Faculty of Tropical Medicine
Mahidol University

Annual Report 2002

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Faculty of Tropical Medicine Mahidol University, Annual Report 2002
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Foreword

The Faculty of Tropical Medicine, Mahidol University was founded in 1960. From the outset, with its focus on teaching, research and services, the Faculty was destined to develop into "Asia's Leader in Tropical Medicine", and has gone from strength to strength each year since its establishment.

The Faculty currently consists of 11 Departments plus essential administrative and support services. The on-campus Hospital for Tropical Diseases specializes in such tropical diseases as malaria, dengue fever, gnathostomiasis, opisthorchiasis, strongyloidiasis, paragonimiasis and taeniasis, as well as providing special clinical services in, for example, STD's, gastro-enterology and dermatology, as well as Chinese and Thai traditional medicine.

Through the Bangkok School of Tropical Medicine, the Faculty provides five international postgraduate programmes, from diploma to doctoral levels, which attract students from all over the world each year. Our graduates then distribute the benefits of their learning, through their services and training, all around the globe. The Diploma in Tropical Medicine and Hygiene (DTM&H), a postgraduate training programme for medical doctors, was accredited by the American Society of Tropical Medicine and Hygiene (ASTMH).

The Faculty also conducts international meetings, conferences, seminars and special training courses. In the reporting period, the annual Joint International Tropical Medicine Meeting (JITMM 2002) was co-organized with the Department of Disease Control, Ministry of Public Health, the Bernhard-Nocht Institute for Tropical Medicine (Hamburg, Germany), the Parasitology and Tropical Medicine Association of Thailand, TROPMED Alumni Association, SEAMEO TROPMED Network and the Asian Centre of International Parasite Control (ACIPAC). Internationally renowned, Mr. Mechai Viravaidya presented the 8th Chamlong-Tranakchit Harinasuta Lecture entitled "The Privatization of Poverty Reduction". In JITMM 2002, there were 101 oral presentations and 88 poster presentations, and the Meeting attracted 1,000 delegates from 27 countries. In line with previous trends, this was an increase in participants of 150 over the previous year.

Faculty collaborations located on-campus include the Wellcome-Mahidol University Oxford Tropical Medicine Research Programme (the Wellcome Unit), SEAMEO TROPMED Regional Centre for Tropical Medicine, ACIPAC (a cooperative regional parasite control project with JICA, the Thai Ministry of Public Health, and other contributors), the Joint WHO/UNEP/UNCHS Collaborating Centre for Environmental Management for Vector Control, the Vaccine Trial Centre, and the SEAMEO TROPMED Regional GIS Unit (supported by the EC Regional Malaria Control Programme). The Faculty has ongoing collaborative relationships in research and training with over 30 institutions internationally. Three new Memoranda of Understanding were signed in respect of Nippon Medicine Care (Singapore), the University of Leicester (UK), and Japanese Technical Cooperation for the ACIPAC Project.

Over the past 42 years, the Faculty has continuously expanded and improved its operations, services and research activities in line with its objectives and its wider social responsibilities, nationally, regionally and internationally. Recent developments have included the establishment of the new Field Research Station in Kanchanaburi Province, which complements the existing station at Suan Phung in Ratchaburi Province. At these sites, the Faculty conducts research into endemic tropical diseases, particularly communicable vector-borne diseases like malaria. The Kanchanaburi site will be fully operational in March 2003.

In the reporting period, the Faculty attracted internal grants of 24 million Baht and external grants of 112 million Baht. The Faculty's staff reported 103 research works, most of which were published in peer-reviewed international journals. In the Year 2002, there were 76 ongoing research projects, with 19 new projects being instigated.

Prof. Dwip Kitayaporn was appointed Director of the Thailand-Tropical Diseases Research Programme (T2). Prof. Wanpen Chaicumpa was honored with the National Outstanding Lecturer award. Prof. Sornchai Looareesuwan was presented with the Siriraj Medical School Alumni Outstanding Academic Productivity Award and plaque by Her Royal Highness Princess Chulabhorn, was elected to the Fellowship of the Royal College of Physicians (FRCP), and presented the Priscilla Kincaid-Smith Oration at the RACP/FRCP Meeting in Australia.

Finally, I wish to convey my sincere appreciation to all members of the Faculty, to our supporters and collaborators for their excellent work throughout the Year 2002. I trust that the Faculty of Tropical Medicine Annual Report for the Year 2002 provides a comprehensive summary of the Faculty's activities in the reporting period, and commend it to you.

Sornchai Looareesuwan

Prof. Sornchai Looareesuwan
Dean

Editor's Note

It is a tradition for the members of the Faculty of Tropical Medicine, Mahidol University to report their activities each year. For this fiscal year, October 2001-September 2002, the successful completion of the Annual Report can be attributed to the collaboration of the Departments and Divisions, the Hospital for Tropical Diseases, and affiliated organizations, i.e. SEAMEO TROPMED Network, the Wellcome Mahidol-Oxford Tropical Medicine Research Programme (or Wellcome Unit), and the Asian Centre of International Parasite Control (ACIPAC).

The three main activities of the Faculty focus on teaching and training, research, and academic and health services. Five regular international postgraduate programmes have continued to progress very well, with 227 students enrolled in the courses this year, 69 of those being new enrollments. There have been, in addition, national and international short training courses.

In the reporting period, 103 papers reporting our research activities were published in international and national journals. There were at least 94 on-going research projects. In addition, there were 78 research projects related to Master and Doctor of Philosophy in Tropical Medicine theses. Collaborative research and training programmes have been maintained with at least 30 institutions internationally.

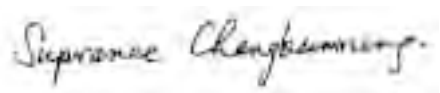
As part of the Faculty's commitment to academic services, we organized the annual Joint International Tropical Medicine Meeting (JITMM), which was held in August 2001. One thousand participants, from 27 countries, attended. National and international conferences and workshops were held. The Faculty also provides in-service training for domestic and overseas trainees. In order to distribute knowledge of tropical diseases and related fields to the public, many kinds of leaflets were published. Furthermore, other mass media were utilized, such as television and radio programmes. Three hundred and twenty-four overseas and local visitors came to the Faculty via the SEAMEO TROPMED Network and via the Faculty itself during the year.

The Hospital for Tropical Diseases provides health services to the public, with 250 beds for in-patients. The most distinctive cases are malaria, for which the determination of malaria in patient blood is a 24-hour service. Besides routine laboratory examinations for tropical diseases, the Faculty and the Hospital also provide many other specialized tests.

Not only have there been matters of academic interest, but also our cultural heritage has been preserved in such events as the 'Tak Baht for New Year Festival', 'Wan Wai Kru' and the 'Songkran Festival'.

However, more details are in the full text.

Finally, the members of the Editorial Committee would like to express our sincere gratitude to all members of the Faculty for their excellent cooperation in the preparation of this Annual Report for the fiscal year 2002.



Assoc. Prof. Supranee Changbumrung
Editor

Organization and Administration

The Faculty of Tropical Medicine, Mahidol University

Dean, Deputy Deans, Assistant Deans and Secretary of the Faculty

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

Dr. Chotechuang Panasoponkul
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for Student Affairs

Assoc. Prof. Kanjana Hongtong
Deputy Dean
for Welfare

Assist. Prof. Chalit Komalamisra
Deputy Dean
for Educational and InformationTechnology

Miss Kobsiri Chalermrut
Assistant Dean
for Special Activities

Miss Suparp Vannaphan
Assistant Dean
for Professional Development

Assist. Prof. Chukiat Sirivichayakul
Deputy Dean
for Educational Affairs

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

Assoc. Prof. Pratap Singhasivanon
Deputy Dean
for Policy and Development

Dr. Wirach Maek-A-Nantawat
Assistant Dean
for Educational Affairs

Assoc. Prof. Parnpen Viriyavejakul
Assistant Dean
for International Relations

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

Mrs. Vorapan Singhsilarak
Secretary of the Faculty

Special Events 2002







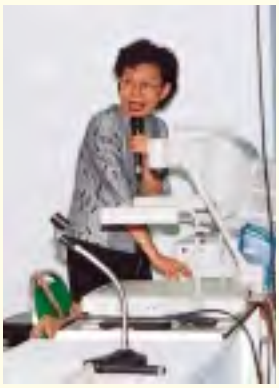


■ JITMM 2002

Joint International Tropical Medicine Meeting 2002,
20-22 November 2002, at the Montien Riverside Hotel, Bangkok, Thailand

Special Events 2002

Prof. Sornchai Looareesuwan was presented with the Siriraj Medical School Alumni Outstanding Academic Productivity Award, and plaque, by Her Royal Highness Princess Chulabhorn, on 4 March 2002



Workshop on Self Assessment Report (SAR)
10-11 July 2002

Special Events 2002

■ Seminar on “Office of the Dean and Quality Assurance”
15-16 December 2001, at Tawaravadi Resort, Prachinburi

Special Events 2002

Charity Horse Race, proceeds to the Hospital for Tropical Diseases Foundation under the Patronage of Her Royal Highness Princess Galayani Vadhana Krom Luang Naradhivas Rajanagarindra, on 14 July 2002

Rajvithi Campus
Sport Day, 20 February 2002

Consultants

1. Prof. Emeritus Chamlong Harinasuta
2. Prof. Emeritus Danai Bunnag
3. Prof. Emeritus Arunee Sabchareon
4. Prof. Emeritus Chaisin Viravan
5. Prof. Emeritus Prayong Radomyos
6. Assoc. Prof. Mario Riganti
7. Prof. Emeritus Mukda Trishnananda
8. Prof. Emeritus Sommai Wilairatana
9. Dr. Peter Echeverria

Visiting Professors

Name	Country
Professor Walther H. Wernsdorfer	Austria
Professor Frank P. Schelp	Germany
Dr.Gertrud Elise Schmidt - Ehry	Germany
Professor Gunther Wernsdorfer	Germany
Dr.Frédérick Gay	France
Professor Masamichi Aikawa	Japan
Associate Professor Dr.Shigeyuki Kano	Japan
Professor Somei Kojima	Japan
Prof.Akira Ito	Japan
Professor C.P. Ramachandran	Malaysia
Datuk Dr.Manikavasagam Jegathesan	Malaysia
Dr.P.F. Beales	Switzerland
Dr.Chev Kidson	Australia
Dr.David Warrell	United Kingdom
Prof.Gary M. Brittenham	USA
Professor John H. Cross	USA
Dr.Stephen L Hoffman	USA
Prof.Myron Max Levine	USA
Prof.James Carroll	USA
Prof.Victor R. Gordeuk	USA
Prof.Ralf Clemens	Belgium
Prof.Herbert M. Gilles	United Kingdom
Dr.Karl A. Western	USA

Faculty Board

(1 October 2001-30 September 2002)

No.	Name	Position
1.	Prof. Sornchai Looareesuwan	Dean
2.	Assoc. Prof. Pratap Singhasivanon	Deputy Dean for Policy and Development
3.	Prof. Polrat Wilairatana	Deputy Dean for Hospital Services
4.	Assoc. Prof. Suvanee Supavej	Deputy Dean for International Relations
5.	Assoc. Prof. Jitra Waikagul	Deputy Dean for Academic Affairs
6.	Assoc. Prof. Chukiat Sirivichayakul	Deputy Dean for Educational Affairs
7.	Assoc. Prof. Thaiyooth Chintana	Deputy Dean for Area and Financial Affairs
8.	Assist. Prof. Chotechuang Panasoponkul	Deputy Dean for Student Affairs
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10.	Assist. Prof. Chalit Komalamisra	Deputy Dean for Educational and Information Technology
11.	Assoc. Prof. Somjai Leemingsawat	Head of Department of Medical Entomology
12.	Assoc. Prof. Pornthep Chanthavanich	Head of Department of Tropical Pediatrics
13.	Prof. Srisin Khusmith	Head of Department of Microbiology and Immunology
14.	Assoc. Prof. Malinee Thairungoj	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 Sanghirun	Head of Department of Tropical Radioisotopes
19.	Assist. Prof. Kasinee Buchachart	Head of Department of Tropical Hygiene

20.	Prof. Dwip Kitayaporn	Head of Department of Social and Environmental Medicine
21.	Assoc. Prof. Wichai Supanaranond	Head of Department of Clinical Tropical Medicine
*22.	Prof. Wanpen Chaicumpa	Elected Member
*23.	Assoc. Prof. Surang Tantivanich	Elected Member
24.	Assist. Prof. Achara Asavanich	Elected Member
25.	Assoc. Prof. Yupaporn Wattanagoon	Elected Member
**26.	Assoc. Prof. Wichit Rojekittikhun	Elected Member
**27.	Assoc. Prof. Porntip Petmitr	Elected Member
	*	Until 13 January 2002
	**	From 14 January 2002

Faculty Senate

No.	Name	Position
1.	Assoc. Prof. Surang Tantivanich	Chairman/Mahidol University Faculty Senate Member
2.	Assist. Prof. Achara Asavanich	Vice Chairman / Lecturer Representative
3.	Prof. Wanpen Chaicumpa	Representative until 13 January 2002
4.	Assoc. Prof. Yupaporn Wattanagoon	Representative until 13 January 2002
5.	Assist. Prof. Supatra Thongrungkiat	Representative, Department of Medical Entomology, Assistant Secretary General (21 January 2002-Present)
6.	Dr. Kriengsak Limkittikul	Representative, Department of Tropical Pediatrics (1 October 2000-20 January 2001, 1 July 2002-Present)
7.	Assoc. Prof. Wipawee Usawattanakul	Representative, Department of Microbiology and Immunology (21 January -17 December 2002)
8.	Assist. Prof. Yuvadee Mahakunkitjaroen	Representative, Department of Microbiology and Immunology (27 December 2002 - Present)
9.	Assist. Prof. Panyawut Hiranyachattada	Representative, Department of Helminthology (21 January 2002 - Present)
10.	Assoc. Prof. Wichit Rojekittikhun	Representative, Department of Helminthology (14 January 2002 - 1 October 2002)
11.	Assoc. Prof. Porntip Petmitr	Representative, Department of Protozoology (until 14 January 2002) Lecturer Representative, Department of Protozoology (14 January 2002-Present)
12.	Assist. Prof. Chutatip Siripanth	Representative, Department of Protozoology (21 January 2002-Present)
13.	Assoc. Prof. Yaowapa Maneerat	Representative, Department of Tropical Pathology, Secretary General (21 January 2002 - Present)
14.	Assist. Prof. Talabporn Harnroongroj	Representative, Department of Tropical Nutrition and Food Science
15.	Assist. Prof. Petcharin Yamarat	Representative, Department of Tropical Radioisotopes
16.	Assist. Prof. Chantima Lohachit	Representative, Department of Social and Environmental Medicine
17.	Assoc. Prof. Srivicha Krudsood	Representative, Department of Tropical Hygiene (6 November 2001-Present)
18.	Assist. Prof. Udomsak Silachamroon	Representative, Department of Clinical Tropical Medicine (until 20 January 2002)
19.	Assoc. Prof. Punnee Pitisuttithum	Representative, Department of Clinical Tropical Medicine (18 October 2002-Present)
20.	Dr. Wirach Maek-A-Nantawat	Representative, Department of Clinical Tropical Medicine (21 January 2001-Present)
21.	Assist. Prof. Varee Wongchotigul	Representative, Department of Microbiology and Immunology
22.	Assist. Prof. Paron Dekumyoy	Representative, Department of Helminthology, Secretary General (11 May 2001 -20 January 2002)

Mahidol University Senate

1.	Prof. Wanpen Chaicumpa	(until 23 December 2001)
2.	Assoc. Prof. Surang Tantivanich	(24 December 2001-23 December 2003)

Annual Report 2002
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Assoc. Prof. Benjaluck Phonrat	Member
Assist. Prof. Achara Asavanich	Member
Mr. Paul Adams	Member
Mr. Sompoch Thanuvathana	Member
Mrs. Thitika Teeranetr	Member
Mr. Tawan Wathanakul	Member
Mr. Ronnachai Rarerng	Member
Mr. Phaibul Vasanakomut	Member
Ms. Warissara Chaiyabhandhu	Member
Mrs. Siwaporn Samung	Member
Ms. Pitchapa Vutikes	Member
Mrs. Pornpimon Adams	Member and Secretary

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Lecturer

Chuanpit Preechawuthiwong
B.A (Political Science)
General Affairs Officer

Pannamas Maneekarn
B.Sc. (Nursing), M.Sc. (Preventive Medical)
Researcher

CURRENT RESEARCH ACTIVITIES

The Department has published more than 300 papers and has continued to pursue its mission in 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% mixed infections of the 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 antigens in cerebral and non-cerebral malaria patients, of lymphocyte subpopulations during the 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 drugs trials for gnathostomiasis, strongyloidiasis, opisthorchiasis, paragonimiasis and teniasis.

Research series are continuing involving new antifungal drugs for AIDS with fungal disease. Traditional medicine for the treatment of HIV/AIDS is also being studied.

Research into skin diseases in HIV patients has been conducted in many aspects, the epidemilogy of cutaneous manisfestations in HIV patients in Thailand, fungal infection in leukoplakia patients, superficial fungal infections in normal and HIV patients.

The titles of current departmental research activites are as follows :

1. 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.
2. Neurotoxicity of oral artemether in animal model following intermittent intramuscular injections.
3. Open-label, treatment protocol for the safety and efficacy of SCH 56592 (oral suspension) in the treatment of invasive fungal infections.
4. Efficacy and tolerability of ivermectin for gnathostomiasis (pilot study)
5. Efficacy and tolerability of ivermectin for gnathostomiasis.
6. Effect of insecticide or female reproductive system.
7. Health risk from trihalomethane contamination in tap water in Bangkok Metropolitan area and boundary.
8. Development of genotyping technique for *Plasmodium vivax* parasite.
9. Study of auto-agglutination phenotype and disease severity in *P. falciparum* infection..
10. Research and development for Thai people living at Thai-Myanmar border to be free from tropical diseases
11. Effect of drug accumulation in the neurotoxicity of artemether, dosing regimens with variable drug-free intervals in a mouse model.
12. Safety and therapeutic effects of Jin Huang Chinese medicine in uncomplicated HIV-1 patients.
13. Observational probe study of *in vitro* immune response parameters to candidate HIV-1 vaccine antigens among subjects from Thailand.

14. Biochemical abnormalities of renal function in patients with falciparum malaria.
15. Neoropathological toxicity of artemisinin derivatives in a mouse model.
16. Advirse effect of rifampicin on quinine efficacy in falciparum malaria.
17. *Plasmodium vivax*: Polymerase Chain Reaction amplification artifacts limit the suitablility of pugam 1 as a genetic marker.
18. Efficacy of the combination of antimalarial with ursodeoxycholic acid comparing to antimalaria and placebo in the prevention of acute renal failure in severely jaundiced falciparum malaria patients: a randomized controlled trial.

LIST OF ABSTRACTS

LIST OF ABSTRACTS

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Departmental On-going Research (2002)

Gnathostomiasis

- A seven-year retrospective evaluation of gnathostomiasis.
- The diagnostic specificity of gnathostomiasis by immunoblot. Gnathostomiasis: an emerging imported disease
- Sequence variation in *Gnathostoma spinigerum* mitochondrial DNA by single-strand confirmation polymorphism analysis.
- Effect of ivermectin on *Gnathostoma spinigerum* morphology.
- *Gnathostoma* infection in Nakhon Nayok and Prachin Buri.
- *Gnathostoma* infection in fish caught for local consumption in Nakhon Nayok Province.
- Seasonal variation of *Gnathostoma* infection in swamp eels in Nakhon Nayok.

Angiostrongyliasis

- Angiostrongyliasis: partially purified antigens of *Angiostrongylus cantonensis* adult worms for diagnosis using immunoblot.
- Angiostrongyliasis: potential fractionated antigens of *Angiostrongylus cantonensis* adult worms for diagnosis using ELISA and an elimination of cross-reactive components.
- *Angiostrongylus cantonensis*: s-adenosyl methionine decarboxylase.
- Experimental infection of freshwater fish in Thailand with infective stage of *Angiostrongylus*.

Cysticercosis

- Comparison of biochemical extract preparations of *Cysticercus cellulosae* by SDS-polyacrylamide gel electrophoresis and immunoblot technique.
- Differentiation of fractionated larval antigens (*Cysticercus cellulosae*) responsible for antibody of neurocysticercosis patients

Opisthorchiasis

- Diagnosis of human opisthorchiasis with *Bithynia* snail antigen by ELISA.
- Studies on the efficacy of Thai traditional herbal medicines in the treatment of opisthorchiasis in hamsters.

Trichinellosis

- Monoclonal antibody-based competitive ELISA and indirect ELISA for immunodiagnosis of trichinellosis.

Toxocariasis

- *Toxocara canis* larval antigens for serodiagnosis of human toxocarosis.
- Evaluation of excretory-secretory and partially purified antigens of adult *Toxocara canis* againt toxocariasis by ELISA and immunoblot.

Filariasis

- Study on prevalence of *Wuchereria bancrofti* infection in Kanchanaburi and Ratchaburi provinces.
- Urine ELISA for diagnosis of Bancroftian filariasis

Soil-transmitted helminthiasis

- Soil-transmitted helminthiases control through school-based intervention.
- Effect of mebendazole on *Trichuris trichiura* morphology.
- Efficacy of high dose mebendazole against trichuriasis in adult patients.
- Strongyloidiasis: improvement of antigen preparation for increasing the specificty of IgG-ELISA.

Other helminthiases

- Analysis of fluid antigens of *Echinococcus* cyst for diagnosis.
- Fish-borne trematodes in Thailand.

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CURRENT RESEARCH ACTIVITIES

The Department of Medical Entomology has conducted 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.

Laboratory colonies of different strains of mosquito vector species of *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.

Study of 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.

In addition, an entomological survey is being carried out in Pa Rai, Sa Kaeo Province, to investigate malaria transmission potential by *An. campestris*. This will be the first evidence of the species acting as a malaria vector in Thailand.

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 complexes of these mosquitoes from various locations in Thailand are also investigated by enzymatic studies.

Effective controls for mosquito vectors are investigated both in laboratory and field trials. The efficacy of chemical insecticides, microbial insecticide, insect growth regulator and chemosterilant are evaluated against the vectors. Studies on the development of insect resistance to these chemicals are also conducted. Non-polluting control methods, such as the use of medicinal plants, are tested. The use of insecticide-impregnated bed nets, especially for malaria control, has been introduced. The selection of mosquito resistance to permethrin-impregnated bed nets is conducted in the laboratory to study the impact on mosquito vectors.

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

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

CURRENT RESEARCH ACTIVITIES

The current research activities of the Department involve studies on biology, molecular biology and immunology of infectious agents/diseases, particularly those causing problems in tropical areas, with the ultimate aims 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 of host responses and immunity; 4) understanding pathogenic mechanisms and virulence factors of pathogens and pathophysiology in hosts; and 5) acquisition of, and acquaintance with, modern technologies, e.g. genetic analysis of bacterial pathogens for epidemiological study, immunogenetic characteristics of severe malaria, gene polymorphism of malaria parasites. Further details are given below:

Sodium dodecyl sulphate-polyacrylamide gel electrophoresis and immunoblotting have been used for the identification of the specific antigens of various pathogens, including *Opisthorchis viverrini, Paragonimus heterotremus, Trichinella spiralis, Strongyloides stercoralis, Gnathostoma spinigerum, Entamoeba histolytica, Plasmodium falciparum* and *P. vivax, Leptospira*, etc. Successful identifications of the specific antigens of these pathogens lead to the development of 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 crude extract by column chromatography. 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* and *P. vivax*; bacteria or their toxins including *Bordetella pertussis, Vibrio cholerae* O:1 and O:139, *Salmonella*, enterotoxigenic *E. coli*, enterohemorrhagic *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 the 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 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, e.g. *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, hemagglutinin, procholeragenoid and lipopolysaccharide of a bacterial pathogen, *Vibrio cholerae*, associated with liposome adjuvant were also studied. It was shown that oral immunization by the combination of these components provides strong local immunity against the bacterium. Phase I and II trials of the oral cholera vaccines 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.

Other areas of research activity 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 Prachin Buri 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.

In malaria, studies on the mechanism of protective immunity, on the one hand, and of immunopathology, on the other hand, have been carried out aiming at how manipulation of the immune system may best be achieved. These include the regulation of the balance between T helper 1 and T helper 2 CD4+ T lymphocytes in immunity to blood stage *P. falciparum*; the immunopathogenesis of severe malaria, including cytokine profile, lymphocyte responses, IgE and IgG and their subclasses and the presence of specific HLA-types, cytokine promoter gene variants in severe and uncomplicated malaria in order to detect patient characteristics of importance for the development of protection against severe *P. falciparum* malaria. For vaccine development, the genetic diversity of the circumsporozoite protein as an epidemiological marker for the efficacy of pre-erythrocytic immunity was also studied.

Studies of *E. histolytica* revealed that its genome organization consisted of at least a circular supercoiled-like and a linear DNA molecule that behave 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 pyruvateferrodoxin oxidoreductase was not decreased. A monoclonal antibody specific against *E. histolytica* conjugated with red phycoerythrin (R-PE) was used successfully for the detection of trophozoites in human fecal samples. An immunotoxin (IT) consisting of a monoclonal antibody against pyruvateferredoxin 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, IT would be one approach for future immunotherapy for invasive amebiasis.

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 the PCR technique and tissue culture, it should be used in every laboratory.

Parts of this research work are being carried out in collaboration with various international universities and institutions, i.e. the Department of Immunology, University of Stockholm, Sweden; Unit of Biomedical Parasitology, Pasteur Institute, France; 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; 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, 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, Laos 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.

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CURRENT RESEARCH ACTIVITIES

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 created at the beginning of the Faculty of Tropical Medicine in the year 1960. Its responsibilities are teaching training, research and service in the field of medical protozoa.

1. Study on DNA replication enzymes of *Plasmodium falciparum* as new chemotherapeutic targets against malaria.
2. Toxoplasmosis in population at risk in Thailand
3. Light and electron microscopic features of acute Ttoxoplasmosis in animal model.
4. Dog and cat parasitic zoonoses.
5. Inhibition of *Giardia intestinalis* and *Entamoeba histolytica* by medicinal plants.
6. Studies on ultrastructure of *Giardia intestinalis* trophozoites after exposure to drugs.
7. *Blastocystis hominis* in children with diarrhea in children hospitals.

8. *In vitro* cultivation for *Cryptosporidium* spp.
9. Rapid detection of *Entamoeba histolytica* antibody.
10. Detection of malaria parasites in patients after-drug treatment by using QBC method.
11. *In-vitro* sensitivities of *Plasmodium falciparum* to medicinal plant.
12. Study on antimalarial drug sensitivites to *Plasmodium falciparum* in community of Thailand.
13. Invention of Thai medicinal plant for treatment of coccidiosis.
14. Establish double antibody ELISA method (sandwich ELISA) for detection of *G. intestinalis, E. histolytica, B. hominis* in fecal specimens
15. Isolation and characterization of DNA helicase from *P. falciparum*.

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- A phase III trial of Aventis Pasteur live recombinant ALVAC-HIV (vCP1521) priming with VaxGen gp120 B/E (AIDSVAX™ B/E) boosting in HIV-uninfected Thai adults
- Socio-cultural and behavioral component for shigellosis disease burden studies in Kaeng Koi District, Saraburi Province, Thailand
- Socio-environmental management for sustainable dengue hemorrhagic fever control in Chaiyaphum Province
- Local wisdom in the treatment of herpes complex diseases: a case study on the treatment of herpes simplex by monk healer (Moh-Pra)
- Tuberculosis infection among household contacts under 15 years old in Bangkok, Thailand
- Hazardous substance management and development of computerized database inventory list on major hazardous substances used in the Faculty of Tropical Medicine
- Environmental health models for sustainable agriculture
- Distribution and genetic variations of the *Pila* snails
- Leptospirosis vaccine design using T7 phage display technique
- Control of soil-transmitted helminths in primary schools in Southern Thailand
- Detection of a possible specific serum marker in opisthorchiasis-associated cholangiocarcinoma patients
- Determination of zinc in soil and sludge from pig farm

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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 of the department, 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 field stations for conducting research in the field of 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 majority of the population are 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. Control of soil-Transmitted helminthiasis in Children through the School Health Program in a Rural Community
3. Base-line Epidemiological and Socio-behavioral Survey of Malaria and Soil-Transmitted Helminthiasis in a Rural Community Near Thai-Myanmar Border in Suan Phung, Ratchaburi Province.
4. Application of GIS in Monitoring Multi-Drug Resistance Malaria in Greater Mekong Sub-Region of Southeast Asia.
5. Effects of Constant Lead Exposure and Health Status of Government Employees Working on the Express Way.
6. Epidemiological Study of Paragonimiasis in Ratchaburi Province.
7. Epidemiology and Drug Sensitivity of Enterbacteriaceae in a Rural Community near Thai-Myanmar border in Suan Phung, Ratchaburi Province.
8. Studies on the Water Quality of River Pachi at Tanawsri Sub-district, Suan Phung District, Ratchaburi Province.
9. Immunological Level of Scrub Typhus of People along Thai-Burmese Border in Suan Phung District, Ratchaburi Province.

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CURRENT RESEARCH ACTIVITIES

Research activities of the Department of Tropical Nutrition and Food Science are concerning 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 especially dislipidemia and coronary heart disease, the effect of smoking on work performance in relation to homocysteine concentration. Furthermore, molecular biology in cancers of lung, liver, breast cholangiocarcinoma, colon and cervix were investigated. Food and health relationship in population of Asian countries are of interest for study and the data will be compared.

At the present time using food practice as the food for disease prevention and treatment is of particular interest. This has led to the project on the development of food and medicinal plants.

In collaboration with the Departments of Helminthology, Protozoology, Tropical Pathology, Tropical Radioisotopes, Social Medicine and Environmental Health, Tropical Pedriatrics, Medical Entomology, Microbiology and Immunology, Clinical Tropical Medicine and the Hospital for Tropical Diseases, the projects for using medicinal plants for the treatment of hookworm and medicinal plants to combat malaria are being carried out.

The topics of the current research projects are as follows:

1. Food and health relationship in the Asian population
2. Micronutrients and oxidative stress in obese subjects
3. Antioxidants and antioxidant enzymes, vitamins, trace elements in patients with dislipidemia and coronary heart disease
4. Relationship of folic acid and cervic cancer
5. Development of food and medicinal plants
6. Medicinal plants for the treatment of hookworm
7. Medicinal plants against malaria

8. Mutational analysis of hMSH2 and hMSH6 genes in sporadic colon cance
9. Determination of genomic instability in cholangiocarcinoma tissues using the random amplified polymorphic DNA technique
10. Identification of genetic alterations in breast cancer by arbitrarily primed polymerase chain reaction in Thai patients.
11. Identification of genetic alterations of epithelial ovarian tumors by arbitrarily-primed polymerase chain reaction (AP-PCR).

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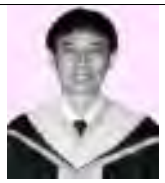

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CURRENT RESEARCH ACTIVITIES

1. Malaria: histopathologic and electronmicroscopic studies on various tissues and organs in humans
2. Light and electron microscopic correlation of knob proteins and staging *in vitro*: *Plasmodium falciparum*
3. Pathogenic effects of cytokines and nitric oxide in severe malaria
4. Endothelial cell activation by *Plasmodium falciparum*
5. Role of nitric oxide in vascular pathologic changes in atherosclerosis: *in vitro* study
6. Response of mast cells in falciparum malaria
7. Cytokines in HIV infection and malaria

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CURRENT RESEARCH ACTIVITIES

Safety and Immunogenicity of Tetravalent Dengue Vaccine Formulation in Thai Adult Volunteers : *Eight-year antibody persistence*

Safety and Immunogenicity of Tetravalent Dengue Vaccine Formulations in Healthy Thai Children : *Evaluation of a booster dose and five-year antibodies persistence*

A phase II, pilot, randomized, open-label, single-center study to evaluate immunogenicity, safety and booster respense of 3 full IM doses versus 3 half IM doses versus 3 ID doses versus 2 ID doses of PCEC rabies vaccine (RabipurX administered concomitantly with JE vaccine as a pre-exposure regimen in 12 to 18 months old toddlers in Thailand

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CURRENT ACTIVITIES

RESEARCH

1. The Department's current research has been carried out as follows:

1.1 Comparison of non-radiological technique and ^{125}I-labeled method for measurement of folic acid in normal RBC and sera patients with cervical dysplasia.

1.2 Effect of helminthic infection on RBC deformability and splenic clearance of patients with *Plasmodium falciparum*

1.3 Comparison of non-radiological technique and ^{125}I-labeled method for measurement of folic acid in patients with Alzheimer's disease.

2. The Department has corporated with other departments, as follows :

2.1 Treatment of hookworm with medicinal plants LD50

2.2 Determination of total folate analysis in food

2.3 Erythrocyte glutathione peroxidase (GSH-Px) and plasma selenium levels in patients with cervical sysplasia.

2.4 The influence of vitamin B_{12} and folate deficient indices on whole blood viscosity in pregnancy.

2.5 The correlation between folic acid status and the cervical cytologic abnormality in Thai women.

3. The Department has corporated with Neuro-Behavioural Biology Center, Institute of Science and Technology for Research and Development in "Determination of Serum Vitamin B_{12} and Folic Acid in Thai Alzheimer's Patients"

4. The Department has corporated with Department of Pediatrics, Faculty of Medicine Ramathibodi Hospital in "Homocysteinemia and Thrombosis in Thai Children Patients"

SERVICES

The Department has two projects for services : (1) service for the measurement of folic acid in red blood cells and sera ; and (2) service for the measurement of vitamin B_{12} in sera. Annual services are shown below

The Department also provides assistance and facilities to measure vitamin B_{12} and folic acid levels of 200 serum samples in ECONUT project, Faculty of Medicine, Chiangmai University.

One hundred and ninety serum samples are measured for vitamin B_{12} and folic acid for the M.Sc. student of the Department of Nutrition, Faculty of Public Health.

January 2002 – December 2002

	Serum vitamin B_{12} (number)	Serum folate (number)	Red cell folate (number)
Children	4	7	4
Man	78	154	51
Women	126	164	93
Total	**208**	**325**	**148**

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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 four 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 ethic minority on the north-western Thai-Myanmar border (studies of the epidemiology, prevention and treatment of malaria and tuberculosis),
- in Sappasitprasong Hospital, Ubon Ratchatani (studies of melioidosis and fungal infections in patients with AIDS),
- in Udon Thani Hospital, Udon Thani (studies of prospective clinical, epidemiological, and treatment of leptospirosis).

The current research activities of the unit on malaria include studies of pathophysiological mechanisms in severe malaria, descriptions of the pharmacokinetic and pharmacodynamic properties of the antimalarial drugs, and studies of the epidemiology, prevention and treatment of malaria in the area of low or unstable transmission of the western border.

The unit's work has provided the currently accepted dose regimens for chloroquine, quinine, artesunate, mefloquine, and artemether-lumefantrine. In the treatment of severe malaria a major objective is to characterize the relative advantages of the artemisinin derivatives over current treatments. Studies are also underway to define the optimum treatment of vivax malaria, and the best methods of preventing and treating malaria in pregnancy. 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.

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.

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VACCINE TRIAL CENTRE

The Vaccine Trial Centre 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.

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.

CURRENT RESEARCH

1. Development of new vaccines against cholera due to *Vibro cholerae* 0139 (Part III)
2. A phase I/II, double-blind, placebo-controlled study of the Chiron biocine HIV Thai Egp 120/MF 59 vaccine administered alone or combined with the chiron biocine HIV SF 2 gp 120 antigen in healthy HIV-seronegative Thai adults
3. A phase I/II trial to evaluation the safety and immunogenicity of AIDSVAX™ B/E vaccine in Bangkok, Thailand
4. A Phase III trial to determine the efficacy of AIDSVAX™ B/E Vaccine in intravenous drug users in Bangkok, Thailand
5. Phase I/II trial of Pasteur Merieux Connaught (PMC) live recombinant ALVAC-HIV (VCP 1521) Priming with Vaxgen gp 120 B/E (AIDSVAX™ B/E) Boost in Thai HIV-Seronegative adults

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DATA MANAGEMENT UNIT

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 AIDSVAX™ B/E vaccine in injecting drug users in Bangkok, Thailand. In September 2002, its Chief and Deputy Chief received technological transfer from VaxGen on preparation of data for the Data and Safety Monitoring Board (DSMB) meeting to consider interim efficacy analysis of this trial.

In the meantime, five additional staff were recruited in preparation for the second - generation HIV vaccine efficacy trial. This will be the largest HIV vaccine efficacy trial in the world to test the prime-boost concept of HIV candidate vaccines. The trial, A Phase III Trial of Aventis Pasteur Live Recombinant ALVAC-HIV (vCP1521) Priming With VaxGen gp120 B/E (AIDSVAX™ B/E) Boosting in HIV-uninfected Thai Adults, is scheduled to launch in early 2003.

The Data Management Unit also renders service on data management for biomedical research through Mahidol University Applied and Technological Service Center.

AIDS Vaccine Trial Project

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Ms. Kessuda Maneegrajangseang	CRC
Ms. Ketsuda Tanchun	CRC
Ms. Khuandaw Chotchompoo	CRC
Ms. Jirasanun Tepboon	CRC
Mrs. Jeerapa Tharasukh	CRC
Mrs. Jiraporn Intarajinda	CRC
Ms. Jutarat Watanakitwichai	CRC
Mrs. Chanida Liangthorachon	CRC
Ms. Duangkamol Promlukkano	CRC
Ms. Tassaneeya Lumabeaboul	CRC
Ms. Tanaporn Thammatuksa	CRC
Mrs. Tamonwan Petchsuk	CRC
Ms. Napatsakorn Gonthong	CRC
Ms. Nawinda Kongmuang	CRC
Mr. Nawin Phudphad	CRC
Ms. Nisakorn Ratnaratorn	CRC
Ms. Benjawan Boonchokchai	CRC
Ms. Preyanuch Chonweerawong	CRC
Mrs. Puntip Wongduen	CRC
Ms. Pornrat Pansrimangkorn	CRC
Ms. Maliwan Hongsuwan	CRC

Project Staff (Continued)

Ms. Rojchana Whangwatanakul	CRC
Ms. Rawiwan Rachsomboon	CRC
Ms. Rapin Own-On	CRC
Ms. Roongthip Boondao	CRC
Ms. Rungnapa Chaiyapin	CRC
Ms. Wanwisa Pongpun	CRC
Mrs. Wipa Sumrej	CRC
Ms. Sivaporm Keowsangk	CRC
Ms. Sabaithip Sriwichai	CRC
Ms. Somchit Ruenthong	CRC
Ms. Sarawan Maythaarttaphong	CRC
Mrs. Sukanya Tomkum	CRC
Ms. Sunisa Phanphruk	CRC
Ms. Amonrat Aiyasiri	CRC
Ms. Aagkana Rukwongrit	CRC
Ms. Achariya Kanchanapradith	CRC
Ms. Anchalee Yamklin	CRC
Ms. Anchalee Iammaleerat	CRC
Ms. Umaporn Suksawad	CRC
Ms. Urairat Phantong	CRC
Ms. Suparnee Suradach	CRC
Ms. Chompunuch Boonchansri	CRC
Ms. Benjakan Sopasiravatana	CRC
Ms. Penpak Chantasorn	CRC
Ms. Sunee Yam-Wong	CRC
Ms. Peingruthai Sirrat	CRA
Mrs. Kanokporn Apichanapong	CRA
Ms. Jaruwan Laowarakul	CRA
Ms. Rapeeporn Sangsawang	CRA
Ms. Bussarin Thungmeephol	CRA
Mr. Pronsak Chaiyaporn	CRA
Ms. Montira Yuayai	CRA
Ms. Nalin Rungnapapai	CRA
Ms. Pawinee Jarujareet	CRA
Ms. Siriluck Jaiwan	CRA
Ms. Pikul Kulchatchai	CRA
Ms. Sukkasem Photo	CRA
Ms. Supinda Hanwisai	CRA
Ms. Areewan Teo-Rawb	CRA
Ms. Chonticha Rodragkwan	CRA
Mr. Suwit Numpa	CRA
Ms. Phuangthong Mangked	CRA

LIST OF ABSTRACTS

The Bangkok School of Tropical Medicine

The Bangkok School of Tropical Medicine was established in 1960 to teach Thai medical doctors, especially those working in rural areas, tropical medicine, parasitology and the preventive aspects of endemic diseases. The School now provides continuing education to doctors, researchers, medical personnel and professionals concerned with tropical medicine and public health through its five programmes, from post-graduate diploma to PhD levels. Lectures are in English. The courses are open to students from all around the world. Details of the School's programmes can be viewed on the Faculty's website at: *http://www.tm.mahidol.ac.th* or may be requested by e-mail from the School at e-mail address: *tmedu@diamond.mahidol.ac.th*

Regular Postgraduate Programmes

1. Graduate Diploma in Tropical Medicine and Hygiene

The course provides medical doctors with the concepts and principles of clinical management of tropical diseases, epidemiology, prevention and control, and health problems in tropical areas.

2. Master of Clinical Tropical Medicine and Master of Clinical Tropical Medicine in Tropical Pediatrics

The M.C.T.M. programme is an extension of the D.T.M.&H. Its purpose is to train medical doctors in tropical and endemic diseases in relation to their causes, epidemiology, pathogenic mechanisms, prevention and control; to be able to efficiently examine, diagnose and treat patients suffering from tropical and endemic diseases; to be able to provide consultation, disseminate and impart knowledge of tropical medicine; and, competently to conduct clinical research.

3. Master of Science in Tropical Medicine

This programme develops competency in research, and the capacity to deliver technical services related to tropical medicine. There are 14 major fields: 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.

4. Doctor of Philosophy in Tropical Medicine

This doctoral programme provides advanced knowledge and skills for competency in research, particularly in tropical medicine. There are 14 major fields, as for the Master of Science in Tropical Medicine, listed above.

5. Doctor of Philosophy in Clinical Tropical Medicine

This programme enables medical doctors to gain advanced knowledge and study new techniques, and apply them to areas of research in clinical tropical medicine. Students conduct an original extensive research project related to clinical tropical medicine.

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. Each university issues its own degree in accordance with its own degree regulations.

2. Master of Science in Clinical Epidemiology

The Faculty, with the Faculties of Public Health and Medicine, Ramathibodhi Hospital, offers this international programme. The objective is to provide academic and health service leadership, which will facilitate effective public health and medical care programmes at every level in various countries.

