or specialty trained clinical pharmacologist. Its aim is to determine safety and clinical pharmacology with single or repeat dosage in an open study design.

Phase II (trial) is aimed to determine clinical efficacy, safety and side effects of an investigational drug in patients. It is normally done as a single blind design in a limited number of subjects in special research centers.

Phase III (clinical trial in a large group of patients) is aimed to confirm efficacy and occurrence of adverse events. It is normally done as a double blind or comparative design with a standard regimen in a large group of patients. This phase can be performed in special group of patients (eg. pediatric, pregnant, geriatric) and can also be performed as multicenter studies. If the trial succeeds

this phase, the investigational drug is normally granted registration from regulatory authority for using in public patients.

Phase IV (continuing or observation after marketing) is a post marketing surveillance study. It is aimed to find rare adverse events that cannot be detected in phase II or III trials (incident of adverse event < 1:10,000 population). Moreover, it aims to find evidences on drug interaction, compliance and pharmacogenetic when the study drug has been extensively used in public.

To perform a clinical trial, a scientific research proposal is needed. This proposal must include the primary and secondary endpoints of the study, why (problem), how to be done (subjects, inclusion and exclusion criteria), what (variables, ethics, costs) and when (to start, analysis, and publication).

There are many types of protocols and designs (prospective or retrospective studies). They need planning, organizing, executing, evaluating, and finally publishing the results.

The planning of a research project includes the proposal of the study, known problems, design to be used, and the method of choosing subjects. Planning also includes the intervention in the study, the method of defining and measuring variables, data to be collected and analyzed, the possible ethical problems, arrangements to be made, the

starting time, and the costs of the project. Types of investigations include place (field, hospital, laboratory), time (retrospective, concurrent, or experimental) and purposes (epidemiological, evaluative, surveillance).

Study protocol operation must include inclusion and exclusion criteria, study drug allocation (random or open) and discontinuation criteria. In addition, all these data (control, randomization, blind or unblind, sample size) should be specified in the protocol in order to reduce clinical trial errors. Any clinical trial must answer a specific scientific question.

Developing a good protocol is a difficult part of a project or it must be performed according to Good Clinical Practice (GCP). GCP is an international ethical and scientific quality standard for designing, conduction, recording and reporting trials that involve the participation of human subjects. Compliance with this standard provides public assurance that the rights, safety and well-being of trial subjects are protected, consistent with the principles that have their origin in the Declaration of Helsinki, and that the clinical trial data are

creditable.

The objective of GCP must facilitate the mutual acceptance of clinical data by the regulatory authorities. The principles of GCP include: ethic, risk and benefit, rights, safety and well-being of the subjects. Available non-clinical and clinical information on an investigational product, scientifically sound and clearly described in protocol, prior to be approved by institutional review board (IRB). Before a trial starts, it is the responsibility of qualified physicians to explain and clearly inform subjects about the risks/benefits. Study subjects should also be informed consent procedure and free withdrawal from the study at any time, data/records handled accurately for interpretation in a confidential manner. The investigational products manufactured/ handled and stored in accordance with good manufacturing practice (GMP). Unless these points met, GCP cannot be obtained. □

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AVERTING A MALARIA DISASTER

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There is considerable variation in antimalarial drug sensitivity in the southeast Asia region, even over short geographical distances. Thus treatment recommendations must be based on precise, up-to-date local knowledge. In some areas within the region *Plasmodium falciparum*, surprisingly, still retains sensitivity to chloroquine, and in others sulphadoxine-pyrimethamine sensitivity is retained by chloroquine resistant parasites. Both these drugs are inexpensive and relatively well tolerated. They

should be used if there is unequivocal evidence of sensitivity. Unfortunately, in many parts of the region, resistance to both these compounds is prevalent, and quinine, mefloquine, or the artemisinin derivatives are used. In Papua New Guinea, where low grade chloroquine-resistant *P. falciparum* infections exists, amodiaquine has largely replaced chloroquine. □

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AN *IN VIVO* – *IN VITRO* MODEL FOR THE ASSESSMENT OF CLINICALLY RELEVANT ANTIMALARIAL CROSS-RESISTANCE

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Cross-resistance may be considered one of the most important factors leading to decreased drug susceptibility of *Plasmodium falciparum*. The results of this study are highly suggestive of a clinically relevant cross-sensitivity between artemisinin and mefloquine. 76 patients with falciparum malaria were admitted and treated with artemisinin-derivatives. Treatment response parameters were assessed and *in vitro* drug sensitivity tests were performed with artemisinin, mefloquine, quinine and chloroquine. Distinct *in vitro* cross-sensitivity between artemisinin and mefloquine was observed ($\rho = 0.604$; $P < 0.001$).

To assess the relevance of this finding for a clinical cross-resistance, an analytical model was employed, based on the relation of *in vivo* treatment response parameters (fever, parasite and symptom clearance) to a single reference drug with *in vitro* drug sensitivity data of several other drugs. Artemisinin ($R = 0.554$; $P = 0.009$) and mefloquine ($R = 0.615$; $P = 0.002$) *in vitro* drug sensitivities were equally well reflected in the *in vivo* treatment response to artemisinin, thereby confirming the clinical relevance of *in vitro* cross-resistance. □

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HOOKWORM INFECTION IS ASSOCIATED WITH DECREASED BODY TEMPERATURE DURING MILD *PLASMODIUM FALCIPARUM* MALARIA

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Malaria's pyrogenic threshold seems to depend on factors such as age and transmission patterns. We have studied the admission temperature of 200 mild malaria cases and observed after adjusting for body mass index, other helminths and other confounders, that only hookworm infected patients had less fever on

admission that those without hookworm ($37.5 \pm 0.9 / 38 \pm 0.8$ $P < 0.001$). Thus, we suggest the age dependence of the pyrogenic threshold could have been confounded by the epidemiology of iron deficiency. □

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CONTEMPORANEOUS AND SUCCESSIVE MIXED *PLASMODIUM FALCIPARUM* AND *PLASMODIUM VIVAX* INFECTIONS ARE ASSOCIATED WITH *ASCARIS LUMBRICOIDES*: AN IMMUNOMODULATING EFFECT?

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Following an investigation suggesting a protective role for *Ascaris* against cerebral malaria, possibly through immunomodulation, we examined whether *Ascaris* had any impact on mixed *P. falciparum* and *P. vivax* infections. We studied a cross section of 928 patient files between 1991 and 1999. Forty patients had contemporaneous mixed infections and 40 patients had *P. falciparum* infections, followed by *P. vivax* infections. There was a significant association between *Ascaris* infection and risk of having both

contemporaneous or successive mixed *P. falciparum* and *P. vivax* infections (adjusted odds ratios respectively 6 [2-18] $P=0.001$ and 3.6 [1.2-11.1] $P=0.02$). There was a positive linear trend between the burden of *Ascaris* and the risk of mixed infections $P<0.0001$. These results suggested the possibility that pre-existing *Ascaris* infection may increase tolerance of the host to different *Plasmodium* spp., thus facilitating their co-existence. □

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A POINT-PREVALENCE SURVEY OF MOLECULAR MARKERS FOR DRUG-RESISTANT *PLASMODIUM FALCIPARUM* MALARIA IN THAILAND AND LAO PDR

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Chloroquine-resistant *Plasmodium falciparum* is well documented in Thailand. Lao PDR, however, continues to use chloroquine as first-line therapy for the treatment of falciparum malaria. The objective of this study was to determine the prevalence of *cg2*, *pfmdr1* and *pfcr1* allelic types that have previously been associated with chloroquine resistance in these two areas. *P. falciparum* isolates were collected from participants in ongoing treatment studies conducted near the Thai-Cambodian border and in Vang Vieng District of Lao PDR. *Pfmdr1* and *pfcr1* alleles were characterized by PCR-RFLP and mutations in *cg2* were characterized by PCR-SSCP. Of the 50 samples analysed, 32% of Lao isolates (8/25) were found to contain the *pfmdr1* mutation N86Y,

versus only 4% of Thai isolates (1/25; $p = 0.02$). The *cg2* polymorphism previously associated with chloroquine resistance was present in 40% of isolates from Lao PDR (10/25) compared to 96% of Thai isolates (24/25; $p < 0.001$). All samples from both countries (50/50) contained the *pfcr1* K76T mutant allele reported to confer resistance to chloroquine. The differences observed in the prevalence of Tyr86 and *cg2* alleles suggest that there is selective pressure for the maintenance of *pfmdr1* and *cg2* mutations. This drug pressure may be attributable to differences in malaria treatment policies between Thailand and Lao PDR. □

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ARTEMETHER-LUMEFANTRINE FOR THE TREATMENT OF MULTIDRUG-RESISTANT FALCIPARUM MALARIA

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The efficacy and safety of the 6-dose regimen of artemether-lumefantrine were assessed in an open randomized trial in children and adults presenting with acute, uncomplicated *Plasmodium falciparum* malaria in Thailand between November 1997 and March 1998. 200 patients were enrolled in 2 centres: 150 received artemether-lumefantrine (i.e., a median total dose of 9.6 mg/kg [interquartile range 8.7-10.7] and 57.9 mg/kg of lumefantrine [52.4-64.0]) and 50 the standard combination of artesunate (12 mg/kg over 3d) and mefloquine (25 mg/kg). All patients had rapid initial clinical and

parasitological responses. The 28 d cure rates were high: 97.7% (95% confidence interval [95% CI] 93.5-99.5%) for artemether-lumefantrine and 100% (95% CI 92.5-100) for artesunate-mefloquine. The 6-dose regimen of artemether-lumefantrine was better tolerated than, and as effective as, artesunate-mefloquine, the current standard treatment in this area of multidrug-resistant *P. falciparum* malaria. □

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THE CLINICAL USE OF ARTEMISININ DERIVATIVES IN THE TREATMENT OF MALARIA

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The use of artemisinin and its derivatives with other antimalarials seems to be obligatory if a high cure rate is to be obtained. Because of their short half-lives, artemisinin and its derivatives have to be given once or twice daily for 5-7 days. The shorter the duration of drug administration, the higher the rate of recrudescence. A three-day course of these compounds has been associated with about 50% recrudescence. A longer treatment duration, for example of 5-7 days, improves the cure rate to 90-98%, however, patient compliance is poor. The use of antimalarial combinations (i.e. an artemisinin

derivative plus mefloquine, tetracycline or doxycycline), may be used for treatment on an out-patient basis because it reduces the duration of drug administration (i.e. 2-3 days vs. 5-7 days) and increases patient compliance. Many studies have shown that combination of these drugs with other antimalarials having a longer half-life gives more a advantage. Mefloquine combinations (Karbwang *et al.*, 1992a; Looareesuwan *et al.*, 1992b, c, 1993, 1994a,b, 1995, 1996b,d; Luxemburger *et al.*, 1994; Nosten *et al.*, 1994) with either artemisinin rectally, artesunate orally or parenterally or rectally, artemether orally

or parenterally have been studied extensively in uncomplicated and severe malaria. Mefloquine allows a short treatment course due to its long-half life. Combination treatment gives a rapid initial therapeutic response and protects the artemisinin

compounds from resistance since the other antimalarial drug should eliminate residual parasites. □

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PLASMODIUM FALCIPARUM ANTIMALARIAL DRUG SUSCEPTIBILITY ON THE NORTH-WESTERN BORDER OF THAILAND DURING FIVE YEARS OF EXTENSIVE USE OF ARTESUNATE-MEFLOQUINE

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Following a marked decline in the efficacy *in vivo* of mefloquine between 1990 and 1994, a combination of artesunate (4 mg/kg/d for 3 d) and mefloquine (25 mg/kg) has been used as first line treatment of uncomplicated falciparum malaria in camps for displaced persons located along the north-western border of Thailand. Antimalarial drug susceptibility of fresh isolates of *Plasmodium falciparum* from this population was evaluated using a radioisotope microdilution assay between 1995 and 1999. In total, 268 isolates were collected, of which 189 were from primary infections and 79 from recrudescence infections. The geometric mean 50% inhibitory concentration (IC₅₀) values from

primary infections were: dihydroartemisinin 1.2 ng/mL, artesunate 1.6 ng/mL, artemether 4.8 ng/mL, atovaquone 0.4 ng/mL, lumefantrine 32 ng/mL, chloroquine 149 ng/mL, quinine 354 ng/mL, mefloquine 27 ng/mL and halofantrine 4.1 ng/mL. A significant improvement in mefloquine sensitivity ($P < 0.001$), and halofantrine ($r = 0.51$, $P < 0.001$). This supports observations *in vivo* that the combination of artesunate and mefloquine has reversed the previous decline in mefloquine sensitivity. □

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A COMPARATIVE CLINICAL TRIAL OF A COMBINATION OF ARTESUNATE AND MEFLOROQUINE VERSUS A COMBINATION OF QUININE AND TETRACYCLINE FOR THE TREATMENT OF ACUTE UNCOMPLICATED FALCIPARUM MALARIA IN SOMDEJPRACHAOTAKSINMAHARAJ HOSPITAL, TAK PROVINCE

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A combination of quinine and tetracycline is a standard regimen for the treatment of acute uncomplicated falciparum malaria. Frequent administration due to its short half-life (6-8 hours), long duration of drug administration (7 days), and side effects of quinine (cinchonism e.g., tinnitus, nausea, vomiting, palpitation, etc) may cause the patient not to complete the whole course of treatment and recrudescence ensues. A previous study of artesunate followed by mefloquine given once daily for 3 days gave a greater than 95% cure rate. The objective of this study is to determine the efficacy and tolerability of a combination of artesunate and mefloquine (ASM group) compared with a combination of quinine and tetracycline (QT group) in 120 uncomplicated falciparum malaria cases. In the ASM group, 60 patients received 200 mg artesunate and 312.5 mg mefloquine 12-hourly for 2 days (a total of 800 mg artesunate and 1,250 mg mefloquine). Another 60 cases received 600 mg quinine sulfate 8-hourly and 250 mg tetracycline

6-hourly for 7 days. Both groups were admitted to the Somdejprachaotaksinmaharaj Hospital, Tak Province until either parasite negative or until there were no clinical signs or symptoms of malaria. 108 cases complete the 28-day follow-up. The results showed a similar 28-day cure rate (96.2% in the ASM group vs 94.6% in the PT group), however side effects such as tinnitus (25.8% vs 83.3%), vomiting (51.6% vs 80.6%), and palpitation (32.3% vs 80.6%) were less common in the ASM group. In addition, parasite clearance time (PCT) and the time taken to produce clinical improvement were significantly shorter in the ASM group ($p < 0.05$). In conclusion, a combination of artesunate and mefloquine may be an alternative regimen for treatment of uncomplicated falciparum malaria especially for outpatients in remote areas. In addition, this will shorten the duration of patients' hospital stay. □

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FREQUENCY OF EARLY RISING PARASITEMIA IN FALCIPARUM MALARIA TREATED WITH ARTEMISININ DERIVATIVES

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To define the frequency of the early rising of parasitemia in falciparum malaria patients treated with artemisinin derivatives, a retrospective chart review of 497 patients admitted to the Hospital for Tropical Diseases, Bangkok in 1996 was carried out. Early rising parasitemia, which was defined as an increase in the parasite count over the baseline pretreatment level during the first 24 hours of treatment, was found in 59/229 episodes (25.8%) of uncomplicated, and 111/268 episodes (41.3%) of complicated, falciparum malaria. All uncomplicated

cases were successfully treated without developing any complications. There were 2 deaths and 13 changes of drug regimen in the complicated group. Only one of these unfavorable responses was due to parasite response. Early rising parasitemia was very common in falciparum malaria treated with artemisinin derivatives, despite their ability to clear the parasitemia, and did not indicate failure of the drug used. □

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PROGNOSTIC SIGNIFICANCE OF SKIN AND SUBCUTANEOUS FAT SEQUESTRATION OF PARASITES IN SEVERE FALCIPARUM MALARIA

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Intradermal blood smear, histopathologic and immunohistologic studies were performed in severe malaria (n=10) and uncomplicated malaria (n=10) patients during positive parasitemia and within 6 hours after negative parasitemia by finger prick smears. Intradermal blood smears showed asexual forms and intraleukocytic pigments when finger prick blood smears showed negative results; however intradermal blood smear did not indicate disease severity within 6 hours after negative parasitemia by finger prick. Histopathologic findings showed 15 fold higher parasitized red blood cells sequestered in vessels of subcutaneous fatty tissue in severe malaria than in uncomplicated

malaria ($p < 0.001$) and may indicate disease severity. A panel of polyclonal antibodies against cytokines applied to skin biopsies clearly detected a higher titer against tumor necrosis factor-alpha (TNF) and interleukin-10 (IL-10) in dermal vessels and stratum granulosum respectively, in severe malaria compared with uncomplicated malaria. Results of the study suggest that histopathology and immunohistology of skin and subcutaneous fatty tissue may indicate prognostic severity of malaria and may be associated with focal accumulation of cytokines. □

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MANAGEMENT OF MALARIA WITH ACUTE RENAL FAILURE

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In parts of the world, such as Africa, where *Plasmodium falciparum* is endemic and its transmission stable, severe malaria affects mainly children. Cerebral malaria and severe anaemia are common but multi-organ failure involving the kidneys or liver is very rare. Surviving children develop immunity and thus adults rarely develop severe disease. In contrast, in other tropical countries where transmission of *P. falciparum* is unstable and the risk of infection low, severe malaria can occur at any age. Severe malaria is defined as parasitaemia greater than 5% or vital organ dysfunction. Acute renal failure (ARF) is a common complication of severe falciparum malaria in non-

immune individuals.

At the Bangkok Hospital for Tropical Disease, 5,210 patients with falciparum malaria were admitted during the period 1991-1997 of whom 112 patients (2.12%) had ARF. In a recent study of 560 cases of severe adult malaria in Vietnam, 28% of patients had renal failure on admission and 41% at some stage, with 14% overall requiring dialysis. Overall, however, ARF is not a common complication of malaria. During the Vietnam war, the reported incidence was 19 cases in 3,300 malaria admissions in 1965/6 and 8 of 2003 admission in 1966/7. □

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AN *IN VIVO* - *IN VITRO* MODEL FOR THE ASSESSMENT OF CLINICALLY RELEVANT ANTIMALARIAL CROSS-RESISTANCE

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Cross-resistance may be considered one of the most important factors leading to decreased drug susceptibility of *Plasmodium falciparum*. The results of this study are highly suggestive of a clinically relevant cross-sensitivity between artemisinin and mefloquine. 76 patients with falciparum malaria were admitted and treated with artemisinin-derivatives. Treatment response parameters were assessed and *in vitro* drug sensitivity tests were performed with artemisinin, mefloquine, quinine and chloroquine. Distinct *in vitro* cross-sensitivity between artemisinin and mefloquine was observed ($\rho = 0.604$; $P < 0.001$).

To assess the relevance of this finding for a clinical cross-resistance, an analytical model was employed, based on the relation of *in vivo* treatment response parameters (fever, parasite and symptom clearance) to a single reference drug with *in vitro* drug sensitivity data of several other drugs. Artemisinin ($R = 0.554$; $P = 0.009$) and mefloquine ($R = 0.615$; $P = 0.002$) *in vitro* drug sensitivities were equally well reflected in the *in vivo* treatment response to artemisinin, thereby confirming the clinical relevance of *in vitro* cross-resistance. □

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HELMINTH INFECTIONS ARE ASSOCIATED WITH INCREASED GAMETOCYTE CARRIAGE DURING MILD *FALCIPARUM* MALARIA IN THAILAND.

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The objective of the study was to determine whether preexisting helminth infections could affect sexual forms of *Plasmodium falciparum*. A cross-sectional case record study, compared 120 mild *Plasmodium falciparum* malaria cases with patent gametocyte carriage and 187 without gametocytes for helminth exposure. Relevant crude odds ratios and potential confounders were included in a logistic regression model.

Helminth infections were associated with the presence of gametocytes with a crude odds ratio of 1.9 [1.1-3.3] ($P = 0.01$). A positive linear trend was observed between the odds of having patent

gametocytemia and the number of different helminth species ($P = 0.003$). However, when adjusting for hemoglobin concentration the significance of the association between helminths and gametocytes disappeared ($P = 0.15$). Pre-existing helminth infections may increase the severity of malarial anemia and therefore increase the likelihood of carrying gametocytes. At a population level, helminth infections may thus have a significant influence on malaria transmission. □

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CONTEMPORANEOUS AND SUCCESSIVE MIXED *PLASMODIUM FALCIPARUM* AND *PLASMODIUM VIVAX* INFECTIONS ARE ASSOCIATED WITH *ASCARIS LUMBRICOIDES*: AN IMMUNOMODULATING EFFECT?

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Following an investigation suggesting a protective role for *Ascaris* against cerebral malaria, possibly through immunomodulation, we examined whether *Ascaris* had any impact on mixed *P. falciparum* and *P. vivax* infections. We studied a cross section of 928 patient files between 1991 and 1999. Forty patients had contemporaneous mixed infections and 40 patients had *P. falciparum* infections, followed by *P. vivax* infections. There was a significant association between *Ascaris* infection and risk of having both contemporaneous

or successive mixed *P. falciparum* and *P. vivax* infections (adjusted odds ratios respectively 6 [2-18] $P = 0.001$ and 3.6 [1.2-11.1] $P = 0.02$). There was a positive linear trend between the burden of *Ascaris* and the risk of mixed infections $P < 0.0001$. These results suggested the possibility that pre-existing *Ascaris* infection may increase tolerance of the host to different *Plasmodium* spp., thus facilitating their co-existence. □

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A PROSPECTIVE STUDY OF AIDS ASSOCIATED CRYPTOCOCCAL MENINGITIS IN THAILAND TREATED WITH HIGH DOSE AMPHOTERICIN B

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A prospectively study Thai adults (N=106) with cryptococcal meningitis associated with the Acquired Immune Deficiency Syndrome was conducted to determine the prognostic factors affecting survival after high dose Amphotericin B (0.7 mg/kg/day) followed by oral azole treatment. Presenting symptoms were headache (91%), vomiting (62%) and fever (62%), marked weight loss was reported in (37%), anorexia (36%), diarrhea (20%) and cough (18%). 7% had a Glasgow Coma Score <13. The geometric mean (range) total and viable cryptococcal counts in the cerebrospinal fluid on admission were 430,000 (1,000 to 3.4x10⁷) and 31,000 (10 to 1.4x10⁷) per mL respectively. Both total and viable cryptococcal counts declined monoexponentially with an elimination half life of

4 days. The cumulative CSF yeast clearance rates were 38% and 56% at two and four weeks respectively. Cumulative mortalities at 2 weeks, 4 weeks and one year were 16%, 24% and 76% respectively. Early death was associated significantly with previous history of weight loss (relative risk (RR) = 2.2 ; 95% CI, 1.2 to 3.9), Glasgow Coma Score <13 (RR=2.33; 95% CI, 1.55 to 3.50), and hypoalbuminaemia (P<0.001). Later mortality was associated with visual impairment (RR=4.8; 95% CI, 1.4 to 15.9), delayed CSF yeast clearance (RR=3.6; 95% CI, 1.9 to 6.4) and relapse (RR=3.9; 95% CI, 1.4 to 10.8). In the absence of effective antiretroviral treatment cryptococcal meningitis in Thai patients with AIDS is associated with a high mortality despite high dose antifungal treatment. □

APPLICATION OF YEAST ENOLASE AS ANTIGEN FOR IMMUNODIAGNOSIS OF MALARIA

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In 1998, we reported that *Plasmodium falciparum* (*P.f.*) enolase was useful as the capture antigen for the immunodiagnosis of malaria. In the present study, we modified a fluorescence-ELISA for the diagnosis of malaria by applying yeast enolase or rabbit muscle enolase as antigen. Sera from 67 *falciparum* malaria patients and 15 *vivax* malaria

patients were tested by the method. Positivity rates of the former was 82.1% against yeast enolase antigen and 90.5% against rabbit muscle enolase antigen, and those of latter was 93.3% against both enolase antigens. Mean antibody titers (RFU values) of sera from *falciparum* and *vivax* malaria patients were significantly higher than that from healthy

individuals. There was a significant correlation between anti-yeast and anti-rabbit muscle enolase antibody titers (RFU values) in the group of falciparum subjects ($r=0.401$, $P<0.001$). A significant correlation between RFU values against yeast enolase antigen and indirect fluorescent antibody titers against crude *P.f.* antigen in the same subjects was recognized ($r=0.518$, $P<0.001$). Longitudinal changes of RFU values against yeast enolase for the following 4 weeks after admission were also examined for sera from falciparum malaria

patients. Patients with severe malaria showed increasing RFU values as the clinical course progressed. However, in the mild cases, each RFU value stayed unchanged during the course. We concluded that yeast and rabbit muscle enolase could be appropriately used as antigen for the immunodiagnosis of malaria. □

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THE MALARIA CAULDRON OF SOUTHEAST ASIA: CONFLICTING STRATEGIES OF CONTIGUOUS NATION STATES

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The past half-century or so has witnessed dramatic failures but also some successes in control of malaria in the world at large. South and Southeast Asia have had their share of both outcomes, a scenario that reflects many variables in control programs: technology, management strategy, human and financial resources. However, at least equally culpable have been major wars and minor conflicts, economic growth and stagnation, inequity of opportunity, urbanization, deforestation, changing transport and communications. The history of malaria is thus an integral part of the broader political and economic evolution of the region, as well as the story of the wisdom and unwisdom of malaria specialists. In positive reflection on the latter, systematic organizational effort using standard tools of trade has seen the gradual elimination of major malaria foci from central plain regions of a number of nations in this large region, with residual foci at forested border areas. In many cases there is good evidence of sustainability of elimination in defined areas but the differing success stories reflect in part conflicting strategies in neighboring nation states. On

the other hand, physical conflicts, population migration, inequitable economic change, border instability and many other socio-economic variables can be clearly seen to undermine the most ingenious strategies. Undoubtedly the single most important negative ingredient is the rise and spread of multi-drug resistant falciparum malaria that has its epicenter in Southeast Asia, from which it threatens the world in insidious fashion. Containment of this phenomenon has been the focus of attention for 30 years, more particularly the past decade, and represents the greatest challenge at this time in predicting the continuing impact of malaria globally on human history. So too does the compelling necessity to link malaria control with macro and micro economic planning. This challenge impinges on the sovereignty of individual nations in this region, for they exist in contiguity, so that successful applications of technology require collaborative political determination. □

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Somchit Pubampen



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CURRENT RESEARCH ACTIVITIES

1. Comparative studies on surface ultrastructure of adult worm of *Paragonimus* spp. in Thailand.
2. Soil-transmitted helminthiasis among fishermen, farmers, gardeners and urban communities in southern Thailand.
3. Reinfection of soil-transmitted helminthiasis in village with one hundred percent latrine.
4. Control of soil-transmitted helminths in primary school in southern Thailand.
5. Efficacy of high dose mebendazole against trichuriasis in adult patients.
6. Hookworm species in school children in Nakhon Si Thammarat province, southern Thailand.
7. Zoonotic potential of dog's intestinal helminths transmitting to man.
8. Effect of mebendazole on *Trichuris trichiura* morphology.
9. Current status of *Gnathostoma* infection in swamp eels in Nakhon Nayok and Prachin Buri.
10. *Gnathostoma* infection in fishes caught for local consumption and sale in Nakhon Nayok province.
11. Seasonal variation of *Gnathostoma* infection in swamp eels in Nakhon Nayok province.
13. Effect of ivermectin on *Gnathostoma spinigerum* morphology.
14. Detection of immune response of *Gnathostoma spinigerum* by IFAT.
15. A five-year retrospective evaluation of gnathostomiasis and diagnostic specificity by immunoblot.
16. Experimental infection of freshwater fish in Thailand with infective stage of *Angiostrongylus*.
17. Angiostrongyliasis: potential fractionated antigens of *Angiostrongylus cantonensis* adult worms for diagnosis using ELISA.
18. Angiostrongyliasis: partially purified antigens of *Angiostrongylus cantonensis* adult worms for diagnosis using immunoblot.
19. *Angiostrongylus cantonensis*: S-adenosyl methionine decarboxylase.
20. Fish-borne trematodes in Thailand.
21. Studies on the efficacy of Thai traditional herbal medicines in the treatment of opisthorchiasis in hamsters.
22. Diagnosis of human opisthorchiasis with cocktail and eluted *Bithynia siamensis goniomphalos* snail antigen by ELISA.
23. Monoclonal antibody-based competitive ELISA and indirect ELISA for immunodiagnosis of trichinosis.
24. *Trichinella* spp. in Thailand: differentiation of isolates by biological and molecular biological methods.
25. The effect of *Trichinella* infection on renal function.
26. *Toxocara canis* larval antigens for serodiagnosis of human toxocariasis.
27. Comparison of biochemical extract preparations of *Cysticercus cellulosae* by SDS-PAGE and immunoblot technique.
28. Differentiation of fractionated larval antigens (*Cysticercus cellulosae*) responsible to antibody of neurocysticercosis patients.
29. Analysis of fluid antigens of *Echinococcus* cyst for diagnosis.
30. Strongyloidiasis: crude, molecular weight cut-off and eluted antigens of third-stage larvae for immunodiagnosis.

Abstracts

NEUROCYSTICERCOSIS: UTILIZING THE CYSTIC FLUID ANTIGEN FROM *TAENIA SOLIUM* METACESTODES FOR DIAGNOSIS BY IGG -ELISA

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Cystic fluid, which has antigenic properties of whole *Taenia solium* cysticerci, was used to discriminate neurocysticercosis cases and other parasitic infections, especially helminthiasis. Twenty-one neurocysticercosis and several kinds of 22 different parasitic infections, including HIV cases (n=234) evaluated a 90.48% sensitivity and 86.32% specificity of indirect ELISA as follows; a low antigen concentration of 5 µg/ml, serum dilution of 1:400, conjugate dilution of 1:2,000 and a cut-off value of 0.349. Eight different helminthic infections (n=25); echinococcosis (8/10), gnathostomiasis (6/8), strongyloidiasis (5/14), hookworm infection (1/18), angiostrongyliasis (2/25), opisthorchiasis (1/18), onchocercosis (1/3)

and toxocariasis (1/6) were cross-reactive with this antigen. No serum antibody from other brain infections in the study gave a reaction with the antigen. In this study, the cystic fluid antigen gave high sensitivity of the test. However, the antigen contains various antigenic molecules able to bind with antibodies from several of the above helminthic sera, especially echinococcosis and gnathostomiasis. In Thailand, gnathostomiasis is one of the more famous tropical diseases but echinococcosis is quite rare. Cystic fluid antigen should be further investigated for its specific finding in diagnosis. □

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CHROMOSOME AND C-BANDING OF *OPISTHORCHIS VIVERRINI*

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Chromosome of *Opisthorchis viverrini* was observed by air-drying and C-banding techniques. The result revealed that the chromosome number was 2n=12 and n=6 consisting of one large-sized metacentric, one medium-sized metacentric, one small-sized metacentric, one small-sized submetacentric or subtelecentric, one small-sized subtolocentric or acrocentric and one small-sized acrocentric. The

relative lengths of the chromosomes were 32.02±2.52, 23.28±1.98, 15.24±3.40, 13.39±3.11, 10.18±1.56 and 5.82±0.59% respectively. After C-banding treatment, two of the small-sized chromosomes showed a remarkable constitutive heterochromatin. □

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COMPARATIVE STUDIES ON GENERAL PROTEINS, ISOENZYME AND DNA RESTRICTION ENDONUCLEASE PROFILES OF THAI *PARAGONIMUS METACERCARIAE*

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General proteins and 14 enzymes from metacercariae of *Paragonimus heterotremus*, *P. siamensis* and *P. westermani* were determined by vertical polyacrylamide gel electrophoresis. The isoenzyme profiles were considerable interspecific polymorphism for general protein (PT), malate dehydrogenase (MDH), malic enzyme (ME) and tetrazolium oxidase (TO) while those of glucose phosphate isomerase (GPI) and phosphoglucosmutase (PGM) showed similarity. The *Pt-6* and *To-I* loci can be used as identification markers for these three species. The preliminary study of molecular biology of *Paragonimus heterotremus*, *P. siamensis* and *P. westermani* was based on restriction endonuclease analysis of

metacercarial genomic DNA with restriction endonuclease, *Pst*I. Agarose gel electrophoresis revealed restriction fragment length differences among the three species studied. The DNA restriction fragments were approximately 4-6 fragments, ranging from 5.35 to 14.67 kb. Among these, *P. westermani* shared two homologous fragments with *P. siamensis*, i.e., 5.35 and 7.22 kb, none with *P. heterotremus* while *P. heterotremus* shared only one of that with *P. siamensis*, i.e., 8.16 kb. Thus, the DNA restriction fragment length differences can be used to differentiate one from another among these three species. □

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THE KARYOTYPE OF LUNG FLUKE, *PARAGONIMUS SIAMENSIS*

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The karyotype of chromosomes obtained from the germ cells of *Paragonimus siamensis* was analyzed by air-drying technique. The result revealed the diploid number of chromosome to be $2n=22$. The entire chromosomes consisted of one large-sized metacentric, four medium-sized subtelocentric, three small-sized metacentric or submetacentric and three small-sized

submetacentric or subtelecentric. The relative lengths of the chromosomes were 20.13 ± 1.21 , 13.16 ± 0.42 , 11.07 ± 0.48 , 10.37 ± 0.84 , 9.29 ± 0.52 , 6.50 ± 0.39 , 6.42 ± 0.34 , 6.27 ± 0.28 , 6.04 ± 0.58 , 5.65 ± 0.39 and 5.03 ± 0.40 % respectively. □

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HOOKWORM SPECIES IN SCHOOLCHILDREN IN NAKHON SI THAMMARAT PROVINCE, SOUTHERN THAILAND

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Ninty-nine point nine percent of 2,940 hookworms recovered from schoolchildren in Nakhon Si Thammarat Province, in the South of Thailand were *Necator americanus*. Only 3 worms (0.1%) were identified as *Ancylostoma duodenale*, and all were female worms. No *A. ceylanicum* was found in the present study.

As regards worm expulsion from the schoolchildren, there were 17 cases of light intensity hookworm infection. Fifteen cases (88.2%) expelled worms in the range corresponding with

the worm burden estimated from the number of eggs per gram of feces. Two cases (11.8%) expelled worms numbering above the estimate. In 16 moderate intensity cases, 5 cases (31.3%) expelled worms corresponding with the estimated worm burden. Eleven cases (68.7%) expelled worms lower than the number estimated. All cases of heavy intensity expelled worms below the estimate. □

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COMPARISON OF IVERMECTIN AND ALBENDAZOLE TREATMENT FOR GNATHOSTOMIASIS

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Comparative treatment of ivermectin in 21 patients (Group 1) and albendazole in 49 patients (Group 2) of gnathostomiasis gave the cure at 95.2% and 93.8% respectively. The ELISA OD and eosinophil counts were reduced after treatment. Side effects in ivermectin were hypotension, dizziness, weakness and diuresis; and

side effects of albendazole were nausea, dizziness and increased alkaline phosphatase in two cases. Ivermectin should be an effective drug against gnathostomiasis and more convenient in treatment single dose. □

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STRONGYLOIDES STERCORALIS INFECTION AND CHRONOLOGICAL CHANGES OF OTHER SOIL-TRANSMITTED HELMINTHIASIS IN THE ENDEMIC AREA OF SOUTHERN THAILAND.

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A field survey was conducted in 4 primary schools in Nakhon Si Thammarat Province, southern Thailand. By Sasa modified Harada-Mori cultivation method, 1.8% of the schoolchildren were found to be infected with *Strongyloides stercoralis*, and 25.1% with hookworm infection. By Kato's thick smear method, the overall prevalence of soil-transmitted helminths was 46.8%, being *Trichuris trichiura* 28.5% hookworm 18.0% and *Ascaris lumbricoides* 5.7%. Fecal examination, performed by Kato's thick smear and culture method, indicated that the prevalence of hookworm infection was 26.9%. The prevalence in the present study was very much lower than many previous reports in the past decade. This may indicate the partial success of the parasite

control project in Thailand by mass treatment, improving the sanitation and personal hygiene of the people in the endemic area.

In light infection with *Trichuris*, albendazole administered at a dosage of 200 mg daily for 3 days showed a 48.7% cure rate. When mebendazole was given at 100 mg twice daily for 3 days, its effectiveness was 88.5%. A lower cure rate was obtained (70.0%) in moderate to heavy infection. □

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THE EFFECTS OF TRICHINELLA SPIRALIS INFECTION ON RENAL FUNCTIONS IN RATS

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Trichinella spiralis infection was induced in rat by oral feeding of infective larvae. Four weeks later, renal function including renal plasma flow (RPF), glomerular filtration rate (GFR), excretion rate of protein, sodium and potassium were determined using clearance technics. There were no significant changes in these parameters.

However, plasma urea nitrogen was significantly higher in the infected group, suggesting that either an impaired regulation of renal tubular urea transport or an increased skeletal muscle breakdown is likely. □

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SOIL-TRANSMITTED HELMINTHIASES AMONG FISHERMEN, FARMERS, GARDENERS AND TOWNSPEOPLE IN SOUTHERN THAILAND

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Soil-transmitted helminths are abundant in the southern part of Thailand due to the suitable climate for egg development, and the eating habits and unsanitary conditions of the inhabitants. The occupations of the villagers in the particular community may play an important role in the prevalence rate of these helminthic infections. This study aimed to study the prevalence rate of STH in primary school children living in the community of fishermen, farmers, gardeners and those who live in the town (townspeople). Examination of 1930 fecal samples of school children (in fishermen 593, farmers 554, gardeners 326 and townspeople

457) by Kato-Katz's modified thick smear technique showed that in the group of fishermen 72.8% had STH infection, while in farmers and gardeners the infection rates were lower, being 33.8% and 31.9%, respectively. Townspeople comprised only 11.5% of STH cases. More moderately and heavily infected cases were also found among the group of fishermen, and more than 50% of the fishermen had 2-3 kinds of STH in their bodies. There was no difference in the prevalence rate between males and females. □

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SHARED ANTIGENS BETWEEN *PARASTRONGYLUS CANTONENSIS* AND *BIOMPHALARIA GLABRATA* AND THEIR POSSIBLE USE IN IMMUNODIAGNOSIS OF HUMAN PARASTRONGYLIASIS

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We have previously demonstrated by immunoblot analysis the presence of at least 12 common antigenic components between *Parastrongylus cantonensis* and *Biomphalaria glabrata* an intermediate snail host of *Parastrongylus*, using a serum from rabbit immunized with the antigens of *P. cantonensis* adult worms. In the present study, it was further demonstrated by immunoblotting that many of the shared components found in *B. glabrata* antigens were also recognized by sera from patients with parasitologically confirmed parastrongyliasis. The more distinct shared immunogenic bands were those of 190, 110, 70, 60, 48, 39.5, 24, 22 and 19.5 kDa. Most of these antigenic bands were, however, considered non-specific since they also appeared with sera from patients with gnathostomiasis,

toxocariasis, filariasis, ascariasis and strongyloidiasis. Only two antigenic components of *B. glabrata* antigens with molecular weight of 48 and 24 kDa appeared to give consistent reactions with sera from all the parastrongyliasis patients but not with other parasitic infections. These *B. glabrata*/*P. cantonensis*-specific shared antigens may have the potential for the immunodiagnosis of *P. cantonensis* in humans. Unlike the specific 31-kDa antigen of *P. cantonensis*, the immunogenic component with molecular weight of 31 kDa in *B. glabrata* snail did not appear to be *P. cantonensis* specific and thus cannot be used as an alternative antigen for specific immunodiagnosis of human parastrongyliasis. □

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A MOLECULAR PERSPECTIVE ON THE GENERA *PARAGONIMUS* BRAUN, *EUPARAGONIMUS* CHEN AND *PAGUMOGONIMUS* CHEN

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The status of the genera *Euparagonimus* Chen, 1963 and *Pagumogonimus* Chen, 1963 relative to *Paragonimus* Braun, 1899 was investigated using DNA sequences from the mitochondrial cytochrome c oxidase subunit I (CO1) gene (partial) and the nuclear ribosomal DNA second internal transcribed spacer (ITS2). In the phylogenetic trees constructed, the genus *Pagumogonimus* is clearly not monophyletic and therefore not a natural taxon. Indeed, the type species of *Pagumogonimus*, *P. skrjabini* from China, is very closely related to *Paragonimus*

miyazakii from Japan. The status of *Euparagonimus* is less obvious. *Euparagonimus cenocopiosus* lies distant from other lungflukes included in the analysis. It can be placed as sister to *Paragonimus* in some analyses and falls within the genus in others. A recently published morphological study placed *E. cenocopiosus* within the genus *Paragonimus* and probably this is where it should remain. □

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COMPARATIVE MORPHOMETRY, MORPHOLOGY OF EGG AND ADULT SURFACE TOPOGRAPHY UNDER LIGHT AND SCANNING ELECTRON MICROSCOPIES, AND METAPHASE KARYOTYPE AMONG THREE SIZE-RACES OF *FASCIOLA GIGANTICA* IN THAILAND

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Comparative morphometry of eggs and adults under light microscope, and morphology of adults under scanning electron microscope (SEM) were undertaken in the three size-races (<25 mm, 25-35 mm, > 35 mm) of *Fasciola gigantica* (Thailand strain). Morphometric examination revealed intraspecific variation with respects to the dimensions of eggs and adults, whereas surface topography of the three size-race adults under SEM was morphologically similar. The observations

on mitotic metaphase chromosomes of spermatogonial cells from testes of the three size-races revealed $2n=20$ (diploid type), and no karyotypic difference was observed among them. The meiotic metaphase chromosome was 10 bivalents in primary spermatocyte in diplotene to diakinesis, and many mature spermatozoa were seen in the testicular preparations. □

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A SURVEY OF INFECTIVE LARVAE OF *GNATHOSTOMA* IN EELS SOLD IN HO CHI MINH CITY

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To investigate the distribution of *Gnathostoma* spp. in Ho Chi Minh City (HCM city), 1,081 eels were purchased from a local market twice a month from March 1998 to February 1999. Infective larvae of *Gnathostoma* spp. detected from the flesh and liver of eels by the press preparation technique were examined and identified. Three hundred and fifty advanced third-stage larvae were recovered from liver, none from the flesh. The average rate of infection was 0.11; a high rate of infection was found from August to November and a low rate of infection from February to May. The average number of larvae/eel was 2.9; the greatest number

of larvae/eel was in January whereas the lowest was in March and April. There was a marked decrease in both prevalence and intensity of infection from February to May, followed by a rise from June. The finding suggests that in HCM city, the infection rate abruptly decreases soon after the end of the rainy season and starts to rise when the rain comes and reaches its peak at the end of the rainy season. All recovered larvae were identified as *G. spinigerum*. □

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ZOONOTIC POTENTIAL OF DOGS' INTESTINAL HELMINTHS TRANSMITTING TO MAN

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One hundred and ninety-three stray dogs from the Rabies Control Subdivision, Veterinary Public Health Division, Bangkok Metropolitan Administration were investigated for gastrointestinal helminths. Ninety-five percent of dogs harbored one or more helminths. The most prominent infection was hookworm with a 92.2% infection rate. *Ancylostoma braziliense* male was first reported in Thailand with a 2.6% prevalence; the other common species of hookworm found were *A. caninum* and *A. ceylanicum* with 84.5% and 72.5%. *Toxocara canis* had a high prevalence

(42.0%) and a high intensity in young dogs. *Dipylidium caninum* was found moderately in young dogs (26.8%) and to be relatively high (50.0%) in mature dogs, but vice versa in intensity. All helminths reported may be infectious to humans either by invading intestinal tract or other tissues. Children are the population at greatest risk since they are in closer contact with young dogs. □

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CURRENT RESEARCH ACTIVITIES

The Department of Medical Entomology conducts research involving 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, fleas, ticks and mites are also studied in various aspects.

Laboratory colonies of different strains of mosquito vector species, *Anopheles*, *Aedes*, *Culex*, and *Mansonia* are continuously maintained in the insectarium for further use. The filarial parasite, *Brugia pahangi*, is also maintained in the reservoir host.

Studies on the biology and ecology of mosquito vectors of malaria at Amphoe Suan Phung, 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 these studies 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 tested both in laboratory and field trials. The efficacy of chemical insecticides, microbial insecticide, insect growth regulator and chemosterilant is evaluated against the vectors. Studies on the development of insect resistance to these chemicals are also conducted. Non-pollutant control methods such as the use of medicinal plants are tested. The use of insecticide impregnated bed nets and blankets (permethrin, etofenprox), especially for malaria control, has been introduced. Mosquito resistance to permethrin- and etofenprox-impregnated bed nets is being evaluated in the laboratory to study the impact on mosquito vectors.

Surveys of commensal rat distribution and their infestation with fleas are conducted in the Bangkok Metropolitan area. The data collected are basic information on surveillance of rats, fleas and plague.

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 provides academic consultation, especially on mosquito-borne diseases and their control measures, and also provide services on detection of filarial parasites, identification of mosquitoes and other medically important insects and arthropods.

Abstracts

AUTOGENOUS *Aedes togoi* SUB-COLONIES (CHANTHABURI, THAILAND STRAIN), AN EFFICIENT LABORATORY VECTOR IN STUDY OF FILARIASIS

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Comparative filarial susceptibility and biology between stock colony and selectively autogenous *Aedes togoi* sub-colony were carried out to determine the laboratorial vector capacity and viability of autogenous sub-colony. The results of susceptibility revealed that the selectively autogenous *Ae. togoi* sub-colony yielded higher susceptibility than the stock colony, i.e. *Dirofilaria immitis*: susceptibility rates = 80.00% [Exp1 (F₈)] and 76.19% [Exp2 (F₁₇)] (autogenous sub-colony), 53.33% (Exp1) and 71.43% (Exp2) (stock colony); *Brugia malayi*: susceptibility rates = 83.33% [Exp1 (F₁₇)] and 84.38% [Exp2 (F₁₉)] (autogenous sub-colony), 81.25% (Exp1) and 75.00% (Exp2) (stock colony), but not at the level of statistically significant differences except the Exp1 of *D. immitis*, which showed a significant difference. In addition, the average No. L3 per infected mosquito in the selective autogenous sub-colony (*D. immitis*: Exp1 = 3.37, Exp2 = 3.19; *B. malayi*: Exp1 = 8.80, Exp2 = 3.37) was also higher than in the stock

colony (*D. immitis*: Exp1 = 2.44, Exp2 = 2.73; *B. malayi*: Exp1 = 7.85, Exp2 = 3.02), but not at the level of a statistically significant difference. The results of comparing some biological aspects demonstrated that most of the cases have similar biology, except the average egg deposition per gravid female of stock colony (130.17±43.33) was significantly more than the selectively autogenous sub-colony (F₉) (94.33±13.69), egg length x width 575.62±18.06 mm x 186.15±9.35 mm of stock colony was significantly larger than selectively autogenous sub-colony (F₉) (560.49±18.96) μ m x 177.99±8.40 mm, and mean longevity of adult females of the stock colony [41.60(6-61)] was significantly longer than the selectively autogenous sub-colony (F₉) [(35.00(5-39))]. A selectively autogenous sub-colony was established and 22 successive generations have been colonized. □

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DEVELOPMENT OF COMPREHENSIVE RAPID TESTS FOR THE SCREENING OF CHEMICAL INSECTICIDE RESISTANCE IN MEDICALLY IMPORTANT INSECTS

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Kits for the detection of resistance mechanism due to mixed function oxidases and acetylcholinesterases were developed. The shelf life of substrates was a major factor for kit development. Therefore, the substrates were kept under 2 conditions: at room temperature and 4°C. The freshly prepared solution was used as the reference standard. The substrates were 3,3',5,5' tetramethylbenzidine (TMBZ) for the mixed function oxidases test kit (MFO test kit) and acetylthiocholine iodine (ACTH) for the acetylcholinesterases test kit (AChE test kit). The substrates from those conditions were used to detect insecticide resistance in *Culex quinquefasciatus* by enzyme microassay and detection by ELISA reader.

As a result, the MFO test kit, which contained either solid or liquid TMBZ, was stable for 5 weeks at 4°C but only 3 days at room temperature. For the AChE test kit, the solid ACTH was stable for 4 weeks at 4°C, while the liquid ACTH was stable 3 days either at room temperature or at 4°C. Comparison of effectiveness between the test kit and the standard method of enzyme microassay showed no differences.

There was a direct correlation between the intensity of colour due to enzyme and resistance to insecticide. The eye-score method can be adapted for use in the field for the rapid detection of resistance status due to mixed function oxidases and acetylcholinesterases. □

STUDY ON DISTRIBUTION OF FLEAS AND FLEA INDEX IN COMMENSAL RATS IN BANGKOK METROPOLITAN AREA

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The occurrence of plague in India in 1994 was a warning sign of the possible reemergence of this disease in Thailand. Surveillance of plague is of interest, especially in the Bangkok Metropolitan area where commensal rats are abundant. Therefore, rat and flea surveys were conducted in 47 districts of Bangkok Metropolitan area. Rats were trapped for 3 consecutive nights in a market which was a sample from each district of the

Bangkok Metropolis. The trapped rats were identified, then fleas and other ectoparasites were removed by combing. The fleas were mounted on microscopic slides and identified. From the surveys conducted from March to May 2000 in 47 markets, a total of 600 rats was trapped and classified into 5 species, namely *Rattus norvegicus*, *R. rattus*, *R. exulans*, *Mus musculus* and *Suncus murinus* in which *R. norvegicus* was the dominant

species (91.67%). Only 119 rats (24.05%) were infested with fleas. The total number of fleas was 347 and they were identified as *Xenopsylla cheopis* (99.71%) and *Ctenocephalides felis felis* (0.29%).