D.T.M. & H. 2002

1.	Dr. Ananta Kumar Barua	Bangladesh
2.	Dr. Andrea Rotheneder	Austria
3.	Dr. Ariane Doris Knauer	Austria
4.	Dr. Asis Kumar Das	Bangladesh
5.	Dr. Aung-Thu	Myanmar
6.	Dr. Bouachanh Sengphilom	Lao PDR
7.	Dr. Catherine Extermann	Switzerland
8.	Dr. Christopher John Newman	Switzerland
9.	Dr. Dang Van Phuc	Vietnam
10.	Dr. Djatnika Setiabudi	Indonesia
11.	Dr. Duong Van Thanh	Pakistan
12.	Dr. Hiromitsu Kusagaya	Japan
13.	Dr. Joshua Paul Hanson	Australia
14.	Dr. Karma Lhazeen	Bhutan
15.	Dr. Khornsavanh Luangxay	Lao PDR
16.	Dr. Lim Yi	Cambodia
17.	Dr. Naksit Kamolsin	Thailand
18.	Dr. Nathalie Mezger	Switzerland
19.	Dr. Nguyen Kieu Uyen	Vietnam
20.	Dr. Nguyen Van Thinh	Vietnam
21.	Dr. Phung Duc Thuan	Vietnam
22.	Dr. Robert Chen	Canada
23.	Dr. Satit Vichitbandha	Thailand
24.	Dr. Sengdeuane Phouthsavath	Lao PDR
25.	Dr. Subha Rajan	India
26.	Dr. Suradet Vichengalayarat	Thailand
27.	Dr. Truong Ngoc Phuoc	Vietnam
28.	Dr. Umar Zein	Indonesia
29.	Dr.Vongsavanh Banchongphanitt	Lao PDR
30.	Dr. Yok Sovann	Cambodia

M.C.T.M. 2002-2003

1.	Dr. Ariane Doris Knauer	Austria
2.	Dr. Asis Kumar Das	Bangladesh
3.	Dr. Karma Lhazeen	Bhutan
4.	Dr. Lim Yi	Cambodia
5.	Dr. Ole Wichmann	German
6.	Dr. Subha Rajan	India
7.	Dr.Vongsavanh Banchongphanitt	Lao PDR
8.	Dr. Aung-Thu	Myanmar
9.	Dr. Maung Myo Nyunt Naing	Myanmar
10.	Dr. Dang Van Phuc	Vietnam
11.	Dr. Nguyen Van Thinh	Vietnam
12.	Dr. Phung Duc Thuan	Vietnam
13.	Dr. Nguyen Kieu Uyen	Vietnam

M.C.T.M. (Trop.Ped.) 2002-2003

1.	Dr. Djatnika Setiabudi	Indonesia
2.	Dr. Khornsavanh Luangxay	Lao PDR

M.C.T.M. (Trop.Ped.) 2002-2003 *(Continued)*

3.	Dr. Christopher John Newman	Switzerland
4.	Dr. Truong Ngoc Phuoc	Vietnam

Ph.D. (Clin.Trop.Med.) 2002

1st year students

1.	Dr. Prakaykaw Tipmanee	Thailand

3rd year students

1.	Dr. Hla Yin Mint	Myanmar

5th year students

1.	Dr. Yoshinari Moriyama	Japan

M.Sc.(Trop.Med.) 2002

1st year students

1.	Miss Kaesinee Phuwao	Thailand
2.	Pol. Maj. Kitanapa Napakorn	Thailand
3.	Miss Chanthanee Nitigaroon	Thailand
4.	Miss Chantira Suttikornchai	Thailand
5.	Miss Jiraporn Kuljiraruk	Thailand
6.	Miss Jitbanjong Toomphong	Thailand
7.	Miss Thipawan Kanghae	Thailand
8.	Miss Nada Petabut	Thailand
9.	Miss Preeyaporn Monatrakul	Thailand
10.	Miss Pattamaporn Sirima	Thailand
11.	Miss Piyawan Sricharoen	Thailand
12.	Miss Muncharee Tattiyapong	Thailand
13.	Miss Ratana Tacharoenmuang	Thailand
14.	Miss Wilaiwan Rugsarash	Thailand
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16.	Miss Saranya Siribal	Thailand
17.	Miss Pedcharad Satheanmethakul	Thailand
18.	Mr. Jakkrawarn Chompoosri	Thailand
19.	Mr. Prasan Kankaew	Thailand
20.	Mr.Phiromsak Phattanapaigitkun	Thailand
21.	Ms. Wachirapon F. Piluek	USA
22.	Ms. Elizabeth Legge	Australia
23.	Mr. Seth Sy Koeut	USA
24.	Dr. Do Hoang Long	Vietnam

2nd year students

1.	Miss Kanlaya Boonpen	Thailand
2.	Miss Kanchana Usuwanthim	Thailand
3.	Miss Kevalin Vongthoung	Thailand
4.	Miss Jaruwadee Rattanadakul	Thailand
5.	Lt. Jittima Hirunrussamee	Thailand
6.	Mr. Chalermpon Kaewjai	Thailand
7.	Lt. Chanakarn Kalambaheti	Thailand
8.	Mrs. Chamaiporn Suwanasophon	Thailand

2nd year students (*Continued*)

9.	Miss Nattawan Rachapaew	Thailand
10.	Mr. Danai Sisuan	Thailand
11.	Mrs. Teerarut Chanket	Thailand
12.	Mr. Narin Hoisanks	Thailand
13.	Mr. Nitipon Ratanasetyuth	Thailand
14.	Mr. Nukool Limpairojn	Thailand
15.	Miss Natefa Uthaichotiwan	Thailand
16.	Miss Busakorn Promsarin	Thailand
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18.	Miss Pannumthip Pitaksajjakul	Thailand
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20.	Miss Potjamas Pansri	Thailand
21.	Miss Pimolrat Thongngarm	Thailand
22.	Miss Wijitporn Siriphapapun	Thailand
23.	Mr. Wichai Purisa	Thailand
24.	Mr. Weerapong Deumtan	Thailand
25.	Mr. Sompoj Chalermtaranukul	Thailand
26.	Mr. Santipong Sirikajorndachsakul	Thailand
27.	Miss Supawan Piyaratanavarasakul	Thailand
28.	Mr. Sangchai Yingsakmongkon	Thailand
29.	Mr. Amornthep Archawakulathep	Thailand
30.	Miss Oranuch Kongpechsatit	Thailand
31.	Mr. Ittisak Subrungruang	Thailand
32.	Miss Uraiwan Krainara	Thailand
33.	Dr. Phonephouminh Simeuang	Lao PDR
34.	Dr. Au Bich Thuy	Vietnam
35.	Miss Yoko Oshima	Japan

3rd year students

1.	Mr. Krasae Kanakupt	Thailand
2.	Miss Tanyalak Khuntamoon	Thailand
3.	Pol.Capt.Natsuda Jamornthanyawat	Thailand
4.	Miss Busaba Tuntithavorn	Thailand
5.	Mr. Prasert Rukmanee	Thailand
6.	Miss Penapa Yutayong	Thailand
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8.	Miss Matukorn Na Ubol	Thailand
9.	Miss Ladawan Wasinpiyamongkol	Thailand
10.	Mr. Sasipon Pumkumarn	Thailand
11.	Mr. Sith Premashthira	Thailand
12.	Miss Saichon Chimsumang	Thailand
13.	Dr. Manikip Outhayphone	Lao PDR
14.	Miss Charinthon Ngamamonpirat	Thailand

4th year students

1.	Miss Nahathai Chulakarat	Thailand
2.	Lt. Tossapon Chaiyasith	Thailand
3.	Miss Piyaporn Suebtrakul	Thailand
4.	Miss Risara Jaksuwan	Thailand
5.	Miss Souwanit Nakasiri	Thailand

5th year students

1.	Mr. Pornchai Kirdsiri	Thailand
2.	Miss Yupa Nakkinkun	Thailand

Ph.D. (Trop.Med.) 2002

1st year students

1.	Miss Sudarat Nguansangiam	Thailand
2.	Mr. Prasert Thavondunstid	Thailand
3.	Miss Patchara Sriwichai	Thailand
4.	Miss Pornsawan Amarapal	Thailand
5.	Miss Pachuen Potup	Thailand
6.	Miss Piyada Wongroongsarb	Thailand
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11.	Miss Chintana Phawong	Thailand
12.	Mr. Narong Nitatpattana	Thailand
13.	Miss Manirat Therawiwat	Thailand
14.	Miss Naowarat Tanomsing	Thailand
15.	Dr. Trinh Van Hung	Vietnam

2nd year students

1.	Dr. Kittipong Kongsomboon	Thailand
2.	Ms. Chomrach Sirigul	Thailand
3.	Mr. Tavorn Maton	Thailand
4.	Mr. Narisorn Na-ngam	Thailand
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17.	Miss Sunanta Chariyalertsak	Thailand
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20.	Dr. Kim Jung Ryong	Korea
21.	Dr. Sompong Srisaenpang	Thailand
22.	Miss Pannapa Susomboon	Thailand
23.	Miss Doungrat Riyong	Thailand
24.	Miss Siriporn Chanchay	Thailand
25.	Miss Kanjana Suriyaprom	Thailand

3rd year students

1.	Miss Nantawan Kaewpoonsri	Thailand
2.	Mr. Parin Suwannaprapha	Thailand

3rd year students (*Continued*)

3. Miss Petchara Tussana	Thailand
4. Miss Waraporn Aumarm	Thailand
5. Miss Supawadee Konchom	Thailand
6. Miss Suwanna Chaorattanakawee	Thailand
7. Miss Onguma Natalang	Thailand
8. Miss Orntipa Sethabutr	Thailand
9. Dr. Gias Uddin Ahsan	Thailand
10. Mr. Rongdej Tungtrakanpoung	Thailand
11. Mr. Somchai Jadsri	Thailand
12. Mr. Somphong Sithiprom	Thailand
13. Mrs. Tippayarat Yoonuan	Thailand
14. Mr. Apichai Srijan	Thailand
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16. Miss Thanida Tangwanicharoen	Thailand
17. Mr. Songpol Tornee	Thailand
18. Mrs. Pimsurang Taechaboonsermsak	Thailand
19. Mrs. Ratana Sithiprasasna	Thailand
20. Mrs. Soontaree Akawat	Thailand
21. Mr. Adisak Bhumiratana	Thailand
22. Mrs. Anamai Tadkatuk	Thailand

4th year students

1. Mr. Kamon Foihirun	Thailand
2. Miss Chutima Kamkhaek	Thailand
3. Miss Nantika Panutdaporn	Thailand
4. Miss Naowarut Dechkum	Thailand
5. Mrs. Prapa Nunthawarasilp	Thailand
6. Mr. Piyanan Taweethavonsawat	Thailand
7. Mr. Panas Thumkiratiwong	Thailand
8. Miss Pornphan Diraphat	Thailand
9. Miss Pattra Suntornthiticharoen	Thailand
10. Mr. Yuttana Sudjaroen	Thailand

4th year students (*Continued*)

11. Mrs. Ratree Leelawongtawon	Thailand
12. Miss Waraphon Phimpraphi	Thailand
13. Miss Walairut Tuntaprasart	Thailand
14. Miss Suwalee Tantawiwat	Thailand
15. Mrs. Oranan Prommano	Thailand
16. Mr. Hari Har Joshi	Nepal
17. Mr. Rajendra Kumar B.C.	Nepal
18. Miss Nitaya Poosanthanasarn	Thailand
19. Miss Panee Chaksangchaichot	Thailand
20. Miss Sirichit Wongkamchai	Thailand
21. Dr. Aree Kantachuvessiri	Thailand

5th year students

1. Miss Kriyaporn Songmuaeng	Thailand
2. Miss Kleebkaew Pitasawad	Thailand
3. Mrs. Prapin Tharnpoophasiam	Thailand
4. Miss Pungasem Paeporn	Thailand
5. Mrs. Yupadee Sirissinsuk	Thailand
6. Miss Wanida Pongstaporn	Thailand
7. Miss Sawanee Tengrungsun	Thailand
8. Miss Nitchakarn Noranate	Thailand
9. Miss Pittayaporn Moungnoi	Thailand
10. Miss Yuwadee Trongtokit	Thailand

6th year students

1. Mrs. Kanjana Hongtong	Thailand
2. Mr. Paron Dekumyoy	Thailand
3. Miss Siriwan Chancharoen	Thailand

7th year student

1. Mr. Ruangyuth Chaiworaporn	Thailand

THESIS TITLES

M.C.T.M. (Thematic Papers)

Department	Name	Title of Thesis	Advisor
Clinical Tropical Medicine	Dr. Ariane Doris Knauer	Clinical features, aetiology and short-term outcome of interstitial pneumonitis in HIV/AIDS patients at Bamrajnaradura Hospital	Assoc. Prof. Punnee Pitisuttithum
Clinical Tropical Medicine	Dr. Asis Kumar Das	Clinical features, aetiology and short-term outcome of interstitial pneumonitis in HIV/AIDS patients at Bamrajnaradura Hospital	Assoc. Prof. Wichai Supanaranond
Clinical Tropical Medicine	Dr. Karma Lhazeen	Efficacy and adverse effects of three antiretroviral drug combination stavudine, lamivudine and nevirapine in the treatment of adult AIDS patients at Chonburi Regional Hospital	Prof. Polrat Wilairatana
Clinical Tropical Medicine	Dr. Lim Yi	Prospective study of the treatment of cryptococcal meningitis in AIDS patients with short course amphotericin B followed by fluconazole at Bamrajnaradura Hospital, Nonthaburi, Thailand	Assoc. Prof. Punnee Pitisuttithum
Clinical Tropical Medicine	Dr. Ole Wichmann	Clinical manifestation of dengue haemorrhagic fever at Chonburi in 2001	Prof. Sasithon Pukrittayakamee
Clinical Tropical Medicine	Dr. Subha Rajan	Prospective study of the treatment of cryptococcal meningitis in AIDS patients with short course amphotericin B followed by fluconazole at Bamrajnaradura Hospital, Nonthaburi, Thailand	Assoc. Prof. Wichai Supanaranond
Clinical Tropical Medicine	Dr. Vongsavanh Banchongphanitt	Evaluation WHO clinical criteria for diagnosis of leptospirosis among Thai patients in Khon Kaen Province, Thailand	Dr. Wirach Maek-A-Nantawat
Clinical Tropical Medicine	Dr. Aung-Thu	Gastrointestinal manifestations of scrub typhus in septic patients	Assoc. Prof. Wichai Supanaranond
Clinical Tropical Medicine	Dr. Maung Myo Nyunt Naing	Renal manifestations of scrub typhus in septic patients	Asst. Prof. Weerapong Phumratanaprapin
Clinical Tropical Medicine	Dr. Dang Van Phuc	Efficacy and adverse effects of three antiretroviral drug combination stavudine, lamivudine and nevirapine in the treatment of adult AIDS patients at Chonburi Regional Hospital	Prof. Polrat Wilairatana
Clinical Tropical Medicine	Dr. Nguyen Van Thinh	Evaluation WHO clinical criteria for diagnosis of leptospirosis among thai patients in Khon Kaen Province, Thailand	Asst. Prof. Udomsak Silachamroon

M.C.T.M.

Department	Name	Title of Thesis	Advisor
Clinical Tropical Medicine	Dr. Phung Duc Thuan	Clinical manifestations of patients admitted with acute diarrhea at Samut Sakhon Provincial Hospital: retrospective study	Assoc.Prof. Yupaporn Wattanagoon
Clinical Tropical Medicine	Dr. Nguyen Kien Uyen	Clinical manifestations of patients admitted with acute diarrhea at Samut Sakhon Provincial Hospital: retrospective study	Asst. Prof. Sombat Treeprasertsuk

M.C.T.M. (*Continued*)

Department	Name	Title of Thesis	Advisor
Tropical Pediatrics	Dr. Djatnika Setiabudi	Antimicrobial susceptibility patterns and clinical features of *Streptococcus pneumoniae* infection in children	Assoc. Prof. Krisana Pengsaa
Tropical Pediatrics	Dr. Khornsavanh Luangxay	Assessment of pain in children with HIV/AIDS: a pilot study	Assoc. Prof. Chukiat Sirivichayakul
Tropical Pediatrics	Dr. Christopher John Newman	Assessment of pain in children with HIV/AIDS: a pilot study	Assoc. Prof.Pornthep Chanthavanich
Tropical Pediatrics	Dr. Truong Ngoc Phuoc	Antimicrobial susceptibility patterns and clinical features of *Streptococcus pneumoniae* infection in children	Dr. Kriengsak Limkittikul

M. Sc. (Trop. Med.) 2nd year students

Department	Name	Title of Thesis	Advisor
Microbiology and Immunology	Miss Kanchana Usuwanthim	Mimotope searching of bound phage to monoclonal antibodies against Shigella spp. and shiga toxin using T7 phage display technique	Assist. Prof. Pongrama Ramasoota
Microbiology and Immunology	Mr. Preeda Wutthinuntiwong	Prevalence of cytomegalovirus in periodontitis patients and healthy people in Thailand	Assoc. Prof. Surang Tantivanich
Microbiology and Immunology	Miss Potjamas Pansri	Prevalenct Epstein-Barr virus infection in periodontitis patients and healthy oral cavity persons in Thailand	Assoc. Prof. Surang Tantivanich
Tropical Hygiene	Mr. Weerapong Deumtan	Serosurvey of leptospirosis among domestic animals in Bangkok and the Northeast of Thailand	Assoc. Prof. Pratap Singhasivanon
Microbiology and Immunology	Mr. Sompoj Chalermtaranukul	Prevalence of human *Herpesvirus* type 6 in periodontitis lesions in Thailand	Assoc. Prof. Surang Tantivanich
Social and Environmental Medicine	Miss Yoko Oshima	Molecular epidemiology of *Aeromonas* spp. by using ERIC-PCR	Assist. Prof. Pongrama Ramasoota
Social and Environmental Medicine	Dr. Au Bich Thuy	Cholinesterase screening test among organophosphate exposure of rice farmers in Southern Vietnam	Assist. Prof. Voranuch Wangsuphachart

M. Sc. (Trop. Med.) 3rd year students

Department	Name	Title of Thesis	Advisor
Helminthology	Mr. Krasae Kanakupt	Evaluation of excretory-secretary and partially purified antigens of adult *Toxocara canis* against human toxocariasis by ELISA and immunoblot	Assoc. Prof. Malinee Thairungroj
Tropical Nutrition & Food Science	Miss Tanyalak Khuntamoon	Seasonal variation of fresh, sterilized and pasteurized cow milk	Assoc. Prof. Supranee Changbumrung
Tropical Nutrition & Food Science	Miss Busaba Tantithavorn	Homocysteine, folic acid and cobalamin in subjects with coronary heart disease and healthy controls	Assoc. Prof. Supranee Changbumrung

M. Sc. (Trop. Med.) 3rd year students (*Continued*)

Department	Name	Title of Thesis	Advisor
Helminthology	Miss Pennapa Yutayong	*Toxocara canis* larval antigens for serodiagnosis of human toxocarosis	Assoc. Prof. Wichit Rojekittikhun
Microbiology and Immunology	Miss Matukorn Na Ubol	Virulenced genes of *Vibrio cholerae* Thailand isolates	Prof. Wanpen Chaicumpa
Medical Entomology	Miss Ladawan Wasinpiyamongkol	Morphological variations for susceptibility and transovarial transmission of dengue virus in *Aedes aegypti*	Assoc. Prof. Chamnarn Apiwathnasorn
Tropical Nutrition & Food Science	Mr. Sasipon Pumkumarn	Antioxidant enzymes and trace elements in subjects with coronary heart disease and healthy controls	Assoc. Prof. Supranee Changbumrung
Microbiology and Immunology	Miss Saichon Chimsumang	Indirect immunoperoxidase test for dual serodiagnosis of scrub typhus and leptospirosis	Assist. Prof. Varee Wongchotikul
Tropical Hygiene	Dr. Manikip Outhayphone	Belief and behavior of people in the use of insecticide IBN to control malaria transmission in Khammuane Province in Lao PDR	Assoc. Prof. Pratap Singhasivanon
Helminthology	Ms. Charinthon Ngamamonpirat	Sequence variation in *Gnathostoma spinigerum* mitochondrial DNA by single-strand conformation polymorphism analysis	Assoc. Prof. Jitra Waikagul

M. Sc. (Trop. Med.) 4th year students

Department	Name	Title of Thesis	Advisor
Tropical Hygiene	Miss Nahathai Chulakavat	Sputum conversion among newly adult positive-smear pulmonary tuberculosis patients	Assoc. Prof. Pratap Singhasivanon
Helminthology	Lt. Tossapon Chaiyasith	Gnathostomiasis in Nakhon Nayok Province: prevalence and intensity of infection in fish caught for local consumption and the seasonal variation of infection in swamp eels	Assoc. Prof. Wichit Rojekittikhun
Microbiology and Immunology	Miss Piyaporn Suebtrakul	Seroprevalence of antibodies to *Orientia tsutsugamushi* in primary school children at Saiyoke District, Kanchanaburi	Assist. Prof. Varee Wongchotikul
Tropical Pathology	Miss Souwanit Nakasiri	Light and electron microscopic correlation of knob proteins and staging *in vitro*: *Plasmodium falciparum*	Assoc. Prof. Emsri Pongponrat

M. Sc. (Trop. Med.) 5th year students

Department	Name	Title of Thesis	Advisor
Social and Environmental Medicine	Mr. Pornchai Kirdsiri	HIV/AIDS counseling service at hospitals in Kanchanaburi Province	Assist. Prof. Jaranit Kaewkungwal
Microbiology and Immunology	Miss Yupa Nakkinkun	Platelet dysfunction in immune thrombocytopenic	Prof. Wanpen Chaicumpa

Ph.D. (Trop. Med.) 2nd year students

Department	Name	Title of Thesis	Advisor
Tropical Hygiene	Dr. Sompong Srisaenpang	Burden & trend of infectious tuberculosis patients, their treatment outcomes and the associated factors for the treatment success at Khon Kaen medical school during 1997-2001	Assoc. Prof. Pratap Singhasivanon
Microbiology and Immunology	Miss Piyatida Tangteerawatana	Cytokine gene polymorphisms in severe malaria	Prof. Srisin Khusmith

Ph.D. (Trop. Med.) 3rd year students

Department	Name	Title of Thesis	Advisor
Microbiology and Immunology	Miss Petchara Tussana	Serogrouping of *Leptospira* spp. by DNA technology	Dr. Thareerat Kalambaheti
Tropical Hygiene	Miss Supawadee Konchom	Development of early detection system of malaria epidemics in Thailand	Assoc. Prof. Pratap Singhasivanon
Microbiology and Immunology	Mr. Rongdej Tungtrakanpoung	Leptospirosis vaccine designed using T7 phage display technique	Assist. Prof. Pongrama Ramasoota
Tropical Hygiene	Dr. Gias Uddin Ahsan	Gender and tuberculosis control epidemiological pattern of gender differences in tuberculosis case detection, treatment seeking behavior and treatment compliance in rural Bangladesh	Assoc. Prof. Pratap Singhasivanon
Helminthology	Mrs. Tippayarat Yoonuan	*Paragonimus mexicanus* and its difference from some Asian species	Assoc. Prof. Jitra Waikagul
Tropical Nutrition & Food Science	Mr. Tanett Pakeetoot	Identification of genetic alterations in breast cancer by arbitrarily primed polymerase chain reaction and gene cloning	Assoc. Prof. Songsak Petmitr
Social and Environmental Medicine	Mr. Songpol Tornee	Tuberculosis infection among household contacts under 15 years old in Bangkok, Thailand	Assist. Prof. Jaranit Kaewkungwal
Tropical Hygiene	Mrs. Ratana Sithiprasasna	Application of a remote-sensing based geographic information system to predict malaria transmission risks in villages in western Thailand	Assoc. Prof. Pratap Singhasivanon
Microbiology and Immunology	Miss Sirichit Wongkamchai	Development of Iimmunodiagnostic assay for brugian filariasis	Prof. Wanpen Chaicumpa
Microbiology and Immunology	Miss Chutima Kamkhaek	Analysis of sequence polymorphism of T-cell epitope regions, Th 2R and Th 3, on *Plasmodium falciparum* circumsporozoite proteins in Thai isolates	Prof. Srisin Khusmith

Ph.D. (Trop. Med.) 4th year students

Department	Name	Title of Thesis	Advisor
Microbiology and Immunology	Miss Nantika Panutdaporn	Genotypic and phenotypic analysis of clinical and environmental Shiga toxin producing *Escherichia coli* (STEC) to identify pathogenic clones and their pathogenic mechanism	Prof. Wanpen Chaicumpa

Ph.D. (Trop. Med.) 4th year students (*Continued*)

Department	Name	Title of Thesis	Advisor
Protozoology	Mrs. Prapa Nunthawarasilp	Purification and characterization of DNA polymerase b from *Plasmodium falciparum*	Assoc. Prof. Porntip Petmitr
Microbiology and Immunology	Mr. Piyanan Taweethavonsawat	Development of specific serological test(s) for diagnosis of strongyloidiasis and genetic variation of *Strongyloides stercoralis* Thailand isolates	Prof. Wanpen Chaicumpa
Tropical Nutrition & Food Science	Mr. Panas Thumkiratiwong	The synergistic effects of riboflavin deficiency to trichinellosis in Wistar rat model	Assoc. Prof. Rungsunn Tungtrongchitr
Microbiology and Immunology	Miss Pornphan Diraphat	Production of recombinant cockroach allergens	Prof. Wanpen Chaicumpa
Protozoology	Miss Pattra Suntornthiticharoen	Purification and characterization of DNA helicase from *Plasmodium falciparum*	Assoc. Prof. Porntip Petmitr
Tropical Nutrition & Food Science	Mr. Yuttana Sudjaroen	The isolation and characterization of phenolic antioxidants (potential cancer chemopreventive agents) in by-products of tropical fruits from Thailand	Assoc. Prof. Supranee Changbumrung
Microbiology and Immunology	Mrs. Ratree Leelawongtawon	Role of liposome and bacterial CpG DNA in immune response to oral cholera vaccine	Prof. Wanpen Chaicumpa
Clinical Tropical Medicine	Miss Waraphon Phimpraphi	Host cenetic susceptibility to clinical malaria	Prof. Sornchai Looareesuwan
Medical Entomology	Miss Walairut Tuntaprasart	Study on vritical indices of *Aedes aegypti* correlated to transmission of dengue viruses	Assoc. Prof. Somjai Leemingsawat
Tropical Pathology	Mrs. Oranan Prommano	A quantitative ultrastructural study of the pathology of falciparum malaria in human heart, lung, liver and spleen	Assoc. Prof. Emsri Pongponrat
Microbiology and Immunology	Mr. Hari Har Joshi	Monoclonal antibody based ELISA for detection of *P. falciparum* and *P. vivax* antigens in malaria endemic populations in Southern Nepal	Prof. Srisin Khusmith
Tropical Hygiene	Mr. Rajendra Kumar	Epidemiological pattern in relation to gender difference in leprosy case detection, and case holding with treatment compliance in the top hyper-endemic district of Nepal	Assoc. Prof. Pratap Singhasivanon
Tropical Nutrition and Food Science	Miss Panee Chaksangchaichot	Identification of genetic alterations in colon cancer by arbitrarily primed polymerase chain reaction and gene cloning	Assoc. Prof. Songsak Petmitr

Ph.D. (Trop. Med.) 5th year students

Department	Name	Title of Thesis	Advisor
Social and Environmental Medicine	Mrs. Kleebkaew Pitasawad	Environmental health model of pesticide utilization for sustainable agriculture in Donka Subdistrict, Bang Pae District, Ratchaburi Province	Assist. Prof. Piyarat Butraporn
Social and Environmental Medicine	Mrs. Prapin Tharnpoophasiam	Simultaneous determination of T, T-muconic acid and S-phenyl mercapturic acid and its application in monitoring of occupational benzene exposure	Prof. Dwip Kitayaporn

Ph.D. (Trop. Med.) 5th year students *(Continued)*

Department	Name	Title of Thesis	Advisor
Medical Entomology	Miss Pungasem Paeporn	Temephos resistance in *Aedes aegypti* and its significance to the mechanism and dengue infection	Assist. Prof. Narumol Komalamisra
Social and Environmental Medicine	Mrs. Yupadee Sirisinsuk	Access and patterns of health services utilization among insured persons under the Social Security Act, 1990	Assoc. Prof. Wijitr Fungladda
Tropical Nutrition and Food Science	Miss Wanida Pongstaporn	Identification of genetic alterations in ovarian cancer by arbitrarily primed polymerase chain reaction and gene cloning	Assoc. Prof. Songsak Petmitr
Tropical Hygiene	Miss Sawanee Tengrungsun	Survival analysis of Thai adult AIDS patients in the tertiary care hospital, Thailand	Assoc. Prof. Pratap Singhasivanon
Medical Entomology	Miss Yuwadee Trongtokit	Promising insecticidal activity of Thai phytochemical plants for control of mosquito vectors of diseases	Assist. Prof. Narumol Komalamisra

Ph.D. (Trop. Med.) 6th year students

Department	Name	Title of Thesis	Advisor
Tropical Nutrition and Food Science	Mrs. Kanjana Hongtong	Platelet fatty acids and serum lipoprotein A in subjects with coronary heart disease and healthy controls	Assoc. Prof. Supranee Changbumrung
Helminthology	Mr. Paron Dekumyoy	Evaluation of metacestode antigens in serodiagnosis of neurocysticercosis	Assoc. Prof. Jitra Waikagul

Ph.D. (Trop. Med.) 7th year students

Department	Name	Title of Thesis	Advisor
Social and Environmental Medicine	Mr. Ruangyuth Chaiworaporn	Studies on *Schistosoma spindale* Montgomery, 1906 : the effects of antiparasitic drugs on *Schistosoma spindale* in mice and the resistance to reinfection after treatment	Assoc. Prof. Yaowapa Maneerat

Ph.D. (Clin. Trop. Med.)

Department	Name	Title of Thesis	Advisor
Clinical Tropical Medicine	Dr. Yoshinari Moriyama	The clinical relevances of cytokines on severe malaria patients and effects of prostagladin derivatives	Prof. Polrat Walairatana
Clinical Tropical Medicine	Dr. Hla Yin Mint	A systematic overview of antimalarial drug trials	Prof. Sornchai Looareesuwan

The Hospital for Tropical Diseases

Office Telephone: 0-2248-3183, 0-2246-9000-12 ext. 1624, 1625

Prof. Polrat Wilairatana
Director

Assist. Prof. Weerapong Phumratanaprapin
Deputy-director

Assoc. Prof. Srivicha Krudsood
Deputy-director

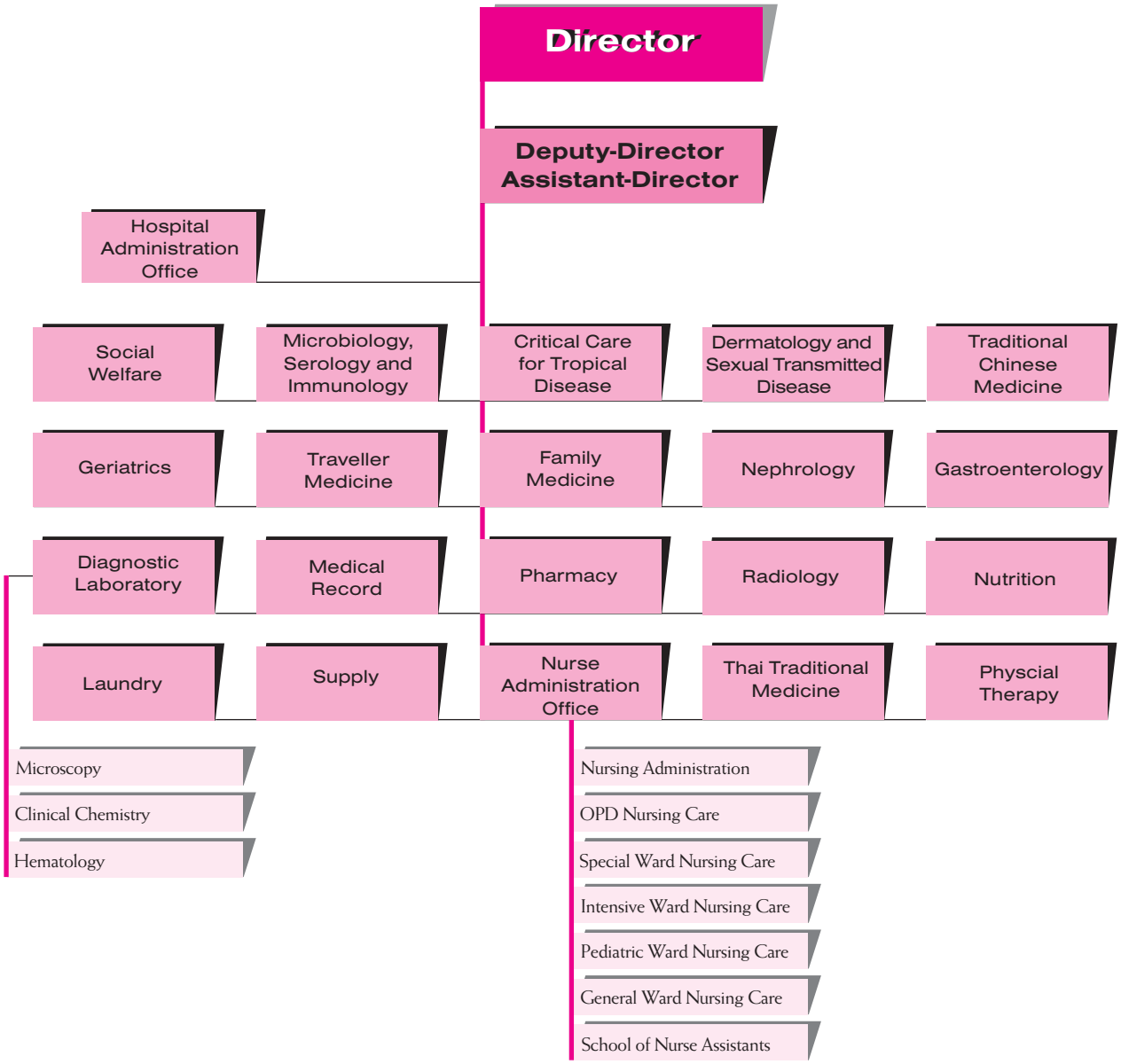
Dr. Wirach Maek-A-Nantawat
Assistant-director

Assist. Prof. Sombat Treeprasertsuk
Deputy-director

Dr. Teerachai Kusolsuk
Assistant-director

Assist. Prof. Udomsak Silachamroon
Deputy-director

Organization and Administration of The Hospital for Tropical Disease



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 ward, 2 special care wards, a geriatric ward, an intensive care unit, 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.
- 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: 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, 13.00-16.00 hr.
- Thai Traditional massage: everyday, 8.00-20.00 hr.
- Chinese Traditional acupuncture: Monday, Wednesday, 9.00-12.00 hr.

Nursing Unit

Mrs. Ladawun Supeeranuntha
Chief of Nurshing Unit

Mrs. Wanna Plooksawasadi
Deputy Chief for Administration/ Supervisor

Mrs. Kingkan A. Indravijit
Head of Ward 4

Mrs. Kingkaew Nakharutai
Head of Ward 5

Mrs. Suwatana Siripiphat
Head of Ward 11

Mrs. Pinkaew Nipattasopone
Head of Ward OPD

Mrs. Yupin Rattanapong
Deputy Chief for Education/Supervisor

Mrs. Vipa Prariyanupharb
Head of Ward 9

Mrs. Monthira Ditta-in
Head of Ward 10

Miss Suparp Vannaphan
Head of Ward ICU

Mrs. Rachanida Glanarongran
Director School of Nurse Assistants

Miss Kobsiri Chahermrut
Deputy Chief for Service/Supervisor

Miss Arun Chantra
Head of Ward 2

Miss Sunee Chittamas
Head of Ward 3

Miss Aurathai Thanavibul
Head of Ward 7

Mrs. Siripan Srivilairit
Head of Ward 8

In the fiscal year 2002 (October 2001-September 2002), the number of patients treated in the Hospital for Tropical Disease are classified according to disease as follows:

Diseases	No.of out-patients	No. of in-patients
1. Falciparum malaria	369	350
2. Vivax malaria	402	266
3. Mixed falciparum and vivax malaria	1	1
4. Malariae malaria	6	4
5. Ovale malaria	1	1
6. Unidentifed infections	49	22
7. Scrub typhus	21	7
8. Typhoid	1	1
9. Diarrhea	149	46
10. Food poisoning	29	2
11. Hepatitis	578	53
12. Dengue hemorrhagic fever	229	213
13. Leptosprirosis	2	2
14. Taeniasis	45	-
15. Hookworm	21	-
16. Ascariasis	2	-
17. Liver flukes	53	-
18. Pinworm	2	-
19. Strongyloidiasis	20	1
20. Gnathostomiasis	1,257	1
21. Trichuriasis	1	-
22. Filariasis	2	-
23. Dematitis	2,132	21
24. Tuberculosis (pulmonary)	269	11
25. HIV infections	118	6
26. Hypertention	1,874	37
27. Diabetes mellitus	1,433	52
28. Hyperlipidemia	1,008	1
29. Diseases of oral cavity, salivary glands and jaws	200	198
30. Others	28,597 (73.6%)	741 (36.4%)
Total	**38,871**	**2,037**

Special Laboratory Services

Disease / Infection	Serological Test used	Specimen required	Time required (days)	Cost per test (Baht)	Place where specimen should be sent
Strongyloidosis	Immunoblot , ELISA	Serum 1-2 ml.	2	200	Dept. Helminthology via OPD
Toxocariasis	Immunoblot , ELISA	Serum 1-2 ml.	2	200	Dept. Helminthology via OPD
Angiostrongyliasis	Immunoblot	Serum 1-2 ml.	2	200	Dept. Helminthology via OPD
Cysticercosis	Immunoblot	Serum 1-2 ml.	2	200	Dept. Helminthology via OPD
Filariasis	ICT	Serum1-2 ml.	2	200	Dept. Helminthology via OPD
Gnathostomiasis	Immunoblot	Serum 1-2 ml.	2	200	Dept. Helminthology via OPD
Paragonimiasis	Immunoblot	Serum 1-2 ml.	2	200	Dept. Helminthology via OPD
Filaria	Knott's concentration Technique	Thick blood film, Mix blood 1-2 ml + 2% formalin 9 ml.	1	120	Dept. Medical Entomology via OPD
Entomology	Microscope (insects + arthropods)	in 70% alcohol	1	80	Dept. Medical Entomology via OPD
Toxoplasma antibody	Dye test	Serum 0.5 ml.	2	300	Dept. Protozoology *
Cryptosporidiosis	Special stain	Feces sputum	2	100	Dept. Protozoology *
Serum Vitamin B12	Dilution technique	Serum 2 ml.	7	450	Dept. Tropical Radioisotopes *
Serum folate	Microbiological assay (57 C°)	Serum 2 ml.	7	250	Dept. Tropical Radioisotopes *
Red cell folate	Lactobacillus casei	Clot blood 2-3 cc.	7	250	Dept. Tropical Radioisotopes *
Schistosoma Antibody	COPT	Serum 1-2 cc. for Schistosoma ova	3	400	Dept. Social and Environmental Medicine via OPD
Red blood cell Vitamin B1	Enzymatic method	Heparinized blood 1-2 ml	7	400	Dept. Tropical Nutrition and food Science *
Red blood cell Vitamin B2	Enzymatic method	Heparinized blood 1-2 ml	7	400	Dept. Tropical Nutrition and food Science *
Red blood cell Vitamin B6	Enzymatic method	Heparinized blood 1-2 ml	7	400	Dept. Tropical Nutrition and food Science *
Pap smear-cervical, vaginal smear	Cytology	vaginal smear, cervical smear	1	150/300	Dept. Pathology via OPD
Fluids	Cytology	Pleural effusion, Ascites, Urine	1	350/700	Dept. Pathology via OPD
Small pieces of Biopsy	Histopathology	Small pieces of Biopsy	3	300/600	Dept. Pathology via OPD
Organ	Histopathology	Organ	3	400/800	Dept. Pathology via OPD
Small pieces of Biopsy	Frozen section	Small pieces of Biopsy	3	300/600	Dept. Pathology via OPD
Organ	Frozen section	Organ	3	900/1,800	Dept. Pathology via OPD
Special stain		-	1	100	Dept. Pathology via OPD
Detection of heavy metals in blood	Atomic absorption	Heparinized whole blood 1 ml.	7	160	Central Equipment Unit via OPD
Amphetamine	Commercial test	Urine	1	100	Central Equipment Unit via OPD
Morphine	Strip (lateral flow chromatographic immunoassay)	Urine	1	100	Central Equipment Unit via OPD

Disease / Infection	Serological Test used	Specimen required	Time required (days)	Cost per test (Baht)	Place where specimen should be sent
Blood	Aerobic bacteria	Blood 5 ml. in T.S.B.	3	200	Div. of Microbiology, Serology and Immunology
Urine	1) Culture 2) Gram stain	Urine 5-10 ml	3 1	120	Div. of Microbiology, Serology and Immunology
Stool	1) Culture 2) Gram stain	Rectal swab	3 1	160	Div. of Microbiology, Serology and Immunology
Sputum	1) Culture 2) Gram stain	Sputum	3 1	120	Div. of Microbiology, Serology and Immunology
C.S.F.	1) Culture 2) Gram stain	C.S.F. 5-10 ml	3 1	120	Div. of Microbiology, Serology and Immunology
Wound, Fluid	1) Culture 2) Gram stain	Wound, Fluid 5-10 ml	3 1	120	Div. of Microbiology, Serology and Immunology
Fungus	KOH	All specimens	1	50	Div. of Microbiology, Serology and Immunology
V.D.R.L.	Agglutination	Clot blood 3 ml	1-2	60	Div. of Microbiology, Serology and Immunology
Widal test	Agglutination	Clot blood 5 ml	2	100	Div. of Microbiology, Serology and Immunology
Weil Felix test	Agglutination	Clot blood 5 ml	2	120	Div. of Microbiology, Serology and Immunology
Scrub typhus	Indirect immunofluorescent	Clot blood 5 ml	2	150	Div. of Microbiology, Serology and Immunology
E. histolytica	Immunodiffusion	Clot blood 3 ml	2	150	Div. of Microbiology, Serology and Immunology
Alpha-fetoprotein	Immunodiffusion	Clot blood 3 ml	2	200	Div. of Microbiology, Serology and Immunology
HBs Ag	Enzyme immunoassay	Clot blood 5 ml	2	120	Div. of Microbiology, Serology and Immunology
HBs Ab	Enzyme immunoassay	Clot blood 5 ml	2	120	Div. of Microbiology, Serology and Immunology
HBc Ab	Enzyme immunoassay	Clot blood 5 ml	2	120	Div. of Microbiology, Serology and Immunology
Anti HIV	Agglutination Enzyme immunoassay	Clot blood 5 ml	1	250	Div. of Microbiology, Serology and Immunology
Anti HIV quick test	Enzyme immunoassay	Clot blood 3 ml	2 hr.	250	Div. of Microbiology, Serology and Immunology
Leptospirosis	Microagglutination	Clot blood 5 ml.	7	200	Div. of Microbiology, Serology and Immunology
Anti DNA	Agglutination	Clot blood 5 ml.	2	80	Div. of Microbiology, Serology and Immunology
Anti HAV IgM	Enzyme immunoassay	Clot blood 5 ml.	2	250	Div. of Microbiology, Serology and Immunology
Anti HCV	Enzyme immunoassay	Clot blood 5 ml.	2	250	Div. of Microbiology, Serology and Immunology

Disease / Infection	Serological Test used	Specimen required	Time required (days)	Cost per test (Baht)	Place where specimen should be sent
Cryptococcal/Ag	Agglutination	Clot blood 5 ml.	2	150	Div. of Microbiology, Serology and Immunology
Dengue IgG&IgM	HAI	Clotted blood 5 ml.	2	250	Div. of Microbiology, Serology and Immunology
Mycoplasma/Ab	Agglutination	Clotted blood 5 ml.	2	200	Div. of Microbiology, Serology and Immunology
B.pseudomallei/Ab	Agglutination	Clotted blood 5 ml.	2	80	Div. of Microbiology, Serology and Immunology
Rheumatoid factor	Agglutination	Clotted blood 5 ml.	2	100	Div. of Microbiology, Serology and Immunology

* *Directly sent specimens to the department*

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

Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

Prof. Sornchai Looareesuwan
Director

Assoc. Prof. Suvanee Supavej
Deputy Director

TROPMED/Thailand has 3 major functions namely 1) Teaching and training 2) research and 3) services. Activities of the 3 functions are reported according to the 5 KEY 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 offered by TROPMED/Thailand with a total of 223 students from 20 countries. There were 71 graduates in the academic year 2001/2002.

1.2 **Undergraduate courses**

TROPMED/Thailand also offers 2 undergraduate courses :

1) Elective programme in tropical medicine with 23 medical students from 9 countries;
2) Certificate in Nurse Assistant with 170 students.

In the FY 2001/2002, TROPMED/Thailand had 416 students from 24 countries; among these, 304 were new enrolled students in 7 courses offered by TROPMED/Thailand. Ninety-six percent of these students were fee paying attendants and 264 (63.46%) graduated in the year under review.

Table 1: 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)	34	15 (Austria, Bangladesh, Cambodia, Ethiopia, Germany, Japan, Lao PDR, Myanmar, Netherlands, Nigeria, Pakistan, Sweden, Thailand, Vietnam, USA)	28 (82%)	34 (100%)
MCTM (1 year course)	18	12 (Austria, Bangladesh, Cambodia, Ethiopia, Germany, Japan, Lao PDR, Myanmar, Netherlands, Pakistan, Vietnam, Thailand)	15 (83%)	18 (100%)
MSc (TM)				
1st year	36	4 (Japan, Lao PDR, Thailand, Vietnam)	69 (94.5%)	18 (24.6%)
2nd year	27	6 (Lao PDR, Malaysia, Tanzania, USA, Vietnam, Thailand)		
3rd year	8	1 (Thailand)		
5th year	2	1 (Thailand)		
PhD (TM)				
1st year	23	4 (Austria, Korea, Switzerland, Thailand)	96 (100%)	1 (11.4%)
2nd year	24	2 (Bangladesh, Thailand)		
3rd year	23	2 (Nepal, Thailand)		
4th year	14	1 (Thailand)		
5th year	10	1 (Thailand)		
6th year	1	1 (Thailand)		
9th year	1	1 (Thailand)		
PhD (CTM)				
2nd year	1	1 (Myanmar)	1 (100%)	0
4th year	1	1 (Japan)	1 (100%)	0
Subtotal	**223**		**210 (94.1%)**	**71 (31.8%)**

Course	Number	No. of nationalities	No. of fee paying students	No. of graduates
Undergraduate				
Elective programme in Tropical Medicine	23	9 (Austria, Australia, Canada, Germany, Ireland, Japan, Switzerland, UK, USA)	23 (100%)	23 (100%)
Certificate in Nurse Assistants	170	1 (Thailand)	170 (100%)	170 (100%)
Sub total	**193**		**193 (100%)**	**193 (100%)**
Grand Total	**416**	**24**	**403 (96.87%)**	**264 (63.46%)**

1.3 **Training courses/Workshop/Meetings.** Three training courses at the regional level, one at the international level, 1 international workshop and 1 international meeting were convened during FY 2001/2002 with a total number of 961 participants from 42 countries.

KRA2. INCREASED ACCESS TO MARKET

2.1 **Active Marketing.** Seven TV series and 6 news spots were broadcasted, 10 news were published in local newspapers, 1 radio announcement and 1other media.