In addition, the results provided update information on the specific flea index in Bangkok

Metropolitan area. It was 0.69 which indicated no risk of plague outbreak. However, surveillance of rats and fleas should be done periodically along with community participation, since the oriental rat flea (*X. cheopis*) is of great importance as a vector of plague. □

ISOZYMES AND DIFFERENT FORMS OF *Aedes aegypti*, THE VECTOR OF DENGUE VIRUS

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Dengue fever, dengue haemorrhagic fever and dengue shock syndrome are widely distributed in the tropical and subtropical regions. Since 1958, the first serious epidemic of DHF occurred in Bangkok, further outbreaks have occurred annually with peaks every two years; the outbreaks are more confined to the rainy season. Though the mortality rate has decreased dengue cases are increasing every year. *Aedes aegypti* is the main vector of these diseases. Many aspects of research study on these disease agents and vectors have been carried out. In this paper, variation between mosquito strains and morphology were studied using isozyme.

Aedes aegypti larvae were collected from various provinces as representative provinces of each part of Thailand. The collected larvae were brought to the insectariums of the Department of Medical Entomology, Faculty of Tropical Medicine, Mahidol University, to rear until adulthood, identification and continued rearing of the next generation for further studies.

For the morphological study, adult mosquitoes 3-5 days old were used to examine the abdominal tergite scale patterns. There are 3 forms of *Aedes aegypti* following McClelland (1974); 1. the formosus form never has any pale scales on the first abdominal tergite, 2. the type form with pale scales on the first abdominal tergite and 3. the var. *queenlandensis* with any extension of the pale

scales on the thorax, tergites beyond the first and legs. But the quantified records following the CKM system (Hartbertberg *et al.*, 1986) can be classified into 8 classes, class 0-7 depends on the presence of white scales on the abdominal tergite segment 1 to 7. Therefore, the CKM class-0 is formosus form, class-1 is type form and class-2 to 7 is var. *queenlandensis* or pale form. In Thailand there were two forms of *Ae. aegypti*, the type form and the pale form. The type form or dark form was predominant and widely distributed from the north to the south of Thailand. More variation of the pale form was found southwards, but the greatest proportion with an exohitic habit, was found outdoors. The type form with endophitic and peridomestic habit was found predominant indoors.

Twenty-one isozymes were studied in mosquitoes from various provinces by vertical polyacrylamide slab gel electrophoresis. They revealed some variation in allele frequencies but no significance difference between these mosquito populations. Some esterase loci (Est-7 allele 102) showed a difference in allele frequencies of mosquitoes from indoors vs. outdoors and dark form vs. pale form. Mosquitoes from indoors have allele frequencies proportion of the dark form and the pale form higher (D:P = 2:1) than those form outdoors (D:P = 1.1:1). □

ARTEMISIA OIL AS A REPELLENT AGAINST MOSQUITO VECTORS IN THAILAND

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The efficacy of essential oils obtain from steam distillation of natural *Artemisia annua* (flower) and *Citrus hystri* (fruit) were tested against *Aedes aegypti*, *Culex quinquefasciatus*, *Anopheles dirus*, *An. maculatus* biting in laboratory. The mixture solution of the essential oil consists of 1% *Artemisia annua*, 5% *Citrus hystrix*, 0.5% Vanillin and 93.5%

sesame oil. The protection time of this formulation was 3 hours for *Ae. aegypti*, while 4 hours for *Cx. quinquefasciatus*, *An. dirus* and *An. maculatus*. The efficacies of the same concentration in the field against *Ae. aegypti*, and *Mansonia* spp. were 3 hours. *Cx. quinquefasciatus* was 4 hours. □

A BIOLOGICAL STUDY OF *PACHYCREPOIDEUS VINDEMMIAE* (RONDANI), A HYMENOPTEROUS PARASITOID OF MEDICAL IMPORTANCE

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The biology of a hymenopteran parasitoid, *Pachycrepoideus vindemmiae* Rondani, and its efficiency in the control of flies of medical importance was investigated in the laboratory.

The life cycle study revealed that *Pachycrepoideus vindemmiae*, when developed in house fly puparia, the egg, the first, second, third, fourth and fifth instar larvae, and prepupa and pupal stages lasted 1-2, 1-2, 2-3, 1-2, 2-3, 3-4, 1-2 and 9-12 days respectively. The average development period from egg to adult emergence was 20.35±1.43 days for males and 21.30±1.16 days for females. The characteristics of each development stage of the parasitoid were also

described in this study.

Adult longevity, when reared with 10% sugar solution, averaged 13.63±4.06 days in males and 18.22±2.93 in females. The mean fecundity was 112.18±25.24 offspring per female. The sex ratio, female per male, of offspring produced by mated females was 1.58:1, while only males were obtained from unmated females. The parasitism rate in *Musca domestica* was 75.12±10.97%.

Regarding the host preference in the laboratory, *Musca domestica* was the most preferred, followed by *Chrysomya megacephala* and *Parasarcophaga orchidae*, respectively. □

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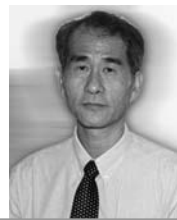
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The main responsibilities of the Department of Microbiology and Immunology are teaching and training, research, laboratory services and academic consultations.

TEACHING AND TRAINING

Fourteen international courses at the postgraduate level in microbiology and immunology including core subjects, elective and advanced courses are offered to the students of the D.T.M. & H. as well as M.Sc. and Ph.D. in Tropical Medicine. Our Department also shares some parts in teaching microbiology, immunology and molecular biology in other courses offered at the Faculty and other faculties of Mahidol University and other universities and institutions. As of September 2000, 47 students selected to work for their theses towards the M.Sc./Ph.D. degrees in various laboratories of the Department. Short courses on the subjects are given periodically.

CURRENT RESEARCH ACTIVITIES

The current research activities of the Department involve studies on the biology, molecular biology and immunology of infectious agents/diseases, particularly those causing problems in tropical areas with the ultimate aims being 1) development of simple, rapid, specific, sensitive, cost-effective and practical diagnostic methods for use in remote areas and for the self-reliance of the country; 2) identification of potential protective antigens for vaccine development; 3) understanding host responses and immunity; 4) understanding pathogenic mechanisms and virulence factors of pathogens and pathophysiology in hosts; and 5) acquisition of knowledge of modern technologies, eg. genetic analysis of bacterial pathogens for epidemiology study. 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*, *P. vivax*, *Leptospira*, etc. Successful identification of the specific antigens of these pathogens leads to the development of more simple, rapid, sensitive and specific immunodiagnostic methods for patients suffering from these diseases. For example, in human gnathostomiasis, a 24 kDa specific diagnostic component of *G. spinigerum* was further purified from the crude extract by column chromatographies. For affinity chromatography, the antigen used in the plate/membrane enzyme-linked immunosorbent assay (ELISA) gave 100% sensitivity and specificity for the disease. Attempts to produce the antigen either by 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*, *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), *Leptospira*, *Shigella*, *Vibrio parahaemolyticus*, *Listeria*, *Campylobacter rickettsia*, Japanese encephalitis 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 simple, specific, sensitive, rapid and cost-effective methods which are practical for use in 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, have been carried out.

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

Pathogenic mechanisms and virulence factors of certain pathogens, e.g. EHEC and uropathogenic *E. coli*, and pathological changes of the host target tissues caused by the virulent factors have been studied.

Protective activities of various antigens such as frimbriae, haemagglutinin, procholeraenoid and lipopolysaccharide of a bacterial pathogen, *Vibrio cholerae*, associated with liposome adjuvant are also studied. It was shown that oral immunization by the combination of these components provides strong local immunity against the bacterium. Phases I and II trials of the oral cholera vaccines, both against *V. cholerae* O:1 for tolerability and immunogenicity, have been successful. Clinical trials on the protective role in volunteers and field trials of the oral cholera vaccine are planned.

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 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. 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.

The study of nonfermentative gram negative aerobic bacteria, to find a simpler and faster diagnostic scheme, is continuing for the development of an identification method that can be used in any hospital laboratory.

The Leptospirosis Unit is collaborating with Chulalongkorn University in a study of leptospirosis in suspected patients in Prachinburi Province.

A more specific immunofluorescent technique has been developed to diagnose scrub typhus, and it is being evaluated with clinical samples in the Hospital for Tropical Diseases and other hospitals, in order to replace the Weil-Felix test for routine laboratory service next year.

Research work on viral infections, especially the detection of cytomegalovirus (CMV) infection by the immunostaining method is helpful for early diagnosis, particularly in congenital infection or after organ transplantation. This method can detect the presence of CMV in leukocytes very early during the course of an active infection and before the presence of specific IgM antibody. Since this immunostaining method is very simple to perform, inexpensive and more rapid than other diagnostic methods, such as PCR technique and tissue culture, it should be used in every laboratory.

Parts of these research works are being carried out in collaboration with various international universities and institutions, *i.e.* the Department of Microbiology, Institute of Basic Medical Sciences, University of Tsukuba; the Institute of Tropical Medicine, Nagasaki University; the Department of Parasitology, University of Tokyo; the Department of Medical Technology, University of Okayama; the Research Institute, International Medical Center of Japan; and the National Institute of Infectious Diseases, Tokyo, Japan; the London School of Hygiene and Tropical Medicine; International Vaccine Institute, Seoul, Korea; the Department of Microbiology and Immunology, Faculty of Medicine, Monash University, Melbourne, Australia; the Department of Microbiology and Immunology, Faculty of Medicine, University of Adelaide, Adelaide, Australia; the Queensland Institute of Medical Research and the University of Queensland, Australia; the Institute for Clinical Research in Tropical Medicine, Hanoi, Vietnam; Institute of Malaria, Parasitic Diseases and Entomology, Lao PDR; the University of Vienna and the University of Innsbruck, Austria; the University of Stellenbosch, South Africa; the National Institute of Cholera and Enteric Diseases, Calcutta, India; the International Centre for Diarrhoeal Disease Research, Bangladesh; etc.



Abstracts

MONOCLONAL ANTIBODY CAPTURE ENZYME-LINKED IMMUNOSORBENT ASSAY FOR IMMUNODIAGNOSIS OF HUMAN PARAGONIMIASIS HETEROTREMUS

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A monoclonal antibody (MAb) capture enzyme-linked immunosorbent assay (MAb capture ELISA) was developed and evaluated for its application in the detection of circulating antibodies to *Paragonimus heterotremus* in infected human sera. Mouse IgG monoclonal antibodies derived from a hybridoma clone 10F2 which reacted to 31.5 and 22 kDa components of the excretory-secretory (ES) antigen of the parasite were used to sensitize a microtiter plate; the bound antibodies captured their respective epitopes in the subsequent added ES antigen. Individual sera of patients with either parasitologically confirmed paragonimiasis heterotremus, other parasitic infections or pulmonary tuberculosis, and parasite-free healthy controls were incubated to the appropriate antigen containing wells. Finally, the bound human antibodies were detected by the anti-

human immunoglobulin-horseradish peroxidase conjugate and substrate. The MAb capture ELISA had 100%, 97%, 91.6% and 100% diagnostic sensitivity, diagnostic specificity, and positive and negative predictive values, respectively, when tested on sera of 33 patients with parasitologically confirmed paragonimiasis heterotremus, when tested on sera of 33 patients with parasitologically confirmed paragonimiasis heterotremus, 68 patients with other parasitic infections, eight patients with pulmonary tuberculosis and 29 normal controls. The MAb capture ELISA offers an alternative for sensitive and specific diagnosis of paragonimiasis by means of antibody detection without the requirement of purified, specific antigen of the parasites. □

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PREVALENCE OF ANTIBODIES TO *SCHISTOSOMA MEKONGI* AMONG INHABITANTS OF THE HIGH RISK AREA OF THAILAND

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Serum samples were collected from 339 inhabitants of Ubon Ratchathani province, Thailand, which is located in the immediate vicinity of Kong island, Lao PDR, where schistosomiasis is endemic (group 1). The samples were subjected to indirect- and dot-blot ELISA using a *Schistosoma* heterophile substance, i.e. keyhole limpet hemocyanin (KLH), as the antigen. Thirty five serum samples of residents of Bangkok, a low risk area for the blood fluke infection, were tested concurrently (group 2). It was found that 10 of 339 samples of group 1 revealed KLH-indirect ELISA optical densities higher than the uppermost limit of samples of group 2. These 10 serum samples were negative when tested by the indirect ELISA using affinity purified, specific antigen of *Trichinella spiralis*. The finding implied that the high optical densities found when the samples were

tested by the KLH-indirect ELISA, were not incited by *T. spiralis*, the infection which had been known to stimulate antibodies reactive also to the KLH. All sera of both groups 1 and 2 were negative when tested against KLH and specific *T. spiralis* antigen in dot-blot ELISA. Evaluation of the ages and occupations of the 10 individuals of group 1 revealed that their age range was 18 to 72 years, and 50% or more were farmers, with a high chance of exposure to water where the *S. mekongi* infective cercariae might be present. Moreover, none of the 10 individuals denied swimming in the Mekong river. Thus, the possibility exists that the high optical densities of the 10 serum samples in the KLH-ELISA is due to natural exposure or undetectable (light) infection by the *Schistosoma mekongi*. □

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DETECTION OF *SALMONELLA* CONTAMINATION IN FOOD SAMPLES BY DOT-ELISA, DNA AMPLIFICATION AND BACTERIAL CULTURE

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A dot-blot enzyme-linked immunosorbent assay (dot-ELISA) employing a genus *Salmonella* specific monoclonal antibody (MAb) was used for detection of the bacteria in food samples in comparison with the conventional culture method and the DNA amplification. Among the 200 chicken and pork samples (100 each) tested, 9% and 33%, 7% and 20% and 7 and 23% were positive for salmonellae by the dot-ELISA, the culture method and the DNA amplification, respectively. Statistical analyses revealed that the sensitivity, specificity, efficacy, and positive and negative predictive values of the detection of *Salmonella* in the food samples by dot-ELISA compared with the culture method were 93.33%, 91.76%, 92%, 66.66% and 98.73%, respectively. Comparison of the DNA amplification and the culture method revealed the sensitivity, specificity, efficacy, and positive and negative

predictive values of 100%, 91.58%, 92%, 65.21% and 100%, respectively. The dot-ELISA and the DNA amplification results were in a better agreement when the two assays were compared. The sensitivity, specificity, efficacy, positive and negative predictive values of the dot-ELISA compared to the DNA amplification were 91.3%, 100%, 98%, 100% and 97.5%, respectively. From this study, the dot-ELISA is rapid, simple, sensitive, specific at low cost with limited amount of infectious waste to be disposed and offers another advantage in that it detects only the smooth LPS of *Salmonella* which implies the possible presence of the virulent organisms. □

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MONOCLONAL ANTIBODIES PRODUCTION SPECIFIC TO VITELLIN AND VITELLOGENIN OF GIANT TIGER PRAWN *PENAEUS MONODON*

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Monoclonal antibodies specific to *Penaeus monodon* vitellin and vitellogenin were produced using crude ovarian extract from gravid *P. monodon* ovaries. After immunization and fusion of the mouse spleen cells with P3X myeloma,

hybridomas were selected by indirect immunoperoxidase ELISA against *P. monodon* 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 bound with ovarian extract proteins and with female haemolymph, but not with male haemolymph. One antibody (PMV-64) bound with both native and denatured proteins. Using Western blot analysis of ovarian extract separated by PAGE, all four monoclonal antibodies bound with the same lipoglycoprotein band. Using Western blot analysis

of proteins separated by SDS-PAGE, PMV-64 antibody bound with MW 80 and 83 kD proteins in ovarian extract, and with MW 83 and 200 kD proteins in female haemolymph, respectively. All four monoclonal antibodies belong to IgG1 subclass. □

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GENETIC ANALYSIS OF *TRICHINELLA SPIRALIS* THAI ISOLATES

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The gap genes within LSU rRNA of the individual infective larvae of human and pig *T. spiralis* of Thailand isolates were identified. Polymerase chain reaction was performed to increase DNA extracted from each larva of the parasite. Electrophoretic analysis of the PCR amplicons revealed that the length of the gap gene was less than 500 bp. PCR amplicons were ligated into pGEM-T Easy vector and then transformed into *E. coli* JM 107. Recombinant clones were identified using *Lac* selection and then subjected to automatic DNA sequencing. It was found that the gap region was flanked by the consensus sequence CGAAAG, which have been implicated in gap processing or recognition site, at both termini. From sequencing data, the gap genes of the *T. spiralis* larvae of the human isolate could be divided into four different groups and of the pig isolate could be divided

into three groups. Comparisons of the sequences of gap genes of the parasites of both isolates revealed that they were genetically similar, both in length and in base sequences. Nevertheless, the difference of nucleotides at the position 93 could be observed. There were many variables at this position in gap genes of the larvae of the pig isolate such as pig L2, pig L4-10 contained T, pig L3 contained G and pig L1 showed the deletion at the positions 93-95 whereas those of the human isolate showed consistency at the same position. □

The work was financially supported in part by BIOTEC, NSTDA and Faculty of Tropical Medicine, Mahidol University.

Presented at: the XVth International Congress for Tropical Medicine and Malaria, Cartagena de Indias, Colombia, August 20-25, 2000.

CHARACTERIZATION OF A PUTATIVE VIRULENCE ISLAND IN THE CHROMOSOME OF UROPATHOGENIC *ESCHERICHIA COLI* POSSESSING A GENE ENCODING A UROPATHOGENIC-SPECIFIC PROTEIN

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This study was initiated to search for a homologue of the *Vibrio cholerae zot* gene in uropathogenic *Escherichia coli* (UPEC) using a specific DNA probe. The faint signal obtained at low stringency with some UPEC strains associated with prostatitis cases prompted us to examine UPEC strains by PCR using primers designed from the conserved regions of the proteins of the Zot group of putative NTPases containing the classical NTP binding motif. This led to the discovery of a DNA fragment revealed an ORF which was designed from the PCR. Further analysis of this DNA fragment revealed an ORF which was designated as uropathogenic specific protein (Usp). The gene encoding Usp was 1038 bp long and codes for

346 amino acids with an appropriate SD sequence. Upstream and downstream analysis of *usp* revealed motifs of prokaryotic consensus promoters and three small ORFs with SDs and ribosome binding sites transcribed in the same direction of *usp*. The proximity of these sets of genes in a specific area of the bacterial chromosome resembling a block of genes preferentially associated with UPEC coupled with the presence of a motif matching that of a Tn3 transposon family lead us to believe that this could be an hitherto unknown pathogenicity island. □

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DIFFERENTIAL DIAGNOSIS OF SCHISTOSOMIASIS MEKONGI AND TRICHINELLOSIS IN HUMAN

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An indirect (plate) ELISA and, a more convenient version, a dot-blot (membrane) ELISA have been developed using haemocyanin of a mollusk, *Megathura crenulata*, i.e. keyhole limpet haemocyanin (KLH) and purified, specific antigen of *Trichinella spiralis* (APTsAg) obtained from a monoclonal antibody-affinity column chromatography, for differential diagnosis of schistosomiasis mekongi and trichinellosis. Serum samples of patients with parasitologically confirmed trichinellosis were reactive to both antigens in both

versions of ELISA while sera of patients with schistosomiasis mekongi were positive only to the KLH. Both ELISA were negative when used to test sera of normal controls and patients with gnathostomiasis, paragonimiasis and opisthorchiasis. □

Supported by National Sciences and Technology Development Agency (NSTDA), Ministry of Sciences Technology and Environment and Thailand Research Fund (TRF) through the Royal Golden Jubilee Ph.D. Program

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BLINDED, PLACEBO-CONTROLLED TRIAL OF ANTIPARASITIC DRUGS FOR TRICHINOSIS MYOSITIS

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There is no consensus on the benefits of treatment with any specific anthelmintic compound on muscle-stage trichinosis. A double-blinded, placebo-controlled comparison was done of 3 antiparasitic drugs during an outbreak of trichinosis in Chiangrai Province, northern Thailand. Forty-six adults were randomized to receive 10 days of oral treatment with mebendazole (200 mg twice a day), thiabendazole (25 mg/kg twice a day), fluconazole (400 mg initially, then 200 mg daily), or placebo. All patients received treatment to eradicate adult intestinal worms. *Trichinella spiralis* infection was proved

parasitologically in 19 (41%) of 46 patients and by serodiagnosis in all cases. Significantly more patients improved after treatment with mebendazole (12/12) and thiabendazole (7/7) than after treatment with placebo (6/12; $p < .05$) or fluconazole (6/12). Muscle tenderness resolved in more patients treated with thiabendazole and mebendazole than in those treated with placebo ($p < .05$). However, 30% of volunteers could not tolerate the side effects of thiabendazole. In summary, *Trichinella* myositis responds to thiabendazole and to mebendazole. □

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DIAGNOSIS OF HUMAN LEPTOSPIROSIS BY MONOCLONAL ANTIBODY BASED-ANTIGEN DETECTION IN URINE

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Hybridomas secreting specific monoclonal antibodies (MAb) to all members of the genus *Leptospira* (clone LF 9) and those that are specific only to the pathogenic species *interrogans* (clones LD5 and LE1) were produced. MAbLF9, which were IgG1, reacted to a 38 kDa component of the SDS-PAGE separated whole cell lysates of all *Leptospira* spp., while MAbLD5 and MABLE1, which were IgG1 and IgG2a respectively, reacted to the 33 to 35 kDa of all *Leptospira interrogans* but only CH 11 strain of serovar andamana of *L. biflexa*. All MAb-recognized epitopes were heat-stable, non-protein. The MAbLF9 were used as a capture reagent in a dot-ELISA to detect *Leptospira* antigen in urine samples of patients presumptively diagnosed leptospirosis. In one hospital, the MAb-based dot-ELISA had 61.67% sensitivity, 97.26% specificity and 86.97% accuracy when tested single urine samples of 60 presumptive leptospirosis patients at acute illness and 26 patients with fever of unknown origins compared to 120 healthy counterparts. In another hospital, the ELISA gave

100% sensitivity when tested two urine samples of individual patients collected at different time intervals. The ELISA was more sensitive than the standard microagglutination test (MAT) and the IgM dipstick. Besides high sensitivity, the urine antigen test does not require maintenance of living *Leptospira* cultures. Urine collection is not an invasive procedure and several samples can be tested at the same time without significant increase in the turn-around time. The results are read visually without microscope and they can be preserved for further study. The ELISA is rapid, simple and inexpensive. It does not produce any contaminated waste as do the standard MAT and the bacterial culture method. Thus, the MAb-based dot-ELISA has high potential as a rapid diagnostic test for patients suspected leptospirosis. □

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LOCALIZATION OF SHIGA TOXINS OF ENTEROHAEMORRHAGIC *ESCHERICHIA COLI* IN KIDNEYS OF PAEDIATRIC AND GERIATRIC PATIENTS WITH FATAL HAEMOLYTIC URAEMIC SYNDROME

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Haemolytic uraemic syndrome (HUS) is characterized by haemolytic anaemia, thrombocytopenia and renal failure. Infection with enterohaemorrhagic or Shiga toxin (Stx)-producing *Escherichia coli* (STEC), mainly O157:H7, has been strongly implicated as the major cause of HUS in children. The pathogenesis of HUS caused by the infection is not well understood and the defined sites of Stx in kidney of STEC-infected human has not been clearly demonstrated. The aim of this study was to investigate and compare the locations of Stx deposition in kidneys of paediatric and geriatric patients who died from enterohaemorrhagic *E. coli* O157 (EHEC) associated HUS, using an immunoperoxidase staining of the tissues. Our study revealed that binding of Stx was relatively less and limited only to the renal tubules of an adult case (81 years old), while more

binding was found at both renal tubules and glomeruli of another 21-month old case. The Stx binding in the infant's glomeruli was at podocytes, mesangial and endothelial cells. The findings confirm a hypothesis that synthesis and expression of Stx receptor, i.e., Gb3, correlate with the stage of cell growth and the host's age. They are higher in infants and much less so in the aged individuals. This explains why young children are more susceptible to HUS than adults and why the paediatric incidence of HUS is relatively high after the Stx-producing bacterial infections. □

Supported by Thailand Research Fund through the Senior Researcher Award to Professor Dr. Wanpen Chaicumpa and the Royal Golden Jubilee Ph.D. Program.

Submitted to: *Microbial Pathogenicity*

DETECTION OF *ESCHERICHIA COLI* O157 ANTIGEN AND SHIGA-LIKE TOXINS IN CLINICAL SPECIMENS USING MONOCLONAL ANTIBODIES

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Hybridomas secreting monoclonal antibodies (MAbs) to lipopolysaccharide (LPS) of *E. coli* O157 and A- and B-subunits of Shiga toxin-1 (Stx-1) and Shiga toxin-2 (Stx-2) were produced. Mono-epitope specificities of the MAbs were screened using homologous antigens and a wide range of heterologous antigens. The MAbs, namely MAb to O157 LPS and MAbs to A- and B-subunits of Stx-1 and Stx-2 were used in a dot-ELISA for the detection of their respective antigens in stool samples collected from patients with diarrhea. The MAb-based dot-ELISA, when performed in double-blinded manner, could correctly identified 5 samples of patients with enterohemorrhagic *E. coli* infections, i.e., 1 sample with non-O157, Stx-1 and Stx-2-producing *E. coli*, 2 samples with O157, Stx-2-producing *E. coli*, 1 sample with O157, Stx-1 and Stx-2-producing *E. coli* and 1 sample with O157, Stx-1-producing *E. coli*. The tests were negative for 215 samples collected from patients with diarrhea caused by other enteric pathogens (i.e., 43 samples with *Shigella sonnei*, 22 samples with *S. flexneri*, 8

samples with *Vibrio parahaemolyticus*, 3 samples with enteropathogenic *E. coli* (EPEC), 2 samples with *Staphylococcus aureus*, 1 sample with *Plesiomonas shigelloides*, and 136 samples with untyped *E. coli*). The membrane ELISA is easy to perform and relatively inexpensive compared to the culture and DNA amplification methods. The procedure requires only 90 minutes and it can test multi-samples at a single time without much increase in the turn around time. The dot-ELISA does not require equipment and does not produce large quantities of contaminated waste. Most of all, the test using a cocktail of MAbs to A- and B-subunits of both Stx offers advantage in detection of their respective antigen(s) in clinical specimens of patients infected with non-O157 Shiga toxin-producing bacteria. □

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CLONAL DISSEMINATION OF *VIBRIO PARAHAEMOLYTICUS* DISPLAYING SIMILAR DNA FINGERPRINT BUT BELONGING TO TWO DIFFERENT SEROVARS (O3:K6 AND O4:K68) IN THAILAND AND INDIA

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Active surveillance of *Vibrio parahaemolyticus* infection among hospitalized patients in Calcutta, India, showed the appearance of the O4:K68 serovar for the first time in March 1998 alongside the continued predominant incidence of the O3:K6 serovar. Strains belonging to both these serovars have been reported to possess pandemic potential. The genomes of O3:K6 and O4:K68 strains and for comparison, non-O3:K6 and non-O4:K68 strains isolated from two different countries, India and Thailand, were examined by different molecular techniques to determine their relatedness. The O3:K6 and O4:K68 strains from Calcutta and Bangkok carried the *tdh* gene but not *trh* gene. Characterization of representative strains of these two serovars by ribotyping and by arbitrarily primed-polymerase chain reaction (AP-

PCR) showed that the isolates had identical ribotype and DNA fingerprint. Pulsed-field gel electrophoresis (PFGE) performed with the same set of strains yielded nearly similar restriction fragment length polymorphism (RFLP) patterns for the O3:K6 and O4:K68 isolates from Calcutta and Thailand. Phylogenetic analysis of the *NotI* RFLP showed that the O3:K6 and O4:K68 strains formed a cluster with 78-97% similarity thus indicating close genetic relationship between the two different serovars isolated during the same time-frame but from widely separated geographical regions. The non-O3:K6 and non-O4:K68, in contrast, showed different ribotype, AP-PCR and PFGE patterns. □

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REGULATION OF IMMUNITY TO MALARIA: THE INTERPLAY BETWEEN TH1 AND TH2 CELLS

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Immunity to asexual blood stages malaria parasite is regulated by the CD4⁺ T cells in both Th1 and Th2 subsets on the basis of distinct patterns of cytokine secretion. Several lines of research have converged to provide a picture of how the relative contributions of these two subsets appear to change during the infection. In falciparum malaria the immune response was characterized by polarized Th1-like versus Th2-like cytokine responses in which it induces both in protection and pathogenesis. Evidence for the involvement of IFN- γ responses in resistance to *P. falciparum* reinfection has been reported in African children. *In vitro*, the responses of CD4⁺ T cells from Thai malaria exposed individuals to *P. falciparum* crude schizont extract could inhibit the growth of *P. falciparum* with variable production of IFN- γ in supernatants. However, ten antigen specific CD4⁺ T cell clones showed high level of parasite growth inhibition and seven of the ten produced high level of IFN- γ . The *P. falciparum* specific antibody production and their isotype expression during blood stage infection are regulated by IL-4 and probably

together with IL-5 and IL-10. Thus, the antibodies inhibit erythrocyte invasion and promote opsonization of merozoites and infected erythrocytes by monocytes. However, the balance between Th1-like cytokines such as TNF- α and IFN- γ and Th2-like cytokines such as IL-4 and IL-10 may determined the severity of falciparum malaria. Over production of TNF- α , IL-1 and IL-6 has been shown to implicate in severity and pathogenesis of cerebral malaria. The IL-10 and IL-12 may function as immune modulators in *P. falciparum* infection by the finding of the elevation of IL-10 and IL-12 levels in plasma of individuals with complicated malaria. Such increase of IL-10 correlated with parasite clearance, while that of IL-12 did not. The finding of IL-15 is still debatable. However, the question of the differences in the Th1/Th2 cytokine balance that link to the control of parasite multiplication and/or inducing pathogenesis remains to be answered. □

Presented at: the Symposium Session, Second Congress of the Federation of Immunological Societies of Asia-Oceania (FIMSA 2000), Bangkok, Thailand, January 23-27, 2000

DO IgE ANTIBODIES AND RELATED CYTOKINES HAVE A ROLE IN PATHOGENESIS OR PROTECTION IN FALCIPARUM MALARIA?

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Immunoglobulin E (IgE) involved in atopic disease is found to elevate in many parasitic infections. In malaria, although the increase of serum concentration IgE has been reported, however, the possible role of IgE for protection and/or pathogenesis remains to be elucidated. Our recent studies of IgE in falciparum malaria have shown that approximately 73% of individuals tested who have been living in malaria endemic areas in Thailand had increased levels of total IgE in serum whereas only 20.5% of this was specific to *P. falciparum* blood stage antigens. The levels of such specific serum IgE were not rising as those of IgG. The increase of anti-*P. falciparum* IgE antibodies seems to be malaria exposure- and age-dependent. However, the possibility of the anti-*P. falciparum* IgE antibodies from malaria individuals in activation of various effector cells such as monocytes/macrophages which might contribute to inhibition of malaria parasite is under investigation. While the relative importance of specific anti-plasmodial IgE for protection against malaria has not yet been well clarified, there is an evidence for its involvement in pathogenesis. This is based on the findings of significantly higher levels of total IgE and anti-*P. falciparum* IgE antibodies

in sera of patients with cerebral malaria compared to those with uncomplicated malaria. However, the results are reverse with anti-*P. falciparum* IgG antibodies which suggested that anti-*P. falciparum* IgE antibodies play a role in malaria pathogenesis. The severity of malaria was also associated with an increase concentration of serum tumor necrosis factor (TNF) in parallel with an increase of anti-*P. falciparum* IgE antibodies. In addition, the results from *in vitro* studies have shown that the concentration of specific IgE was usually in the form of immune complexes which activated adherent peripheral blood mononuclear cells (PBMC) to produce TNF- α . These data supported in part the previous finding that the levels of immune complexes in sera of patients with cerebral malaria were significantly higher than those with uncomplicated malaria. Other related cytokines such as IL-1, IL-6, IL-10, IL-12 and IFN- γ involved together with TNF- α in control of infection or implication in severity and pathogenesis will be included in the discussion. □

Presented at: the Symposium Session, XVth International Tropical Medicine and Malaria, Cartagena, Colombia, August 20-25 2000

CHARACTERIZATION OF SPECIFIC MONOCLONAL ANTIBODIES FOR DETECTION OF MEFLOROQUINE IN BODY FLUIDS.

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Specific monoclonal antibodies (MAbs) to mefloquine conjugated to bovine serum albumin (mefloquine-BSA) were produced by hybridoma technology. The mefloquine-BSA was

synthesized by converting mefloquine into hemisuccinate followed by covalently linked to bovine serum albumin (BSA) and coupling with N,N' disuccinimidyl carbonate (DSC). The

conjugate was purified by Sephadex G-75 gel filtration using 0.01M PBS pH 7.2. An average of 19.34 molecules of mefloquine were conjugated to each molecule of protein determined by differential UV absorption spectra of hapten and protein carrier. Sixteen monoclonal antibodies producing antibody specific to mefloquine were screened by indirect ELISA using homologous antigens. The specificity of MAbs was determined by reacting with BSA and the structurally related antimalarial drug, quinine. Three, three, five and two MAbs belonged to IgG1, IgG2a, IgG2b and IgG3, respectively. Most of the MAbs slightly reacted

with quinine-BSA due to the closely related structure of mefloquine to quinine. The selected Mab designated 11F9(G5)G9 which showed no cross reaction with quinine-BSA gave high reactivity with blood samples from malaria patients previously treated with mefloquine when compared to normal blood by indirect ELISA. The preliminary results indicated that such specific Mab could be used as antibody probe for detection of mefloquine in biological fluids. □

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CYTOADHERENCE CHARACTERISTICS OF *FALCIPARUM* ISOLATES IN THAILAND USING AN *IN VITRO* HUMAN LUNG ENDOTHELIAL CELLS MODEL

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Using an *in vitro* model of human lung endothelial cells, we studied different characteristics of *Plasmodium falciparum* isolates as potential factors for malaria severity in two Thai patient groups: 27 complicated malaria (CM) and 42 uncomplicated malaria (UM). In regard to binding properties, no association existed between cytoadherence and rosette phenotypes ($p=0.1$) and hypochromocytometry increased the cytoadherence level ($p=0.007$). Cytoadherence was significantly associated with malaria severity ($p=0.05$) contrary to rosette formation ($p=0.9$). ICAM-1 and Chondroitin-4-sulfate were major receptors of

cytoadherence in CM in comparison to UM ($p<10^{-4}$). Chondroitin-4-sulfate could act as putative receptor in non-pregnant malaria complications. CD36 was a main receptor in UM versus CM ($p<10^{-3}$). VCAM-1 and E-selectin played a minor role in two groups ($p=0.6$). Derivatives qinghaosu were more efficient than other antimalarial drugs, but a positive correlation was observed between IC50 of HF, QN and number of adhesive PRBCs suggesting their influence on the cytoadherence phenomenon. □

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COMPLICATED MALARIA IS ASSOCIATED WITH DIFFERENTIAL ELEVATIONS IN SERUM LEVELS OF INTERLEUKINS 10, 12, AND 15 *

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Complicated malaria, caused by *Plasmodium falciparum*, is characterized by multiple organ dysfunction. The pathogenesis of complicated malaria involves complex host-parasite interactions that include polarized cytokine responses. Recently, correlates between Th1-like and Th2-like cytokines, especially interleukin-10 (IL), IL-12, and TNF-, and specific types of organ dysfunction have been noted. Here, we measured IL-10, IL-12, and for the first time, IL-15, in 19 patients aged 16-55 years old with complicated malaria on days 0 (admission), 3, 7, and 14. For analysis, patients were grouped together or sub-categorized into hyperparasitemias or cerebral malaria (CM). For IL-10, a dramatic increase was noted on admission,

followed by a reduction toward control values that closely paralleled parasite clearance. For IL-12, modest but persistent increases were noted over the entire 14 day period that did not correlate with parasitemia. In general, especially on days 0 and 3, hyperparasitemic patients had, in comparison with CM patients, higher IL-10 and IL-12 levels. In contrast, IL-15 was generally below detection in most samples. These results provide further insight into the pathogenesis of complicated malaria by strengthening the contention that cytokines such as IL-10 and IL-12 are involved in modulating the immune response to *P. falciparum*. □

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RAPID DETECTION OF DENGUE VIRAL RNA BY NUCLEIC ACID SEQUENCE BASED AMPLIFICATION (NASBA)

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In this study, the suitability of RNA amplification by nucleic acid sequence-based amplification (NASBA) for detection of dengue viral RNA was investigated. NASBA is an enzymatic amplification of RNA sequence employing avian myoblastosis virus reverse transcriptase (AMV-RT), Rnase-H and T7-RNA polymerase under isothermal condition (usually at 41°C). A set of primers and probe synthesized based on a selected RNA sequence from the non-coding region at the 3' end of dengue viral RNA was used in

the NASBA assay. The NASBA reaction product was then determined by agarose gel electrophoresis and electrochemiluminescence (ECL) signal count. The sensitivity of NASBA assay was at 1-10 PFU/ml for all of the four dengue virus serotypes. There was no false positive result with Japanese encephalitis virus. This method was used successfully to detect dengue virus in the infected tissue culture cell. This test has potential use will be useful for detection of the dengue viruses in the clinical specimens. □

DETECTION OF DENGUE VIRAL RNA IN PATIENTS' SERA BY NUCLEIC ACID SEQUENCE-BASED AMPLIFICATION (NASBA) AND POLYMERASE CHAIN REACTION (PCR)

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Nucleic acid sequence-based amplification (NASBA) was employing a set of primers and probe based on the non-coding region at the 3' end of RNA sequence of dengue viruses for detection of the viral RNA in sera of patients clinically diagnosed of having dengue virus infection and compared with polymerase chain reaction (PCR). NASBA is an enzymatic amplification reaction by the three enzymes: avian myoblastosis virus-reverse transcriptase (AMV-RT), Rnase-H and T7-RNA polymerase for the continuous amplification of nucleic acids in a single mixture at isothermal temperature (usually at 41°C). Fifty-five acute sera were obtained from patients suspected of having dengue haemorrhagic fever. There are twenty-seven samples gave the positive results for both of NASBA and PCR and twenty-seven samples gave the negative results for both of NASBA and PCR. There are one sample gave positive results with NASBA but gave negative result with PCR and one sample gave negative results with NASBA but gave positive result with were found in this study. NASBA will be useful in early detection of acute dengue virus infection and the molecular study. □

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The Department of Protozoology is one of the eleven departments within the Faculty of Tropical Medicine, Mahidol University. It was one of the first five departments established at the founding of the Faculty of Tropical Medicine in 1960. Its responsibilities are teaching training, research and services in the field of medical protozoa.

CURRENT RESEARCH ACTIVITIES

1. Study on DNA replication enzymes of *Plasmodium falciparum* as new chemotherapeutic targets against malaria.
2. Effects of DNA gyrase inhibitors on *Trichomonas vaginalis* in cultures.
3. Isolation and characterization of DNA topoisomerase II from *Trichomonas vaginalis*
4. Toxoplasma antibody in healthy Thai population.
5. Inhibition of *Giardia intestinalis* and *Entamoeba histolytica* by medicinal plants.
6. *Blastocystis hominis* in children with diarrhea in children hospitals.
7. *In vitro* cultivation of *Cryptosporidium* spp.
8. Rapid detection of *Entamoeba histolytica* antibody.
9. Comparison of *Toxoplasma gondii* detection between in-house latex agglutination and commercial test.
10. Effects of DNA topoisomerase I inhibitors on *Trichomonas vaginalis in vitro*.
11. *In vitro* cultivation of *Blastocystis hominis*.

TEACHING AND TRAINING

1. Regular courses
 - 1.1 Diploma in Tropical Medicine and Hygiene (D.T.M.&H.)
 - 1.1.1 Core Subject TMPZ 501: Protozoology
 - 1.1.2 Elective subject TMID 505: Parasitology
 - 1.2 Master of Science in Tropical Medicine (M.Sc. Trop. Med.) and Doctor of Philosophy in Tropical Medicine (Ph.D.Trop.Med.).



1.2.1 Core Subject

TMID 512 : Tropical Medicine

1.2.2 Elective Core Subject

TMID 503 : Medical Protozoology

TMID 516 : Practical Parasitology

1.2.3 Free Elective

TMID 517 : Biochemistry of Parasites

TMID 518 : Advanced Parasitology

TMID 519 : Experimental Technique in Parasitology

TMID 520 : Molecular Biology of Parasites

TMID 521 : Antiparasitic Agents



OTHERS

The Department

- 2.1 The Department in conjunction with some international organizations, has provided international training courses.
- 2.2 Provides opportunities for both local and foreign medical personnel to train in special topics within the Department.
- 2.3 Teaches special topics in other universities.

TRAINING COURSES

1. Laboratory Diagnosis of AIDS-related Protozoa.
2. Workshop on Clinical and Laboratory Diagnostic Parasitology.

SERVICES

The Department of Protozoology provides the following services:

1. Special techniques for diagnosis of protozoal diseases such as
 - 1.1 Diagnosis of toxoplasmosis by Dye-Test technique.
 - 1.2 Diagnosis of cryptosporidiasis, *Cyclospora* spp., *Microspora* by special staining techniques.
 - 1.3. Identifying intestinal protozoa by nuclear staining.
2. Provides protozoal specimens for teaching to other institutes upon request.



Abstracts

INHIBITORY EFFECTS OF 9-ANILINOACRIDINES ON *PLASMODIUM FALCIPARUM* GAMETOCYTES

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Two gametocyte-producing isolates of *Plasmodium falciparum*, KT1 and KT3 were cultivated *in vitro*. On day 11 of cultivation, pure gametocytes containing stage II, III and IV were used to test the gametocytocidal activity of 9-anilinoacridines that had previously demonstrated their activity against the asexual stage of the parasite. After drug exposure for 48 hours, gametocytes were maintained without drug for another two days before thin films were prepared for parasite counting. Gametocytocidal activities of 13 analogs of 9-anilinoacridine were observed

with 50% inhibitory concentrations in the range of 0.6 μ M to greater than 100 μ M. The most active compound was 1'-CH₂NMe-9-anilinoacridine. Anilinoacridine derivatives² with 3,6-diamino substitution had reduced gametocytocidal activity in contrast to their enhancing effect against the asexual forms. Morphological abnormalities of gametocytes were observed following drug exposure. □

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PARTIAL PURIFICATION AND CHARACTERIZATION OF MITOCHONDRIAL DNA POLYMERASE FROM *PLASMODIUM FALCIPARUM*

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Mitochondria of chloroquine-resistant *Plasmodium falciparum* (K1 strain) were isolated from mature trophozoites by differential centrifugation. The mitochondrial marker enzyme cytochrome c reductase was employed to monitor the steps of mitochondria isolation. Partial purification of DNA polymerase from *P. falciparum*

mitochondria was performed using fast protein liquid chromatography (FPLC). DNA polymerase of *P. falciparum* mitochondria was characterized as a γ -like DNA polymerase based on its sensitivity to the inhibitors aphidicolin, N-ethylmaleimide and 1- β -D-arabinofuranosyladenine-5'-triphosphate. In contrast, the enzyme was found to be strongly resistant to 2',3'-

dideoxy-thymidine-5'-triphosphate ($IC_{50} > 400 \mu M$) and differed in this aspect from the human homologue, possibly indicating structural differences between human and *P. falciparum* DNA polymerase γ . In addition, the DNA polymerase of parasite mitochondria was shown to be resistant ($IC_{50} > 1mM$) to the nucleotide analogue (S)-1-[3-hydroxy-2-

phosphonyl-methoxypropyl]adenine diphosphate (HPMPApp). □

This work was supported by the *Thailand Research Fund*.

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

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Gametocytocidal activities of pyronaridine and DNA topoisomerase II inhibitors against two isolates of multidrug-resistant *Plasmodium falciparum*, KT1 and KT3 were 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 was the most effective gametocytocidal drug against *Plasmodium falciparum* isolates KT1 and KT3; with 50% inhibitory concentration of 6 and 20 nM, respectively. Moreover, the 50% inhibitory

concentration of pyronaridine was lower than that of primaquine which is the only drug used to treat malaria patients harbouring gametocytes. Prokaryotic (norfloxacin) and eukaryotic (amsacrine and etoposide) DNA topoisomerase II inhibitors were only effective against asexual but not sexual stages of the malaria parasites. Based on the results, pyronaridine has both schizontocidal and gametocytocidal activities against the human malaria parasite, *Plasmodium falciparum*. □

This work was supported by the *Thailand Research Fund*.

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IN VITRO SENSITIVITY OF *TRICHOMONAS VAGINALIS* TO DNA TOPOISOMERASE II INHIBITORS

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Vaginal trichomoniasis is a highly prevalent sexually transmitted disease caused by a microaerophilic protozoan *Trichomonas vaginalis*. The disease is one of the most common sexually transmitted disease and can augment the

predisposition of individuals to human immunodeficiency virus (HIV) infection. Although the disease can be treated with metronidazole and related 5-nitroimidazole, cases of trichomonal vaginitis which are refractory to standard treatment

seems to be increasing. Clearly, new antitrichomonal agents are needed and DNA topoisomerase II may act as a new target for antitrichomonal agents. In this study, *in vitro* sensitivity of *Trichomonas vaginalis* to DNA topoisomerase II was investigated. Axenic culture of local strain of *Trichomonas vaginalis* was performed. Both eukaryotic and prokaryotic DNA topoisomerase II inhibitors such as ellipticine, amsacrine and fluoroquinolones were tested for effectiveness against *Trichomonas vaginalis in vitro* compared to metronidazole. The result showed that *Trichomonas vaginalis* was sensitive to metronidazole under aerobic condition. Minimal inhibition concentrations (MICs) of eukaryotic DNA

topoisomerase II; ellipticine and amsacrine were 6.4 μ M and 64 μ M, respectively. The MICs of prokaryotic DNA topoisomerase II or DNA gyrase inhibitors; ciprofloxacin, ofloxacin and norfloxacin were 64, 960 and 1280 μ M, respectively. Based on the results, among DNA topoisomerase II inhibitors ellipticine was the most effective drug against *Trichomonas vaginalis in vitro* whereas fluoroquinolones did not show high antitrichomonal activity. □

This study was supported by a grant from Mahidol University.

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SEROLOGICAL STUDY OF *TOXOPLASMA GONDII* IN KIDNEY RECIPIENTS

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Toxoplasma gondii IgG antibodies were determined in 200 kidney recipients by the Sabin-Felmand dye test. Twenty-two (11%) cases were positive for antibody detection. There was a statistically significant difference in history of taking under-cooked meat, when compared the number of sero-positive cases with those of sero-negative subjects (63.6% vs. 28.8%, $p=0.02$). No such significant difference was evident regarding cat ownership (13.6% vs. 22.0%, $p=0.3$).

Sixteen (72.6%) of the 22 subjects with positive *T.gondii* antibody had undergone kidney transplantation for less than one year during which high dose of immunosuppressive drugs were prescribed. The remaining six (27.3%) had transplantation for more than one year which the dosage of immunosuppressants are lower. It was

known those people who positive for *T.gondii* antibody harbour viable cyst in their body and potential flare up when immune system was impaired. Therefore, the potential of toxoplasma reactivation seems to be higher in the former group, which should be closely followed up. Preventive chemoprophylaxis should be considered if there is any indication of toxoplasma reactivation.

Since there have been occasional reports of donor-to-host transmission of toxoplasmosis in kidney transplant recipients, serological screening of toxoplasma antibody in kidney donors is advisable. Potential donors with positive toxoplasma antibody should be rejected; but if that is unavoidable, 6-week prophylactic treatment of primary infection in kidney recipients should be administered. □

COMPARISON STUDY ON *TOXOPLASMA GONDII* ANTIBODY USING LATEX AGGLUTINATION AND SABIN-FELDMAN DYE TEST

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Study on toxoplasma IgG antibody was carried out to evaluate the sensitivity and specificity of the commercial latex agglutination kit (Toxo-Screen DA, bioMerieux) with the gold standard, Sabin-Feldman dye test. Five hundred serum samples were enrolled from 200 blood donors and each 100 from kidney recipients, pregnant women and HIV infected persons.

There were 80 subjects out of 500 (16.0 %) positive for toxoplasma IgG antibody by Toxo-Screen DA (bioMerieux), whilst 11.4 % (57 out of 500) was positive by Sabin-Feldman dye test. There were 23 samples positive by Toxo-Screen DA (bioMerieux) but not by Sabin-Feldman dye

test, but all samples, which were positive by Sabin-Feldman dye test, were positive by Toxo-Screen DA (bioMerieux). Therefore, the sensitivity of Toxo-Screen DA (bioMerieux) is 100 % whilst the specificity is 94.8 %.

Toxo-Screen DA (bioMerieux) is highly sensitivity and rather high specificity when compare with the gold standard, Sabin-Feldman dye test. To expand the assessment of toxoplasma sero-prevalence in Thailand, it is advisable to use Latex Agglutination method as a screening test for toxoplasma IgG antibody. The questionable results could be confirmed by the gold standard test. □

STUDY ON *TOXOPLASMA GONDII* ANTIBODY IN THE POPULATION OF PROVINCES WITH A HIGH RISK OF HIV INFECTION

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Serological study on *Toxoplasma gondii* antibody was performed in the healthy population of 6 provinces, which are high risk of HIV infection. These are Bangkok, Chiang Rai, Phayao, Chonburi, Khon Kaen and Ranong. One thousand and six hundred serum samples were enrolled. Sabin-Feldman dye test is used to determine toxoplasma IgG antibody.

The average of *T.gondii* antibody is 9.6 % where as the seropositive in Bangkok, Chiang Rai, Phayao,

Chonburi, Khon Kaen and Ranong are 15.7% (74/480), 7.2% (13/180), 2.4% (2/250), 15.6% (39/250), 2.0% (4/200) and 7.1% (13/180) respectively. Among the seropositive subjects, the male to female ratio is 2.6:1.

Sero-prevalence of *T.gondii* antibody in Thai healthy population is low even in the provinces with a high risk of HIV infection. □

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Chonlawan Koolapant

CURRENT RESEARCH ACTIVITIES

The research activities of the Department involve both laboratory research and field investigation.

1. Multiple mutations in the *rpoB* gene of *Mycobacterium leprae* strains from leprosy patients in Thailand
2. Identification of *Escherichia coli* recovered from milk of sows with coliform mastitis by random amplified polymorphic DNA (RAPD) using standardized reagents
3. Effect of insecticide on female reproductive system
4. Appropriate biological sample for determination of manganese concentration among welders
5. Detection of a possible specific serum marker in opisthorchiasis-associated cholangiocarcinoma patients
6. Hazardous substance management and development of computerized database inventory list on major hazardous substance used at the Faculty of Tropical Medicine
7. Air pollution mitigation from industrial sector
8. Uses of CFCs alternatives in Thailand
9. Control of soil-transmitted helminths in primary school in Southern Thailand
10. A phase III trial to determine the efficacy of AIDS VAX™ B/E vaccine in intravenous drug users in Bangkok, Thailand
11. Environmental health impact assessment for adverse effects of water resources development



TRAINING COURSES

The Department of Social and Environmental Medicine offered 2 training courses in the year 2000. The first training course, entitled "Management of Municipal Solid Wastes and Hazardous Substances", was held during July 3-5, 2000 and was attended by 145 participants from the academic sector, which included those from higher education institutions, the Ministry of Science Technology and Environment, Ministry of Education, Ministry of Public Health, Ministry of Interior and the Bangkok Metropolitan Administration.

The second training course on "Pollution Prevention/Clean Technology" held during August 21-23, 2000 also provided more than 150 participants with concrete information of clean technology along with successful case studies.



Abstracts

MULTIPLE MUTATIONS IN THE *RPOB* GENE OF *MYCOBACTERIUM LEPRAE* STRAINS FROM LEPROSY PATIENTS IN THAILAND

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A new finding is reported of multiple mutations in the *rpoB* gene of 9 *Mycobacterium leprae* strains from leprosy patients in Thailand, who did not respond to therapy even when rifampicin, the main drug in multi-drug therapy was used. By means of sequence analysis of 9 Thai *M. leprae* strains, various mutations in 289 bps of the *rpoB* gene revealed forms of mutation never before described, such as multiple mutations (*i.e.*, mutation at two, three, six, seven, eight and nine positions in the *rpoB*

gene), most of which were point-mutation substitutions (a few of which were silent) and some insertions. This investigation demonstrates that mutation in the *rpoB* gene of *M. leprae* strains from Thailand involves more variety than previously reported for *rpoB* mutation patterns in rifampicin resistance *M. leprae* strains. □

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IDENTIFICATION OF *ESCHERICHIA COLI* RECOVERED FROM MILK OF SOWS WITH COLIFORM MASTITIS BY RANDOM AMPLIFIED POLYMORPHIC DNA (RAPD) USING STANDARDIZED REAGENTS

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A standardized-reagents commercial kit for random amplified polymorphic DNA (RAPD) analysis was used for typing 58 *Escherichia coli* strains that were recovered from the milk of sows, having coliform mastitis, within a single swineherd in Sweden. Previously, the 58 *E. coli* strains were characterized serologically and profiled biochemically. They were also evaluated for their

serum resistance and their ability to adhere to fibronectin and bovine fetal fibroblasts. The RAPD analysis was fast, easily performed, and required only a nanogram of DNA. The indistinguishable banding patterns obtained with repeated analyses of 2 isolates from each strain demonstrated that RAPD analysis using standardized beads is a technique that provides reproducible results for

typing *E. coli* strains that cause mastitis in sows. The results of the RAPD analyses demonstrated that *E. coli* sow mastitis strains are highly variable in serotype, biochemical profiles, virulence factors, and RAPD type, and that all 58 strains can be differentiated by means of the RAPD technique. The strains grouped into 24 RAPD types by combining the results of 2

primers, and into 38 groups by combining the results of serotype and RAPD type. No relationship between serotypes, virulence factors and RAPD types was found. □

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MULTIPLE MUTATION IN THE *RPOB* GENE OF RIFAMPICIN-RESISTANT *MYCOBACTERIUM TUBERCULOSIS* STRAINS FROM THAILAND

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Forms of mutation never before described in the *rpoB* gene are reported for a sample of 70 rifampicin-resistant (RIF^r) *M. tuberculosis* strains from Thailand. Sequence analysis of these strains revealed mutations in a 435 base-pair region of the *rpoB* gene. Twenty-eight strains (40.0%) had single mutations, and 26 of those strains had mutations at positions never before reported. Of those 26, just one had a substitution at Val-432 (Asp), and the remaining 25, a silent mutation at Gln-517. All other strains had multiple mutations. Twenty-four (34.3%) had mutations at two positions; nine (12.8%), at three positions; two (2.8%), at five positions; and one (1.4%), at six positions. Five strains (7.1%), reported to have the RIF^r phenotype, contained no mutation in the

examined region of the *rpoB* gene. Surprisingly, one RIF^r strain had silent mutations at twenty-nine positions. By far the dominant mutation was the silent mutations at Gln-517 (85.7% of strains). This investigation demonstrates that mutation in the *rpoB* gene of *M. tuberculosis* strains from Thailand are more varied than previously reported for RIF^r *M. tuberculosis* strains. Screening by means of PCR-SSCP clearly separated RIF^r strains from rifampicin-susceptible (RIF^s) strains. Based upon random amplified polymorphic DNA (RAPD) analyses, there was no correlation between RIF^r mutations and RAPD types. □

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COMPARISON OF *MYCOBACTERIUM AVIUM* COMPLEX (MAC) STRAINS FROM PIGS AND HUMANS IN SWEDEN BY RANDOM AMPLIFIED POLYMORPHIC DNA (RAPD) USING STANDARDIZED REAGENTS

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Infections with atypical mycobacteria belonging to the *Mycobacterium avium* / intracellular complex (MAC) can cause infection in both animals and humans. Using a standardized-reagents commercial kit for random amplified polymorphic DNA (RAPD) analysis, forty-nine MAC strains isolated from 32 slaughter pigs and 17 humans in Sweden were identified and sorted out, yielding 6 RAPD types. By combining the results of RAPD primers 4 and 5, and the primer IS 1245A, we found that pigs and humans may be infected with the same types of MAC strains, since 14 strains from humans and 8 strains from pigs were essentially identical, and together, comprised RAPD

type 2, the largest group of stains (44.8 % of strains). With respect to grouping of strains, serotype and RAPD type were uncorrelated, except for serotype 20 and RAPD type 6. Using standardized beads, RAPD analysis is a reproducible technique for typing MAC strains, as the indistinguishable banding patterns obtained with repeated analyses of two isolates from each strain in this study demonstrate. However, primer selection and DNA purity were crucial for differentiating closely related strains. □

Published in: *Veterinary Microbiology* 2000.



APPLICATION OF RANDOMLY AMPLIFIED POLYMORPHIC DNA (RAPD) ANALYSIS FOR TYPING AVIAN *SALMONELLA ENTERICA* SUBSP.

ENTERICA

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Randomly Amplified Polymorphic DNA (RAPD) analysis was performed for the molecular genetic typing of 30 *Salmonella enterica* subsp. *enterica* strains isolated from chickens and ducks in Thailand. Six different primers were tested for their discriminatory ability. While some of the primers only could differentiate between the different serovars the use of multiple primers showed that the RAPD method could subdivide also within a given

serovar. The Ready-To-Go RAPD analysis beads used resulted in reproducible and stable banding patterns. As the RAPD technique is simple, rapid and rather cheap we suggest that it may be a valuable new tool for studying the molecular genetic epidemiology of *Salmonella enterica* subsp. *enterica* both inter- and intra-serovars. □

Published in: *FEMS Immunology and Medical Microbiology* 2000;29(3):221-5.

EVALUATION OF THE RANDOM AMPLIFIED DNA METHOD FOR IDENTIFICATION AND DIFFERENTIATION OF AVIAN PATHOGENIC *ESCHERICHIA COLI* (APEC) STRAINS

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Here we describe the application of a random amplified polymorphic DNA (RAPD) analysis for molecular genetic typing of such APEC strains. The RAPD technique was shown to be highly reproducible. Stable banding patterns with a high discriminatory capacity were obtained using two different primers. Overall, 55 *E. coli* strains were analyzed with a RAPD technique. The RAPD analysis showed that the *E. coli* strains isolated from poultry in Thailand and Sweden could be grouped into 50 of RAPD types by using these

two different primer sets. Most of these different *E. coli* RAPD types were not geographically restricted. There was, as expected, a tendency of higher genetic relationship among *E. coli* strains isolated from the same farm. It is suggested that the RAPD technique may provide a rapid, low cost, simple and powerful tool to study the clonal epidemiology of avian *E. coli* infections. □

Published in: *Veterinary Microbiology* 2000.

GENETIC CHARACTERIZATION OF INCIDENT HIV TYPE 1 SUBTYPE E AND B STRAINS FROM A PROSPECTIVE COHORT OF INJECTING DRUG USERS IN BANGKOK, THAILAND

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We obtained specimens from 128 HIV-1 seroconverters identified from 1995 through 1998 in a prospective cohort study of 1,209 HIV-negative injecting drug users (IDUs) in Bangkok, Thailand. Epidemiologic data indicated that parenteral transmission accounted for nearly all infections. HIV-1 DNA from the C2-V4 env region was sequenced, and phylogenetic analyses determined that 102 (79.7%) of the specimens were subtype E and 26 (20.3%) subtype B strains. All subtype B strains clustered with strains often referred to in previous studies as Thai B or B'. The interstrain nucleotide distance (C2-V4) within subtype E strains was low (mean, 6.8%), and pairwise comparisons with a prototype subtype E strain, CM244, showed limited divergence (mean, 5.6%). The subtype B strains showed greater interstrain divergence (mean, 9.2%) and were significantly divergent from the prototype B strain HIV-MN (mean, 13.0%; $p < 0.0001$). The subtype

E strains had significantly lower mean V3 loop charge than did subtype B strains ($p = 0.017$) and, on the basis of analysis of amino acid sequences, were predicted to be predominantly (91%) non-syncytium-inducing (NSI), chemokine coreceptor CCR5-using (CCR5+) viruses. The subtype B strains had a higher mean V3 loop charge, and a smaller proportion (23%) were predicted to be NSI/CCR5+ viruses. This study demonstrates that most incident HIV-1 infections among Bangkok IDUs are due to subtype E viruses, with a narrow spectrum of genetic diversity. The characterization of incident HIV-1 strains from 1995 to 1998 will provide important baseline information for comparison with any breakthrough infections that occur among IDUs in Bangkok who are participating in an HIV-1 vaccine efficacy trial initiated in 1999. □

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AIDSVAX (MN) IN BANGKOK INJECTING DRUG USERS: A REPORT ON SAFETY AND IMMUNOGENICITY, INCLUDING MACROPHAGE-TROPIC VIRUS NEUTRALIZATION

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A randomized, double-blind, placebo-controlled phase I/II study of AIDSVAX (MN) was conducted among injecting drug users in Bangkok, Thailand. Four doses of vaccine (300 µg of MN-rgp120 in alum) or placebo (alum) were given at study entry and at 1, 6, and 12 months. The objectives of the study were to evaluate (1) the feasibility of conducting vaccine trials in this population; (2) the safety of this candidate AIDS vaccine; and (3) the immunogenicity of this vaccine. Thirty-three volunteers (22 vaccine and 11 placebo recipients) were recruited. None were lost to follow-up during the 18-month study. Mild reactogenicity was noted, which was similar in both vaccine and placebo recipients. The vaccine induced anti-HIV-1 antibody in all vaccine recipients. Maximal titers of binding antibodies of MN-rgp120 and

the V3 domain of MN-rgp120 were induced after the third (6 month) dose while maximal neutralizing antibodies followed the fourth (12 month) dose. The vaccine-induced antibodies from several volunteers were capable of neutralizing macrophage-tropic, subtype B viruses (301660 and JRCSF) detected in a PBMC-based assay. Binding and neutralizing antibodies declined about 10-fold in the 6 months after the last boost. Two vaccines became infected during the trial, both with subtype E viruses. A phase III efficacy trial, using a bivalent gp120 vaccine containing antigens from a subtype B virus (MN) and a subtype E virus (A244), was initiated in March 1999 in injecting drug users in Bangkok. □

Published in: *AIDS Res Hum Retroviruses* 2000;16:655-63.

DISEASE PROGRESSION AND SURVIVAL WITH HUMAN IMMUNODEFICIENCY VIRUS TYPE 1 SUBTYPE E INFECTION AMONG FEMALE SEX WORKERS IN THAILAND

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This study describes rates and correlates of disease progression and survival among 194 female sex workers in northern Thailand who were infected with human immunodeficiency virus type 1 (HIV-1; 96% with subtype E). The median rate of CD4 T lymphocyte decline (3.9 cells/L/month), median time from infection to <200 CD4 T lymphocytes/L (6.9 years), and time to 25% mortality (6.0 years) were similar to those found in studies performed in Western countries before highly active antiretroviral therapy was available to populations

infected with HIV-1 subtype B. Mortality rates among women with >100,000 HIV-1 RNA copies/mL were 15.4 times higher (95% confidence interval, 5.2-45.2) than among women with <10,000 copies. Initial CD4 T lymphocyte counts and serum virus load were independently strong predictors of survival. These results can help in assessing the effects of the epidemic in Thailand and in determining the prognoses for individual patients. □

Published in: *JID* 2000;18(15):1598-606.

LONG-TERM TRENDS IN THREE HIGH HIV SEROPREVALENCE EPIDEMICS: IDUs IN BANGKOK, THAILAND, NEW YORK CITY, USA AND SANTOS, BRAZIL

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Objective: To assess trends in (A) HIV prevalence, (B) HIV incidence, (C) Behaviors that risk exposure for HIV, and (D) Behaviors that risk transmission of HIV in three high seroprevalence epidemics among injecting drug users. One epidemic has occurred within a context of heroin injection (Bangkok), one within cocaine injection (Santos), and one within both heroin and cocaine injection (New York).

Methods: From 1989 through 1997, multiple cross-sectional HIV prevalence and behavior surveys were conducted in each city - 5 surveys in New York, 3 in Bangkok and 2 in Santos. A total of over 12,000 IDUs participated. HIV incidence cohort studies were also conducted in Bangkok and New York, with a total of over 1500 IDU participants. Risk behaviors were measured in terms of the % of subjects engaging in a behavior in the 6 months prior to interview. All changes were significant at $p > 0.05$ by chi square tests for trends.

Results: (A) HIV prevalence declined from 43% to approximately 35% among IDUs in Bangkok, declined from 50% to 29% in New York, and declined from 63% to 42% in Santos. (B) HIV incidence remained stable at 6% per year in

Bangkok, and declined from 4% per year to 1% per year in New York. (C) Risk for exposure behavior (injecting with needles and syringes used by someone else in the previous 6 months) declined from 35% to 22% in Bangkok, remained constant at approximately 22% in New York, and declined from 55% to 24% in Santos. (D) Risk for transmission behavior (passing on used needles and syringes to others) remained constant at approximately 18% in Bangkok, declined from 22% to 5% in New York, and from 59% to 18% in Santos.

Conclusions: These 3 cities illustrate the possibilities of “stabilizing” and potentially “reversing” high seroprevalence epidemics. The data from New York present a strong case for a “declining” epidemic. While reducing risk for exposure behavior is obviously important in HIV prevention, reducing risk for transmission behavior may also be critical in controlling high seroprevalence HIV epidemics. HIV prevention programs should include more efforts to reduce transmission behaviors among seropositives. □

Presented at: the XIII International AIDS Conference, Durban, South Africa, July 2000.

SOCIAL HARM MONITORING AMONG INJECTING DRUG USERS (IDUs) IN A PHASE III HIV VACCINE TRIAL IN BANGKOK, THAILAND – PRELIMINARY RESULTS

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Issues: HIV vaccine trial participants may be subject to social harms such as stigmatization (by identification of high-risk group membership); misclassification of HIV infection status (due to vaccine-induced antibody) resulting in loss of employment, insurance, or travel restrictions; or increased risk behavior due to false perceptions of vaccine protection.

Description: In Mar-1999, a phase III trial was initiated in Bangkok among 2500 IDUs to evaluate the efficacy of AIDSVAX(tm) B/E vaccine. As of 17-Jan-2000, 1304 volunteers were enrolled. All participants receive intensive education, counseling, informed consent, and monitoring at 6-month intervals for risk behavior and study-related social harms. Thus far, 5 (0.4%) volunteers have reported disturbances in personal relationships; 4 were with friends or family following voluntary disclosure of trial involvement and resolved with counseling of the concerned parties. The other report described difficulty with an employer and resolved with the volunteer taking

a new job. In all cases counseling was provided to address the specific problems. No social harm events have been reported due to false-positive HIV tests conducted outside of the study. The proportion of IDUs reporting high-risk behavior has decreased at month 6 compared to baseline. Injecting drug use overall decreased from 96% to 83% (regular use dropped from 30 to 20%; sharing needles dropped from 30% to 14%), and methadone maintenance increased from 45% to 78%. In addition, 100% condom use increased from 55% to 69%.

Conclusions: In HIV vaccine trials, it is important to establish effective education and risk reduction counseling as an integral part of the trial. Emphasis should be placed on how volunteers can avoid potential social harms. Interventions should be available to assist trial volunteers with problems as they occur. □

Presented at: the XIII International AIDS Conference, Durban, South Africa, July 2000.

INITIATION OF A PHASE III EFFICACY TRIAL OF BIVALENT B/E RGP120 HIV VACCINE (AIDSVAX? B/E) IN BANGKOK, THAILAND

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* Presenting author for BVEG

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²Bangkok, Thailand [D. Kitayaporn and J. Kaewkungwal members]

Background: Since 1988, injecting drug users (IDUs) in Bangkok have experienced a severe epidemic of HIV infection. A 1995-98 study conducted in this group showed an annual incidence rate of at least 6%, willingness to participate in HIV vaccine trials, and high rates of follow-up. The bivalent B(MN)/E(A244) rgp120 HIV vaccine, specifically designed to match HIV strains in Thailand, was previously found to be safe and highly immunogenic in phase I/II trials. In March 1999, a phase III efficacy trial was initiated in Bangkok using AIDSVAXTM B/E vaccine.

Methods: Following informed consent, 2500 IDUs attending 17 drug treatment clinics will be randomized in a blinded fashion to AIDSVAX B/E vaccine (300ug of each antigen) or placebo (1:1 ratio) at months 0, 1, and 6, with booster doses at months 12, 18, 24, and 30. Interim safety and efficacy analyses will be conducted by an independent DSMB. The study is designed to last 3 years following recruitment and to detect efficacy of at least 30% (1st endpoint - protective "sterilizing"

immunity as measured by ELISA and Western blot; 2nd endpoint - reduced viral load measured by RNA PCR).

Results: As of 17 January 2000, 2463 volunteers were screened and 1304 were enrolled (93% male; mean age 30 years). Immunization compliance has been 100% (1198 and 517 received the second and third doses, respectively). Thus far, only 6 volunteers have been lost to follow-up and 5 deaths have occurred (none were vaccine related). Immunizations have been well tolerated with no severe vaccine-related side effects.

Conclusions: The first phase III efficacy trial of an HIV vaccine among a high-risk population of IDUs has been initiated in Bangkok, Thailand. To date, recruitment is proceeding well, follow-up is excellent, and adverse effects are unremarkable. With completed enrollment, an interim efficacy analysis is expected in 2002. □

Presented at: the XIII International AIDS Conference, Durban, South Africa, July 2000.

BASELINE CHARACTERISTICS OF INJECTING DRUG USERS (IDUS) ENROLLED IN A PHASE III HIV VACCINE EFFICACY TRIAL – PRELIMINARY RESULTS FROM BANGKOK, THAILAND

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Background: Since 1988, IDUs in Bangkok have experienced a severe epidemic of HIV infection with a sustained annual incidence rate of 6%. Previous studies have suggested that this population is highly motivated to participate in HIV vaccine trials. In March 1999, a phase III trial was initiated among 2500 IDUs to evaluate the protective efficacy of bivalent B/E rgp120 HIV vaccine (AIDSVAXTM) B/E). An important outcome of this trial is the first description of baseline characteristics of this high-risk group participating in the first international phase III HIV vaccine efficacy trial.

Methods: At enrollment into the trial, standardized questionnaires were used to interview IDUs on demographics, risk behavior, and motivations and reasons for participating in the trial.

Results: As of 17 January 2000, 1304 IDUs have been enrolled. The volunteers are mostly male

(93%), Thai (99%), young (mean age 30.6 yr.), have at least primary education (94%), and have been incarcerated in the past (15%). Almost all (99.7%) inject heroin on a regular (30%) or sporadic (70%) basis, and 30% have reported sharing needles. The primary reasons or motivations to participate in this trial are altruistic with 96% wanting to do something to stop the spread of HIV. Thus far, loss to follow-up has been minimal (0.5%) and immunization compliance has been 100%.

Conclusions: IDUs in Bangkok continue to be at high risk of HIV infection and appear to be highly motivated to enroll and participate in this first international phase III efficacy trial. Results of this trial will provide important information on the protective efficacy of AIDSVAX B/E vaccine against parenteral HIV infection. □

Presented at: the XIII International AIDS Conference, Durban, South Africa, July 2000.

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Kasinee Buchachart



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Apichai Tuanyok



Supalarp Puangsa-art



Pitak Wuthisen



Surapon Yimsamran



Nipon Thanyavanich



Wanchai Maneeboonyong



Natefa Uthaichotiwat



Prasert Rakmanee



Muntana Nakmun



Chotima Charusabha



Supit Sungnoi



Kamornwan Chaipakdee

The Department of Tropical Hygiene is responsible for teaching, training as well as research in the field of epidemiology and hygiene. Most of the research activities related to tropical diseases are being conducted at the Suan Phung Research Unit in Ratchaburi province. The Suan Phung Research Unit, supported by Her Royal Highness Princess Fund, is one of the faculty's research station for conducting research



on tropical diseases. Various activities at the Suan Phung Research Unit, such as the provision of health services for the local people and field epidemiology training for students, are conducted under the supervision of personnel from the Department of Tropical Hygiene.

Suan Phung is a small district in Ratchaburi Province located on the western border of Thailand with Myanmar. It has an area of 2,545 square kilometers, consisting of 7 sub-districts with 8,254 households and a population of 33,972. The population is mainly Thai-Karen of low socio-economic status who carry Thai identity cards. There is one community hospital with fifty beds and a total of 13 health centers. The common health problems of the people living in the area are: malaria, dengue hemorrhagic fever, filariasis, tropical skin diseases, intestinal helminthiasis and malnutrition.

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.
5. Assessment of risk factors of mortality associated with vehicular crashes in a central province of Thailand: before and after enforcement of safety device law, 1994-1998.

TEACHING AND TRAINING COURSES

The Department is responsible for the Faculty's teaching and training courses as well as international training courses in epidemiology.

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 Software 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

1.2 Centre de Formation et de Recherche en Medecine et Santé Tropicales, Hôpital Felix Houphouet-Boigny, Marseille, France.

1.3 Department des Maladies Infectieuses et Tropicales, Hôpital de la Salpêtrière, 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 Philippines, Manila

2.4 Faculty of Public Health, University of Indonesia, Indonesia

2.5 Institute for Medical Research, Malaysia

2.6 Freie Universität Berlin

TRAINING COURSES

Regional Field-based Training Programme in Epidemiology and Control of Tropical Disease, May 22-August 8, 2000 (Supported by WHO)

Training on the Health Mapper for Mekong Countries, Bangkok, Thailand, September 25-29, 2000 (Supported by WHO)

INTERNATIONAL LINKAGES

1. Research

- 1.1 Clinica di Malattie Infetive e Tropicali, Universit Degli Studi Di Brescia



Abstracts

ASSESSMENT OF RISK FACTORS OF MORTALITY ASSOCIATED WITH VEHICULAR CRASHES IN A CENTRAL PROVINCE OF THAILAND: BEFORE AND AFTER ENFORCEMENT OF SAFETY DEVICE LAW, 1994-1998,

Nilarat Premmanisakul

Vehicular crashes are currently one of the most important public health problems in Thailand. They are responsible for 35.3-43.9% of mortality resulting from accidents of all types. The study conducted in the year 1996 revealed a total of 16,268 deaths resulting from vehicular crashes, or 44.5 persons per day or 1.9 persons an hour. It was also revealed that if no immediate and effective measures are taken by the year 2000, vehicular crashes in Thailand will soon claim as many as 8 deaths an hour.

A study conducted during the year of 1996-1997 disclosed that a majority of injuries, i.e., 71.8-73.7%, were found among motorcycle drivers, out of these, 90% did not wear protective helmets. The risk of head injuries, that usually resulted in loss of lives, was found to be 3.5 times more among drivers and passengers who did not wear a protective helmet. This is supported by another study that revealed the reduction of mortality by 27% among those who wore a protective helmet. With this revelation, the Government of Thailand intervened by passing a law on January 1, 1996 enforcing motorcycle drivers and passengers (nationwide) to put on protective helmets while driving.

Thereafter, the government passed another law enforcing all motor car users to fasten their seat belt while driving, so as to further reduce injuries caused by vehicular crashes. There is no report, as to how much will this help to reduce fatal outcome, However, one study revealed that the use

of safety belts reduced the occurrence of injuries by 40-70%.

This study was conducted with the aim of determining the impact of law promulgation enforcing the use of safety devices in reducing the fatal outcome in vehicular crashes. The site of study selected was Saraburi province. The recorded cases of accidents that occurred at Saraburi province from the year 1994 to 1998 were used for this study. Analysis was performed to compare the magnitude of fatal outcome and the various risk factors of fatal accident before and after intervention. For this presentation, only descriptive analysis was performed.

The study revealed that after intervention, there was a reduction in the number of total crashes among motorcycle drivers and not the other group of drivers. The percentage of people using the safety device also showed an increasing trend after law enforcement. Other factors, such as age and sex, also demonstrated a decline. But due to a large number of missing data, this study is not conclusive. Thus, more data will be collected and thereafter, an analytical analysis will be performed to reach a conclusion regarding the effect of law promulgation in reducing the number of fatal cases. □

Presented at: *SEAGTEC Research Forum*, College of Public Health, Manila, Philippines, August 7, 2000.

APPLICATION OF GEOGRAPHICAL INFORMATION SYSTEMS TO EPIDEMIOLOGY AND DISEASE SURVEILLANCE

Singhasivanon P, Chupraphawan S, Kidson C

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The advent of Geographical Information Systems (GIS) has opened up a new dimension in quantitative descriptive epidemiology that can serve a number of objectives, e.g

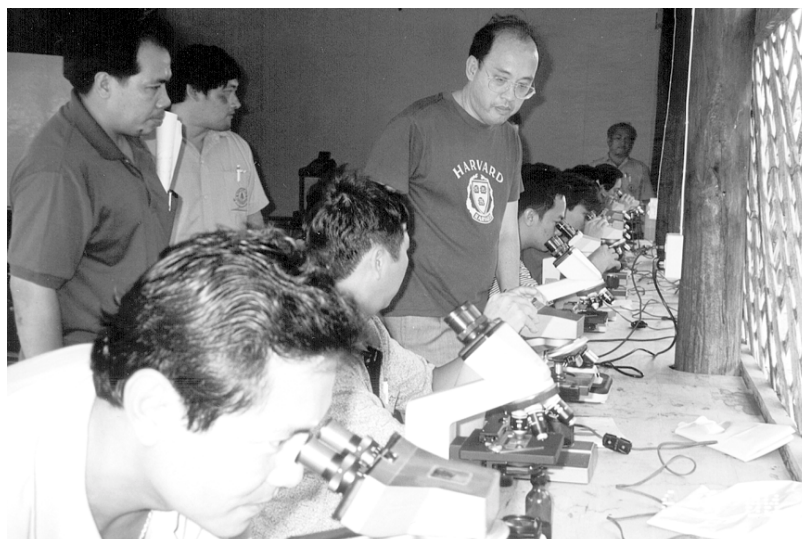
- Correlation of spatial data with population density and migration dynamics
- Delineation of environmental perspectives in relation to climate and climate change
- Interspersion of 3-dimensional satellite imaging with 2 dimensional land use data
- Precise definition of international border areas at macro to micro levels
- Detailed depiction of disease patterns as a function of space, time, population distribution, intervention tactics/ outcomes
- Rapid overview presentation of shifting disease profiles to decision makers
- Correlation of disease distribution with health services provision and economic costs

For vector-borne diseases like malaria, GIS provides a multi-faceted, dynamic picture of short an long term change at local, provincial, national, regional and global levels. This capability has recently been exploited on a multi-country collaborative basis in the Mekong region of Southeast Asia, focused on changing geographic

patterns of falciparum and vivax malaria in relation to international border areas, to population mobility, to multi-drug resistance and to control activities. The joint presentation of data from the 6 Mekong countries provides an information base of coordinated regional development at technical and policy levels; if this type of database can be regularly updated and acted upon it can contribute to substantial relief of the disease burden over time. Similar approaches can be developed for diseases of high priority such as dengue, severe diarrhoea, tuberculosis, HIV/DIDS which have regional connotations in relation to economic development.

Technically, GIS has already reached the stage where it is easy to operate at both field operational and research levels. Internet sharing of data facilitates multi-site downloading for collaborative planning. Given adequate frequency of data collection and entry, internet data sharing and analysis can potentially lead to the development of regionally-based disease surveillance and to useful conjoint effort to contain outbreaks of disease. □

Presented at: the Joint International Tropical Medicine Meeting 2000



A STUDY OF THE MOLECULAR EPIDEMIOLOGY OF *SHIGELLA SONNEI* INFECTIONS IN THE NORTH-WEST OF ENGLAND

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²Centre for Tropical Medical Microbiology, University of Liverpool, UK

Shigella sonnei remains an important public health problem in England, occurring both sporadically and in outbreaks. This study involved the epidemiology of infections caused by *Shigella sonnei* over a 12-month period in the north-west of England, and compared the value of different typing methods for characterising the strains. Two-hundred and twenty-three laboratory confirmed cases of *Shigella sonnei* occurred during the study period. Of four molecular typing methods used, plasmid profiling was the most useful in

distinguishing strains from different outbreaks, and showing associations among localised “endemic” strains.. PFGE, PCR-ribotyping, and ERIC-PCR were less discriminatory, and were not obviously related to epidemiological differences in the cases. The study showed that the relatively simple technique of plasmid profiling can contribute to more effective surveillance and subsequent public health action. □

Presented at: the Joint International Tropical Medicine Meeting 2000

POST-GRADUATE STUDY AT THE FACULTY OF TROPICAL MEDICINE, MAHIDOL UNIVERSITY AND THE ROLE OF SEAMEO TROPMED IN EDUCATION IN THE SOUTHEAST ASIAN REGION

Srivicha Krudsood

The Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand, was established by the Thai Government on 5 April 1960. Its mission is post-graduate teaching through the Bangkok School of Tropical Medicine, medical service through the Hospital for Tropical Diseases, and research. Post-graduate teaching was initially for Thai medical doctors who had obtained the degree of Bachelor of Medicine. The post graduate course was designed especially for those doctors who worked in rural areas in tropical medicine, parasitology and the preventive aspects of endemic diseases. Since that time, the extent and impact of the Faculty’s educational and research activities have extended throughout Southeast Asia and to tropical regions all over the world, and it now serves as an international institute. The Bangkok School of Tropical Medicine, Faculty of Tropical Medicine, offers 5 regular international-post-

graduate programs, taught in English, to doctors, researchers, medical personnel and professionals concerned with tropical medicine and public health. These are the graduate Diploma in Tropical Medicine and Hygiene and Master of Clinical Tropical Medicine (courses for qualified medical doctors only); the Master of Science in Tropical Medicine; Doctor of Philosophy in Tropical Medicine; and Doctor of Philosophy in Clinical Tropical Medicine. Overall, 2,234 students from 42 countries have graduated. Students enrolled in the Faculty’s programs originate from SEAMEO member countries (Brunei Darussalam, Cambodia, Indonesia, Lao People’s Democratic Republic, Malaysia, Myanmar, the Philippines, Singapore, Thailand, and Vietnam) and other countries (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, Romania, Russia, the U.S.A. and Venezuela). In recent years, the number of self-supporting participants has increased markedly. The Faculty of Tropical Medicine is a leader in postgraduate tropical medicine education in the Southeast Asian Region and beyond, together with its collaborative and cooperative programs and linkages in training and research, especially with the Southeast Asian Ministers of Education Organization (SEAMEO) through SEAMEO TROPMED. SEAMEO TROPMED

was established in 1967 with its primary activities being teaching, research and training in tropical medicine and public health, under SEAMEO. The Faculty has been the SEAMEO TROPMED in relation to education, training and research are detailed, as well as emerging regional trends in education and research. The Faculty has ongoing collaborative activities in teaching, research and academic services with more than 25 universities and institutions from 13 countries. The Faculty recently became the Asian Centre of International Parasite Control (ACIPAC). □

Presented at: ASAIHL Conference 2000

MEKONG MALARIA. MALARIA, MULTI-DRUG RESISTANCE AND ECONOMIC DEVELOPMENT IN THE GREATER MEKONG SUBREGION OF SOUTHEAST ASIA

Singhasivanon P, Chupraphawan S, Kidson C, Supavej S, Looreesuwan S, Baimai V, *et al.*

Department of Tropical Hygiene, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

This monograph brings together national malaria databases for 1996, 1997 and 1998 from the 6 countries comprising the Greater Mekong Subregion of Southeast Asia: Cambodia, China (southern provinces), Lao People's Democratic Republic, Myanmar, Thailand, Viet Nam. The objective is to create a regional perspective in what is a global epicenter of drug resistant falciparum malaria, so to enhance the information flow required to improve malaria control on a regional basis in the context of economic and social change. Geographical Information Systems technology has been applied to the regional mapping of total reported malaria cases, malaria incidence, confirmed cases, parasite species distribution. There is great diversity in disease patterns in the 6 countries and at subnational administrative unit area level in each country, so that in the region as a whole there is marked asymmetry in disease distribution, with many areas of high endemicity. Focal expansion of maps in the vicinity of international border areas delineates the differential

trans-border malaria distribution that presents a challenge for disease control. The malaria pattern is also depicted in environmental context against regional elevation and forest cover profiles, which affect mosquito breeding site distribution and agricultural activity. Data on resistance of falciparum malaria to a range of anti-malarial drugs summarise the historical and recent context of resistance development and spread in terms of geography and time frame. Data on population movement across international borders identify the magnitude of a major factor in the dispersal of malaria, including resistant parasite strains. Malaria control involves consideration of microeconomic capacity and operates in the broader context of macroeconomic policy: economic and social profiles of the region are included to provide this perspective. So too are maps depicting major economic development projects in the region, projects that have and will continue to have profound, dynamic impacts on malaria epidemiology. The geographic collation of regional

malaria databases is thus placed in overall geographic, health, environmental and economic perspective. This beginning can form a basis for the development of an effective regional malaria surveillance system in the context of rapidly evolving social and

infrastructural change, leading eventually to a multi-disease surveillance network. □

Published in: *Southeast Asian J Trop Med Public Health* 1999;30 Suppl 4.

HIDDEN *PLASMODIUM FALCIPARUM* INFECTIONS

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Mixed infection of *P. vivax* and *P. falciparum* malaria frequently recorded in field survey. However mixed infection was frequently misdiagnosed as single infection due to low parasite density, difficult species identification and procedure error of microscopic examination. Our previous report showed high rates (32-33%) of *P. vivax* infection following treatment of previously assumed to be only *P. falciparum* infection. In a study

of 992 patients with initial presentation with *P. falciparum*, we found that 104 (10.5%) of patients had *P. falciparum* appearing during 28 days in the hospital (ranged 1-28 days) following chloroquine treatment for *P. vivax*. The potential for *P. falciparum* appearing following elimination of *P. vivax* must be considered in malaria treatment. □

Published in: *Southeast Asian J Trop Med Public Health* 1999.

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

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Before field application of the direct agglutination test (DAT) for leishmaniasis, it was assessed as a diagnostic tool. Fifteen confirmed visceral leishmaniasis cases (bone marrow aspiration positive), 120 tuberculosis, 58 leprosy, 15 malaria, 26 intestinal parasitic infection cases, 24 endemic healthy controls from adjacent to the study area, and 18 controls from Kathmandu (who had never visited the VL endemic areas) were tested for anti-leishmanial antibody agglutination titers. Two of the tuberculosis cases were positive for anti-leishmanial agglutinating antibodies at 1:800. All the visceral leishmaniasis confirmed cases were reactive to anti-leishmanial antibody at > or =

1:3,200. Other specimens were negative for serology. The sensitivity of the direct agglutination test was 100% and the specificity was 99.2%. The direct agglutination test had positive and negative predictive values of 100% and 99.2% respectively. The direct agglutination test has been found to be simple, rapid, reliable, economic, safe and adaptable to micro-techniques using microtiter plates. It is specific and sensitive. The direct agglutination test is simple enough for it to be performed in a field laboratory. □

Published in: *Southeast Asian J Trop Med Public Health* 1999.

PRIMARY VERIFICATION: IS THE TRISS APPROPRIATE FOR THAILAND?

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The Trauma and Injury Severity Score (TRISS) is a well-accepted model used to evaluate quality of trauma care in America. This research aims to study whether TRISS can be applied to evaluate trauma care and classify outcome of road traffic injury patients in Thailand. A retrospective study was used to review the Injury Surveillance System database from Thailand from 1st January to 31st December 1996. Study subjects were severe road traffic injury patients with blunt injuries. The TRISS model was applied to compute the survival probability for each patient. The chi-square goodness-of-fit was used to compare the survival probability distribution between the American Major Trauma Outcome of Study (MTOS) and the road traffic injuries in Thailand. Further the accuracy, sensitivity and specificity of the survival prediction by TRISS were evaluated. The

distribution of survival probability between American trauma patients and Thai road traffic injury patients was significantly different ($\chi^2=544.512$, $df=5$, $p\text{ value}<0.00001$). The TRISS model had high accuracy and sensitivity, but low specificity, in predicting the survival of Thai road traffic injuries. MTOS and Thai road traffic injuries have different distributions for various factors such as Revised Trauma Score (RTS), Injury Severity Score (ISS), and age which effect the injury survival. Due to these factors the distribution of survival probability between MTOS and Thai road traffic injuries is also significant different. By applying TRISS, the survival prediction of Thai road traffic injuries resulted in a high number of false positive cases. □

Manuscript in preparation for publication.

ALTERNATIVE COEFFICIENTS OF THE TRISS MODEL IN THAILAND

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The Trauma and Injury Severity Score (TRISS) model is used worldwide to evaluate trauma care, but is an unsuitable model to use for other data sets. The purpose of this study is to develop a survival probability model based on road traffic injuries in Thailand and test its appreciative for the prediction of survival in this country. retrospective analysis study of road traffic injuries in Thailand was utilized during 1st January to 31st

December 1996. Their physical indices were used to generate a new Revised Trauma Score (new RTS) by using logistic regression method. The accuracy, sensitivity and specificity of the original RTS and new TRS were compared. Only the study subjects with blunt injury were divided into a model and a test group. Using the logistic regression method, survival probability was developed in the model group. The best survival probability model was the

model with high Receiver Operating Characteristics (ROC) in the test group. The TRISS and new survival model were used to estimate the survival probability of each of study subject in the test group. Accuracy, sensitivity and specificity were used to compare the classification of the TRISS and new survival model. The specificity rate of the new RTS was higher than the original RTS, while accuracy and sensitivity were almost the same. The new survival probability contained new RTS, ISS and age of patient the same with the original TRISS model. The accuracy and

sensitivity of new survival probability or Thai-TRISS model were comparable to the original TRISS model when applying it to the Thai injuries, but specificity was almost two times higher than the original TRISS model. The new survival probability model for Thailand has the same variables as the TRISS model but the coefficients were different. Its classification was more precise than the original TRISS model. □

Manuscript in preparation for publication.

A COMPARATIVE CLINICAL TRIAL OF A COMBINATION OF ARTESUNATE AND MEFLUQUINE VERSUS A COMBINATION OF QUININE AND TETRACYCLINE FOR THE TREATMENT OF ACUTE UNCOMPLICATED FALCIPARUM MALARIA IN SOMDEJ PRACHAO TAKSIN MAHARAJ HOSPITAL, TAK PROVINCE

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¹Department of Medicine, Somdej Prachao Taksin Maharaj Hospital, Tak, Thailand

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

A combination of quinine and tetracycline is a standard regimen for the treatment of acute uncomplicated falciparum malaria. Frequent administration due to its short half-life (6-8 hours), long duration of drug administration (7 days), and side effects of quinine (cinchonism e.g. tinnitus, nausea, vomiting, palpitation, etc) may cause the patient not to complete the whole course of treatment and recrudescence ensues. A previous study of artesunate followed by mefloquine given once daily for 3 days gave a greater than 95% cure rate. The objective of this study is to determine the efficacy and tolerability of a combination of artesunate and mefloquine (ASM group) compared with a combination of quinine and tetracycline (QT group) in 120 uncomplicated falciparum malaria cases. In the ASM group, 60 patients received 200 mg artesunate and 312.5 mg mefloquine 12-hourly for 2 days (a total of 800 mg artesunate and 1,250 mg mefloquine). Another 60 cases received 600 mg quinine sulfate 8-hourly and 250 mg tetracycline

6-hourly for 7 days. Both groups were admitted to the Somdejprachaotaksinmaharaj Hospital, Tak Province until either parasite negative or until there were no clinical signs or symptoms of malaria 108 cases completed the 28-day follow-up. The results showed a similar 28-day cure rate (96.2% in the ASM group vs 94.6% in the QT group), however side effects such as tinnitus (25.8% vs 83.3%), vomiting (51.6% vs 80.6%), and palpitation (32.3% vs 80.6%) were less common in the ASM group. In addition, parasite clearance time (PCT) and the time taken to produce clinical improvement were significantly shorter in the ASM group ($p < 0.05$). In conclusion, a combination of artesunate and mefloquine may be an alternative regimen for treatment of uncomplicated falciparum malaria especially for outpatients in remote areas. In addition, this will shorten the duration of patients' hospital stay. □

Published in: *J Trop Med Parasitol* 1999.

ASCARIS LUMBRICOIDES INFECTION IS ASSOCIATED WITH PROTECTION FROM CEREBRAL MALARIA

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Following reports of increased IgE in severe malaria and hypothesizing that helminth coinfections could modify its outcome, we conducted a retrospective case-control study to establish whether helminths affect the evolution of *Plasmodium falciparum* malaria. Some 182 severe cases, 315 mild controls and 40 controls with circulating schizonts were examined for intestinal helminths. Comparing cerebral malaria with mild controls, *Ascaris lumbricoides* was associated with a protective adjusted odds ratio (OR) of 0.58 (0.32-1.03) $P = 0.06$, for coinfection with *Ascaris* and *Necator americanus*, OR = 0.39 (0.17-0.88) $P = 0.02$. Protection followed a dose-effect trend ($P = 0.008$).

When comparing cerebral malaria cases and controls with circulating schizonts the OR was 0.25 (0.009-0.67) $P = 0.006$. We hypothesized that *Ascaris* infected patients may have had decreased cytoadherence, possibly through endothelial cell receptor downregulation and/or decreased splenic clearance leading to the absence of selection of virulent *P. falciparum* strains. IgE-anti-IgE immune complexes resulting from helminth preinfection may have an important role in influencing clinical presentation of severe malaria, and in establishing malaria tolerance, through the CD23/NO pathway. □

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EFFICACY OF PRIMAQUINE REGIMENS FOR PRIMAQUINE-RESISTANT *PLASMODIUM VIVAX* MALARIA IN THAILAND

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To define the current efficacy of Fansidar (F. Hoffmann-La Roche Ltd., Basel Switzerland) (pyrimethamine and sulfadoxine), primaquine in a high dose, and artesunate for treating acute *Plasmodium vivax* malaria, we conducted a comparative clinical trial of these 3 drugs in an open-label study. Patients (15-65 years old) were assigned to 1 of 4 treatments regimens in a serial order. Ninety percent of the patients were infected at Thailand-Myanmar border. Patients in group I (n = 23) received Fansidar (3 tablets, 75 mg of pyrimethamine and 1,500 mg of sulfadoxine, a single dose on the first day), group II (n = 23) received

Fansidar (3 tablets, 75 mg of pyrimethamine and 1,500 mg of sulfadoxine, a single dose on the first day) and then received primaquine (30 mg a day for 14 days), group III (n = 23) received primaquine (30 mg a day for 14 days), and group IV (n = 23) received artesunate (200 mg once a day for 3 days) and then primaquine (30 mg a day for 14 days). Cure rates on day 28 of follow-up were 40%, 100%, 100%, and 100% in groups I, II, III, and IV, respectively. There were 4 and 5 patients in group I showing post-treatment reappearance of parasitemia at $t = 16$ days and between 17 and 28 days, respectively. Patients in the other 3 groups showed negative parasitemias within

7 days after treatment. Artesunate plus primaquine (group IV) cleared parasitemia faster than the other 3 regimens. There is a high proportion of ineffectiveness of Fansidar for treatment of *P. vivax* malaria and it should be no longer used for treatment of *P. vivax* malaria acquired at the Thailand-Myanmar

border. A high dose of primaquine is safe and effective in the treatment of *P. vivax* malaria during the 28-day follow-up period. □

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FREQUENCY OF PRURITUS IN *PLASMODIUM VIVAX* MALARIA PATIENTS TREATED WITH CHLOROQUINE IN THAILAND

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Chloroquine-induced itch in black-skinned African malaria patients is common and frequently leads to poor compliance or treatment defaulting. To assess the frequency and severity of chloroquine-induced pruritus in an Asian population, we reviewed case records of 1189 *Plasmodium vivax* malaria patients treated with chloroquine (25 mg/kg over 3 days) at the Bangkok Hospital for Tropical Diseases from 1992 through 1997. The majority of patients were Thais or ethnic Burmese (light brown skin), referred from the western border of Thailand. Overall, there were 23 patients (1.9%) with complaints of pruritus during chloroquine therapy. Of these, 12 (52%) had palm and sole involvement, eight (35%) had generalized pruritus including the palms and soles, and three (13%) had palm itching only. One patient developed pruritus on the palms and soles on two

consecutive admissions. The pruritus did not interfere with daily activity, was reduced in intensity by anti-histamine therapy, and did not affect the patient's willingness to complete the chloroquine regimen. Therapeutic responses in the 23 patients with chloroquine itch was similar to those without itch. Among the itch patients, there was no association with gender or level of parasitaemias. Our findings indicate that the frequency of chloroquine-induced pruritus in Asian patients treated with chloroquine for *P. vivax* malaria is low in comparison with black-skinned Africans. This may be related to pharmacogenetic factors, the infective *Plasmodium* species, drug metabolism or drug-parasite interactions, or a lower affinity of chloroquine for less pigmented skin. □

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CONTRASTING FUNCTIONS OF IgG AND IgE ANTIMALARIAL ANTIBODIES IN UNCOMPLICATED AND SEVERE *PLASMODIUM FALCIPARUM* MALARIA

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Plasmodial infection results in a significant elevation of the blood concentrations of immunoglobulins including IgE. Two well-characterized groups of adult Thai patients with either uncomplicated or severe *Plasmodium falciparum* malaria were studied over a period of four weeks. The mean parasitemias were approximately three-fold higher in patients with severe malaria than in those with uncomplicated disease. The mean concentrations of both total IgG and IgE

antiplasmodial antibodies tended to be highest in the group with uncomplicated disease while total IgE and IgE antibodies were higher in the group with severe disease. The IgE antibodies detected in approximately 65% of the patients were positively correlated to parasitemia. These results suggest that antiplasmodial IgG antibodies are involved in reducing the severity of *P. falciparum* malaria, while IgE antibodies may contribute to the pathogenesis of this infection. □

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PROGNOSTIC SIGNIFICANCE OF SKIN AND SUBCUTANEOUS FAT SEQUESTRATION OF PARASITES IN SEVERE *FALCIPARUM* MALARIA

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Intradermal blood smear, histopathologic and immunohistologic studies were performed in severe malaria (n=10) and uncomplicated malaria (n=10) patients during positive parasitemia and within 6 hours after negative parasitemia by finger prick smears. Intradermal blood smears showed asexual forms and intraleukocytic pigments when finger prick blood smears showed negative results; however intradermal blood smear did not indicate disease severity within 6 hours after negative parasitemia by finger prick. Histopathologic findings showed 15 fold higher parasitized red blood cells sequestered in vessels of subcutaneous fatty tissue in severe malaria than in uncomplicated

malaria (p<0.001) and may indicated disease severity. A panel of polyclonal antibodies against cytokines applied to skin biopsies clearly detected a higher titer against tumor necrosis factor-alpha (TNF α) and interleukin-10 (IL-10) in dermal vessels and stratum granulosum respectively, in severe malaria compared with uncomplicated malaria. Results of the study suggest that histopathology and immuno-histology of skin and subcutaneous fatty tissue may indicate prognostic severity of malaria and may be associated with focal accumulation of cytokines. □

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CURRENT RESEARCH ACTIVITIES

Research activities of the Department of Tropical Nutrition and Food Science are concerned with nutritional problems in Thailand such as micronutrient deficiencies, lifestyle and dietary patterns of different age groups, the impact of overnutrition, oxidative stress and antioxidants in relation to health, and the effect of smoking on work performance in relation to the phenotype of α_1 -antitrypsin. Furthermore, molecular biology in lung cancer, e.g. identification of gene mutation in Thai patients, is investigated. Food and health relationship in populations of Asian countries are of interest for study and the data will be compared.