KRA3. INCREASED LINKAGES

3.1 **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	1	1 wk
2. SEAMEO TROPMED Network-Rockefeller Foundation	Health Equity	Rockefeller Foundation	2	4 days
3. Scientific and Ethical Review Group	Ethical Review	WHO	3	3 days

3.2 **Visitors.** Two hundred and ninety-eight visitors from 24 countries visited TROPMED/Thailand during FY 2002/2003.

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 / Decreased
1. Government budget	156.250	-30.29
2. Revenue from services and other activities	89.00	+14.32
3. Research funds from other organizations	111.5	+56.99

KRA5. ENHANCED QUALITY OF SEAMEO MANAGEMENT

TROPMED/Thailand has a total of 770 staff comprising 73 academic staff, 135 academic assistants and research staff, 106 administrative personnel, 71 university employees and 385 employees. The qualification and academic posts holding by these 84 academic staff are shown in Table 4.

Table 4: Qualification of 84 academic staff.

Qualification	No	%
PhD	63	75.0
Master	19	23.0
Bachelor	2	2.0
Total	**84**	**100.0**

The academic posts of 84 academic staff compared to those of Mahidol University are shown in Table 5.

Table 5: Academic posts of 84 staff of TROPMED/Thailand.

	Academic Posts			
	holding by FTM staff		holding by Mahidol University staff	
	No	(%)	No	(%)
Professors	5	(5.95%)	129	(4.68%)
Associate Professors	32	(38.09%)	767	(27.85%)
Assistant Professors	28	(33.03%)	833	(30.24%)
Lecturers	19	(22.06%)	1,025	(37.21%)
Total	**84**	**(100.00%)**	**2,754**	**(100.00%)**

5.1 Number of staff promoted or obtaining higher qualification

Table 6: Number of staff promoted.

Academic rank	:	Professor	=	3
		Associate Professors	=	1
		Assistant Professors	=	-
Career rank	:	Higher rank	=	43
Higher qualification	:	Higher degree	=	19
		Total	**=**	**66**

5.2 **Number of research projects and publication.** TROPMED/Thailand staff undertake 128 research projects with a total research grants of 111.5 million Baht and published research papers.

	New project	On-going	Accomplished
No of research projects	19 (15%)	83 (65%)	26 (20%)
No of published papers	= 100		

5.3 Number of staff taking study leave, attending training courses and attending meetings/seminars/workshops.

Fourteen staff (1.8%) took study leaves for higher education. Sixty (7.7%) attended training courses in Thailand and abroad. Seven hundred and thirty staff (94.8%) 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	13 (1.7%)	1 (0.1%)	14 (1.8%)
Attending training courses	51 (6.6%)	9 (1.1%)	60 (7.7%)
Attending meetings/ seminars/workshops			
No of staff	**634 (82.3%)**	**96 (12.4 %)**	**730 (94.8%)**

5.4 Special talks/lectures

To develop and/or improve knowledge of staff, 4 lunch talks/lecturers on various topics for 110 attendants, 45 CME lectures (Continuing Medical Education) including information technology were organized for 779 attendants.

5.5 Patients treated for tropical diseases

The Hospital for Tropical Diseases offers medical care services to patients suffering from tropical and other diseases. The Hospital has 250 beds with 30 medical doctors, 94 nurses and 80 nurse assistants. The total number of outpatients treated were 38,871 and the number of patients admitted to the Hospital were 2,037. 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 TROPMED Thailand in May 2000.

5.7 Number of staff awarded

1) **Distinguished staff**. Two staff; one from Office of the Dean and another one from the Hospital for Tropical Diseases were awarded as 2001 Distinguished Staff of the Faculty of Tropical Medicine.

2) **Local Awards :**

Recipients	Awards
1. Prof. Sornchai Looareesuwan	1. Outstanding for research project. (Senior Level) The Siriraj Medical Alumni Association

3) **National Awards :**

Recipients	Awards
1. Prof. Wanpen Chaicumpa	1. National Outstanding Lecturer for the year 2002 Lecturer Council of Thailand

The Asian Centre of International Parasite Control (ACIPAC)

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Prof. Somei Kojima
Chief Advisor

Assoc. Prof. Jitra Waikagul
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Miss Karinee Khaothiar
Asistant Secretary

ACTIVITES BETWEEN OCTOBER 1, 2001 TO SEPTEMBER 30, 2002

During the Thai Fiscal Year 2001, the main activities of the Asian Centre of International Parasite Control (ACIPAC) were concerned with human resource development to establish networking among ACIPAC and partner countries in the Greater Mekong Sub-region – Cambodia, Lao PDR, Myanmar, Thailand, and Vietnam. ACIPAC also intensively worked on propelling school-based parasite control in this region with a catchphrase of "Save Wormy Schoolchildren".

1) International Training Course 2002

ACIPAC organized the international training course on "School-based Malaria and Soil-transmitted Helminthiasis Control for Programme Managers" held from September 2 to November 22 at the Faculty of Tropical Medicine. There were 27 participants; seven trainees from Lao PDR, six trainees from each of Cambodia, Thailand and Vietnam and one each from Ghana and Kenya. The trainees also attended Joint International Tropical Medicine Meeting 2002.

2) Model Activities in Thailand

Two model sites have been established in Rujirapat School in Ratchabrui province and Wat Thangphoon School in Nakhon Si Thammarat province in cooperation with Office of National Primary Education Commission (ONPEC), Ministry of Education, and Department of Communicable Disease Control, Ministry of Public Health. ONPEC conducted trainings for teachers with technical support from Faculty of Tropical Medicine, Mahidol University, promoting child centered learning for parasite prevention. ACIPAC Training Course participants visited these sites for their field training.

3) Small Scale Pilot Projects in Partner Countries

Partner countries started small scale pilot projects. Equipments and budget were allocated by ACIPAC to partner countries. Ex-participants of the ACIPAC International Training Course 2001 played central role in conducting baseline survey and further implementation.

4) ACIPAC International Workshop

On March 25-26, 2002, ACIPAC organized a

workshop on "School-based Approaches for Malaria and STH Control" with the presence of Dr. E.A. Padmasiri WHO SEARO, Mr. Gamini Abeysekera UNICEF, and Dr. Punya kaewkeeyoon, ONPEC MoE as invited speakers. Two participants from respective partner countries reported the progress of the small scale pilot projects.

5) Information Network

ACIPAC website (http://www.tmacipac.mahidol.ac.th/) was established in the Information Technology Unit of Faculty of Tropical Medicine to promote Human/ Information network. ACIPAC Times, a newsletter, has been published since 30 August regularly. Copies were delivered by postal mail or e-mail to ex-participants and other persons concerned, and also can be seen on the website.

6) Short Term Experts

ACIPAC invited three short-term experts from Japan: Prof. Kazuhiko Moji (January 21-February 3) propelled health education in a model activities in Thailand, Prof. Shigeyuki Kano (February10-23) conducted a survey for drug resistant strain of malaria in a model area, and Prof. Akira Ishii (February 27-March 9) took on the job of technical guidance for malaria survey in the pilot project site in Lao PDR.

7) Conferment of a Honorary Degree to H.E. Mr. Ryutaro Hashimoto

H.E. Mr. Ryutaro Hashimoto, a former Prime Minister of Japan, was conferred a degree of Doctor of Philosophy in Clinical Tropical Medicine, *Honoris Causa*, from the Mahidol University on 4 July 2002 due to his great contribution toward a global parasite control including the establishment of the ACIPAC. The degree was bestowed by H.R.H.Princess Maha Chakri Sirindhorn.

Office of the Dean

Tel. 0-2246-9000 ext. 1326, 1328 Fax. 0-2246-8340

ORGANIZATION CHART

Management Information

Personnel Management

In 2002, there was a total of 769 staff, comprised of 319 government service staff, 41 University employees (Government budget), 22 University employees (Faculty budget), 282 permanent staff and 103 temporary staff. In the fiscal year 2002, there were 16 new staff, 65 transferred and resigned, and 5 retired (3 governments staff and 2 permanent staff).

Budget Management

Total expenses were 243.8 million Baht, of which 157 million Baht were supported by the government budget, and 86.9 million Baht was Faculty revenue, in the percentage ratio 84:16. The expenditure can be broken down as follows:

- Personnel Budget = 109.5 million Baht (44.89%)
- Operational Budget = 86.1 million Baht (35.33%)
- Investment Budget = 48.2 million Baht (19.78%)

Construction and Area Development

The new field research station in Kanchanaburi Province is now under going internal fit-out. It will be finished in March 2003.

Mrs. Vorapan Singhsilarak
B.A.
Secretary 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:

Administrative and General Affairs Unit

Tel. 0-2246-9000 ext. 1302, 1304, 1801
The Unit is divided into 4 subunits, as follows:

Mrs. Kannikarkaew Pinit
B.A. (General Management), B.A. (Business Education)
Head

Documentation Subunit

General Affairs Office

Aree Masngammuang B.A. (Political Science)
Maninthorn Phanumaphorn M.B.A.
Patra Kreekul B.A. (General Management)
Nathaneeporn Panampai B.A. (General Management)
Supavadee Yaowasang B.A. (Lib.Info.Sc)

Office Clerk

Pranee Kraisorn
Prachum Bauprasert
Sanchai Meeprom

Operator

Chanpen Ronsuk

Data Input Clerk

Yupa Jarernrit

Area and Transportation Subunit

Civil Engineer

Savek Chomming B.En.

Architect

Thep Ngamnetr B.Arch.

Security Guard

Somjai Promduang

Gardener

Sombat Khamthanee

Driver

Kasem Kaewbangkerd

Public Relations Subunit

Public Relations Officer

Thitika Teeranetr B.A. (Communication Arts)

General Affairs Office

Wandee Srasalee B.A. (General Management)
Varee Viriyarat B.A. (General Management)

Maintenance and Repairs Subunit

Electrician

Chaiyaporn Phoopan Voc. Cert. (Electric)
Panumas Tunritsa Voc. Cert. (Electric)
Tumrongsak Wimolsut

The Educational Affairs Unit

Tel. 0-2246-9000 ext. 1921, 1662, 1664, 1668

Wanpen Puttitanun
B.A. (General Management)
Head

Education Affairs Officer
- **Benjarat Prompakdee** B.Ed., M.Ed.
- **Somporn Ngamsirisomsakul** B.B.A. (Marketing)

Scientist
- **Chutamas Chaiworaporn**
  B.Sc. (Biology), M.Sc.(Trop.Med.)

General Affairs Officer
- **Chutarat Pradabprachr** B.Ed.
- **Sivaporn Pisitsak** B.B.A. (Marketing)
- **Rasamee Wongititarkul** B.B.A. (Accounting)
- **Kittaya Bureerat** B.A. (English)

General Affairs Associate
- **Rangson Praevanit** Cert. Commercial
- **Nutjanat Taewrob** Cert. Commercial
- **Chiraporn Praevanit** Voc. Cert. Commercial
- **Aree Buaprae** Voc. Cert. Commercial

Specialist
- **Paul R. Adams** B.A., Grad.Dip.Lib., M.Mgt.

Staff
- **Anurat Kalasen** Cert. Commercial
- **Srisuchart Mongkhonmu** Cert. Commercial

Financial and Procurement Unit

Tel. 0-2246-9000 ext. 1204, 1305, 1323, 1325

The Unit is divided into 2 subunits, as follows:

Somkid Nima

B.B.A. (General Management), LL.B.

Head

Financial and Accounting Subunit

Accountant Officer

- **Ketsinee Nima** B.B.A. (Accounting)
- **Tham Chermkhuntod** B.A. (General Management), B.B.A. (Accounting)
- **Chuenboon Aimpraneet** B.A. (General Management)
- **Arayaporn Sawangrungrueng** B.A.
- **Souavalak Chomchai**

Accountant Staff

- **Jeeranat Kumseranee** B.A. (General Management)
- **Prapaporn Krootmas**
- **Vantana Theprod** Voc. Cert.
- **Chayan Muanom** Cert. in Commercial
- **Nopadol Preechasunthorn** Voc. Cert.

Officer Clerk

- **Porntiva Sen-im** B.A.

Procurement Subunit

Procurement Officer

- **Prapaiporn Tiacharoen** B.B.A. (General Management)
- **Montri Noochan** B.B.A. (Econ)
- **Inthira Pansuebchuea** B.B.A.

Procurement Staff

- **Kanjanaporn Sukasem** B.B.A.
- **Rangsi Prathumrat** Cert. in Commerce
- **Tuenjai Ketanond** Voc. Cert.

Officer Clerk

- **Oranart Supaka**

Typist

- **Mongkol Bunchakorn**

Photographer

- **Wattana Prechasunthorn**

Policy and Planning Unit

Tel. 0-2246-9000 ext. 1303

The Unit is divided into 3 subunits

1. Coordination and development planning
2. Budget preparation, monitoring, review
3. Management database

Yaowapa Pratumsuwan
B.A. (Political Science), M.P.A.
Head

Policy and Planning Officer

Thanormsri Ketsuk B.B.A. (Money & Banking)
Jitra Suriya B.B.A. (Money & Banking)

Officer Clerk

Pramote Ketsuk B.Sc. (Computer Science)

Personel Unit

Tel. 0-2246-9000 ext. 1324, 1330

Sukanya Ongaree
B.A. (Soc. Ant.)
Head

Personnel Officer

Phongsri Konthong B.A. (General Management)
Chuleeporn Rumyarungsi

Personnel Staff

Surang Wattanakamolgul Cert. Marketing
Supaporn Chotivatin Cert. Computer
Buarun Nilapa

Education Technology Unit

Tel. 0-2246-9000 ext. 1841, 1842

The unit is comprised of 2 divisions:

1. Audio-Visual Division
2. Museum of Tropical Medicine

Sompoch Thanuvathana
Cert. Med. Illus., B.Sc. (Med. Illus.&A.V. Tech.)
M.Ed. (Ed.Tech.)
Head

Illustration Officer

Saranya Vongngernyuang
B.Sc. (Med.Illus.&A.V. Tech.)

Tawan Wathanakul
Voc. Cert., B.Ed. (Ed.Tech.Inn.)

Vatcharin Nagpong
B.F.A. (Comm. Desi.)

Sivaporn Kanchanamai
B.F.A. (Appli. Art)

Chamnan Egasonth
Cert. Graphic Art

General Affairs Officer

Kannika Petporee
B.A. (General Management)

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.

Information Technology unit

Duangjai Sahassananda
B.Sc. (Med.Tech.), M.Sc. (Information Technology in Business)
tmdsh@mahidol.ac.th
Head

System Administrator
Wimol Chotithammapiwat B.Sc. (Computer Science)
tewct@mahidol.ac.th

Computer Scientist
Wuttichai Kitpremthaworn B.Sc. (Computer Science)
tewkp@mahidol.ac.th
Seksan Sawadiraksa B.A. (Business Computer)
teswd@mahidol.ac.th
Kamphon Sophapis B.A. (General Management)

Electronic Associate
Pongnatee Kingsawat Dip. In Voc. Ed. (Electronic)
tepkn@mahidol.ac.th

Illustration Officer
Anakanun Hinjiranan B.A. (Visual Communication Design)
teahj@mahidol.ac.th

General Affairs Officer
Jetsadaporn Chantachorn B.A. (General Management)
tejct@mahidol.ac.th

The Information Technology Unit provided information and computer services throughout FY 2000/2001 for the Faculty's staff, students and participants in short training courses, such as:

I. Teaching & Training

1.1 Teaching faculty students; MSc, Ph.D, DTM&H and MCTM

Course

TMHG511, TMHG511-3, TMCD518, TMSE521, TMSE505, TMSE504, TMSE502, TMNU605, TMID513, TMMI523, TMHG509, TMID510, TMHG514

1.2 Training faculty staff

- Computer software training 7 times for 141 faculty staff (30 terminals each time) which consist of MS Office
- Basic Knowledge on Computer/Windows 98/MS Word
- MS PowerPoint/Imaging/WinZip
- MS Excel

Statistics

- SPSS Program

Graphic

- Photoshop & Scanner

Web

- Web page & Imaging

1.3 Trianing for workshop

- Health Mapper
- Third Regional Field-based Training Programme in Epidemiological Research Methods and Control of Tropical Diseases (Refit 2002)
- Basic Data Analysis for Epidemiologic Research
- ACIPAC Course

II. 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.

III. Network and Application Development

The Unit is responsible for development of the computer system and programming in

- Network for IT unit
- Network for Chalermprakiet Building
- Hospital database development in a client/server environment; case study of the Hospital for Tropical Diseases
- Database development for the services of the Information Technology Unit
- Faculty homepage at http://www.tm.mahidol.ac.th
- Intranet for the administration section

International Relations Unit

Tel: 0-2246-9000-12 ext. 1327, 1318; 0-2643-5614
Fax: 0-2246-9013, E-mail: tmknt@mahidol.ac.th

Keeratiya Nontabutra
B.A.
Head

General Affairs Officer

Wandia Onwan B.A. (Thai & Eng)
Sethavudh Kaewviset B.A.
Ratanawadee Nanlar B.A.

Central Equipment Unit

Tel: 0-2246-9000 ext. 1291, 1662, 1664, 1668

Scientist

Hathairad Hananantachai
Rachaneekorn Mingkhwan

Secretary

Nuttaporn Kotchasri

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 ot the Faculty's staff
3. To provide a general scientific consultancy service for members of the Faculty

Research and Academic Affairs Unit

Tel: 0-2246-9000 ext. 1524, 1525 Fax: 0-2643-5578
Homepage: http:/www.tm.mahidol.ac.th./research
E-mail: tmpww@mahidol.ac.th.

Pornpimon Adams
B.Sc. (Biology), M.Sc. (Trop. Med.)
Head

General Affairs Officer
Warissara Chaiyabhandhu
B.A. (General Management)
Sivaporn Samung B.A. (Lib. Info. Sc.)

Database Developer
Pitchapa Vutikes B.B.A. (Business Computer)

Illustration Officer
Ronnachai Rarerng B.Ed. (Tech. Inn.)

Illustration Staff
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 International Meeting (JITMM) and the Chamlong-Tranakchit Harinasuta Lecture, and secretarial services for the Ethics Committee of the Faculty of Tropical Medicine, Mahidol University.

In the fiscal year 2002, the Unit provided the following services:

1. Circulated 25 research funds
2. Circulated 7 awards
3. Provided/helped organize 4 special lectures
4. Provided secretarial services for the Ethics Committee of the Faculty of Tropical Medicine; 50 projects
5. Produced 4 volumes of the *Mosquito Borne Diseases Bulletin,* 2 volumes of the *Journal of Tropical Medicine, and Parasitology,* 1 issue of the Annual Report, and 1 issue of JITMM/FBPZ abstract book
6. Provided publication services to external clients

Training Courses / Workshops

No.	Course / Workshops	Duration	Total No.of Participated	Countries Participated
1.	School-based Malaria and Soil-transmitted Helminthiases Control for Programme Managers	17 Sep - 7 Dec 01	27	Cambodia, Kenya, Lao PDR, Myanmar, Thailand, Vietnam
2.	Infectious Diseases/Tropical Medicine/ AIDS	8 - 25 Oct 01	1	USA
3.	Special Training in Tropical Diseases Management	19 Oct - 14 Dec 01	2	Japan
4.	Training in Tropical Medicine	22 Oct - 2 Nov 01	1	Sweden
5.	Total Quality Management at Clinical Medical Laboratories in Developing Countries	29 Oct - 9 Nov 01	1	Japan
6.	Training for the International Infectious Diseases Control	29 Oct - 23 Nov 01	6	Japan
7.	Training in Information Exchange on Malaria Control Activities	5 - 9 Nov 01	12	Vietnam
8.	Training in Tropical Paediatrics	6 -30 Nov 01	3	USA
9.	Training in Skill Laboratory	12 - 21 Nov 01	9	Vietnam
10.	Training in Tropical Nutrition and Food Science	4 Jan - 15 Feb 02	2	Germany
11.	Special Training Programme in Tropical Diseases	13 Jan - 1 Feb 02	4	Lao PDR
12.	Special Training in Tropical Diseases Management	28 Jan - 1 Feb 02	1	Japan
13.	Training in Tropical Paediatrics	4 - 8 Feb 02	1	USA
14.	Training Workshop on Family Health/Reproductive Health : Participatory Learning towards Operational Research in Reproductive Health	4 - 29 Mar 02	4	Sri Lanka
15.	ACIPAC International Workshop	25 - 26 Mar 02	10	Cambodia, Lao PDR Myanmar, Thailand, Vietnam,
16.	Study Visit of Community-oriented Teaching Group	25 - 30 Mar 02	10	Vietnam
17.	Special Training in Tropical Medicine	13 - 27 Mar 02	3	Japan
18.	Training in Tropical Medicine	9 Apr - 2 May 02	5	Japan
19.	Training in Tropical Medicine	5 -9 May 02	2	Japan
20.	Third Regional Field-based Training Programme in Epidemiological Research Method and Control of Tropical Diseases	13 May - 31 July 02	16	Myanmar, Vietnam, Cambodia, Lao PDR, India
21.	Training on Skill Laboratory for Thaibinh Medical University	20 - 31 May 02	7	Vietnam

No.	Course / Workshops	Duration	Total No.of Participated	Countries Participated
22.	Special Training in Tropical Medicine Management	28 May - 28 June	1	Japan
23.	Study Tour for Managerial Officers for Hanoi Medical College	9 -16 June 02	8	Vietnam
24.	Laboratory Diapnosis of AIDS related Protozoa	19 - 20 Aug 02	60	Thailand
25.	Regional Basic Course on Data Analysis for Epidemiologic Research	2 - 20 Sept 02	6	India
26.	Workshop on Food Safety Education Network in Thailand	5 Sept 02	36	England, Indonesia, USA
27.	The ACIPAC International Training Course on School-Based Malaria and Soil-Transmitted Helminthiases Control for Programme Managers	2 Sept - 22 Nov 02	27	Cambodia, Ghana, Kenya, Lao PDR, Thailand, Vietnam
28.	Regional Advanced Course on Data Analysis for Epidemiologic Research	23 Sept - 11 Oct 02	17	Cambodia, India, Indonesia, Lao PDR, Vietnam
29.	Study Tour in Thailand on Malaria Control	8 - 21 Sept 02	8	Vietnam

International Linkages

AUSTRALIA
- Queensland Institute of Medical Research, University of Queensland, Brisbane
- Tropical Health Program, University of Queensland Medical School
- The Walter and Eliza Hall Institute of Medical Research

AUSTRIA
- Austrian Society of Tropical Medicine and Parasitology, Vienna
- Department of Infectious Diseases, Faculty of Medicine, University of Vienna
- Department of Tropical Medicine and Specific Prophylaxis, Faculty of Medicine, University of Vienna

CANADA
- Cross Cancer Institute, Edmonton, Alberta
- Department of Medicine, University of Toronto
- Department of Microbiology and Infectious Diseases, Faculty of Medicine, University of Calgary

FRANCE
- Association Sante Sud Medical Humanitarian French Association, Marseille
- Aventis Pasteur SA
- Centre de Formation et de Rechherche en Medicine et Sant Tropicales, Hopital Felix
- Houphouet-Boigny, Marseille
- Department des Maladies Infectieuses et Tropicales, Hopital de la Salpetriere, Paris

GERMANY
- Free University, Berlin
- German Cancer Research Center, Heidelberg
- Humboldt University of Berlin, Berlin

INDONESIA
- Faculty of Public Health, University of Indonesia
- SEAMEO TROPMED Regional Centre for Community Nutrition, University of Indonesia

ITALY
- Chiron S.p.a, Siena
- Clinica Malattie Infetive e Tropicali, Univrsit Degli Studi Di Brescia

JAPAN

KENYA
- Wellcome Trust Research Laboratories, Nairobi

MALAYSIA
- Institute for Medical Research, Kuala Lumpur

NORWAY
- Department of Infectious Diseases, Ullevaal Hospital, University of Oslo

PHILIPPINES
- College of Public Health, University of the Philippines, Manila

UNITED KINGDOM
- Division of Parasitology, NIMR, Mill Hill, London
- Institute of Molecular Medicine, University of Oxford
- Liverpool School of Tropical Medicine
- Nuffield Department of Clinical Medicine, University of Oxford
- The Wellcome Trust

UNITED STATES OF AMERICA
- Case Western Reserve University, Ohio
- Department of Epidemiology, University of Michigan
- Department of Medicine, George Washington University Medical Center, Washington DC
- Hahnemann University, Philadelphia, Pennsylvania

SEAMEO-TROPMED Network

WHO/TDR

MOU in FY 2002
1. Memorandum of understanding between the Faculty of Tropical Medicine, Mahidol University and the Nippon Medicine Care, Singapore pertaining to the establishment of a collaborative programme 24/09/2002
2. Memorandum of understanding between the Faculty of Tropical Medicine, Mahidol University and the University of Leicester, United Kingdom 7/03/2002
3. Minutes of Meetings between the Japanese mid-term evaluation team and the authorities concerned of the government of the Kingdom of Thailand on Japanese Technical Cooperation for the project for the Asian of International Parasite Control 1/07/2002

Visitors

During 1 October 2001 – 30 September 2002

No.	Name	Country/Institute
1.	Dr. Khamhoung Heangvongsy	Lao PDR
2.	Dr. Onsy Phommalat	Lao PDR
3.	Dr. Prasongsidh Boupha	Lao PDR
4.	Dr. Somphone Phanmanisay	Lao PDR
5.	Dr. Pavit Khemmanit	Lao PDR
6.	Dr. Heio Hohmann	Lao PDR
7.	Dr. Supachai Douangchak	Lao PDR
8.	Dr. Suresh Kumar	Malaysia
9.	H.E. Prof. C.P. Thakur	India
10.	Dr. Galappaththy	Sri-Lanka
11.	Dr. Cherise Rohr	USA
12.	Mr. Anupong Preamjai	Mahidol-Vittayanusorn School
13.	Mr. Sithichok Somaum	Mahidol-Vittayanusorn School
14.	Mr. Sakarin Pupanil	Mahidol-Vittayanusorn School
15.	Mr. Pavit Meankong	Mahidol-Vittayanusorn School
16.	Mr. Amnart Kartsanook	Mahidol-Vittayanusorn School
17.	Mr. Kittikun Kertsomboon	Mahidol-Vittayanusorn School
18.	Ms. Nutta Hensawang	Mahidol-Vittayanusorn School
19.	Ms. Patwilai Nootpramul	Mahidol-Vittayanusorn School
20.	Ms. Montira Oilsrisakul	Mahidol-Vittayanusorn School
21.	Ms. Chamlika Pormmapan	Mahidol-Vittayanusorn School
22.	Ms. Chanokporn Downwan	Mahidol-Vittayanusorn School
23.	Ms. Pannawan Innulak	Mahidol-Vittayanusorn School
24.	Mr. Pongpol Chauwanitwanil	Mahidol-Vittayanusorn School
25.	Mr. Attapol Sahakarnarenakul	Mahidol-Vittayanusorn School
26.	Mr. Passarat Kongkaw	Mahidol-Vittayanusorn School
27.	Ms. Kulwalang Jumnianwai	Mahidol-Vittayanusorn School
28.	Mr. Panyo Wootilakchainan	Mahidol-Vittayanusorn School
29.	Ms. Pattarapa Rungwichaniwat	Mahidol-Vittayanusorn School
30.	Ms. Sasikarn Panyadee	Mahidol-Vittayanusorn School
31.	Ms. Chonikarn Chawanasean	Mahidol-Vittayanusorn School
32.	Ms. Pornpan Watanarungchai	Mahidol-Vittayanusorn School
33.	Ms. Munchuta Dangkulwanit	Mahidol-Vittayanusorn School
34.	Ms. Karnsinee Payarkjumlearn	Mahidol-Vittayanusorn School
35.	Mr. Pattana Thanakorn	Mahidol-Vittayanusorn School
36.	Mr. Salawoot Sangaulai	Mahidol-Vittayanusorn School
37.	Mr. Somluthai Homechein	Mahidol-Vittayanusorn School
38.	Ms. Aree Sakyim	Mahidol-Vittayanusorn School
39.	Dr. S.K. Shrivastava	India
40.	Dr. P.K. Bholanath Das	India
41.	Dr. T.S. Chaluvaraj	India
42.	Dr. N.J. Rathod	India
43.	Dr. K.K. Rout	India
44.	Dr. P.K. Srivastava	India
45.	Dr. P. Chandra Dash	India
46.	Ms. Christine M. Allen	USA
47.	Ms. Corazon (Cora) G. Barrios	USA
48.	Mrs. Elaine C. Forbes	USA
49.	Dr. Mark A. Fredrickson	USA
50.	Ms. Ann Hilt-Garro	USA
51.	Ms. Linda Lou Scribner	USA
52.	Prof. Hidenori Kobayashi	Japan
53.	Dr. Robert Edwards	Australia
54.	Ms. Miriam Paul	Germany
55.	Mr. Walter Scholer	Germany
56.	Mrs. Franziska Eichstadt-Bohlig	Germany
57.	Dr. Barbara Holl	Germany
58.	Dr. Michael Luther	Germany
59.	Mrs. Waltrand Lehn	Germany
60.	Mrs. Clemens Schwalbe	Germany
61.	Mrs. Antje-Marie Steen	Germany
62.	Mr. Karl-Friedrich Schulze	Germany
63.	Mr. Klaus Kruger	Germany
64.	Mr. Alexander Nowak	Germany
65.	H.E. Andreas von Stechow	Germany
66.	Dr. Juergen Erherdt	Germany
67.	Prof. Nevin Scrimshaw	USA
68.	Dr. James Carroll	USA
69.	Mr. Niklas Lindegardh	Sweden
70.	Ms. Anna Annerberg	Sweden
71.	Prof. Yutaro Kaneko	Japan

No.	Name	Country/Institute
72.	Prof. Naohiro Watanabe	Japan
73.	Prof. Nguyen Van Dip	Vietnam
74.	Dr. Pham Quoc Bao	Vietnam
75.	Dr. Pham Van Tac	Vietnam
76.	Mr. Le Chi Thanh	Vietnam
77.	Mr. Le Hanh	Vietnam
78.	Mr. Nguyen Chien Thang	Vietnam
79.	Dr. Tong Ban Quy	Vietnam
80.	Ms. Tran Thi Oanh	Vietnam
81.	Mr. Le Van Quan	Vietnam
82.	Dr. Pham Kim Thu	Vietnam
83.	Dr. Le Thi Xuan	Vietnam
84.	Dr. Nguyen Van Hien	Vietnam
85.	Dr. Hoang Kim Ha	Vietnam
86.	Mr. Cao Ngoc Anh	Vietnam
87.	Dr. Tran Trung Hoa	Vietnam
88.	Dr. Hguyen Van Nam	Vietnam
89.	Dr. Pham Van Linh	Vietnam
90.	Dr. Bui Thi Minh Thu	Vietnam
91.	Mrs. Lai Hong Loan	Vietnam
92.	Dr. Denise Mattei	France
93.	Dr. Anthony Pearson	UK
94.	Ms. Kanikar Pilomrat	Thai
95.	Dr. Ben-Aroya Yehuda	Israel
96.	Dr. Danon Yehuda	Israel
97.	Dr. Yaari Joseph	Israel
98.	Dr. Yaari Israael	Israel
99.	Dr. Maia Funk	Switzerland
100.	Dr. Erich Schmutzhard	Austria
101.	Dr. Leonard Levy	UK
102.	Dr. Lesley Rushton	UK
103.	Dr. Grant Gall	Canada
104.	Dr. Taj Jadavji	Canada
105.	Dr. David Warrell	UK
106.	Dr. Nathalie Cambon	Switzerland
107.	Mr. Kenji Tanii	Japan
108.	Dr. Eisaku Kimura	Japan
109.	Dr. Makoto Itoh	Japan
110.	Ms. Kasumi Tabita	Lao PDR
111.	Ms. Junko Nagasawa	Japan
112.	Ms. Ikuyo Yoneda	Japan
113.	Mr. Takeshi Kouga	Japan
114.	Ms. Noriko Kinosita	Japan
115.	Mr. Yuya Mituhasi	Japan
116.	Ms. Kyoko Invi	Japan
117.	Mr. Kotaro Miyake	Japan
118.	Mr. Hiratako Kato	Japan
119.	Mr. Ko Inbe	Japan
120.	Ms. Sayaka Asahata	Japan
121.	Ms. Syuno Uemura	Japan
122.	Mr. Toshihito Sakamoto	Japan
123.	Ms. Nari Yamanoto	Japan
124.	Ms. Kulkanya Sahawatkul	Thai
125.	Ms. Nisa Puttikul	Thai
126.	Ms. Patchala Pattanajarit	Thai
127.	Ms. Yulee Yanasay	Thai
128.	Mr. Akawoot Sousakul	Thai
129.	Ms. Chanikarn Kaewplung	Thai
130.	Ms. Vilonlong Suratniti	Thai
131.	Ms. Vorawan Amritchote	Thai
132.	Ms. Nunkanya Satilapongsasutti	Thai
133.	Mr. Tanan Deesomchok	Thai
134.	Ms. Pilayan Tamlongteelakul	Thai
135.	Ms. Manika Naparat	Thai
136.	Mr. Abul Kalarn Azad	Bangladesh
137.	Dr. Abdur Rashid	Bangladesh
138.	Dr. Aung Swi Prue Marma	Bangladesh
139.	Dr. Yim Khun Khoeun	Cambodia
140.	Dr. Xiaodong Sun	PR China
141.	Dr. Guowei Chen	PR China
142.	Dr. Marti Kusumaningsih	Indonesia
143.	SKM. Yety Intarti	Indonesia
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146.	Dr. Viengporn Sengsawath	Lao PDR
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148.	Ms. Mastura Bt	Malaysia
149.	Dr. Joel Pama	Philippines
150.	Mr. John Porto	Philippines
151.	Mr. Suebskul Sakolwaree	Thailand
152.	Ms. Nardlada Khuntikul	Thailand
153.	Mr. Somkait Choosrithong	Thailand
154.	Dr. Phi Duc Toan	Vietnam
155.	Dr. Dao Minh Tuan	Vietnam
156.	Dr. Nguyen Chinh Phong	Vietnam
157.	Dr. Ravinder Kumar Kataria	India
158.	Dr. Vimal Kishore Gupta	India
159.	Dr. Utsuk Datta	India
160.	Dr. Pramod Gandhi	India
161.	Dr. Chandra Shekhar Aggarwal	India
162.	Dr. Sunil Kamar Bhat	India
163.	Dr. Neeraj Bedi	India
164.	Dr. S.M. Bandappa	India
165.	Dr. Pramod Murlidhar Chapalgaonkar	India
166.	Dr. Motiram Govindrao Kamble	India
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169.	Dr. Kenji Yamanoto	Japan
170.	Dr. Fumihiko Takeuchi	Japan
171.	Prof. John Harris	UK
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179.	Dr.Pavit Khemmanit	Lao PDR
180.	Dr.Heio Hohmann	Lao PDR

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195.	Miss Nalinee Tuntisevi	Thailand
196.	Miss Dusanee Srimanikarn	Thailand
197.	Miss Nathaporn Parinyaprom	Thailand
198.	Miss Thitipron Polimthana	Thailand
199.	Miss Nathya Pookkhwan	Thailand
200.	Miss Thapanee Songseeyon	Thailand
201.	Miss Nispasinee Wongthongsiri	Thailand
202.	Miss Narisa Thamweerapong	Thailand
203.	Miss Nuthaporn Sungwichai	Thailand
204.	Miss Duangdao Muanprasat	Thailand
205.	Miss Nutha Wannissorn	Thailand
206.	Miss Thip-apa Thammongkut	Thailand
207.	Miss Nongluck Arunjit	Thailand
208.	Mr.Nuthapong Surawan	Thailand
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212.	Mr.Thanakarn Wongleelaseth	Thailand
213.	Mr.Nuthaphol Suwathrungkool	Thailand
214.	Mr.Thavichai Kulwong	Thailand
215.	Mr.Nuthakit Paisithviroj	Thailand
216.	Mr.Thanawith Mekhavuthidul	Thailand
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222.	Miss Thanisa Twichsri	Thailand
223.	Miss Theeraruk Tharavuth	Thailand
224.	Miss Thanitha Singkhibut	Thailand
225.	Miss Thanaporn Nimitrbancha	Thailand
226.	Miss Napaporn Poolsin	Thailand
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240.	Mr.John H. Thomas	SEAMEO
241.	Dr.GA Deye	AFRIMS
242.	Dr.Ng Conger	AFRIMS
243.	Dr.HM Chun	AFRIMS
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245.	Ms.Rikke Moller Pedersen	Denmark
246.	Miss Siritheera Srichanthapong	Thailand
247.	Miss Oraporn Rojanasakul	Thailand
248.	Ms.Aya Tanaloe	Japan
249.	Prof.Peter Beales	WHO/Geneva
250.	MAJ Nicholas J Vietri	AFRIMS
251.	CPT Mathew J Hepburn	AFRIMS
252.	Prof.Shigeyuki Kano	Japan
253.	Dr.Hatabu	Japan
254.	Mr.Kenji Yamada	Japan
255.	Ms.Anwara Khatun	WHO/SEARO
256.	Ms.Nima Sangay	WHO/SEARO
257.	Dr.Asha Sharma	WHO/SEARO
258.	Ms.Masyitha L	WHO/SEARO
259.	Ms.Ashiyath Rasheed	WHO/SEARO
260.	Ms.M T Amarsinghe	WHO/SEARO
261.	Dr.Thira Worathanarat	WHO/SEARO
262.	Dr.Pragai Jirojanakul	WHO/SEARO
263.	Dr.William L Holzemer	WHO/SEARO
264.	Mr.Wittaya Fukfon	WHO/SEARO
265.	Ms.Chiraporn Yachompoo	WHO/SEARO
266.	Dr. D C S Reddy	WHO/SEARO
267.	Dr.Hedwig Goede	WHO/SEARO
268.	Dr.Kobkul Phancharoenworakul	WHO/SEARO
269.	Mr.Paul Toh	WHO/SEARO
270.	Ms.Shamsun Nahar	WHO/SEARO
271.	Dr.Kim Sang Ho	WHO/SEARO
272.	Dr.Kim Jong On	WHO/SEARO
273.	Mr.Ryan Hui Chol	WHO/SEARO
274.	Dr.Punitha Vijaya Ezhilarasu	WHO/SEARO
275.	Ms.Etty Rekawati	WHO/SEARO
276.	Ms.Savitri Singh	WHO/SEARO
277.	Dr.Daranee Jamjuree	WHO/SEARO
278.	Dr.Rutja Phuphaibool	WHO/SEARO
279.	Ms.Yaowarat Inthong	WHO/SEARO
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283.	Dr.Arvind Mathur	WHO/SEARO
284.	Dr.Rose Johnson	WHO/SEARO
285.	Ms.Manikala Laygoi	WHO/SEARO
286.	Dr.Indarjit Walia	WHO/SEARO
287.	Mr.Asik	WHO/SEARO
288.	Ms.Husna Mohamed	WHO/SEARO
289.	Ms.Sarala Shrestha	WHO/SEARO
290.	Ms. K P S Wijayalakshmi	WHO/SEARO
291.	Mrs.Pornpimol Ngamtao	WHO/SEARO
292.	Dr.Kanaungnit Pongthavornkamol	WHO/SEARO
293.	Assoc.Prof.Dr.Tassana Boontong	WHO/SEARO
294.	Dr.Leana Uys	WHO/SEARO
295.	Ms.Laksami Suebsaeng	WHO/SEARO
296.	Ms.Else Melgaard	WHO/SEARO
297.	Assoc.Prof. Supanee Senadesai	WHO/SEARO
298.	Dr.Krongkarn Saugkard	WHO/SEARO

Research and Voluntary Attachment

No.	Name	Duration	Institute/Country
1.	Dr. Methieu P Nacher	Since 1999	University Paris VI
2.	Mr. Martin Dodd	Nov 2001 - Oct 2002	Nurse Volunteer, UK
3.	Dr. Yaghoob H Bazzaz	21 Nov 2001 - 21 Feb 2002	University of Medical Sciences Tehran, Iran
4.	Mr. Maresa F Bodenberger	16 Mar -30 Apr 2002	University of Innsbruck, Austria

Elective Students in Tropical Medicine

No.	Name	Duration	Institute/Country
1.	Ms. Phoebe Brodie	9 - 26 Oct 2001	University of Queensland, Australia
2.	Ms. Janet McLeaire	9 -26 Oct 2001	University of Queensland, Australia
3.	Ms. Kate Macdonald	19 Nov - 14 Dec 2001	University of Tasmania, Australia
4.	Ms. Saowarat Snidvongs	26 Nov - 7 Dec 2001	Imperial College of Science, Technology and Medicine, United Kingdom
5.	Ms. Morishita Mariko	25 -29 Mar 2002	Kyoto Prefectural, University of Medicine, Japan
6.	Ms. Aya Nishimura	25 -29 Mar 2002	Kyoto Prefectural, University of Medicine, Japan
7.	Ms. Nina Salomon	14 Jan - 11 Feb 2002	Universitaetsklinikum Benjamin Franklinder Freien Universitaet, Germany
8.	Mr. Sekon Won	25 Mar - 15 Apr 2002	Boston University, USA
9.	Mr. Bharath Chakravarthy	25 Mar - 15 Apr 2002	Boston University, USA
10.	Ms.Jessica Lyons	1 - 26 July 2002	University of Calgary, Canada
11.	Mr.Jimmy Vantanajal	1 - 26 July 2002	University of Calgary, Canada
12.	Ms.Jenny Souster	1 - 26 July 2002	University of Calgary, Canada
13.	Mr.Harvey Hawes	1 - 26 July 2002	University of Calgary, Canada
14.	Dr.J.A. Skalsky	1 - 26 July 2002	General and Tropical Medicine FMH, Switzerland University College Dublin, Ireland
15.	Mr.John Burke	1 - 21 August 2002	University College Dublin, Ireland
16.	Ms.Evelyn O'Neill	1 -21 August 2002	University College Dublin, Ireland
17.	Ms.Julia Engl	2 - 27 Sept 2002	University of Innsbruck, Austria
18.	Ms.Margit Furtmuller	2 - 27 Sept 2002	University of Innsbruck, Austria
19.	Ms.Verena Kainzwalder	2 - 27 Sept 2002	University of Innsbruck, Austria
20.	Ms.Vera Prugger	2 - 27 Sept 2002	University of Graz, Austria
21.	Mr.Ramin Sotoudeh	2 - 27 Sept 2002	University of Vienna, Austria
22.	Ms.Petra Novak	2 - 27 Sept 2002	University of Vienna, Austria
23.	Ms.Shoko Ohinata	2 - 27 Sept 2002	Chiba University Medical Department, Japan

Fellows

No.	Name	Duration	Institute/Country
	WHO Fellow		
1.	Ms. Chee Chean Gan	Advanced Laboratory Diagnosis for Parasitic Diseases 5 – 30 Nov. 01	Malasia
	Thai Government Fellow		
1.	Dr. Ung Sophal	DTM&H, MCTM 1 Apr - 31 Mar 02	Cambodia
2.	Dr. Khamphanh Prabouasone	MCTM 1 Sept 01 - 31 Mar 02	Lao PDR
3.	Ms. Khonesavanh Luangxay	DTM&H 11 Mar 02 - present	Lao PDR
4.	Ms. Karma Lhazeen	DTM&H 11 Mar 02 - present	Bhutan
5.	Mr. Djamika Setiabudi	DTM&H 31 Mar 02 - present	Indonesia

Lecturers and their Areas of Expertise

Lecturer	E-mail Address	Field of Specialization/Expertise
Achara Asavanich	tmaas@mahidol.ac.th	Malaria vector/Medical entomology
Anong Kitjaroentham	tmakj@mahidol.ac.th	Biochemical nutrition
Arunee Sabchareon	tmasc@mahidol.ac.th	Malaria in children
Chalit Komalamisra	tmckm@mahidol.ac.th	Helminthology
Chamnarn Apiwathnasorn	tmcaw@mahidol.ac.th	Medical entomology/Mosquito taxonomy/Ecology/Field study
Channarong Sanghirun	rd123@mahidol.ac.th headtmrd@mahidol.ac.th	Radioisotopes in medical science and biology Monoclonal antibody for diagnosis of parasites
Chanathep Pojjaroen-anant	tmcpj@mahidol.ac.th	Cultivation and drug sensitivity test of *P. falciparum*
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Paron Dekumyoy	tmpdk@mahidol.ac.th	Immunodiagnosis of helminthiases
Petcharin Yamarat	tmpym@mahidol.ac.th	Rheology of malarial blood, blood of subjects digested garlic, cord blood
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Ratanaporn Kasemsuth	tmrks@mahidol.ac.th	Radioisotopes in medical science and biology RIA. (Radio immunoassay)
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Thongchai Deesin	-	Ecology/Mosquito-borne diseases/Field study
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Usanee Suthisarnsuntorn	-	Clinical microbiology/Bacteriology Infectious diseases/Pediatrics
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Varaporn Suphadtanaphongs	tmwsp@mahidol.ac.th headtmpz@mahidol.ac.th	Cultivation and drug sensitivity test of *P. falciparum*
Varee Wongchotigul	tmvwc@mahidol.ac.th	Rickettsiology (Scrub typhus)
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Yuvadee Mahakunkijcharoen	tmymh@mahidol.ac.th	Immunology of parasitic infections and bacterial infections

Ongoing Research Project of the Faculty of Tropical Medicine in 2002

No.	Ongoing Research Projects in 2002	Grants	Principal Investigator
	Department of Clinical Tropical Medicine		
1	Research and development for Thai people living at Thai-Myanmar border to free from tropical diseases	Mahidol University	Prof. Sornchai Looareesuwan
2	Adverse effect of rifampicin on quinine efficacy in falciparum malaria	Wellcome Trust of Great Britain	Prof. Sasithon Pukrittayakamee
3	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
4	Open-label, treatment protocol for the safety and efficacy of SCH 56592 (Oral Suspension) in the treatment of invasive fungal infections	Schering Plough Research Institute	Assoc. Prof. Punnee Pitisuttithum
5	Safety and therapeutic effects of Jin Huang Chinese Medicine in uncomplicated HIV-1 patients	Huatai Pharmacy, Co., Ltd.	Assoc. Prof. Punnee Pitisuttithum
6	Observational probe study of *in vitro* immune response parameters to candidate HIV-1 vaccine antigens among subject from Thailand	MERCK and Co., Inc	Assoc. Prof. Punnee Pitisuttithum
7	Effect of insecticide to female reproductive system	Tokyo University, Japan	Assist. Prof. Ladda Tangbanluekal
8	Health risk from trihalomethane contamination in tap water in Bangkok Metropolitan area and boundary	Mahidol University	Assist. Prof. Ladda Tangbanluekal
9	Biochemical abnormalities of renal function in patients with falciparum malaria	Government Budget	Assist. Prof. Udomsak Silachamroon
10	Efficacy of the combination of antimalaria with ursodeoxycholic acid comparing to antimalaria and placebo in the prevention of acute renal failure in severely jaundiced falciparum malaria patients: a randomized controlled trial	Mahidol University	Assist. Prof. Sombat Treeprasertsuk
11	Efficacy and tolerability of ivermectin on gnathostomiasis (pilot study)	Mahidol University	Dr. Valai Bussaratid
12	Efficacy and tolerability of ivermectin on gnathostomiasis	Thailand - Tropical Diseases Research Programme (T-2)	Dr. Valai Bussaratid
13	Study of auto-agglutination phenotype and disease severity in *P. falciparum* infection	TRF and Wellcome Trust of Great Britain	Dr. Kesinee Chotivanich
14	Neurotoxicity of artemether in animal model following intermittent intramuscular injections	Wellcome Trust of Great Britain and SEAMEO-TROPMED	Dr. Apichart Nontprasert

No.	Ongoing Research Projects in 2002	Grants	Principal Investigator
	Department of Clinical Tropical Medicine (Continued)		
15	Effect of drug accumulation in the neurotoxicity of artemether, dosing regimens with variable drug-free intervals in a mouse model	Wellcome Research Unit	Dr. Apichart Nontprasert
16	Neuropathological toxicity of artemisinin derivatives in a mouse model	Wellcome Trust of Great Britain	Dr. Apichart Nontprasert
17	Development of field methods and investigators of the molecular basis of Sulfonamide resistance in *Plasmodium vivax*	Wellcome Trust of Great Britain	Dr. Mallika Imwong
18	Novel point mutations in the dihydrofolate reductase gene of *Plasmodium vivax*: evidence for sequential selection by drug pressure	Wellcome Trust of Great Britain	Dr. Mallika Imwong
	Department of Helminthology		
19	Research and development of the intergrated project on chemotherapy and control of malaria and parasitic infections	Government Budget	Assoc. Prof. Jitra Waikagul
20	Seasonal variation in the intensity of Gnathostoma larvae in eels in Nakhon Nayok Province	Mahidol University	Assoc. Prof. Wichit Rojekittikhun
21	Experimental infection of freshwater fish in Thailand with the infective stage of *Angiostrongylus cantonensis*	Mahidol University	Assist. Prof. Chalit Komalamisra
22	Comparison of biochemical extract preparations of *Cysticercus cellulosae* by SDS - polyacrylamide gel electrophoresis and immunoblot technique	Mahidol University	Assist. Prof. Paron Dekumyoy
23	Studies on the efficacy of Thai traditional herbal medicines in the treatment of opisthorchiasis in Hamsters	Mahidol University	Assist. Prof. Panyawut Hiranyachattada
24	*Toxocara* canis larval antigens for serodiagnosis of human toxocariasis	Mahidol University	Assoc. Prof. Wanna Maipanich
25	Comparative studies on surface ultrastructure of adult worm of *Paragonimus* sp. in Thailand	Mahidol University	Assist. Prof. Sanan Yaemput
26	Monoclonal antibody-based competitive ELISA and indirect ELISA for immunodiagnosis of trichinosis	Mahidol University	Mrs. Supaporn Nuamtanong
27	*Angiostrongylus* cantonensis: S-Adenosylmethionine decarboxylase	Government Budget	Mrs. Supaporn Nuamtanong
	Department of Medical Entomology		
28	Study on fauna of medically important vectors at Kanchanaburi Campus Sai Yok District, Kanchanaburi Province	Mahidol University	Assoc. Prof. Somjai Leemingsawat
29	Specificity of the synthetic primers from sequencing DNA fragments of *Anopheles minimus*	Faculty of Tropical Medicine	Assist. Prof. Narumon Komalamisra
30	Mosquito repellent from medicinal plants	Mahidol University	Assist. Prof. Narumon Komalamisra
31	Effect of heavy metals (Pb2+, Cd2+) on enzymes of *Culex quinquefasciatus* larvae	Mahidol University	Mrs. Raweewan Srisawat
	Department of Microbiology and Immunology		
32	Rapid diagnosis of salmonellosis using dip stick method	Mahidol University	Prof. Wanpen Chaicumpa

No.	Ongoing Research Projects in 2002	Grants	Principal Investigator
	Department of Microbiology and Immunology (Continued)		
33	Production of allergenic components of cockroaches by genetic engineering	National Research Council of Thailand	Prof. Wanpen Chaicumpa
34	Efficacy testing of new vaccine adjuvant CpG DNA		Prof. Wanpen Chaicumpa
35	Development of molecular biological method for serotyping of *Leptospira*	NSTDA and TRF	Prof. Wanpen Chaicumpa
36	Development of a rapid test for detection of *Vibrio parahaemolyticus*		Prof. Wanpen Chaicumpa
37	Epidemiological survey of enterohemorrhagic *Escherchia*	Royal Golden Jubilee, TRF	Prof. Wanpen Chaicumpa
38	Towards the *Strongyloides stercoralis* Thai isolates	Royal Golden Jubilee, TRF	Prof. Wanpen Chaicumpa
39	Identification and characterization of T cell epitopes on *P. falciparum* sporozoite surface protein 2 recognized by human	Naval Medical Research Institute	Prof. Srisin Khusmith
40	Analysis of sequence polymorphism of T-cell epitope regions, Th2R and Th3R on *Plasmodium falciparum* circumsporozoite proteins in Thai isolates	Royal Golden Jubilee, TRF	Prof. Srisin Khusmith
41	Genetic diversity of the CS protein as an epidemiological marker for the efficacy of pre-erythrocytic stage immunity	IRD (French Ministry of Research) and TRF	Prof. Srisin Khusmith
42	Cytokine gene polymorphism in severe malaria	Royal Golden Jubilee, TRF	Prof. Srisin Khusmith
43	Relationship between cytokine gene polymorphism and severity of falciparum malaria	TRF	Prof. Srisin Khusmith
44	Development of opisthorchiasis by immunological method	MoPH, Faculty of Tropical Medicine and NRCT	Prof. Wanpen Chaicumpa
45	Typing of *Entamoeba histolytica* isolates obtained from Southeast Asian countries	Japanese Health Sciences Foundation (JHSF)	Assoc. Prof. Nitaya Thammapalerd
46	Production of monoclonal antibodies to *Bordetella pertussis* filamentous hemagglutinin	Faculty of Tropical Medicine, NSTDA and University of Tsukuba, Japan	Assoc. Prof. Manas Chongsa-nguan
47	Detection of dengue virus in mosquitoes (*Aedes* sp) by Nucleic Acid Based-Amplification (NASBA) and Polymerase Chain Reaction (PCR)	Mahidol University	Assoc. Prof. Wipawee Usawattanakul
48	Serotype of dengue and dengue-like illness in 3 hospitals along the Thai borderline	Mahidol University	Assoc. Prof. Wipawee Usawattanakul
49	Production of monoclonal antibodies for use in the diagnosis of scrub typhus	Faculty of Tropical Medicine	Assist. Prof. Varee Wongchotigul
50	A simple and rapid detection of scrub typhus	Mahidol University	Assist. Prof. Varee Wongchotigul
51	Detection of Leptospira spp. in urine by polymerase chain reaction (PCR)	Thailand Research Fund	Dr. Thareerat Kalambaheti
52	Prevalence of antibody encoding for Tat gene in HIV infected patients and AIDS patients	Mahidol University	Miss Pornsawan Amarapal
	Department of Protozoology		
53	Isolation and characterization of DNA helicase from *Plasmodium falciparum*	Thailand Research Fund	Assoc. Prof. Pornthip Petmitr
54	Toxoplasmosis in population at risk in Thailand	Mahidol University	Assoc. Prof. Yaowalark Sukthana
55	Comparative study of the affects of parasitic drug treatment alone with drug treatment and health education in primary school students in Bangkok and suburban area	Government Budget	Assoc. Prof. Yaowalark Sukthana

No.	Ongoing Research Projects in 2002	Grants	Principal Investigator
	Department of Protozoology (Continued)		
56	Comparison of *Toxoplasma gondii* antibody detection between in-house latex agglutination and commercial test	Thanad-Molee Choman Foundation	Assist. Prof. Varaporn Suphadtanapongs
57	Detection of malaria parasites in after-drug treatment patients by using QBC method	Government Budget	Assist. Prof. Varaporn Suphadtanapongs
58	Studies on the effect of Thai medicinal plants to *Cryptosporidium* and *Isopora in vitro*	Mahidol University	Assist. Prof. Chutatip Siripanth
59	Established Thai medicinal plants for treatment of coccidiosis in pig poultry and cow	Ministry of University Affairs	Assist. Prof. Chutatip Siripanth
60	Established double antibody ELISA method for detection of pathogenic protozoal antigens in the feces	National Science and Technology Development Agency	Assist. Prof. Chutatip Siripanth
	Department of Social and Environmental Medicine		
61	A phase III trial of Aventis Pasteur live recombinant ALVAC-HIV (vCP 1521) priming with VaxGen gp120 B/E (AIDSVAX™ B/E) Boosting in HIV-uninfected Thai-Adults	The Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc.	Dr. Supachai Reukngam (Prof. Dwip Kitayaporn)
62	A phase III trial to determine the efficacy of AIDSVAX™ B/E vaccine in intravenous drug users in Bangkok, Thailand	VAXGEN Co., Ltd.	Bangkok AIDS Vaccine Evaluation Group (Database management by Prof. Dwip Kitayaporn)
63	Socio-cultural and behavioral factors of Shigellosis burden studies in Kaeng Koi District	The International Vaccine Institute	Assoc. Prof. Piyarat Butraporn
64	Socio-environmental management for sustainable dengue hemorrhagic fever control in Chaiyahuum Province	Mahidol University	Assoc. Prof. Piyarat Butraporn
65	Leptospirosis vaccine designed using T7 phage display technique	Thailand Reserch Fund	Assist. Prof. Pongrama Ramasoota
66	Local wisdom in the treatment of herpes simplex diseases case study: the treatment of herpes simplex by monk healer (mor-pra)	Mahidol University	Mr. Wiwat Wanarangsikul
	Department of Tropical Nutrition and Food Science		
67	Food and health relationship in Asian population Institute of Malaysia	Palm oil Research	Assoc. Prof. Supranee Changbumrung
68	Development of food and medicinal plants	Government Budget	Assoc. Prof. Supranee Changbumrung
69	Medicinal plants for treatment of hookworm	Government Budget	Assoc. Prof. Supranee Changbumrung
70	Medicinal plants against malaria	Government Budget	Assoc. Prof. Supranee Changbumrung
71	Identification of gene alterations in breast cancer	BIOTEC	Assoc. Prof. Songsak Petmitr
72	The correlation between folic acid status and cervical cytologic abnormalities in Thai women	Mahidol University	Assist. Prof. Karunee Kwanbunjan
	Department of Tropical Pathology		
73	Hematopoietic features of the bone marrow of *Plasmodium falciparum* infected patients	Mahidol University	Assoc. Prof. Yaowapa Maneerat
74	The effects of *Plasmodium falciparum* - induced cellular responses on activation of endothelial cells	Mahidol University	Assoc. Prof. Yaowapa Maneerat

No.	Ongoing Research Projects in 2002	Grants	Principal Investigator
	Department of Tropical Pathology (Continued)		
75	Pathology and Immunohistochemistry of liver in AIDS: a necropsy study	Mahidol University	Assoc. Prof. Parnpen Viriyavejakul
76	Causes of diarrhea in HIV/AIDS patients	Mahidol University	Assoc. Prof. Parnpen Viriyavejakul
	Department of Tropical Pediatrics		
77	A phase II, pilot, randomized, open-label, single-center study to evaluate immunogenicity and safety after PCECV rabies vaccine (Rabipur^{R}) administered concomitantly with Japanesse encephalitis vaccine as a pre-exposure regimen in 12 to 18 month old toddlers in Thailand	Chiron Vaccines, Co, Ltd., Italy	Prof. Arunee Sabchareon
78	Safety and immunogenicity of tetravalent dengue vaccine formulations in Thai adult volunteers: evaluation of three-year persistence	Aventis Pasteur (France)	Assoc. Prof. Pornthep Chanthavanich
79	Immunogenicity and adverse reaction of liquid form of Japanese encephalitis vaccine (Beijing strain) in healthy Thai children	Government Pharmaceutical Organization, Thailand	Assoc. Prof. Pornthep Chanthavanich
80	Follow up of Thai school children immunized with live attenuated tetravalent dengue vaccine 3 to 8 years ago: current immunity response and history of serious medical events since vaccination (EPI 10)	Aventis Pasteur (France)	Assoc. Prof. Pornthep Chanthavanich
81	Health problems, knowledge, attitudes and practices of children in Saiyok District, Kanchanaburi Province	Mahidol University	Assoc. Prof. Pornthep Chanthavanich
82	Early immune response to multi-sites intramuscular injection of purified Vero cell rabies vaccine (PVRN) for rabies post-exposure treatment (RAB 24)	Aventis Pasteur (Thailand)	Assoc. Prof. Pornthep Chanthavanich
83	Single dose therapy for treatment of *Giardia* infection in children	Mahidol University	Assoc. Prof. Krisana Pengsaa
84	Dengue antibodies in Thai infants: age-specific seroprevalence and kinetics of transplacentally transferred dengue antibodies (EPI 11)	Aventis Pasteur (France)	Assoc. Prof. Krisana Pengsaa
85	Clinical efficacy and pharmacokinetics of suppositoried artesunate combined with mefloquine in the treatment of uncomplicated childhood falciparum malaria	Department of Tropical Pediatrics	Assoc. Prof. Chukiat Sirivichayakul
86	A comparative study of the efficacy and ease of administering salbutamol delivered from conventional meter dose inhalers and easyhaler in asthmatic Thai children	Mahidol University	Dr. Wimol Nganthavee
87	Prevalence and risk factors of atopic diseases in rural children in Saiyok District, Kanchanaburi Province	Mahidol University	Dr. Wimol Nganthavee
	Department of Tropical Radioisotopes		
88	Studies on serum transcobalamin II in patients with pyrexia of unknown origin	Mahidol University	Miss Cheeraratana Cheeramakara
	Vaccine Trial Centre		
89	Development of new vaccines against cholera due to *Vibro cholerae* 0139 (Part III)	WHO	Assoc. Prof. Punnee Pitisuttithum

No.	Ongoing Research Projects in 2002	Grants	Principal Investigator
	Vaccine Trial Centre (Continued)		
90	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	Walter Reed Army Institute of Research, USA	Assoc. Prof. Punnee Pitisuttithum
91	A phase I/II trial to evaluation the safety and immunogenicity of AIDSVAX™ B/E vaccine in Bangkok, Thailand	VAXGEN Co, Ltd.	Assoc. Prof. Punnee Pitisuttithum
92	Phase I/II trial of Pasteur Merieux Connaught (PMC) live recombinant ALVAC-HIV (VCP 1521) Priming with Vaxgen gp 120 B/E (AIDVAX™ B/E) Boost in Thai HIV-Seronegative adults	Walter Reed Army Institute of Research, USA	Assoc. Prof. Punnee Pitisuttithum
93	A phase III trial to determine the efficacy of AIDSVAX™ B/E Vaccine in intravenous drug users in Bangkok, Thailand	AIDSVAX	Bangkok AIDS Vaccine Evaluation Group (Assoc. Prof. Punnee Pitisuttithum)
94	A phase III trial of Aventis Pasteur live recombinant ALVAC-HIV (VCP1521) priming with Vaxgen gp 120 B/E (AIDSVAX B/E) boosting in HIV-uninfected Thai adults	Walter Reed Army Institute of Research, USA	Dr. Supachai Rueknggam (Assoc. Prof. Punnee Pitisuttithum)

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(1 October 2001-30 September 2002)

1. Apiwathnasorn C, Prommongkol S, Samung Y, Limrat D, Rojruthai B. Potential for *Anopheles campestris* (Diptera: Culicidae) to Transmit Malaria Parasites in Pa Rai Subdistrict (Aranyaprathet, Sa Kaeo Province), Thailand. *J Med Entomol* 2002;39:583-6.
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5. Chavalitshewinkoon-Petmitr P, Worasing R, Wilairat P. Partial purification of mitochondrial DNA topoisomerase II from *Plasmodium falciparum* and its sensitivity to inhibitors. *Southeast Asian J Trop Med Public Health* 2001;32:733-8.
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9. Chotivanich K, Silamut K, Udomsangpetch R, Stepniewska KA, Pukrittayakamee S, Looareesuwan S, White NJ. *Ex-vivo* short-term culture and developmental assessment of *Plasmodium vivax*. *Trans R Soc Trop Med Hyg* 2001;95:677-80.
10. Chotivanich K, Udomsangpetch R, McGready R, Stephane Proux, Newton P, Pukrittayakamee S, Looareesuwan S, White NJ. Central role of the spleen in malaria parasite clearance. *J Infect Dis* 2002;185:1538-41.
11. Chotivanich K, Udomsangpetch R, Pattanapanyasat K, Chierakul W, Simpson J, Looareesuwan S, White NJ. Hemoglobin E: a balanced polymorphism protective against high parasitemias and thus severe *P. falciparum* malaria. *Blood* 2002; 100:1172-6.
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1 seroconversion during a period of high incidence among injection drug users in Bangkok. *J Acquir Immune Defic Syndr* 2002;30:240-7.

15. Hudgens MG, Longini IM Jr, Vanichseni S, Hu DJ, Kitayaporn D, Mock PA, Halloran ME, Satten GA, Choopanya K, Mastro TD. Subtype-specific transmission probabilities for human immunodeficiency virus type 1 among injecting drug users in Bangkok, Thailand. *Am J Epidemiol* 2002;155:159-68.
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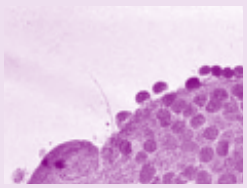
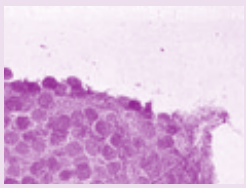


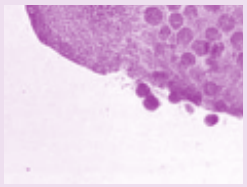
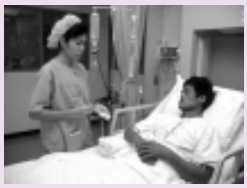
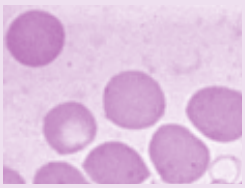
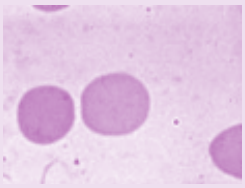


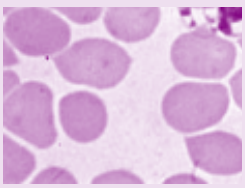
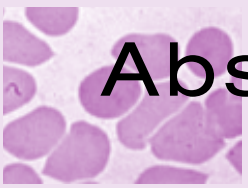

Abstracts

2002

A COMPARISON OF ARTESUNATE ALONE WITH COMBINED ARTESUNATE AND QUININE IN THE PARENTERAL TREATMENT OF ACUTE FALCIPARUM MALARIA.

Newton PN[1,2], Chierakul W[1], Ruangveerayuth R[3], Silamut K[1], Teerapong P[4], Krudsood S[1], Looareesuwan S[1], White NJ[1,2]

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In some areas clinicians have combined parenteral artesunate and quinine in the belief that the 2 drugs would be additive or synergistic in severe malaria. A randomized comparison of the effectiveness of intravenous (i.v.) artesunate versus i.v. artesunate and i.v. quinine together on parasite clearance was conducted in 1998/99 amongst 69 patients with uncomplicated and severe *Plasmodium falciparum* malaria in western Thailand. The parasite clearance time did not differ significantly between the 2 treatment groups (P = 0.12), but adverse events were significantly more frequent in the artesunate plus quinine group (P = 0.05). Quinine did not have a significant antipyretic effect and artesunate did not affect the electrocardiographic QTc interval. There is no benefit evident from combining parenteral administration of these 2 antimalarial drugs in the acute phase of treatment. •

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A CROSS-SECTIONAL STUDY OF INTESTINAL PARASITIC INFECTIONS AMONG SCHOOLCHILDREN IN NAN PROVINCE, NORTHERN THAILAND

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A cross-sectional study of the prevalence of intestinal parasitic infections at eight schools in Bo Klau district and four schools in Chalerm Prakiet district, Nan Province, in January and February, 2001. A total of 1,010 fecal samples were examined using the formalin-ether sedimentation technique. Results revealed that the rate of helminthic infection was 60.0%, while protozoa accounted for 36.2% of infections; mixed infections were common, resulting in a total prevalence of both parasites of 68.1%. Helminthic parasites, listed by frequency of infections, were *Ascaris lumbricoides* (21.7%), hookworm (18.5%), *Trichuris trichiura* (16.3%), *Opisthorchis viverrini* (1.7%), *Strongyloides stercoralis* (0.9%) and *Enterobius vermicularis* (0.9%). The protozoal infections were *Entamoeba coli* (25.8%), *Giardia lamblia* (5.3%), *Endolimax nana* (2.5%), *Entamoeba histolytica* (1.4%), *Blastocystis hominis* (0.8%), *Chilomastix mesnili* (0.3%) and *Iodamoeba butschlii* (0.1%). This study emphasizes the need for improved environmental hygiene ie clean water supplies and enhanced sanitation, in affected communities. Health promotion, by means of a school-based educational approach is recommended; regular check-ups should be implemented, and a continuos program of treatment should be considered. •

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A HUMAN VOLUNTEER CHALLENGE MODEL USING FROZEN BACTERIA OF THE NEW EPIDEMIC SEROTYPE, *V. CHOLERAE* O139 IN THAI VOLUNTEERS

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A total of 35 volunteers were recruited for an IRB-approved inpatient dose-escalation challenge. The goal was to identify a dose that produced and observed cholera attack rate ≥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. Only 2 out of 5 volunteers who received the lowest dose (4.3×10^4 cfu) had diarrhea. As the inoculum size increased, the attack rate of diarrhea increased to 3-4 of 5 volunteers. At the highest dose tested, approximately 5×10^7 cfu, the attack rate was 73%. We recommend the use of frozen *V. cholera* O139 in a human experimental challenge model to assess cholera vaccine efficacy (VE) in a cholera endemic area but with 4 days observation period before initiation of tetracycline to allow assessment of severity. •

Published in: Vaccine 2001;20:920-5.

A PILOT FIELD TRIAL OF AN *IN VITRO* DRUG SUSCEPTIBILITY TEST USING ANAEROPACK® MALARIA CULTURE SYSTEM IN THAI-MYANMAR BORDER

Hatabu T[1,2], Kawazu S[1], Kojima S[3], Singhasivanon P[4], Krudsood S[4], Looareesuwan S[4], Kano S[1]

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Since chloroquine-resistant *Plasmodium (P.) falciparum* was first reported in 1959 in Thailand, it has developed resistance to all commonly used drugs. Development and its expanding distribution of multi-drug resistant *P. falciparum* is now a major public health problem word wide, with prophylactic and therapeutic implications. Therefore, evidence-based detection of drug-resistant parasites is important for the accurate evaluation of susceptibility against the antimalarial drugs. However, isolation of the fresh parasites for *in vitro* drug susceptibility test is often difficult in the field because of the limited experimental conditions needed for the test. *In vitro* susceptibility test are likely to be conducted but they sometimes fail because of the difficulties in following up the patients. In fact, we sometimes don't know whether the drug concentration has been successfully attained in the patients' blood. Therefore in *in vitro* test are indispensable for us to know bthe exact degree of resistance acquired by the parasites. •

Submitted

A RANDOMIZED TRIAL OF INTRAVENOUS QUININE, INTRAVENOUS ARTESUNATE OR INTRAMUSCULAR ARTEMETHER FOR THE TREATMENT OF SEVERE MALARIA IN THAILAND

Krudsood S[1], Looareesuwan S[2], Wilairatana P[2], Wadmanee N[2], Treeprasertsuk S[2], Silachumroon U[2], Tosukhowong T[2], Susomboon P[2], Gourdeuk VR[3], Brittenham GM[4]

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The optimal choice of antimalarial drugs for the treatment of severe falciparum malaria remains problematic. Artemisinin derivatives (intramuscular artemether and intravenous artesunate) are the most useful drug in Southeast Asian but are not available in all areas. Quinine is generally available but resistance (1, 2) and poor response to this drug have been encountered. Two large randomized trials have compared the mortality rate of intravenous quinine and intramuscular artemether in severe malaria, one in the Gambia (3) and the other in Vietnam (4). However, there is no trial comparing artemisinin derivatives given the intravenous or intramuscular routes, clinical and parasites responses and the effects of adding mefloquine high dose at the end of the treatment course to intravenous quinine yet. We report here a randomized clinical trial of the three drugs alone and with mefloquine high dose at the end of artesunate/artemether in severe falciparum malaria. The aims of study are to see the efficacy and tolerability of the most use of available antimalarial drugs (artesunate i.v./ artemether i.m./ quinine i.v.) for severe malaria on the initial responses and the effect of sequential treatment will mefloquine on day 28. •

Submitted

AN OPEN RANDOMIZED CLINICAL TRIAL OF ARTECOM® *VS* ARTESUNATE-MEFLOQUINE IN THE TREATMENT OF ACUTE UNCOMPLICATED FALCIPARUM MALARIA IN THAILAND

Wilairatana P, Krudsood S, Chalermrut K, Pengruksa C, Srivilairit S, Silachamroon U, Treeprasertsuk S, Looareesuwan S

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

The efficacy and safety of Artecom® were assessed in an open randomized trial in adults presenting with acute, uncomplicated *Plasmodium falciparum* malaria in Thailand. Three hundred and fifty-two patients were randomly enrolled at the ratio of 2:1 into group A:B and received Artecom® (group A) and the standard combination of artesunate and mefloquine (group B) respectively. All patients had rapid initial clinical and parasitological responses. There were no significant differences in fever clearance time and parasite clearance time between the two groups. The 28 day cure rates were high as 97% in both groups. Artecom® was effective and well tolerated as artesunate-mefloquine, the current treatment in this area of multidrug-resistant *P. falciparum* malaria. •

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ARTEMISININ ANTIMALARIALS IN PREGNANCY: A PROSPECTIVE TREATMENT STUDY OF 539 EPISODES OF MULTIDRUG-RESISTANT PLASMODIUM FALCIPARUM

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The emergence and spread of multidrug-resistant *Plasmodium falciparum* compromises the treatment of malaria, especially during pregnancy, where the choice of antimalarials is already limited. Artesunate (n=528) or artemether (n=11) was used to treat 539 episodes of acute *P. falciparum* malaria in 461 pregnant women, including 44 first-trimester episodes. Most patients (310 [57.5%]) received re-treatments after earlier treatment with quinine or mefloquine. By use of survival analysis, the cumulative artemisinin failure rate for primary infections was 6.6% (95% confidence interval, 1.0-12.3), compared with the re-treatment failure rate of 21.7% (95% confidence interval, 15.4-28.0; P=.004). The artemisinins were well tolerated with no evidence of adverse effects. Birth outcomes did not differ significantly to community rates for abortion, stillbirth, congenital abnormality, and mean gestation at delivery. These results are reassuring, but further information about the safety of these valuable antimalarials in pregnancy is needed. •

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ARTESUNATE AND MEFLOQUINE GIVEN SIMULTANEOUSLY FOR 3 DAYS VIA A PREPACKED BLISTER IS EQUALLY EFFECTIVE AND TOLERATED AS A STANDARD SEQUENTIAL TREATMENT OF UNCOMPLICATED ACUTE *PLASMODIUM FALCIPARUM* MALARIA: RANDOMIZED, DOUBLE-BLIND STUDY IN THAILAND

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Currently the combination of artesunate and mefloquine is one of the most effective treatments against multidrug-resistant *P. falciparum* malaria. In order to improve patient compliance to such a combination, the two agents have been combined in a prepacked single blister and the patients were instructed to simultaneously co-administer the drugs once daily for three days. In the present randomized, double-blind, parallel group, comparative, single center study in Thailand, this concept was investigated in 204 adults and children with acute, uncomplicated *P. falciparum* malaria. Patients were randomized to two treatment groups and received once daily over three days: Group A: artesunate 4-5 mg/kg/day and mefloquine 25 mg/kg total dose (~8.5 mg/kg/day) simultaneously; Group B: artesunate 4-5 mg/kg/day and mefloquine 25 mg/kg total dose sequentially (i.e., no mefloquine dose on the first day, 15 mg/kg on the second day and 10 mg/kg on the third day).

Both treatment groups did not relevantly differ as for baseline demographic and clinical characteristics. Intent to treat analysis revealed a cure rate at day 28 (primary endpoint) of 100% in group A and 99% in group B (n.s.). The secondary endpoints mean time to fever clearance (group A 34 h vs. B 31 h) and mean time to parasite clearance (group A 44 h vs. B 48 h) were similar between groups (both n.s.). Tolerability was good in both treatment groups with no difference in the overall incidence of AEs. There was a low incidence of nausea/vomiting (4.9% in both groups) and CNS side effects (4.9% [A] vs. 8.8% [B]) which were comparable between groups and generally of mild nature. In conclusion, the 3-day combination of artesunate and mefloquine (Artequin,) with introduction of mefloquine already on day 1 offers a practical dosing regimen, which is highly effective and well tolerated in patients of different age suffering from uncomplicated *P. falciparum*. It is likely that the prepacked blister approach translates clinically into a better patient compliance thereby contributing to limit the development of drug resistance. •

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ASSESSMENT OF THE NEUROTOXICITY OF ORAL DIHYDROARTEMISININ IN MICE

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High doses of the oil-soluble antimalarial artemisinin derivatives artemether and arteether, given by intramuscular injection to experimental mammals, produce an unusual pattern of selective damage to brainstem centres predominantly involved in auditory processing and vestibular reflexes. We have shown recently, in adult Swiss albino mice, that constant exposure either from depot intramuscular injection of oil-based artemisinin derivatives, or constant oral intake carries relatively greater neurotoxic potential than other methods of drug administration. Using the same model, oral dihydroartemisinin suspended in water was administered once or twice daily at different doses ranging from 50 to 300 mg/kg/day for 28 days. The neurotoxic potential of the oral dihydroartemisinin was assessed and compared to that of oral artemether and artesunate. Oral artemether, artesunate, and dihydroartemisinin had similar neurotoxic effects with no significant clinical or neuropathological evidence of toxicity at doses below 200 mg/kg/day. These data indicate that once and twice daily oral administration of artemether, artesunate and dihydroartemisinin is relatively safe when compared to intramuscular administration of the oil-based compounds. •

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ASSOCIATION OF ADHESION MOLECULE PECAM-1/CD31 POLYMORPHISM WITH SUSCEPTIBILITY TO CEREBRAL MALARIA IN THAIS

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Adhesion molecules on endothelial cells are known to be important ligands for malaria infected red blood cells (PRBC) [Mol Biochem Parasitol, 76, (1996) 1], and may be involved in the pathogenic process of cerebral malaria (CM) which is the most serious complication of falciparum malaria, through enhancing micro embolism or sequestration in the capillaries of the brain. PECAM-1/CD31 is one of these candidate ligands and is coded by a polymorphic gene. Two hundred and ten Thai malaria patients (43 cerebral, 89 severe and 78 uncomplicated) were analyzed for their genetic polymorphism of CD31 to examine the clinical relationship between the disease and specific genotypes. Four alleles were defined 125 valine (V)-563 asparagine (N); 125V-563 serine (S); 125 leucine (L)-563N; and 125L-563S. We found that the frequency of the 125 V/V 563 N/N genotype was significantly high in CM patients as compared with severe cases without CM ($P<0.01$, OR=2.92), suggesting that this genotype is one of the risk factors for CM. •

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ASSOCIATION OF GENETIC MUTATIONS IN *PLASMODIUM VIVAX DHFR* WITH RESISTANCE TO SULFADOXINE-PYRIMETHAMINE: GEOGRAPHICAL AND CLINICAL CORRELATES

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Mutations in the *Plasmodium falciparum* gene (dhfr) encoding dihydrofolate reductase are associated with resistance to antifols. *Plasmodium vivax*, the more prevalent malaria parasite in Asia and the Americas, is considered antifol resistant. Functional polymorphisms in the *dhfr* gene of *P. vivax* (*pvdhfr*) were assessed by PCR-restriction fragment length polymorphism using blood samples taken from 125 patients with acute vivax malaria from three widely separated locations, Thailand (n = 100), India (n = 16), and Madagascar and the Comoros Islands (n = 9). Upon evaluation of the three important codons (encoding residues 57, 58, and 117) of *P. vivax dhfr* (*pvdhfr*), double- or triple-mutation genotypes were found in all but one case from Thailand (99%), in only three cases from India (19%) and in no cases from Madagascar or the Comoros Islands ($P < 0.0001$). The *dhfr* PCR products of *P. vivax* from 32 Thai patients treated with the antifolate sulfadoxine-pyrimethamine (S-P) were investigated. All samples showed either double (53%) or triple (47%) mutations. Following treatment, 34% of the patients had early treatment failures and only 10 (31%) of the patients cleared their parasitemias for 28 days. There were no significant differences in cure rates, but parasite reduction ratios at 48 h were significantly lower for patients whose samples showed triple mutations than for those whose samples showed double mutations ($P = 0.01$). The three mutations at the *pvdhfr* codons for residues 57, 58, and 117 are associated with high levels of S-P resistance in *P. vivax*. These mutations presumably arose from selection pressure. •

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ASSOCIATION OF HELMINTH INFECTION WITH DECREASED RETICULOCYTE COUNTS AND HEMOGLOBIN CONCENTRATION IN THAI FALCIPARUM MALARIA

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Following a study showing an association between Ascaris and protection from cerebral malaria, we conducted a cross-sectional study comparing admission hemoglobin concentrations in relation to exposure to helminth infection in 2 separate groups of patients: 111 cerebral malaria cases and 180 mild *Plasmodium falciparum* malaria cases. Hookworm infections were excluded. Mean hemoglobin concentrations were significantly lower in helminth-infected patients compared to those without helminths, both in the cerebral malaria group (10.1+/-3 [n = 47] versus 11.2+/-2.4 g/dl [n = 64], $P = 0.04$) and the mild malaria group (11+/-2.5 [n = 89] vs 12.2+/-2.7 g/dl [n = 91], $P = 0.004$). Median reticulocyte counts, only available in the cerebral malaria group, were lower in helminth-infected patients compared to those without helminths (15,340/23,760 per microl, $P = 0.03$). Adjustments for confounders such as body mass index did not alter these associations. These data are consistent with a mechanism causing anemia linked to differences in the immune response of helminth-infected patients during malaria. •

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ASSOCIATION OF HELMINTH INFECTIONS WITH INCREASED GAMETOCYTE CARRIAGE DURING MILD FALCIPARUM MALARIA IN THAILAND

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The objective of this study was to determine whether pre-existing helminth infections could affect sexual forms of *Plasmodium falciparum*. A cross-sectional case record study compared 120 mild *P. 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 (95% confidence interval = 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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ASSOCIATION OF HEPATOMEGALY AND JAUNDICE WITH ACUTE RENAL FAILURE BUT NOT WITH CEREBRAL MALARIA IN SEVERE FALCIPARUM MALARIA IN THAILAND

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We conducted a case record study comparing liver tests abnormalities in 20 malaria-related acute renal failure cases without cerebral malaria, 52 cerebral malaria cases without other organ impairment, 189 cases of nonsevere malaria associated with a high parasite burden, and 131 cases of mild Plasmodiumfalciparum malaria. Jaundice and hepatomegaly were significantly associated with renal failure (adjusted odds ratio [AOR], 3.3, 95% confidence interval [CI], 1.3-8.6, P = 0.01; and AOR, 1.7 95% CI, 1.13-2.4, P = 0.01) but not with cerebral malaria (AOR, 1, 95% CI, 0.5-2, P = 0.8; and AOR, 1.08, 95% CI, 0.8-1.8, P = 0.5). Patients with acute renal failure were significantly older and had increased liver abnormalities compared with other groups. Although an increase in the proportion of mature schizonts over ring forms was significantly associated with cerebral malaria, it did not seem to have affected acute renal failure. These results suggested that cytoadherence was not the main determinant for renal failure and that jaundice itself may have potentiated the effects of hypovolemia. •

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ASSOCIATION OF INTESTINAL HELMINTHS WITH DECREASED LIVER SIZE AND SCD23 CONCENTRATIONS DURING FALCIPARUM MALARIA

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Liver enlargement is a common feature of malaria (Manson *et al.*, 1996). Its pathophysiology, however, is not clear. Erythrocytic and may be preerythrocytic parasite multiplication are thought to lead to mononuclear proliferation and non-specific hepatitis (Ramachandran and Perera, 1976). Intrahepatic sequestration of parasitized red blood cells may also contribute to hepatomegaly.