At the present time, using food practice as the way to disease prevention and treatment, is particularly interesting. This is part of the project on development of food and medicinal plants.

The topics of the current research projects are as follows:

1. Food and health relationship in the 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
6. The effect of smoking on work performance in relation to the phenotype of α_1 -antitrypsin
7. Identification of gene mutation in lung cancer cells in Thai patients
8. Molecular biology of carcinogenesis in lung cancer
9. Development of food and/or medicinal plants

Abstracts

ERYTHROCYTE ANTIOXIDANT ENZYMES AND BLOOD PRESSURE IN RELATION TO OVERWEIGHT AND OBESE THAI IN BANGKOK

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The specific activities of antioxidant enzymes, (e.g. superoxide dismutases (SOD), glutathione peroxidase (GPX) and catalase (CAT)), anthropometric measurements, including waist/hip ratio of 48 male and 167 female overweight (body mass index (BMI) $\geq 25.0 \text{ kg/m}^2$) compared with a 26 male and 80 female control group (BMI = 18.5-24.9 kg/m^2) Thai volunteers who attended the Out-patient Department, General Practice Section, Rajvithi Hospital, Bangkok, for a physical check-up during March-October, 1998, were investigated. There was a slightly significant difference between the median age of the sexes. The medians of height, weight, and waist/hip ratio in males were significantly higher than those in female overweight and obese subjects. The median of arm circumference (AC), mid arm muscle circumference (MAMC) in males was significantly higher than those in female overweight and obese subjects ($p < 0.05$). The prevalence of hypertension based on systolic and diastolic blood pressure of $\geq 160/\geq 95 \text{ mmHg}$, were 8.3% and 37.5% for males and 5.4% and 18.6% for females, respectively. There was no significant difference between the median

of antioxidant enzymes (SOD, GPX and CAT) between the sexes. No significant differences in the antioxidant enzymes in male overweight/obese and normal controls were presented, whereas antioxidant enzymes in female overweight/obese were statistically lower than control females ($p < 0.05$). A significantly higher SOD, GPX, and CAT status was observed in normal subjects compared with overweight/obese subjects ($p < 0.01$). A higher prevalence of SOD 2866 U/gHb, GPX $\leq 15.96 \text{ U/gHb}$ in females was found, compared with males. High percentage of lower catalase (CAT $\leq 19.2 \times 10^4 \text{ IU/gHb}$) was found in both sexes (64.5% in males and 64.5% in females). In obese subjects (BMI $\geq 30.0 \text{ kg/m}^2$), there were significantly positive relationships between systolic and diastolic blood pressure, systolic blood pressure and waist/hip ratio, and SOD could be related to weight, BMI as well as GPX and CAT, whereas the opposite result was observed for age and SOD. □

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ACTIVITY, DIETARY INTAKE, AND ANTHROPOMETRY OF AN INFORMAL SOCIAL GROUP OF THAI ELDERLY IN BANGKOK

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Socio-demographic, anthropometric assessment, dietary pattern, lifestyle and 3 day dietary records of 384 Thai elderly (55 males and 329 females) aged 60-94 years, who were members of an informal social activity groups, were investigated. Most males were married (88.9%) whereas 42.9% of females were widowed. Nearly all of the elderly lived with their relatives. Only 3% of the elderly had never attended school. Males smoked or had smoked in the past, more than the female elderly, and their drinking habits were similar to their smoking habits. The health situation of the individuals under investigation seemed to be satisfactory, however, the most frequent diseases among the elderly were chronic diseases such as hypertension, hyperlipidemia and diabetes mellitus. No statistically significant difference in body mass index (BMI), arm circumference (AMC), and hip circumference was found between males and females. Weight, height, mid-arm muscle circumference (MAMC), armspan, waist, waist/hip

ratio and blood pressure of the males were significantly higher than those of the females. Tricep skinfold thickness (TSF) and subscapular skinfold thickness (SST) were lower for males in comparison with females. 54.5% of males and 50.5% of females were found to be overnourished and less than 2% of all the individuals under investigation were undernourished. There were no significant differences for all nutrients between the males and females. Intake of dietary energy from food of males and females were 69.8% and 75.5 % respectively, compared with Thai RDA. When calculating the intake of macro-nutrients as the percentage of total calorie intake, about 17% of the total calorie intake is attributed to fat, 13% to protein and 70% to carbohydrate for males, whereas the figures for females were 17%, 15%, and 68%. Intake of calcium, phosphorus, vitamin B1, B2 and niacin seem to be inadequate for both sexes. □

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THE EFFECTS OF SMOKING ON WORK PERFORMANCE IN RELATION TO THE PHENOTYPE OF ALPHA-1-ANTITRYPSIN

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Serum alpha-1-antitrypsin, vitamin C, and thiocyanate including alpha-1-antitrypsin phenotype in 123 male smokers and 66 male non-smokers were investigated. There were statistically significantly higher levels of serum alpha-1-antitrypsin and thiocyanate concentrations in smokers than in non-smokers. The thiocyanate level correlated with the duration and quantity of cigarette smoking. However, vitamin C concentration in smokers was found to be statistically significantly lower when compared with non-smokers. Vitamin C might be used to detoxify some free radicals and cyanide derived from cigarettes. The prevalence of non-MM alpha-1-

antitrypsin phenotype in smokers was not significantly different from non-smokers, but the smokers with non-MM had a significantly lower vitamin C level than non smokers of the same phenotype. In addition, smokers with non-MM phenotype reported a higher prevalence of illness from respiratory tract infections within the past 3 months. Smokers with an abnormal phenotype of serum protein alpha-1-antitrypsin are likely to have a higher risk of suffering from respiratory tract infections or other related diseases. □

Report to Institute of Tobacco Control, Department of Medical Services, Ministry of Public Health, Thailand.

DIETARY PATTERN, LIFESTYLE AND NUTRITIONAL STATUS OF HEALTH SCIENCE UNIVERSITY STUDENTS IN BANGKOK

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Sixty-two Thai university students, comprising 22 males and 40 females, aged between 19-24 years, were randomly selected from students of the Faculty of Medical Technology, Rangsit University, Bangkok. The median age for the males was 22 yrs and for the females 21 yrs. Anthropometric assessment, dietary pattern, lifestyle and prospective seven-day 24-hr records were performed, as well as the determination of diastolic and systolic blood pressure. Cigarette smoking, consumption of alcohol and medicines used, were also recorded. 27.3% (6 of 22) had a smoking habit, and 50% (11 of 22) had a drinking

habit. However, no females had a smoking habit, and only 10% (4 of 40) had a history of drinking alcohol. About 30-50% of all 62 students had a history of drinking tea and coffee, and 11.3% (7 of 62) also took vitamin and mineral supplement tablets. The systolic and diastolic blood pressure of all students were found to be normal (122/67 mmHg in males and 110/80 mmHg in females).

Due to attrition, 20 of the 62 total students who started in the study dropped out, leaving 42 remaining. 60% (28 of 42) of these students irregularly skipped breakfast. Total calorie intakes per day were 1196 kilocalories for males and 1225

kilocalories for females. About 11%, 15% and 74% of fat, protein and carbohydrate of the total calories per day were taken by those students. A lower fiber and iron intake (1.4 gm. and 10.3 mg. in males, and 2.1 gm and 11.3 mg. in females) was observed. The male students were statistically higher in weight, height, BMI, AC and MAMC than the female

students. 9.1% and 10% of males and females were undernourished (body mass index (BMI) $<18.5 \text{ kg/m}^2$) while 22.7% of male and 5% of females were found to be overnourished (BMI $>25.0 \text{ kg/m}^2$). □

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CHANGING TRENDS IN DIETARY HABITS IN AGING PROCESS THAI'S CASE

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It is estimated that in the year 1998, in the Kingdom of Thailand approximately 2.3 million males and 2.7 million females were over 60 years of age. This amounts to approximately 8.5% of the total population. It seems that the proportion of elderly among the total population of the country is increasing rapidly. Up to now, information on the health and nutritional status of the elderly on a nation-wide basis is lacking. So far, scattered results have been obtained by conducting various research studies, undertaken by a number of academic institutions without co-ordination, with different research objectives and different methodologies. From those results it appears that there are distinct differences between the elderly belonging to different socio-economic strata of the population. The elderly who are still living a more traditional lifestyle within their families are predominantly doing quite well, and in general have been found to be sufficiently nourished. Generally, family members try to convince elderly relatives not to change their eating behavior drastically and to avoid eating disorders. The majority of the elderly eat three times a day or more. For breakfast, usually rice with side dishes are taken together with coffee,

milk and noodles. For lunch, cooked meals are consumed based on rice and chopped meat with vegetables. Lunch is probably the most important meal of the day. Fruits and sweet desserts are consumed for lunch as well. Dinner is normally a light meal. In this group, overnutrition and obesity were quite common, sometimes associated with subclinical vitamin deficiencies, which however had been found not to be serious. Elevated serum cholesterol is less common, but high triglycerides are found more often. It appears that an increasing proportion of the well-to-do elderly are suffering from non-insulin dependent diabetes mellitus (NIDDM) and hypertension. Due to rapid industrialisation in the past decades, more and more aged people however are living in care homes and institutions for the elderly, or are no longer being cared for intensively by their families. In these groups, malnutrition in terms of undernutrition and anemia are not uncommon, and vitamin deficiencies are prevalent. □

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MOLECULAR CHARACTERIZATION OF MITOCHONDRIA IN ASEQUAL AND SEXUAL BLOOD STAGES OF *PLASMODIUM FALCIPARUM*

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Molecular mechanisms that regulate gene expression during development of asexual stage to sexual stage of *Plasmodium falciparum* in the human erythrocyte are largely unknown. There were apparent variations in ultrastructural characteristics of the mitochondrion between the two developing stages. The asexual stage's mitochondrion had developed less than that of the sexual stage. The respiratory complexes of the mitochondrial electron transport system in the asexual stage were ~8-10 times less active than those in the sexual stage. Using quantitative polymerase chain reaction to amplify the cytochrome b gene encoding a subunit of mitochondrial cytochrome c reductase, the amount of the cytochrome b gene of the sexual stage was calculated to be ~3 times higher than

that obtained from the asexual stage. Moreover, using quantitative reverse-transcription polymerase chain reaction, a relatively high level of ~1.3-kb transcript mRNA of the cytochrome b gene was observed in the sexual stage compared to the asexual stage. A known single-copy chromosomal dihydrofolate reductase gene was found to have a similar amount in the two stages. These results suggest that the copy number of the mitochondrial gene, including transcriptional and translational mechanisms, plays a major regulatory role in differential expression during the development of the asexual to sexual stage of *P. falciparum* in the human cell. □

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LEPTIN CONCENTRATION IN RELATION TO BODY MASS INDEX (BMI) AND HEMATOLOGICAL MEASUREMENTS IN THAI OBESE AND OVERWEIGHT SUBJECTS

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The weight, height and body mass index (BMI), including waist/hip ratio, serum leptin and hematological parameters of 48 male and 166 female overweight (BMI ≥ 25.00) Thai volunteers who came for a physical check-up at the Out-

patient Department, General Practice Section, Rajvithi Hospital, Bangkok during the period March-October 1998, were investigated. There were statistically significantly higher levels of serum leptin, mean corpuscular (MCHC) and mean

corpuscular volume (MCV) in the overweight than in the control subjects. The median serum leptin concentration in overweight subjects was 19.6 (2.0-60.0 ng/ml) compared with 9.0 (range 1.0-30.0 ng/ml) in the control subjects ($p < 0.001$). The medians of leptin in overweight and obese males were significantly higher than those of overweight and obese females. 66.7% (32 out of 48) of overweight and obese males were found to have elevated leptin levels, while 87.3% (145 out of 166) were found in overweight and obese females. Anemia was found

in 18.7% of female overweight and obese subjects, using hemoglobin as an indicator. Significant associations were found between weight, height, BMI, waist, hip, waist/hip ratio, hemoglobin, hematocrit, and serum leptin in both male and female overweight subjects. A negative correlation was found between serum leptin and hemoglobin, and hematocrit in both overweight and obese subjects. □

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SERUM LEPTIN AND LIPID PROFILES IN THAI OBESE AND OVERWEIGHT SUBJECTS

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The weight, height, body mass index (BMI), waist/hip ratio, serum leptin and lipid profiles of 48 overweight (BMI ≥ 25.00) Thai males and 166 overweight Thai females, compared with a 26 males and 81 females in a control group (BMI = 18.5-24.9 kg/m²), were investigated. Subjects for the study were those persons who turned up regularly for physical check-ups at the Out-patient Department, General Practice Section of the Rajvithi Hospital, Bangkok. The study was conducted between March-October, 1998. Statistically significantly higher levels of serum leptin, cholesterol, LDL-C, LDL-C/HDL-C ratio and triglyceride were found in the overweight compared with the control subjects. The median serum leptin concentration in overweight subjects was 19.6 (2.0-60.0 ng/ml) compared with 9.0 (range 1.0-30.0 ng/ml) in the control subjects ($p < 0.001$). The median values of leptin serum concentration in the overweight and obese males were

significantly higher than those of the overweight and obese females. A total of 66.7% (32 out of 48) of the overweight and obese males had elevated leptin levels, while elevated leptin levels were found in 87.3% (145 out of 166) of the overweight and obese females. A total of 18.8% and 21.1% of the overweight and obese males and females respectively had cholesterol concentrations of ≥ 6.48 mmol/l. However, the prevalence of low HDL-C (HDL-C ≥ 0.91 mmol/l) was found to be 41.7% in the overweight and obese males and 4.2% in the overweight and obese females. Statistically significant associations were found between weight, height, BMI, waist, hip, waist/hip ratio, HDL-C, and serum leptin in both overweight male and female subjects. A negative correlation was found between serum leptin and LDL-C/HDL-C ratio in both the overweight and obese subjects. □

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PROMOTION OF THE HEALTH OF RURAL WOMEN TOWARDS SAFE MOTHERHOOD – AN INTERVENTION PROJECT IN NORTHEAST THAILAND

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An intervention project focusing on the health of women in the reproductive age were conducted in three districts of the Khon Kaen province, Northeast Thailand between 1991 and 1996. The main emphasis was laid on improving reproductive health, the nutritional status including the iron deficiency anaemia (IDA) as well as iodine deficiency disorder (IDD), and the parasitic diseases, liver fluke (*Opisthorchis viverrini*) and hookworm. For implementation a community based Primary Health Care approach was used including the training in health matters of health officials, primary health care workers and villagers as well as enhancing health education and the dissemination of health information. The health delivery system was encouraged to take appropriate actions such as in the treatment of parasitic diseases and the control of IDA and IDD. Monitoring was done on a regular basis. The outcome of the project was assessed by comparing baseline data compiled from a random sample of the target population with the results of the final evaluation. An attempt to compare results obtained from villages within and outside of the project area failed most probably because of spill over effects. A number of important indicators on family planning and mother and child health care

improved during the time the project was implemented, this included practising family planning, and participation in antenatal care (ANC). Also the proportion of females being pregnant for the first time when 20 years or older increased. Child-raising also improved in that almost all females gave colostrum to their babies by this time. Almost 75% of the women breast-fed their children. Improvements occurred in the nutritional status as far as the micronutrients iron and iodine is concerned however the overall nutritional status of females as far as undernutrition is concerned did not change, however a rather high proportion of females were found to be overnourished. The project failed in reducing abortion and the proportion of females becoming pregnant when they are 18 years old or younger. It was also not possible to improve the usage of postnatal care (PNC). As anticipated, the results achieved so far are most suitable in serving as a training ground and providing a favourable example to improve family planning, mother and child health care, and also the general health of females in the region, particularly in the neighbouring countries, such as in Lao PDR Cambodia and Vietnam. □

Submitted to: *Southeast Asian J Trop Med Public Health* 2000

NUTRITIONAL STATUS OF PRESCHOOL CHILDREN AND WOMEN IN SELECTED VILLAGES IN SAVANNAKHET PROVINCE, LAO PDR - AN INTERVENTION TRIAL

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A project to promote the health and nutritional status of women and pre-school children was started from 1995 to 1997 in three villages in the Savannakhet province, Lao PDR. One village served as control. In 1995, for the baseline survey, 456 females, and in 1997, for the final evaluation, 363 females from the four villages volunteered for further investigations. An attempt was undertaken to involve all females in the reproductive age residing in the villages. At the same time also the nutritional status of 321 and about 540 randomly selected pre-school children respectively was also assessed through physical examination and anthropometric measurements. Intervention measures included introducing growth charts and taking regular anthropometric measurements of women in the reproductive age and of pre-school children. Training in nutritional aspects such as giving colostrum to newborns, prepare proper weaning food and supplementary feeding, animal-raising and home gardening was also introduced and provided to health personnel, village leaders and in women clubs. Special

attention was given to the control of acute infectious diseases. The conventional EPI program was enforced as well. Health education in matters of mother and child health care was also provided. The proportion of undernourished women was rather high at about 15%. For pre-school children, the proportion of wasting was around 5%, and of stunting 50% and above. Intervention did not improve the nutritional status either of the women or of the children. It was concluded that the time span of two years is too short for a decrease in the proportion of undernourishment to be observed. An improvement was achieved for some indicators of mother and child health care. This seems to indicate the population's willingness to follow suggestions to improve their health. Most probably, if attempts to improve the nutritional status were continued, an improvement in this aspect could also be observed, if the population can be encouraged to take actions and develop initiatives by themselves. □

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IODINE CONTENT IN COW'S MILK, SOY BEAN MILK AND MILK PRODUCTS

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The iodine content of cow's milk, milk products and soy bean milk were investigated. The results show that the iodine content in cow milk and milk products are significantly higher compared to soybean milk ($p < 0.05$). The highest iodine concentration was found in ultra high temperature (UHT) cow's milk. Sterilization and pasturization do not alter iodine content of milk and milk products. □

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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 pathology in AIDS, including immunohistochemistry study
4. Evaluation of stool samples in HIV infected patients
5. Opportunistic infections in AIDS

Abstracts

SKELETAL MUSCLE INVOLVEMENT IN FALCIPARUM MALARIA: BIOCHEMICAL AND ULTRASTRUCTURAL STUDY

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Biochemical evidence of skeletal muscle damage is common in malaria, but rhabdomyolysis appears to be rare. To investigate the relationship between serum creatine kinase and myoglobin levels, muscle histology, and renal function in *Plasmodium falciparum* infections, we studied 13 patients with uncomplicated malaria, 13 with severe noncerebral malaria, and 10 with cerebral malaria. A muscle biopsy specimen was obtained from each patient for light microscopy and electron microscopy. Mean serum creatine kinase concentrations \pm SD were raised but similar for the three groups (258 ± 277 , 149 ± 158 , and 203 ± 197 U/L, respectively; $P = .5$). The mean serum

myoglobin level \pm SD was highest in cerebral malaria (457 ± 246 vs. 170 ± 150 and 209 ± 125 ng/mL in uncomplicated and severe malaria, respectively; $P < .01$) and correlated with the mean serum creatinine level ($r = .39$ for 36 patients; $P = .02$). The number of intravascular parasites, proportion of mature forms, and glycogen depletion were highest in biopsy specimens from patients with cerebral malaria. Myonecrosis was not observed. Muscle appears to be an important site for *P. falciparum* sequestration, which could contribute to metabolic and renal complications. □

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ABSENCE OF KNOB ON PARASITIZED RED BLOOD CELLS IN A SPLENECTOMIZED PATIENT IN FATAL FALCIPARUM MALARIA

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We present a case report of fatal falciparum malaria of a splenectomized adult Thai patient. The patient developed high peripheral parasitaemia and showed signs of severe malaria with multiorgans involvement. Ultrastructure of *Plasmodium falciparum*-infected red blood cells in fatal splenectomized patient and pathological features are reported for the first time with special emphasis on the role of the spleen as a modulating cytoadherence phenotype of parasitized red blood cells (PRBC). In this patient, adherence of the PRBC to the vascular endothelium of brain, kidney and lung including blood circulating cells, was noted, despite the absence of knob on the surface of the PRBC. □

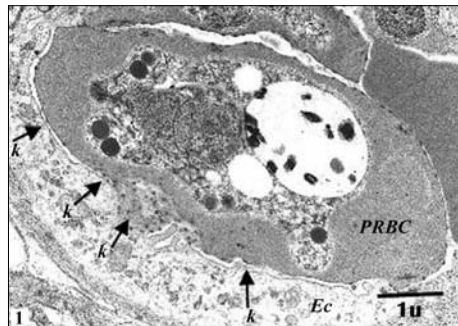


Figure 1
Sequestration of *Plasmodium falciparum*-infected red blood cell (PRBC) to the endothelial cell (Ec) of a cerebral microvessel, is mediated by contacts between electron dense knobs (k) on its surface (arrows).

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THE DISCREPANCY BETWEEN MALARIA PARASITE IN THE BRAIN AND PERIPHERAL BLOOD PARASITAEMIA

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In severe and fatal *Plasmodium falciparum* malaria, sometimes no parasites can be found in peripheral blood smears. This may be explained by previous antimalarial treatment or by sequestration of parasitized red blood cells (PRBC) in deep vascular beds. Sequestration is thought to

cause much of the pathology of severe falciparum malaria. It also accounts for the discrepancy between peripheral blood parasitaemia and the total body parasite burden.

We report here a quantitative ultrastructural analysis of microvascular sequestration of malaria

parasites in the brains of 50 patients who died from severe malaria, compared with the peripheral parasite counts.

The parasite count in the brain was significantly higher than in the peripheral blood. Significantly more PRBC sequestration was seen in the cerebrum of cerebral malaria patients (CM) compared to non-cerebral cases (NCM) ($p=0.039$). Within the CM group there was a marked trend for more mature stages when sequestered parasites were seen. The median (range) ratio of the proportion of PRBC in

the brain to the peripheral blood parasitaemia was higher in the CM group [66.1(1.6-1618)] than in the NCM group [34.9(1.4-981.2)] ($p=0.045$).

This study provides sequestration index reflecting the proportion of PRBC sequestered in the microvasculature and hidden from the examining microscopist, and might therefore provide important prognostic information. □

This study was supported by The Wellcome Trust of Great Britain and The Faculty of Tropical Medicine, Mahidol University.

CYTOKINES ASSOCIATED WITH PATHOLOGY IN THE BRAIN TISSUE OF FATAL MALARIA

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Cytoadherence of *Plasmodium falciparum*-infected erythrocytes to the brain microvascular endothelial cells is believed to be an important cause of circulatory blockage in cerebral malaria. Cytokines released during acute infection may activate brain endothelial cells leading to increased binding of infected erythrocytes in the brain and reduced cerebral blood flow. This effect may be direct and more potent with the tissue-localized cytokines in the brain. In order to establish this relationship, brain tissues of cerebral and noncerebral malaria were compared. The most prominent histopathologic changes in the brain included edema, neuronal degeneration, ring hemorrhage, and percentage of parasitized erythrocytes sequestration were observed in

cerebral malaria. Immunohistochemical staining of the brain sections demonstrated that tissue-localized TNF- α , IFN- γ , IL-1 β , and IL-10 were associated with the histopathology. However, IL-4 was the only cytokine presented at moderate level in the brain tissue of noncerebral malaria which histopathology was the least. No tissue-localized cytokine was observed in the brain of *P. vivax* infection or of the car accident control cases. □

This work received financial support from The Thailand Research Fund (TRF) for the development of research in Thailand. Rachanee Udomsangpetch is a TRF-Research Scholar.

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INDUCIBLE NITRIC OXIDE SYNTHASE EXPRESSION IS INCREASED IN THE BRAIN IN FATAL CEREBRAL MALARIA

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Aims: Nitric oxide (NO) has been hypothesized to play a major role in the pathogenesis of cerebral malaria caused by *P. falciparum* infection. NO may act as a local neuroactive mediator contributing to the coma of cerebral malaria (CM). We hypothesized that increased expression of inducible nitric oxide synthase (iNOS) may cause increased release of NO, and examined the expression and distribution of iNOS in the brain during CM.

Material and results: Brain tissues from fatal cases of cerebral malaria in Thai adults were examined using immunohistochemical staining to detect iNOS. The distribution and strength of staining was compared between 14 patients with CM, three of whom were recovering from coma, and controls. iNOS expression was found in endothelial cells, neurones, astrocytes and microglial cells in CM cases. There was also strong staining in macrophages surrounding ring haemorrhages. iNOS staining was decreased in recovering malaria cases compared to acute CM,

and was low in controls. Quantification showed a significant association between the intensity and number of iNOS positive vessels with the severity of malaria related histopathological changes, although the total number of cells staining was not increased compared to recovering CM cases.

Conclusions: This study indicates that an acute induction of iNOS expression occurs in the brain during CM. This occurs in a number of different cells types, and is increased in the acute phase of CM compared to cases recovering from coma. As NO may activate a number of secondary neuropathological mechanisms in the brain, including modulators of synaptic function, induction of iNOS expression in cerebral malaria may contribute to coma, seizures and death.

This study was supported by The Wellcome Trust of Great Britain, The Thailand Research Fund, and Mahidol University.

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OPPORTUNISTIC INFECTIONS IN THE LIVER OF HIV-INFECTED PATIENTS IN THAILAND: A NECROPSY STUDY

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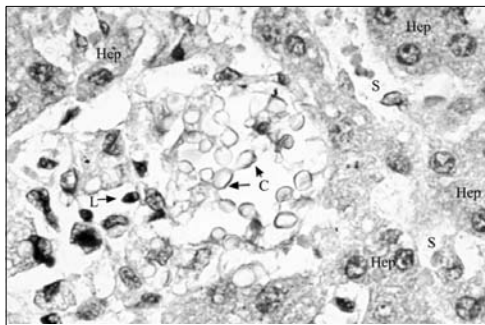


Figure 1
Cryptococcus neoformans in the liver. Some show budding activities. Note the destruction of hepatocytes. Mucin stain, 400x.
 C= *Cryptococcus neoformans*,
 Hep= hepatocytes, S= sinusoids,
 L= lymphocytes

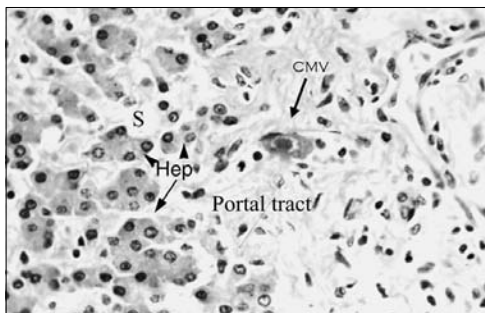


Figure 2
 Cytomegalovirus infecting the endothelium of hepatic vein. Note the enlargement of the endothelium, the typical intranuclear inclusion and perinuclear halo. Modified hematoxylin and eosin stain, 400x. Hep= hepatocytes, S= sinusoids

Liver necropsy from patients infected with human immunodeficiency virus was analyzed in 117 cases. Wide ranges of opportunistic infections were recorded in 47%. Cryptococcosis (21.4%) was the most outstanding infection among others, which was followed by tuberculosis (16.2%), cytomegalovirus (5.1%) and penicillosis (3.4%). Non specific alterations of the liver tissues include fatty steatosis (49.6%), fibrosis (55.6%), portal inflammation and reactive hepatitis. Cases of chronic active and chronic passive hepatitis and one case of hepatocellular carcinoma were reported. In the infected liver, predominant pathological changes included granuloma and spotty necrosis, which were attributed to tuberculous hepatitis. Infection with cryptococcus usually showed no associated pathological change. The sensitivity for the clinical diagnosis of cryptococcus was 88.8% and specificity was 91.7%. For tuberculosis, sensitivity was 20% and specificity was 67.9%.

This study received financial support from the Ministry of University Affairs, Thailand. It is a part of a project supported by the World Health Organization (Thailand) (Project no. 980256 THA OCD 001). This work is being submitted for publication in the *Southeast Asian Journal of Tropical Medicine and Hygiene*.

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Chanathep Pojjaroen-anant



Patraporn Wisetsing



Udomluk Thangtaweewaroaj

CURRENT RESEARCH ACTIVITIES

Vaccine

1. Immunogenicity and adverse reaction after immunization with liquid form of Beijing strain Japanese encephalitis vaccine in healthy Thai children (vaccine trial Phase I/II).
2. Safety and immunogenicity of tetravalent dengue vaccine formulations in Thai adult volunteers.
3. Safety and immunogenicity of live attenuated tetravalent dengue vaccine formulation in Thai children.

Dengue

1. Dengue antibodies in Thai infants: age-specific seroprevalence and kinetics of transplacentally transferred dengue antibodies.
2. Follow-up Thai schoolchildren immunized with live attenuated tetravalent dengue vaccine 3 to 8 years ago: current immunity response and history of serious medical events since vaccination.

Parasite

1. Single dose therapy for treatment of *Giardia* infection in children.
2. Clinical efficacy and pharmacokinetics of suppositoried artesunate combined with mefloquine in the treatment of severe childhood falciparum malaria.
3. Clinical efficacy and pharmacokinetics of suppositoried artesunate combined with mefloquine in the treatment of uncomplicated childhood falciparum malaria.

Allergy

1. A comparative study of the efficacy and ease of administering of sulbutamol delivered from conventional meter dose inhalers and easyhaler in asthmatic Thai children.

Abstracts

INCIDENCE AND CLINICAL MANIFESTATIONS OF INFLUENZA IN NURSE ASSISTANT STUDENTS

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A prospective study was conducted to find the incidence and clinical manifestations of influenza in 201 nurse assistant students of the Faculty of Tropical Medicine during June 1998 to May 1999. There were 106 episodes of influenza-like illness (incidence 52.7%) of which only 33% were proved to be influenza (incidence 17.4%). Main clinical manifestations of influenza included headache, fever, malaise, myalgia, rhinorrhea, cough, and sore throat. We found that influenza

could not be diagnosed solely by using clinical manifestations. Respiratory pathogenic bacteria were rare etiologies of influenza-like illness and this led to our suggestion that routine pharyngeal culture and antibiotic therapy would not be helpful. Influenza vaccination in every nurse assistant students would be beneficial. □

Published in: *Southeast Asian J Trop Med Public Health* 2000;31(1):57-61.

PREVALENCE OF ENTEROBIASIS AND ITS INCIDENCE AFTER BLANKET CHEMOTHERAPY IN MALE ORPHANAGE

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A prospective observational study was conducted in a male orphanage to find out the prevalence of enterobiasis and its incidence after blanket chemotherapy using mebendazole. We found that the prevalence of enterobiasis was 28.9%. The incidence density of enterobiasis after blanket

chemotherapy was 379.82 per 1000 person-year, which was quite high. We suggest that blanket chemotherapy should be repeated at every 6 months interval to control enterobiasis in orphanages. □

Published in: *Southeast Asian J Trop Med Public Health* 2000;31(1):144-6.

CASE REPORT: PLEURAL EFFUSION IN CHILDHOOD FALCIPARUM MALARIA

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Pulmonary complication is a rare manifestation of childhood malaria and isolated pleural effusion without pulmonary edema has never been reported in children. We report here an 11-year-old boy who suffered from cerebral malaria and massive right pleural effusion. The patient was treated with intravenous artesunate, albumin, and other

supportive treatments. He recovered completely after eight days. The clinical and laboratory courses suggested that the plasma leakage played a role in the pathogenesis of pleural effusion. □

Published in: *Southeast Asian J Trop Med Public Health* 2000;31(1):187-9.

EFFECTS OF RICE POWDER SALT SOLUTION AND MILK-RICE MIXTURE ON ACUTE WATERY DIARRHEA IN YOUNG CHILDREN

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A randomized pilot study was carried out to compare the safety and effectiveness of rice powder salt solution (RPSS) in combination with milk-rice mixture (RPSS-MR group, n = 17) with other two regimens, glucose-based oral rehydration solution (ORS) combined with MR (ORS-MR group, n = 17) and ORS combined with formula milk (ORS-milk group, n = 14) in the treatment of acute watery diarrhea with mild to moderate dehydration in 48 boys younger than 2 years. Results showed that in the first 24 hours patients in the RPSS-MR group had significantly smaller amount of stool weight (32.7 g/kg) than those in the ORS-MR group (67.5 g/kg) and ORS- milk group (59.2 g/kg) (p < 0.05 for both measurements). Patients in the RPSS-MR

group also had significantly shorter duration of diarrhea (29.6 h) than the other two groups (43.8 h and 49.6 h, respectively) (p < 0.05 for both measurements). The stool weight and duration of diarrhea between the ORS-MR group and the ORS-milk group were not significantly different. The positive effect of milk rice mixture was not demonstrated in the study due to the significantly more severe diarrhea in the ORS-MR group. The effectiveness of the RPSS-MR is therefore likely due to mainly RPSS. □

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DENGUE INFECTION WITH UNUSUAL MANIFESTATIONS: A CASE REPORT

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Since 1978, there has been an increasing number of reported cases of dengue infection with unusual manifestations and most of them had dengue shock syndrome. We report here one patient who had dengue hemorrhagic fever grade II with liver failure and hepatic encephalopathy and very high elevation of liver enzymes. She made a complete recovery after conservative therapy. She is the fourth case of reported dengue hemorrhagic fever grade II who had unusual manifestation. □

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CURRENT ACTIVITIES

Teaching

The Department has established two new subjects for the Ph.D. student. They are Nuclear Physics (TMRD 502) and Biological Effects of Radiation (TMRD 503). The other two subjects that have been continuously provided for the Ph.D. student are Radioisotopes in Medicine and Biology (TMRD 504) and Radiation Protection (TMRD 505). These subjects have been organized with the cooperation of the Department of Radiological Science, Faculty of Medicine, Ramathibodi Hospital; the Department of Tropical Nutrition and Food Science, Faculty of Tropical Medicine; and the Office of Atomic Energy Commission for Peace, Ministry of Science, Technology and Environment.



The Department has provided teaching to M.Sc. students (Radiological Science), Faculty of Medicine, Siriraj Hospital in Practical Applications of Atomic Energy for Peaceful Uses in Environment and Nutritional Research (SIRA 609) on Nuclear Techniques in Parasitic Infection. Moreover, the Department has provided assistance to two M.Sc. students from the Faculty of Pharmacy, Chulalongkorn University, and the Faculty of Public Health, Mahidol University in folic acid determination.

Research

The Department has established research and cooperation with other departments, as follows:

1. Test for toxicity of herbal extract used for treatment of hookworm infection
2. A clinical trial of modified bovine colostrum in HIV-infected Thai patient
3. Effects of helminthic infection on RBC deformability and splenic clearance of patients with *Plasmodium falciparum*
4. Blood viscosity in cerebral malaria
5. Plasma selenium, glutathione peroxidase in erythrocytes and cervical dysplasia

Services

The Department has two projects for services: (1) service for the measurement of folic acid; and (2) service for the measurement of vitamin B₁₂. The annual service details are shown below.

1 October 1998 – 29 September 1999

	Vitamin B number ¹²	Serum folate number	Red cell folate number
Child	5	5	1
Woman	249	354	113
Man	176	272	72
Total	430	631	186

Abstracts

A COMPARISON OF THE INTERNAL VISCOSITY OF RED CELLS OF ADULTS AND NEWBORN

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The internal viscosity of red cells of adult and cord blood was determined by the blood viscosity equation which was proposed by Dintenfass in 1968. The % HbF and plasma fibrinogen concentration were also determined in all subjects. It was found that the mean values of the internal viscosity of red cells (η_i), blood viscosity (η_b), and plasma viscosity (η_p) of newborn were significantly less than those of adults. A decrease in blood viscosity of newborns in spite of an increase in actual volume concentration indicates a decrease in η_i . There were no significant differences between the T_k and plasma trapping of

adults and newborns. There were no significant relationships between the η_i and plasma fibrinogen concentration in both adults and newborns. There was no relationship between the η_i and HbF. It seems that a decrease in the internal viscosity of the red cell of cord blood may be due to a decrease in membrane rigidity of new borns' RBC rather than due to the HbF. □

The work was supported financially by the National Research Council of Thailand.



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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 and tuberculosis),
- 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 on 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

EMPIRICAL CEPHALOSPORIN TREATMENT OF MELIOIDOSIS

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Melioidosis, or infection by *Burkholderia pseudomallei*, remains a serious cause of mortality and morbidity in northeastern Thailand [1]. During the months of the rainy season, *B.pseudomallei* is the commonest cause of community-acquired septicemia [1]. Empirical antibiotic regimens for the treatment of presumed community-acquired sepsis, such as penicillin/aminoglycoside combinations, have no activity against this organism. In areas of endemicity such as this, more expensive empirical antibiotic regimens that possess activity against *B.pseudomallei* are therefore needed. Amoxicillin/clavulanic acid is widely used and has been shown to be an effective treatment of melioidosis [2], although ceftazidime remains the treatment of choice for severe disease [3]. Other third-generation cephalosporins, particularly cefotaxime and ceftriaxone, are being used increasingly. These antibiotics are active in vitro against *B.pseudomallei* [4,5] but have never been formally assessed in controlled treatment trials.

We therefore retrospectively reviewed the treatment records of all adult patients with melioidosis (primary presentations only) who were admitted to Sappasitprasong Hospital, Ubon Ratchathani, Thailand, between May 1987 and September 1998.

Of the 1,440 cases, 1,353 could be evaluated (i.e., the acute outcome was known). Overall, 733 patients (54.2%) died. Ceftazidime (adult dosage, 40 mg/kg q8h) was used as first-line therapy for *B.pseudomallei* infection in 528 patients

(39.0%); 138 patients (10.2%) received primary treatment with either cefotaxime (20 mg/kg q6h) or ceftriaxone (20 mg/kg q12h), and 167 patients (12.3%) received first-line therapy with amoxicillin/clavulanic acid (24 mg/kg q4h). The mortality rate among all ceftazidime-treated patients was 41.7%, which is comparable with findings of previously reported series [2,3]. This rate compares with 53.9% associated with amoxicillin/clavulanic acid ($P=.006$) and 71.0% associated with cefotaxime or ceftriaxone ($P<.001$; 2 test with Yates' correction). Amoxicillin/clavulanic acid was also significantly more effective than cefotaxime or ceftriaxone ($P=.002$). Blood cultures were positive for 62.3% of ceftazidime-treated patients, 68.3% of amoxicillin/clavulanic acid-treated patients, and 78.3% of cefotaxime- or ceftriaxone-treated patients. Among these septicemia patients, the mortality rates were 59.6%, 67.5% ($P=.13$), and 81.5% ($P<.001$), respectively, and among a subgroup of septicemic patients surviving at least 48 hours, the rates were 47.0%, 47.1%, and 74.4% ($P<.001$) respectively.

Forty-eight (61%) of 79 cefotaxime- or ceftriaxone-treated patients whose therapy was switched to ceftazidime when culture results became available died subsequently. Therapy for the further 13 patients was switched to amoxicillin/clavulanic acid.

Cefotaxime and ceftriaxone are both marginally less active than ceftazidime against *B.pseudomallei* in vitro [4,5], and at the doses currently used, these drugs are associated with a significantly higher mortality rate among patients with melioidosis.

These results suggest that, in areas in which melioidosis is endemic, empirical regimens for treatment of presumed community-acquired septicemia that contain cefotaxime or ceftriaxone are not appropriate. □

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SKELETAL MUSCLE INVOLVEMENT IN FALCIPARUM MALARIA: BIOCHEMICAL AND ULTRASTRUCTURAL STUDY

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Biochemical evidence of skeletal muscle damage is common in malaria, but rhabdomyolysis appears to be rare. To investigate the relationship between serum creatine kinase and myoglobin levels, muscle histology, and renal function in *Plasmodium falciparum* infections, we studied 13 patients with uncomplicated malaria, 13 with severe noncerebral malaria, and 10 with cerebral malaria. A muscle biopsy specimen was obtained from each patient for light microscopy and electron microscopy. Mean serum creatine kinase concentrations \pm SD were raised but similar for the three groups (258 ± 277 , 149 ± 158 , and 203 ± 197 U/L, respectively; $P = .5$). The mean serum myoglobin level \pm SD was highest in cerebral malaria (457 ± 246 vs. 170 ± 150 and 209 ± 125

ng/mL in uncomplicated and severe malaria, respectively; $P < .01$) and correlated with the mean serum creatinine level ($r = .39$ for 36 patients; $P = .02$). The number of intravascular parasites, proportion of mature forms, and glycogen depletion were highest in biopsy specimens from patients with cerebral malaria. Myonecrosis was not observed. Muscle appears to be an important site for *P.falciparum* sequestration, which could contribute to metabolic and renal complications. □

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MOLECULAR MECHANISMS OF CYTOADHERENCE IN MALARIA

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Microbial pathogens subvert host adhesion molecules to disseminate or to enter host cells to promote their own survival. One such subversion is the cytoadherence of *Plasmodium falciparum*-infected erythrocytes (IRBC) to vascular endothelium, which protects the parasite from being removed by the spleen. The process results in microcirculatory obstruction and subsequent hypoxia, metabolic disturbances, and multi-organ failure, which are detrimental to the host. Understanding the molecular events involved in these adhesive interactions is therefore critical both in terms of pathogenesis and implications for therapeutic intervention. Under physiological flow conditions, cytoadherence occurs in a stepwise fashion through parasite ligands expressed on the

surface of IRBC and the endothelial receptors CD36, intercellular adhesion molecule-1 (ICAM-1), P-selection, and vascular adhesion molecule-1. Moreover, rolling on ICAM-1 and P-selection increases subsequent adhesion to CD36, indicating that receptors can act synergistically. Cytoadherence may activate intracellular signaling pathways in both endothelial cells and IRBC, leading to gene expression of mediators such as cytokines, which could modify the outcome of the infection. □

Wellcome-Mahidol University, Oxford Tropical Medicine Research

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THIAMINE DEFICIENCY AND MALARIA IN ADULTS FROM SOUTHEAST ASIA

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Background Thiamine deficiency (beriberi) is common in some parts of southeast Asia. Acute thiamine deficiency can mimic many complications of malaria, such as encephalopathy and lactic acidosis. We examined the incidence of thiamine deficiency in adults admitted to hospital with malaria in Thailand.

Methods For this prospective study, we recruited consecutive patients with malaria or other febrile illness who presented to Pahlpolpayuhasena Hospital, Kanchanaburi, Thailand, between May and July, 1992. We used

the activation coefficient (α) for transketolase activity in erythrocytes to measure thiamine deficiency (defined as >1.31) in patients with severe and uncomplicated malaria and in controls (patients' relatives and healthy volunteers). To exclude the possibility of interference in the assays, transketolase activity was also measured in erythrocytes used to culture parasites.

Findings 12 (52%) of 23 patients with severe malaria and ten (19%) of 54 patients with uncomplicated malaria had values above the normal range ($p < 0.0001$ and $p = 0.0014$, respectively,

compared with controls), which indicated severe thiamine deficiency. Thiamine deficiency was more severe in patients with cerebral malaria than in those with uncomplicated malaria and the controls (p=0.008).

Interpretation In adults admitted to hospital in Thailand, thiamine deficiency commonly complicates acute falciparum malaria, particularly

in severe infections, and could contribute to dysfunction of the central nervous system. □

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ELEVATED PLASMA CONCENTRATIONS OF INTERFERON (IFN)- AND THE IFN-INDUCING CYTOKINES INTERLEUKIN (IL)-18, IL-12, AND IL-15 IN SEVERE MELIOIDOSIS

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Interferon (IFN)- plays an important role in the pathogenesis of sepsis. Production of IFN- is stimulated by synergistic effects of interleukin (IL)-18, IL-12, and IL-15. To investigate the regulation of IFN- production during severe gram-negative infection, the plasma concentrations of IFN-, IL-18, IL-12, and IL-15 were measured in 83 patients with suspected melioidosis. The diagnosis was confirmed in 62 patients, 31 of whom had blood cultures positive of *Burkholderia pseudomallei*, of whom 12 died. Compared with healthy controls, patients had elevated levels of IFN-, IL-18, IL-12p40, and IL-15 on admission, with significantly higher levels in blood culture-positive patients, and these

levels remained elevated during the 72-h study period. In whole blood stimulated with heat-killed *B.pseudomallei*, anti-IL-12 had a stronger inhibitory effect than anti-IL-18 and anti-IL-15 on IFN- production. This effect of anti-IL-12 was further enhanced by anti-IL-18. These data suggest that during gram-negative sepsis, IFN- production is controlled at least in part by endogenous IL-18, IL-12 and IL-15. □

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A REVIEW OF THE SPECTRUM OF CLINICAL OCULAR FUNDUS FINDINGS IN *P.FALCIPARUM* MALARIA IN AFRICAN CHILDREN WITH A PROPOSED CLASSIFICATION AND GRADING SYTEM

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Ocular fundus pathology in *Plasmodium falciparum* malaria is common and has prognostic significance. We have made a collaborative effort to document the ocular features in several populations. Based on examination of 735 patients in Malawi, Kenya and The Gambia by direct and indirect ophthalmoscopy with dilated pupils, we have determined that the 5 distinct clinical features (in order of frequency) include

retinal whitening, haemorrhages, unique vessel abnormalities, papilloedema, and cotton wool spots. Photographs and descriptions of these are presented, along with a proposed grading scheme. □

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THE THAI-BURMESE BORDER: DRUG STUDIES OF *PLASMODIUM FALCIPARUM* IN PREGNANCY

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Plasmodium falciparum malaria is increasing world-wide, as is resistance to the available antimalarials. On the Thai-Burmese border this problem is most acute in pregnant women, as options for their treatment are even more restricted because of the unknown effects of antimalarials

on the foetus. Presented here are the results of descriptive, clinical, drug studies on quinine, mefloquine and artemisinin derivatives for *P.falciparum* in pregnant women. Mefloquine and quinine have high failure rates for primary and recrudescence infections. Artemisinin-based

treatments in pregnant women have proved safe, tolerable and efficacious. However, randomized drug studies with these drugs and other new antimalarials are required to define the true safety and efficacy of these drugs in pregnant women. □

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THE EFFECTS OF *PLASMODIUM VIVAX* MALARIA IN PREGNANCY

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Background *Plasmodium vivax* is more common than *P.falciparum* as a cause of malaria in many parts of the tropics outside Africa. *P.falciparum* infection has harmful effects in pregnancy, but the effects of *P.vivax* have not been characterized. We investigated the effects of *P.vivax* infection during pregnancy.

Methods Since 1986, pregnant Karen women living in camps for displaced people on the western border of Thailand have been encouraged to attend antenatal clinics. Karen women were screened for malaria and anaemia at each week of pregnancy until delivery, and pregnancy outcome recorded. We compared the effects of *P.vivax* infection on anaemia and pregnancy outcome with those of *P.falciparum* and no malaria infection in the first pregnancy recorded at the antenatal clinics.

Findings There were 634 first episodes of pure *P.vivax* malaria in 9956 women. *P.vivax* malaria was more common in primigravidae than in multigravidae and was associated with mild

anaemia and an increased risk of low birthweight (odds ratio 1.64 [95% CI 1.29-2.08], $p < 0.001$). The birthweight was a mean of 107 g (95% CI 61-154) lower in women with *P.vivax* infection than in uninfected women. By contrast with *P.falciparum* malaria, the decrease in birthweight was greater in multigravidae. *P.vivax* malaria was not associated with miscarriage, stillbirth, or with a shortened duration of pregnancy.

Interpretation *P.vivax* malaria during pregnancy is associated with maternal anaemia and low birthweight. The effects of *P.vivax* infection are less striking than those of *P.falciparum* infection, but antimalarial prophylaxis against *P.vivax* in pregnancy may be justified. □

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THE *PFMDR1* GENE IS ASSOCIATED WITH A MULTIDRUG-RESISTANT PHENOTYPE IN *PLASMODIUM FALCIPARUM* FROM THE WESTERN BORDER OF THAILAND

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On the western border of Thailand, *Plasmodium falciparum* has become resistant to almost all antimalarial agents. The molecular basis of resistance in these parasite populations has not been well characterized. This study assessed genetic polymorphisms in the *pfmdr1* gene in 54 parasites collected from the western border of Thailand to determine the relationship of *pfmdr1* copy number and codon mutations with parasite sensitivities to mefloquine, chloroquine, halofantrine, quinine, and artesunate assessed in vitro. A point mutation at codon 86 (resulting in a change of Asn to Tyr) was associated with a significantly lower 50% inhibitory concentration (IC50) of mefloquine (median, 9 ng/

ml versus 52.4 ng/ml; $P = 0.003$). Overall 35% of the isolates (19 of 54) had an increase in *pfmdr1* copy number, and all 19 carried the wild-type allele at codon 86. Increased *pfmdr1* copy number was associated with higher IC50s of mefloquine ($P = 0.04$) and artesunate ($P = 0.005$), independent of polymorphism at codon 86. The relationship between *pfmdr1* and resistance to structurally distinct antimalarial agents confirms the presence of a true multidrug-resistant phenotype. □

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COMBINATION ANTIBIOTIC THERAPY FOR SEVERE MELIOIDOSIS

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Sir-We read with interest the article by Dorman et al. [1] concerning a case of melioidosis in chronic granulomatous disease. We would like to comment on the therapeutic regimens used in this case.