Nitric oxide (NO) is a key mediator of anti malarial immunity (Anstey *et al*, 1996) but also has antiproliferative properties (Taylor-Robinson and Smith, 1999). Its generation requires the induction of the inducible NO synthase (iNOS), which can be achieved by a variety of immune mediators (Bogdan, 2001). Among these, the F_{ce}RII/ CD23 receptor, upon ligation, can generate large quantities of NO (Dugas *et al*, 1995. In the absence of ligands, CD23 is normally physiologically cleaved into soluble CD23 (sCD23) (Delespeses *et al*, 1991), which has pleiotropic properties and is measurable in the plasma. On the contrary, upon ligation, the membrane CD23 receptor is stabilized, and cleavage is reduced (Pritchard *et al*, 1993). Recently, it was shown that helminth-infections were associated with protection from cerebral malaria. Adjustments for socioeconomic, nutritional factors and malaria history did not alter this association (Nacher *et al*, 2001a). It was suggested that the CD23/NO pathway had a protective role against cytoadherence and severe complications of malaria (Nacher *et al*, 2000; 2002). It was shown in Thailand that helminth-infected patients had a lower incidence of renal failure and jaundice during malaria (Nacher *et al*, 2001b), and that helminth-infected had higher reactive nitrogen intermediates concentrations (RNI), which correlated with IgE and sCD23 (Nacher *et al*, 2002). Here, the objective was to look for a possible influence of helminthes and the CD23/NO pathway on liver size. •

Submitted

ASSOCIATION OF SPLENOMEGALY WITH CEREBRAL MALARIA AND DECREASED CONCENTRATIONS OF REACTIVE NITROGEN INTERMEDIATES IN THAILAND

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The role of the spleen during *Plasmodium falciparum* malaria in humans is unclear. In Thailand, malaria transmission is low and splenomegaly is rarer than in high transmission areas. We compared the prevalence of splenomegaly between 52 cerebral malaria patients and 191 patients without complications despite a high parasite biomass. We also measured concentrations of reactive nitrogen intermediates (RNIs) in a fraction of these cases recruited in 1998 (24 cerebral malaria and 56 controls). Splenomegaly was significantly associated with cerebral malaria (adjusted odds ratio = 2.07 [95% confidence interval = 1-4.2]; P = 0.048). There was a linear trend for this association (P = 0.0003). After adjusting for potential confounders, concentrations of RNIs were significantly lower in the presence of splenomegaly (P = 0.01). These results suggest that in humans, as in animal models, the spleen may be involved in the pathogenesis of cerebral malaria. The relationship between RNI concentrations and the spleen suggest that nitric oxide may have a regulating role in the complex physiology of the spleen during malaria. •

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CENTRAL ROLE OF THE SPLEEN IN MALARIA PARASITE CLEARANCE

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In acute malaria, red blood cells (RBCs) that have been parasitized, but no longer contain a malaria parasite, are found in the circulation (ring-infected erythrocyte surface antigen [RESA]-RBCs). These are thought to arise by splenic removal of dead or damaged intraerythrocytic parasites and return of the intact RBCs to the circulation. In a study of 5 patients with acute falciparum malaria who had previously undergone splenectomy, it was found that none of these 5 patients had any circulating RESA-RBCs, in contrast to the uniform finding of RESA-RBCs in all patients with acute malaria and intact spleens. Parasite clearance after artesunate treatment was markedly prolonged, although the parasites appeared to be dead and could not be cultured *ex vivo*. These observations confirm the central role of the spleen in the clearance of parasitized RBCs after antimalarial treatment with an artemisinin derivative. Current criteria for high-grade antimalarial drug resistance that are based on changes in parasitemia are not appropriate for asplenic patients. •

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CLINICAL TRIAL OF DESFEROXAMINE AND ARTESUNATE IN ADULTS WITH SEVERE BUT NOT CEREBRAL FALCIPARUM MALARIA

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Cerebral malaria caries high mortality rate (10-80%) even though a potent antimalarial drug has been used (1, 2, 3) and yet pathogenesis and pathophysiology of cerebral is still unclear. With an effective adjuvant therapy and its early implication, mortality rate could be reduced. In Thailand, various adjuvant such as dexamethasone, pentoxifylline and antibody to tumor necrotic factor failed to show their efficacous (4, 5, 6). However, desferoxamine has shown both antimalarial effect (7) and antioxidative process through home which could enhance artemisinine derivatives in killing parasites and protective role in cells in juried. In addition, desferoxamine has shown its protective role in restoring cell injury in cerebral malaria in African children as an evidence of shortening in coma time. In an attempt to investigate desferoxamine in cerebral malaria in adult Thai patients, we reported here the tolerability and safety of desferoxamine in severe malaria (but not cerebral malaria) in adult who were treated with artesunate i.v. •

Submitted

CLINICAL TRIAL OF DEFEROXAMINE AND ARTESUNATE IN CEREBRAL MALARIA

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Cerebral malaria carries high mortality rate ranging between 10-80% (1-4) depend upon its complications. Strictly defined cerebral malaria studied in a hospital at the eastern part of Thailand in 1990 had 20% mortality (2). At the same hospital (5), cerebral malaria with renal failure carried double mortality rate (40%). At a teaching hospital in Thailand (6), cerebral malaria with acute renal failure and pulmonary oedema, the mortality rate was up to 80%. From our earlier study in African children suffering from cerebral malaria treated with quinine with and without desferoxamine, it revealed that recovering from coma of those children treated with quinine i.v. and desferoxamine i.v. was shorten than those treated with i.v. quinine alone (7), Victor & Gary studied in African children NEJM). Our double blind randomized study in adult Thai patients suffering from severe malaria but not cerebral malaria showed that those who were treated with artesunate i.v. together with desferoxamine i.v. for 3 days had clinical and laboratories improved faster than those treated with artesunate i.v. alone (in preparation). In this report, we report here the results of a double-blind clinical trial of desferoxamine in cerebral malaria with material and method followed as our previous study (in preparation) showed the outcome of the some method we randomized study in cerebral malaria patients. •

Submitted

CLINICAL TRIAL OF ORAL ARTESUNATE WITH OR WITHOUT HIGH DOSE PRIMAQUINE FOR THE TREATMENT OF VIVAX MALARIA IN THAILAND

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We studied 801 Thai patients admitted to the Bangkok Hospital for Tropical Diseases with acute, symptomatic *P. vivax* malaria to determine the preferred duration of treatment with oral artesunate and the safety, tolerability and effectiveness of a high dose of primaquine in prevention of relapse. Patients were assigned at random to one of four treatment groups: (i) a 5-day course of artesunate, Group A5; (ii) a 7-day course of artesunate, Group A7; (iii) a 5-day course of artesunate plus a 14-day course of high dose primaquine (0.6mg/kg; maximum dose 30mg), Group A5+P; and (iv) a 7-day course of artesunate plus a 14-day course of high dose primaquine, Group A7+P. During 28 days of observation, *P. vivax* reappeared in the blood of roughly half of those who received artesunate alone (Groups A5 and A7). The addition of primaquine to either the 5- or 7-day treatment with artesunate (Groups A5+P and A7+P) prevented reappearance of vivax malaria in all patients by day 28. Adverse effects were confined to the subpopulation of patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency. Among the 13 patients with G6PD deficiency who completed the 28 day study, high dose primaquine (0.6 mg/kg of base) had to be stopped because of a fall in hematocrit in 4 (31%). Overall, these results provide guidance in the development of a therapeutic regimen for acute malaria in Thailand that can be used in the absence of reliable microscopic diagnosis. •

Submitted

CONTRIBUTION OF HUMORAL IMMUNITY TO THE THERAPEUTIC RESPONSE IN FALCIPARUM MALARIA

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The contribution of humoral immunity to the therapeutic response in acute falciparum malaria was assessed in a case-control study. Forty adult Thai patients with acute falciparum malaria who had subsequent recrudescent infections and 40 patients matched for age, therapeutic regimen, and disease severity who were cured by Day 28 were studied. All cured patients had positive immunoglobulin (Ig) G to ring-infected erythrocyte surface antigen (RESA) in their admission plasma, compared with only 60% of patients who failed to respond to treatment (P < 0.001). The proportion of IgM-positive cases at admission was also higher in the successfully treated group than in the group with failure (70% versus 30%) (P < 0.001). The geometric mean (95% confidence interval) reciprocal IgG titer at admission was significantly higher in cured patients (187.0 [83.5-418.3]) compared with those who experienced treatment failure (11.6 [5.1-26.5]) (P < 0.001). The patients with uncomplicated malaria who were both IgG and IgM positive at admission had significantly shorter fever clearance times and lower admission parasitemia levels compared with those who were negative (P = 0.01 and P = 0.02, respectively). The median (range) *in vitro* parasite multiplication rate was significantly lower in cultures containing positive anti-RESA antibody plasma compared with those containing normal plasma (0.7 [0.1-3.5] versus 2.6 [0.1-12.1]; P < 0.001). These results suggest that antimalarial antibodies may play an important supportive role in the therapeutic response to antimalarial drugs during acute falciparum malaria. •

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DOSE-FINDING AND EFFICACY STUDY FOR I.M. ARTEMOTIL (BETA-ARTEETHER) AND COMPARISON WITH I.M. ARTEMETHER IN ACUTE UNCOMPLICATED *P. FALCIPARUM* MALARIA

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AIMS: The antimalarial efficacy/pharmacodynamics and pharmacokinetics of intramuscular (i.m.) artemotil in Thai patients with acute uncomplicated falciparum malaria were studied to determine effective dose regimens and to compare these with the standard dose regimen of artemether. METHODS: In part I of the study three different artemotil dose regimens were explored in three groups of 6-9 patients for dose finding: 3.2 mg kg-1 on day 0 and 1.6 mg kg-1 on days 1-4 (treatment A), 1.6 mg kg-1 on day 0 and 0.8 mg kg-1 on days 1-4 (treatment B), 3.2 mg kg-1 on day 0 and 0.8 mg kg-1 on days 1-4 (treatment C). In part II of the study, artemotil treatments A and C were compared in three groups of 20-22 patients with standard i.m. artemether treatment: 3.2 mg kg-1 on day 0 and 0.8 mg kg-1 on days 1-4 (treatment R). RESULTS: Full parasite clearance was achieved in all patients in Part I, but parasite clearance time (PCT) and fever clearance time (FCT) tended to be longer in treatment B. Also the incidence of recrudescence before day 28 (RI) tended to be higher for treatment B. In part II, the mean PCT for each of the two artemotil treatments (52 and 55 h, respectively) was significantly longer than for artemether (43 h). The 95% CI for the difference A vs R was 0, 16 h (P=0.0408) and for difference C vs R it was 2, 19 h (P=0.0140). FCT was similar for the three treatments. The incidence of RI ranged from 5 out of 19 for treatment C to 3 out of 20 for treatment R. Plasma concentration-time profiles of artemotil indicated an irregular and variable rate of absorption after i.m. injection. A late onset of parasite clearance was associated with delayed absorption and/or very low initial artemotil plasma concentrations. Pharmacokinetic-pharmacodynamic evaluations supported a relationship between the rate of parasite clearance and exposure to artemotil during approximately the first 2 days of treatment, and suggested that artemotil has a slower rate of absorption than artemether. Safety assessment, including neurological and audiometric examinations showed no clinically relevant findings. Adverse events before and during treatment included headache, dizziness, nausea, vomiting

and abdominal pain. These are characteristic of acute malaria infections and resolved during treatment. CONCLUSIONS: The optimum dose regimen for artemotil in this study was identical to the standard dose regimen of artemether. The findings that artemotil is more slowly absorbed from the i.m. injection site than artemether, and that early systemic availability may be insufficient for an immediate onset of parasite clearance contributed to the decision to choose a higher loading dose of artemotil (divided over two injection sites) and to omit the fifth dose in later studies. With this optimized dosing schedule, the more pronounced depot characteristics of i.m. artemotil can be an advantage, since it may allow shorter hospitalization. •

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EFFECT OF PRIMAQUINE STANDARD DOSE (15 MG/DAY FOR 14 DAYS) IN THE TREATMENT OF VIVAX MALARIA PATIENTS IN THAILAND

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Primaquine (8-aminoquinoline), the only effective drug to prevent relapses of the persistent liver forms of *Plasmodium vivax* and *Plasmodium ovale*, can induce hemolytic anemia in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency. The severity varies considerably among affected individuals. Three hundred and sixty-four *Plasmodium vivax* cases (342 G6PD-normal and 22 G6PD-deficient) were given a 3-day course of chloroquine (total dose 1,500 mg) followed by primaquine 15 mg a day for 14 days and completed a 28-day follow-up. All G6PD-deficient patients were male; there were no relapses or serious adverse events during the study. Although a significant decrease in hematocrit levels and an increase in the percent reduction of hematocrit levels were observed on day 7 (34.9+/-5.0 vs 26.7+/-5.4; (-1.2)+/-14.4 vs (-24.5) +/-13.9 respectively) and on day 14 (35.7+/-4.3 vs 30.9+/-3.1; 1.6+/-17.8 vs (-11.0) +/-19.3 respectively) blood transfusion was not required. Daily doses of 15 mg of primaquine for 14 days following a full course of chloroquine when prescribed to Thai G6PD deficient patients where Mahidol variant is predominant, are relatively safe. •

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EX-VIVO SHORT-TERM CULTURE AND DEVELOPMENTAL ASSESSMENT OF *PLASMODIUM VIVAX*

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A simple reproducible method for short-term *ex-vivo Plasmodium vivax* culture is presented in which glucose, ascorbic acid, thiamine, hypoxanthine, and 50% human AB+ serum are added to the standard *P. falciparum in-vitro* culture medium. Culture of freshly obtained blood samples from patients with acute vivax malaria with > 0.5% parasitaemia resulted in > 95% complete schizogony. Culture could be continued for 5-6 cycles without the addition of red cells. Criteria for staging the erythrocytic development of *P. vivax* in the first schizogonic cycle based on synchronous *ex-vivo* culture are presented. The asexual cycle was divided into 7 morphological stages: tiny ring (0-6 h), small ring (6-12 h), large ring (12-18 h), early trophozoite (18-28 h), late trophozoite (28-36 h), early schizont (36-42 h) and mature schizont (42-48 h). This simple method of culturing *P. vivax ex vivo* is suitable for antimalarial susceptibility and immunoparasitology studies. •

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FEBRILE TEMPERATURES INDUCE CYTOADHERENCE OF RING-STAGE *PLASMODIUM FALCIPARUM*-INFECTED ERYTHROCYTES

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In falciparum malaria, the malaria parasite induces changes at the infected red blood cell surface that lead to adherence to vascular endothelium and other red blood cells. As a result, the more mature stages of *Plasmodium falciparum* are sequestered in the microvasculature and cause vital organ dysfunction, whereas the ring stages circulate in the blood stream. Malaria is characterized by fever. We have studied the effect of febrile temperatures on the cytoadherence *in vitro* of *P. falciparum*-infected erythrocytes. Freshly obtained ring-stage-infected red blood cells from 10 patients with acute falciparum malaria did not adhere to the principle vascular adherence receptors CD36 or intercellular adhesion molecule-1 (ICAM-1). However, after a brief period of heating to 40 degrees C, all ring-infected red blood cells adhered to CD36, and some isolates adhered to ICAM-1, whereas controls incubated at 37 degrees C did not. Heating to 40 degrees C accelerated cytoadherence and doubled the maximum cytoadherence observed ($P < 0.01$). Erythrocytes infected by ring-stages of the ICAM-1 binding clone A4var also did not cytoadhere at 37 degrees C, but after heating to febrile temperatures bound to both CD36 and ICAM-1. Adherence of red blood cells infected with trophozoites was also increased considerably by brief heating. The factor responsible for heat induced adherence was shown to be the parasite derived variant surface protein PfEMP-1. RNA analysis showed that levels of var mRNA did not differ between heated and unheated ring-stage parasites. Thus fever-induced adherence appeared to involve increased trafficking of PfEMP-1 to the erythrocyte membrane. Fever induced cytoadherence is likely to have important pathological consequences and may explain both clinical deterioration with fever in severe malaria and the effects of antipyretics on parasite clearance. •

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FOOD-AND WATER-BORNE PARASITIC ZOONOSES IN THE 21ST CENTURY

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This, the third in a series of Seminars, had as its theme the prospects for improved mitigation of food (and water)-borne parasitic zoonoses (FBPZ) in the coming decade. The instigation of this series of conferences focusing on Asia, grew out of a recognition in the 1980s that problems related to FBPZ, when considered in the aggregate, were substantial, and for this region, appeared to be increasing inspite of economic growth and development. Concern existed over the unpredictable consequences of population growth and development, forces which can have an impact on food production systems, the demands for water, and which can cause dramatic demographic and social changes such as urbanization, travel, immigration, and political shift. The importance of these factors lies in their potential adverse influences on the Human-Domestic animal-Wildlife diseases continuum characteristic of zoonoses. Obvious examples are the movement of people and animals, the creation of water cachements for agriculture and power, and because of increased demand for meat (especially exotic foods), intensification of livestock production, with their impacts on water safety and environmental quality. Thus, these FBPZ meetings were created around specific objectives: (1) To determine the extent of FBPZ, especially in Asia; (2) to stimulate greater epidemiological study; (3) to identify and address research needs; and (4) to facilitate the development of practical and sustainable control projects. The Seminar organizers also wanted the opportunity to increase collaboration between researchers and public health workers throughout the

region (and world), to improve access to knowledge and data on the status of FBPZ in various countries, and to raise the visibility and awareness of FBPZ both within and outside of the scientific community.

Looking back from this 3rd Seminar to the 1st Seminar in 1990, it is clear that much has been achieved in meeting the original objectives. The presentations and discussions at this meeting reflected major advances in the understanding of the epidemiology of FBPZ in the region, in devising effective educational tools and strategies, in the development of reliable diagnostic tools, in vaccine development for certain zoonoses, and in the development of new approaches to effective control. The latter was especially prominent at this meeting, reflecting the maturing of the FBPZ research agenda. The following are only a few highlights pertaining to these aspects. Because of the large number of participants (over 600), it is beyond the scope of this brief report to summarize all of the presentations and discussions. A complete record of the papers and lectures for this 3rd Seminar will be published in 2001 by *the Southeast Asian Journal for Tropical Medicine and Public Health*. •

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GLOBAL CAMPAIGN TO ERADICATE MALARIA. MALARIA IS PARADIGM OF AN EMERGENT DISEASE

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One of lessons is that any chemotherapeutic, prophylactic, or insecticide based tool has a finite duration of efficacy: chloroquine and dicophane (DDT) rapidly induced resistance in *Plasmodium spp and Anopheles spp* respectively. These organisms reproduce rapidly and as vector/parasite systems have an unrivalled capacity to change, have coevolved an efficient host-parasite relationship, and are hugely diverse below the species level. *Anopheles* adapts rapidly to ecological, environmental, and climate change; such change is often local and operationally relevant to malaria control. The development of drug and insecticide resistance and ecological and demographic change will outstrip the capacity of any health system to respond even if human resources were available to implement changes in policy on the basis of good evidence. •

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HAEMATOPOIETIC FEATURES OF THE BONE MARROW *OF PLASMODIUM FALCIPARUM*-INFECTED PATIENTS

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Mechanism of anaemia in severe falciparum malaria is incompletely understood. The purpose of this study was to determine whether apoptosis in erythroid lineage attributes causing anaemia in falciparum malaria. Bone marrow aspirates from 8 severe falciparum malaria patients, 3 normal volunteers and 5 retrospective normal bone marrow smears were investigated. By light microscopic study, five of eight hyperparasitemia patients had hypocellular bone marrow and erythroid hypoplasia whereas the other three patients had normal cellularity. The mean myeloid :erythroid ratio of these 5 patients was significantly ($p < 0.05$) higher than that of normal. Apoptosis of bone marrow nucleated cells (BMNC) was determined from the exposure of phosphaidylserine (PS) on

cell membrane, and DNA fragmentation. The mean percentage of apoptotic BMNC in the patients was significantly (p £ 0.05) lower than that of normal. Whereas the mean percentage of apoptotic erythroid cells alone was neither different from that of normal ($p > 0.05$) nor associated with parasitemia. There was no DNA fragmentation (180-250 bp), confirmed by TUNEL and ultrastructural investigation, in BMNC of both patients and control. This study suggested that destruction of erythroid lineage particularly through apoptosis regulation could not solely account for anaemia in falciparum malaria. •

submitted

HELMINTH INFECTIONS ARE ASSOCIATED WITH PROTECTION FROM CEREBRAL MALARIA AND INCREASED NITROGEN DERIVATIVES CONCENTRATIONS IN THAILAND

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Following a study showing an association between Ascaris and protection from cerebral malaria, we hypothesized helminths may have induced protection through immunoglobulin E (IgE) and the CD23/NO pathway. We compared the prevalence of helminth infections in 67 cerebral malaria patients and 217 hyperparasitemic controls with no complications. For 24 cerebral malaria cases and 56 controls, we compared reactive nitrogen intermediates (RNI) concentrations and their correlations to total IgE and sCD23 concentrations in helminth-infected and noninfected patients. We observed a dose-dependent association between helminth infections and protection from cerebral malaria (adjusted odds ratio [OR] = 0.36, 95% CI = 0.19-0.7, P = 0.002, linear trend P = 0.0007). Helminth-infected controls had higher RNI concentrations than those without helminths: 72 OD +/- 19 SD and 57 OD +/- 20 SD, respectively (P = 0.006). Logistic regression, including interaction terms between RNI and sCD23, showed that an increase of RNI could be both protective and pathogenic depending on the concentration of sCD23. Helminths increasing both the CD23 receptor and its ligand may have a role in the establishment of malaria tolerance through the CD23/NO pathway. •

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HELMINTH INFECTIONS ARE ASSOCIATED WITH PROTECTION FROM MALARIA-RELATED ACUTE RENAL FAILURE AND JAUNDICE IN THAILAND

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Following studies showing an association between helminth infections and protection from cerebral malaria, we compared 22 patients with malaria-associated acute renal failure with 157 patients with moderately severe malaria. Helminths were associated with protection from renal failure (adjusted odds ratio [AOR], 0.16 [0.03-0.85], P = 0.03). Helminth-infected controls were less likely to have jaundice (AOR, 0.39 [0.16-0.96], P = 0.04) or to have peripheral mature schizonts (AOR, 0.2 [0.07-0.62], P = 0.005) than controls without helminths. This suggested that preexisting helminth infections may have been protective by influencing sequestration and obstructive jaundice, 2 possible determinants of acute tubular necrosis. •

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HEMOGLOBIN E: A BALANCED POLYMORPHISM PROTECTIVE AGAINST HIGH PARASITEMIAS AND THUS SEVERE P FALCIPARUM MALARIA

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Hemoglobin E is very common in parts of Southeast Asia. The possible malaria protective effects of this and other inherited hemoglobin abnormalities prevalent in Thailand were assessed in a mixed erythrocyte invasion assay. *In vitro*, starting at 1% parasitemia, *Plasmodium falciparum* preferentially invaded normal (HbAA) compared to abnormal hemoglobin (HbH, AE, EE, HCS, beta-thalassemia E) red cells (HRBCs). The median (range) ratio of parasitization of HRBCs (n = 109) compared to the controls of different major blood groups was 0.40 (0.08, 0.98), less than half that of the normal red cells (NRBCs) compared to their controls 0.88 (0.53, 1.4; P = 0.001). The median (range) parasitemia in the HRBCs was 2% (0.1%-9%) compared to 5.2% (1.2%-16.3%) in the NRBCs (P = 0.001). The proportion of the RBC population that is susceptible to malaria parasite invasion can be described by a selectivity index (SI; observed number of multiply invaded RBCs/ number predicted). The heterozygote AE cells differed markedly from all the other cells tested with invasion restricted to approximately 25% of the RBCs; the median (range) SI was 3.8 (1-15) compared with 0.75 (0.1-0.9) for EE RBCs (P < 0.01). Despite their microcytosis, AE cells are functionally relatively normal in contrast to the RBCs from the other hemoglobinopathies studied. These findings suggest that HbAE erythrocytes have an unidentified membrane abnormality that renders the majority of the RBC population relatively resistant to invasion by *P falciparum*. This would not protect from uncomplicated malaria infections but would prevent the development of heavy parasite burdens and is consistent with the "Haldane" hypothesis of heterozygote protection against severe malaria for hemoglobin E. •

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IDENTIFICATION OF CRYPTIC *COINFECTION* WITH *PLASMODIUM FALCIPARUM* IN PATIENTS PRESENTING WITH VIVAX MALARIA

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In Thailand, approximately 8% of patients treated for vivax malaria are found subsequently to have coinfection with *Plasmodium falciparum*. A *P. falciparum* histidine rich protein 2 (PfHRP-2) dipstick test was evaluated as a predictor of mixed infections with subpatent *P. falciparum* in a prospective study of 238 patients admitted to the hospital with acute vivax malaria. Of these, 23 (10%) had subsequent development of falciparum malaria without reexposure. Patients with cryptic *P. falciparum* infection had a significantly lower mean (standard deviation) hematocrit than those with *P. vivax* alone: 29.6 (7.6%) versus 37.2 (6.4%) (P < 0.0001). Using microscopic appearance of *P. falciparum* after the start of treatment as the reference standard, the PfHRP-2 test was 74% sensitive and 99% specific in predicting mixed infections with subpatent *P. falciparum* parasitemia at presentation. The PfHRP-2 dipstick test may be a useful adjunct to microscopy in areas where mixed infections are common. •

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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 study aimed to determine whether clinically relevant cross-sensitivity of *P. falciparum* existed between artemisinin and mefloquine. Seventy-six 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 ($p = 0.604$; $P < 0.001$). To assess the relevance of this finding for clinical cross-resistance, we used an analytical model 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 suggesting the clinical relevance of *in vitro* cross-sensitivity. •

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INTESTINAL HELMINTHS AND MALNUTRITION ARE INDEPENDENTLY ASSOCIATED WITH PROTECTION FROM CEREBRAL MALARIA IN THAILAND

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Although human infection with *Ascaris* appears to be associated with protection from cerebral malaria, there are many potential socio-economic and nutritional confounders related to helminth infection that need to be considered. In a hospital-based study, 37 cases of cerebral malaria and 61 cases of non-severe malaria with high parasite biomass (i.e. hyperparasitaemia and / or circulating schizonts) answered a structured questionnaire and were screened for intestinal helminthes. Logistic regression was then used to adjust for the potential confounders. The adjusted odds ratios (OR) and their 95% confidence intervals (CI) still showed a significant protective association for helminthes (OR=0.24; CI=0.07-0.78; P=0.02) and malnutrition (OR=0.11; CI=0.02-0.58; P=0.01), with no evidence of interaction between the two. There was also a significant dose-effect trend for the helminth infections (P=0.048).

There results, despite coming from a hospital-based study, indicate that the apparent association between helminthes and protection from cerebral malaria is not the result of socio-economic or nutritional confounders. •

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INVOLVEMENT OF INTERLEUKIN 18 IN SEVERE FALCIPARUM MALARIA

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Serum levels of IL-18, IFN-α, and IgE were determined for 96 patients with falciparum malaria. They were divided into three groups, i.e., uncomplicated, severe, and cerebral malaria (CM) according to WHO criteria (2000). Elevation of IL-18 levels was observed in all of the groups, with a tendency of higher levels in cases with severe malaria throughout the course of the disease. Moreover, there was a significant correlation between IL-18 levels and the extent of parasitemia among patients with severe malaria. However, IL-18 levels decreased more significantly in patients with CM compared to the other groups in the late stage of the disease. Elevated levels of IFN-α were also observed in all groups of patients, especially in those with severe malaria or CM, and the levels in patients with CM remained significantly higher than in those with uncomplicated malaria during the time of day 4 to 7 post treatment, suggesting the involvement of IFN-α in disease severity. Meanwhile, no significant difference was observed in IgE levels between severe and uncomplicated groups, although IgE levels were significantly higher in helminth-infected patients than uninfected patients. These results suggest that IL-18 plays a key role in inducing severe malaria through another pathway, such as elevation of IFN-α rather than its IgE inducing activity. •

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MALARIA IN THAILAND IN FORMER TIMES

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Malaria has existed in Thailand for a long time. Malaria is a tropical disease and, since antiquity, Thailand has had forests in which the malaria vector, the Anopheles mosquito, has lived. Malaria in Thailand was first documented during the reign of King Narai of Ayuthaya (BE 2203-2230). Today, malaria remains an important health problem in Thailand: there are many cases and many fatalities every year, which impose an economic burden of some 2 billion Baht per year on the country. Multidrug-resistant malaria is also an important problem in the country, thus, new effective antimalarials need to be developed to address the problem. •

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MEFLOQUINE SUSCEPTIBILITY OF FRESH ISOLATES *OF PLASMODIUM FALCIPARUM* ON THE SOUTHWESTERN BORDER OF THAILAND

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In *vitro* drug sensitivity tests were performed with mefloquine using blood samples collected from falciparum malaria patients followed the standard methodology for the assessment of the inhibition of schizont maturation. A total of 37 successful fresh isolates demonstrated mean IC50, IC90 and IC99 (with 95% confidence intervals) of 0.036 (0.031-0.041), 0.118 (0.099-0.147) and 0.305 (0.230-0.449) _M, respectively, indicating that all of them were sensitive to mefloquine. This result supports the current first line drug policy, by which the Ministry of Public Health, Thailand recommended mefloquine monotherapy in the southwestern area of Thailand. •

Submitted

MOLECULAR MARKERS FOR CHLOROQUINE-RESISTANT *PLASMODIUM FALCIPARUM* MALARIA IN THAILAND AND LAOS

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Chloroquine-resistant *Plasmodium falciparum* is well documented in Thailand. Laos, however, continues to use chloroquine (CQ) as the first-line therapy for the treatment of *P. falciparum* malaria. The objective of the present study was to determine the prevalence, in these two areas, of the *cg2*, *pfmdr1* and *pfcrt* allelic types that have previously been associated with CQ resistance. Isolates of *P. falciparum* were collected from participants in ongoing treatment studies conducted in Thailand (near the Thai-Cambodian border) and in Laos (Vang Vieng district). The *pfmdr1* and *pfcrt* alleles were characterized by PCR-RFLP and mutations in *cg2* were characterized by PCR and single-stranded-conformation-polymorphism (SSCP) electrophoresis. Eight (32%) of the 25 Laotian isolates but only one (4%) of the 25 Thai isolates were found to contain the *pfmdr1* mutation N86Y ($P = 0.02$). In contrast, the *cg2* polymorphisms previously associated with CQ resistance were present in only 10 of the isolates from Laos but 24 of those from Thailand (40% v. 96%; $P < 0.001$). All the samples from both countries contained the *pfcrt* K76T mutant allele reported to confer resistance to CQ. The results may indicate that drug pressure for the maintenance of the *pfmdr1* and *cg2* alleles varies in intensity in the Thai and Laotian study areas, probably reflecting differences in the national malaria-treatment policies of Thailand and Laos. •

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MULTIDRUG-RESISTANT MALARIA: RESEARCH ON ANTIMALARIALS AND WHERE DO WE GO FROM HERE?

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With the emergence of multidrug-resistant falciparum malaria, new drugs and drugs in combination are urgently needed. However, it may take over five years to discover one new antimalarial drug. Combination of existing effective antimalarials currently may be helpful for increased efficacy of treatment and delayed drug resistance.

Many new antimalarials and new regimes studied at the Hospital for Tropical Diseases include atovaquone alone and in combination with proguanil; artemisinin derivatives alone and in combination with other antimalarials; and tafenoquine for preventing relapse. Artemisinin derivatives such as artesunate, artemether, artemether, and dihydroartemisinin were studied. In general, artemisinin derivatives (12 mg/kg given over 2-3 days) combined with mefloquine (25 mg/kg total dose) comprise a standard treatment of multidrug-resistant falciparum malaria in Thailand. Until proven otherwise, drug combinations are still recommended for all adult patients suffering from acute uncomplicated falciparum malaria contracted in multidrug-resistant areas.

The aim of treatment in uncomplicated falciparum malaria is radical cure. Effective drugs in multidrug-resistant areas include artesunate-mefloquine, artemether-lumefantrine, atovaquone-proguanil, and quinine-tetracycline (or doxycycline). In treatment of severe malaria, early diagnosis and prompt appropriate treatment with potent antimalarials are recommended to save the patient's life. Antimalarial drugs for severe malaria include artemisinin derivatives [such as artesunate (intravenously or intramuscularly or by suppository), artemether (intramuscularly), dihydroartemisinin (suppository)] combination with mefloquine; and quinine (intravenously). Apart from early recognition of malaria complications, supportive treatment also plays an important role in the management of severe malaria. In spite of these efforts, however, mortality from severe malaria is still high. •

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PHARMACOEPIDEMIOLOGY OF ARTEMISININ DERIVATIVES IN BANGKOK HOSPITAL FOR TROPICAL DISEASES

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With the emergence of multidrug resistant falciparum malaria in Thailand, various approaches have been taken. Artemisinin derivatives are potent antimalarials agents available in oral, parenteral and rectal formulations. Drug combinations recommended for treatment of patients suffering from falciparum malaria include artemisinin derivatives plus mefloquine for severe falciparum malaria, and artemisinin derivatives plus mefloquine or artemether-lumefantrine for uncomplicated falciparum malaria. The cure rate was high with no serious adverse effect. •

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PLASMODIUM VIVAX MALARIA IN SOUTHEAST IRAN IN 1999-2001: ESTABLISHING THE RESPONSE TO CHLOROQUINE *IN VITRO* AND *IN VIVO*

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Chloroquine-resistant *Plasmodium vivax* is emerging in Oceania, Asia and Latin America. The drug sensitivity of *P. vivax* to chloroquine both *in vivo* and *in vitro* in the southern part of Iran was assessed; chloroquine-resistant *Plasmodium falciparum* has already been documented in this area. The *in vitro* sensitivity of 39 *P. vivax* isolates was assessed: the mean IC50 and IC90 were 189 ng/ml and 698 ng/ml blood respectively; for *in vivo* testing, all 39 vivax malaria patients were treated with a standard regimen of choloquine and followed-up at 28 days: the mean parasite clearance time was 67.2±22.5 hours. The *in vitro* development of young parasites to mature schizonts in standard test medium was compared with that obtained in McCoy's 5A medium: no significant difference was observed. Synchronization of the blood-stage parasites was performed according to Lambros's method: the method was not suitable because it was detrimental to the parasites. A number of *in vitro* test were performed using both our own laboratory-predosed microplates and WHO microplates: there was no significant difference between the results. •

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PLASMODIUM VIVAX: POLYMERASE CHAIN REACTION AMPLIFICATION ARTIFACTS LIMIT THE SUITABILITY OF *PVGAM1* AS A GENETIC MARKER

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Plasmodium *vivax* is the most prevalent of the four human malaria parasites. The morbidity from malaria in endemic areas of Central and South America, North Africa, the Middle East and the sub-Indian continent results primarily from infections by this species. In Thailand as in other parts of Southeast Asia and in Oceania, the prevalcnce of this parasite species rivals that of *Plasmodium falciparum*, and the emergence and spread of *P. vivax* parasites resistant to chloroquine and to Fansidar in these regions, which mirrors ominously that of *P. falciparum*, is of major concern. The availability of polymorphic genetic markers for *P. falciparum* parasites has proven to be of great value in clinical and epidemiological studies. A similar ability to distinguish between different *P. vivax* populations would therefore be desirable. •

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PREDICTIVE ROLE OF LABORATORY AND CLINICAL TREATMENT RESPONSE PARAMETERS AND GLUCOSE-6-PHOSPHATE DEHYDROGENASE STATUS IN THE THERAPY OF FALCIPARUM MALARIA

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Beyond the criteria of success or failure, the treatment response in malaria may be characterized by a number of clinical parameters such as fever and parasite clearance. These factors are influenced by various biochemical and haematological factors and the parasite's drug response. The aim of the study was the determination of the value of treatment response parameters and their relation to laboratory findings in the treatment of falciparum malaria, irrespective of the severity of disease and the treatment used. The study was conducted at the Hospital for Tropical Diseases in Bangkok with 119 inpatients suffering from falciparum malaria. The median fever (FCT), parasite (PCT) and symptom (SCT) clearance times were 29.75, 43.00 and 48.00 hours respectively. Fever clearance was found to be closely associated with the other two response parameters as well as with the parasite count on admission ($P < 0.001$), which was therefore found to be a good predictor for the expected duration of the clinical disease. Another important predictor for the persistence of fever may be the glucose-6-phosphate dehydrogenase (G6PD) status of the patients. Individuals with normal G6PD-values had almost double the FCT as compared to those with G6PD-deficiencies (46.5 versus 27.2 hrs), an indication of a protective role conferred by low G6PD-levels. A positive association between red blood cell count and FCT ($P = 0.009$), may be attributed to a similar protection mediated by anaemia. A possible explanation could lie in the high frequency of haemoglobinopathies in Southeast Asia and their relation to malaria. No comparable associations were noted for PCT and SCT. Particularly the fever clearance was therefore found to be a good indicator of treatment response. Several parasitological and haematological parameters, such as G6PD level and parasitaemia, were identified as reliable predictors of the expected duration of clinical disease in malaria. •

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RANDOMIZED COMPARISON OF QUININE-CLINDAMYCIN VERSUS ARTESUNATE IN THE TREATMENT OF FALCIPARUM MALARIA IN PREGNANCY

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In areas where multidrug-resistant *Plasmodium falciparum* (MDR-Pf) is prevalent, only quinine is known to be safe and effective in pregnant women. On the western border of Thailand, 7 days of supervised quinine (30 mg/kg daily) cures two-thirds of *P. falciparum*-infected women in the 2nd and 3rd trimesters of pregnancy. Artesunate is effective against MDR-Pf and the limited data on its use in pregnancy suggest it is safe. An open randomized comparison of supervised quinine (10 mg salt/kg every 8 h) in combination with clindamycin (5 mg/kg every 8 h) for 7 days (QC7) versus artesunate 2 mg/kg per day for 7 days (A7) was conducted in 1997-2000 in 129 Karen women with acute uncomplicated falciparum malaria in the 2nd or 3rd trimesters of pregnancy. There was no difference in the day-42 cure rates between the QC7 ($n = 65$) and A7 ($n = 64$) regimens with an efficacy of 100% in both, confirmed by parasite genotyping. The A7 regimen was also associated with less gametocyte carriage; the average person-gametocyte-weeks for A7 was 3 (95% CI 0-19) and for QC7 was 39 (95% CI 21-66) per 1000 person-weeks, respectively ($P < 0.01$). There was no difference in gastrointestinal symptoms between the groups but there was significantly more tinnitus in the QC7 group compared to the A7 group

(44.9% vs 8.9%; RR 5.1; 95% CI 1.9-13.5; P < 0.001). The favourable results with quinine-clindamycin mean that there is a useful back-up treatment for women with falciparum malaria who experience quinine and artesunate failures in pregnancy. Adherence to the 7-day regimen and cost (US$18.50 per treatment) are likely to be the main obstacles to this regimen. •

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RECRUDESCENCE IN FALCIPARUM PATIENTS TREATED WITH ARTEMISININ DERIVATIVES IS DEPENDENT ON PARASITE BURDEN NOT ON PARASITE FACTORS

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Artemisinin derivative, especially artesunate, have become first-line antimalarial drugs in Thailand. There is no firm evidence yet of clinically relevant artemisinin resistance. When used as monotherapy, artesunate therapy has been associated with a high treatment failure (recrudescence) rate. In order to determine whether recrudescence might be associated with low-level artemisinin resistance, we attempted to identify risk factors for recrudescence in a cohort of 104 malaria patients treated with artesunate monotherapy, 32 of whom recrudesced. There was no difference in the *in vitro* sensitivities to artesunate between 6 non-recrudescent isolates and paired admission and recrudescent isolates from 16 patients. Also, paired admission and recrudescent isolates from 10 patients were genotyped and only 3 had mutations in *pfmdr1*. On the other hand, patients with admission parasitemias greater than 40,000 per microliter had an 11-fold higher likelihood of recrudescence (adjusted Odds Ratio) compared to patients with lower parasitemias. These results suggest that (1) inherent resistance to artesunate is not associated with artesunate recrudescence and (2) admission parasitemia may be a useful criterion in choosing therapeutic options. •

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SAFETY OF THE INSECT REPELLENT N,N-DIETHYL-M-TOLUAMIDE (DEET) IN PREGNANCY

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The safety of daily application of N, N-diethyl-m-toluamide (DEET) (1.7 g of DEET/day) in the second and third trimesters of pregnancy was assessed as part of a double-blind, randomized, therapeutic trial of insect repellents for the prevention of malaria in pregnancy (n = 897). No adverse neurologic, gastrointestinal, or dermatologic effects were observed for women who applied a median total dose of 214.2 g of DEET per pregnancy (range = 0-345.1 g). DEET crossed the placenta and was detected in 8% (95% confidence interval = 2.6-18.2) of cord blood samples from a randomly selected subgroup of DEET users (n = 50). No adverse effects on survival, growth, or development at birth, or at one year, were found. This is the first study to document the safety of DEET applied regularly in the second and third trimesters of pregnancy. The results suggest that the risk of DEET accumulating in the fetus is low and that DEET is safe to use in later pregnancy. •

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SIGNIFICANT ASSOCIATION OF LONGER FORMS OF CCTTT MICROSATELLITE REPEAT IN THE INDUCIBLE NITRIC OXIDE SYNTHASE PROMOTER WITH SEVERE MALARIA IN THAILAND

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A CCTTT microsatellite repeat in the inducible nitric oxide synthase (iNOS) promoter was analyzed among 256 adult patients with severe *Plasmodium falciparum* malaria and 179 adult patients with mild malaria living in northwestern Thailand. Genotypes with longer forms of the CCTTT repeat (alleles of > or =15 repeats) were significantly associated with severe malaria (odds ratio [OR], 2.14; P = 0.0029, chi(2) test). More interestingly, the summed repeat number of both microsatellite alleles in an individual was found to be a significant risk factor for severe malaria (OR, 1.11; logistic regression analysis, P = 0.0041). The single nucleotide substitution, -954G—>C, in the iNOS promoter was rare in Thai patients with malaria. No variations were detected in the iNOS promoter region containing functional NF-kappaß elements at -5.2, -5.5, -5.8, and -6.1 kb upstream of the iNOS transcriptional start site. Thus, a CCTTT repeat in the iNOS promoter may play a key role in the pathogenesis of severe malaria. •

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THE CLINICAL USE OF ARTEMISININ DERIVATIVES IN THE TREATMENT OF MALARIA

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Malaria is one of the world's most important tropical diseases, causing great human suffering and loss of life in the affected countries. There are four species of *Plasmodia* causing human malaria: *P. falciparum*, *P. vivax*, *P. ovale*, and *P. malariae*. Of the four species of *Plasmodia*, it is *P. falciparum* with which causes the most problems. Mosquito control if often not cost-effective in areas where the disease is most severe and where transmission interruption cannot be sustained. Therefore, current malaria control places emphasis on early diagnosis, treatment with effective antimalarials, and selective use of preventive measures including vector control where they can be sustained. The treatment of malaria has changed over the past two decades in response to declining drug sensitivity in *P. falciparum* and a resurgence of the disease in tropical areas. Some other problems are increasing numbers of severe and cerebral malaria cases, the high cost of drugs, side effects and the need for multiple dose regimens. Although chloroquine was recently the drug of choice in Africa, resistance has now spread to all major malarial-endemic areas. For multidrug resistant *P. falciparum* malaria, the choice of treatment is mefloquine, halofantrine, or quinine plus tetracycline. After mefloquine became the drug of choice in some Southeast Asian countries, *P. falciparum* malaria resistant to mefloquine developed. The alternative treatment with oral quinine or quinidine is not well tolerated. Although the combination of quinine with tetracycline or doxycycline remains more than 85 percent effective nearly everywhere, compliance with seven-day courses of treatment required for resistant *P. falciparum* infections is poor. The second-line drug, a combination of a long-acting sulfonamide (usually sulfadoxine) and pyrimethamine carries a risk of severe side effects and is facing growing resistance. •

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THE EFFECTS OF QUININE AND CHLOROQUINE ANTIMALARIAL TREATMENTS IN THE FIRST TRIMESTER OF PREGNANCY

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Quinine (n = 246) was used to treat uncomplicated *Plasmodium falciparum* and chloroquine (n = 130) was used to treat *P. vivax*, in a total of 376 episodes of malaria in the first trimester of pregnancy, in 300 Karen women (Thailand, 1995-2000). Parasites were still present on day 6 or 7 in 4.7% (11/234) of episodes treated with quinine. The overall 28 day parasite reappearance rate following quinine was 28.7% (60/209) for primary treatments and 44% (11/25) for re-treatments. Quinine treatment resulted in a high rate of gametocyte carriage: person-gametocyte-weeks = 42.5 (95% CI 27.8-62.1) per 1000 woman-weeks. For *P. vivax*, the reappearance rate for all episodes by day 28 was 4.5% (5/111). Significantly more women complained of tinnitus following quinine treatment compared to on admission: 64.5% (78/121) vs 31.6% (59/187), P < 0.001. Using survival analysis, the community rate of spontaneous abortion in women who never had malaria in pregnancy, 17.8% (16.5-19.0), did not differ significantly from rates in women treated with quinine: 22.9% (95% CI 15.5-30.3), or chloroquine: 18.3% (95% CI 9.3-27.3), P = 0.42. Pregnancies exposed to quinine or chloroquine and carried to term did not have increased rates of congenital abnormality, stillbirth or low birthweight. These results suggest that therapeutic doses of quinine and chloroquine are safe to use in the first trimester of pregnancy. •

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THE FUTURE OUTLOOK OF ANTIMALARIAL DRUGS AND RECENT WORK ON THE TREATMENT OF MALARIA

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With the emergence of multidrug-resistant falciparum malaria, new drugs and drugs in combination are urgently needed. New antimalarial drugs investigated at the Hospital for Tropical Diseases of the Faculty of Tropical Medicine at Mahidol University in Bangkok, Thailand in recent years for treatment of uncomplicated and severe falciparum malaria are as follows: atovaquone, and artemisinin derivatives (artesunate, artemether, arteether, and dihydroartemisinin) combined with other antimalarials.Malarone, artemisinin derivatives combined with lumefantrine or doxycycline, and mefloquine combined with tetracycline or doxycycline have been evaluated with improvement of the cure rate in uncomplicated malaria. Artemisinin derivatives intravenously or intrarectally combined with mefloquine may be alternatives to intravenous quinine for treatment of severe malaria. In Thailand, drug treatment for uncomplicated malaria consists of the combinations or artesunate plus mefloquine or artemether plus lumefantrine or quinine plus tetracycline. In treatment of severe malaria, antimalarial drugs of choice are intravenous quinine or artemisinin derivatives. •

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THE TREATMENT OF MALARIA IN THAILAND

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The treatment of uncomplicated malaria is intended to produce a radical cure. One of the following combinations may be used: artesunate (4 mg/kg/day) and mefloquine (8 mg/kg/day) for three days; a fixed dose of artemether and lumefantrine (Coartem®; 20/120 mg tablets; four tablets twice a day for three days for adults weighing more than 35 kg); quinine 10mg/kg eight-hourly and tetracycline 250 mg six-hourly for seven days (or doxycycline 200 mg once a day for seven days) in patients aged eight years and over; a combination of atovaquone and proguanil (Malarone®; four tablets given daily for three days in adults). In severe malaria, early diagnosis and prompt treatment with a potent antimalarial drug are recommended and may prove life-saving. The antimalarial drugs of choice are: intravenous quinine or a parenteral form of an artemisinin derivative (artesunate i.v. or i.m. 2.4 mg/kg followed by 1.2 mg/kg injection at 12 and 24 hours and then daily for five days; artemether i.m. 3.2 mg/kg injection followed by 1.6 mg/kg at 12 and 24 hours and then daily for five days; arteether i.m. [Artemotil®] with the same dose of artemether; artesunate suppository [5 mg/kg] given rectally 12 hourly for three days). Oral artemisinin derivatives (artesunate, artemether, dihydroartemisinin in doses of 4 mg/kg/day) should replace parenteral forms when patients can tolerate oral medication. Oral mefloquine (25 mg/kg divided into two doses eight hours apart) should be given at the end of the artemisinin treatment course to reduce recrudescence. Early recognition of malaria's complications and their adequate treatment also play an important role as these complications (hypoglycemia, pulmonary edema, acute renal failure, metabolic acidosis, convulsions) often increase the mortality rate. Other symptomatic and supportive treatments include the careful monitoring of fluid input and urine output, the provision of good nursing care and the avoidance of harmful adjuvant treatment. In spite of these efforts, mortality from severe malaria is still high. •

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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 1995-98 in 92 adult patients in Thailand with *Plasmodium vivax* malaria. All patients recovered following treatment and the early therapeutic responses were similar among the 4 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; 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 time taken for detection of falciparum malaria was 13 (4) days after starting treatment for vivax malaria. The 28-day cumulative cure rates of clindamycin (n = 12), tetracycline (n = 18) and doxycycline (n = 18) groups were similar ($P \geq$ or = 0.14) and all were significantly higher compared to the azithromycin group (n = 18; $P \leq$ or = 0.04). The intervals until vivax reappearance were also significantly shorter in the azithromycin group [mean (SD) = 21 (6) vs 25 (3) days, $P < 0.05$] suggesting that some of these were recrudescences. The apparent success rate (no subsequent appearances of either vivax or falciparum infection) was significantly lower for the azithromycin group (11%) compared to the other groups (34-78%; $P < 0.01$). In current antibacterial treatment regimens, short-course azithromycin has inferior antimalarial activity compared to clindamycin or the tetracyclines. •

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A SEVEN-YEAR RETROSPECTIVE EVALUATION OF GNATHOSTOMIASIS

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Our routine laboratory immunoblot has been employed for antibody detection of human gnathostomiasis. The antibody against *Gnathostoma* parasite reacted with the diagnostic 24 kDa antigen, which is provided from *Gnathostoma spinigerum* L3 extract. On data between 1995-2001, 3,262 suspected cases were collected in a 7-year record of gnathostomiasis. A number of 274 samples (non-Thai patients) were included and delivered from Australia, Austria, Canada, China, Germany, France, Ireland, Malaysia, Myanmar, Peru, Switzerland, the United Kingdom, U.S.A. and Vietnam, including those in Thailand. The incidence of positive gnathostomiasis was 47.3% (1543/3262 cases) by immunoblot of which 274 cases of non-Thai patients were 44.9% (123/274) positive. Most of the eosinophilia of the positive-immunoblot cases was in the range 0-10%. In the parasitologically confirmed cases, 1-2% of eosinophil was present. Many patients treated with albendazole and ivermectin, *Gnathostoma* worms were removed from the swollen skin or migrated areas, in contrast, also removed from a few untreated patients. A few patients show symptoms relapsing. •

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ANTIGENIC COMMUNITY BETWEEN *OPISTHORCHIS VIVERRINI* ADULT WORMS AND THEIR INTERMEDIATE HOSTS, *BITHYNIA* SNAILS AS A SUPPORT FOR CONCOMITANT ANTIGENS

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The concept that parasites share antigens with their snail intermediate hosts has received considerable experimental support. In this study, comparison between three species of *Bithynia* snails: *Bithynia funiculata, B. siamensis siamensis, B. siamensis goniomphalos* and crude somatic antigens of *Opisthorchis viverrini* adult worms were immunologically characterized with antibodies (IgG) in sera of opisthorchiasis patients by SDS-PAGE and Western blot analysis. All of these snail antigens reacted with *O. viverrini* infected human sera, which revealed only 13 – 15 protein bands by Western blot analysis when compared with sera from healthy controls. *B. funiculata* was proven to have more shared antigens with *O. viverrini* than the other two species, particularly three pairs with molecular weights (MW) of 29 & 30, 47 & 50 and 86 & 90 kDa, which reacted consistently with all infected sera. Extensive cross reactions of the *B. funiculata* snail antigen with sera from patients with other parasitic infections still occurred. However, the three pairs of proteins mentioned above mostly failed to give any cross reaction with the sera of paragonimiasis, schistosomiasis, fascioliasis, sparganosis, larval toxocariasis, trichuriasis and capillariasis, or at least just one or two protein bands out of the six appeared to cross react with sera of taeniasis, cysticercosis, echinococcosis, gnathostomiasis, angiostrongyliasis, trichinosis, ascariasis, filariasis, strongyloidiasis, hookworm infections and HIV infections. This study suggests that the antigen prepared from *B. funiculata* snails, one of the snail intermediate hosts of *O. viverrini*, could possibly be used as an alternative diagnostic antigen for opisthorchiasis in the future. •

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CURRENT STATUS OF *GNATHOSTOMA* INFECTION IN THAILAND

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At least five species of *Gnathostoma*: *G. spinigerum*, *G. hispidum*, *G. doloresi*, *G. vietnamicum* and *G. malaysiae* have been documented in Thailand, but only *G. spinigerum* is known to cause human infection. From 1961 to 1963, about 900 patients were clinically diagnosed each year as having gnathostomosis, and about 10 deaths were reported between 1967-1981. Each year, from 1985 to 1988, between 300-600 suspected gnathostomosis patients came to the gnathostomosis clinic at the Hospital for Tropical Diseases, Faculty of Tropical Medicine, Mahidol University. From 1989 until now, about 100-400 new cases of suspected gnathostomosis have been seen each year at this hospital.

In Nakhon Nayok and Prachin Buri Provinces, central Thailand, the prevalences of *Gnathostoma* infection in eels were 38.1% and 24.0%, respectively. Most of the positive eels harbored only 1-9 larvae. In Nakhon Nayok, about 12,000 fresh-water fish were examined: 8 out of 72 species were found to be infected with gnathostome larvae. The infection rates in *Monopterus albus*, *Anabas testudineus*, *Channa striata*, *Clarias macrocephalus* and *Channa micropeltes* were 30.1%, 7.7%, 7.4%, 6.7% and 5.1%, respectively. The overall positive rate for *G. spinigerum* eggs in dog fecal samples, which were collected from 21 localities in Nakhon Nayok, was 1.2%. In Bangkok, no infections with *G. spinigerum* were found in the stomachs and intestines of 200 stray dogs; negative results for the worm eggs were also obtained with fecal samples of 370 cats and 518 dogs. A cyclops survey in each of two areas (Ban Phrao, Nakhon Nayok and Tha Ngam, Prachin Buri) found no evidence of natural cyclops infection. •

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GNATHOSTOMIASIS: AN EMERGING IMPORTED DISEASE

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Increasing international travel brings the more adventurous traveler into contact with helminthic parasites rarely seen outside the tropics. Infection with *Gnathostoma spinigerum* leading to the clinical syndrome of gnathostomiasis is a typical example and one with which few clinicians in non-endemic areas will be familiar. We report a case series of patients seen over a 12-month period at the Hospital For Tropical Diseases (London, UK) to draw attention to this underdiagnosed parasitic infection which may present to a range of different medical specialities. •

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IMMUNODIAGNOSIS OF GNATHOSTOMIASIS

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Several immunological methods for diagnosis of gnathostomiasis have appeared in the literature. The oldest method was the skin test that was established initially by Japanese scientists in the 1960s. It was the convenient and relatively reliable diagnostic means in that period. During the 1980s, ELISA was evaluated by several investigators, and it was found that the sensitivity varied from 56% to 100%. The antigen used in the assay was crude larval antigen of *G. spinigerum*, crude adult antigen of *G. doloresi* or larval excretory-secretory antigen. The immunoblotting technique was studied during the 1990s. The specific diagnostic band was the protein component with a molecular weight of 24 kDa. The routine current diagnostic method for human gnathostomiasis is the immunoblotting technique. Monoclonal antibodies (mAbs) to the crude soluble extract, 24 kDa protein component of *G. spinigerum* advanced third stage larvae (GsAL3) have been produced. Moreover, hybridoma cell lines derived from spleen cells of an infected mouse secreted antibodies

which reacted with the cuticle of GsAL3 sections by IFA. These mAbs were produced. However, the diagnostic value of these mAbs is not applicable for the diagnosis of human gnathostomiasis. •

Presented at: The First International Meeting on Gnathostomiasis, Culican, Mexico, March 2002.

INTESTINAL PARASITOSES AMONG HILLTRIBE PEOPLE AND SOIL CONTAMINATION IN NAN PROVINCE, NORTHERN THAILAND

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Hilltribe people in the north of Thailand reside in mountainous areas. In Nan Province, these people inhabit hill-side and plain areas, keeping the highlands for agriculture. Tropical climate, clustered housing and the traditional lifestyle of the people intensify the transmission of intestinal parasitic diseases in the area. When residents are parasitized and contaminate the land with their feces, the soil around the households becomes a source of infection. In this study, the prevalence rates of intestinal parasitic infections among 453 hilltribe people were assessed by fecal examination using simple direct smear, DMSO Modified Acid Fast staining, Kato-Katz's modified thick smear and polyethylene tube cultivation methods. Contamination of soil samples with fecal matter was studied by sugar floatation technique. Fecal examination showed that the hilltribe people in Nan Province had protozoan infections with *Giardia lamblia* (3.5%), *Entamoeba coli* (7.5%), and *Endolimax nana* (0.2%), none of them was detected for *Cryptosporidium parvum* and 38.0% of the population had helminthic infections. Major helminthic infections detected in this study were *Necator americanus* (30.7%) and *Ascaris lumbricoides* (13.9%). For *Trichuris trichiura*, *Enterobius vermicularis*, *Taenia* spp., *Opisthorchis viverrini* and minute intestinal fluke; detection rates were only 0.2% for each infection.

The prevalence rate of helminthic infection among hilltribe people in Muang District was higher than the group from Pua District and soil samples collected around the household of Muang District also showed positive findings for *A. lumbricoides* eggs. Since the prevalence rate of hookworm infection in both districts were significant, 22.4% in Pua District and 39.4% in Muang District, the hilltribe group should be considered as a risk group or target group in the Intestinal Helminthiosis Control Program in Thailand. •

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MULTIPLE DOSE TREATMENT OF TRICHURIASIS WITH MEBENDAZOLE: EFFICACY, EXPULSION PATTERN AND MORPHOLOGICAL CHANGES AFFECTING THE WORMS

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A study on the efficacy of multiple doses of mebendazole against *Trichuris trichiura* was carried out in Nakhon Si Thammarat Province in southern Thailand. Cure rates obtained from mebendazole at 500 mg x 3 in light and moderately infected groups were significantly different, 94% and 71%, respectively. Mebendazole at 100 mg x 2 x 3 exhibited similar cure rates, 89% and 75%, among light and moderately infected groups, respectively. About 90% of worms were expelled between Day 3 to Day 6 post-treatment with the 500 mg x 3 regimen, and between Day 3 and Day 5 post-treatment with the 100 mg x 2 x 3 regimen. Regarding the cost of treatment, the standard dose of mebendazole at 100 mg x 2 x 3 is still the drug of choice for trichuriasis.

Microscopic study of expelled worms revealed slight changes in morphology. About 100 to 200 m from the anterior tip of the worm had degenerated, the anterior part of the esophagus had contracted, and the cuticular sheath covering the anterior end had become detached.

Degeneration of stichocytes of the esophagus occurred in treated worms. In hematoxylin and eosin cross-sectioned slides, there was distinct destruction and fragmentation of stichocytic cells after treatment with mebendazole. •

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RECORD NUMBERS OF *GNATHOSTOMA* LARVAE IN SWAMP EELS!

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From 1986 to 2001, thousands of swamp eels (*Monopterus albus*, previously *Fluta alba*) from several provinces in Thailand were examined for the presence of *Gnathostoma* larvae. Three different record numbers of the larvae per eel were documented. Two thousand, five hundred and eighty-two larvae were collected from one eel (the heaviest record ever) in Nakhon Nayok Province by Akahane *et al* in 1987. Nuamtanong *et al* in 1992 recovered 2,283 larvae from one eel (the second heaviest record) in Nakhon Nayok as well. Recently, in 2000, Rojekittikhun & Chaiyasith found 698 gnathostome larvae from an eel in the same province. About half (43%-52%) of the total number of larvae was concentrated in the liver, whereas the other half (48%-57%) was in the whole muscles. In the muscles, the larvae preferred encysting in the ventral part (54%-71%) to the dorsal part (29%-46%), and in the middle portion (43%-53%) rather than the anterior (32%-33%) or posterior (15%-24%) portions of the eels. The most preferred region among the six divided parts of the eels is the medioventral, where about 23%-30% of the larvae were present. •

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THE DIAGNOSTIC SPECIFICITY OF GNATHOSTOMIASIS BY IMMUNOBLOT

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The diagnostic antigen (24 kDa) produced from *Gnathostoma spinigerum* L3 extract was previously shown its specificity to gnathostomiasis. The antigen did not react with antibodies of other parasitic infections; seven diseases of nematodiasis, three diseases each of cestodiasis and trematodiasis, two protozoan diseases and 14 cases of mixed infection with two or more helminth and protozoan parasites. Due to the antigen has been used for antibody detection against *Gn. spinigerum* in serum and CSF, which are delivered from endemic and non-endemic countries of gnathostomiasis. A further cross-reactivity was carried out for its specificity. A number of serum samples were employed in the reactions; enterobiasis, entrobiasis appendicitis, toxocariasis, onchocercosis, Bancroftian filariasis, cappilariasis, hymenolepiasis nana, hydatidosis, fascioliasis, schistosomiasis, paragonimiasis westermani, other visceral larva migrans, *Blastocystis hominis* infection, *Trichomonas hominis* infection, entamebiasis nana, leptospirosis, other brain disorders, occula mass formation, appendicitis, rhuematoid, and autoimmune disease. By the results, no antibodies of those diseases reacted with the 24 kDa antigen. Besides, both cases of *Leptospira pyrogenese* infections gave a weak reaction. Additionally, four of five *L. pyrogenese*-infected cases with same and higher antibody titers to two previous cases could prove an unbinding reaction with the antigen. In this study, antibodies of those serum samples did not from a complex with the diagnostic antigen of 24 kDa. •

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POTENTIAL FOR *ANOPHELES CAMPESTRIS* (DIPTERA: CULICIDAE) TO TRANSMIT MALARIA PARASITES IN PA RAI SUBDISTRICT (ARANYAPRATHET, SA KAEO PROVINCE), THAILAND

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Member(s) of the *Anopheles barbirostris* group Reid, particularly *Anopheles barbirostris* and *Anopheles campestris* Reid are the suspected vectors of *Plasmodium vivax* in Pa Rai (Aranyaprathet, Sa Kaeo province). To determine if *An. barbirostris*, *An. campestris*, or both, are present in Pa Rai and to determine their potential to transmit malaria, a field and laboratory study was conducted. Isofemale colonizations of wild caught mosquitoes captured by landing catches were made for species confirmation and to determine the mosquito life cycle. Pupal morphology indicated all mosquitoes were *An. campestris*. During the late rainy season (October and November), *An. campestris* populations comprised 78.6% of all females captured by human landing catches and 7.1% of mosquitoes in a cow-baited trap. The biting activity cycle peaked between 20.00 and 01.00 hours and was highest (17.6 bites per person per hour) at 23.00 hours. More *An. campestris* bit people indoors (nine bites per person per hour) than outdoors (four bites per person per hour). Immature *An. campestris* were found in ponds, swamps, rice-fields, puddles, marshes, ground pools, and pits with open sunlight to partial shade. The time from egg hatch to adult was 18-47 d and 14-22 d under laboratory (25.0-27.0°C) and ambient (26.0-32.0°C) conditions, respectively. The fecundity of *An. campestris* ranged from 173 to 311 eggs. Based on experimental infections, *An. campestris* was able to support the sporogonic cycle of *P. vivax* with 76.2 and 23.8% oocyst and sporozoite formation rate, respectively. *An. campestris* shows high potential as a malaria vector in Pa Rai. •

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THE APPLICATION OF ETHANOL-EXTRACTED *GLORIOSA SUPERBA* FOR METAPHASE CHROMOSOME PREPARATION IN MOSQUITOES

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The application of ethanol-extracted *Gloriosa superba* for metaphase chromosome preparation in adult and 4th larva *Aedes aegypti* revealed that 0.5-8% ethanol-extracted *Gl. superba* solution could be used instead of 1% colchicine in Hanks' balanced salt solution. For adult mosquitoes, the metaphase rates and average number of metaphase chromosome per positive mosquito after intrathoracic inoculation with 1-2% ethanol-extracted *Gl. superba* solution were 100% and 11.8 (2-16) - 12.6 (3-28) in females, and 80-90% and 16.5 (1-52) - 29.89 (1-72) in males, whereas the inoculation with 1% colchicine solution yielded 80% and 50% metaphase rates, and 18.25 (1-40) and 16.5 (2-53) average number of metaphase chromosomes per positive mosquito in females and males, respectively. For 4th stage larvae, the metaphase rates and average number of metaphase chromosomes per positive mosquito after incubation with 0.5-8% ethanol-extracted *Gl. superba* soluation were 90-100% and 14.42 (1-65) - 64 (19-137), while incubation with 1% colchicine solution yield 100% metaphase rate and 10.9 (7-15) average number of metaphase chromosome per positive mosquito. •

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AEDES ALBOLATERALIS, A POTENTIAL VECTOR OF NOCTURNALLY SUBPERIODIC *WUCHERERIA BANCROFTI* AND DENGUE TYPE 2 VIRUS

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The susceptibility of *Aedes albolateralis* to nocturnally subperiodic *Wuchereria bancrofti* and dengue type 2 virus was investigated by using artificial membrance feeding and intrathoracic inoculation techniques, respectively. The results indicated that *Ae. albolateralis* was susceptible to nocturnally subperiodic *W. bancrofti* (susceptibility rate = 9.43%) and dengue type 2 virus (susceptibility rate = 100%), suggesting the potential vector of the two pathogens. •

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ANOPHELES BARBIROSTRIS/CAMPESTRIS AS A PROBABLE VECTOR OF MALARIA IN ARANYAPRATHET, SA KAEO PROVINCE

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As a result of dramatic increase in malaria cases in Sa Kaeo Province from 666 cases in 1995 to 4,381 in 1997, a brief entomological study was carried out during January 1998 to December, 1999 in Pa Rai subdistrict where most malaria cases were reported. Of fourteen species of mosquitos found, only *Anopheles barbirostris* group was the most abundant species throughout the year. Adult identification was not able to confirm species within *An. barbirostris* group, particularly between *An. barbirostris* and *An. campestris* because of morphological resemblance. Therefore, the *barbirostris* group captured in this study is reported to be either *An. barbirostris* or *An. campestris*. The seasonal prevalence of *barbirostris/campestris* was bimodal in distribution (September and November) and coincided well with malaria occurrence in this area. Human landing collections revealed high adult densities with 20 bites/person-night for mean indoor density and 53.5 bites/person-night for mean outdoor density. The biting peak was during 21.00-24.00 hours. Among 223 *barbirostris/campestris* dissected for oocysts and sporozoites only one gut from the outdoor collection in November was infected with oocysts. There were no sporozoites detected in salivary glands of all mosquitoes collected. This appears to indicate that in the absence of major vectors local species may serve as potential transmitters of malaria in Thailand. •

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LARVAL OCCURRENCE, OVIPOSITION BEHAVIOR AND BITING ACTIVITY OF PETENTIAL MOSQUITO VECTORS OF DENGUE ON SAMUI ISLAND, THAILAND

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A 1995 outbreak of dengue haemorrhagic fever (DHF) occurred on Samui Island in Thailand with an incidence of almost 500 cases/100,000 population. To find and develop effective strategies to control this disease through cost-effective vector control programs, entomological studies were carried out on the island between 1996 and 1998. There were two species of DHF vectors, *Aedes aegypti* and *Ae. albopictus* prevailing on the island, and the population of *Ae. aegypti* remained relatively constant throughout the year while the abundance of *Ae. albopictus* increased substantially during the rainy season (May-December) and then declined

drastically in the dry season (January - April). The ranges of the three *Aedes* larval indices, Breteau index (BI), house index (HI) and container index (CI) were 93 - 310, 43 - 89 and 16 - 50 respectively. The creamic or earthen jars both inside and outside the dwellings and concrete water storage tanks (mostly in toilets and bathrooms) served as the main breeding places of *Ae. aegypti* whereas coconut husks and coconut floral spathes found outdoors were the major breeding sites of *Ae. albopictus*. The number of washing water jars, concrete tanks and natural sites infested with *Aedes* larvae increased significantly in rainy season, with 60% of ovitraps become positive for *Ae. albopictus* eggs with an average number of 26 eggs/trap in 3 days of setting. There was a complete lack of oviposition by *Ae. aegypti* in outdoor ovitraps (15 m away from the houses). The indoorbiting rate ranged from 1.5 to 8.1 mosquitoes/man-hour, while the outdoor rate was between 5 and 78 mosquitoes/man-hour. Of the indoor biting mosquitoes, 75.4% were identified as *Ae. aegypti* and 99% of the outdoor ones were *Ae. albopictus*. The diel biting activity of *Aedes* during the period from 08.00 h to 17.00 h in the houses was higher in the morning than in the afternoon period, with a low prevalence between 13.00 h and 14.00 h. •

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APPLICATION OF GIS TO THE CHARACTERIZATION OF FILARIASIS TRANSMISSION IN NARATHIWAT PROVINCE

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Geographical information system (GIS) and available survey data (both from the Filariasis Annual Reports, 1985-1999 and from the published literatures) for the microfilarial infection rates and vector densities are used to develop first subdistrict-level endemicity map of lymphatic filariasis in Narathiwat province. The maps demonstrated subdistrict-level geographical distribution of filariasis and the subdistricts at varied degrees of infection rate. The maps also indicate that, since 1985, there was a marked decrease in endemicity at the subdistrict level and even in some areas, the infection rates were zero. However, the transmission remained in the subdistricts covering peat swamp forest (Su Ngai Padi, Paluru Puyo, Pasemat, Bang Khunthong, and Phron subdistrict). The house locations of infected cases as well as the vector breeding places were, therefore, georegistered and placed as symbolic dots on the base maps obtained from Landsat's Thematic Mapper (TM) 5 and the land use map of Narathiwat to display distribution of filariasis foci. Of 102 houses mapped, there were 40 houses in primary peat swamp forest (39.22%), 26 houses in rice fields (25.49%), 15 houses in fruit orchards (14.70%), 10 houses in coconut fields (9.80%) and others (10.78%). All the houses were closed to the larval habitats presented in the survey. A 2-km buffer zone around the conservative boundary of primary peat swamp forest was created to locate risk areas of filariasis transmission. The buffer zone covered an area of 544.11 sq km and included 88.89% of houses of infected cases found in 2002. It was able to identify 54 villages located in the buffer area which might help in determination resource needs and resource allocation for filariasis control in Narathiwat province. •

Presented at: Joint International Tropical Medicine Meeting 2002, Montien Riverside Hotel, Bangkok, Thailand, 20-22 November 2002.

THE REPELLENT EFFICIENCY OF MOSQUITO COIL WITH EMPHASIS ON COVERAGE AREA IN LABORATORY CONDITIONS

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Assessment/evaluation of the efficiency of a mosquito coil formulation containing d-aleethrin 0.3% w/w was conducted in order to find the protective coverage area for *Aedes aegypti* in a closed room condition. Eight volunteers sat at positions 1 m, 2.5 m, 4 m and 7 m away from the coil. When the mosquito coil was ignited, the mosquito-landing number was counted at 2, 4, 6, 8, 10, 15, 20, 25, 30, 45 and 60 min. The results revealed

that at a distance of 1 m from the burning coil, there was a 50% reduction in the mosquito-landing number at 10 minutes. The repellency of this mosquito coil could prevent mosquito bite at 4 m and 7 m distance when the coil was lit for 30 minutes and 60 minutes, respectively. •

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POTENTIAL DEVELOPMENT OF TEMEPHOS RESISTANCE IN *AEDES AEGYPTI* RELATED TO ITS MECHANISM AND SUSCEPTIBILITY TO DENGUE VIRUS

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The addition of temephos to water containers as a larvicide against *Aedes aegypti* was commonly used as a part of DHF control programs. The widespread, or long-term, application of insecticides can lead to the development of mosquito resistance to the insecticides as a result of selection pressure. This presents a problem for a disease control. Therefore, this study was conducted in the laboratory to observe the potential development of resistance to temephos and the mechanism involved in *Ae. aegypti*, and to study the significance for dengue infection. The larvae were selected in consecutive generations. The level of resistance to temephos was detected by WHO assay technique. After 19 generations of selection, a low level of resistance was found. The resistance ratio at LC_{50} was 4.64 when compared with the non-selected group. The assay for major enzyme-based resistance mechnisms was done in a microtiter plate to detect elevated non-specific esterases, monooxygenase, and insensitive acetylcholinesterase in the temephos-selected and non-selected groups. It revealed a significant increase in esterase activity when compared with the non-selected group. There was no elevation of monooxygenase and the insensitive acetylcholinesterase activities. However, when an esterase inhibitor (S, S, S, -tributyl phosphorotrithioate or DEF) was added to temephos and susceptibility in the selected group was studied, the resistance ratio was reduced from 16.92 to 3.57 when compared with a standard susceptible strain (Bora Bora). This indicates that the esterases play an important role in temephos resistance.

Dengue-2 virus susceptibility was studied by oral feeding to females of the temephos-selected (S19) and the non-selected groups. The dissemination rate, when the titer of virus in the blood meal was 7.30 MID_{50}/ml were 11.11% and 9.38% for selected and non-selected groups respectively. When the titer of virus in blood meal was 8.15 MID_{50}/ml, the dissemination rates increased to 24.24% and 33.33%, respectively. A statistical difference in viral susceptibility was not found between the two groups. This suggested that the low level of temephos resistance might not affect oral susceptibility. However, this needs further study. •

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ZYMOGRAM PATTERNS OF *NAEGLERIA* SPP ISOLATED FROM NATURAL WATER RESOURCES AT THALING CHUN DISTRICT

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A genetic approach to species criteria in the amoeba genus *Naegleria* using allozyme electrophoresis to characterize to trophozoite stage of three *Naegleria fowleri* isolated from patients with primary amoebic meningoencephalitis, five thermophilic (42 C) *Naegleria* spp isolated from natural water resources at Thaling Chun District and reference control strain *Naegleria fowleri* CDC VO 3081 was conducted. Isoenzymes of amoebae whole-cell extracts were resolved and analyzed by the vertical polyacrylamide slab gel electrophoresis (Takai 1986) to determine whether three were correlations between divergenic of the amoebae. The results revealed that four out of eleven enzymes; Aldehyde oxidase (ALDOX), Aldolase (ALD), a-Glycerophosphate dehydrogenase (a-GPDH), Xanthine dehydrogenase (XDH) were undetectable from the pathogenic

strains, while the other enzymes; Esterase (EST), Glucose phosphate isomerase (GPI), Isocitate dehydrogenase (IDH), Lactate dehydrogenase (LDH), Malic enzyme (ME), Glucose phosphomutase (GPM) and Malate dehydrogenase (MDH) were determined. *Naegleria fowleri* strains were biochemically the most homogeneous, they showed intraspecific isoenzyme variation that allowed them to be grouped. In contrast, their allozyme patterns (EST 1-7, IDH) of *Naegleria* spp isolated from the environment were interspecific isoenzyme variations to the pathogenic *Naegleria* strain. Conclusion, this study recognized that genetic interpretation of these zymograms of *Naegleria fowleri* strains were too different heterogenicity particularly from thermophilic 42°C *Naegleria* spp isolated from the environment. •

Poster Presentations at: Joint International Tropical Medicine Meeting 2002, Montien Riverside Hotel, Bangkok, Thailand, 20-22 November 2002.

COMPARATIVE STUDIES ON THE BIOLOGY AND FILARIAL SUSCEPTIBILITY OF SELECTED BLOOD-FEEDING AND AUTOGENY *AEDES TOGOI* SUB-COLONIES

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Blood-feeding and autogenous sub-colonies were selected from a laboratory, stock colony of *Aedes togoi*, which was originally collected from Koh Nom Sao, Chanthaburi province, southeast Thailand. Comparative biology and filarial susceptibility between the two sub-colonies (blood-feeding: F_{11}, F_{13}; autogeny: F_{38}, F_{40}) were investigated to evaluate their viability and vectorial capacity. The results of comparison on biology revealed intraspecific differences, i.e.; the average egg deposition/gravid female (F_{11} / F_{38}; F_{13} / F_{40}), embryonation rate (F_{13} / F_{40}), hatchability rate (F_{11} / F_{38}; F_{13} / F_{40}), egg width (F_{11} / F_{38}), wing length of females (F_{13} / F_{40}), and wing length and width of males (F_{11} / F_{38}) in the blood-feeding sub-colony were significantly greater than that in the autogenous sub-colony; and egg length (F_{11} / F_{38}) and width (F_{13} / F_{40}), and mean longevity of adult females (F_{11} / F_{38}) and males (F_{13} / F_{40}) in the blood-feeding sub-colony were significantly less than that in the autogenous sub-colony. The results of comparison on filarial susceptibility demonstrated that both sub-colonies yielded similar susceptibilities to *Brugia malayi* [blood-feeding / autogeny = 56.67% (F_{11}) / 53.33% (F_{38}), 60.00% (F_{13}) / 83.33% (F_{40})] and *Dirofilaria immitis* [blood-feeding/autogeny = 85.71% (F_{11}) / 75.00% (F_{38}), 45.00% (F_{13}) / 29.41% (F_{40})]. •

Poster Presentations at: Joint International Tropical Medicine Meeting 2002, Montien Riverside Hotel, Bangkok, Thailand, 20-22 November 2002.

PRELIMINARY STUDY ON MORPHOLOGICAL VARIATIONS FOR SUSCEPTIBILITY AND TRANSOVARIAL TRANSMISSION OF DENGUE VIRUS IN *AEDES AEGYPTI*

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Two types of morphological variants, the dark form and the pale form of *Aedes aegypti* were selected from wild-caught mosquitoes. Ascertaining any differences in susceptibility to dengue type 2 virus was performed by oral feeding. Transovarial transmission was determined from the progenies of infected mosquitoes by tracing it in 3 generations. Significant differences in oral infection were not observed between these two forms of mosquitoes. Transovarial transmission was found in the progenies of infected females of both forms, and the filial infection rates (FIR) were also similar. However, there was a trend of declining FIR in the later generation. In order to achieve an accurate result, more tests are currently studied to obtain a larger number of progeny. Although the FIR was low in the present study under laboratory conditions, higher rates might occur under field conditions which could have a significant impact on the maintenance of dengue viruses in nature. •

Poster Presentations at: Joint International Tropical Medicine Meeting 2002, Montien Riverside Hotel, Bangkok, Thailand, 20-22 November 2002.

PREVALENCE OF CONGENITAL CYTOMEGALOVIRUS AND TOXOPLASMA ANTIBODIES IN THAILAND

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Prevalence of CMV and toxoplasmosis antibodies was determined among the normal newborn infants, the suspected congenital neonates and the pregnant women. Seropositive rates of CMV and toxoplasmosis were similar. Most of the pregnant women had CMV antibodies. The in-house ELISA for detection of toxoplasma antibodies was developed and compared with the commercial kit with sensitivity and specificity of 90.47% and 96.74% respectively. •

RAPID DIAGNOSIS OF CYTOMEGALOVIRUS IN THAI PEDIATRIC AIDS PATIENTS

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One hundred blood samples were collected from pediatric AIDS patients for the detection of CMV in PBLs by immunoperoxidase staining (IP) and PCR. IgM antibody was also performed to determine the correlation of antigen and antibody. IP and PCR can be used as early diagnosis methods for the detection of CMV prior to the presence of IgM antibody. The sensitivity and specificity of IP were 73% and 97%, respectively. IP has more advantages than PCR in that it is very easy to perform, less time consuming, less expensive, and does not require expensive instruments. •

PREVALENCE OF CYTOMEGALOVIRUS IN THAI BLOOD DONORS BY MONOCLONAL STAINING OF BLOOD LEUKOCYTES

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Four hundred and forty-one blood and serum samples were collected during August to October 1998 from the blood donors at blood bank of Rajvithi Hospital, Bangkok, Thailand. Their ages were varied between 18-55 years. All specimens were tested by immunostaining and ELISA method. Forty-seven specimens (10.66%) gave positive results by immunostaining. Among these, 20 cases were seropositive and 27 cases were seronegative.The age groups between 41-50 years had high percentage of CMV infection by immunostaining method more than the others age groups. From ELISA, 231 cases (52.38%) had positive IgG antibody to CMV, 42 cases (9.52%) had IgM antibody positive and 39 cases (8.84%) had positive results both in IgG and IgM antibodies. The age groups between 36-40 years had higher percentage of IgM antibody than the other age group. Since immunostaining method can detect early CMV infection. Therefore screening for the presence of antibodies alone is not enough to avoid CMV infection. Immunostaining along with ELISA detection of antibodies were useful for decrease the CMV infection. The information thereafter may be used for prevention of the CMV transmission.•

THE EFFECT OF EYESTALK EXTRACT ON VITELLOGENIN LEVELS IN THE HAEMOLYMPH OF THE GIANT TIGER PRAWN *PENAEUS MONODON*

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Competitive ELISA using combination of monoclonal antibodies specific to vitellin subunits was used to monitor the fluctuation of haemolymph vitellogenin levels in *Penaeus monodon* during ovarian development induced by bilateral eye-ablation and to monitor the effect of eyestalk extract injection in prawn with developing ovary. The haemolymph vitellogenin levels were undetectable in the prawn with ovary at the resting stage but elevated sharply when the ovary began to develop. The haemolymph vitellogenin levels remained high during the ovary developing into ripe stage and fallen down to the low levels before spawning and spent stage. The results from injection of eyestalk extract into prawn with developing ovary revealed that haemolyph vitellogenin levels elevated sharphy within 2 hr, reached the maximal levels and remained high during 4-10 hr, then slightly declined at 24 hr. This respones directly depended on the amount of injected eyestalk extract and it was species specific. The application of eyestalk extract from *Metapenaeus affinis* demonstrated the same results but less effective whereas the eyestalk extract from *Macrobrachium rosenbergii* did not cause any changes in haemolymph vitellogenin levels. Therefore, the assay is specific and indicative for use to determine the activity of the putative gonad inhibiting hormone by monitoring the alteration of vitellogenin levels. •

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A RAPID-COOLING METHOD FOR CRYOPRESERVING *ENTAMOEBA HISTOLYTICA*

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The rapid-cooling method containing 50% horse serum in the suspension frozen has now been used to cryopreserve strains of HTH-56 : MUTM, HM-1: IMSS metronidazole-resistant *E. histolytica*, and emetine-resistant *E. histolytica* successfully for more than 2 years. The technique described gives reasonable recoveries of about 25% after storage at -196°C with a relatively simple, uncontrolled, cooling schedule. The longterm storage is also possible at -70°C. •

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DIAGNOSIS OF AMEBIASIS USING IMMUNOLOGICAL AND MOLECULAR BIOLOGICAL METHODS

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Intestinal and extra-intestinal infection with *Entamoeba histolytica* is one of the major causes of worldwide morbidity and mortality. Therefore, rapid, sensitive and specific diagnostic tests would pave ways for prompt treatment and prevention of transmission of the disease, amebic colitis and liver abscess. Direct stool examination for the presence of hematophagous *E. histolytica* trophozoites and/or cysts and culture method would have been useful, nevertheless, in asymptomatic cyst passers, the output is in an acyclic manner and not concentrated enough. It is also rather difficult in cases of extra-intestinal amebiasis to exhibit trophozoites in clinical specimens such as liver abscess. The existence of two species, *E.histolytica* Schaudinn 1903 and *E. dispar* Brumpt 1925, is now recognized. They were previously known as pathogenic and non-pathogenic *E.histolytica*, respectively. The former is used in reference to the species capable of causing invasive amebiasis and the latter as the luminal commensal and is not evidenced to cause amebiasis. They are morphologically indistinguishable but genetically different. Therefore, ordinary microscopy can no longer be reliable except when hematophagous trophozoites are being seen. The techniques for immunodiagnosis of amebiasis are 1) detection of amebic antigens, 2) detection of anti-amebic antibodies, 3) detection of immune complexes, and 4) detection of cell-mediated immune responses. Molecular biological techniques that can simultaneously distinguish *E.histolytica* from *E. dispar* have been developed; they include 1) the culture of stool samples and/or liver abscess followed by isoenzyme typing, 2) the detection of an *E.histolytica* antigen using the enzyme-linked immunosorbent assay(ELISA), 3) the detection of an *E.histolytica* antigen using the MAb- based IFA test, and 4) the use of the polymerase chain reaction (PCR)- based technique to amplify amebic DNA. Of these methods, antigen detection using the MAb-based ELISA and IFA can be performed easily and rapidly, making it the diagnostic method of choice for clinical use. The PCR-based methods are powerful tools for genetic typing of different amebic strains with high sensitivity and specificity for simultaneous diagnosis and distinguishing *E.histolytica* from *E. dispar* that are currently being developed in our laboratory. Isoenzyme typing takes a long time, while detection of anti-amebic IgM isotype and salivary IgA confirm recent infection. The WHO, PAHO and UNESCO stressed the urgent need to develop improved methods for the specific diagnosis of *E.histolytica* using appropriate technologies for developing countries. Knowledge of the true prevalence of *E. histolytica* will not only be useful for public health control programs but also facilitate the application of vaccines against invasive amebiasis. •

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DISEASES CAUSED BY PATHOGENIC FREE-LIVING AMOEBAE AND THEIR MOLECULAR-BASED DIAGNOSIS

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At present, three genera of free-living amoebae capable of infecting human central nervous system (CNS) and eyes are *Naegleria fowleri, Acanthamoeba* and *Balamuthia mandrillaris*. Small free-living amoebae, belonging to the genera *Naegleria* and *Acanthamoeba*, occur world-wide and cause fatal primary amoebic meningoencephalitis (PAM) and granulomatous acanthamoebic encephalitis/meningoencephalitis (GAE/GAM) and chronic acanthamoebic keratitis (CAK) with invasion of other tissues in man, respectively. A relatively large amoeba *Balamuthia mandrillaris*, like *Acanthamoeba* causes a chronic GAE in humans and animals. Delay in diagnosis or misdiagnosis together with unavailability of drug treatment often lead to fatality, especially in PAM and GAE/GAM. Both PAM and CAK occur in healthy individuals while GAE and related diseases are associated with immunodeficient states. Only *Balamuthia* is soil amoeba, those other two could be found as facultative parasites in the intestine of both cold-blooded and warm-blooded animals; and as free-living stages in seawater, soil and mud, dust and even in the air. In Thailand, only 9 cases of PAM,7 cases of GAE/GAM, 19 confirmed cases of CAK, one case of acanthamoebic infection of peptic ulcer and 2 cases of *Acanthamoeba* pluropeumonitits have been reported. Survey in industrial plants and stagnant water revealed the prevalence of these free-living amoebae. However, *Balamuthia* causing GAE has never been reported in this country but reported elsewhere in Peru 32 cases, in Brazil 1 case, and in the USA 4 cases as well as 1 case in mandrill baboon. Since there are good evidences supporting that the facultative intracellular parasites, such as *Legionella pneumophila* and *Pseudomonas aeruginosa* are capable of growing inside on natural host, *Acanthamoeba castellanii* present in domestic water supplies, whirlpool bathes, and even in hot spring spas. The other ones, *Burkholderia cepacia* and *Candidatus Odyssellaa thessalonicensis*' gen.nov.,sp.nov., are obligate intracellular bacteria of free-living amoeba *Acanthamoeba* polyphage. Therefore, special attention should be paid to these potentially pathogebic protozoa alone of as biofilms in various aspects including early detection for prompt treatment, parasitology, taxonomy, epidemiology, molecular biology, and vaccine development.

For *Balamuthia mandrillaris*, the simple IFA test using specific polyclonal antibodies can serve definitively diagnostic purpose (Dr. Govinda S. Visvesvara, Division of Parasitic Diseases, Center for Disease Control and Prevention, Atlanta, Georgia). For the other two, their molecular-based diagnoses include isoenzyme typing and interstrain polymorphisms of isoenzyme profiles, monoclonal antibodies (MAbs)-based UFA/ELISA and flow cytometry, polyclonal antibodies (PAbs)-based IFA test, restriction fragment length polymorphism (RFLP), restriction endonuclease digestion of whole cell DNA/ELISA and flow cytometry, polyclonal antiodies (PAbs)-based IFA test, restriction fragment length polymorphism (RFLP), restriction endonuclease digestion of whole cell DNA/mitochondrial DNA and PCR, rDNA PCR-RFLP patterns and their specific small subunit rRNA/rDNA (SSrRNA/SSrDNA) genes are of most valuable achievements. MAbs produced are specific to each stage of the parasite, either cyst or trophozoite forms. However, observations under conventional microscope, conventional staining with dyes (Giemsa, Haematoxylin and Eosin for trophoxoites and fluorescent dye Calcoflour white for cysts in smears) and culture methods on non-nutrient agar (NNA) plates with an overlay of live *Escherichia coli* of fresh clinical specimens such as CSF, corneal scrapings or biopsy specimens, water or washing solutions inside and scrapings attached to all sides of cases for keeping contact lensm etc., are of first aids which are useful for physicians to decide whether to treat or not to treat the victims. Observations using enflagellation and animal inoculation experiment to confirm pathogenicity of suspected isolates, scanning and/or transmission electron microscopy are second choice. The special test, *in situ* hybridization and an immunogold assay is used to identify *Legionella* associations with *Acanthamoeba*. Culture of CSF sample upon 1.5% non-nutrient agar coated with washed *E.coli* bacteria is recommended for the cultivation of pathogenic free-living *Naegleria*. Collections of clinical specimens, their transportation to and processing in the laboratories must be performed simultaneously and accordingly with special care. •

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MOLECULAR-BASED DIAGNOSIS OF *ENTAMOEBA* INFECTIONS AND VACCINE DEVELOPMENT IN THE 21ST CENTURY

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There exists two species within what has been called *E. histolytica* which are *E. histolytica* Schaudinn, 1903 (equivalent to *E. dysenteriae*) and *E. dispar* Brumpt, 1925, previously known as pathogenic and non-pathogenic *E.histolytica*, respectively. When diagnosis using light microscope, the cysts and trophozoites of the two species are morphological indistinguishable and should be reported as *E. histolytical E. dispar.*Biochemical, immunological and genetic data now indicate their difference. Only *E. histolytica* us caoable of causing invasive disease where as *E. dispar* or with asymptomatic *E.histolytica*, colonisation never develop symptoms and spontaneously clear the infection. Therefore, amoebiasis researchers have been trying in the 21st century to develop molecular-based diagnoses of *E.histolytica* infection which could simultaneously identify and differentiate between these two species, the tests of which could lead to the real prevalence of *E. histolytica* infection.

Applications of specific monoclonal antiboidies (Mabs), small subunit rRNA (SSrRNA) genes and nested PCR using specific primers of these two species are of most valuable achievements. All new techniques developed should be appropriate for the detection of antigens in clinical specimens in under-developed, developing, and developed countries.

Vaccine development against invasive amoebiasis include using serine-rich *E.histolytica* protein (SPEHP), anti-amoebic adherence lectin, cysteine proteinases in animal models. Protection against invasive amebiasis by a single monoclonal directed against a lipophosphoglycan antigen localized on the *E. histotytica* was documented. Knowledge of the real prevalence of amoebiasis will be useful for the control of parasite and amoebiasis, as well as for testing of anti-amoebic vaccine in the endemic area. •

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DIAGNOSIS OF INTESTINAL AMEBIASIS USING SALIVARY IGA ANTIBODY DETECTION

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Attempts were made to use soluble antigen extract of strain HK-9 of *E. histolytica* to detect salivary IgA antibodies in intestinal amoebiasis patients by using ELISA. Total salivary samples of 109 individuals were divided into four groups. Group I comprised 32 patients whose stools were positive only for *E. histolytica* cysts and/or trophozoites. Group II comprised 12 individuals whose stools were positive for *E. histolytica* and other intestinal parasites. Group III comprised 36 individuals whose stools were negative for *E. histolytica* but contained other intestinal parasites such as *E. coli, E. nana, Blastocystis hominis, T. hominis, Giardia lamblia, Opisthorchis viverrini,* and hookworm. Group IV comprised 29 healthy individuals whose stools were free from any intestinal parasitic infections. Based on the mean optical density, OD ±SD of the results from 29 parasitologically. Negative healthy individuals, the cut-off OD value for salivary IgA antibodies was 1.265. Therefore, the assays were positive in 14 out of 32 (43.75%) of group I and 2 out of 12 (16.6%) of group II. The assays were positive in 16 out of 36 (44.44%) for group III whereas 2 out of 29 (6.90%) for group IV were positive. The overall sensitivity and specificity of the assays were 36% and 72%, respectively. The false positive rate was 28% and the false negative rate was 64%. The predictive values of positive and negative results were 47% and 63%, respectively. The diagnostic accuracy of ELISA for the presence of salivary IgA antibodies was 58%. •

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COMPARISON BETWEEN R-PHYCOCYANIN-LABELED AND R-PHYCOERYTHRIN-LABELED MONOCLONAL ANTIBODY (MAB) PROBES FOR THE DETECTION OF *ENTAMOEBA HISTOLYTICA* TROPHOZOITES

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Comparison between R-Phycocyanin-labeled monoclonal antibody (MAb) probes and R-phycoerythrin-labeled probes for the detection of the three standard refernce strains of the cultured-derived *Entamoeba histolytica* trophozoites, namely HK-9, HM-1:IMSS and HTH-56:MUTM strains by using direct immunofluorescence antibody (DIFA) assay, five times each. The R-Phycocyanin-labeled probes showed greenish-yellow trophozoites while the R-phycoerythrin-labeled probes showed orange-yellow trophozoites under the blue irradiation of the fluorescence microscope. The R-phycoerythrin-labeled MAb probe stained the trophozoites more brightly and clear than those stained by the R-Phycocyanin-labeled probe of the same Eh208C2-2MAb. When the fluorescence microscope, under green irradiation, was used, both probes showed the same bright red colour. The sensitivity of both tests was used, both probes showed the same bright red colour. The sensitivity of both test was 100%. Since this Eh208-C2-2MAb could recognise specifically *Entamoeba histalytica* pyruvate : ferredoxin oxidoreductase enzyme, therefore, our two antibody probes would be valuable for use as a rapid, easy and sensitive test for diagnosis of invasive amoebiasis. •

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AMEBIASIS

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Particular highlights of research studies have inculded : 1) successful treatment of ALA by using a single dose of 2.4 grams of metronidazole or 1.2 to 1.5 grams of tinidazole or in divided doses; 2) molecular cloning and sequencing of genes encoding for RMLC (new gene sequence), PFOR (new gene sequence), actin, Hsp 70 and alkyl-hydroperoxide reductase of *E. histolytica* via MAb and PAbs; 3) immunodiagnostic applications of Eh 208C2-2MAb which recognizes EhPFOR, one in particular, to produce R-PE-and R-PC-MAb probes for the detection of trophozoite antigens by IFA test, to detect trophozoite antigens in liver section by MAb-based immunoperoxidase test and to detect amebic antigens in circulation and in feces by PAb-MAb-based ELISA; 4) therapeutic application of immunotoxin (IT) in hamster model; and 5) axenization of one local strain, HTH-56:MUTM and one monoxenic culture of HTH-65:MUTM of *E. histolytica* and many xenic cultures. On going researches aim at surveillance and control of amoebiasis, and improved methods for specific diagnosis of *E. histolytica/E. dispar* with simple test or technologies appropriate for Thailand, other developing and underdeveloped countries. •

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SENSITIVE AND RAPID DETECTION OF *VIBRIO CHOLERAE* CONTAMINATION IN FOOD USING THE COMBINATION OF IMMUNOMAGNETIC ENRICHMENT AND MAB-BASED DOT-BLOT ELISA

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Sensitive and rapid detection of *Vibrio cholerae* (Vc) is important for study and prevention of cholerae transmission in endemic area. For this purpose, we have developed an immunomagnetic enrichment (IME)/ monoclonal antibody-based dot blot ELISA (MAb-dot ELISA) method to detect the bacteria in food. Goat anti-rabbit IgG-coated superparamagnetic beads reacted with Vc-specific rabbit Igs were used to capture the bacteria in food samples. The captured Vc were then detected by MAb-dot ELISA. This method was able to detect as low as 10^6 cfu Vc/ml and also able to detect the bacteria in all artificially seeded food samples while only 32% of them were detected by conventional culture method. Furthermore, enrichment of the bacteria by IME prior to conventional culturing increased percent positivity from 20.59% (7 of 34 samples) to 52.94% (18 of 34 samples) or about 2.5 times. The method would be therefore useful for large scale screening, as its being simple and rapid, and giving less waste compared to conventional culture method. •

RECOMBINANT FIMBRIAE ANTIGEN OF *V. CHOLERAE*

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Attachment of the *Vibrio cholerae* at the intestinal epithelium is the first prerequisite step in cholera pathogenesis, which will allow bacteria to multiply and produce toxins near the sites of their action, *i.e*, intestinal epithelium. It is believed that *Vibrio cholerae* attachment is mediated by toxin-coregulated pili (TCP) which are expressed on the bacterial surface. The major subunit of TCP is encoded by *tcpA*. The *tcpA* deletant mutant of *V. cholerae* O1 was shown to have a dramatic attenuation *in vivo*. Antibody raised against TcpA was also conferred protection in cholera infant mouse model. This project was then aimed to clone and express TcpA from *V. cholerae* O1 El Tor biotype, which were reported to be epidemic in Southeast Asia. PCR primers were designed from *tcpA* of *V. cholerae* O1 Classical biotype (Genebank; accession no.M33514). PCR probe was prepared using genomic DNA of *V. cholerae* O1 Classical biotype as template with an incoperation of Digoxegenic labeling. This PCR probe was used for screening the genomic DNA library of *Cla*I fragment from *V. cholerae* O1 El Tor biotype. The plasmid vector pBluescript II KS vector was used for genomic library construction. The VC1 clone containing 4 kb *Cla*I insert was obtained and sequencing analysis revealed that this insert was identical to *tcp* locus from *V. cholerae* O1 El Tor biotype, and the complete *tcpA* gene was found to locate in the 0.8 kb. *Eco*RV fragment.