The authors state that combination therapy is recommended for severe disease. While it is true that some investigators have recommended intravenous combination therapy for treatment of

severe disease [2], there is no evidence to support its use. There are only four reported randomized comparative trials of antibiotic therapy for severe melioidosis. The first two trials compared ceftazidime alone [3], or ceftazidime plus trimethoprim-sulfamethoxazole (TMP-SMZ) [4], with a combination of chloramphenicol, doxycycline, and TMP-SMZ. The results of both trials demonstrated a substantial reduction in

mortality with use of the ceftazidime-containing regimens. We do not know whether the use of TMP-SMZ provides additional benefit. The results of two further trials of β -lactamase inhibitor-containing regimens (amoxicillin/clavulanate or cefoperazone/sulbactam) vs. ceftazidime alone [5] or ceftazidime plus TMP-SMZ [6], did not show significant differences in mortality. Imipenem has also been evaluated as therapy for melioidosis and appears to be effective as a single-agent therapy (A. Simpson, unpublished data)

The combination of imipenem and doxycycline as therapy for melioidosis has never been the subject of clinical investigation. Doxycycline has been shown to antagonize the cidal action of

ceftazidime against *Burkholderia pseudomallei* in vitro [7], and it is possible that doxycycline may antagonize imipenem. We recommend caution in the use of untested, potentially antagonistic regimens in treatment of a disease associated with high mortality and relapse rates. This same point applied to the combination of oral cefixime and doxycycline used for maintenance treatment in this case. □

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COMPARISON OF IMIPENEM AND CEFTAZIDIME AS THERAPY FOR SEVERE MELIOIDOSIS

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An open, prospective, randomized, comparative treatment trial was conducted to compare the therapeutic efficacy of high-dose intravenous imipenem and ceftazidime for acute severe melioidosis. Adult Thai patients with suspected acute, severe melioidosis were randomized to receive either imipenem, at a dosage of 50 mg/(kg.d), or ceftazidime, at a dosage of 120 mg/(kg.d), for a minimum of 10 days. The main outcome measures were death or treatment failure. Of the 296 patients enrolled, 214 had culture-confirmed melioidosis, and 132 (61.7%) of them had positive blood cultures. Mortality among patients with

melioidosis was 36.9% overall. There were no differences in survival overall ($P = .96$) or after 48 hours ($P = .3$). Treatment failure after 48 hours was more common among patients treated with ceftazidime ($P = .011$). Both treatments were well tolerated. Imipenem is a safe and effective treatment for acute severe melioidosis and may be considered an alternative to ceftazidime. □

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AMINOGLYCOSIDE AND MACROLIDE RESISTANCE IN *BURKHOLDERIA PSEUDOMALLEI*

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We were very interested in the recent paper by Moore et al. (3) in which the authors used transposon mutants to demonstrate efflux-mediated resistance to aminoglycosides and macrolides in *Burkholderia* (formerly *Pseudomonas*) *pseudomallei*. Melioidosis is very difficult to treat because of intrinsic resistance to many antimicrobial agents, particularly the aminoglycosides. Aminoglycoside-lactam combinations are used empirically to treat suspected community-acquired sepsis in many areas of the world, but they are ineffective in melioidosis.

We have been conducting clinical and laboratory studies of melioidosis in Thailand since 1986. During this time we have collected over 3,700 clinical isolates of *B.pseudomallei* from more than 1,800 patients with melioidosis admitted to Sappasitprasong Hospital, Ubon Ratchathani, northeast Thailand. We have performed susceptibility testing using the disk diffusion method on most of these isolates, according to the guidelines of the National Committee for Clinical Laboratory Standards (4), for ceftazidime, co-amoxiclav, chloramphenicol, doxycycline, ciprofloxacin, gentamicin, polymyxin B, and, more recently, imipenem. MIC determinations, using an agar incorporation method (5), have been performed for representative isolates.

During this time we have isolated three strains of *B.pseudomallei*, from two patients, which were susceptible to gentamicin by disk testing. The isolates were from a splenic aspirate of one patient (708a) (2) and from blood and knee aspirate

cultures of the second (2188a and b).

All other isolates were resistant to gentamicin by disk testing (disk content, 10 g). *B.pseudomallei* is usually highly resistant to aminoglycosides, with a gentamicin MIC at which 50% of the isolates are inhibited of 128 mg/liter (1), and also to the macrolide antibiotics. The MIC results of 100 clinical isolates of *B.pseudomallei*, collected during 1998, for the macrolides erythromycin, clarithromycin, and azithromycin are listed in Table 1. In contrast, the three gentamicin-susceptible isolates were also susceptible to these macrolide antibiotics (Table 1).

For all three isolates the MICs of ceftazidime, imipenem, chloramphenicol, ciprofloxacin, and doxycycline were within the expected ranges for each agent. All three were resistant to polymyxin B.

Thus, there are very rare wild strains of *B.pseudomallei* which exhibit antibiotic susceptibility patterns similar to those of the transposon mutants created by Moore et al. (3), i.e., with linked loss of resistance to aminoglycosides and macrolides. By definition the three clinical isolates described here are virulent. This is consistent with the evidence for retention of virulence in hamsters by the mutant strains. Whether these findings have therapeutic implications remains to be seen. □

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POPULATION PHARMACOKINETICS OF MEFLOQUINE IN PATIENTS WITH ACUTE FALCIPARUM MALARIA

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Objective: To construct a population pharmacokinetic model for mefloquine in the treatment of falciparum malaria.

Background: Mefloquine is the treatment of choice for multidrug-resistant falciparum malaria. The factors that influence the pharmacokinetic properties of mefloquine in acute malaria are not well characterized.

Methods: The pharmacokinetic properties of mefloquine were evaluated in 257 patients with acute falciparum malaria by use of nonlinear mixed-effects modeling. Two different oral dose regimens were used: (1) a split dose of 15 mg/kg initially followed by 10 mg/kg 24 hours later (n = 159) and (2) a single dose of 25 mg/kg (n = 98). Mefloquine was combined with artesunate in 105 (41%) patients (74 received a split dose and 31 received a single dose).

Results: Splitting the mefloquine dose increased the area under the concentration-time curve [AUC(0-)] by 50% (95% confidence interval [CI], 36% to 65%) for monotherapy and by 20% (95% CI, 3% to 40%) for combined therapy. The apparent volume of distribution (V/F) was significantly lower in patients receiving split doses of mefloquine

monotherapy (mean, 8.14 L/kg; 95% CI, 7.49 to 8.86 L/kg) compared with a single dose (mean, 20.37 L/kg; 95% CI, 16.26 to 25.51 L/kg). Patients who received mefloquine monotherapy and cleared parasitemia in less than 48 hours had a significantly higher AUC(0-) independent of any confounders, compared with patients with slower parasite clearance (geometric mean [95% CI], 50,373 ng/mL.day [46,121 to 55,017 ng/mL.day] versus 45,583 ng/mL.day [42,306 to 49,125 ng/mL.day]).

Conclusion: The pharmacokinetic properties of mefloquine in malaria were relatively unaffected by demographic variables (other than body weight) or disease severity. If it is assumed that apparent clearance and volume of distribution are unaffected by dose regimen, then splitting the 25 mg/kg mefloquine dose improves oral bioavailability and the therapeutic response in the treatment of acute falciparum malaria. □

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RAPID IDENTIFICATION OF *BURKHOLDERIA PSEUDOMALLEI* BY LATEX AGGLUTINATION BASED ON AN EXOPOLYSACCHARIDE-SPECIFIC MONOCLONAL ANTIBODY

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We recently identified a constitutively expressed exopolysaccharide of *Burkholderia pseudomallei* which is composed of a unique linear tetrasaccharide repeating unit consisting of three galactose residues and one 3-deoxy-D-manno-2octulosonic acid residue. In this study we developed a latex agglutination test based on monoclonal antibody 3015, which is specific for this exopolysaccharide, and evaluated this test for rapid identification of *B.pseudomallei* grown on agar plates. All 74 environmental and clinical *B.pseudomallei* strains tested, originating from different areas of Southeast Asia, northern Australia,

and Africa, showed a strong and specific agglutination. *B.pseudomallei*-like organisms and a variety of other bacteria did not react. In conclusion this monoclonal antibody-based test is a simple, rapid, and highly specific method for identifying *B.pseudomallei* culture isolates from different geographic areas. □

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RISK FACTORS FOR MELIOIDOSIS AND BACTEREMIC MELIOIDOSIS

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A case-control study was conducted in four hospitals in northeastern Thailand to identify risk factors for melioidosis and bacteremic melioidosis. Cases were patients with culture-proven melioidosis, and there were two types of controls (those with infections, i.e. with community-acquired septicemia caused by other bacteria, and those without infection, i.e. randomly selected patients admitted with noninfectious diseases to

the same hospitals). Demographic data, clinical presentations, and suspected risk factors were analyzed. Diabetes mellitus, preexisting renal diseases, thalassemia, and occupational exposure, classified by the soil and water risk assessment, were confirmed to be significant risk factors for melioidosis and bacteremic melioidosis. Only diabetes mellitus was a significant factor associated with bacteremic melioidosis, as compared with

nonbacteremia. A significant interaction was found between diabetes mellitus and occupational exposure. Thus, diabetic rice farmers would be the most appropriate population group for targeted control measures such as vaccination in the future. □

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ABSENCE OF AN INTERACTION BETWEEN ARTESUNATE AND ATOVAQUONE-PROGUANIL

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Objective: Atovaquone plus proguanil is a new, well-tolerated and highly effective antimalarial drug. In order to protect it from the development of resistance, it may be deployed in combination with an artemisinin derivative. To investigate whether artesunate affects the pharmacokinetics of atovaquone plus proguanil, and to provide preliminary information regarding the tolerability of the triple drug combination (artesunate plus atovaquone plus proguanil), a crossover study was conducted in adult volunteers.

Methods: Twelve healthy Karen adults were randomized to receive atovaquone-proguanil (1000/400 mg) with or without artesunate (250 mg) and, at least 90 days later, the study was repeated. Blood was sampled over a 10-day period.

Results: The three-drug combination was well tolerated. Artesunate did not alter the pharmacokinetic properties of atovaquone and

proguanil (maximum plasma concentrations: 13.02 g/ml and 742 ng/ml; elimination half-lives: 42.2 h and 14.4 h; oral plasma clearance estimates: 90 ml/h/kg and 710 ml/h/kg; and apparent volumes of distribution: 4.91/kg and 14.51 kg, respectively). There was also no effect of artesunate on the biotransformation of proguanil to cycloguanil. The pharmacokinetic variables were similar to those reported previously for the individual drugs.

Conclusion: Artesunate does not influence atovaquone or proguanil pharmacokinetics. The triple-drug combination of atovaquone and proguanil and artesunate was well tolerated. □

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NO EVIDENCE OF CARDIOTOXICITY DURING ANTIMALARIAL TREATMENT WITH ARTEMETHER-LUMEFANTRINE

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Artemether-lumefantrine is a new fixed antimalarial combination effective against multidrug-resistant falciparum malaria. A prospective electrocardiographic study was conducted in 150 patients receiving artemether-lumefantrine and 50 treated with artesunate-mefloquine. There was no evidence for clinically significant changes in the electrocardiographic

intervals and in particular no relationship between plasma concentrations of lumefantrine and QTc prolongation. Artemether-lumefantrine does not have significant cardiac effects at therapeutic doses. □

Wellcome-Mahidol University, Oxford Tropical Medicine Research

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ANTIFUNGAL SUSCEPTIBILITIES OF *CRYPTOCOCCUS NEOFORMANS* IN NORTHEAST THAILAND

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Thailand is currently experiencing a rapid rise in the numbers of patients presenting with AIDS and opportunistic fungal infections such as cryptococcal meningitis, disseminated *Penicillium marneffei* infection, and *Pneumocystis carinii* pneumonia. As there are limited therapeutic options in systemic antifungal treatment and, until recently, considerable variability in the results of susceptibility testing *in vitro* (BSAC WORKING PARTY 1991), many isolates, including cryptococci, are not tested routinely for their susceptibilities to antifungal agents. Broth microdilution methods have been validated and standardized in recent years (BARCH-IESI *et al.*, 1994; HACEK *et al.*, 1995). We tested antifungal susceptibilities for human isolates of *Cryptococcus neoformans*, using a broth microdilution method based on the National Committee for Clinical Laboratory Standards M27-

P Proposed Standard (NCCLS, 1992), to provide information about minimum inhibitory concentrations (MICs) in the north-east of Thailand. Strains of *C. neoformans* were isolated from AIDS patients admitted to Sappasitprasong hospital in Ubon Ratchathani, north-east Thailand with suspected cryptococcal meningitis. A total of 140 isolates (cerebrospinal fluid 88, blood 34, urine 9, skin 3, sputum 3, bone marrow 2, pharynx 1) were collected from 96 adult patients over a 3-year period. *C. neoformans* was isolated from between 1 and 5 sites for any individual patient. All isolates were from the first episode, i.e. were primary infections. □

Wellcome-Mahidol University, Oxford Tropical Medicine Research

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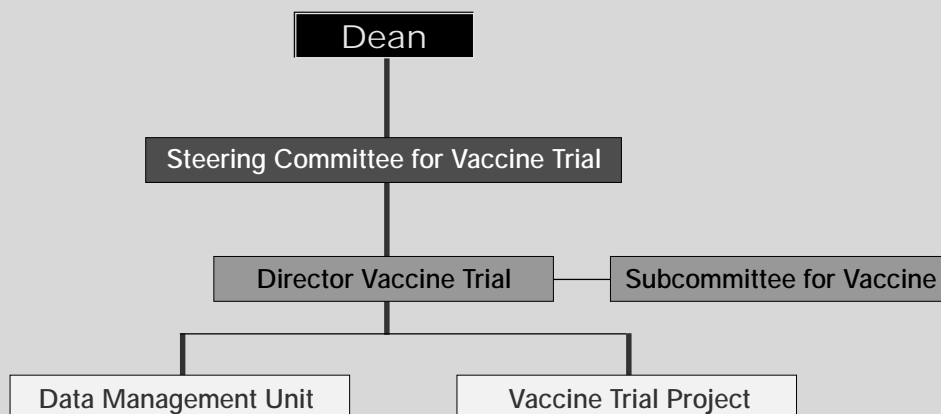
VACCINE TRIAL CENTRE

Despite advancement in medical technology and therapeutics, infectious diseases, including diarrheal 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 Diarrheal Diseases supported the establishment of such a facility in the tropics, where diarrheal diseases are endemic and the vaccines specifically needed are different from Western countries. With the initiation of Professor Dr.Natth Bhamarapravati, 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, 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 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 in September 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 disease in developing countries.

ORGANIZATION CHART



Physical facilities

The Centre occupies the tenth and eleventh floors of the Chamlong Harinasuta 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

C. Administrative office on the 11th floor

D. HIV Vaccine Trial Project on the 9th floor of the Anek Prasong Building

- Registration and data entry room
- Volunteer waiting area
- Counselling rooms
- Physical examination room
- Vaccination room

E. Data Management Unit on the 9th floor of the Anek Prasong Building

Work scope

The VTC was planned to serve as a clinical facility for the evaluation of newly developed vaccines, in terms of reactogenicity, immunogenicity and protective efficacy, against various infectious diseases prevalent in the area. There are three disease areas for vaccine studies identified at this time: diarrheal diseases, malaria and viral infections. All volunteer studies will be carried out on informed consenting adults.

The costs of each vaccine study should be borne by either the individual or the institution wanting the vaccine to be tested. It could be supported by funds from interested vaccine developers, pharmaceutical companies, or donor agencies.

Types of studies planned

- Evaluation of reactogenicity and immunogenicity of living (attenuated) and non-living vaccines.
- Assessment of vaccine formulation and dose schedules for optimum immune response.
- Evaluation of the efficacy of vaccines for partial or complete protection from illness.
- Study of the pathogenesis and immune response to pathogenic agents.
- Determination of the level and mechanisms of natural immunity to pathogenic agents.

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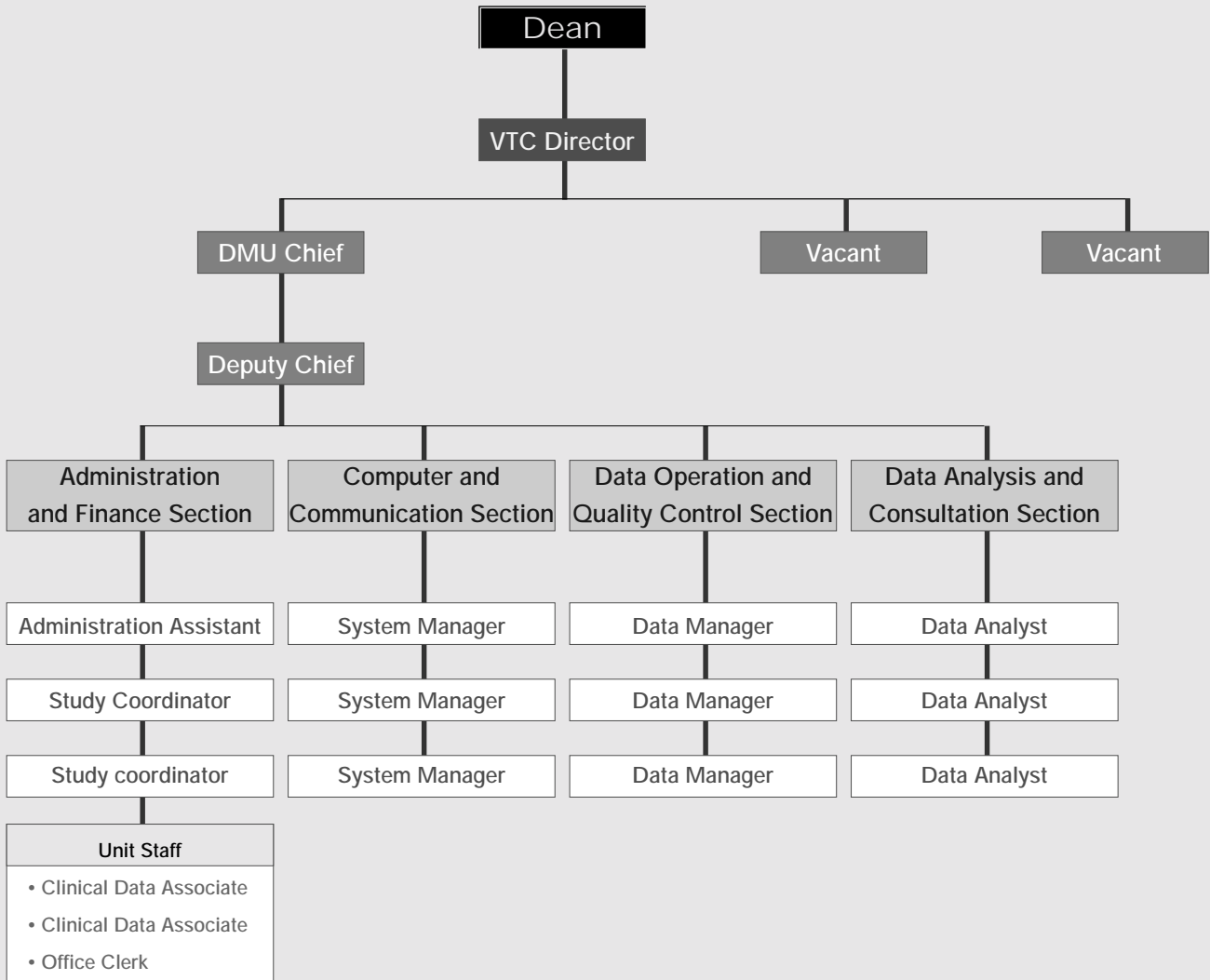


Klinsukon Sritanaittipol



Urairat Kerdmuangbua

DMU ORGANIZATION CHART



The Data Management Unit or DMU was established in late 1998 and is located on the 9th floor of the Anek Prasong Building, Faculty of Tropical Medicine, to fulfill national requirements under the Thailand National AIDS Committee. Its establishment and the early-year operation have been sponsored by VaxGen Inc., Brisbane, CA, U.S.A.

The primary objective of the Unit is to provide “data management” and “data analysis” services to research projects, particularly clinical trials; meanwhile, its current commitment is put mainly into the Phase III Trial to determine the efficacy of AIDS VAX™ B/E vaccine in intravenous drug users in Bangkok, Thailand.

Vaccine Trial Projects

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Punnee Pitisuttithum



CURRENT RESEARCH ACTIVITIES:

1. Addendum : A Phase I/II, Double-blind, Placebo-controlled Study of the Chiron Vaccines HIV Thai E gp120/MF59 Vaccine Administered Alone or Combined with the Chiron Vaccines HIV SF2 gp120 Antigen in Healthy HIV-Seronegative Thai Adults

Objective:

- A Phase II Trial of a subtype E-specific gp120 candidate vaccine was carried out in healthy Thai adults to determine safety and immunogenicity

Sites:

- four clinical sites situated within academic centers, 3 in Bangkok and 1 in Chiang Mai

Protocol summary:

- Vaccine-Chiron Vaccines' recombinant Thai E gp120 protein, adjuvanted with MF59 in 9 dose combinations
- Immunizations-intramuscular injections at 0,1 and 6 months
- Referring to the Thai E, SF2 gp120A dose respectively
are : 25/0 50/0 100/0 25/25 50/50 100/25 25/50 50/50
and : 100/50
- Design-randomized, double-blind, placebo-control study
- Volunteers are subjects-HIV-seronegative, Thai adults at low risk of HIV exposure

Measures of immunogenicity:

- Binding antibodies to SF2 and Thai E gp120 antigens, measured by enzyme-linked immunosorbent assay (ELISA)
- Neutralizing antibodies to SF2 and Thai E HIV-1, measured by a neutralization assay or an equivalent functional assay

2. A Phase I/II Trial to Evaluate The Safety and Immunogenicity of AIDSVAX™ B/E Vaccine in Bangkok,Thailand

Objective:

- To evaluate the safety and immunogenicity of three different doses of AIDSVAX™ B/E vaccine (100, 300 or 600 µg of each antigen) given at 0, 1, 6 and 12 months in Thailand

Candidate vaccine:

- AIDSVAX™ B/E containing MN gp120 and A244 gp120 in aluminum hydroxide adjuvant.

Design:

- Open-label, randomized dose escalation (100 mg, 300 mg and 600 mg of each antigen) given at 0, 1, 6 and 12 months

Population:

- 92 HIV-negative, healthy volunteers, 69 males and 23 females (approximately 30 volunteers in each group)

3. A Phase III Trial to Determine the Efficacy of AIDSVAX™ B/E Vaccine in Intravenous Drug Users in Bangkok, Thailand

Primary objective:

- To determine whether immunization with AIDSVAX™ B/E vaccine protects intravenous drug users from HIV-1 infection

Secondary objective:

- To determine whether prior immunization with AIDSVAX™ B/E vaccine prevents persistent viremia

Other objectives:

- To evaluate whether immunization with AIDSVAX™ B/E affects the genetic characteristics of HIV-1 “breakthrough viruses”
- To evaluate possible immunologic markers which correlate with protection from HIV-1 infection
- To assess any behavioral effect (positive or negative) associated with participation in a vaccine efficacy trial

4. Phase I/II Trial of Pasteur Merieux Connaught (PMC) Live Recombinant ALVAC-HIV (vCP1521) Priming with Vaxgen gp120 (AIDSVAX™ B/E) Boost in Thai HIV-Seronegative Adults

Objective :

- Phase I : Phase I (open label) description of the acute safety and tolerability of ALVAC – HIV (vCP1521 : $10^{6.53}$ CCID₅₀)
- Phase II : Description of the safety and immunogenicity of ALVAC – HIV (vCP1521) priming with either 200 µg or 600 µg (100 or 300 µg each B and E gp120) of the bivalent AIDSVAX™ B/E gp120 boosting.

Study design :

- Group I : ALVAC – HIV (vCP1521; $10^{6.53}$ CCID₅₀) will be tested for acute safety and tolerability in a group of 5 low risk, HIV seronegative Thai adults. If there are no serious vaccine-related adverse events or severe laboratory abnormalities after vaccination #2 in Phase I , Phase II will be initiated.
- Group II : 45 low – risk HIV seronegative Thai adults will be given ALVAC – HIV (vCP1521; $10^{6.53}$ CCID₅₀) priming at weeks 0, 4, 12 and 24. At weeks 12 and 24 , vCP1521 will be administered with 200 g of a bivalent AIDSVAX™ B/E gp120 (100 µg for each B and E gp120). 15 other subjects will receive a placebo.
- Group III: 45 low – risk HIV seronegative Thai adults will be given ALVAC – HIV (vCP1521; $10^{6.53}$ CCID₅₀) at weeks 0, 4, 12 and 24. At weeks 12 and 24, vCP1521 will be administered with 600 g of a bivalent AIDSVAX™ B/E gp120 (300 µg for each B and E gp120). 15 other subjects will receive a placebo.

Abstracts

LONG-TERM TRENDS IN THREE HIGH HIV SEROPREVALENCE EPIDEMICS: IDUs IN BANGKOK, THAILAND, NEW YORK CITY, USA, AND SANTOS, BRAZIL

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Objective: To assess trends in (A) HIV prevalence, (B) HIV incidence, (C) Behaviors that risk exposure for HIV, and (D). Behaviors that risk transmission of HIV in three high seroprevalence epidemics among injecting drug users. One epidemic has occurred within a context of heroin injection (Bangkok), one within cocaine injection (Santos), and one within both heroin and cocaine injection (New York).

Methods: From 1989 through 1997, multiple cross-sectional HIV prevalence and behavior surveys were conducted in each city - 5 surveys in New York, 3 in Bangkok and 2 in Santos. A total of over 12,000 IDUs participated. HIV incidence cohort studies were also conducted in Bangkok and New York, with a total of over 1500 IDU participants. Risk behaviors were measured in terms of the % of subjects engaging in a behavior in the 6 months prior to interview. All changes were significant at $p > 0.05$ by chi square tests for trends.

Results: (A) HIV prevalence declined from 43% to approximately 35% among IDUs in Bangkok, declined from 50% to 29% in New York, and declined from 63% to 42% in Santos. (B) HIV incidence remained stable at 6% per year in Bangkok, and declined from 4% per year to 1%

per year in New York. (C) Risk for exposure behavior (injecting with needles and syringes used by someone else in the previous 6 months) declined from 35% to 22% in Bangkok, remained constant at approximately 22% in New York, and declined from 55% to 24% in Santos. (D) Risk for transmission behavior (passing on used needles and syringes to others) remained constant at approximately 18% in Bangkok, declined from 22% to 5% in New York, and from 59% to 18% in Santos.

Conclusions: These 3 cities illustrate the possibilities of “stabilizing” and potentially “reversing” high seroprevalence epidemics. The data from New York present a strong case for a “declining” epidemic. While reducing risk for exposure behavior is obviously important in HIV prevention, reducing risk for transmission behavior may also be critical in controlling high seroprevalence HIV epidemics. HIV prevention programs should include more efforts to reduce transmission behaviors among seropositives. □

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SOCIAL HARM MONITORING AMONG INJECTING DRUG USERS (IDUs) IN A PHASE III HIV VACCINE TRIAL IN BANGKOK, THAILAND - PRELIMINARY RESULTS

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Issues: HIV vaccine trial participants may be subjected to social harms such as stigmatization (by identification of high-risk group membership); misclassification of HIV infection status (due to vaccine-induced antibody) resulting in loss of employment, insurance, or travel restrictions; or increased risk behavior due to false perceptions of vaccine protection.

Description: In Mar-99, a phase III trial was initiated in Bangkok among 2500 IDUs to evaluate the efficacy of AIDSVAX™ B/E vaccine. As of 17-Jan-2000, 1304 volunteers were enrolled. All participants receive intensive education, counseling, informed consent, and monitoring at 6-month intervals for risk behavior and study-related social harms. Thus far, 5 (0.4%) volunteers have reported disturbances in personal relationships; 4 were with friends or family following voluntary disclosure of trial involvement and resolved with counseling of the concerned parties. The other report described difficulty with an employer and resolved with the volunteer taking a new job. In all cases counseling was provided

to address the specific problems. No social harm events have been reported due to false-positive HIV tests conducted outside of the study. The proportion of IDUs reporting high-risk behavior has decreased at month 6 compared to baseline. Injecting drug use overall decreased from 96% to 83% (regular use dropped from 30 to 20%; sharing needles dropped from 30% to 14%), and methadone maintenance increased from 45% to 78%. In addition, 100% condom use increased from 55% to 69%.

Conclusions: In HIV vaccine trials, it is important to establish effective education and risk reduction counseling as an integral part of the trial. Emphasis should be placed on how volunteers can avoid potential social harms. Interventions should be available to assist trial volunteers with problems as they occur. □

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INITIATION OF A PHASE III EFFICACY TRIAL OF BIVALENT B/E RGP120 HIV VACCINE (AIDSVAX™ B/E) IN BANGKOK, THAILAND

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Background: Since 1988, injecting drug users (IDUs) in Bangkok have experienced a severe epidemic of HIV infection. A 1995-98 study conducted in this group showed an annual incidence rate of at least 6%, willingness to participate in HIV vaccine trials, and high rates of follow-up. The bivalent B(MN)/E(A244) rgp120 HIV vaccine, specifically designed to match HIV strains in Thailand, was previously found to be safe and highly immunogenic in phase I/II trials. In March 1999, a phase III efficacy trial was initiated in Bangkok using AIDSVAX™ B/E vaccine.

Methods: Following informed consent, 2500 IDUs attending 17 drug treatment clinics will be randomized in a blinded fashion to AIDSVAX B/E vaccine (300 µg of each antigen) or placebo (1:1 ratio) at months 0, 1, and 6, with booster doses at months 12, 18, 24, and 30. Interim safety and efficacy analyses will be conducted by an independent DSMB. The study is designed to last 3 years following recruitment and to detect efficacy of at least 30% (1° endpoint - protective “sterilizing” immunity as measured by ELISA and Western blot;

2° endpoint-reduced viral load measured by RNA PCR).

Results: As of 17 January 2000, 2463 volunteers were screened and 1304 were enrolled (93% male; mean age 30 years). Immunization compliance has been 100% (1198 and 517 received the second and third doses, respectively). Thus far, only 6 volunteers have been lost to follow-up and 5 deaths have occurred (none were vaccine related). Immunizations have been well tolerated with no severe vaccine-related side effects.

Conclusions: The first phase III efficacy trial of an HIV vaccine among a high-risk population of IDUs has been initiated in Bangkok, Thailand. To date, recruitment is proceeding well, follow-up is excellent, and adverse effects are unremarkable. With completed enrollment, an interim efficacy analysis is expected in 2002. □

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BASELINE CHARACTERISTICS OF INJECTING DRUG USERS (IDUs) ENROLLED IN A PHASE III HIV VACCINE EFFICACY TRIAL - PRELIMINARY RESULTS FROM BANGKOK, THAILAND

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Background: Since 1988, IDUs in Bangkok have experienced a severe epidemic of HIV infection with a sustained annual incidence rate of 6%. Previous studies have suggested that this population is highly motivated to participate in HIV vaccine trials. In March 1999, a phase III trial was initiated among 2500 IDUs to evaluate the protective efficacy of bivalent B/E rgp120 HIV vaccine (AIDSVAXTM B/E). An important outcome of this trial is the first description of baseline characteristics of this high-risk group participating in the first international phase III HIV vaccine efficacy trial.

Methods: At enrollment into the trial, standardized questionnaires were used to interview IDUs on demographics, risk behavior, and motivations and reasons for participating in the trial.

Results: As of 17 January 2000, 1304 IDUs have been enrolled. The volunteers are mostly male (93%), Thai (99%), young (mean age 30.6 yr.), have at least

primary education (94%), and have been incarcerated in the past (15%). Almost all (99.7%) inject heroin on a regular (30%) or sporadic (70%) basis, and 30% have reported sharing needles. The primary reasons or motivations to participate in this trial are altruistic with 96% wanting to do something to stop the spread of HIV. Thus far, loss to follow-up has been minimal (0.5%) and immunization compliance has been 100%.

Conclusions: IDUs in Bangkok continue to be at high risk of HIV infection and appear to be highly motivated to enroll and participate in this first international phase III efficacy trial. Results of this trial will provide important information on the protective efficacy of AIDSVAX B/E vaccine against parenteral HIV infection. □

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COMMUNITY PARTICIPATION IN HIV-I VACCINE TRIAL IN THAILAND

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Issue: To assess the community interest and participation in HIV-I vaccine trial in Thailand. The results of this will be useful for future HIV-I vaccine efficacy trial in Thailand

Project: A Phase I/II HIV vaccine trial involving general healthy seronegative volunteers was initiated in 1998. Various types of campaign on health education and HIV-1 vaccine trial project were done at various institutions.

Results: 5 types of campaign were performed within 5 months period in order to get 98 volunteer interested to participate in the HIV-I vaccine trial. 834 listened to brief lecture in a classroom or conference room including booth presentation including question and answer after the lecture at universities, college and air force. 451 interested in booth or board presentation at the student union; Red Cross fair, Blood donor site and Buddhist temples only, about 20 came and sought more

informations on the trial after listening to the media via radio or watching TV. Only 159 out of 1285 volunteers really showed their interest and made appointment for screening, but 151 volunteer did come for volunteer screening process. 40% of volunteers who came for screening are monks from Buddhist Colleges or monk followers. 84% expressed the reason of participating in the trial as wanting to help the country and society to get HIV-I vaccine for general use.

Conclusion: Brief lecture together with booth presentation followed by questioning and answer individually or in group seemed to be the most effective way to find the target population. This procedure can be applied to get target population for future vaccine efficacy trial. □

Presented at: Fifth International Congress on AIDS in Asia and the Pacific, Kuala Lumpur, 23-28 October 1999

SPECIES OF *CANDIDA* IN ORO-PHARYNGEAL CANDIDIASIS IN HIV AIDS PATIENTS IN THAILAND-PRILIMINARY RESULT

Valai Bussaratid, Punnee Pitisuttithum, Somsit Tansuphaswadikul, Benjaluck Phonrat, Paul Howe, Nicholas J White

Objective: To determine the prevalence of various species of *Candida* in oro-pharyngeal candidiasis (OPC) in HIV AIDS patients in Thailand

Methods: After the confirmation of OPC by KOH preparation, the samples were cultured and species of *Candida* were identified.

Results: Nineteen of 23 cases (83%) were singularly infected with *C.albicans*. Four cases (18%) had mixed infections between *C.ablicans* and *C.glabrata*. *C.albicans* was predominant in 2 cases

while in the other two cases, the predominant infection was *C.gabrata*.

Conclusion: The finding that *C.albicans* is the most prevalent species in OPC in HIV which is similar to other studies. Other species that have been known to coinfect *C.albicans* include *C.krusei* and *C.lipotica*. The study still continues for another 8 months. □

Presented at: Fifth International Congress on AIDS in Asia and the Pacific, Kuala Lumpur, 23-28 October 1999

VALIDATION OF A HUMAN VOLUNTEER CHALLENGE MODEL USING FROZEN BACTERIA OF THE NEW EPIDEMIC SEROTYPE, *V.CHOLERAE* O139: COMPARISON OF THE INOCULUM DOSE RESPONSE BETWEEN NORTH AMERICAN AND THAI VOLUNTEERS

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Background: Until recently, all epidemic strains of *Vibrio cholerae* have been of the O1 serotype. Current epidemics have also been caused by a new serotype, O139, synonym Bengal. Although serotype O1 does not confer immunity to the Bengal serotype and no licensed vaccine is available for testing this serotype vaccines, challenge studies with freshly harvested *V.cholerae* O139 organisms have produced variable results between centers. In previously published challenge studies from the Center for Vaccine Development using freshly prepared *V.cholerae* O139, strain Al1837, North American volunteers demonstrated an 82% attack rate (purge range 400 mL –16,500 mL). However, in separate studies even at dosed up to 108 CFU in Thai volunteers, using the same freshly prepared strain (Al1837), the attack rate never exceeded 1/5 volunteers (purge range 220 mL-3,690 mL). Therefore, prior to beginning multi-center vaccine efficacy studies, we sought to validate the use of a large standardized frozen inoculum of virulent *V.cholerae* O139, strain 4260B.

Methods: A total of 60 volunteers (25 in Cincinnati, OH, USA, and 35 in Bangkok, Thailand) were recruited for an IRB-approved inpatient dose-escalation challenge. Our goal was to identify a dose that produced an observed cholera attack rate $\geq 80\%$ and an illness of sufficient severity during the defined study period such that the model would be useful for determining vaccine protection. Volunteers were challenged in groups of 5 with *V.*

cholerae O139 that had been reconstituted immediately before use, with no further incubation or bacterial growth. After challenge, the volunteers were monitored for the development and severity of diarrhea and related symptoms.

Results: In North American volunteers, all 25/25 who were challenged were colonized with *V.cholerae* O139. At a dose of 10^5 CFU, 8/10 volunteers met the study criteria for diarrhea and had a geometric mean stool volume of 2,175 mL. At a dose of 10^6 CFU, 14/15 (93%) volunteers experienced purging with a geometric mean stool volume of 5,621 mL (range 1,300-20,300 mL). In Thai volunteers challenge with the identically prepared frozen organisms, 34/35 volunteers became colonized with *V.cholerae* O139. However, at doses up to 10^6 CFU, only 2/5 or 3/5 volunteers in each group experienced purging; the geometric mean stool volumes at these doses were 1,505-2,355 mL (range 580 mL- 4,360 mL). In Thai volunteers challenged at doses $\geq 10^7$ CFU, 11/15 (73%) volunteers experienced purging (range 470-16,020 mL) as shown in table 1

Conclusions: In contrast to the freshly prepared challenge stain, in both North American and Thai volunteers, the frozen inoculum model produced an illness with an adequate attack rate and sufficient severity to test the efficacy of new O139 or combined O1/O139 vaccines. However, the challenge dose required to produce an adequate attack rate and disease severity with the

identical frozen organism was significantly higher in Thai volunteers than in North American volunteers. This suggests an inherent difference between immunologically naive North American volunteers and Thai volunteers who may have had prior environmental exposure to *V.cholerae* and/or

enterotoxigenic *E. coli*. This observation has potential dosing implications both for future challenge studies and for vaccine trials. □

Presented at: US-Japan Conference on Cholera.

Table 1 Clinical and bacteriology response of volunteer after challenge with frozen inoculum *Vibrio cholerae* O139

Inoculum size	4.3x10 ⁴	3.9x10 ⁵	2.4x10 ⁶	8.1x10 ⁶	5x10 ⁷
Volunteer	5	5	5	5	15
Number of Blood gr. O	3	2	3	3	6
Age (yrs.) (mean ± SD)	25±4	31±9	21±5	29±8	27±6
Diarrhea (≥grade3)(attack rate)	2/5 (40%)	3/5 (60%)	3/5 (60%)	4/5* (80%)	11/15 (73.33%)
Mean time to onset of diarrhea (hr) (range)	46 (31-61)	41 (27-50)	40 (27-65)	34 (11-47)	35 (10-73)
Geometric mean stool volume (min-max) (ml) (≥ grade 3)	1946 (1820-2080)	1505 (580-3390)	2355 (1280-4360)	1665 (170-16020)	1391 (470-5705)
Stool volume (mean ± SD)	1950±184	1902±1412	2660±1565	5305±7261	1838±1330
Positive stool culture	4/5	5/5	5/5	5/5	15/15
Max excretion in stool (cfu/ml)(mean ± SD)	2133333± 808290.4	8844500± 1.5E+07	7.1E+08± 1.3E+09	7.7E+08± 1.5E+09	1.7E+0.8± 3.0E+08
Nausea/Omiting	2/5	0/5	0/5	0/5	1/15
Fever	0/5	0/5	0/5	0/5	1/15

HIV SUBTYPE E GP120 VACCINE TRIAL (PHASE II) IN SERONEGATIVE THAI ADULTS

Punnee Pitisuttiithum, Prasert Tongcharoen, Chirasak Khamboonruang, Sorachai Nitayaphan, Joseph Chiu, Arthur Brown, John G McNeil

Background: A phase II trial of a subtype E-specific gp120 candidate vaccine was carried out in healthy Thai adults to determine safety and immunogenicity.

Methods: Vaccine – ChironVaccines’ recombinant Thai E gp120 protein with or without SF2 gp120 protein, adjuvanted with MF59, in 9 dose combinations (Dr. Duliege).

Immunizations – Intramuscular injections at 0, 1 and 6 months.

Design – Randomized, double-blind, placebo-controlled. (At writing of abstract, investigators are still blinded.)

Subjects – HIV-seronegative, Thai adults at low risk of HIV exposure; four clinical sites situated within academic centers, 3 in Bangkok and 1 in Chiang Mai.

Results: 368 volunteers completed the full course of immunization; 288 received the vaccine

and 80 the placebo. Immunizations were well tolerated and no serious adverse events occurred related to the vaccine. Among the total 368 subjects, neutralizing antibody to T-cell line adapted viruses were detected in 68% and 69% to the E and B viruses, respectively. Of the 180 subjects assayed to date for binding antibody, 78% seroconverted to the gp120 immunogen.

Conclusions: This gp120 vaccine, derived from the amino acid sequence of a Thai E isolate, was found to be safe and immunogenic in Thai volunteers. The optimal dose combination for advancement to phase III evaluation will be determined after unblinding. □

Presented at: Fifth International Congress on AIDS in Asia and the Pacific, Kuala Lumpur, 23-28 October 1999.

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

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Objective: To evaluate the safety and immunogenicity of three different doses of AIDSVAX™ B/E vaccine (100, 300 or 600 µg of each antigen) given at 0, 1, 6 and 12 months in Thailand

Design: Open-label, randomized dose escalation (100 µg, 300 µg and 600 µg of each antigen)

Population: 90 HIV-negative, healthy volunteers

(30 volunteers in each group)

Safety: Safety assessments are conducted 1 hr, 3 days and 14 days after each immunization.

Immunogenicity: Overall immunogenicity is evaluated by measuring antibody titers to gp120 at baseline, prior to and two weeks following each immunization. Antigen-specific immunity is evaluated by measuring antibody titers to a V2 peptide.

Results: Reactogenicity: The vaccine was well tolerated. Pain and tenderness at the injection site were the most commonly reported symptoms across all dose groups. Most reactogenicity symptoms reported were self-limiting typically resolved within 14 days of onset. However, pain and tenderness appeared to increase with escalating doses (26.7% of subjects at the 100 µg dose group, as compared to 66.7% and 55.2% of subjects at the 300 µg and 600 µg dose groups).

Month 1.5 Immunogenicity: Greater than 95% seroconversion was detected to all of the gp120 antigens at the 6.5 month time-point. When antigen specificity was examined, it was found that peptides from the V2 domains of the three envelope glycoprotein antigens clearly distinguished antibodies to each antigen. These, antigen specific immune responses were dose dependent.

Month 6.5 Immunogenicity: Both MN-rgp120 and A244-rgp120 titers approach maximum values after two immunizations whereas MN V2 titers continue to increase (two to three-fold) after the third (6.5 month) immunization with the mean optical density values for the 600, 300 and 100 µg dose groups were 0.545, 0.248 and 0.069, respectively at the 1.5 month timepoint and 1.202, 0.570, and 0.213, respectively at the 6.5 month timepoint.

AIDSVAX B/E Vaccine is highly safe and immunogenic as AIDSVAX MN monovalent vaccine. Together with previous evidences phase III efficacy trial of AIDSVAX B/E Vaccine was initiated this year in Thailand □

Presented at: Fifth International Congress on AIDS in Asia and the Pacific, Kuala Lumpur, 23-28 October 1999.

INITIAL REPORT OF A PHASE I/II TRIAL OF AIDSVAX™ B/E RGP120 HIV VACCINE – BANGKOK, THAILAND

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Background: To evaluate the safety and immunogenicity of 3 doses of bivalent AIDSVAX™ B/E (MN/A244) and determine if bivalent vaccines induce antigen-specific immune responses.

Methods: Feb 98 to Aug 99, 92 healthy HIV-seronegative volunteers (75% male) received either 100 g, 300 g, or 600 g doses (31, 31, and 30 subjects respectively) of each antigen at 0, 1, 6, and 12 mos. Of the 92, 40 were at high risk of HIV infection. Antibody titers to gp120 were measured at baseline, prior to immunization and 2 wks later. Antigen specific immune responses to MN and A244 were measured using peptide based assays to V2 and V3.

Results: Reactogenicity was greater for 300 g and

600 g doses than 100 g with pain and tenderness at the injection site being the most commonly reported (48% of all events). No severe vaccine-related adverse events were reported. After 2 doses, 100% of subjects had detectable antibodies to gp120 antigens. At 18 mos, antibodies were still present in 100% of subjects in all dose groups. Antigen specific V2 and V3 domain mean antibody responses were dose dependent and nadirs of the group mean antibody responses increased with successive immunization. V2 and V3 antibody responses to MN and A244 were highest (80-100%) for the 300 g and 600 g dose groups after 3 immunizations and remained at the same level or increased for the 300 g dose after 4th immunization, but declined slightly for the 600 g dose group. Neutralizing antibodies to MN were detected

in 100% of subjects in all dose groups at 6.5 and 12.5 mos.

Conclusions: This study shows for the first time that gp120 antigens derived from different genetic subtypes can be combined to elicit antigen specific immune responses. These preliminary results demonstrate that AIDS-VAX is safe, well-tolerated

and immunogenic. A phase III efficacy trial using AIDS-VAX B/E vaccine was initiated in March 99 among 2500 IDUs in Bangkok. □

Presented at: XII International AIDS Conference, Durban, South Africa, 9-14 July 2000.

PHASE II TRIAL OF HIV-1 SUBTYPE E AND B GP120 VACCINES IN SERONEGATIVE THAI ADULTS

Background: A phase II trial of a subtype E (+ B)-specific gp120 candidate vaccine was carried out to determine the vaccines' safety, immunogenicity and dose response in healthy Thai adults.

Methods: Vaccine - Recombinant Thai E (CM235; 25, 50 and 100 ug) and B (SF2; 25 and 50 ug) gp120 proteins produced in Chinese hamster ovary cells, adjuvanted with MF59 and administered in 9 dose combinations.

Immunization route and schedule - Intramuscular injections at 0, 1 and 6 months.

Design - Complete factorial, randomized, double-blind, placebo-controlled.

Subjects - HIV-seronegative, Thai adults at low risk of HIV exposure; four clinical sites situated within academic centers, three in Bangkok and one in Chiang Mai.

Immunogenicity assays - Neutralizing antibody (NAb) to a heterologous Thai E (NP03) and homologous B (SF2) strains, adapted to T lymphocyte cell lines, was defined as 50% reduction

in viral growth in comparison of post-3rd injection and pre-immune sera.

Results: 368 volunteers completed the full course of immunization, 288 received vaccine and 80 placebo. Immunizations were well tolerated and no serious adverse events occurred related to the vaccine. At one month-post 3rd injection, E-specific and B-specific NAb were detected in 85% of the 288 E-vaccinated subjects and 84% of the 193 B-vaccinated subjects, respectively. 50% geometric mean neutralization titers to NP03 were 155, 169 and 147 to 100, 50 and 25 ug CM235, respectively.

Conclusions: These gp120 subtypes E and B recombinant vaccines were found to be safe and immunogenic in healthy Thai adults. These results, and further analyses of NAb to CM235 in PBMCs, will identify optimal dose combinations and provide the basis for phase III trial planning. □

Presented at: XII International AIDS Conference, Durban, South Africa, 9-14 July 2000

PRELIMINARY RESULTS OF THE PHASE I/II SAFETY AND IMMUNOGENICITY TRIAL OF BIVALENT B/E RGP120 HIV VACCINE (AIDSVAX™) – BANGKOK, THAILAND

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Background: To evaluate the safety and immunogenicity of three different doses (100 µg, 300 µg, 600 µg of each antigen) of bivalent B(MN)/E(A244) rgp120 vaccine (AIDSVAX™) among low and high risk volunteers in Bangkok, Thailand.

Methods: In an open-label trial, 92 HIV-seronegative healthy volunteers (69 males, 23 females) were randomized to immunization with either 100 µg, 300 µg, or 600 µg doses (31, 31, and 30 subjects respectively) of each antigen of B/E rgp120 vaccine, given at 0, 1, 6, and 12 months. Of the 92, 40 were at high risk of HIV infection (1 homosexual, 39 injecting drug users). Safety was assessed at 1hr, 3 days, and 14 days post immunization. Overall immunogenicity was evaluated by measuring antibody titers to gp120 at baseline, prior to and 2 weeks following each immunization. MN and A244 antigen-specific immune responses were measured using V2 and V3 peptide based assays.

Results: Pain and tenderness at the injection site were the most commonly reported adverse events for all three dose groups (>92%); reactogenicity was greater for the 300 µg and 600 µg doses than for 100 µg. No severe vaccine-related adverse events were reported. After 3 doses

of vaccine (month 6.5), 100% of subjects had detectable antibodies to gp120 antigens. At 18 months, detectable antibodies were present in 92.9% of those receiving the 100 µg dose, and 100% in those receiving the 300 µg and 600 µg doses. Overall, V2/V3 mean antibody responses were dose dependent for the three dose groups, and the nadir of the group mean antibody response increased slightly with each successive immunization. V2/V3 antibody responses to MN and A244 were highest (97-100%) for the 300 µg and 600 µg dose groups after 3 immunizations. This level was sustained for the 300 µg dose after 4th immunization, but declined slightly for the 600 µg dose group.