It was attempted to express the TcpA protein in *E. coli* clone containing pBluescript II SK under *lacZ* promotor, however after induction with 1 mM IPTG, there is no extra protein band as view by SDS-Polyacrylamide gel electrophoresis when comparing with *E. coli* clone containing vector only. We then utilised the T7 RNA polymerase promoter system, which composed of pGP 1-2 plasmid, which enables T7 RNA polymerase to produce by heat induction in any *E. coli* host. The VC7 clone, that has *tcpA* insert and contain the T7 promoter sequence upstream its start codon, was then transformed into this vector. This plasmid system need to be maintaing at low temperature about 30°C, but after increase the temperature to 42°C to inactivate the repressor protein, this will allow the T7 RNA polymerase to produce and then drive the expression of TcpA. The prominent protein band of approximately 23 kDa was observed in comparison to the system that contain pBluescript II KS vector only. This protein was mainly included in inclusion body thus require lysis buffer containing 1% Triton X-100 and 8 M urea to solubilise the protein. This solubilised product was then used in immunisation experiment in mice. By intraperitoneal injection, the crude TcpA protein of approximately 250 ug per dose was mixed with Complete Freud adjuvant in the first dose and subsequently with Incomplete Freud adjuvant for the second and third dose, by two week interval. Furthermore, the crude TcpA of approximately 1 mg was orally given in three doses, by two weeks interval. The serum collected after the course of immunisation was then use in Westernblot analysis, all immune serum all reacted with the protein band of approximately 23 kDa, which is the expected molecular weight of the expressed protein TcpA. This result showed a the promising immunogenicity of TcpA. •

IgE ELEVATION AND ANTI-*P.FALCIPARUM* IGE ANTIBODIES: ASSOCIATION OF HIGH LEVEL WITH MALARIA RESISTANCE

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The total IgE and anti-*Plasmodium falciparum* IgE antibodies were determined by enzyme link immunosorbent assay (ELISA) in 480 children and adults living in malaria endemic area along Thai-Myanmar border, Kanjanaburi province, western Thailand. Approximately 73.13% of tested individuals had elevated levels of total IgE with the range of 160-998 ng/ml. Whereas 20.5% of these IgE were specific to *P. falciparum* blood stage antigens, ranged from 78-353 ng/ml. However, the levels of total IgE were not significantly correlated with those of specific IgE (r=0.083). The elevation of anti-*P. falciparum* IgE antibodies seems to be age dependent. The prolonged or repeated exposure to malaria parasite is necessary for the induction of specific IgE response by the finding of significant correlation between the levels of *P. falciparum* specific IgE and number of malaria attacks (r=0.551, p=0.01). Interestingly, among the specific IgE responders, 20 individuals naturally exposed to malaria without clinical malaria reported had high levels of both total IgE and anti- *P.falciparum* IgE antibodies with the mean values of 418.67 mg/ml and 146.25 ng/ml, respectively. It is likely that the antibodies from such specific IgE responders could mediate phagocytosis *in vitro*. •

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NATURAL HUMAN IGG SUBCLASS ANTIBODIES TO *PLASMODIUM FALCIPARUM* BLOOD STAGE ANTIGENS AND THEIR RELATION TO MALARIA RESISTANCE IN ENDEMIC AREA OF THAILAND

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The immunoglobulin G (IgG) subclass antibodies to *Plasmodium falciparum* blood stage antigens in the sera of 181 individuals living in malaria endemic area in Karnchanaburi province, western Thailand, were determined by enzyme linked immunosorbent assay (ELISA). In this study, IgG3 and IgG1 were shown to be the predominant subclasses. Generally, IgG2 were coexpressed with IgG1 and IgG3 while IgG4 were found to coexpress with other three IgG subclasses. The levels of specific IgG1, IgG2, and IgG3 increased significantly with age (r=0.295, p=0.000; r=0.416, p=0.000; r=0.320, p= 0.000, respectively). The data seem to indicate that the higher antibodies producing required continuous stimulation under natural condition. Furthermore, the levels of specific IgG1, IgG2 and IgG3 increased in immune individuals without clinical malaria reported in adolescents and adults were associated with malaria resistance. The similar results were found in children with different pattern of IgG subclasses in which the specific IgG2 and IgG3, but not IgG1 related to resistance. The findings may contribute to the development of protective immunity against malaria. •

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MOLECULAR AND PHENOTYPIC CHARACTERISTICS OF NEUROTROPIC HIV-1 SUBTYPE E

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Although HIV-1 subtype E associated with neurological dysfunction is common, the virological characteristics of HIV-1 isolated from CNS in this subtype have not yet been identified. In this study, paired blood and CSF isolated from AIDS defining patients were cultured, sequenced and aligned. Phylogenetic tree, nucleotide-distances from both blood and CSF were investigated. Cytopathicity and co-receptor usage of paired blood and CSF isolates were compared to define the specific characteristics of CNS isolates. The results confirmed that CSF isolates showed less cytopathicity. In addition to co-receptor usage, both blood and CSF isolates used either CXCR4 or CXCR4 and CCR5. Interestingly, one of the CSF isolates using CCR3 as a co-receptor had been identified. By sequence analysis, the pair-wise distances of envelope gp 120 sequence and those of all variable regions (except V3 region) between blood and CSF isolates were significantly different. The genetic distances in V1/V2 regions of CSF isolates showed more diverse than those of V1/V2 of blood isolates. These findings suggested that the evolution of V1/V2 regions of CSF isolates seem to be advantage for HIV-1 in CNS infection. In contrast, the genetic distance in V4 and V5 regions of CSF isolates showed less diverse suggesting that the conservation in these regions might be necessary during the process of HIV-1 in CNS infection. •

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COMPARATIVE TREATMENT BETWEEN ANTI-PARASITIC DRUG ALONE AND DRUG COMBINED WITH HEALTH EDUCATION IN INTESTINAL PROTOZOA IN THAI SCHOOL CHILDREN

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Experimental longitudinal studies on intestinal protozoa infestation in 972 Thai school children were performed with the purpose of comparison the result of treatment between anti-parasitic drug alone and drug combine with health education. Infection rate before intervention was 6.4%. Proper anti- parasitic drugs were given to the positive cases in control group as well as drugs combined with health education provided to children in experimental group. The re-infection rate was 4.2% in control group, whilst it was 3.2% in experimental group. The result of treatment between two groups was not statistically significantly different (p=0.54). •

LIGHT AND ELECTRON MICROSCOPIC PATHOLOGICAL FEATURES OF ACUTE TOXOPLASMOSIS IN EXPERIMENTAL ANIMAL

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Toxoplasma *gondii* is an obligate intracellular protozoan that infects a variety of vertebrate hosts including man. In immunocompetent host, symptoms are mild and non-specific, thus pathological information of acute toxoplasmosis in man is rare. Toxoplasmosis as a life-threatening disease in AIDS patients results from reactivation of previously quiescent infection. The presently available evidence suggests that host tissue pathology associated with *T. gondii* infection may play an important role in latent infection and reactivation process.

We, therefore, studied the pathology of acute toxoplasma in experimental mice inoculated with 5 x 10^5 RH strain of *Toxoplasma gondii*. Light and electron microscopic pathological features found disseminated toxoplasmosis the liver, spleen, and pancreas of those mice studied, could be applied in man for the further understanding of the pathogenesis of *Toxoplasma* reaction. •

Presented at: Joint International Tropical Medicine Meeting, Bangkok 20-22 November 2002.

COMPARISON OF *CRYPTOSPORIDIUM PARVUM* DEVELOPMENT IN VARIOUS CELL LINES FOR SCREENING *IN-VITRO* DRUG TESTING

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The study described development of *Cryptosporidium parvum* in MDCK, MA-104, Hep-2 and Vero cell lines. Differences of susceptibility, infectivity, and methodology of excystation were determined. Various solutions were adjusted to determine the factors, which enhanced the excystation e.g. with and without sodium hypochlorite, trypsin or sodium taurocholate. It was shown that the sporozoites could be excysted in media either with or without trypsin and sodium taurocholate but the number of sporozoites in the latter solution was less than the former one. Only digested oocysts by sodium hypochlorite and trypsin could enter the culture cells. Numerous meronts and oocysts were demonstrated and persisted for 9 days. Asexual stages could not be observed in MA-104. Only few oocysts could be detected during 1-3 day post inoculations. There was a significant difference between the number of oocysts, which invaded MDCK, MA- 104, and Hep-2 cells. MDCK gave the highest susceptibility to oocyst invasion among three cell lines and asexual stages were also found. Among 25 isolates, which had been cultivated, 23 isolates could be infected in MDCK and Hep-2. Only 2 isolates could not be infected in MDCK cell. These 2 isolates could be infected to Vero cell and yielded high numbers of trophozoites. PZQ, doxycycline and PRM were tested to the infected parasites. The drugs were added either with inoculum or 24 hours after inoculation. None of them was effective including PRM, which has been previously reported. •

Poster presentation at: Joint International Tropical Medicine Meeting Bangkok, 20-22 November 2002.

CAT AND THE TRANSMISSION OF DISEASES FROM CATS TO MAN

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The relationship between cats and man dates back about 5,000 years ago when African wild cats, which previously preyed on mice and birds that caused damage to agricultural products, become domesticated and eventually were kept as pets by man. Currently, cats are household members worldwide and live happily in harmony with their owners except for a very small minority that are utilized as experimental animals in scientific research. Owing to their close relationship with man, certain infectious diseases can be transmitted to their human host. These include bacterial, viral and parasitic infections. Although a few of these could cause serious harm and death, this fact should not hinder or discourage man from keeping cats as pets. All that is required to prevent disease are health education and simple public health measures. •

CEREBROSPINAL FLUID ANALYSIS IN EOSINOPHILIC MENINGOENCEPHALITIS

Tangwanicharoen T, Viriyavejakul P, Punpoowong B, Wilairatana P, Kaewkungwal J, Pongponratn E, Riganti M

Eosinophilic meningoencephalitis (EME) remains an important neurological disease and is widely distributed in Thailand. We analyzed the cytological specimens of 56 EME cases. Pertinent clinical data were analyzed retrospectively and correlated with the cerebrospinal fluid (CSF) analysis. Headache was the commonest symptom seen in all EME cases. History of raw or partially cooked *Pila* snail ingestion was elicited from most patients. There was a marked seasonal occurrence between July to January. Patients received specific treatment as supportive therapy, which included spinal taps, analgesics and corticosteroids, was adequate. No fatal cases were seen. The CSF specimens were sorted into two categories: fresh CSF and hematoxylin and eosin (H&E) stained centrifuged CSF sediment. There was a statistically significant difference between the number of eosinophils and lymphocytes of fresh CSF and the H&E stained centrifuged CSF sediment ($p = 0.001$ and 0.001 respectively). The CSF glucose and the number of eosinophils in both methods were significantly correlated ($p = 0.000$, $p = 0.008$ for fresh CSF and the H&E stained centrifuged CSF sediment respectively). Moreover, the number of eosinophils was statistically significant with the protein in the CSF ($p = 0.013$), and intracranial pressure (ICP) ($p = 0.025$). Higher yields of eosinophils, especially in the early course of the disease, can readily be detected in the H&E stained centrifuged CSF sediment, whereas fresh specimens were negative. Further tests may increase the sensitivity and specificity of EME diagnostic results. •

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COST-EFFECTIVENESS AND SUSTAINABILITY OF LAMBDACYHALOTHRIN-TREATED MOSQUITO-NETS IN COMPARISON TO DDT SPRAYING FOR MALARIA CONTROL IN WESTERN THAILAND

Kamolratanakul P, Butraporn P, Prasittisuk M, Prasittisuk C, Indaratna K

The cost-effectiveness of lambdacyhalothrin-treated nets in comparison with conventional DDT spraying for malaria control among migrant populations was evaluated in a malaria hyperendemic area along the Thai-Myanmar border. Ten hamlets of 243 houses with 948 inhabitants were given only treated nets. Twelve hamlets of 294 houses and 1,315 population were in the DDT area, and another 6 hamlets with 171 houses and 695 inhabitants were in the non-DDT-treated area. The impregnated net program was most cost-effective (US$1.54 per 1 case of prevented malaria). Spraying with DDT was more cost-effective than malaria surveillance alone ($1.87 versus $2.50 per 1 case of prevented malaria). These data suggest that personal protection measures with insecticide-impregnated mosquito net are justified in their use to control malaria in highly malaria-endemic areas in western Thailand. •

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GENETIC ANALYSIS OF INCIDENT HIV-1 STRAINS AMONG INJECTION DRUG USERS IN BANGKOK: EVIDENCE FOR MULTIPLE TRANSMISSION CLUSTERS DURING A PERIOD OF HIGH INCIDENCE

Nguyen L, Hu DJ, Choopanya K, Vanichseni S, Kitayaporn D, van Griensven F, Mock PA, Kittikraisak W, Young NL, Mastro TD, Subbarao S

During 1995-1996, 1,209 HIV-1-negative injection drug users (IDUs) attending methadone treatment clinics operated by the Bangkok Metropolitan Administration in Bangkok, Thailand, were enrolled in a prospective cohort study. Through 1998, 133 of these IDUs had seroconverted to HIV-1; 130 of these seroconverters were included in this study. HIV-1 CRF01_AE and subtype B strains accounted for 79% and 21% of the incident infections, respectively. To examine phylogenetic relationships among these incident HIV-1 strains, we used several phylogenetic inference methodologies to analyze the env (C2-V4) sequences in blood samples collected soon after seroconversion. These analyses consistently revealed eight phylogenetic clusters comprising 21 incident strains (bootstrap method, >80%; six CRF01_AE and two subtype B clusters). Two factors were found to be associated with the eight clusters. The first factor was temporal: seven of the eight clusters comprised 17 sequences from IDUs whose estimated dates of seroconversion were within a period of high incidence from July 1996 through January 1997. The second factor was a possible geographic association: four clusters were observed among IDUs who had attended the same methadone treatment clinics. These phylogenetic clusters likely represent subgroups within larger HIV transmission networks among IDUs in Bangkok. Despite prevention efforts, the incidence of HIV-1 infection among the Bangkok IDU population continues to be high. A better understanding of transmission networks and factors associated with such networks can help guide prevention efforts. •

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HIGHER VIRAL LOADS AND OTHER RISK FACTORS ASSOCIATED WITH HIV-1 SEROCONVERSION DURING A PERIOD OF HIGH INCIDENCE AMONG INJECTION DRUG USERS IN BANGKOK

Hu DJ, Subbarao S, Vanichseni S, Mock PA, van Griensven F, Nelson R, Nguyen L, Kitayaporn D, Young NL, Des Jarlais D, Byers R Jr, Choopanya K, Mastro TD

We analyzed data from a prospective cohort study of injection drug users (IDUs) attending methadone treatment clinics in Bangkok, Thailand, during 1995-1998 to characterize factors associated with a period of high incidence (PHI) from July 1996 through January 1997 compared with periods of lower incidence. Sociobehavioral characteristics were similar for all participants during and outside the PHI except for the following: there was more reported drug injection while IDUs were incarcerated during the PHI (odds ratio, 1.67; p = 0.02) and significantly higher proportions of persons reported heroin injection (91% vs. 75%, respectively; p = 0.02) and higher frequencies of daily injection and sharing of injection equipment (40% vs. 25%, respectively; p = 0.05) during the PHI than outside the PHI. Through most of the first year after seroconversion, plasma HIV-1 loads were significantly higher in persons who seroconverted during the PHI than in those who seroconverted outside the PHI. Higher viral loads may potentially contribute to faster disease progression and increased infectiousness or transmissibility to subsequent contacts. Our findings suggest that prevention efforts to reduce the effective size and turnover within IDU sharing networks may have a significant impact on the epidemic by disrupting the rapid transmission of HIV-1 from recently infected, highly infectious individuals. •

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INCARCERATION AND RISK FOR HIV INFECTION DRUG USERS IN BANGKOK

Choopanya K, Des Jarlais DC, Vanichseni S, Kitayaporn D, Mock PA, Raktham S, Hireanras K, Heyward WL, Sujarita S, Mastro TD

Objective: To assess potential multiple relationships between incarceration and HIV infection among injecting drug users (IDUs) in Bangkok. Previous cross-sectional studies have shown strong relationships between incarceration and HIV infection but have not been able to assess potential causal pathways.

METHODS: Injection drug users seen at methadone treatment programs in Bangkok were screened during 1995 to 1996 for enrollment into the study. With informed consent, 1,209 seronegative IDUs were enrolled in a cohort study to determine HIV incidence and identify factors associated with incident infections. Follow-up visits were conducted every 4 months, with HIV testing and assessment of risk behaviors.

Results: Overall incidence rate was 5.8 per 100 person-years (95% confidence interval [CI], 4.8-6.8) of follow-up. A four-step "injection risk" scale was constructed that included less frequent than daily injection, daily injection, daily injection with reported sharing of injection equipment, and injection while incarcerated. This scale was strongly related to HIV incidence, with incidence approximately doubling for each step in the scale. Incidence rate for follow-up periods that contained drug injection while incarcerated was 35/100 person-years at risk. In multivariate analyses, incarceration was related to incident HIV infection in multiple ways: previous incarceration and recent incarceration without drug injection, and the injection risk scale were all independently predictors of incident HIV infection.

Conclusions: Incarceration is related to incident HIV infection through multiple pathways. Previous incarcerations are likely to serve as markers for unmeasured high-risk behaviors, and it is also highly likely that HIV is transmitted during periods of incarceration. Programs to reduce HIV transmission in jails and prisons, including drug abuse treatment of inmates and programs to reduce the likelihood of incarceration of IDUs, are needed urgently. Given the current diffusion of injecting drug use, of HIV infection among drug injectors, and of the common policy of incarcerating drug users, it is very likely that the problem of HIV transmission in jails and prisons is increasing in many countries throughout the world. •

Published in: J Acquir Immune Defic Syndr 2002;29:86-94.

RELATIONSHIP BETWEEN REACTIVE NITROGEN INTERMEDIATES AND TOTAL IMMUNOGLOBULIN E, SOLUBLE CD21 AND SOLUBLE CD23: COMPARISON BETWEEN CEREBRAL MALARIA AND NONSEVERE MALARIA

Nacher M, Singhasivanon P, Kaewkungwal J, Silachamroon U, Treeprasertsuk S, Tosukhowong T, Vannaphan S, Looareesuwan S

To search for evidence of a protective role of the CD23/NO pathway against cerebral malaria, concentrations of reactive nitrogen intermediates (RNI) and sCD21, total immunoglobulin (Ig)E and sCD23 were compared between 17 cases of cerebral malaria and 33 controls. The geometric mean of sCD23 concentration was higher among cerebral malaria cases than among controls (optical density 2643/1495, P = 0.01). The ratio between sCD21 and sCD23 was significantly lower in cerebral malaria cases than in controls (0.67 +/- 0.02 versus 0.77 +/- 0.02, respectively, P = 0.009). Multiple linear regression analysis showed that, among cerebral malaria cases, there was a clear correlation between RNI and both IgE (P = 0.007) and sCD21 (P < 0.0001). Among controls, there was a strong negative correlation between RNI and sCD23 concentrations (r = -0.61, P < 0.0001). However, multivariate analysis unmasked the fact that, in controls, there was also a positive correlation between RNI and IgE (P = 0.045). Logistic regression showed that increased RNI concentrations were associated with a cerebral malaria adjusted odds ratio of 1.05 per unit increase [95% confidence interval (CI) 1.006-1.1, P = 0.02] and that an increased ratio between sCD21 and sCD23 was associated with protection from cerebral malaria (adjusted OR = 0.00001 per unit increase (95% CI 0-0.03, P = 0.005). These different immunological profiles suggest that, among controls, the CD23/NO pathway was chronically stimulated whereas, in cerebral malaria, its stimulation was acute, which could explain why some patients developed cerebral malaria and others did not. •

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SUBTYPE-SPECIFIC TRANSMISSION PROBABILITIES FOR HUMAN IMMUNODEFICIENCY VIRUS TYPE 1 AMONG INJECTING DRUG USERS IN BANGKOK, THAILAND

Hudgens MG, Longini IM Jr, Vanichseni S, Hu DJ, Kitayaporn D, Mock PA, Halloran ME, Satten GA, Choopanya K, Mastro TD

The Bangkok (Thailand) Metropolitan Administration cohort of injecting drug users (IDUs) consisted of 1,209 IDUs initially seronegative for human immunodeficiency virus (HIV) who were followed from 1995 to 1998 at 15 Administration drug treatment clinics. At enrollment and approximately every 4 months thereafter, participants were assessed for HIV seropositivity. As of December 1998, there were 133 HIV type 1 seroconversions and approximately 2,300 person-years of follow-up. Of the 133 observed seroconversions, specimens from 126 persons were available for subtyping (27 subtype B, 99 subtype E). In this analysis, the authors assessed differences in subtype-specific transmission while controlling for important risk factors. The methodology used accounts for left truncation, interval censoring, and competing risks as well as for time-varying covariates such as each IDU's history of reported frequency of injection and of incarceration. Using plausible epidemiologic assumptions and controlling for behavioral risks, the authors found that a significantly higher transmission probability was associated with subtype E compared with subtype B in this population. Since many epidemiologic, virologic, and host factors can influence HIV transmission, it was difficult to conclude whether these differences in transmission probabilities were due to biologic properties associated with subtype. •

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COMPLETION OF ENROLLMENT AND ONGOING FOLLOW-UP OF INJECTING DRUG USERS (IDUS) IN THE AIDSVAX B/E VACCINE EFFICACY TRIAL IN BANGKOK, THAILAND

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Background: Since 1988, IDUs in Bangkok, Thailand, have experienced an explosive HIV epidemic. As a consequence, Thailand, with support of UNAIDS, has made development of an effective AIDS vaccine a national commitment. A 1995-1998 cohort study of Bangkok IDUs revealed high rates of follow-up, an annual HIV-1 incidence rate of 5.8 per 100 person-years (21% subtype B, 79% subtype E), and willingness to participate in HIV vaccine trials. In 1995, a phase I trial of a bivalent B (MN)/E (A244) rgp120 HIV vaccine (AIDSVAX B/E, VaxGen, Inc., USA) showed the vaccine to be safe and immunogenic in Bangkok IDUs, prompting the initiation of a phase III efficacy trial.

Methods: Following informed consent, HIV-seronegative IDUs meeting eligibility criteria were randomized to receive AIDSVAX B/E 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. All participants are being followed for 3 years to detect > 30% efficacy (1st endpoint, infection measured by ELISA and Western blot; 2nd endpoint, reduced progression of disease as measured by RNA PCR viral load and CD4). Interim safety and efficacy analyses are conducted by and independent data and safety monitoring board (DSMB).

Results: Screening began on March 10, 1999 and the first participant was vaccinated on March 24; enrollment was completed on August 31, 2000. A total of 4,939 IDUs were screened, 1,689 (34%) were HIV-seropositive (HIV-1 subtype, March thru Dec. 1999: 26% B, 74% E; Jan. thru Aug. 2000: 23% B, 77% E). 2,545 IDUs were enrolled with a median age of 26 years and 93% were male. Through March 18, 2001, follow-up has been well tolerated. No vaccine-related serious adverse events have occurred, with pain and tenderness at the injection site (reported by 65% of subjects after 1 or more vaccinations) being the most commonly experienced side effect. Immunization compliance was 98%, with 2,513 (99%) subjects receiving the 2nd dose, 2,426 (97%) receiving the 3rd, and 1,717 (96%) receiving the 4th dose, respectively. The DSMB advised trial continuation following safety reviews in September 1999, April and October 2000, and April 2001.

Conclusion: Through March 18,2001, study follow-up has been excellent (97.4%), and adverse effects have been unremarkable. The first combined interim safety and efficacy DSMB review is scheduled for late 2002 and final results are expected in late 2003. •

Presented at the 6th International Congress on AIDS in Asia and Pacific, Melbourne, Australia, 5-10 October 2001.

LEARNING FROM LONG-TERM BEHAVIORAL SURVEILLANCE: BANGKOK, THAILAND AND NEW YORK CITY, USA

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Objective: To assess validity of self-reported HIV risk behavior within the long-term structure of high HIV prevalence epidemics among injecting drug users (IDUs) in Bangkok (BKK) and New York City (NYC).

Methods: Multiple risk behavior and HIV seroprevalence surveys were conducted from 1989-1997 in BKK and 1984-2000 in NYC. IDU subjects were recruited from persons entering drug abuse treatment programs with N=1500 in BKK and N=6400 in NYC. Cohort studies were also conducted in each city to estimate HIV incidence. Implementation of new HIV prevention programs was also recorded.

Results: In both cities, self-reported HIV risk behaviors tracked HIV prevalence and incidence over time. Injection risk behavior declined from 1988 to 1993 and then remained stable in BKK. HIV prevalence

stabilized during this time in BKK at 30-40%. Estimated HIV incidence was moderate to high at 5.8% per year in BKK from 1995-98. Injection risk behavior initially declined in NYC in the middle 1980s, and then further declined after implementation of large syringe exchange programs in 1992. HIV prevalence stabilized at approximately 50% from 1984 to 1992, and then declined to 20% in 2000 in NYC. Estimated HIV incidence declined from 4.4%/year in the early 1990s to 1%/year in the late 1990s in NYC.

Conclusions: The consistency of parallel trends in self-reported risk behavior, HIV prevalence and HIV incidence in both cities supports the group-level validity of self-reported risk behavior among IDUs. Initial risk reduction tends to stabilize high HIV prevalence epidemics among IDUs for long time periods with "moderate to high" 4-6%/year incidence rates. Introduction of new, large-scale HIV prevention programs may lead to declines in such large epidemics. Monitoring self-reported HIV risk behavior may be a critical component in public health efforts to control HIV epidemics. •

Presented at the 6th International Congress on AIDS in Asia and Pacific, Melbourne, Australia, 5-10 October 2001.

RISK BEHAVIOUR MONITORING AMONG INJECTING DRUG USERS (IDUS) PARTICIPATING IN THE AIDSVAX B/E VACCINE TRIAL IN BANGKOK, THAILAND

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Background: In March 1999, a randomized, double-blinded, placebo-controlled phase III trial was initiated among 2,545 IDUs in Bangkok, Thailand, to evaluate the protective efficacy of a bivalent B/E rgp120 HIV-1 Vaccine (AIDSVAX B/E). Concern exists that trial participation may lead to enhanced HIV risk behavior, attributed to expectations about the efficacy of the vaccine. We evaluated drug use and sexual behaviors at baseline and during follow up among IDUs participating in this first HIV vaccine efficacy trial in a developing country.

Methods: At enrollment and every 6 months thereafter, standardized questionnaires are administered to assess demographic characteristics, drug use, and sexual behaviors. Participants receive continued behavioral risk reduction counseling during the trial. Results: Participants are predominantly male (93.4%) with a median age of 26 years. Most (95.0%) of the 2,545 IDUs had completed at least primary education. At enrollment, reported HIV risk behaviors during the previous 6 months were: injection drug use 93.8%, needle sharing 33.0%, injection drug use while incarcerated 13.0%, no or inconsistent condom use with steady partner 92.8%, and no or inconsistent condom use with casual partner 54.3%. Among 1,727 IDUs at 12 months of follow up, injection drug use had decreased significantly to 72.1% ($p<0.001$), needles sharing to 16.3% ($p<0.001$) and injection drug use while being incarcerated to 3.6% ($p<0.01$). No significant changes were observed in condom use with steady and casual sexual partners.

Conclusion: There are no indications of adverse effects of trial participation on risk behavior among IDUs enrolled in the AIDSVAX B/E vaccine trial. Participants report significant education in injection drug use and needle sharing, which are the main routes of HIV transmission in this group. HIV risk behaviors will be monitored on an ongoing basis during the course of the trial, and if indicted, risk reduction counseling will be adapted. •

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B VITAMINS, VITAMIN C AND HAEMATOLOGICAL MEASUREMENTS IN OVERWEIGHT AND OBESE THAI IN BANGKOK

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The dynamic changes of socio-economics leading to the industrialisation of countries are known to affect lifestyle and nutritional behaviours of the population. Review of the literature on the prevalence of obesity showed increasing numbers of overweight and obese during the past decade. For this contribution, information on health and nutritional status of obese in Thailand has not been widely publicized. This study is one trial on revealing the vitamin status and haematological picture in 270 overweight and obese in Bangkok, Thailand, compared with 175 normal subjects. No statistically significant differences in haemoglobin and haematocrit were observed in the overweight comparing with control subjects. The prevalence of hypertension exhibited in both male and female overweight and obese subjects. The prevalence of anaemia was 17.2% among female and 9.8% among male overweight and obese subjects. Even if there were no statistically significant differences in vitamins B_1, B_2 and B_6 in overweight and obese subjects compared with the controls, high percentages of vitamin C and vitamin B_2 deficiencies were observed. Vitamin B_2 deficiency was detected in 19.7% of overweight and obese males as well as in 28.7% of overweight and obese females. However clinical signs of vitamin B_2 deficiencies are rare. There was also a high percentage of vitamin C deficiency in 51.5% of overweight and obese subjects and 41.7% of controls, respectively. The results suggest more attention to health study and nutritional problems for the overweight and obese population, especially vitamins and oxidative stress. More research is still needed in these respects. •

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MICROSATELLITE ALTERATIONS IN NON-SMALL CELL LUNG CANCER

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Genetic alterations at 12 dinucleotide repeat loci located on human chromosomes 2, 3, 12, and 17 have been analyzed in non-small cell lung cancer from Thai patients. Seventeen out of 30 cases (57%) harboured the microsatellite alterations. Of the 30 cases, 19 patients had a history of tobacco smoking, of whom 14 (74%) were in the group with microsatellite alterations, whereas 3 out of 11 non-smokers (26%) had these alterations. The frequency of microsatellite alterations among smokers was significantly higher than it was in non-smokers (P = 0.01 Fisher' s exact test; odds ratio = 7.47). •

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IODINE DEFICIENCY DISORDER - AN OLD PROBLEM TACKLED AGAIN: A REVIEW OF A COMPREHENSIVE OPERATIONAL STUDY IN THE NORTHEAST OF THAILAND

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Between 1991 and 1996 attempts were made to control iodine deficiency disorder (IDD) in the Northeast of Thailand. The project was conducted within the framework of an intervention project with emphasis on women's health in the reproductive age. IDD was found to be highly prevalent in the project area. The goitre rate of the women was 50.6%. In school children it was between 27 to 93%. The use of iodinated water was not successful. In the project area, iodinated fish sauce was favoured over iodinated salt. This was because the local population mostly use fish sauce instead of salt in their cooking. The results of two independent intervention trials, one with females and another with school children, indicated that iodinated fish sauce could be the best means to control IDD in the area. The experiences gained in the trials were used to control IDD in the whole project area. From 1991 to 1996 the goitre rate of females in the reproductive age decreased to about 20%. •

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CIGARETTE SMOKING EFFECT ON CERULOPLASMIN AND C3 COMPLEMENT: RISK OF CARDIOVASCULAR DISEASE (ATHEROSCLEROSIS)

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Serum ceruloplasmin, C3 complement and albumin in 119 male smokers and 65 male non-smokers from a military unit in Bangkok were investigated in the study. The scrum ceruloplasmin concentration was found to be significantly higher in smokers compared with non-smokers. However, the serum albumin concentration in smokers was statistically lower than in non-smokers. Significant associations were found between age, albumin and quantity of cigarettes smoked. There were significantly positive correlations between serum ceruloplasmin and C3 complement concentration. An association between the quantity of cigarettes smoked and albumin was also found. A significant relationship between smoking and the quantities of cigarettes smoked to serum ceruloplasmin was found when smoking and the quantity of cigarettes smoked were taken as independent variables, and serum ceruloplasmin as a dependent variable. It might be suggestive that high concentrations of the acute-phase protein, ceruloplasmin, might be linked to the risk of developing atherogenesis or cardiovascular disease in smokers. •

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IRON BIOAVAILABILITY IN THAI DIETS

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Dietary low iron bioavailability intake is an important causation factor of iron deficiency anemia in Asian countries including Thailand. The aim of this study was to estimate the iron bioavailability in the Thai diet by a calculation method that is based on dependent factors, dietary components and physiological iron store. Based on the latest national nutrition survey of the Thai diet, 1995, the data of nutrient intake per capita per day by region were used for calculating the iron bioavailability at physiological iron store levels; 0, 250, 500 and 1,000 mg of iron. The results showed that the diets consumed by the populations in the Central, North, Northeast and South of Thailand were classified under the calculation method as being of moderate nonheme iron availability. The per cent iron bioavailability values of the Thai diets were within the range 3.7-12.4 percent of total iron, depending on physiological iron store. The values of all region Thai diets at each iron store level were similar. By the same method, the dietary iron bioavailability of the total Thai diet at any iron store level was markedly lower than the general US diet, which was classified as high nonheme iron availability. When comparison of the iron bioavailability among other different diets was carried out, the values of the total Thai diet were slightly lower than Utah, but higher than US vegetarian and Regional Latin American diet. •

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STAGE SPECIFIC OF *PLASMODIUM FALCIPARUM* TELOMERASE AND ITS INHIBITION BY BERBERINE

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Telomerase activity in asynchronized and synchronized *Plasmodium falciparum* during its erythrocytic cycle was examined using the TRAP assay. Telomerase activity was detected at all stages of the parasite intraerythrocyte development, with higher activity in trophozoite and schizont stages compared with ring form. In addition, the inhibitory effect of berberine, extracted from *Arcangelisia flava* (L.) Merr. against *P. falciparum* telomerase was investigated. Berberine inhibited telomerase activity in a dose-dependent manner over a range of 30-300 mM, indicating that *P. falciparum* telomerase might be a potential target for future malaria chemotherapy. •

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RELATIONSHIP BETWEEN ALPHA-2-MACROGLOBULIN, ANTHROPOMETRIC PARAMETERS AND LIPID PROFILES IN THAI OVERWEIGHT AND OBESE IN BANGKOK

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The aim of this study was to assess anthropometrical variables and the lipid pattern in relation to alpha-2-

macroglobulin in normal- and over-nourished Thai individuals, to further support the hypothesis that alpha-2-macroglobulin plays a beneficial role in the determining of the nutritional status. The study population comprised of 48 male and 166 female overweight and obese Thai volunteers and 26 male and 81 female normal subjects. The group of overweight individuals had statistically significantly lower alpha-2-macroglobulin serum levels. The lipid status between the two groups was also statistically significantly different, in that total serum cholesterol, LDL and triglycerides were higher and HDL lower in the over-nourished group. The LDL/HDL ratio was slightly but significantly higher in the over-nourished group, but still well below the value of 5 for both groups. In using a stepwise multiple linear regression, the model, which best explained the variation of alpha-2-macroglobulin for all individuals, includes age, HDL, BMI, and gender. The relationship of alpha-2-macroglobulin to the variables under study differed between males and females. For males, a model which includes cholesterol and BMI explained best the variation of the proteinase inhibitor. For the females, the best model includes age, HDL and BMI. The role of protease inhibitors has hardly been explored in human epidemiological studies despite its relationship to important public health issues including nutrition, smoking cancer and cardiovascular diseases. The results of this study indicate, that alpha-2-macroglobulin might be a potential indicator for the interrelationship of the nutritional status with the occurrence and the prevention of diseases. •

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SERUM HOMOCYSTEINE, B_{12} AND FOLIC ACID CONCENTRATION IN THAI OVERWEIGHT AND OBESE SUBJECTS

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This study investigated serum homocysteine, vitamin B_{12}, folic acid, vitamin B_6 and vitamin C, including anthropometric measurements and waist/hip ratios, of 37 male and 112 female overweight and obese Thai volunteers (BMI $\geq$ 25.00), and 23 male and 90 female normal Thai volunteers, who came for a physical check-up at the Out-patient Department, General Practice Section, Rajvithi Hospital, Bangkok from March to October, 2000. All anthropometric variables, except height, were significantly higher for the overweight subjects than for the normal subjects. Statistically significantly higher levels of serum homocysteine were found in the overweight subjects. Serum homocysteine concentrations in overweight and obese males were significantly higher than in overweight and obese females. Serum folic acid and vitamin C in the overweight and obese were found to be statistically significantly lower than in the control subjects. No statistically significant difference in vitamin B_{12} was found in the overweight and obese subjects compared with the normal control subjects. The medians of serum folic acid and vitamin C concentrations for the overweight and obese males were significantly lower than of those for the overweight and obese females. A negative correlation was found between serum folic acid and homocysteine concentrations in all overweight and obese subjects. A significant negative correlation between serum folic acid and vitamin B_6 was observed in both male and female overweight and obese subjects. The results of the investigation suggest that homocysteine levels in overweight and obese subjects seem to be caused by insufficient dietary folic acid intake and probably not by B_{12} deficiency. •

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THE RELATIONSHIPS BETWEEN ANTHROPOMETRIC MEASUREMENTS, SERUM VITAMIN A AND E CONCENTRATIONS AND LIPID PROFILES IN OVERWEIGHT AND OBESE SUBJECTS

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The weight, height, body mass index (BMI), waist/hip ratio, serum retinol and a-tocopherol and lipid profiles of 16 overweight (BMI ⩾ 25.0 kg/m^2) Thai males and 56 overweight females, compared with 14 males and 58 females in a controlj group (BMI 18.5-24.9 kg/m^2), were investigated. Subjects for the study were those persons who turned up regularly for physical check-up at the Outpatient Department, General Practice Section of Rajvithi Hospital, Bangkok. The study was conducted between December 2000-March 2001. Higher levels of cholesterol, LDL-C, LDL-C/HDL-C ratio were found in the overweight compared with the control subjects. Statistically significantly higher triglyceride levels were found in the overweight compared with the control subjects. The median serum retinol concentration in overweight subjects was 2.80 μmol/L (range 0.53-4.62 μmol/L) compared with 2.97 μmol/L (range 1.21-4.12 μmol/L) in control subjects (p=0.0736). The median serum α-tocopherol concentration in overweight subjects was 17.30 μmol/L (range 6.29-28.65 μmol/L) compared with 18.75 μmol/L (range 5.30-30.28 μmol/L) in control subjects (p<0.05). The median values of retinol and α-tocopherol serum concentrations in the overweight and obese males were lower than those of the overweight and obese females. A total of 6.3% (1 out of 16) and 12.5% (2 out of 16) of the overweight/obese males had decreased retinol and α-tocopherol levels, while the overweight/obese females had decreased retinol and α-tocopherol level of 1.8% (1 out of 56) and 10.7% (6 out of 56), respectively. A total of 12.5% and 39.3% of the overweight/obese males and females 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 50% in the overweight and obese males and 10.7% in the overweight and obese females. Statistically significant associations were found between age, cholesterol, LDL-C, and serum α- tocopherol in the overweight and obese male and female subjects. A negative correlation was found between weight, BMI, AC, MAMC, hip circumference and serum retinol in both the overweight and obese subjects. A negative correlation was found between weight, BMI, MAMC, waist, hip circumferences and serum α-tocopherol in both the overweight and obese subjects. •

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DETERMINATION OF GENOMIC INSTABILITY IN CHOLANGIOCARCINOMA TISSUES USING THE RANDOM AMPLIFIED POLYMORPHIC DNA TECHNIQUE

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The random amplified polymorphic DNA (RAPD) technique was used to determine genomic instability in cholangiocarcinoma tissues compared to corresponding normal tissues from the same patients. DNA from tumor and corresponding normal tissues of 30 patients were extracted and amplified separately with 60 random 10-base arbitrary primers using RAPD technique. Genomic instabilities were analyzed as banding pattern changes between normal and tumour DNA. Interestingly, one primer yielded genomic instabilities in 29 out of the 30 case (97%). These finding demonstrate that genomic changes are related to cholangiocarcinogenesis. •

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IDENTIFICATION OF GENETIC ALTERATIONS IN BREAST CANCER BY ARBITRARILY PRIMED POLYMERASE CHAIN REACTION IN THAI PATIENTS

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Genetic alterations in 15 Thai patients with breast cancer were analyzed by arbitrarily primed polymerase chain reaction (AP-PCR) with sixty random arbitrary primers. Six primers exhibit high frequency of abnormal patterns in breast cancer when compared with their corresponding normal DNA (60-86%). Of these one primer presence most frequency of a band which greatly increased intensity in 13 cases, (86%), while the other primers show banding pattern changes in 66% of the cases. The combination of two primers can detect genetic alteration of all breast cancer tissues (100%). These results estimated that AP-PCR analysis is useful for the detection of genetic alteration in breast cancer tissues. •

Present at the 4th HUGO Pacific Meeting and the 5th Asia-Pacific Conference on Human Genetics, Ambassador City Jomtien, Cholburi, Thailand October 27-30, 2002.

IDENTIFICATION OF GENETIC ALTERATIONS OF EPITHELIAL OVARIAN TUMORS BY ARBITRARILY-PRIMED POLYMERASE CHAIN REACTION (AP-PCR)

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DNA fingerprinting by Arbitrarily-Primed Polymerase Chain Reaction (AP-PCR) was employed to identify genetic alterations in 15 epithelial ovarian tumors. DNA from tumor and corresponding normal tissues were extracted and amplified with 60 arbitrary primers. Genomic instabilities which appeared as banding pattern changes between normal and tumor DNA were detected. Result shows that the combination of 3 arbitrarily primers have a relatively high frequency (93%) of genetic alterations in these patients. The identification of these genetic alterations were further investigated. In summary, AP-PCR is a useful method to detect genetic alterations in epithelial ovarian tumors. •

Present at the 4th HUGO Pacific Meeting and the 5th Asia-Pacific Conference on Human Genetics, Ambassador City Jomtien, Cholburi, Thailand October 27-30, 2002.