Conclusions: Bivalent B/E rgp120 HIV Vaccine (AIDSVAX™) is safe, well-tolerated, and highly immunogenic. These results are consistent with previous safety and immunogenicity data of monovalent B(MN) rgp120 vaccine. With this and other supporting data, a phase III efficacy trial using AIDSVAX B/E vaccine was initiated among 2500 IDUs in Bangkok in March 1999. □

Presented at: Third Annual Conference on Vaccine Research, Washington DC., 30 April-2 May 2000.



SALUTE THE TEACHER DAY
29 JUNE 2000

The Bangkok School of Tropical Medicine

Office Telephone: 245 8270 or 246 9000-12 ext. 1532,1533



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, 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.) has been organized as an international course 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 all 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 medicine 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. Master and Doctorate degree programmes in Clinical Tropical Medicine were first 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. 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 from April to 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. Course duration is approximately two years, which includes a minimum of 24 credits for coursework and 12 credits for thesis. The programme offers 14 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, Environmental Toxicology, Environmental Health, Parasitology and Medical Entomology. Applicants who are qualified to enrol in this programme are those who have graduated with an M.D., D.D.S., D.V.M. Pharmacy, or B.Sc. degree.

3. Master of Clinical Tropical Medicine (M.C.T.M.) and (M.C.T.M. (Trop. Ped.))

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 study abnormalities mainly in adults, while in the major field of Tropical Pediatrics, students study only abnormalities in children.
- c) able to give consultative advice, disseminate and impart knowledge of tropical medicine.
- d) able to conduct clinical research.

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.

4. 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, Environmental Toxicology, 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 an M.D., D.D.S., D.V.M., M.Sc., or B.Sc. (Hons) degree.

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 in clinical tropical medicine. Students are required to conduct an extensive research project related to clinical tropical medicine which should be original work. The minimum length of 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 the 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 been 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, Lao 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 the U.S.A.).



COLLABORATIVE TRAINING PROGRAMMES

1. Master of Clinical Tropical Pediatrics**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 Pediatrics, 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 pediatrics 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 hemorrhagic 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.

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 participants have attended lectures for 3 months in Austria, they continue attending for more clinical experience for 1 month in Thailand at the Faculty of Tropical Medicine, Mahidol University. Apart from lectures, participants also have the opportunity to see many patients suffering from tropical diseases 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 Assoc. Prof. Wichai Supanaranond.

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.

D.T.M. & H. 2000

1.	Dr. Chrysanthus Pradeep Kumar Henry	Sri Lanka
2.	Dr. Khampanh Prabouasone	Lao PDR
3.	Dr. Syed Ashraf Ali	Bangladesh
4.	Dr. Soe Naing	Myanmar
5.	Dr. Sovann Ly	Cambodia
6.	Dr. Thein Si	Myanmar
7.	Dr. Nimfa M Putong	Philippines
8.	Dr. Bun Sreng	Cambodia
9.	Dr. Bounseng Akhavongsa	Lao PDR
10.	Dr. Pirjo Inkeri Hauvonen	Finland
11.	Dr. Michiko Arai	Japan
12.	Dr. Matthew John Howes	Australia
13.	Dr. Lon Chan Thell	Cambodia
14.	Dr. Layim Tipsing	Thailand
15.	Dr. Ly Van Ngo	Vietnam
16.	Dr. Le Hung Thai	Vietnam
17.	Dr. Wimol Ngantawee	Thailand
18.	Dr. Siriluck Anunnatsiri	Thailand
19.	Dr. Somchanh Souksavarn	Lao PDR
20.	Dr. Sunam Kumar Barua	Bangladesh
21.	Dr. Nguyen Quoc Tip	Vietnam
22.	Dr. Anggun Sari	Indonesia
23.	Dr. Ei Ei Tin	Myanmar
24.	Dr. Udomsak Silachamroon	Thailand
25.	Dr. Oudayvone Rattanavong	Lao PDR
26.	Dr. Huot Chan Yuda	Cambodia
27.	Dr. Fauzima Anwar Bhatti	Pakistan
28.	Dr. Le Kien Ngai	Vietnam
29.	Dr. Maria Guevara	Venezuela
30.	Dr. Maqsood Anwar Arain	Pakistan
31.	Dr. Yasin Ismail Hassan	Ethiopia

M.C.T.M. 2000

1.	Dr. Chrysanthus Pradeep Kumar Henry	Sri Lanka
2.	Dr. Syed Ashraf Ali	Bangladesh
3.	Dr. Soe Naing	Myanmar
4.	Dr. Sovann Ly	Cambodia
5.	Dr. Thein Si	Myanmar
6.	Dr. Nimfa M. Putong	Philippines
7.	Dr. Bun Sreng	Cambodia
8.	Dr. Maqsood Anwar Arain	Pakistan
9.	Dr. Layim Tipsing	Thailand
10.	Dr. Le Hung Thai	Vietnam
11.	Dr. Siriluck Anunnatsiri	Thailand

M.C.T.M. 2000		
12.	Dr. Nguyen Quoc Tip	Vietnam
13.	Dr. Anggun Sari	Indonesia
14.	Dr. Oudayvone Rattnavong	Lao PDR
15.	Dr. Huot Chan Yuda	Cambodia
ATTEND		
1.	Dr. Ly Van Ngo	Vietnam
M.Sc.(TROP.MED.) 2000		
	1st year students	
1.	Mr. Krasae Kanakupt	Thailand
2.	Miss Chutima Naksongsak	Thailand
3.	Miss Tanyalak Khuntamoon	Thailand
4.	Pol.Capt.Natsuda Jamornthanyawat	Thailand
5.	Mr. Nitat Sookrung	Thailand
6.	Mr. Nirut Suwanna	Thailand
7.	Miss Busaba Tuntithavorn	Thailand
8.	Mr. Prasert Rukmanee	Thailand
9.	Miss Pitchapa Yungyuen	Thailand
10.	Mr. Phitsanu Tulayakul	Thailand
11.	Miss Penapa Yutayong	Thailand
12.	Miss Pensri Saelee	Thailand
13.	Mr. Panop Wilainam	Thailand
14.	Miss Matukorn Na Ubol	Thailand
15.	Miss Ladawan Vasinpiyamongcone	Thailand
16.	Mr. Vongsavanh Pongsisay	Lao PDR
17.	Mr. Sasipon Pumkumarn	Thailand
18.	Mr. Sith Premashtira	Thailand
19.	Miss Saichon Chimsumang	Thailand
20.	Miss Supranee Linthaworndee	Thailand
21.	Mrs. Sira Ubwa Mamboya	Tanzania
22.	Mr. Zulhainan bin Hamzah	Malaysia
23.	Mr. Donald Edward Bryant	USA
24.	Dr. Manikip Outhayphone	Lao PDR
25.	Dr. Nguyen Xuan Xa	Vietnam
26.	Dr. Ta Van Thong	Vietnam
27.	Dr. Tran Manh Ha	Vietnam
28.	Miss Charinthon Ngamamonpirat	Thailand
	2nd year students	
1.	Miss Kanjana Sonji	Thailand
2.	Miss Gaysorn Bunyaraksyotin	Thailand
3.	Miss Junpen Suwimonteerabut	Thailand
4.	Mr. Narong Nitatpattana	Thailand

M.Sc.(TROP.MED.) 2000 (CON'T)**2nd year students**

5. Miss Nahathai Chulakarat	Thailand
6. Lt. Tossapon Chaiyasith	Thailand
7. Miss Piyaporn Suebrakul	Thailand
8. Mrs. Phimonsri Saengkar	Thailand
9. Miss Malida Soontornruengyot	Thailand
10. Miss Ratchanok Kumsiri	Thailand
11. Mr. Ram Chandra Silwal	Nepal
12. Miss Risara Jaksuwan	Thailand
13. Dr. Lek-Dysoley	Cambodia
14. Miss Wandee Sawatmongkonkun	Thailand
15. Mr. Sumate Aumpawong	Thailand
16. Miss Suwanee Sungkawasee	Thailand
17. Miss Souwanit Nakasiri	Thailand

3rd year students

1. Pol. LT. Kitiyaporn Chaichana	Thailand
2. Miss Chuthaporn Toonboonchoo	Thailand
3. Miss Bunguorn Sermsart	Thailand
4. Mr. Pornchai Kirdsiri	Thailand
5. Miss Yupa Nakkinkun	Thailand
6. Miss Varangkana Visemanee	Thailand
7. Miss Waraporn Chaimchitpanid	Thailand
8. Miss. Wacharee Tiyasuttipan	Thailand
9. Miss Suwaporn Anantrakulsin	Thailand
10. Miss Akanitt Jittmittraphap	Thailand
11. Mr. Apichai Supasansatorn	Thailand
12. Miss Umaporn Pinyosirikul	Thailand

4th year students

1. Miss Napa Onvimala	Thailand
2. Miss Watcharee Saisongkorh	Thailand
3. Miss Siriwan Tribanyatkul	Thailand
4. Miss Searmsap Riengrod	Thailand
5. Miss Saowaluk Julnimi	Thailand
6. Dr. Tran Do Hung	Vietnam

5th year students

1. Mr. Vick Banmairuoy	Thailand
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Ph.D. (TROP.MED.) 2000**1st year students**

1. Mr. Tawadchai Suppadit	Thailand
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Ph.D. (TROP.MED.) 2000

1st year students

2.	Miss Nantawan Kaewpoonsri	Thailand
3.	Mr. Parin Suwannapha	Thailand
4.	Miss Petchara Tussana	Thailand
5.	Miss Waraporn Aumarm	Thailand
6.	Mr. Wanchai Phatihatakorn)	Thailand
7.	Miss Supawadee Konchom	Thailand
8.	Miss Suwanna Chaorattanakawee	Thailand
9.	Miss Onguma Natalang	Thailand
10.	Miss Orntipa Sethabutr	Thailand
11.	Dr. Gias Uddin Ahsan	Thailand
12.	Mr. Rongdej Tungtrakanpoung	Thailand
13.	Mr. Somchai Jadsri	Thailand
14.	Mr. Somphong Sithiprom	Thailand
15.	Mrs. Tippayarat Yoonuan	Thailand
16.	Mr. Apichai Srijan	Thailand
17.	Mr. Tanett Pakeetoot	Thailand
18.	Miss Thanida Tangwanicharoen	Thailand
19.	Mr. Songpol Tornee	Thailand
20.	Mrs. Pimsurang Taechaboonsermsak	Thailand
21.	Mrs. Ratana Sithiprasasna	Thailand
22.	Mrs. Soontaree Akawat	Thailand
23.	Mr. Adisak Bhumiratana	Thailand
24.	Miss Anamai Thiravirojana	Thailand

2nd year students

1.	Mr. Preecha Liangpunsakul	Thailand
2.	Miss Duangkamol Viroonudomphol	Thailand
3.	Mr. Kamon Foihirun	Thailand
4.	Miss Chutima Kamkhaek	Thailand
5.	Miss Nantika Panutdaporn	Thailand
6.	Miss Naowarut Dechkum	Thailand
7.	Mrs. Prapa Nunthawarasilp	Thailand
8.	Mr. Piyanan Taweethavonsawat	Thailand
9.	Mr. Panas Thumkiratiwong	Thailand
10.	Miss Pornphan Diraphat	Thailand
11.	Miss Pattra Suntornthiticharoen	Thailand
12.	Mr. Yuttana Sudjaroen	Thailand
13.	Mrs. Ratee Leelawongtawon	Thailand
14.	Miss Waraphon Phimpraphi	Thailand
15.	Miss Walairut Tuntaprasart	Thailand
16.	Miss Suwalee Tantawiwat	Thailand
17.	Mrs. Oranan Prommano	Thailand
18.	Mr. Hari Har Joshi	Nepal

Ph.D. (TROP.MED.) 2000 (CONT)

2nd year students

- | | | |
|-----|-----------------------------|----------|
| 19. | Mr. Rajendra Kumar B.C. | Nepal |
| 20. | Miss Nitaya Poosanthanasarn | Thailand |
| 21. | Miss Panee Chaksangchaichot | Thailand |
| 22. | Miss Sirichit Wongkamchai | Thailand |
| 23. | Dr. Aree Kantachuversiri | Thailand |

3rd year students

- | | | |
|-----|-----------------------------|------------|
| 1. | Miss Kriyaporn Songmuaeng | Thailand |
| 2. | Miss Kleebkaew Pitasawad | Thailand |
| 3. | Mrs. Prapin Tharnpoophasiam | Thailand |
| 4. | Miss Pungasem Paeporn | Thailand |
| 5. | Miss Mallika Imwong | Thailand |
| 6. | Mr. Mana Vatakul | Thailand |
| 7. | Mrs. Yupadee Sirissinsuk | Thailand |
| 8. | Miss Wanida Pongstaporn | Thailand |
| 9. | Miss Sawanee Tengrunsun | Thailand |
| 10. | Miss Surangrat Srisurapanon | Thailand |
| 11. | Miss Nitchakarn Noranate | Thailand |
| 12. | Miss Pittayaporn Mounnoi | Thailand |
| 13. | Miss Wannaporn Ittiprasert | Thailand |
| 14. | Miss Yuwadee Trongtokit | Thailand |
| 15. | Dr. Mayfong Mayxay | Lao P.D.R. |

4th year students

- | | | |
|-----|----------------------------|----------|
| 1. | Mrs Kamolrat Silamut | Thailand |
| 2. | Mrs. Kanjana Hongtong | Thailand |
| 3. | Mrs. Chantima Lohachit | Thailand |
| 4. | Mr. Chamnarn Apiwathnasorn | Thailand |
| 5. | Mr. Paron Dekumyoy | Thailand |
| 6. | Mrs. Patcharin Saengjaruk | Thailand |
| 7. | Miss Siriwan Chancharoen | Thailand |
| 8. | Mr. Apichart Nontprasert | Thailand |
| 9. | Miss Urai Chaisri | Thailand |
| 10. | Miss Usavadee Thavara | Thailand |
| 11. | Mrs. Emsri Pongponrat | Thailand |
| 12. | Miss Thitima Wongsaroj | Thailand |

5th year student

- | | | |
|----|----------------------------|----------|
| 1. | Mr. Ruangyuth Chaiworaporn | Thailand |
|----|----------------------------|----------|

8th year student

- | | | |
|----|---------------------------|----------|
| 1. | Miss Prakaidown Srimuzipo | Thailand |
|----|---------------------------|----------|

THESIS TITLES

M.C.T.M. 2000

Department	Name	Title of Thesis	Adviser
Clinical Tropical Medicine	Dr. Syed Ashraf Ali	Clinical manifestations of childhood and adult dengue hemorrhagic fever in Chonburi Hospital	Assoc. Prof. Pornthep Chanthavanich
Clinical Tropical Medicine	Dr. Anggun Sari	Clinical manifestations of childhood and adult dengue hemorrhagic fever in Chonburi Hospital	Assist.Prof. Chukiat Sirivichayakul
Clinical Tropical Medicine	Dr. Thien Si	Clinical manifestations and outcome of non-tuberculosis mycobacterium in HIV/AIDS patients	Assoc.Prof. Punnee Pitisuttithum
Clinical Tropical Medicine	Dr. Layim Tipsing	Clinical manifestations and outcome of non-tuberculosis mycobacterium in HIV/AIDS patients	Assoc.Prof. Punnee Pitisuttithum
Clinical Tropical Medicine	Dr. Nguyen Quoc Tip	A randomized, double-blind, placebo controlled trial of acetazolamide therapy in the adjunctive treatment of AIDS associated cryptococcal meningitis	Assoc.Prof. Punnee Pitisuttithum
Clinical Tropical Medicine	Dr. Le Hung Thai	A randomized, double-blind, placebo controlled trial of acetazolamide therapy in the adjunctive treatment of AIDS associated cryptococcal meningitis	Assoc.Prof. Punnee Pitisuttithum
Clinical Tropical Medicine	Dr. Nimfa M Putong	Clinical manifestations and outcome of tuberculosis in HIV infected patients	Assoc.Prof. Punnee Pitisuttithum
Clinical Tropical Medicine	Dr. Maqsood Anwar Arian	Clinical manifestations and outcome of tuberculosis in HIV infected patients	Assoc.Prof. Wichai Supanaranond
Clinical Tropical Medicine	Dr. Huot Chan Yuda	Clinical manifestations and outcome of tuberculosis in HIV infected patients	Assoc.Prof. Wichai Supanaranond
Clinical Tropical Medicine	Dr. Sovann Ly	Gastrointestinal manifestations in AIDS patients at Chonburi Regional Hospital	Prof. Polrat Wilairatana
Clinical Tropical Medicine	Dr. Bun Sreng	Gastrointestinal manifestations in AIDS patients at Chonburi Regional Hospital	Dr. Sombat Treeprasertsuk
Clinical Tropical Medicine	Dr. Soe Naing	Anti-retroviral therapy in HIV infection	Prof. Sirivan Vanijanonta
Clinical Tropical Medicine	Dr. Chrysanthus Pradeep Kumar Henry	Anti-retroviral therapy in HIV infection	Prof. Sasithorn Pukrittayakamee
Clinical Tropical Medicine	Dr. Oudayvone Rattanavong	Value of liver function test for predicting melioidotic liver abscess	Assoc.Prof. Yupaporn Wattanagoon
Clinical Tropical Medicine	Dr. Siriluck Anunnatsiri	Value of liver function test for predicting melioidotic liver abscess	Assoc.Prof. Yupaporn Wattanagoon

M.SC. (TROP.MED.)

Department	Name	Title of Thesis	Adviser
Clinical Tropical Medicine	Mr. Vick Banmairuoy	Development of a high performance liquid chromatographic method for determination of mycophenolic acid in biological fluids and preliminary investigation of its pharmacokinetics in Thai recipients of kidney transplantation	Assoc. Prof. Wichai Supanaranond
Helminthology	Col.LT. Kitiyaporn Chaichana	Diagnosis of human opisthorchiasis with cocktail and eluted <i>Bithynia siamensis goniomphalosnail</i> antigens by ELISA	Assoc.Prof. Jitra Waikagul
Helminthology	Lt. Tossapon Chaiyasith	Seasonal variation of <i>Gnatho-stoma</i> infection in eels in Nakhon Nayok province	Assoc.Prof. Wichit Rojekittikhun
Helminthology	Ms. Charinthon Ngamamonpirat	<i>Trichinella spiralis</i> in Thailand: differentiation of isolates by polymerase chain reaction (PCR) method	Assoc.Prof. Jitra Waikagul
Microbiology and Immunology	Dr. Tran Do Hung	Epidemiology study of beta hemolytic streptococcus group A in the pharynx of school children in Cantho Province, Vietnam	Assist.Prof. Usanee Suthisarnsunton
Microbiology and Immunology	Ms. Watcharee Saisongkorh	DNA amplification for <i>Vibrio cholerae</i> O:139 Detection	Assoc.Prof.Pramuan Tapchaisri
Microbiology and Immunology	Ms. Searmsap Riengrod	A rapid direct-agent detection system for <i>Orientia tsutsugemusi</i>	Assist.Prof. Varee Wongchotikul
Microbiology and Immunology	Ms. Saowaluk Julnimi	Diagnosis of pertussis using MAb-based dot-blot ELISA, indirect ELISA and DNA amplification	Assoc. Prof. Manas Chongsa-nguan
Microbiology and Immunology	Miss Bunguorn Sermsart	Diagnosis of trichinellosis using specific antigen purified from monoclonal antibody based-affinity chromatography	Prof. Wanpen Chaicumpa
Microbiology and Immunology	Miss Yupa Nakkinkun	Platelet dysfunction in immune thrombocytopenic disorder	Prof. Wanpen Chaicumpa
Microbiology and Immunology	Miss Wacharee Tiyasuttiapan	Genetic analysis of <i>Vibrio cholerae</i> isolated in Thailand for epidemic tracing	Assoc.Prof.Pramuan Tapchaisri
Microbiology and Immunology	Miss Akanitt Jittmittraphap	Detection of dengue viral RNA in patient sera by nucleic acid sequence-based amplification (NASBA) and polymerase chain reaction (PCR)	Assoc.Prof. Wipawee Usawattanakul

M.Sc. (TROP.MED.)

Department	Name	Title of Thesis	Adviser
Microbiology and Immunology	Mr. Apichai Supasansatorn	Towards the monoclonal antibodies to filamentous hemagglutinin of <i>Bordetella pertussis</i>	Assoc. Prof. Manas Chongsa-nguan
Microbiology and Immunology	Miss Kanjana Sonji	Evaluation of cholera and salmonellosis diagnostic test kits in a provincial hospital	Prof. Wanpen Chaicumpa
Microbiology and Immunology	Miss Gaysorn Bunyaraksyotin	Evaluation of an antigen detection test kit for leptospirosis	Assoc. Prof. Pramuan Tapchaisri
Microbiology and Immunology	Miss Junpen Suwimonteerabutr	Detection of <i>Leptospira interrogans</i> in urine samples of liverstocks	Prof. Wanpen Chaicumpa
Microbiology and Immunology	Miss Piyaporn Suebrakul	-	Assoc. Prof. Usanee Suthisarnsunthorn
Microbiology and Immunology	Miss Wandee Sawatmongkonkun	Rapid diagnosis of cytomegalovirus in Thai pediatric AIDS patients	Assoc. Prof. Surang Tantivanich
Microbiology and Immunology	Miss Suwaneer Sungkawasee	Detection of <i>Vibrio parahaemolyticus</i> by monoclonal – antibody based immunoassay	Prof. Wanpen Chaicumpa
Microbiology and Immunology	Mrs. Kesaree Chewachatrekasem	The multistage character of immunity to <i>Plasmodium falciparum</i> antigens in naturally exposed malaria endemic populations	Prof. Srisin Khusmith
Social Environmental of Medicine	Mr. Pornchai Kirdsiri	HIV/AIDS counselling service at hospitals in Kanchanaburi province	Dr. Jaranit Kaewkungwal
Social Environmental of Medicine	Miss Varangkana Visemanee	Biomonitoring of manganese concentration among workers in dry cell battery factory	Assist. Prof. Waranya Wongwit
Social Environmental of Medicine	Miss Waraporn Chaimchitpanid	Relationship between chromium and glucose levels in blood and urine of electroplating manufacturing workers	Assist. Prof. Waranya Wongwit
Social Environmental of Medicine	Miss Umaporn Pinyosirikul	Biomarker of aniline exposure in rubber manufacturer	Assist. Prof. Ladda Tangbanluekal
Social Environmental of Medicine	Mr. Ram Chandra Silwal	Health education model to control soil transmitted helminthiasis among self-help group women in rural Nepal	Assist. Prof. Piyarat Buttraporn
Social Environmental of Medicine	Miss Risara Jaksuwan	-	Assoc. Prof. Kamolnetr Okanurak
Social Environmental of Medicine	Mr. Phitsanu Tulayakul	-	Assist. Prof. Waranya Wongwit
Tropical Hygiene	Mr. Narong Nitatpattana	Study on potential association between arbovirus incidence and ground temperature computation by satellite in the central plain of Thailand, 1998	Assist. Prof. Pratap Singhasivanon

M.Sc. (TROP.MED.)

Department	Name	Title of Thesis	Adviser
Microbiology and Immunology	Miss Nitchakarn Noranate	-	Dr. Jintana
Tropical Hygiene	Miss Nahathai Chulakavat	-	Assist.Prof. Pratap Singhasivanon
Tropical Hygiene	Mr. Sumate Aumpawong	Epizootiology of Japanese encephalitis virus and West Nile Virus : zoonosis of medical importance”	Assist.Prof. Pratap Singhasivanon
Tropical Hygiene	Dr. Lek Dysoley	Role of GIS in malaria and DHF control programme in Cambodia	Assist.Prof. Pratap Singhasivanon
Tropical Nutrition and Food Science	Ms. Napa Onvimala	Application of reverse transcriptase polymerase chain reaction for identification of rotavirus serotypes	Assoc.Prof. Supanee Changbumrung
Tropical Nutrition and Food Science	Ms. Siriwan Tribanyatkul	Serum leptin concentrations in obese subjects and healthy controls	Assoc.Prof.Rungsumn Tungtrongchitr
Tropical Nutrition and Food Science	Miss Chuthaporn Toonboonchoo	Vitamin B ₁₂ folic acid and haematological parameters in overweight and obese Thais	Assoc.Prof.Rungsumn Tungtrongchitr
Tropical Nutrition and Food Science	Miss Phimonsri Saengkar	Vitamin B ₁₂ and folate status in cervical cytologic abnormalities in Thai women	Dr. Karunee Kwanbunjan
Tropical Nutrition and Food Science	Miss Malida Soontornruengyot	Relationships between smoking habits, hematological changes, B ₁₂ and folic acid in Thai smokers	Assoc.Prof.Rungsumn Tungtrongchitr
Tropical Pathology	Miss Suwaporn Anantrakulsin	Haematopoietic features of the bone marrow of <i>Plasmodium falciparum</i> -infected patients	Assoc.Prof.Yaowapa Maneerat
Tropical Pathology	Miss Ratchanok Kumsiri	Nitric oxide production by <i>Plasmodium falciparum</i> infected endothelial cells”	Assist.Prof. Yaowapa Maneerat
Tropical Pathology	Miss Souwanit Nakasiri	Light and electron microscopic correlation of knob proteins and staging <i>in vitro</i> : <i>plasmodium falciparum</i>	Assoc.Prof. Emsri Pongponrat

Ph.D. (TROP.MED.)

Department	Name	Title of Thesis	Adviser
Clinical Tropical Medicine	Dr. Mayfong Mayxay	<i>In vivo</i> and <i>in vitro</i> studies in acute malaria	Prof. Sasithon Pukrittayakamee
Clinical Tropical Medicine	Mrs. Kamolrat Silamut	Stage specific morphology, of <i>Plasmodium falciparum in vitro</i> and <i>in vivo</i>	Prof. Sasithorn Pukrittayakamee

Ph.D. (TROP. MED.)

Department	Name	Title of Thesis	Adviser
Clinical Tropical Medicine	Mr. Apichart Nontprasert	Neurotoxicity of antimalarial drugs in animal model	Prof. Sasithorn Pukrittayakamee
Clinical Tropical Medicine	Mrs. Emsri Pongponratn	Ultrastructural studies of <i>Plasmodium falciparum</i> in human organs the interactions between the parasitized erythrocytes and the host cells.	Prof. Sornchai Looareesuwan
Clinical Tropical Medicine	Miss Mallika Imwong	Genotyping of <i>plasmodium Vivax</i>	Prof. Sasithorn Pukrittayakamee
Helminthology	Mr. Paron Dekumyoy	Cloning of antigenic gene from female <i>Angiostrongylus cantonensis</i> adult worms	Assoc.Prof. Jitra Waikagul
Helminthology	Miss Tippayarat Yoonuan	-	Assoc.Prof. Jitra Waikagul
Medical Entomology	Mr. Chamnarn Apiwathnusorn	Some promising phytochemical Thai plants for control of mosquito vectors	Assist.Prof. Achara Asavanich
Medical Entomology	Ms. Usavadee Tharara	Ecological studies of dengue mosquito vectors in four provinces of southern Thailand	Assist.Prof.Narumon Komalamisra
Medical Entomology	Miss Yuwadee Trongtokit	-	-
Medical Entomology	Miss Pungasem Paeporn	Insecticide resistance in <i>Aedes aegypti</i> and the significance to its biochemistry and genetics	Assoc.Prof. Vanida Deesin
Medical Entomology	Miss Walairut Tuntaprasart	A study on critical indices of <i>Aedes aegypti</i> correlated with dengue transmission	Assoc.Prof. Somjai Leemingsawat
Microbiology and Immunology	Ms. Wannaporn Ittiprasert	Towards specific diagnosis of <i>Schistosoma mekongi</i> Infection	Prof. Wanpen Chaicumpa
Microbiology and Immunology	Ms. Urai Chaisri	Pathology of enterohemorrhagic <i>Escherichia coli</i> : infection and protective role of monoclonal antibodies against O-antigen and Shiga-like toxin(s)	Prof. Wanpen Chaicumpa
Microbiology and Immunology	Ms. Patcharin Saengjaruk	Development of immuno-diagnostic method for acute leptospirosis	Prof. Wanpen Chaicumpa
Microbiology and Immunology	Ms. Thitima Wongsaroj	Development of immunodiagnostic method for <i>Opisthorchiasis viverrini</i>	Prof. Wanpen Chaicumpa
Microbiology and Immunology	Ms. Surangrat Srisurapannon	Characterization of B cell-epitope of HIV-1 subtype E	Prof. Srisin Khusmith
Microbiology and Immunology	Mr. Hari Har Joshi	Detection by ELISA of <i>Plasmodium falciparum</i> and <i>Plasmodium vivax</i> antigens in malaria endemic population in Nepal	Prof. Srisin Khusmith

Ph.D. (TROP. MED.)

Department	Name	Title of Thesis	Adviser
Microbiology and Immunology	Miss Chutima Khamkhaek	Analysis of sequence polymorphism of T-cell epitope regions, Th 2 R and Th 3, <i>plasmodium falciparum</i> circumsporozoite proteins in Thai isolates	Prof. Srisin Khusmith
Social and Environmental Medicine	Mr. Ruangyuth Chaiworaporn	Studies on <i>Schistosoma spindale</i> Montgomery, 1906 (Trematoda: Schistosoma-matidae) and related taxa, the causative agent of bovine schistosomiasis in Thailand.	Assoc.Prof. Viroj Kitikoon
Social and Environmental	Mrs. Chantima Lohachit	Ecological Studies of <i>Bithynia goniomphalos</i> a snail Intermediate host of <i>Opisthorchis viverrini</i> in Northeast Thailand.	Assoc.Prof. Viroj Kitikoon
Social and Environmental Medicine	Mrs. Prapin Tharnpoophasiam	Biomarker of toxicity from environmental exposure of benzene, toluene, ethylbenzene and xylene (BTEX)	Assist.Prof. Ladda Tangbanluekal
Social and Environmental Medicine	Mrs. Kleebkaew Pitasawad	-	Assist.Prof. Piyarat Buttraporn
Social and Environmental Medicine	Miss Yupadee Sirisinsuk	Access and patterns of health services utilization among insured persons under the social security act, 1990	Assist.Prof. Wijitr Fungladda
Social and Environmental Medicine	Mr. Tawadchai Suppadit	Modification and development of broiler litter as protein source in concentrate feed for fattening cattle to deducting the environmental impact and improving the farmers' income	Assist.Prof. Piyarat Buttraporn
Tropical Hygiene	Ms. Siriwan Chancharoen	-	Assist.Prof. Pratap Singhasivanon
Tropical Hygiene	Miss Sawanee Tengrungsun	Survival of Thai adult AIDS patients in the tertiary care hospital, Thailand	Assist.Prof. Pratap Singhasivanon
Tropical Nutrition and Food Science	Mrs. Kanjana Hongtong	Platelet fatty acids and serum lipoprotein A in hyperlipidaemia and related heart disease patients and healthy individuals	Assoc.Prof. Supranee Changbumrung
Tropical Nutrition and Food Science	Miss Wanida Pongstaporn	Lipid peroxidant and antio-xidant enzymes in smokers before and after vitamin C and E supplement	Assoc.Prof. Rungsumn Tuntrongchitr
Tropical Nutrition and Food Science	Miss Pittayaporn Moungrnoi	-	Assoc.Prof. Supranee Changbumrung

Ph.D. (TROP. MED.)

Department	Name	Title of Thesis	Adviser
Tropical Nutrition and Food Science	Miss Duangkamol	Levels of antioxidants for health determination in overweight and obese Thais	Assoc.Prof.Rungsun Tungtrongchitr
Tropical Radioisotopes	Mr. Mana Vatakul	Cerebral blood flow in cerebral metalia by using SPECT and MR spectorscopic	Prof. Polrat Wilairatana
Tropical Pathology	Miss Thanida Tangwanicharoen	Production of tissue cytokines in AIDS	Assist.Prof. Parnpen Viriyavejakul

Ph.D. (CLIN.TROP.MED.)

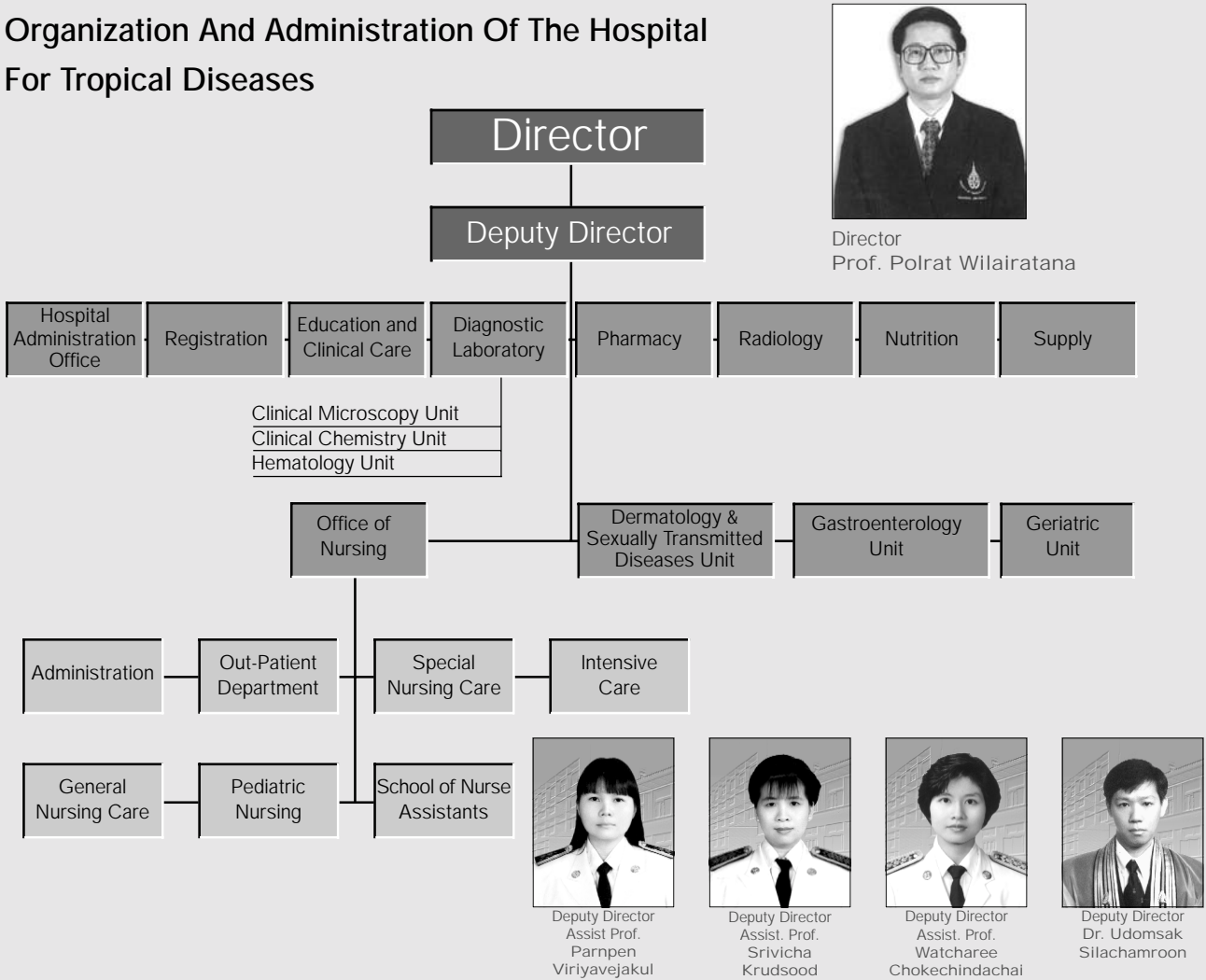
Department	Name	Title of Thesis	Adviser
Clinical Tropical Medicine	Dr. Yoshinari Moriyama	The clinical relevances of cytokines on severe malaria patients and effects of prostagladin derivatives	Prof. Polrat Walairatana

The Hospital for Tropical Diseases

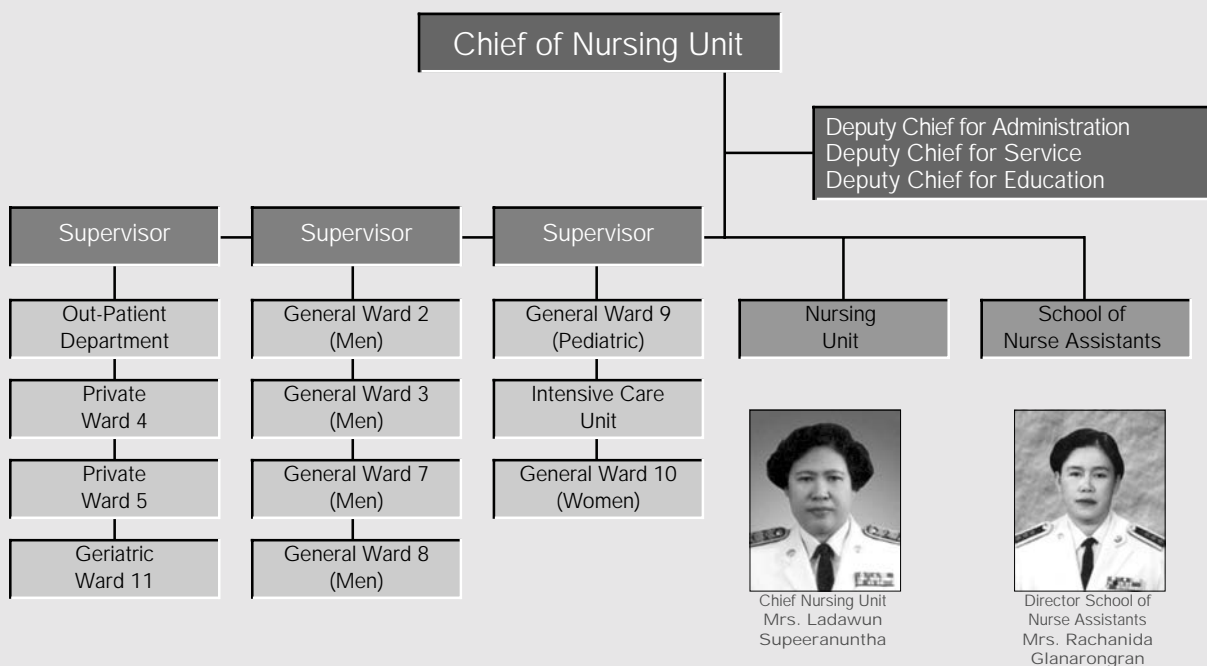
Office Telephone: 248 3183 or 246 9000-12 ext. 1624, 1625



Organization And Administration Of The Hospital For Tropical Diseases



Nursing Unit



MEDICAL CARE SERVICES

Medical care service is one of the main functions of the Faculty of Tropical Medicine. The Hospital for Tropical Diseases, a specialized hospital, provides medical care services for patients suffering from tropical diseases, as well as internal medicine. At present, the Hospital for Tropical Diseases can accommodate up to 250 in-patients. There are services for out-patients, 4 male and female general wards, a children's ward, 2 special care wards, a geriatric ward, an intensive care unit, an intensive care unit for tropical diseases, a gastroenterology division, a dermatology division, and a sexually-transmitted diseases division.

Out-Patient Department services are as follows:

- General medicine: daily except public holidays, 8.00-16.00 hr.
- Malaria clinic: 24 hours daily.
- Electrical stimulation health chair: daily from 6.30-16.00 hr.
- Health examination for emigrant workers: daily except public holidays, 8.00-16.00 hr.
- Laboratory diagnosis for helminthiasis: daily except public holidays, 8.00-10.00 hr.
- Consultation in traveler medicine.
- Center for diagnosis and detection of various specimens in cooperation with other departments and units of the Faculty.
 - Medical care services to all Mahidol University students, staff and their families.
 - Electrocardiography (ECG).
 - Spirometry.
 - Audiogram.
 - Visual acuity test and color blindness test.

Other Special Clinics are:

- Dermatology clinic: Mondays and Wednesdays, 9.00 -12.00 hr.
- Sexually-transmitted diseases clinic: Mondays, 9.00 -12.00 hr.
- Childrens' clinic: Mondays, Wednesdays and Fridays, 13.00 - 16.00 hr.
- Well baby clinic: Mondays, Wednesdays and Fridays, 13.00 - 16.00 hr.
- Chest clinic: Tuesdays, 9.00 -12.00 hr.
- Gastroenterology clinic: Tuesdays and Wednesdays, 9.00 -12.00 hr.
- Geriatric clinic: Tuesdays, 9.00 -12.00 hr.
- Ear, nose, throat clinic: Tuesdays, 9.00 -12.00 hr.
- Gnathostomiasis clinic: Wednesdays and Fridays, 9.00 -12.00 hr.
- Nephrology clinic: Wednesday, 9.00 - 12.00 hr.
- Allergy clinic: Wednesday, 9.00 - 12.00 hr.



In the fiscal year 2000 (October 1999-September 2000), the numbers of patients treated in the Hospital for Tropical Diseases are classified according to disease as follows:

Diseases	No. of out-patients	No. of in-patients
1. Falciparum malaria	779	762
2. Vivax malaria	922	648
3. Mixed, (PF + PV)	35	35
4. Malariae malaria	35	28
5. Unidentified infections	177	159
6. Typhoid	6	4
7. Dengue hemorrhagic fever	73	67
8. Hepatitis	232	34
9. Diarrhea	235	56
10. Tapeworm infections	46	-
11. Liver fluke infections	34	-
12. Round worm infections	-	1
13. Whip worm infections	-	1
14. Hookworm infections	19	-
15. Gnathostomiasis	1,118	6
16. Strongyloides infections	28	1
17. Filariasis	6	1
18. Lung infections and other diseases	370	22
19. Other diseases	23,854	1,021
19. Dermal infections	2,128	14

Activities during the year:

1. Health check-up for Assistant Nurse students.
2. Health check-up for 733 inhabitants at Bong Tee District, Amphoe Sai Yok, Kanchanaburi Province.
3. 4 health exhibitions on various occasions.
4. Health education on malaria and parasitic infections to college students.
5. Higher education as part of staff development.
6. Visit and training for M.Sc. students from the Faculty of Public Health, Mahidol University, Malaria Division, CDC and foreign students and medical staffs.



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 turnaround time for each test, the cost per test and the place where specimens should be sent are included in the table.

Disease/ Infection	Serological test used	Specimen required	Time required (hours)	Cost per test (Baht)	Place where specimen should be sent
Gnathostomiasis	1) Indirect ELISA (uses purified specific antigen)	1) 5 ml of clot blood or	3	300 (Thai)	Dept. Microbiology and Immunology via OPD
	2) Western blot analysis (uses crude extract of the infective larvae)	2) 1-2 ml of serum	1	2,000 (Foreigner)	
	Western blot analysis (crude extract of infective larvae)		3, 1 day*	200 (Thai) 1,000 (Foreigner)	Dept. Helminthology (Western blot only) via OPD, Department
Paragonimiasis	1) Indirect ELISA	1) 5 ml of clot blood or	3	300 (Thai)	Dept. Microbiology and Immunology via OPD
	2) Western blot analysis (partially purified adult worm antigens are used for both assays)	2) 1-2 ml of serum	1	2,000 (Foreigner)	
	3) Western blot analysis (crude extract of adult worms)	3) same	3, 1 day*	200 (Thai) 1,000 (Foreigner)	Dept. Helminthology via OPD
Trichinellosis	1) Indirect ELISA/dot-ELISA	1) 5 ml of clot blood or	3/1	300 (Thai)	Dept. Microbiology and Immunology via OPD
	2) Western blot analysis (the antigen used is either E-S, crude or affinity purified somatic antigens of the infective larvae)	2) 1-2 ml of serum	1	2,000 (Foreigner)	
Strongyloidosis	1) Indirect ELISA/dot-ELISA	1) 5 ml of clot blood or	3/1	300 (Thai)	Dept. Microbiology and Immunology via OPD
	2) Western blot analysis (uses partially purified antigens from filariform larvae)	2) 1-2 ml of serum	1	2,000 (Foreigner)	
	3) Indirect ELISA (Molecular weight cut off antigen from filariform larvae) Western blot (crude extract of filariform larvae)	3) same	3, 1 day*	200 (Thai) 1,000 (Foreigner)	Dept. Helminthology via OPD
Toxocariasis	1) Indirect ELISA (Molecular weight cut off antigens from adult worms)	same	3	200 (Thai)	Dept. Helminthology via OPD
	2) Western blot (crude extract of adult worms)			1,000 (Foreigner)	
Angiostrongyliasis	Western blot (crude extract and partially purified antigens from adult worms)	same	3	200 (Thai) 1,000 (Foreigner)	Dept. Helminthology via OPD
Cysticercosis	Western blot (cystic fluid antigen)	same	3	200 (Thai) 1,000 (Foreigner)	Dept. Helminthology via OPD
Leptospirosis	1) 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

* 2 hours for special request by Western blot analysis

Disease/ Infection	Serological test used	Specimen required	Time required (hours)	Cost per test (Baht)	Place where specimen should be sent
	2) Antigen detection assay	Urine sample (10 ml)	1	100	Directly at the Dept. Microbiology and Immunology
<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) Rectal swab, food/water samples in buffered peptone solution	1-2	300	Dept. Microbiology and Immunology via OPD
Cholera caused by serogroup O: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	Monoclonal antibody-based dot-blot ELISA using specific monoclonal antibodies (antigen detection)	1) Rectal swab in 1% alkaline peptone solution 2) Watery stool	1-3	150	Dept. Microbiology and Immunology via OPD

Other tests

Disease/ Infection	Serological test used	Specimen required	Time required (hours)	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 Radiosotopes
Red cell folate	Microbiological test using <i>Lactobacillus casei</i>	Heparinized blood (2 ml)	7	150	Dept. Tropical Radiosotopes
Vitamin B12	Radiodilution assay	1. 5 ml of clot blood or 2. 1-2 ml of serum	5	150	Dept. Tropical Radiosotopes
Pyrogen free testing	Rabbit test by intravenous injection of the fluid to be tested and determination of body temperatures at intervals	Fluid to be tested	7 days	2,000	Dept. Microbiology and Immunology

Disease/ Infection	Serological test used	Specimen required	Time required (hours)	Cost per test (Baht)	Place where specimen should be sent
Detection of heavy metals in blood (lead, arsenic, cadmium, copper, selenium, chromium, aluminium)	Atomic absorption	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 spectrophotometer (GCMS)	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 and Immunology
Monoclonal antibodies to <i>V. cholerae</i> O:139	Monospecificity to <i>V. cholerae</i> O:139 LPS	150 Baht/ml	Dept. Microbiology and Immunology
Monoclonal antibodies to <i>Salmonella</i> core polysaccharide	Specific to core-polysaccharide of the genus <i>Salmonella</i> (react to all salmonellae)	150 Baht/ml	Dept. Microbiology and Immunology
Monoclonal antibodies to group D <i>Salmonella</i>	Specific to <i>Salmonella</i> antigen 9	150 Baht/ml	Dept. Microbiology and Immunology
Monoclonal antibodies to <i>Pertussis</i> toxin	Specific to S1 component (active, toxic part of pertussis toxin)	150 Baht/ml	Dept. Microbiology and Immunology
Monoclonal antibodies to Verotoxins I and II of enterohemorrhagic <i>Escherichia coli</i>	Specific to A subunit or B subunit	150	Dept. Microbiology and Immunology
Monoclonal antibodies to <i>E. coli</i> O157	Specific to lipopolysaccharide	150	Dept. Microbiology and Immunology
Monoclonal antibodies to the genus <i>Leptospira</i> / pathogenic species <i>interrogans</i>		150	Dept. Microbiology and Immunology
Monoclonal antibodies to E-S antigen of <i>Trichinella spiralis</i>			Dept. Microbiology and 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 and 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	500 Baht/mg	Dept. Microbiology and Immunology
Affinity purified <i>-Trichinella spiralis</i> antigen	Highly purified antigen from MAb-based affinity column chromatography	1,000 Baht/mg	Dept. Microbiology and Immunology

* Order should be made in advance

Annual Report FY 1999-2000

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

FACULTY OF TROPICAL MEDICINE, MAHIDOL UNIVERSITY, BANGKOK, THAILAND



Sornchai Looareesuwan
Director



Suvanee Supavej
Deputy Director

TROPMED/Thailand has 3 major functions, namely 1) Teaching and training, 2) research and 3) services. Activities conducted under the 3 roles are reported according to the 5KEY RESULTS AREAS as follows:

KRA1. ENHANCED PROGRAMME QUALITY AND RELEVANCE

1.1 Post-graduate regular courses. Five post-graduate, regular courses at the international level are being offered by TROPMED/Thailand with a total of 167 students from 14 countries. There were 55 graduates in the academic year 1999/2000. A joint course with The Liverpool School of Tropical Medicine leading to the Master of Tropical Paediatrics was also conducted.

1.2 Undergraduate courses

TROPMED/Thailand also offers 2 undergraduate courses :

- 1) Elective programme in tropical medicine with 19 medical students from 7 countries;
- 2) Certificate in Nurse Assistant with 190 students.

In the FY 1999/2000, 374 students from 17 countries enrolled to study in 8 courses offered by TROPMED/Thailand. Seventy-three percent of these students were fee paying attendants and 274 (73%) graduated in the year under review.

Table I: Number of students attending the 5 regular courses

Course	Number	No. of nationalities	No. of fee paying students	No. of graduates
Postgraduates DTM & H (6 month course)	35	14 (Austria, Bangladesh, Cambodia, Japan, Lao PDR, Malaysia, Myanmar, Pakistan, Philippines, Russia, Thailand, Vietnam, USA)	21 (60%)	33 (94%)
MSc (CTM) (1 year course)	18	13 (Austria, Bangladesh, Cambodia, Lao PDR, Malaysia, Myanmar, Pakistan, Philippines, Russia, Thailand, Vietnam, USA)	14 (77%) ¹	8 (100%)
MSc (TM) 1 st year	21	3 (Cambodia, Nepal, Thailand)	15 (71%) ¹	2 (34%)
2 nd year	14	2 (Philippines, Thailand)		
3 rd year and over	21	4 (Nepal, Philippines, Thailand, Vietnam)		
PhD (TM) 1 st year	20	2 (Nepal, Thailand)	19 (95%)	4 (11%)
2 nd year	17	2 (Lao PDR, Thailand)		
3 rd year	13	1 (Thailand)		
4 th year	6	2 (Thailand, Vietnam)		
Sub total	165	14	71 (42%)	67 (40%)
PhD (CTM) 2 nd year	1	1 (Japan)	0	0
4 th year	1	1 (Thailand)	0	0
MSc (Trop Paediatrics)	1	1	1 (100%)	1 (100%)
Undergraduate Elective programme in Tropical Medicine	16	7 (Austria, Canada, Germany, Japan, Pakistan, Singapore, USA)	16 (100%)	16 (100%)
Certificate in Nurse Assistant	190	1 (Thailand)	190 (100%)	190 (100%)
Grand Total	374	17	278 (74%)	274 (73%)

- 1.3 Training courses/Workshop/Meetings. Five training courses at the national level, and 7 at the international level, 3 international workshops and 1 international meeting were convened during FY 1999/2000 with a total number of 1,250 participants.

KRA2. INCREASED ACCESS TO MARKET

- 2.1 **Active Marketing.** The campaign “Open the door to TROPMED” was organized to allow science related students to see facilities and learning atmosphere at the Faculty of Tropical Medicine on 9 January 2000 with 145 students and 6 lecturers from 5 universities.
- 2.2 **New brochure** produced. Three thousand brochures were produced and over 2,000 were distributed.
- 2.3 Participation of the Seminar and Exhibition on Thai Higher Education. Three staff of TROPMED/Thailand participated in the Seminar and Exhibition on Thai Higher Education organized by Ministry of University Affairs during 25-29 September 1999 in Ho Chi Minh City and Hanoi, Vietnam. Prof.Sornchai Looareesuwan, Director of TROPMED/Thailand was invited as a speaker in the seminar entitled “Vietnam-Thai Cooperation : Opportunities for Linkages”.

KRA3. INCREASED LINKAGES.

1. More MOU/Agreement/Record signed

Three more Memorandum of Understanding/Agreement/Record of Discussions were signed.

1. Agreement on Academic Cooperation with Nagasaki University, Japan and Mahidol University on behalf of the Faculty of Tropical Medicine.
 2. Memorandum of Understanding Pertaining to the Collaboration between the Faculty of Tropical Medicine, Faculty of Social Sciences and Humanities of Mahidol University and the Department of Communicable Diseases Control, Ministry of Public Health, Thailand.
 3. The Record of Discussions between the Japanese Implementation Study Team and the Authorities Concerned of the Government of the Kingdom of Thailand on Japanese Technical Cooperation for the Project for the Asian Centre of International Parasite Control.
2. **SEAMEO-Canada Programme of Corporation FY1999/2000.** The SEAMEO-CIDA Workshop on HIV/AIDS/STD Surveillance was conducted during 20-26 December 1999 in Vientiane, Lao PDR. There were 5 participants from Cambodia and 10 participants from Lao PDR. After the workshop, participants developed the AIDS Surveillance System to be used for their respective countries.
3. **Consulting Services.** Staff of TROPMED/Thailand were invited to provide consulting services in projects supported by other international organizations.

Table 2. Consulting service provided by TROPMED/Thailand staff.

Projects	Nature of the project	Supporting agency of the project	No. of TROPMED staff invited	Duration
1. SEAMEO-GTZ	Epidemiology	GTZ	2	1 wk
2. Malaria Control in Cambodia, Laos and Vietnam	Malaria Control	EC	2	2 wk
3. Lower Genital Tract infection in Vietnam	Infections diseases	WHO	1	3 days
4. EPH Project in Nepal	Qualitative data analysis	USAID	1	10 days
5. Dengue/DHF in Myanmar	DF/DHF	WHO	1	3 wk
6. PDT MIZTEFOSINE Meeting	Tropical Medicine	WHO	1	2 days
7. Health Impact Development	Mosquito-borne diseases	WHO	2	5 days
8. Malaria Control	Data analysis	EC	2	10 days
9. Malaria Research Group	Malaria Research	WHO	1	1 wk
10. Scientific and Ethical Review Group	Ethical review	WHO	1	3 days
11. SEAR/WPR Biregional Meeting	Malaria control	WHO	1	4 days
12. Planning Workshop	Malaria control	EC	1	6 days
13. Roll Back Malaria	Malaria control	WHO	1	5 days
14. Maternal and Child Health in Lao PDR	MCH	WHO	1	3 days
15. Site visit in Vietnam	Research protocol development	WHO	1	4 days

4. **Visitors.** One hundred and fifty-five visitors from 16 countries visited TROPMED/Thailand during FY 1999/2000.

KRA4. IMPROVED FINANCIAL STATUS

There were three sources of revenue for activities pertaining to the three major roles of TROPMED/Thailand : 1) Government budget; 2) Revenue from medical care fees, academic services and other activities; and 3) Research funds.

Table 3: Sources of revenue.

Sources of revenue	Amount in million Baht	% Increased
1. Government budget	272.53	+ 5.8
2. Revenue from services and other activities	37.78	+ 10.4
3. Research funds from other organizations	70.38	+ 30.2

KRA5. ENHANCED QUALITY OF SEAMEO MANAGEMENT

TROPMED/Thailand has a total of 718 staff comprising 89 academic staff, 147 academic assistants and research staff, 141 administrative personnel and 341 employees. The qualification and academic posts holding by these 89 academic staff are shown in Table 4.

Table 4: Qualification of 89 academic staff.

Qualification	No	%
PhD	59	66.0
Master	24	27.0
Bachelor	6	7.0
Total	89	100.0

The academic posts of 89 academic staff compared to those of Mahidol University are shown in Table 5.

Table 5: Academic posts of 89 staff of TROPMED/Thailand.

	Academic Posts			
	holding by FTM staff		holding by Mahidol University staff	
	No.		No.	
Professors	11	(12.4%)	135	(4.8%)
Associate Professors	27	(30.3%)	753	(26.9%)
Assistant Professors	30	(33.7%)	871	(31.1%)
Lecturers	21	(23.6%)	1,044	(37.2%)
Total	89	(100.0%)	2,803	(100.0%)

5.1 Number of staff promoted or obtaining higher qualification

Table 6. Number of staff promoted.

Academic rank	:	Professor	=	1
		Associate Professors	=	1
		Assistant Professors	=	6
Career rank	:	Higher rank	=	56
Higher qualification	:	Higher degree	=	14
Total			=	78

5.2 Number of research projects and publication. TROPED/Thailand staff undertake 140 research projects with a total research grants of 70.4 million Baht and published 117 research papers and 39 books.

	New project	On-going	Accomplished
No of research projects	50 (35%)	58 (42%)	32 (23%)
No of published papers	= 117		
No of published textbooks	= 39		

5.3 Number of staff taking study leave, attending training courses and attending meetings/seminars/workshops.

Thirty-one staff (4.3%) took study leaves for higher education. Twenty-four (3.3%) attended training courses in Thailand and abroad. One hundred and thirty-three staff (32.6%) attended meetings, seminars, workshops. One staff may attend more than one meeting/seminar/workshop.

Table 8. Staff development through higher study, training courses, seminars/workshops.

Category of staff development	In country	Abroad	Total
Study leave	26 (3.6%)	5 (0.7%)	31 (4.3%)
Attending training courses	16 (2.2%)	8 (1.1%)	24 (3.3%)
Attending meetings/ seminars/workshops			
No of staff	85 (25.8%)	49 (16.8%)	34 (18.7%)
No of attendance	491	109	600

5.4 Special talks/lecturers

To develop and/or improve knowledge of staff, 10 special talks/lecturers on various topics including information technology were organized for 367 attendants.

5.5 Patients treated for tropical diseases

The Hospital for Tropical Diseases offers medical care service to patients suffering from tropical and other diseases. The Hospital has 250 beds with 19 medical doctors, 72 nurses and 95 nurse assistants. The total number of outpatients treated were 25,782 and the number of patients admitted to the Hospital were 3,274. Routine and special laboratory services for diagnosis of tropical infections were also provided.

5.6 Improved infrastructure

An international guest house with 66 furnished rooms are opened for students/guests/visitors of TROPED Thailand in May 2000.

5.7 Number of staff awarded

- 1) Distinguished staff. Four staff; two from Department of Medical Entomology and one each from the Hospital for Tropical Diseases and Department of Microbiology and Immunology were awarded as 1999 Distinguished Staff of the Faculty of Tropical Medicine.
- 2) National and International Awards.

Recipients	Awards
1. Prof.Wanpen Chaicumpa	<ol style="list-style-type: none"> 1. Outstanding Scientist in the field of immunology awarded by the Foundation for Promotion of Science and Technology under the Royal Patronage of H.M. the King of Thailand. 2. Best research in the field of Chemistry and Pharmaceutical awarded by the National Research Council of Thailand.
2. Prof.Sornchai Looareesuwan	<ol style="list-style-type: none"> 1. Barons WHO's WHO. In : K Coper, C Kato, B Moon, H Park, eds. The Baron 500 : Leaders of the New Century, 2000 commemorative edition. 2000 : 57. 2. International Man of the Year 2000-2001. International Biographical Centre (IBC), Cambridge, UK. In recognition of his services to tropical medicine.

The Asian Centre of International Parasite Control (ACIPAC)

FACULTY OF TROPICAL MEDICINE, MAHIDOL UNIVERSITY, BANGKOK, THAILAND

Office Telephone : 2469000 – 13 ext. 1338, 1339 Fax : 643-5616

Project Manager

Professor Sornchai Looareesuwan

Chief Advisor

Professor Somei Kojima

Assistant Project Manager

Assoc.Prof. Jitra Waikagul

Longterm Expert

Dr. Nobuhiko Nagai

JICA Coordinator

Mr. Mitsuhiro Iwashita



Sornchai Looareesuwan



Somei Kojima



Jitra Waikagul



Nobuhiko Nagai



Mitsuhiro Iwashita

Secretary

Ms. Wanida Onwan



Wanida Onwan

Assistant Secretary

Ms. Rattanawadee Nanlar



Rattanawadee Nanlar



The Asian Centre of International Parasite Control (A C I P A C)

Under Hashimoto Initiative on the Global Parasite Control Program, the agreement between Japan International Cooperation Agency and Mahidol University and Department of Communicable Diseases Control, Ministry of Public Health, Thailand was signed on 23rd March 2000, to establish the Asian Centre of International Parasite Control attached to the Faculty of Tropical Medicine (FTM), Bangkok. The Project Design Matrix (PDM) has been formulated for its first five years plan, 2000 to 2004. The project purpose defined as the basis for strengthening of parasite control programs in Southeast Asia is established in terms of human resources and information system at ACIPAC. This project will contribute to the super goal that is parasitic diseases are substantially reduced as public health problems in Southeast Asia. The main activities are:

- to develop curriculum and training materials, preparing of training facilities and conduct the training courses of personnel in charge of parasite control
- to develop parasite control models based on operational researches
- to establish human network
- to establish information network
- monitoring and evaluation of the project

Since then infrastructure of the FTM has been renovated to accommodate the ACIPAC activities i.e. classrooms, laboratories, dormitory and field stations. After Chief Advisor, Expert and Coordinator were dispatched from Japan to Bangkok in August 2000, ACIPAC office started to operate. Dean of the Faculty of Tropical Medicine was designated as Project Manager. ACIPAC activities are conducted through three committees, General Management Group, Curriculum Development and Information Network. At present, the first priority is given to the preparation of Third Country Training Course. The administrative members of ACIPAC visited participating countries in the Greater Mekong Subregion (GMS) to gather information on current situation of parasite control program, school health curriculum in primary schools and to promote collaboration between participating countries and ACIPAC.

December 19 – 20, 2000, the Curriculum Development Workshop was held at the FTM. Three representatives each from Cambodia, Lao PDR, Myanmar, Thailand, and one from Vietnam were invited to the workshop to discuss the curriculum developed by ACIPAC and related issues concerning the training. Thai experts from universities, Ministry of Public Health and Ministry of Education were also invited as discussants. Parasitology, Epidemiology, Primary Health Care, Health Education, Project Management, Project Formulation and Field Practice are the main subjects in the curriculum. School Health Approach in Parasite Control is the keyword in conducting this training.

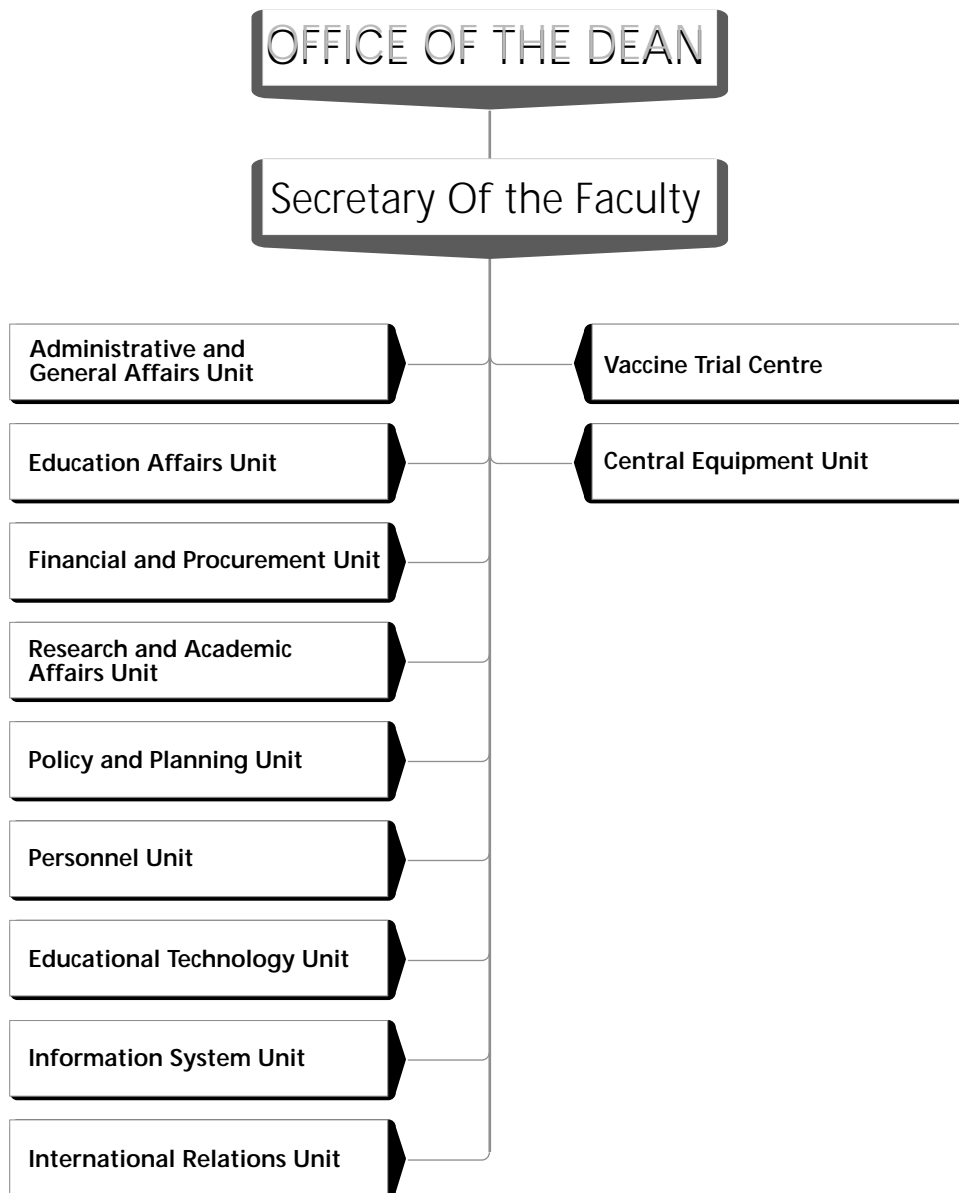
The first training course is expecting to convene in September/October, 2001.

In March 19 – 20, 2001, ACIPAC will organize an International Meeting on Hashimoto Initiative on Global Parasite Control, Bangkok. Representatives from Ministry of Health of GMS Countries, representatives from WHO, UNICEF, The World Bank and other NGOs working in the field of Health Promotion will be invited.

Information network will be developed to distribute ready-in-use information relevant to parasite control and set up links among participating countries as well as Japanese experts as knowledge and experience resources. The structure and contents of information network will be constructed on Internet-basis.

Office of the Dean

Organization and Administration of the Office of the Dean



PERSONNEL MANAGEMENT

There were 736 staff, comprised of 347 government service staff, 27 University employees, 265 permanent employees and 97 temporary staff. In the fiscal year 2000, there were 136 new staff, 94 who transferred and resigned, and 11 who retired or retired early.

Budget Management

Total expenses 226.4 million Baht

Operation statements (Operation budget) 158.5 million Baht

Investment budget 67.8 million

Government budget support 179 million, or 74%

Spent Faculty's revenue 47.3 million or 26%

In fiscal year 2000 Faculty's revenue = 49.9 million from hospital services, educational fees and other academic service fees.

Building and Area Management

In the year 2000, the Faculty opened the new 12-floor "Chalerm Phra Kiat" Building with an area of 24,000 m².

The area is divided into a science laboratory and Tropmed accommodation for students, doctors, nurses, and assistant nurses. In addition, there are patient wards and a car park. This new building has further developed teaching, research and service facilities of the Faculty.

The Office of the Dean Support Services play an important role in the smooth running of the Faculty and School related activities. These include 9 units as follows:



Vorapan Singhsilarak

SECRETARY OF THE FACULTY

Tel. 246 9000 ext. 1322 Fax. 246 9340

Vorapan Singhsilarak B.A.

ADMINISTRATIVE AND GENERAL AFFAIRS UNIT

Tel. 246 9000 ext. 1302, 1304, 1801

Head**Kannikarkaew Pinit**

B.A. (General Management), B.A. (Business Education)

The Unit is divided into 4 subunits as follows :

1.1 Documentation Subunit

Aree Masngammuang B.A. (Political Science)
 Supavadee Yaowasang B.A. (Lib.Info.Sc.)
 Maninthorn Phnumaphorn MBA.
 Pranee Kraisor
 Nathaneeporn Panampai B.A. (General Management)
 Patra Kreekul B.A. (General Management)
 Chanpen Ronsuk

1.2 Area and Transportation Subunit

Savek Chomming B.En.
 Thep Ngamnetr B.Arch.
 Prachuab Kitsupee
 Somjai Promduang
 Sombat Khamthane
 Kasem Kaewbangkerd

1.3 Public Relations Subunit

Thitika Teeranetr B.A. (Communication Arts)
 Wandee Srasalee B.A. (General Management)
 Varee Viriyarat B.A. (General Management)

1.4 Maintenance and Repairs Subunit

Nophadol Siriacharanond B.En.
 Prakorn Chumrum B.En.
 Chaiyaporn Phoopan Voc. Cert. (Electric)
 Kittivatjana Buaban Voc. Cert (Electronics)
 Panumas Tunritsa Voc Cert (Electronics)
 Tuaythep Veeyee Voc. Cert (Electrics)



Kannikarkaew Pinit



Aree Masngammuang



Supavadee Yaowasang



Maninthorn Phnumaphorn



Pranee Kraisor



Patra Kreekul



Savek Chomming



Somjai Promduang



Sombat Khamthane



Kasem Kaewbangkerd



Thitika Teeranetr



Wandee Srasalee



Varee Viriyarat



Nophadol Siriacharanond



Prakorn Chumrum



Wanpen Puttitanun



Benjarat Prompakdee



Somporn Ngamsirisomsakul



Chutamas Koomrungruang



Wannaporn Ittiprasert



Chiraporn Praevanit



Chutarat Pradabprachr



Aree Buaprae



Rangson Praevanit



Nutjanat Taiwrob

EDUCATIONAL AFFAIRS UNIT

Tel. 246 9000 ext. 1291, 1662, 1664, 1668

Head

Wanpen Puttitanun B.A.

Educational Affairs Officer

Benjarat Prompakdee B.Ed., M.Ed.

Somporn Ngamsirisomsakul B.A.

Scientist

Chutamas Koomrungruang B.Sc. (Biology)

Medical Scientist

Wannaporn Ittiprasert B.Sc. (Med. Tech.)

General Affairs Officer

Chiraporn Praevanit Voc.Cert.Commercial

Chutarat Pradabprachr B.Ed.

Aree Buaprae

General Affairs Associate

Rangson Praevanit Cert.Commercial

Nutjanat Taiwrob Cert.Commercial

Nuljun Pochana Cert.Commercial

Staff

Anurat Kalasen Cert.Commercial

Srisuchart Monchonmu Cert.Commercial

Specialist

Paul Adams B.A., Grad. Dip. Lib., M.Mgt.



Nuljun Pochana



Anurat Kalasen



Srisuchart Monchonmu



Paul Adams



Somkid Nima



Ketsinee Nima



Tham Chermkhuntod



Arayaporn Sawangrungrueng

FINANCIAL AND PROCUREMENT UNIT

Tel. 246 9000 ext. 1204, 1205, 1305, 1325

Head

Somkid Nima B.B.A. (General Management), LL.B.

The Unit divided into 3 subunits

1. Finance
2. Accounts
3. Procurement

Accountant Officer

Ketsinee Nima B.B.A. (Accounting)

Tham Chermkhuntod B.A. (General Management), B.B.A. (Accounting)

Prapaiorn Tiacharoen B.B.A. (General Management)

Chuenboon Aimpraneet B.A. (General Management)

Jeeranat Kumseranee B.A. (General Management)

Arayaporn Sawangrungrueng B.A.

Tivaporn Sen-im B.A.
 Vantana Theprod Voc. Cert.
 Chayan Muanom Cert. In Commercial
 Nopadol Preechasunthorn Voc. Cert.
 Mukda Vajrasthira B.A.

Procurement Officer

Prapaiporn Tiacharoen
 B.B.A. (General Management)
 Montri Noochan B.B.A. (Econ.)
 Kanjanaporn Sukasem B.B.A.
 Thapana Khattiwong B.B.A.
 Inthira Pansuebchuea B.B.A.
 Rangsi Prathumrat Cert. in Commerce
 Tuenjai Ketanond Voc. Cert.

Staff

Oranat Puchaka
 Mongkol Bunchakorn
 Wattana Prechasunthorn



Prapaiporn Tiacharoen



Chuenboon Aimpraneet



Jeeranat Kumseranee



Montri Noochan



Kanjanaporn Sukasem



Thapana Khattiwong



Inthira Pansuebchuea



Rangsi Prathumrat



Tuenjai Ketanond

POLICY AND PLANNING UNIT

Tel. 246 9000 ext. 1303

Head

Yaowapa Pratumsuwan B.A. (Political Science), M.P.A.

Policy and Planning Officer

Thanornsri Ketsuk B.B.A. (Money & Banking)
 Jitra Kayee B.B.A. (Money & Banking)
 Pramote Ketsuk B.Sc. (Computer Science)

The Unit is divided into 3 subunits

1. Coordination and development planning
2. Budget preparation, monitoring, review
3. Management database



Yaowapa Pratumsuwan



Thanornsri Ketsuk



Jitra Kayee



Pramote Ketsuk

PERSONNEL UNIT

Tel. 246 9000 ext. 1324, 1330

Head

Sukanya Ongaree B.A. (Soc. Ant.)

Personnel Officer

Pongsri Konthong B.A. (General Management)
 Nathaporn Kotchasri B.Ed.
 Surang Wattanakamolgul Cert. Marketing
 Supaporn Chotivatit Cert. Computer



Sukanya Ongaree



Pongsri Konthong



Nathaporn Kotchasri



Surang Wattanakamolgul



Supaporn Chotivatit



Sompoch Thanuvathana

EDUCATIONAL TECHNOLOGY UNIT

Tel. 246 9000 ext.

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.)

Prastha Kidkian Bachelor of Fine Art (Painting)

Tawan Wathanakul Voc. Cert., B.Ed.(Ed.Tech.Inn.)

Vatcharin Nagpong

General Affairs Officer

Kannika Petporee B.A. (General Management)

The Unit is comprised of 2 divisions :

1. Audio-Visual Division
2. Museum of Tropical Medicine



Saranya Vongngernyuang



Prastha Kidkian



Tawan Wathanakul



Vatcharin Nagpong



Kannika Petporee

Functions of the Unit

1. To produce and service educational media (such as slides, videos, medical illustrations, multimedia of tropical diseases) for staff of the Faculty and the Hospital for Tropical Diseases, and Assistant Nurses of the Hospital School
2. To prepare and control audio-visual equipment for teaching, seminars and workshops
3. To provide instruction in making educational media to staff and others, both inside and outside the Faculty



Duangjai Sahassananda

INFORMATION TECHNOLOGY UNIT

Tel. 246 9000 ext. 1521, 1526

Head

Duangjai Sahassananda B.Sc.(Med.Tech.), M.Sc.
(Information Technology in Business)

Programmer

Somchai Pichaiyongvongdee B.Sc.(Public Health), M.Sc.
(Technology of Information System Management)

Computer

Kitti Thongsri B.Sc. (Computer Science)

Krissada Boonruang B.Sc. (Computer Science)

Wuttichai Kitprethaworn M.6 (General Affairs Assistant)

Wimol Chotithammapiwat B.Sc. (Computer Science)

General Affairs Associate

Jetsadaporn Chantachorn B.A.(General Management)

Electronic Associate

Pongnatee Kingsawat Dip. in Voc. Ed. (Electronic)

Illustration Office

Anakanun Hinjiranan B.A. (Visual Communication Design)

The Information Technology Unit provided information and computer services throughout FY 1999/2000 for the faculty's staff, students and participants in short training courses such as :

I. Lecture

Special lecture in information technology

4 times

II. IT visiting



Krissada Boonruang



Wuttichai Kitprethaworn



Wimol Chotithammapiwat



Jetsadaporn Chantachorn



Pongnatee Kingsawat



Anakanun Hinjiranan

IT visiting to other institutes

4 times

III. Training

Computer software training 12 times for 253 participants (20 terminals each time)

IV. General services

The unit provide services for the faculty such as Computer room, UTP installations, Consulting/Program installation/Virus scan, Computer upgrades, Slide making, Laser print, Color print, Computer scan image and OCR.

V. Database projects

The unit has 2 projects in information technology:

1. 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 health and economic information in GIS form.

2. SEAMEO-TROPMED (Virtual Library, Homepage).

VI. Network and Application development

The unit is responsible for development of the computer system and programming in

- Network for Chalermprakiet building
- 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.
- Faculty Homepage on <http://www.tm.mahidol.ac.th>
- Intranet for the Administration Section.

INTERNATIONAL RELATIONS UNIT

Tel: 2469000-13 ext.1327, 1318 Fax: 2469006 E-mail: tmknt@mahidol.ac.th

Head

Keeratiya Nontabutra, B.A.

General Affairs Officer

Wanida Onwan, B.A.

Sethavudh Kaewwiset, B.A.

Ratanawadee Nanlar, B.A.

Staff

Prachoom Buaprasert



Keeratiya Nontabutra



Wanida Onwan



Sethavudh Kaewwiset



Ratanawadee Nanlar

CENTRAL EQUIPMENT UNIT

Tel. 246 9000 ext. 1291, 1662, 1664, 1668

Head

Yupa Chantachum M.Eng. (Nuclear Tech.)

Scientist

Hathairad Hananantachai M.Sc. (Environment)

Medical Science Associate

Somchai Pooduang Cert. Medical Science Technology

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



Yupa Chantachum



Hathairad Hananantachai



Somchai Pooduang



Pornpimon Adams



Warissara Chaiyabhandhu



Sivaporn Sangpan



Natapong Pensuk



Ronnachai Rarerng



Phaibul Vasanakomut

RESEARCH AND ACADEMIC AFFAIRS UNIT

Tel. 246 9000 ext. 1524, 1525 Fax. 643-5578

Head

Pornpimon Adams B.Sc. (Biology), M.Sc. (Trop. Med.)

General Affairs Officer

Warissara Chaiyabhandhu

B.A. (General Management)

Sivaporn Samung B.A. (Lib.Info.Sc.)

Database Developer

Natapong Pensuk B.Sc. (Computer Science)

Illustration Officer

Ronnachai Rarerng (B.Ed.Tech.Inn.)

Phaibul Vasanakomut

The Unit provides publishing facilities, such as the Annual Report, the *Mosquito Borne Diseases Bulletin*, *The Journal of Tropical Medicine and Parasitology*, prospectuses, 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 secretarial service for the Ethical Committee of the Faculty of Tropical Medicine, Mahidol University.

In the year 2000, the Unit provided the following services

1. Circulated 26 research funds
2. Circulated 14 awards
3. Provided support to organize 16 special lectures
4. Secretarial services for the Ethical committee of the Faculty of Tropical Medicine; 21 projects
5. Produced 4 volumes of the *Mosquito Borne Diseases Bulletin*, 2 volumes of the *Journal of Tropical Medicine and Parasitology*, 18 Brochures and Posters, 1 issue of the Annual Report, and 1 issue of JITMM/FBPZ abstract book
6. Opened a publication service to external clients.

Seminars, Workshops and Training Courses at the Faculty of Tropical Medicine

1. Practical Training on Management of Severe and Complicated Malaria Cases

26 October -5 November 1999

Lao PDR	2	Vietnam	2
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2. APCO Training Course for Senior Administrators and Leaders of Parasite Control Project

10-20 2November 1999

Bangladesh	2	Bhutan	2
Cambodia	2	Indonesia	3
Japan	1	Lao PDR	2
Nepal	2	Philippines	3
Sri Lanka	1	Vietnam	2
Thailand	6		

3. Regional and Field Training Programme in Epidemiology and Control of Tropical Diseases

22 May -11 August 2000

Cambodia	2	Lao PDR	3
Vietnam	3		

4. Training on the Health Mapper for the Mekong Countries

25-29 September 2000

Cambodia	3	China	2
Lao PDR	4	Myanmar	2
Switzerland	3	Vietnam	2

5. Special Training on Tropical Diseases

14 June -13 December 1999

Romania	1
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6. Special Training on Tropical Epidemiology

6 March -28 June 2000

Bangladesh	2
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7. Special Training on Child Health

20 March - 19 December 2000

Bangladesh	1
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INTERNATIONAL MEETING

1. The Toyota Foundation Mini-Symposium on Malaria Diagnosis and Control of Malaria in Asia and Brazil
13-14 January 2000

Brazil	1	China	1
Indonesia	2	Japan	4
Thailand	84	USA	1
Vietnam	2	Singapore	1

2. 1st Conference on Bioplaguicides
23 June 2000

Cuba	3	Thailand	55
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ELECTIVE STUDENT IN TROPICAL MEDICINE

Name	Institute	Country	Duration
1. Mr. Matthew Valentine	The University of Adelaide Medical School	Australia	7-31 Dec.99
2. Ms. Dioni Tai	"	"	"
3. Ms. Caroline Chessex	The University of Toronto	Canada	31 Jan-25 Feb.00
4. Dr. Kahl Monika	Berlin	Germany	25 Jan-25 Feb.00
5. Ms. Hannah Trenkner	Humboldt University Berlin	Germany	7-21 Mar.00
6. Mr. David Hecht	Midwestern University	USA	20-21 April 00
7. Mr. James Hall	"	"	"
8. Mr. Jens Haeter	George Washington University	"	"
9. Mr. Kenneth Muir	University of Dundee School of Medicine	UK	13 Jul.-31 Aug.00
10. Mr. Jonathan Bradley	"	UK	"
11. Mr. Sebastian Brokhaus	Freie Universitat Berlin	Germany	1 Aug.- 1 Sept. 00
12. Mr. Isaak Bruno Wontroba	"	Germany	"
13. Mr. Walter Scholz	University of Vienna	Austria	1-29 Sept.00
14. Mr. Erich Weghofer	"	"	"
15. Mr. Mario Sierenik	"	"	"
16. Mr. Roland Haberl	"	"	"
17. Mr. Gavin Allison	University of Sydney	Australia	"
18. Ms. Mary Stevens	"	"	18 Sept.-13 Oct. 00
19. Mr. Alexander Outhred	"	"	"

International Linkages

The Faculty of Tropical Medicine has ongoing collaborative activities in research and training with the following :

1. WHO/TDR Programme
2. Freie Universität Berlin, Germany, under the assistance of the 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 Association for Parasite Control (JAPC)
11. SEAMEO TROPMED Regional Centres in Indonesia, the 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 Infectieuses et Médecine Tropicale, Groupe Hospitalier Pitié 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
25. Memorandum of Understanding between the Faculty of Tropical Medicine, Mahidol University and Liverpool School of Tropical Medicine, UK.

The nature of these activities are: collaborative research work; consultative services; personnel, specimen and information exchanges; joint training courses, seminars and conferences.

Visitors

Name	Country
1. Dr.Piero Olliaro	WHO/Geneva
2. Prof.Navaratnam	Malaysia
3. Dr.Moriyasu Tsuji	Japan
4. Dr.Kiyoshi Tanaka	Japan
5. Mr.Takaaki Hara	Japan
6. Dr.Tsutomu Takeuchi	Japan
7. Dr.Toshinobu Sata	Japan
8. Mr.Kazumi Jigami	Japan
9. Dr.Nobuhiko Nagai	Japan
10. Dr.Lin-Lin Kaku	Japan
11. Dr.Akira Hashizume	Japan
12. Mr.Ryujiro Sasao	Japan
13. Mr.Dan Jessop	USA
14. Prof.Masamichi Aikawa	Japan
15. Prof. Emeritus Tada	Japan
16. Dr.Toru Obata	Japan
17. Dr.Yamaji Nakano	Japan
18. Dr.Kaki Koku	Japan
19. Prof.Thomas Michael Dexter	UK
20. Prof.Yutaro Kaneko	Japan
21. Prof.Katsushi Tokunaga	Japan
22. Dr.Jun Ohashi	Japan
23. Dr.Tikki Pang	WHO/Geneva
24. Mr.Takeshi Hashimoto	Japan
25. Dr.Craig Stark	AFRIMS
26. Ms.Rebecca Leidel	AFRIMS
27. Ms.Paula Ridge	AFRIMS
28. Dr.Masaji Ono	Japan
29. Dr.Yuji Kawaguchi	WHO/Kobe, Japan
30. Dr.Ataollah Amini	WHO/Kobe, Japan
31. Dr.Jeffrey Miller	WHO/Kobe, Japan
32. Mr.Manuel Menendez	WHO/Kobe, Japan
33. Dr.Mohammad a. Mullick	WHO/Kobe, Japan
34. Dr.Muzaffar Malik	WHO/Kobe, Japan
35. Mr.Tokoi Yamanouchi	WHO/Kobe, Japan
36. Dr.Masato Kawabata	Japan
37. Dr.Kamini Mendis	WHO/Geneva
38. Dr.Charles Delacollette	WHO/Geneva
39. Dr.Pascal Ringwald	WHO/Geneva

Name	Country
40. Mr.Jens Haerter	USA
41. Mr.David Hecht	USA
42. Mr.James Hall	USA
43. Dr.Lin Hwei Chen	USA
44. Dr.Yiming Shao	China
45. Dr.Yuanzhi Zhang	China
46. Dr.Jiapeng Zhang	China
47. Dr.Shigeru Matsuzaki	Japan
48. Dr.Rene Somera	SEAMEO
49. Prof.Nguyen Thi Ke	Vietnam
50. Mrs.Yieng	Vietnam
51. Mr.Vitoon Vonghangool	Thailand
52. Mr.Krishan Mohan Prasad	India
53. Mrs.Dheera Khandelwal	India
54. Mr.Rakesh Bharadwaj	India
55. Dr.(Mrs.) Surraiya Bhat	India
56. Mr.C. Pradeep Kumar	India
57. Mrs.Suprabha Agarwal	India
58. Mr.S.K. Kujur	India
59. Mrs.Loma N. Jyrwa	India
60. Mrs.Chuanzikpuii	India
61. Mr.S. Suryan	India
62. Mr.Shri Krishan Gopal	India
63. Mr.P.K. Chanda	India
64. Mr.Pradeep Kumar	India
65. Mr.R.S. Sharma	India
66. Ms.Myrna Benilda C. Pablo	Philippines
67. Dr.Tran Van Que	Vietnam
68. Dr.Voung Minh Ngoc	Vietnam
69. Dr.Nguyen Xuan Hoa	Vietnam
70. Dr.Nguyen Thi Minh Tam	Vietnam
71. Dr.Le Thi Phu	Vietnam
72. Dr.Nguyen Van Hien	Vietnam
73. Prof.Dao Ngoc Phong	Vietnam
74. Ms.Eri Suzuki	Japan
75. Ms.Akiko Takeyama	Japan
76. Mr.Philippe Lenglet	France
77. Ms.Marie Julien	France
78. Ms.Claire Langlasse	France

	Name	Country		Name	Country
79.	Dr.Mai Ngoc Chan	Vietnam	107.	Dr.Loung Khoeung	Cambodia
80.	Dr.Vu Dang Tinh	Vietnam	108.	Dr.Chan Vanna	Cambodia
81.	Dr.La Dang Tai	Vietnam	109.	Dr.Oung Yeang	Cambodia
82.	Dr.Duong Van Phuc	Vietnam	110.	Dr.Chhiv Lim	Cambodia
83.	Dr.Ban Van Vuong	Vietnam	111.	Dr.Srey Socheat	Cambodia
84.	Mrs.Lai Hong Loan	Vietnam	112.	Dr.Bun Chhum	Cambodia
85.	Mrs.Duong Thi Kim	Vietnam	113.	Dr.Klem Sokun	Cambodia
86.	Dr.Bernard Montaville	France	114.	Dr.Bun Chhem	Cambodia
87.	Ms.Amy McClune	USA	115.	M.A.Se Chou Sithy Chot	Cambodia
88.	Mr.Tom Yan	USA	116.	Captain Kae Shimazaki	Japan
89.	Prof.Somei Kojima	Japan	117.	Prof.Marui	Eiji Japan
90.	Dr.Anthony Arthur Holder	UK	118.	Mr.Takashi	Japan
91.	Mr.Ralph Francis Adam Pine	UK	119.	Mr.Satoshi	Japan
92.	Dr.Richard Paul Lane	UK	120.	Mr.Daisuke	Japan
93.	Dr.Catherine Sarah Davies	UK	121.	Mr.Syuhei	Japan
94.	Dr.Roy Malcolm Anderson	UK	122.	Ms.Rie	Japan
95.	Dr.Weng Kong Chew	UK	123.	Ms.Hiroko	Japan
96.	Dr.Gerald T Keusch	UK	124.	Ms.Ryoko	Japan
97.	Dr.William Ivan Morrison	UK	125.	Ms.Aya	Japan
98.	Dr.Keith Paul Klugman	UK	126.	Ms.Naoko	Japan
99.	Dr.Wendy Rosemary Ewart	UK	127.	Ms.Kaori	Japan
100.	Ms.Bret Purcell	USA	128.	Prof.Dr.Tran Van Nhung	Vietnam
101.	Ms.Ann Suthun	USA	129.	Mr.Takashi Miura	Japan
102.	Ms.Tanya Morgan	USA	130.	Dr.Rob Ridley	WHO/Geneva
103.	Dr.Somer Curtis	USA	131.	Dr.May Ho	Canada
104.	Prof.Jamal Ahmed Essa	Malaysia	132 - 155	The Global Advisory Committee on Health Research (ACHR)	WHO/Geneva
105.	Prof.Gary M. Brittenham	USA			
106.	Dr.Nong Sao Kry	Cambodia			

Lecturers and their Areas of Expertise

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Chantima Lohachit	tmclh@mahidol.ac.th	Medical and freshwater malacology Limnology/Ecology/Spermatogenesis (TEM) Environmental Health
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Dwip Kitayaporn	tmdkt@mahidol.ac.th	Epidemiology of HIV/AIDS Research methodology
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Manas Chongsa-nguan	tmmcs@mahidol.ac.th	Immunology of tropical infections Bacterial identification

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Niyomsri Vudhivai	tmnvd@mahidol.ac.th	Biochemical nutrition/Nutritional epidemiology
Panyawut Hiranyachattada	tmphr@mahidol.ac.th	Helminthology
Parnpen Viriyavejakul	tmpvr@mahidol.ac.th	Anatomical pathology/Oppportunistic infections in AIDS
Paron Dekumyoy	tmpdk@mahidol.ac.th	Immunodiagnosis of helminthiases
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Piyarat Butraporn	tmpbt@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
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Pornratsami Jintaridthi	tmpjt@mahidol.ac.th	Nutritional toxicology/Biochemical nutrition
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
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Lecturers		Field of Specialization/expertise
		Drug trials in AIDS and opportunistic infection, especially oral candidiasis
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Venus Supawan	tmvsp@mahidol.ac.th	Biochemical nutrition/Community nutrition
Vichitra Pornkulprasit	tmvpk@mahidol.ac.th	Radiology

Lecturers	E-mail Address	Field of Specialization/expertise
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Wijitr Fungladda	tmvfd@mahidol.ac.th	Social epidemiology of tropical diseases (malaria, opisthorchiasis)
Wipawee Usawattanakul	tmwus@mahidol.ac.th	Immunology of parasitic infections
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Yuvadee Mahakunkijcharoen	tmymh@mahidol.ac.th	Immunology of parasitic infections and bacterial infections

Ongoing Research Projects of the Faculty of Tropical Medicine in 2000

No.	Ongoing Research Projects in 2000	Grants	Principal Investigator
Department of Clinical Tropical Medicine			
1	Comparative assessment of <i>in vivo</i> and <i>in vitro</i> sensitivity of <i>Plasmodium vivax</i> to chloroquine		Assoc. Prof. Kesara Na Bangchang
2	Investigation of the response of <i>Plasmodium falciparum</i> to a combination regimen of artesunate plus mefloquine in Mae Sot District, Tak Province		Assoc. Prof. Kesara Na Bangchang
3	Study on partition of and antimalarial mefloquine		Assoc. Prof. Kesara Na Bangchang
4	Bioavailability and bioequivalency of suppositories laval artesunate and artemether in healthy volunteers		Assoc. Prof. Kesara Na Bangchang
5	Relationship of <i>Plasmodium</i> antigen and antibody profiles to therapeutic response in falciparum malaria	SEAMEO-TROPED Network and Wellcome Unit of Great Britain	Prof. Sasithon Pukrittayakamee
6	PCR - RFLP detection of <i>Plasmodium vivax dhfr</i> mutations	The Thailand Research Fund	Prof. Sasithon Pukrittayakamee
7	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 Plough Research Institute	Assoc. Prof. Punnee Pitisuttithum
8	Neurotoxicity of artemether in animal model following intermittent intramuscular injections	Great Britain and SEAMEO-TROPED Network	Mr. Apichart Nontprasert
9	Open-label, treatment protocol for the safety and efficacy of SCH 56592 (Oral Suspension) in the treatment of invasive fungal infections	Schering Plough Institute	Assoc. Prof. Punnee Pitisuttithum
10	Research and development of effective antimalarial drugs in combination for widely use in the treatment of malaria	Ministry of University Affairs	Prof. Sornchai Looareesuwan
Department of Helminthology			
1	The IFAT for human gnathostomiasis	Mahidol University	Ms. Wattana Pahuchon
2	Monoclonal antibody-based competitive ELISA and indirect ELISA for immunodiagnosis of trichinosis	Mahidol University	Mrs. Supaporn Nuamtanong
3	Comparison of biochemical extract preparations of <i>Cysticercus cellulosae</i> by SDS - polyacrylamide gel electrophoresis and immunoblot technique	Mahidol University	Assist. Prof. Paron Dekumyoy

No.	Ongoing Research Projects in 2000	Grants	Principal Investigator
Department of Helminthology (Continued)			
4	Experimental infection of freshwater fish in Thailand with infective stage of <i>Angiostrongylus</i>	Mahidol University	Assist. Prof. Chalit Komalamisra
5	<i>Toxocara canis</i> larval antigens for serodiagnosis of human toxocariasis	Mahidol University	Assist. Prof. Wanna Maipanich
6	The effects of <i>Trichinella spiralis</i> Infection on renal furetions in rat	Mahidol University	Mr. Panyawut Hiranyachattada
7	Comparative studies on surface ultrastructure of adult worm of <i>Paragonimus</i> sp. in Thailand	Mahidol University	Assist. Prof. Sanan Yaemput
8	Seasonal variation in the intensity of <i>Gnathostoma</i> larvae in eels in Nakhon Nayok Province	Mahidol University	Assoc. Prof. Wichit Rojekittikhun
9	Studies on the efficacy of Thai traditional herbal medicines in the treatment of opisthorchiasis in hamsters	Mahidol University	Mr. Panyawut Hiranyachattada
10	Epidemiology and prevention of trichinosis in Mae Hong Son	Mahidol University	Assist. Prof. Ponganant Nontasut
11	<i>Angiostrongylus cantonensis</i> : S-Adenosylmethionine decarboxylase	Government Budget FY 2000	Mrs. Supaporn Nuamtanong
12	Study on the killing effect of Thai medicinal plants against mosquitoes vector and parasitic helminths	Mahidol University	Assoc. Prof. Jitra Waikagul
Department of Medical Entomology			
1.	Evaluation of certain chemical stimuli as attractants for sound trapping of <i>Culex tritaeniorhynchus</i>	Faculty of Tropical Medicine	Assoc. Prof. Vanida Deesin
2	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
3.	Critical biology and disease transmission indices in dengue	Faculty of Tropical Medicine	Assoc. Prof. Yupha Rongsriyam
4	Comparative susceptibility to oral infection with dengue virus among local strain of <i>Aedes aegypti</i> collected at different seasons of the year	The National Research Council of Thailand	Assist. Prof. Supatra Thongrungrat
5	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
6	Specificity of the synthetic primers from sequencing DNA fragments of <i>Anopheles minimus</i>	Faculty of Tropical Medicine	Assist. Prof. Narumon Komalamisra
7	Impacts of permethrin impregnated bednets on <i>Anopheles dirus</i>	The National Research Council of Thailand	Assoc. Prof. Vanida Deesin
8	<i>Artemisia annua</i> oil as a repellent against mosquito vectors in Thailand	Mahidol University	Mrs. Kaewmala Palakul
Department of Microbiology and Immunology			
1	Anaerobic bacteria intraabdominal infection	Mahidol University	Assoc. Prof. Suvanee Supavej

No.	Ongoing Research Projects in 2000	Grants	Principal Investigator
Department of Microbiology and Immunology (Continued)			
2	Production of monoclonal antibodies for use in the diagnosis of scrub typhus	Faculty of Tropical Medicine	Assist. Prof. Varee Wongchotigul
3	Detection of dengue virus in mosquitoes (<i>Aedes aegypti</i>) by polymerase chain reaction compare with virus-cultivation	Mahidol University	Assoc. Prof. Wipawee Usawattanakul
4	Development of polymerase chain reaction for the diagnosis of vivax malaria	Mahidol University	Assoc. Prof. Pramuan Tapchaisri
5	Identification and characterization of T cell epitopes on <i>P. falciparum</i> sporozoite surface protein 2 recognized by human	Naval Medical Research Institute	Prof. Srisin Khusmith
6	The use of recombinant <i>Entamoeba histolytica</i> pyruvate : ferredoxin oxidoreductase (rPFOR) as a candidate vaccine against invasive amoebiasis		Assoc. Prof. Nittaya Thammapalerd
7	Production of recombinant pyruvate: ferredoxin oxidoreductase of <i>Entamoeba histolytica</i> (Eh rPFOR) and its application for diagnosis of invasive amebiasis		Assoc. Prof. Nittaya Thammapalerd
8	Pathology of enterohaemorrhagic <i>Escherichia coli</i> infection	The Thailand Research Fund and University of Tsukuba, Japan	Prof. Wanpen Chaicumpa
9	Rapid detection of <i>Salmonella</i> in contaminated foods by immunomagnetic enrichment and enzyme immunoassay	The Thailand Research Fund	Assist. Prof. Yuvadee Mahakunkijcharoen
10	Pathology of enterohaemorrhagic <i>E. coli</i> and the protective role of antibody	The Thailand Research Fund, NSTDA and Tsukuba University, Japan	Prof. Wanpen Chaicumpa
11	Rapid diagnosis of salmonellosis using dip stick method	Mahidol University	Prof. Wanpen Chaicumpa
12	Development of opisthorchiasis by immunological method	MoPH, Faculty of Tropical Medicine and NRCT	Prof. Wanpen Chaicumpa
13	Production of monoclonal antibodies to <i>Bordetella pertussis</i> filamentous haemagglutinin	NSTDA, Faculty of Tropical Medicine and University of Tsukuba, Japan	Assoc. Prof. Manas Chongsa-nguan
14	Antigenic analysis of <i>V. cholerae</i> isolated in Thailand for epidemic tracing	In Cooperation with Japan and Tsukuba University	Assoc. Prof. Pramuan Tapchaisri
15	Production allergenic components of cockroaches by genetic engineering	The National Research Council of Thailand	Prof. Wanpen Chaicumpa
16	Studies on allergic components of cockroaches (<i>Blatta orientales</i>)	The National Research Council of Thailand	Prof. Wanpen Chaicumpa
17	Diagnosis of gnathostomiasis using specifically purified antigen	NSTDA and TRF	Prof. Wanpen Chaicumpa
18	Detection of dengue viral RNA in patient sera by Nucleic Acid Sequence-Based amplification (NASBA) and comparison with Polymerase Chain Reaction (PCR)	Mahidol University	Assoc. Prof. Wipawee Usawattanakul

No.	Ongoing Research Projects in 2000	Grants	Principal Investigator
Department of Microbiology and Immunology (Continued)			
19	Development of rapid detection of <i>Vibrio cholerae</i> in immunomagnetic enriched samples by Mab-based dot-blot ELISA	Mahidol University	Assist. Prof. Yuvadee Mahakunkijcharoen
20	Evaluation of the efficiency of leptospirosis diagnostic test kits	Science Development and Management Company	Prof. Wanpen Chaicumpa
21	Evaluation of <i>Salmonella</i> and <i>Shigella</i> test kits at Petchburi provincial hospital		Prof. Wanpen Chaicumpa
22	Efficacy testing of new vaccine adjuvant CpG DNA		Prof. Wanpen Chaicumpa
23	Development of molecular biological method for serotyping of <i>Leptospira</i>	NSTDA and TRF	Prof. Wanpen Chaicumpa
24	Development of a rapid test for detection of <i>Vibrio parahaemolyticus</i>		Prof. Wanpen Chaicumpa
25	Epidemiological survey of enterohaemorrhagic <i>Escherchia</i>	Royal Golden Jubilee, TRF	Prof. Wanpen Chaicumpa
26	Towards the <i>Strongyloides stercoralis</i> Thai isolates	Royal Golden Jubilee, TRF	Prof. Wanpen Chaicumpa
27	Typing of <i>Entamoeba histolytica</i> isolates obtained from Southeast Asian countries	Japanese Health Sciences Foundation (JHSF)	Assoc. Prof. Nittaya Thammapalerd
28	Detection of <i>Leptospira</i> spp. in urine by polymerase chain reaction (PCR)	The Thailand	Ms. Thareerat Kalambaheti Research Fund
29	Cloning and expression of fimbrial of <i>V. cholerae</i> o1 in the large scale as cholera vaccine candidate molecular biology & immunology	The Thailand Research Fund	Ms. Thareerat Kalambaheti
30	Analysis of sequence polymorphism T-cell epitope regions, Th 2 and Th 3 R on <i>Plasmodium falciparum</i> circumsporozoite proteins in Thai isolates	Royal Golden Jubilee, TRF	Prof. Srisin Khusmith
Department of Protozoology			
1	Prevalence of <i>Toxoplasma gondii</i> in Thai healthy population		Assist. Prof. Yaowalark Sukthana
2	Comparison of <i>Toxoplasma gondii</i> antibody detection between in-house latex agglutination and commercial test	Thanad-Molee Choman Foundation	Assist. Prof. Varaporn Suphadtanongs
3	Isolation and characterization of DNA helicase from <i>Plasmodium falciparum</i>	The Thailand Research Fund	Assist. Prof. Pornthip Petmitr
4	Study of <i>Toxoplasma gondii</i> antibody in the population of provinces with a high risk of HIV	Mahidol University	Assist. Prof. Yaowalark Sukthana
5	Studies on the effect of Thai medicinal plants to <i>Cryptosporidium</i> and <i>Isopora</i> <i>in vitro</i>	Mahidol University	Assist. Prof. Chutatip Siripanth
6	Inhibitory effects of DNA topoisomerase I inhibitors on <i>Trichomonas vaginalis</i> in culture	Mahidol University	Assist. Prof. Pornthip Petmitr

No.	Ongoing Research Projects in 2000	Grants	Principal Investigator
Department of Social and Environmental Medicine			
1	Early detection of Rifampicin resistant of <i>M. leprae</i> among Thai leprosy patient	The National Research Council of Thailand	Dr. Pongrama Ramasoota
2	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
3	Effect of insecticide to female reproductive system	Tokyo	Prof. Ryutaro (Assist. Prof. Ladda Tangbanluekal)
4	Control of soil-transmitted helminths in primary school in Southern Thailand	Mahidol University	Mr. Prasart Vorasant
5	A phase III trial to determine the efficacy of AIDS VAXTM the efficacy of AIDS VAXTM B/E vaccine in intravenous drug users in Bangkok, Thailand	VAXGEN Co., Ltd.	Bangkok (Database by Assoc. Prof. Dwip Kitayaporn)
6	Air pollution mitigation from industrial sector Ministry of Industry	Department of Industrial Works	Dr. Sangsan Panich
7	Uses of CFCs alternatives in Thailand Ministry of Science, Technology and Environment	Office of Environmental Policy and Planning	Assist. Prof. Ladda Tangbanluekal
8	Appropriate biological sample for determination of manganese concentration among welders	Faculty of Tropical Medicine	Assist. Prof. Waranya Wongwit
Department of Tropical Hygiene			
1	Epidemiological study of nutritional deficiency among Karen preschool children	Faculty of Tropical Medicine	Mr. Surapon Yimsamran
2	Malaria in Thai-Burmese border: interaction between host, agent, and environment	Government Budget	Assist. Prof. Pratap Singhasivanon
3	Assessment of risk factors of mortality associated with vehicular crashes in a central province of Thailand : before and after enforcement of safety service law	SEAMEO-GTZ [M.Sc. Epidemiology (Public Health) Project]	Dr. Nilarat Premmanisakul
Department of Tropical Nutrition and Food Science			
1	Identification of genes mutation in lung cancer cells in Thai patients	Mahidol University China Medical Board	Assoc. Prof. Songsak Petmitr
2	Food and health relationship in Asian Population	Palm oil Research Institute of Malaysia	Assoc. Prof. Supranee Changbumrung
3	Molecular biology of carcinogenesis in lung cancer	The Thailand Research Fund	Assoc. Prof. Songsak Petmitr
4	Development of food and medicinal plants	Government Budget	Assoc. Prof. Supranee Changbumrung
5	Serum leptin concentration in obese subjects and Mahidol University	Free University, Berlin Germany	Assoc. Prof. Rungsun Tungtrongchitr
6	Micronutrients and oxidative stress in obese subjects	Free University, Berlin Germany	Assoc. Prof. Rungsun Tungtrongchitr

No.	Ongoing Research Projects in 2000	Grants	Principal Investigator
Department of Tropical Pathology			
1	Study of opportunistic infections in AIDS by needle biopsy	Mahidol University	Assist. Prof. Parnpen Viriyavejakul
2	Nitric oxide production by <i>Plasmodium falciparum</i> stimulated endothelial cell	Mahidol University	Assist. Prof. Yaowapa Maneerat
3	Hematopoietic features of the bone marrow of <i>Plasmodium falciparum</i> infected patients	Mahidol University	Assist. Prof. Yaowapa Maneerat
4	Pathology and immunohistochemistry of liver in AIDS: a necropsy study	Mahidol University	Assist. Prof. Parnpen Viriyavejakul
5	Causes of diarrhea in HIV/AIDS patients	Mahidol University	Assist. Prof. Parnpen Viriyavejakul
Department of Tropical Pediatrics			
1	A phase IV, observer-blind, randomized, controlled, trial to evaluate safety, tolerability and immunogenicity of the chiron acellular pertussis vaccine combined with diphtheria and tetanus toxoids (DTwP), when administered to healthy Thai infants at 2, 4 and 6 months of age		Prof. Arunee Subchareon
2	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
3	Clinical efficacy and pharmacokinetics of suppositoried artesunate combined with mefloquine in the treatment of severe childhood falciparum malaria		Assoc. Prof. Krisana Pengsaa
4	A multicentric, randomised, double blind, placebo-controlled, parallel group study to assess the efficacy, safety and tolerability of acetorphan (TiorfanTM) 1.5 mg/kg body weight tid pa plus oral rehydration therapy in the treatment of acute diarrhea in children	SmithKline Beecham Pharmaceuticals, Co., Ltd.	Assoc. Prof. Pornthep Chanthavanich
5	Clinical efficacy and pharmacokinetics of suppositoried artesunate combined with mefloquine in the treatment of uncomplicated childhood falciparum malaria		Assist. Prof. Chukiat Sirivichayakul
6	The relationship of mixed infection and severity of falciparum malaria		Assist. Prof. Watcharee Chocejindachai
7	Safety and immunogenicity of tetravalent dengue vaccine formulations in Thai adult volunteers: evaluation of three-year persistence	Pasteur Merieux Connaught France	Assoc. Prof. Pornthep Chanthavanich
8	Immunogenicity and adverse reaction of liquid form of Japanese encephalitis vaccine (Beijing strain) in healthy Thai children		Assoc. Prof. Pornthep Chanthavanich
9	Safety and immunogenicity of tetravalent dengue vaccine formulations in Thai children	Pasteur Merieux Connaught France	Prof. Arunee Subchareon
10	Single dose therapy for treatment of <i>Giardia</i> infection in children	Mahidol University	Assoc. Prof. Krisana Pengsaa

No.	Ongoing Research Projects in 2000	Grants	Principal Investigator
Department of Tropical Pediatrics (Continued)			
11	A comparative study of the efficacy and ease of administering of salbutamol delivered from conventional meter dose inhalers and easyhaler in asthmatic Thai children	Mahidol University	Mrs. Wimol Nganthavee
12	A comparative trial of albendazole alone versus combination of albendazole and praziquantel for treatment of <i>Trichuris trichiura</i> infection in children	Department of Tropical Pediatrics	Assist. Prof. Chukiat Sirivichayakul
Department of Tropical Radioisotopes			
1	Study of four Thai medicinal herbs as individuals and combinations for anti-snake venoms.		Assist. Prof. Channarong Sanghirun
2	Viscosity of red cell ghosts and hemoglobin of red cells from patients with <i>Plasmodium falciparum</i> malaria	Mahidol University	Assist. Prof. Petcharin Yamarat
3	Effect of garlic on blood rheology and prevention of thrombolism	The National Research Council of Thailand	Assist. Prof. Petcharin Yamarat
Vaccine Trial Centre			
1	Development of new vaccines against cholera due to <i>Vibrio cholerae</i> 0139 (Part I)	WHO	Assoc. Prof. Punnee Pitisuttithum
2	A phase I/II, double-blind, placebo-controlled study of the chiron biocine HIV Thai Egp 120/MF59 vaccine administered alone or combined with the chiron biocine HIV SF2 gp 120 antigen in healthy HIV-seronegative Thai adults	WRAIR, USA	Assoc. Prof. Punnee Pitisuttithum
3	A phase I/II trial to evaluation the safety and immunogenicity of AIDSVAX TM B/E vaccine in Bangkok, Thailand	VAXGEN Co, Ltd.	Assoc. Prof. Punnee Pitisuttithum
4	A phase III trial to determine the efficacy of AIDSVAXTM B/E vaccine in intravenous drug users in Bangkok, Thailand	AIDSVAX	Dr. Kachit Chupanya Bangkok AIDS Vaccine Evaluation Group
5	Phase I/II trial of Pasteur Merieux Connaught (PMC) live recombinant ALVAC-HIV (VCP 1521) priming with Vaxgen gp 120 B/E (AIDVAXTM B/E) boost in Thai HIV-seronegative adults	Walter Reed Army Institute of Research	Assoc. Prof. Punnee Pitisuttithum

TROPMED Publications

(1 October 1999 – 30 September 2000)

1. Anantaphruti MT, Nuamtanong S, Muennoo C, Sanguankiat S, Pubampen S. *Strongyloides stercoralis* infection and chronological changes of other soil-transmitted helminthiasis in the endemic area of southern Thailand. *Southeast Asian J Trop Med Public Health* 2000;31(2):378-82.

2. Anantaphruti MT, Nuamtanong S, Pubampen S, Rojekittikhun W, Visiadsuk K. Zoonotic potential of dog's intestinal helminths transmitting to man. In: Chen ER, Yamaguchi T, Chung WC, editors. Parasitic zoonoses in Asian-Pacific regions 2000. Proceedings of the sixth Asian-Pacific Congress for Parasitic Zoonoses; 2000 Jul 28-30; Taipei, Taiwan ROC. Taipei: The Organizing Committee; 2000. p. 113-21.

3. Blair D, Wu B, Chang ZS, Gong X, Agatsuma T, Zhang YN, Chen SH, Lin JX, Chen MG, Waikagul J, Guevara Ag, Feng Z, Davis GM. A molecular perspective on the genera *Paragonimus* Braun, *Euparagonimus* Chen and *Pagumogonimus* Chen. *J Helminthol* 1999;73:295-9.

4. Brockman A, Price RN, van Vugt M, Heppner DG, Walsh D, Sookto P, Wimonwattrawatee T, Looareesuwan S, White NJ, Nosten F. *Plasmodium falciparum* antimalarial drug susceptibility on the north-western border of Thailand during five years of extensive use of artesunate-mefloquine. *Trans R Soc Trop Med Hyg*. 2000;94:537-44.

5. Bussaratid V, Walsh DS, Wilairatana P, Krudsood S, Silachamroon U, Looareesuwan S. Frequency of pruritus in *Plasmodium vivax* malaria patients treated with chloroquine in Thailand. *Trop Doct* 2000;30(4):211-4.

6. Camacho LH, Wilairatana P, Weiss G, Mercader MA, Brittenham GM, Looareesuwan S, Gordeuk VR. The eosinophilic response and haematological recovery after treatment for *Plasmodium falciparum* malaria. *Trop Med Int Health* 1999;4(7):471-5.

7. Chaiyaroj SC, Buranakiti A, Angkasekwinai P, Looressuwan S, Cowman AF. Analysis of mefloquine resistance and amplification of pfmdr1 in multidrug-resistant *Plasmodium falciparum* isolates from Thailand. *Am J Trop Health* 1999;61(5):780-3.

8. Changbumrung S, Thesasilpa J, Harnroongroj T, Vorasanta S, Hongtong K, Chantaranipapong Y, Kusolchariya S, Kaewkajee T, Ariyawatana C. Aflatoxin M₁ and M₂ in breast milk. *J Nutr Assoc Thai* 1999;33:42.

9. Chanjanakijskul S, Painupong D, Tungtrongchitr R, Pongpaew P. Relationship between serum C3 and antinuclear antibodies (ANA) in 220 systemic lupus erythematosus (SLE) patients in Institute of Dermatology Bangkok. *Bull Chula Med Tech* 1999;15:175-84.

10. Chansiripornchai N, Ramasoota P, Bangtrakulnonth A, Sasipreeyajan J, Svenson SB. Application of randomly amplified polymorphic DNA (RAPD) analysis for typing avian *Salmonella enterica* subsp. *Enterica*. *FEMS Immunol Med Microbiol* 2000;29(3):221-5.

11. Chansiripornchai N, Ramasoota P, Sasipreeyajan J, Svenson SB. Evaluation of the random amplified DNA method for identification and differentiation of avian pathogenic *Escherichia coli* (APEC) strains. *Vet Microbiol* 2000. (In press)

12. Chaowagul W, Simpson AJH, Suputtamongkol Y, White NJ. Empirical cephalosporin treatment of melioidosis. *Clin Infect Dis* 1999;28:13-28.
13. Chavalitsheewinkoon-Petmitr P, Chawprom S, Naesens L, Balzarini J, Wilairat P. Partial purification and characterization of mitochondrial DNA polymerase from *Plasmodium falciparum*. *Parasitol Int* 2000;49:279-88.
14. Chavalitsheewinkoon-Petmitr P, Pongvilairat G, Auparakkitanon S, Wilairat P. Gametocytocidal activity of pyronaridine and DNA topoisomerase II inhibitors against multidrug-resistant *Plasmodium falciparum* in vitro. *Parasitol Int* 2000;48:275-80.
15. Chavalitsheewinkoon-Petmitr P, Pongvilairat G, Ralph R, Denny WA, Wilairat P. Inhibitory Effects of 9-anilinoacridines on *Plasmodium falciparum* gametocytes. *Trop Med Int Health* 2000 (in press).
16. Chavalitsheewinkoon-Petmitr P, Ramdja M, Kajorndechakiat S. In vitro sensitivity of *Trichomonas vaginalis* to DNA topoisomerase II inhibitors. *Southeast Asian J Trop Med Public Health* 2000;31:118-22.
17. Chotivanich K, Udomsangpetch R, Dondorp A, Williams T, Angus B, Simpson JA, Pukrittayakamee S, Looareesuwan S, Newbold CI, White NJ. The Mechanisms of parasite clearance after antimalarial Treatment of *Plasmodium falciparum* malaria. *JID* 2000;82(2):629-33.
18. Chotivanich K, Udomsangpetch R, Simpson JA, Newton P, Pukrittayakamee S, Looareesuwan S, White NJ. Parasite multiplication potential and the severity of *falciparum* malaria. Published in: *JID* 2000;181:1206-9
19. Chuckpaiwong S, Panvisavas S & Wilairatana P. Health status in Bongtee, Saiyok, Kanchanaburi: Prevalence of malaria and intestinal parasitic infections: Report I. *J Trop Med Parasitol* 1999;22:71-6.
20. Chowdhury NR, Chakraborty S, Eampokalap B, Chaicumpa W, Chongsa-Nguan M, Moolasart P, Mitra R, Ramamurthy T, Bhattacharya SK, Nishibuchi M, Takeda Y, Balakrish Nair G. Clonal dissemination of *Vibrio parahaemolyticus* displaying similar DNA fingerprint but belonging to two different serovars (O3:K6 and O4:K68) in Thailand and India. *Epidemiol Infect* 2000;125:17-25.
21. Davis TME, Pongponratn E, Supanaranond W, Pukrittayakamee S, Helliwell T, Holloway P, White NJ. Skeletal muscle involvement in falciparum malaria: biochemical and ultrastructural study. *Clin Infect Dis* 1999;29:831-35.
22. Dekumyoy P, Anantaphruti MT, Nuamtanong S, Watthanakulpanich D, Waikagul J, Danis M. Neurocysticercosis : Utilizing the cystic fluid antigen from *Taenia solium* metacestodes for diagnosis by IgG –ELISA. *Southeast Asian J Trop Med Public Health*. (in press)
23. Doungnat Riyong, Wej Chhochote, Atchariya Jitpakdi, Saravudh Suvannadabba, Somjai Leemingsawat, Udom Chaithong. Autogenous *Aedes togoi* sub-colony (Chanthaburi, Thailand strain), an efficient laboratory vector in study of filariasis. *Southeast Asian J Trop Med Public Health* 2000;31(2):246-51.
24. Eamsobhana P, Dekumyoy P, Waikagul J. Shared antigens between *Parastrongylus cantonensis* and *Biomphalaria glabrata* and their possible use in immunodiagnosis of human parastrongyliasis. *Trop Biomed* 1999;16:7-13.
25. Ezzet F, van Vugt M, Nosten F, Looareesuwan S, White NJ. Pharmacokinetics and pharmacodynamics of lumefantrine (benflumetol) in acute falciparum malaria. *Antimicrob Agents Chemother* 2000 Mar;44(3):697-704.
26. Gosi P, Khusmith S, Looareesuwan S, Walsh DS. Complicated malaria is associated with differential elevations in serum levels of interleukins 10, 12, and 15. *Southeast Asian J Trop Med Public Health* 1999;30(3):412-7.
27. Ho M, White NJ. Molecular mechanisms of cytoadherence in malaria. *Am J Physiol* 1999;276:C1231-42.
28. Horsawad V, Pongpaew P, Tungtrongchitr R, Phonrat B, Vudhivai N, Chanjanakitskul S, Himman-ngnan T, Supanaranond V, Chantachum Y, Schelp FP. Lead exposure, urinary d-aminolevulinic acid concentration and haematological parameters of road sweepers working in congested areas of Bangkok. *J Nutr Environ Med* 1999;9:109-14.
29. Intapan PM, Maleewong W, Wongkham C, Morakote N, Chaicumpa W. Monoclonal antibody capture enzyme-linked immunosorbent assay for immunodiagnosis of human

- paragonimiasis heterotremus. *J Trop Med Parasitol* 1999;22:41-5.
-
30. Ittarat W, Udomsangpetch R, Chotivanich KT, Looareesuwan S. The effects of quinine and artesunate treatment on plasma tumor necrosis factor levels in malaria-infected patients. *Southeast Asian J Trop Med Public Health* 1999;30(1):7-10.
-
31. Ittiprasert W, Chongsa-nguan M, Manatrakul D, Jongsuksuntigul P, Meesomboon V, Vongsaroj T, Kitikoon V, Sakolvaree Y, Hayashi H, Chaicumpa W. Prevalence of Antibodies to *Schistosoma mekongi* among inhabitants of the High Risk Area of Thailand. *J Trop Med Parasitol* 1999;22(1):7-14.
-
32. Ittipresert W, Butraporn P, Kitikoon V, Klongkamnuankarn K, Pholsena K, Vanisaveth V, Sakolvaree Y, Chongsa-nguan M, Tapchaisri P, Mahakunkijcharoen Y, Kurazono H, Hayashi H, Chaicumpa W. Differential diagnosis of schistosomiasis mekongi and trichinellosis in human. *Parasitol Int* 2000;49:209-18.
-
33. Joshi AB., Singhasivanon P, Khusmith S, Fungladda W, Nandy A. Evaluation of direct agglutination test (DAT) as an immunodiagnostic tool for diagnosis of visceral leishmaniasis in Nepal. *Southeast Asian J Trop Med Public Health* 1999;30(3):583-5.
-
34. Kidson C, Indaratna K, Looareesuwan S. The malaria cauldron of Southeast Asia: conflicting strategies of contiguous nation states. *Parasitologia* 2000;42:101-10.
-
35. Khamhoung K, Bodhisane N, Pathammavong C, Ouenvilay S, Senthavisouk B, Pongpaew P, Tungtrongchitr R, Phonrat B, Saowakontha S, Merkle A, FP. Schelp. Nutritional status of preschool children and women in selected villages in the Suvannakhet province, LAO PDR - an intervention trial. *Southeast Asian J Trop Med Pub Health* 2000. (in press)
-
36. Krudsood S, Wilairatana P, Mason DP, Treeprasertsuk S, Singhasivanon P, Looareesuwan S. Hidden Plasmodium falciparum infections. *Southeast Asian J Trop Med Public Health* 1999;30(4):623-4.
-
37. Khusmith S, Tangteerawatana P, Looareesuwan S. Low CD8+ T lymphocyte response to *P. falciparum* circumsporozoite protein in naturally-exposed malaria endemic populations in Thailand. *Southeast Asian J Trop Med Public Health* 1999;30(3):405-11.
-
38. Kilmarx PH, Limpakarnjanarat K, Kaewkungwal J, Srismith R, Saisorn S, Uthavivoravit W, Young NL, Mastro TD. Disease progression and survival with human immunodeficiency virus type 1 subtype E infection among female sex workers in Thailand. *JID* 2000;18(15):1598-1606.
-
39. Komalamisra C, Boonchuen S, Waikagul J, Dekumyoy P, Komalamisra N. Comparative studies on general proteins, isoenzyme and DNA restriction endonuclease profiles of Thai paragonimus meta cercariae. *Southeast Asian J Trop Med Public Health*. (in press)
-
40. Komalamisra C. Chromosome and C-banding of *Opisthorchis viverrini*. *Southeast Asian J Trop Med Publish Health*. 1999;30(3).
-
41. Kreil A, Wenisch C, Brittenham G, Looareesuwan S, Peck-Radosavljevic M. Thrombopoietin in Plasmodium falciparum malaria. *Br J Haematol* 2000;109(3):534-6.
-
42. Krishna S, Taylor AM, Supanaranond W, Pukrittayakamee S, ter Kuile F, Tawfiq KM, Holloway PAH, White NJ. Thiamine deficiency and malaria in adults from Southeast Asia. *Lancet* 1999;353:546-9.
-
43. Krudsood S, Wilairatana P, Mason DP, Treeprasertsuk S, Singhasivanon P, Looareesuwan. Hidden Plasmodium falciparum infections. *Southeast Asian J Trop Med Public Health* 1999;30(4):623-4.
-
44. Kurazono H, Yamamoto S, Nakano M, Nair GB, Terai A, Chaicumpa W, Hayashi H. Characterization of a putative virulence island in the chromosome of uropathogenic *Escherichia coli* possessing a gene encoding a uropathogenic-specific protein. *Microbial Pathogenicity* 2000;28:183-9.
-
45. Lauw FN, Simpson AJH, Prins JM, Smith MD, Kurimoto M, van Deventer SJH, Speelman P, Chaowagul W, White NJ, van der Poll T. Elevated plasma concentrations of interferon (IFN)- γ and the IFN- γ -inducing cytokines interleukin (IL)-18, IL-12, AND IL-15 in severe melioidosis. *J Infect Dis* 1999;180:1878-85.
-
46. Le XT, Rojekittikhun W. A survey of infective larvae of *Gnathostoma* in eels sold in Ho Chi Minh city. *Southeast Asian J Trop Med Public Health* 2000;31:133-7.
-
47. Learngaramkul P, Petmitr S, Krungkrai SR, Prapunwattana P, Krungkrai J. Molecular

- characterization of mitochondria in asexual and sexual blood stages of *Plasmodium falciparum*. *Mol Cell Biol Res Commun* 1999;2:15-20.
48. Lewallen S, Harding SP, Ajewole J, Schulenburg WE, Molyneus ME, March K, Usen S, White NJ, Taylor TE. A review of the spectrum of clinical ocular fundus findings in *P.falciparum* malaria in African children with a proposed classification and grading system. *Trans Roy Soc Trop Med Hyg* 1999;93:619-22.
49. Longyant S, Sithigorngul P, Thammapalerd N, Sithigorngul W, Menasaveta P. Monoclonal antibodies production specific to vitellin and vitellogenin of giant tiger prawn *Penaeus monodon*. *Invertebrate Reproduction and Development* 1999;35:9-17.
50. Looareesuwan S. Hidden *Plasmodium falciparum* infections. *Southeast Asian J Trop Med Public Health*, 1999;30(4):623-4.
51. Looareesuwan S. Post-graduate study at the Faculty of Tropical Medicine, Mahidol University and the role of SEAMEO TROPMED in education in Southeast Asian Region. Santisirikarnpim, Bangkok, 2000 ISSN 1513-0975:28-50.
52. Looareesuwan S, Wilairatana P, Chokejindachai W, Chalermrut K, Wernsdorfer W, Gemperli B, Gathmann I, Royce C. A randomized, double-blind, comparative trial of a new oral combination of artemether and benflumetol (CGP 56697) with mefloquine in the treatment of acute *Plasmodium falciparum* malaria in Thailand. *Am J Trop Med Hyg* 1999;60(2):238-43.
53. Looareesuwan S, Wilairatana P, Glanarongran R, Indravijit KA, Supeeranontha L, Chinnapha S, Scott TR, Chulay JD. Atovaquone and proguanil hydrochloride followed by primaquine for treatment of *Plasmodium vivax* malaria in Thailand. *Trans R Soc Trop Med Hyg* 1999;93(6):637-40.
54. Looareesuwan S, Wilairatana P, Krudsood S, Treeprasertsuk S, Singhasivanon P, Bussaratid V, Chokjindachai W, Viriyavejakul P, Chalermrut K, Walsh D S, White J. Chloroquine sensitivity of *Plasmodium vivax* in Thailand. *Ann Trop Med Parasitol* 1999;93(3):225-30.
55. Maneerat Y, Pongponratn E, Viriyavejakul P, Punpoowong B, Looareesuwan S, Udomsangpetch R. Cytokines associated with pathology in the brain tissue of fatal malaria. *Southeast Asian J Trop Med Public Health* 1999;30:643-9.
56. Maneerat Y, Viriyavejakul P, Punpoowong B, Jones M, Wilairatana P, Pongponratn E, Turner GDH, Udomsangpetch R. Inducible nitric oxide synthase expression is increased in the brain in fatal cerebral malaria. (This study was supported by The Wellcome Trust of Great Britain, The Thailand Research Fund, and Mahidol University). *Histopathol* 2000;37:269-77.
57. McGready R, Nosten F. The Thai-Burmese border: drug studies of *Plasmodium falciparum* in pregnancy. *Ann Trop Med Parasitol* 1999;93:S19-S23.
58. Migasena S, Suntharasamai P, Pitisuttithum P, Kitayaporn D, Wasi C, Huang W, Vanichseni S, Koompong C, Kaewkungwal J, Raktham S, Ippolito T, Hanson C, Gregory T, Heyward WL, Berman P, Francis D. Aidsvox (MN) in Bangkok injecting drug users: a report on safety and immunogenicity, including macrophage-tropic virus neutralization. *AIDS Res Hum Retroviruses* 2000;16:655-63.
59. Muanza K, Traore B, Gay F, Krudsood S, Danis M, Looareesuwan S. Circulating receptors implicated in the cyto-adherence occurring in severe *Plasmodium falciparum* malaria in Thailand. *Ann Trop Med Parasitol* 1999;93(5):449-55.
60. Muennoo C, Maipanich W, Sanguankiat S, Thairungroj M. Soil-transmitted helminthiasis among fishermen, farmers, gardeners and townspeople in southern Thailand. *J Trop Med Parasitol* 2000;23. (in press)
61. Nacher M, Gay F, Singhasivanon P, Krudsood S, Treeprasertsuk S, Mazier D, Vouldoukis L, Looareesuwan S. *Ascaris lumbricoides* infection is associated with protection from cerebral malaria. *Parasite Immunol* 2000;22(3):107-13.
62. Nacher M, singhasivanon P, Gay F, Silachamroon U, Phumratanapapin W, Looareesuwan S. Contemporaneous and successive mixed *Plasmodium falciparum* and *Plasmodium vivax* infections are associated with *Ascaris lumbricoides*: an immunomodulating effect? *J Parasitology* 2000. (in press)
63. Nacher M, Singhasivanon P, Traore B, Dejvorakul S, Phumratanapapin W, Looareesuwan S, Gay F. Hookworm infection is associated with decreased body temperature during mild *Plasmodium falciparum* malaria. *Am J Trop Med*

- Hyg*2000. (in press)
-
64. Noedl H, Wernsdorfer WH, Krudsood S, Wilairatana P, Viriyavejakul P, Kollaritsch H, Wiedermann G, Looareesuwan S. An *In vivo* – *In vitro* model for the assessment of clinically relevant antimalarial cross-resistance. *Am J Trop Med Hyg*2000. (in press)
-
65. Nontasut P, Bussaratid V, Chullawichit S, Charoensook N, Visetsuk K. Comparison of ivermectin and albendazole treatment for gnathostomiasis. *Southeast Asian J Trop Med Public Health* 2000;31(2):374-7.
-
66. Nosten F. Treatment of vivax malaria on the western border of Thailand. *Trans R Soc Trop Med Hyg* 1999;93(4):433-8.
-
67. Nosten F, McGready R, Simpson JA, Thwai KL, Balkan S, Cho T, Hkirijaroen L, Looareesuwan S, White NJ. The effects of *Plasmodium vivax* malaria in pregnancy. *Lancet* 1999;354:546-9.
-
68. Nosten F, van Vugt M, Price R, Luxemburger C, Thway KL, Brockman A, McGready R, ter Kuile F, Looareesuwan S, White NJ. Effects of artesunate-mefloquine combination on incidence of *Plasmodium falciparum* malaria and mefloquine resistance in western Thailand: a prospective study. *Lancet* 2000;356:297-302.
-
69. Paul RE, Brockman A, Price RN, Luxemburger C, White NJ, Looareesuwan S, Nosten F, Day KP Genetic analysis of *Plasmodium falciparum* infections on the north-western border of Thailand. Published in: *Trans R Soc Trop Med Hyg* 1999;93(6):587-93.
-
70. Perlmann P, Perlmann H, Looareesuwan S, Krudsood S, Kano S, Matsumoto Y, Brittenham G, Troye-Blomberg M, Aikawa M. Contrasting functions of IgG and IgE antimalarial antibodies in uncomplicated and severe *Plasmodium falciparum* malaria. *Am J Trop Med Hyg* 2000;62(3):373-7.
-
71. Pongpaew P, Supawan V, Tungtrongchitr R, Chantaranipapong Y, Phonrat B, Schelp FP. Iodine content in cow's milk, soybean milk and milk products. *J Nutr Assoc Thai* 2000. (in press)
-
72. Pongpaew P, Supawan V, Tungtrongchitr R, Chantaranipapong Y, Phonrat B, Schelp FP. Iodine content in cow's milk, soy bean milk and milk products. Submitted to *J Nutr Assoc Thai* 2000. (in press)
-
73. Pongpaew P, Supawan V, Tungtrongchitr R, Phonrat B, Vudhivai N, Chantaranipapong Y, Kitjaroenatham A, Jintaridhi P, Intarakhao C, Mahaweerawat U, Saowakhontha S, Schelp FP. Urinary iodine excretion as a predictor of the iodine content of breast milk. *J Med Assoc Thai* 1999;82:284-9.
-
74. Pongpaew P, Tungtrongchitr R, Phonrat B, Vudhivai N, Jintaridhi P, Vorasart S, Chantaranipapong Y, Supawan V, Viroonudomphol D, Trivunyatkul S, Tongboonchoo C, Schelp FP. Activity, dietary intake, and anthropometry of an informal social group of thai elderly in Bangkok. *Arch Gerontol Geriatric* 2000;30:245-60.
-
75. Pongponratn E, Viriyavejakul P, Wilairatana P, Ferguson D, Chaisri U, Turner G, Looareesuwan S. Absence of knob on parasitized red blood cells in a splenectomized patient in fatal falciparum malaria. *Southeast Asian J Trop Med Public Health*, December 2000.
-
76. Price RN, Cassar C, Brockman A, Duraisingh M, van Vugt M, White NJ, Nosten F, Krishna S. The *PFMDR1* gene is associated with a multidrug-resistant phenotype in *Plasmodium falciparum* from the western border of Thailand. *Antimicrob Agents Chemother* 1999;43:2943-9.
-
77. Pukrittayakamee S, Chantra A, Simpson JA, Vanijanonta S, Clemens R, Looareesuwan S, White NJ. Therapeutic responses to different antimalarial drugs in vivax malaria. *Antimicrob Agents Chemother* 2000;44(6):1680-5.
-
78. Ramasoota P, Chansiripornchai N, K?llenius G, Hoffner SE, Svenson SB. Comparison of *mycobacterium avium* complex (MAC) strains from pigs and humans in sweden by random amplified polymorphic DNA (RAPD) using standardized reagents. *Veterinary Microbiol*2000. (In press)
-
79. Ramasoota P, Krovacek K, Chansiripornchai N, Morner AP, Svenson SB. Identification of *escherichia coli* recovered from milk of sows with coliform mastitis by random amplified polymorphic DNA (RAPD) using stand ardisized reagents. *Acta Vet Scand*2000;41(3):249-59.
-
80. Ramasoota P, Wongwit W, Sumpunachot P, Unnarat K, Ngamyang M, Svenson SB. Multiple mutations in the *rpob* gene of *mycobacterium leprae* strains from leprosy patients in Thailand. *Southeast Asian J Trop Med Public Health* 2000;31(3):1-5.

81. Riyong D, Choochote W, Jitpakdi A, Suvannadabba S, Leemingsawat S, Chaitong U. Autogenous *Aedes togoi* sub-colony (Chanthaburi, Thailand strain), an efficient laboratory vector in study of filariasis. *Southeast Asian J Trop Med Public Health* 2000;31(2):246-51.
82. Saowakontha S, Pongpaew P, Vudhivai N, Tungtrongchitr R, Sanchaisuriya P, Mahaweerawat U, Laohasiriwong W, Intarakhao C, Leelapanmetha P, Chaisiri K, Vatanasapt V, Merkle A, Schelp FP. Promotion of the health of rural women towards safe motherhood – an intervention project in northeast Thailand. *Southeast Asian J Trop Med Pub Health* 2000. (in press)
83. Sato k, Kano S, Matsumoto Y, Glanarongran R, Krudsood S, Looareesuwan S, Aikawa M, Suzuki M. Application of yeast enolase as antigen for immunodiagnosis of malaria. *Southeast Asian J Trop Med Public Health* 2000;31 (Suppl1):79-84.
84. Sibmooh N, Pipitaporn B, Wilairatana P, Dangdongjai J, Udomsangpetch R, Looareesuwan S, Chantharaksri U. Effect of artemisinin on lipid peroxidation and fluidity of the erythrocyte membrane in malaria. *Biol Pharm Bul* 2000;23(11):1275-80.
85. Silachamroon U, Phumratanaprapin W, Krudsood S, Treeprasertsuk S, Budsaratid V, Pornpininworakij K, Wilairatana P, Looareesuwan S. Frequency of Early Rising Parasitemia in Falciparum Malaria Treated with Artemisinin Derivatives. *Southeast Asian J Trop Med Public Health* (2000).
86. Simpson AJH, Suputtamongkol Y, Smith MD, Angus BJ, Rajanuwong A, Wuthiekanun V, Howe PA, Walsh AL, Chaowagul W, White NJ. Comparison of imipenem and ceftazidime as therapy for severe melioidosis. *Clin Infect Dis* 1999;29:381-7.
87. Simpson AJH, White NJ. Combination antibiotic therapy for severe melioidosis. *Clin Infect Dis* 1999;28:410.
88. Simpson JA, Price R, ter Kuile F, Teja-Isavatharm P, Nosten F, Chongsuphajsiddhi T, Looareesuwan S, Aarons L, White NJ. Population pharmacokinetics of mefloquine in patients with acute falciparum malaria. *Clin Pharmacol Ther* 1999;66(5):472-84.
89. Singhasivanon P. Mekong Malaria. Malaria, multi-drug resistance and economic development in the greater Mekong subregion of Southeast Asia. *Southeast Asian J Trop Med Public Health* 1999;30(Suppl 4: I-iv):1-101.
90. Sirivichayakul C, Sabcharoen A, Chanthavanich P, Chocejindachai W, Thawatsupha P, Suthisarnsunthorn U, Ounkaew W. Incidence and clinical manifestations of influenza in nurse assistant students. *Southeast Asian J Trop Med Public Health* 2000;31(1):57-61.
91. Sirivichayakul C, Chanthavanich P, Chocejindachai W, Pengsaa K, Kabkaew K, Saelim R. Pleural effusion in childhood falciparum malaria *Southeast Asian J Trop Med Public Health* 2000;31(1):187-9.
92. Sirivichayakul C, Chanthavanich P, Chocejindachai W, Sabcharoen A, Pengsaa K, Prarinyanupharb V. Dengue infection with unusual manifestations: a case report. *J Med Assoc Thai* 2000;83:325-9.
93. Sirivichayakul C, Chocejindachai W, Vithayasai N, Chanthavanich P, Pengsaa K, Wisetsing P, Harikul S, Rathvuth H, Sabchareon A. Effects of rice powder salt solution and milk-rice mixture on acute watery diarrhea in young children. *Southeast Asian J Trop Med Public Health* 2000;31(2): 354-9.
94. Sirivichayakul C, Pojjaroen-anant C, Wisetsing P, Lalitphiphat A, Chanthavanich P, Kabkaew K. Prevalence of enterobiasis and its incidence after blanket chemotherapy in male orphanage. *Southeast Asian J Trop Med Public Health* 2000;31(1):144-6.
95. Steinmetz I, Reganzerowski A, Brenneke B, Haussler S, Simpson A, White NJ. Rapid identification of *Burkholderia pseudomallei* by latex agglutination based on an exopolysaccharide-specific monoclonal antibody. *J Clin Microbiol* 1999;37:225-8.
96. Stoiser B, Looareesuwan S, Thalhammer F, Daxbock F, Chullawichit S, El-Menyawi I, Graninger W, Burgmann H. Serum concentrations of granulocyte-colony stimulating factor in complicated Plasmodium falciparum malaria. *Eur Cytokine Netw* 2000;11(1):75-80.
97. Subbarao S, Vanichseni S, Hu DJ, Kitayaporn D, Choopanya K, Raktham S, Young NL, Wasi C, Sutthent R, Luo CC, Ramos A, Mastro TD. Genetic characterization of incident HIV type 1

- subtype E and B strains from A prospective cohort of injecting drug users in Bangkok, Thailand. *AIDS Res Hum Retroviruses* 2000;16:699-707.
-
98. Suputtamongkol Y, Chaowagul W, Chetchotisakd P, Lertpatanasuwan N, Intaranongpai S, Ruchutrakool T, Budhsarawong D, Mootsikapun P, Wuthiekanun V, Teerawatasook N, Lulitanond A. Risk factors for melioidosis and bacteremic melioidosis. *Clin Infect Dis* 1999;29:408-13.
-
99. Tapchaisri P, Wangroongsarb P, Panbangred W, Kalambaheti T, Chongsa-nguan M, Srimanote P, Kurazono H, Hayashi H, Chaicumpa W. Detection of *Salmonella* contamination in food samples by dot-ELISA, DNA amplification and bacterial culture. *Asian Pac J Allergy Immunol* 1999;17:41-51.
-
100. Thepsamarn P, Krudsood S, Looareesuwan S. A comparative clinical trial of a combination of artesunate and mefloquine versus a combination of quinine and tetracycline for the treatment of acute uncomplicated falciparum malaria in Somdejprachaotaksinmaharaj Hospital, Tak province *J Trop Med Parasitol.* 1999;22(2):65-70.
-
101. Timothy ME Davis, Pongponratan E, Supanaranond W, Pukrittayakamee S, Helliwell T, Holloway P, White NJ. Skeletal muscle involvement in falciparum malaria: biochemical and ultrastructural study. *Clin Infect Dis* 1999;29:831-5.
-
102. Traore B, Muanza K, Looareesuwan S, Supavej S, Khusmith S, Danis M, Viriyavejakul P, Gay F. Cytoadherence characteristics of *Plasmodium falciparum* isolates in Thailand using an *In vitro* human lung endothelial cells model. *Am J Trop Med Hyg* 2000; 62(1): 38-44.
-
103. Trisirivanich S, Laothavorn J, Na-Bangchang K, Khusmith S. Characterization of specific monoclonal antibodies for detection of mefloquine in body fluids. *Southeast Asian J Trop Med Public Health* 2000;31(3).
-
104. Tungtrongchitr R, Pongpaew P, Phonrat B, Tribunyatkul S, Viroonudomphol D, Supawan V, Jintaridhi P, Lertchavanakul A, Vudhivai N, Schelp FP. Serum leptin and lipid profiles in Thai obese and overweight subjects. *Int J Vit Nutr Res* 2000. (in press)
-
105. Tungtrongchitr R, Pongpaew P, Phonrat B, Tribunyatkul S, Viroonudomphol D, Supawan V, Jintaridhi P, Lertchavanakul A, Vudhivai N, Schelp FP. Leptin concentration in relation to body mass index (BMI) and hematological measurements in Thai obese and overweight subjects. *Southeast Asian J Trop Med Pub Health* 2000. (in press)
-
106. van Vugt M, Angus BJ, Price RN, Mann C, Simpson JA, Poletto C, Htoo SH, Looareesuwan S, White NJ, and Nosten F. A case-control auditory evaluation of patients treated with artemisinin derivatives for multidrug-resistant *Plasmodium falciparum* malaria. *Am J Trop Med Hyg.* 2000;62(1):65-9.
-
107. van Vugt M, Edstein MD, Proux S, Lay K, Ooh M, Looareesuwan S, White NJ, Nosten F. Absence of an interaction between artesunate and atovaquone – proguanil. *Eur J Clin Pharmacol* 1999;55:469-74.
-
108. van Vugt M, Ezzet F, Nosten F, Gathmann I, Wilairatana P, Looareesuwan S, White NJ. No evidence of cardiotoxicity during antimalarial treatment with artemether-lumefantrine. *Am J Trop Med Hyg* 1999;61(6):964-7.
-
109. van Vugt M, Looareesuwan S, Wilairatana P, McGready R, Villegas L, Gathmann I, Mull R, Brockman A, White NJ, Nosten F. Artemether-lumefantrine for the treatment of multidrug-resistant falciparum malaria. *Trans R Soc Trop Med Hyg* 2000;94:545-8.
-
110. van Vugt M, Wilairatana P, Gemperli B, Gathmann I, Phaipun L, Brockman A, Luxemburger C, White NJ, Nosten F, Looareesuwan S. Efficacy of six doses of artemether-lumefantrine (benflumetol) in multidrug-resistant *Plasmodium falciparum* malaria. *Am J Trop Med Hyg* 1999;60(6):936-42.
-
111. Viroonudomphol D, Pongpaew P, Tungtrongchitr R, Phonrat B, Supawan V, Vudhivai N, Schelp FP. Erythrocyte antioxidant enzymes and blood pressure in relation to overweight and obese Thai in Bangkok. *Southeast Asian J Trop Med Pub Health* 2000;31:325-34.
-
112. Vudhivai N, Pongpaew P, Tungtrongchitr R, Phonrat B, Supawan V, Chantaranipapong Y, Vorasant S, Schelp FP. Dietary pattern, lifestyle and nutritional status of health science university students in Bangkok. *J Nutr Assoc Thai* 2000;35(1):7-21.
-

113. Watt G, Saisorn S, Jongsakul K, Sakolvaree Y, Chaicumpa W. Blinded, Placebo-Controlled Trial of Antiparasitic Drugs for Trichinosis Myositis. *J Infect Dis* 2000;182:371-4.
114. White NJ, Nosten F, Looareesuwan S, Watkins WM, Marsh K, Snow RW, Kokwaro G, Ouma J, Hien TT, Molyneux ME, Taylor TE, Newbold CI, Ruebush TK 2nd, Danis M, Greenwood BM, Anderson RM, Olliaro P. Averting a malaria disaster. *Lancet* 1999;353(9168):1965-7.
115. Wilairatana P, Krudsood S, Silachamroon U, Singhasivanon P, Vannaphan S, Faithong S, Klabprasit M, Na-Bangchang S, Olliaro P & Looareesuwan S. Clinical trial of sequential treatments of moderately severe and severe malaria with dihydroartemisinin suppository followed by mefloquine in Thailand. *Am J Trop Med Hyg* 2000. (in press)
116. Wilairatana P, Looareesuwan S, Neild GH. Management of malaria with acute renal failure (original article). *Afr J Nephrol* 1999;3:67-72.
117. Wilairatana P, Looareesuwan S. The clinical use of artemisinin derivatives in the treatment of malaria. *Medicine Tropical. Med Trop* 2000. (in press)
118. Wilairatana P, Looareesuwan S. Guideline in Management of Severe malaria. *J Indian Med Assoc* 2000;98(10):628-31.
119. Wilairatana P, Riganti M, Puchadapirom P, Punpoowong B, Vannaphan S, Udomsangpetch R, Krudsood S, Brittenham GM, Looareesuwan S. Prognostic significance of skin and subcutaneous fat sequestration of parasites in severe falciparum malaria. *Southeast Asian J Trop Med Public Health*. 2000;31(2):203-12.
120. Wilairatana P, Silachamroon U, Krudsood S, Singhasivanon P, Treeprasertsuk S, Bussaratid V, Pjumratanaprapin W, Srivilirit S, Looareesuwan S. Efficacy of primaquine regimens for primaquine-resistant *Plasmodium vivax* malaria in Thailand. *Am J Trop Med Hyg* 1999;61(6):973-7.
121. Wuthiekanun V, Howe PA, Simpson AJH, Smith MD, Walsh AL, Angus BJ, Rajchanuwong A, White NJ. Antifungal susceptibilities of *Cryptococcus neoformans* in northeast Thailand. *Trans Roy Soc Trop Med Hyg* 1999;93:96-7.
122. Wuthiekanun V, White NJ, Simpson AJH. Aminoglycoside and macrolide resistance in *Burkholderia pseudomallei*. *Antimicrob Agents Chemother* 1999;43:23-32.
123. Xuan LT, Rojekkittikhun W. A survey of inceptive larvae of *Gnathostoma* in eels sold in Ho Chi Minh City. *Southeast Asian J Trop Med Public Health* 2000;31:133-7.
124. Yipp BG, Anand S, Schollaardt T, Patel KD, Looareesuwan S, Ho M. Synergism of multiple adhesion molecules in mediating cytoadherence of *Plasmodium falciparum*-infected erythrocytes to microvascular endothelial cells under flow. *Blood* 2000;96(6):2292-8.
125. Tosukhowong T Eiam-Ong S, Thamutok K, Panomvana Na Ayudhya D, Wittayalertpanya S. Pharmacokinetics of Intraperitoneal Cefazolin and Gentamicin in the Empirical Therapy of Peritonitis in CAPD Patients. *วารสารสมาคมโรคไตแห่งประเทศไทย*. 1999;5(2):166-7.
126. ปราณิต ผ่องแผ้ว, รั้งสรุค์ ตั้งตรงจิตร, ศาสตรี เสาวคนธ์ การเสริมสารไอโอดีนในน้ำปลาเพื่อในการป้องกันโรคขาดสารไอโอดีน: ข้อเสนอแนะ *J Nutr Assoc Thai* 2000. (in press)

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