NECROPSY IN HIV-INFECTED PATIENTS

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Human immunodeficiency virus (HIV) infection is usually followed by opportunistic infections, especially in the full-blown acquired immuno-deficiency syndrome (AIDS). This study details the histopathological changes of different organs in relation to HIV infection, with particular emphasis on the opportunistic infections. Various organs from seventeen HIV-infected patients were collected by necropsy and analyzed for histopathological changes. The major histopathological changes included cytomegalovirus infection, cryptococcosis, penicilliosis, bacterial pneumonia, cryptosporidiosis, pneumocystosis, candidiasis, tuberculosis, granulomatosis of unknown etiology, early cirrhosis and chronic active hepatitis. General organ changes from seventeen cases of HIV-infected patients were described and discussed. •

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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 anemia, 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., Gb_3, 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. •

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A FUNDAMENTAL STUDY ON BIO-CONTROL OF ENVIRONMENTAL MOSQUITO PROBLEMS: GENETIC AND BIOLOGICAL CHARACTERIZATION OF POTENTIALLY NOVEL INSECTICIDE BACTERIA

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We have previously isolated two *Bacillus cereus* strains, Ae10 and Cx5, that displayed stable retention in mosquito larvae guts, indicating a high potential as novel host cells for application in mosquito control. However, *B. cereus* has also been recognized as an enterotoxin-producing strain. In order to elucidate the presence of enterotoxin genes in strains Ae10 and Cx5, primers specific to the structural genes of *B. cereus* enterotoxins, multicomponents haemolysin BL (HBL) and non-haemolytic enterotoxin (Nhe), and single components, BceT and EntFM, were designed and used for gene amplification. The PCR results indicated the presence of seven enterotoxin genes, all except *bceT*, in each bacterium tested. Multicomponent genes were confirmed to be present in a single gene cluster. Southern hybridization with the genomic DNA of strain Cx5 indicated that only single copies of *nheA* and *entFM* genes were present on the chromosome. An immunoassay against the *nheA* gene product displayed positive results in all strains. The bacteria harbored haemolytic activity, and also displayed positive results in Vero cell cytotoxicity testes. Oral feeding to mice did not lead to abnormal symptoms, and negative results were obtained in a rabbit skin irritation assay. •

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RAPID WRIGHT'S STAIN FOR THE DETECTION OF IMPORTED *LEISHMANIA TROPICA*

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Many species of *Leishmania* cause many diseases in tropics and subtropics. There are many ways to detect each of those diseases. We present one of the laboratory confirmation diagnosis *L. tropica* (that causes cutaneous leishmaniasis) by scraping of the skin ulcer smeared and stained with a modified method of Wright staining (used for ordinary laboratory hematological examination). By this method, *L. tropica* could be identified easily, rapidly, and conveniently. •

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ULTRASTRUCTURAL STUDY OF *PLASMODIUM MALARIAE*-INFECTED ERYTHROCYTES IN PERIPHERAL BLOOD AND TISSUE BIOPSIES

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Malaria is one of the most common and important parasitic diseases worldwide. The causative agents of malaria in humans are four species of *Plasmodium* protozoa: *P. falciparum*, *P. vivax*, *P. ovale* and *P. malariae*. Of these, *P. falciparum* accounts for the majority of infections and is the most lethal. While *P. malariae*, the cause of quarten malaria in human, is usually found at low prevalence in Thailand and rarely causes death or persistent sequelae. Ultrastructural studies of *P. falciparum*-infected erythrocyte (PE) showed numerous knobs on the PE surface. The knobs are believed to play a role in the sequestration of the PEs since they are points of contact between the PEs and vascular endothelial cells leading to microvascular obstruction. In addition, parasite species, which express knobs, exhibit the highest level of sequestration and associated with disease severity especially in falciparum malaria. There have been only a few studies that reported the fine structure of erythrocytic stages of *P. malariae*. In this present study we examined the fine structure of *P. malariae*-infected erythrocyte in peripheral blood and in tissue biopsies from liver, duodenum, stomach and kidney of six patients infected with *P. malariae*. Ultrastructural features of *P. malariae*-infected erythrocyte in peripheral blood appear quite similar to those described in *P. falciparum*. The surface membrane of PEs also showed numerous knobs as seen in *P. falciparum*-infected erythrocyte. Examination of PEs from the tissue biopsies showed no evidence of PEs in the microvessels of each organ. This finding may suggest that the presence of knobs in *P. malariae*-infected erythrocytes is not associated with the attachment of the PEs to vascular endothelium and resulting in less severity of malariae malaria. However the failure to find any of the PEs in the tissue biopsies may be due to the very low parasitemia in our patients. More cases with higher parasitemia are needed to confirm the study. •

Presented at: The 3rd ASEAN Microscopy Conference and 19th Annual Conference of The Electron Microscopy Society of Thailand, Chiang Mai, Thailand 30 January - 1 February 2002.

FALCIPARUM MALARIA PARASITES: ULTRASTRUCTURAL STUDIES OF THEIR INTERACTIONS WITH THE HOST CELLS IN HUMAN BRAINS

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Plasmodium *falciparum* malaria parasite is an intraerythrocytic protozoan. Intracellular *Plasmodium* influences the nature of the host plasma membrane. The structures that occur in parasitizeded red blood cell (PRBC) and that can be seen by light microscopy has been given name as Maurer's dot, appear to correspond to narrow slit-like structures in the cytoplasm that could be extrusions of the parasitophorous vacuole membrane. Another prominent change in the PRBC is the development of knobs on the cell membrane. The knobs appear mostly on the PRBC with mature forms of *P. falciparum*. The knobs form focal junctions with the

endothelial cell membrane. They are responsible for the sequestration of the PRBC, leading to vascular obstruction.

Ultrastructural studies of the PRBC in human brains infected with falciparum malaria revealed that the most common interaction is between the PRBC and the vascular endothelium. Many PRBC are irregularly shaped, characterized by distortions and elongated cytoplasmic processes which are always found attached to the endothelium. These are sometimes associated with marked excrescences of the endothelial cell membrane with invagination and endothelial pseudopodia formation. Folding of the PRBC membrane seemed marked in many cells which appear firmly adherent to vessel walls via multiple contacts.

Haemorrhages are represented by extravasation of red blood cells (RBC) around the vessels. Some of these show PRBC including PRBC ghosts among RBC and very occasional leukocytes. These extravasated cells intermixed with neurons, astrocytes, oligodendrocytes, microglial cells and nerve fibers but active interaction between these cells was not observed.

Malarial pigment was always found in phagolysosomes mainly in mononuclear cells. Occasionally the phagocytosed pigment was seen in endothelial cells, fibrous astrocytes or microglial cells. •

Presented at: The 3rd ASEAN Microscopy Conference and 19th Annual Conference of The Electron Microscopy Society of Thailand, Chiang Mai, Thailand 30 January - 1 February 2002.

ULTRASTRUCTURAL ANALYSIS OF THE BRAINS OF PATIENTS DYING OF *PLASMODIUM FALCIPARUM* MALARIA

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Malaria is an extremely important cause of disease in Africa and Asia. There is reported to be over 200 million clinical cases and more than 1 million deaths due to malaria per year. The vast majority of these deaths are due to infection with *Plasmodium falciparum*. A characteristic of falciparum malaria is the ability of red blood cells (RBCs) infected with mature parasites to sequester within the tissues. This is a result of specific parasite produced ligands on the surface of infected RBCs adhering to receptors on endothelial cells. It is believed that this sequestration plays an important role in cerebral malaria but the pathology of the disease is still not clearly understood[1]. In this study be have examined the brains of 65 patients form Thailand and Vietnam who died of malaria. These patients could be dived into two groups; those with coma (cerebral) (36 cases) and those without coma (non-cerebral) (28 cases). It was the purpose the present study was to use electron microscopy to evaluate the degree sequestration in the brains of these two groups to see if it related to disease symptoms.

A detail clinical and haematological record, including coma score and drug treatment, was available for each patient. After death, a rapid post-mortem examination was carried out. Samples from three areas (cerebrum, cerebellum, medulla oblongata) the brain were removed, fixed in glutaraldehyde and processed for routine transmission electron microscopy. To obtain quantitative, information thin sections were examined and the number of events per unit area (grid square) calculated. Factors examined were: number of RBCs, number of infected RBCs, number of blood vessels, number of macrophages, number of ruptured vessels and incidence of thrombus formation. This was carried out without knowledge of the clinical diagnosis.

As this was an autopsy study, the quality of preservation varied markedly and care had to be taken to differentiate between fixation artefact and pathological change. For both the cerebral and non-cerebral groups there were marked differences between patients. In both groups there was evidence of sequestration of infected RBCs although this was more often observed in cerebral cases. The sequestration was characterised by the peripheral location and cyto-adherence of infected RBCs to the endothelial cells of small cerebral blood vessels. In certain cases, all the blood vessel were packed with RBCs, the majority of which were infected as characterised by the presence of knobs at RBC surface. In other patients, the blood vessels were difficult to identify due to the absence of RBCs. When the three areas of the same brain were compared, there was consistently found to be differences in the degree of sequestration with significantly greater sequestration observed in the cerebrum compared to either the cerebellum and medulla oblongata. In addition the total parasite load was higher in the cerebral compared to non-cerebral groups. In fact the sequestration index (base on the ratio of % infected cells in the brain/ % infected cell in peripheral blood) was significantly higher in the cerebral

compared to the non-cerebral group.

This study confirms that sequestration occurs in both cerebral and non-cerebral groups. However, the degree of sequestration is significantly greater in cerebral compared to the non-cerebral cases. There was little evidence of necrotic changes around the vessels, which would point to a 'sludging' effect rather than total blockage of the vessels. •

Presented at: 15th International Conference for Electron Microscopy, Durban, South Africa, July 2002.

MICROVASCULAR SEQUESTRATION IN CEREBRAL MALARIA

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Malaria is an extremely important cause of disease in tropical area especially Asia and Africa. There is reported to be over 200 million clinical cases and more than 1 million deaths due to malaria per year. The vast majority of these deaths are due to infection with *Plasmodium falciparum*. A characteristic of falciparum malaria is the ability of red blood cells (RBCs) infected with mature parasites to sequester within the tissues. This is a result of specific parasite produced ligands on the surface of infected RBCs adhering to receptors on endothelial cells. It is believed that this sequestration plays an important role in cerebral malaria but the pathology of the disease is still not clearly understood. We have examined the brains of 65 patients from Thailand and Vietnam who died of malaria. These patients could be divided into two groups, those with coma (cerebral malaria (CM) 36 cases) and those without coma (non-cerebral malaria (NCM) 29 cases). It was the purpose of the present study to use electron microscopy to evaluate the degree sequestration in the brains of these two groups to see if it related to disease symptoms.

A detail clinical and haematological record, including coma score and drug treatment, was available for each patient. After death, a rapid post-mortem examination was carried out. Samples from three areas (cerebrum, cerebellum, medulla oblongata) of the brain were removed, fixed in glutaraldehyde and processed for routine transmission electron microscopy. To obtain quantitative, information thin sections were examined and the number of events per unit area (grid square) calculated. Factors examined were: number of RBCs, number of infected RBCs, number of blood vessels, number of macrophages, number of ruptured vessels and incidence of thrombus formation. This was carried out without knowledge of the clinical diagnosis.

As this was an autopsy study, the quality of preservation varied markedly and care had to be taken to differentiate between fixation artefact and pathological change. For both the CM and NCM groups there were marked differences between patients. In both groups there was evidence of sequestration of infected RBCs although this was more often observed in CM cases. The sequestration was characterised by the peripheral location and cyto-adherence of infected RBCs to the endothelial cells of cerebral blood vessels. In certain cases, all the blood vessel were packed with RBCs, the majority of which were infected as characterised by the presence of knobs at RBC surface. When the three areas of the same brain were compared, there was consistently found to be differences in the degree of sequestration with significantly greater sequestration observed in the cerebellum compared to either the cerebruum and medulla oblongata. In addition the total parasite load was higher in the CM compared to NCM groups. In fact the sequestration index (base on the ratio of % infected cells in the brain/ % infected cell in peripheral blood) was significantly higher in the CM compared to the NCM group.

This study confirms that sequestration occurs in both CM and NCM groups. However, the degree of sequestration is significantly greater in CM compared to the NCM cases. *P. falciparum* -infected RBCs sequestration in the cerebral microvessels is associated with pre-mortem coma and cerebral malaria. •

Presented at: Asian Union for Microcirculation, Thai Society for Microcirculation, Faculty of Medicine Chulalongkorn University, Bangkok, March 29, 2002.

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TROPICAL NEUROLOGY: PARASITIC INFECTIONS OF THE CENTRAL NERVOUS SYSTEM

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To compress the neurological manifestations of so-called "tropical diseases", the variety of parasitic infection which can damage the nervous system will be presented. This talk will limit itself to describe briefly the neuropathological feature of nervous system as caused by parasitic infection.

For example, epilepsy: this is a major neurological disorder in the tropics and has important medical and social implications. Cysticercosis accounts for about half the cases of epilepsy of late onset in several countries. Other parasitic infections known to cause epilepsy include: hydatid disease, cerebral toxoplasmosis, cerebral amoebiasis and cerebral malaria.

The talk will aim at emphasizing the need for basic and clinical neuroscience research on cerebral malaria, that still represent major health problem and in which severe involvement of the nervous system is frequently the direct cause of death.

This is a neurological syndrome consisting of a diffuse, potentially rapidly reversible encephalopathy associated with loss of consciousness and fitting. The level of consciousness can range from confusion or stupor to coma. The clinical symptoms of cerebral malaria and ultrastructural research aiming at deciphering the pathogenetic mechanism that could affect the nervous system at a molecular level and will be pointed out.

Several mechanisms that might cause damage to host cerebral endothelium and organs have been proposed, including obstruction of blood flow, and systemic or local production and deposition of pro-inflammatory cytokines. Insight into the complexity of cerebral malaria pathogenesis is vital for understanding the disease and will provide a major step towards control and cure of malaria. •

Presented at: Workshop: Neuroscience Research, Adriatic Palace Hotel, Banglamung, Chonburi, 17-19 May 2002.

MICROCIRCULATORY DISTURBANCE IN SEVERE FALCIPARUM MALARIA: AN ELECTRON MICROSCOPIC STUDY

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A key feature of the biology of *Plasmodium falciparum* is its ability to cause infected red blood cells to adhere to the endothelium of blood vessels. The adherence is mediated by contacts between electron dense knobs on the infected cell surfaces and the endothelial membrane. This process is termed "sequestration".

The essential pathological feature of severe falciparum malaria is sequestration of erythrocytes containing mature forms of the parasite in the deep vascular beds of vital organs. Such sequestered parasites cause considerable obstruction to tissue perfusion. Besides their ability to sequester, infected red cells also become rigid. Studies of fatal cases of falciparum malaria in which individual cells were observed under electron microscope have shown that erythrocytes infected with *P. falciparum* have reduced deformability, which is directly proportional to the maturity of the intracellular parasite. This explains the observation that such infected cells are less able to pass through micropore filters than uninfected cells. Normal erythrocytes must undergo considerable deformation in order to traverse the capillary and, when erythrocytes are unuasally rigid, obstruction may occur.

In larger vessels, erythrocytes contain mature parasites formed a layer along the endothelium (margination). A number of young parasites infected red cells and normal red cells were seen in the center of the lumen. Aggregation of normal red cells were observed. When infected cells were seen in the aggregation, special observation was performed in attempt to find out whether there is any rosette formation. Occasionally, an infected cell was found enclosed by red blood cells which may represent rosette formation.

The infected red cells appeared attach to the other infected cells. It was suggested that these cells stuck together and had difficulty passing through the capillary bed and could further slow down microcirculatory flow.

Intermixed with the infected red cells, a good number of mononuclear phagocytes containing malarial pigment were always seen. In some cases, the cerebral microvessel showed residual malarial pigment which was clearly visible deposited within a mass of fibrin and degenerating material.

The observation of these intravascular disturbances suggest that flow would consequently reduced, and finally stopped. The ensuing pathological events were considered to be the result of obstructed microcirculatory flow and/or the local release of unidentified toxic materials from the malaria parasites. •

Presented at: Joint International Tropical Medicine Meeting 2002, Monthien River side Hotel, Bangkok, Thailand, 20-22 November 2002.

This study was supported by The Faculty of Tropical Medicine, Mahidol University, Bangkok Thailand and The Wellcome Trust of Great Britain as part of the Wellcome-Mahidol University, Oxford Tropical Medicine Research Programme.
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FUNCTIONAL SIGNIFICANCE OF AMINO ACID RESIDUES IN THE RECEPTOR BINDING DOMAIN OF THE *BACILLUS THURINGIENSIS* CRY4B TOXIN

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PCR-based mutagenesis was employed to examine the role in insecticidal specificity of two surface-exposed loops (b2-b3 and b4-b5 loops) in the receptor binding domain of the *Bacillus thuringiensis* Cry4B mosquito-larvicidal protein. Total 11 mutants with a single alanine substitution within the b2-b3 loop (Y332A, Q333A, D334A and R336A) and on/near the b4-b5 loop region (Y359A, S361A, S362A, S366A, N367A, T369A and H370A) were initially generated. All mutant toxins were over-expressed as inclusion bodies in *Escherichia coli* and were structurally stable upon solubilisation and trypsin activation. When *E. coli* cells expressing the mutant toxins were tested for toxicity against *Aedes aegypti* mosquito larvae, alanine substitutions at Tyr-332 and Thr-369 completely abolished larvicidal activity, while the replacements at the other positions had no effect on toxicity. The mutagenic effect of these two positions was also confirmed by an *ex vivo* cytotoxicity assay. In addition, Y332A and T369A mutants were still able to release entrapped calcein from liposomes as comparable to the wild type toxin, but showed a decrease in binding activity to larval midgut sections detected by the immuno-histochemical staing. Further mutagenic analysis of these two critical residues showed that only the conversions of ala-332 to phenylalanine or tryptophan, and Ala-369 to serine, cysteine or aspartate were able to restore the larvicidal activity. These results suggest that an aromatic structure at the 332nd residue and the partially negative at a position of the 369th residue play an important role in larvicidal activity of the Cry4B toxin, plausible to be involved in receptor binding rather than membrane insertion and pore formation. •

Presented at: The Protein Sciences Meeting, San Diego, USA, August 16-21, 2002.

ROLE OF CPG DNA AND LIPOSOME IN IMMUNE RESPONSE TO ORAL CHOLERA VACCINE

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An oral cholera vaccine made up of three *Vibrio cholerae* antigens, *i.e.* recombinant TcpA (rTcpA), procholeragenoid (P), which was derived from heat-treated recombinant cholera toxin (rCT), and lipopolysaccharide (LPS), has been formulated into six different formulations. Formulation 1 (V_1; Ag + L + CpG) consisted of the antigens (rTcpA, P, LPS) associated with liposome (L) and bacterial CpG-DNA (ODN#1826); formulation 2 (V_2; Ag + L + Non-CpG) consisted of the three antigens associated with liposome and non-bacterial CpG-DNA (ODN# 1928); formulation 3 (V_3; Ag + L) was the three antigens associated with liposome; formulation 4 (V_4; Ag + CpG) was the three antigens mixed with the bacterial CpG-DNA; formulation 5 (V_5; Ag + Non-CpG) was the three antigens mixed with the bacterial non-CpG-DNA and formulation 6 (V_6; Ag) was the antigen alone. V_1 to V_6 were fed individually to individual rats (young adult Wistar) of six groups (five rats in each group). Liposome, bacterial CpG-DNA (CpG) and 5% $NaHCO_3$ were individually fed to three additional groups (groups 7-9) of rats, respectively, as placebo controls. All formulated vaccines and placebos were administered in three doses at 14-day intervals. The numbers of antigen-specific antibody producing cells in the small intestinal tissues sections of all rats were enumerated at 7 days after the last dose of vaccines and placebos, by a sandwich method of immunofluorescence. It was found that the immunogenicity of the formulated vaccines and placebos, in the order of magnitude of immune response as measured by the numbers of antibody producing cells to all three antigens per one microscopic field (200 ¥), were $V_1 > V_2 > V_3 > V_4 > V_5 = V_6 > L = CpG = NaHCO_3$. •

Presented at: The 6th FIMSA Advance Course and Conference: Molecular Mechanisms of Infection and Immunity, Ayutthaya, Thailand, 20-25 October, 2002.

TYPING OF DENGUE VIRUSES IN CLINICAL SPECIMENS FROM THE CENTRAL OF THAILAND

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Typing of dengue virus in clinical specimens from a total of 136 patients (in children under 15 years old) suspected dengue virus infection and admitted to Pathumthani Provincial Hospital, were performed during May, 1999 to April, 2000. Altogether 44 strains were isolated (isolation rate: 32 %), consisting of 18 DEN-1, 18 DEN-2, 7 DEN-3 and 1 DEN-4. The isolation rate decreased according to the day after onset of the disease from day 4 to day 8. •

Presented in : Joint International Tropical Medicine Meeting, at Bangkok, 20-22 November 2002.

PHARMACOKINETICS OF ALBENDAZOLE SULPHOXIDE WHEN GIVEN ALONE AND IN COMBINATION WITH PRAZIQUANTEL IN THAI CHILDREN WITH *GIARDIA INTESTINALIS* INFECTION

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Background: Plasma concentration of albendazole sulphoxide has been reported to be markedly increased when albendazole is given with food or praziquantel. A single dose combination of albendazole/praziquantel would be more advantage than a 5-7-day course of albendazole in the treatment of children with giardiasis, if pharmacologic synergistic effect is demonstrated without enhanced toxicity.

Objective: To investigate the pharmacokinetics of albendazole/albendazole sulphoxide when albendazole was given concurrently with praziquantel in giardia-infected children.

Materials & Methods: Twenty children with giardia infection were randomly allocated for 400 mg albendazole combined with 20 mg/kg praziquantel group (n=10) or albendazole 400 mg group (n=10) alone. Blood samples were collected through a 24-hour period of drug administration. Concentrations of albendazole/albendazole sulphoxide in plasma were quantified by using high performance liquid chromatography.

Results: A time to peak serum albendazole sulphoxide concentration (t_{max}) ranged from 1.5 to 3 hours when albendazole was given concurrently with praziquantel. Median peak level of albendazole sulphoxide (C_{max}) in the combined regimen was not different when compared with albendazole alone (730 vs 952 ng/ml, $p>0.05$).

Conclusions: Praziquantel at the dose of 20 mg/kg did not alter the pharmacokinetics/bioavailability of albendazole sulphoxide when given concurrently with 400 mg albendazole in children with *G. intestinalis* infection. •

Presented at: The 1st Asian Congress of Pediatric Infectious Diseases, Thailand, 10-13 November 2002.

COMPARATIVE SAFETY AND IMMUNOGENICITY OF AN ACELLULAR VERSUS WHOLE-CELL PERTUSSIS COMPONENT OF DIPHTHERIA-TETANUS-PERTUSSIS VACCINES IN THAI INFANTS

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Background: An acellular component of pertussis in combination with diphtheria, and tetanus toxoid vaccine (DTaP) has been increasingly used to replace the whole-cell component (DTwP) because of its reduced side effects.

Objective: To compare the safety and immunogenicity of the 3-component Chiron DTaP with a DTwP vaccine in Thai infants.

Materials & Methods: Two hundreds and eighty healthy infants were randomly assigned to receive either 3-doses of DTaP or DTwP at two, four and six months of age. Systemic and local reactions were observed after each injection. Antibodies to pertussis toxin (PT), filamentous hemagglutinin (FHA) and pertactin of pertussis and to diphtheria and tetanus toxoid were measured before vaccination and one month after the third dose.

Results: DTaP vaccinees had significantly lower rate of fever (7%), local tenderness (11%), erythema (5%) and induration (3%) when compared to those who received DTwP (22%, 31%, 21% and 14%). More than 95% of infants had seroconversion to at least two components of the acellular pertussis vaccine. GMT of antibodies to PT, pertactin, diphtheria and tetanus toxoid were comparable in both groups but the GMT of antibody to FHA was significantly lower in the DTaP group.

Conclusion: DTaP has a better safety profiles and induces similar immunogenicity to DTwP in Thai infants. •

Presented at: The 1st Asian Congress of Pediatric Infectious Diseases, Thailand, 10-13 November 2002.

ALBENDAZOLE-PRAZIQUANTEL AS A SINGLE DOSE THERAPY FOR GIARDIA INFECTION IN SCHOOL-AGE CHILDREN

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Background: A 5-7-day-course albendazole is effective against giardial infection but drug compliance is still questioned in children. Single-dose drug or drug combination with a comparable cure rate and less side effects should be an important focus.

Objective: To assess the efficacy of combined single dose albendazole and praziquantel in the treatment of giardiasis in Thai school-age children.

Materials & Methods: A randomized controlled trial was carried out in children aged 7-15 years old with giardial infection. Fifty-eight children were allocated into 2 regimens, group 1 (n = 31) albendazole 400 mg combined with praziquantel 20 mg/kg and group 2 (n = 27) tinidazole 50 mg/kg single dose. The treatment was considered as a cure when *Giardia* was not found in two consecutive stool samples.

Results: The parasitological cure rate was 74.2% in the combined single dose albendazole-praziquantel compared with 92.6% cure rates in the tinidazole groups (p = 0.09). This combined regimen was considered safe with minor side effects being observed.

Conclusion: Albendazole-praziquantel combined regimen may be an alternative single dose therapy for giardiasis in children, especially where common intestinal helminthes are co-existed. •

Presented at: The 1st Asian Congress of Pediatric Infectious Diseases, Thailand, 10-13 November 2002.

IMMUNOGENICITY AND ADVERSE REACTIONS AFTER IMMUNISATION WITH LIQUID FORM OF BEIJING STRAIN JAPANESE ENCEPHALITIS VACCINE IN HEALTHY THAI CHILDREN (A PRELIMINARY REPORT)

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Background: GPO has recently produced Beijing strain JEV to replace Nakayama strain JEV. Beijing strain JEV produces higher yield of antigen result in two folds increase in vaccine production.

Objective: To compare the immunogenicity and adverse reactions of Beijing strain JEV GPO, Nakayama strain JEV GPO and Beijing strain JEV BIKEN.

Materials & Methods: Three hundred healthy children with no previous history of JE vaccination were randomly vaccinated with Beijing strain JEV GPO (gr. A, 150 children), Nakayama strain JEV GPO (gr. B, 75 children) and Beijing strain JEV BIKEN (gr. C, 75 children) 3 doses at 0, 1-2 weeks and 1 year later. Local and systemic reactions after each vaccination were recorded. Blood was taken on day 0, one month after the second dose, at six months, at one year, and one month after the third dose for JE neutralizing antibody response using the corresponding JE virus strain.

Results: Preliminary reports of local and systemic reactions one month after the first and second doses of JEV were mild, transient and similar for the 3 groups. The common reactions were fever (1.4-8.2%), vomiting (1.4-8.2%), anorexia (2-4.8%), rash (0-6.7%), pain at the injection site (2.7-6.7%), erythema at the injection site (8-14.5%), swelling at the injection site (1.4-8.2%). A report on 51 children at one month after the second dose showed that the seroconversion rates were 96%, 100% and 100% for gr. A, gr. B and gr. C, respectively. The geometric mean titres of neutralising antibody of gr. A (126) and gr. C (138) were similar and both were significantly higher than that of gr. B (40).

Conclusion: Beijing strain JEV GPO appears to be immunogenic and safe. •

Presented at: The 1st Asian Congress of Pediatric Infectious Diseases, Thailand, 10-13 November 2002.

A META-ANALYSIS USING INDIVIDUAL PATIENT DATA OF TRIALS COMPARING ARTEMETHER WITH QUININE IN THE TREATMENT OF SEVERE FALCIPARUM MALARIA

Stepniewska KA, Day NP, Babiker A, Lalloo D, Warrell D, Olliaro P, White NJ, Garner P, Peto T, Winstanley P, van Hensbroek MB, Danis M, Davies C, Hien TT, Karbwang J, Kwiatkowski D, Marsh K, McIntosh H, Molyneux M, Murphy S, Seaton A, Taylor T, Watkins B.

We conducted a meta-analysis using individual patient data from randomized controlled trials comparing artemether and quinine in severe falciparum malaria. Eleven trials were identified, of which 8 were clearly randomized. Original individual patient data on 1919 patients were obtained from 7 trials, representing 85% of the patients in the original 11 studies. Overall there were 136 deaths among the 961 patients treated with artemether, compared with 164 in the 958 treated with quinine [14% vs 17%, odds ratio (95% confidence interval) 0.8 (0.62 to 1.02), $P = 0.08$]. There were no differences between the 2 treatment groups in coma recovery or fever clearance times, or the development of neurological sequelae. However, the combined "adverse outcome" of either death or neurological sequelae was significantly less common in the artemether group [odds ratio (95% CI) 0.77 (0.62 to 0.96), $P = 0.02$], and treatment with artemether was associated with significantly faster parasite clearance [hazard ratio (95% CI) 0.62 (0.56 to 0.96), $P < 0.001$]. In subgroup analyses artemether was associated with a significantly lower mortality than quinine in adults with multisystem failure. In the treatment of severe falciparum malaria artemether is at least as effective as quinine in terms of mortality and superior to quinine in terms of overall serious adverse events. There was no evidence of clinical neurotoxicity or any other major side-effects associated with its use. •

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EFFECTS OF MALARIA DURING PREGNANCY ON INFANT MORTALITY IN AN AREA OF LOW MALARIA TRANSMISSION

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Malaria during pregnancy reduces birth weight, and low birth weight is a major determinant of infant mortality. The authors estimated the impact of malaria during pregnancy on infant mortality in a Karen population living in Thailand. Between 1993 and 1996, a cohort of 1,495 mothers and their infants was followed weekly from admission of the mother to antenatal clinics until the first birthday of the infant. Both falciparum malaria and vivax malaria during pregnancy were associated with low birth weight but did not shorten gestation. Febrile illness in the week before delivery was associated with premature birth. Preterm and full-term low birth weight and fever in the week before delivery were associated with neonatal mortality. Maternal fevers close to term were also associated with the deaths of infants aged between 1 and 3 months, whereas no risk factors could be identified for deaths that occurred later in infancy. Thus, malaria during pregnancy increased neonatal mortality by lowering birth weight, whereas fever in the week before birth had a further independent effect in addition to inducing premature birth. The prevention of malaria in pregnancy and, thus, of malaria-attributable low birth weight should increase the survival of young babies. •

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PERSISTENCE OF *PLASMODIUM FALCIPARUM* HRP-2 IN SUCCESSFULLY TREATED ACUTE FALCIPARUM MALARIA

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The potential for *Plasmodium falciparum* histidine-rich protein (PfHRP-2) dipstick tests to predict antimalarial treatment failure was investigated in a prospective study in Thailand of 38 patients admitted with severe malaria and 54 hospitalized with uncomplicated *P.falciparum* infections. Of course, 40 had subsequent recrudescence of their infections. Overall, 89% of patients with severe malaria and 61% of patients with uncomplicated malaria had positive PfHRP-2 dipstick tests for >2 weeks following the start of treatment. Persistence was correlated positively with admission parasite counts, PfHRP-2 intensity scores and disease severity. PfHRP-2 tests which remained positive for >2 weeks and PfHRP-2 reactive intensity scores on admission, at day 7 and day 14 did not predict treatment failure independent of admission parasitaemia. Freezing and thawing the blood samples did not significantly affect PfHRP-2 results tested by the dipstick technique. The PfHRP-2 dipstick test provides a useful indicator of recent severe malaria, but does not predict the therapeutic response. •

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POSTPARTUM THIAMINE DEFICIENCY IN A KAREN DISPLACED POPULATION

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***Background*:** Before its recognition, infantile beriberi was the leading cause of infant death in camps for displaced persons of the Karen ethnic minority on Thailand's western border.

Objective: This study aimed to document thiamine status in the peripartum period to examine the current supplementation program and the correlation between the clinical manifestations of thiamine deficiency and a biochemical measure of thiamine status.

Design: Women were enrolled prospectively at 30 wk of gestation and were followed up weekly until delivery and at 3 mo postpartum. Thiamine supplementation during pregnancy was based on patient symptoms.

Results At 3 mo postpartum, thiamine deficiency reflected by an erythrocyte transketolase activity (ETKA) > or = 1.20% was found in 57.7% (15/26) of mothers, 26.9% (7/26) of whom had severe deficiency (ETKA > 1.25%). No significant associations between ETKA and putative maternal symptoms or use of thiamine supplements were found.

Conclusions: Biochemical postpartum thiamine deficiency is still common in Karen refugee women. This situation may be improved by educating lactating women to reduce their consumption of thiaminase-containing foods and by implementing an effective thiamine supplementation program. •

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ORAL QUININE PHARMACOKINETICS AND DIETARY SALT INTAKE

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Objectives: The objective was to determine whether or not dietary salt intake affects the relative bioavailability of oral quinine. Salt intake has been shown to alter quinidine bioavailability.

Methods The pharmacokinetic properties of oral quinine sulphate (600 mg salt) were investigated in seven healthy Caucasian volunteers, in a randomised, cross-over study, on low- and high-salt diets. Plasma quinine concentrations were measured by high-performance liquid chromatography (HPLC) and the 24-h urinary sodium excretion was assayed.

Results Although the 24-h urine sodium excretion was significantly higher when the volunteers were on a high-salt diet, there were no significant differences in quinine AUC0-, *t*MAX, and *c*MAX after the two diets. The median (range) quinine elimination half-life was significantly shorter after a high-salt diet [10.0 (7.6-14.8) h] (P=0.04).

Conclusion Dietary salt does not affect the relative oral bioavailability of quinine sulphate. •

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A COMPARISON OF THE *IN VIVO* KINETICS OF *PLASMODIUM FALCIPARUM* RING-INFECTED ERYTHROCYTE SURFACE ANTIGEN-POSITIVE AND -NEGATIVE ERYTHROCYTES

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Ring-infected erythrocyte surface antigen (RESA)-positive, *Plasmodium falciparum*-negative red blood cells (RBCs) are cells from which the malaria parasite has been removed by the host without the destruction of the erythrocyte ("pitting"). The survival of RESA-RBCs in vivo was assessed in 14 severe and 6 uncomplicated falciparum malaria patients. The mean RESA-RBC life of 183 hours (95% confidence interval [CI], 136-246) was longer than the median parasite clearance time of 66 hours (range, 30-108 hours) but shorter than the mean red cell life of 1027 hours (95% CI, 840-1213) (P = 0.0004), with a median ratio of 0.2:1.0 (range, 0.1-0.7). The estimated median percentage of parasites pitted/body transit was 0.003% (range, 0.001%-0.05%). The rate of rise of the RESA-RBC count during the first 24 hours after antimalarial treatment was significantly faster (P = 0.036) and the subsequent RESA-RBC survival significantly shorter (P = 0.017) after treatment with an artemisinin derivative than after treatment with quinine. Parasitization of red cells leads to changes in the erythrocyte that shorten their survival even if the parasite is removed subsequently. •

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FAKE ARTESUNATE IN SOUTHEAST ASIA

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Artesunate is a key antimalarial drug in the treatment of multidrug-resistant *Plasmodium falciparum* malaria in southeast Asia. We investigated the distribution of counterfeit artesunate tablets by use of the validated, simple, and inexpensive Fast Red TR dye technique. We also aimed to identify distinguishing characteristics of the fake drugs. Of 104 shop-bought "artesunate" samples from Cambodia, Laos, Myanmar (Burma), Thailand, and Vietnam, 38% did not contain artesunate. Characteristics such as cost and physical appearance of the tablets and packaging reliably predicted authenticity. The illicit trade in counterfeit antimalarials is a great threat to the lives of patients with malaria. The dye test will assist national malaria control authorities in urgently needed campaigns to stop this murderous trade. •

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PROTEIN AND ENERGY METABOLISM IN CHRONIC BACTERIAL INFECTION: STUDIES IN MELIOIDOSIS

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Chronic infection is often accompanied by a wasting process, the metabolic basis of which is not fully understood. The aims of the present study were to measure protein and energy metabolism in patients with melioidosis (a serious and antibiotic-refractory Gram-negative bacterial infection which is endemic in South-East Asia) in order to define the metabolic abnormalities that might contribute to wasting. Whole-body protein turnover was measured using the [(13)C]leucine technique, both in the fasted state and while consuming a high-energy meal. Resting energy expenditure was measured by indirect calorimetry, and total energy expenditure by the bicarbonate/urea method. Results were normalized for fat-free mass, as estimated from skinfold thickness. Protein turnover was increased in melioidosis patients compared with healthy controls during fasting (170.9 compared with 124.1 micromol x kg(-1) x h(-1); P=0.04), but the net rate of catabolism (22.2 compared with 20.5 micromol x kg(-1) x h(-1); P=0.77) and the anabolic response to feeding were similar in the two groups. Resting energy expenditure was higher in melioidosis patients compared with controls (191.4 and 157.3 kJ x kg(-1) x day(-1) respectively; P=0.04), but total energy expenditure (measured in a separate group of eight patients with melioidosis) was low (192.1 kJ x kg(-1) x day(-1)). In conclusion, this study found no evidence of metabolic causative factors, such as accelerated net protein catabolism during fasting, a blunted anabolic response to feeding or increased daily energy expenditure, and therefore suggests that reduced energy intake is the prime cause of wasting. The observed normal response to feeding should encourage nutritional approaches to prevent wasting. •

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MELIOIDOSIS AND PANDORA'S BOX IN THE LAO PEOPLE'S DEMOCRATIC REPUBLIC

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Melioidosis has not been recognized previously in Laos, but within months of starting a prospective study of community acquired septicemia in Vientiane, 2 patients with melioidosis were identified. One was a previously healthy, 44-year-old female rice farmer who presented with supraclavicular lymphadenitis and the other was a 74-year-old man with diabetes and renal calculi who was receiving corticosteroids and had septicemia and septic arthritis. •

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

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Objective: To assess kinetic of cryptococci in the cerebrospinal fluid (CSF) and outcome of AIDS-associated cryptococcal meningitis after high-dose amphotericin B.

Patients and Methods: A prospective study involving Thai adults (n=106) with cryptococcal meningitis associated with AIDS was conducted to determine the kinetic of cryptococci in CSF and prognostic factors affecting survival after high-dose amphotericin B (0.7[?]mg/kg/day) followed by oral azole treatment. Cerebrospinal fluids were collected for cryptococcal count and culture at weekly intervals for at least 2 weeks or until CSF cultures were negative for cryptococci. All patients were followed monthly for 1 year or until death in order to detect relapse or occurrence of any other opportunistic infection.

Results: A total of 106 AIDS patients with cryptococcal meningitis were enrolled. The geometric mean (range) total and viable cryptococcal counts in CSF on admission were 430,000 (1000 to 3.4 x 10(7)) and 31,000 (10 to 1.4 x 10(7)) 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 2 and 4 weeks, respectively. Early death was associated significantly with previous history of weight loss [relative risk (RR)=2.2; 95% CI, 1.2-3.9], Glasgow Coma Score <13 (RR=2.33; 95% CI, 1.55-3.50), and hypoalbuminaemia (P<0.001). Later mortality was associated delayed CSF yeast clearance (RR=3.6; 95% CI, 1.9-6.4) and relapse (RR=3.9; 95% CI, 1.4-10.8).

Conclusion: High-dose amphotericin B was not as effective as previously thought. Cumulative mortality at 2 weeks, 4 weeks and 1 year were 16%, 24% and 76%, respectively. •

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FACTORS CONTRIBUTING TO ANEMIA AFTER UNCOMPLICATED FALCIPARUM MALARIA

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The factors contributing to anemia in falciparum malaria were characterized in 4,007 prospectively studied patients on the western border of Thailand. Of these, 727 patients (18%) presented with anemia (haematocrit < 30%), and 1% (55 of 5,253) required blood transfusion. The following were found to be independent risk factors for anemia at admission: age < 5 years, a palpable spleen, a palpable liver, recrudescent infections, being female, a prolonged history of illness (> 2 days) before admission, and pure *Plasmodium falciparum* infections rather than mixed *P. falciparum* and *Plasmodium vivax* infections. The mean maximum fractional fall in hematocrit after antimalarial treatment was 14.1% of the baseline value (95% confidence interval [CI], 13.6-14.6). This reduction was significantly greater in young children (aged < 5 years) and in patients with a prolonged illness, high parasitemia, or delayed parasite clearance. Loss of parasitized erythrocytes accounted for < 10% of overall red blood cell loss. Hematological recovery was usually complete within 6 weeks, but it was slower in patients who were anemic at admission (adjusted hazards ratio [AHR], 1.9, 95% CI, 1.5-2.3), and those whose infections recrudesced (AHR, 1.2, 95% CI, 1.01-1.5). Half the patients with treatment failure were anemic at 6 weeks compared with 19% of successfully treated patients (relative risk, 2.8, 95% CI, 2.0-3.8). Patients coinfected with *P. vivax* (16% of the total) were 1.8 (95% CI, 1.2-2.6) times less likely to become anemic and recovered 1.3 (95% CI, 1.0-1.5) times faster than those with *P. falciparum* only. Anemia is related to drug resistance and treatment failure in uncomplicated malaria. Children aged < 5 years of age were more likely than older children or adults to become anemic. Coinfection with *P. vivax* attenuates the anemia of falciparum malaria, presumably by modifying the severity of the infection. •

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PARACHECK-PF: A NEW, INEXPENSIVE AND RELIABLE RAPID TEST FOR P. FALCIPARUM MALARIA

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We compared the performance of Paracheck-Pf®, a new and cheap rapid malaria test, with ICT-Pf/Pv® and microscopy in two malaria surveys in Thai villages on the Thai-Burmese border. The specificity, sensitivity, predictive positive and negative values of the Paracheck-Pf® and ICT-Pf® tests were calculated taking microscopy results as the gold standard. The 294 ICT-Pf/Pv tests resulted in two invalid (no control line) and 11 doubtful results. Both the ICT-Pf/Pv® and Paracheck-Pf® tests reliably detected *P. falciparum* infections. However, Paracheck-Pf® failed to detect three *P. falciparum* cases and likewise, ICT-Pf/Pv® failed to detect the same three cases and an additional four cases. These seven cases were detected by microscopy and had a parasitaemia under 150 parasites/microl. At a cost of c. US $1.00, the Paracheck-Pf® test, based on the detection of the *P. falciparum* specific HRP-2 protein, is a reliable, easy to use and affordable tool for the diagnosis of *P. falciparum* malaria. •

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HOW CAN WE DO PHARMACOKINETIC STUDIES IN THE TROPICS?

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Information regarding the pharmacokinetic (PK) and pharmacodynamic (PD) properties of a drug provides the basis for optimizing dosing. PK-PD information should be obtained from patients representative of the overall target population, but in many tropical hospitals or health care facilities it may be medically hazardous or logistically difficult for an ill patient or a young child to be sampled repeatedly. Traditional methods used to determine the pharmacokinetic properties of a drug require analysis of a large number of blood samples per subject. However, using modern statistical methods, sparse datasets (i.e. with assay results from only a few, or as little as one blood sample per subject) can now be analysed by a method termed "the population approach". Modern assay techniques can often be adapted to small blood volumes allowing finger prick blood samples to be taken. One of the major aims of the population approach is to distinguish and characterize patient and disease contributors to inter-individual variance in drug pharmacokinetics. The purpose of this paper is to explain the basis of the population approach, to highlight its advantages compared to traditional methods of analysis, and to review the application of the population approach to data from field studies of antimalarial drugs. The design of population pharmacokinetic studies is also discussed briefly. The principles discussed in the paper are also applicable to pharmacodynamic data. •

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A COMPARISON OF ORAL ARTESUNATE AND ARTEMETHER ANTIMALARIAL BIOACTIVITIES IN ACUTE FALCIPARUM MALARIA

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AIMS: Artesunate and artemether are the two most widely used artemisinin derivatives in the treatment of uncomplicated *Plasmodium falciparum* malaria, but there is little information on their comparative pharmacokinetics. The aim of this study was to examine the relative oral antimalarial bioavailability and pharmacokinetics of the two derivatives.

Methods: The pharmacokinetic properties of oral artesunate and artemether (4 mg kg^{-1}) were compared in a randomized cross-over study of 14 adult patients in western Thailand with acute uncomplicated *Plasmodium falciparum* malaria. Antimalarial activity was compared using a previously validated, sensitive bioassay.

Results: Despite a 29% lower molar dose, oral artesunate administration resulted in significantly larger mean area under the plasma antimalarial activity time curve and median maximum plasma antimalarial activity than after oral artemether ($P \leq 0.02$). The mean (95% CI) oral antimalarial bioavailability of artemether, relative to oral artesunate, corrected for molar dose was 58 (40-76)%. The mean (95% CI) relative antimalarial bioavailability of artemether was lower on the first day of treatment, 31 (17-100)%, compared to the second day, 72 (44-118)% ($P = 0.018$). *In vivo* parasite clearance and time above the *in vitro* IC90 were similar for the two drugs, despite considerable differences in Cmax and AUC.

Conclusions: The oral antimalarial bioavailability following artemether was significantly lower than that after artesunate. Artemether oral antimalarial bioavailability is reduced in acute malaria. •

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VALUE OF THROAT SWAB IN DIAGNOSIS OF MELIOIDOSIS

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Throat swab (TS) cultures were performed for 1,011 patients with melioidosis and 3,524 healthy subjects or patients with other diseases. The specificity of TS culture for the diagnosis of melioidosis was 100%, and the overall sensitivity was 36% (24% for sputum-negative patients and 79% for sputum-positive patients). Direct plating of the TS specimen on Ashdown's medium was rapid (colonies were usually evident within 24 h) but only 63% sensitive compared to the results of primary culture in a selective broth. A throat swab should be cultured in all cases of suspected melioidosis. •

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THE CONDUCT OF GOOD CLINICAL PRACTICES (GCP) IN THE FIRST HIV-1 VACCINE EFFICACY TRIAL IN A DEVELOPING COUNTRY – BANGKOK, THAILAND

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Background: A randomized, double blind, placebo-controlled HIV vaccine (AIDSVAX™ B/E) efficacy trial was started in Thailand in March 1999 among 2,545 IDUs attending 17 drug treatment clinics of the Bangkok Metropolitan Administration. To conduct the trial according to GCP standards, i.e. to ensure the quality and integrity of data, and protection of trial participants, methods were established for obtaining informed consent, the monitoring of trial-related social harms, and data collection procedures.

Methods: Starting 9 months prior to trial initiation, clinic personnel were trained in HIV/AIDS, vaccines, GCP, protocol implementation, informed consent process, and various standard operating procedures. Social workers and counselors were trained to deliver health information about HIV/AIDS and to educate potential enrollees about the study design, vaccine, and advantages and disadvantages of participation. Methods included personal and group discussion and written and audio-visual information (brochures and VDO). Prior to enrollment, eligible participants were required to pass a test of understanding (TOU) consisting of 20 true-false questions about study design, vaccine, informed consent etc. After the start of the trial, internal and external monitoring was implemented, and weekly study coordinator meetings were held to calibrate on clinical conduct across all 17 study sites. Standardized questionnaires were administered at enrollment and every 6 months thereafter to monitor risk behavior. Case report forms (CRFs) were simultaneously transmitted to a local data management unit and VaxGen for processing.

Results: Between March 1999 and August 2000, 2,545 participants were enrolled. Their median age is 26 years (range 20 to 59), 93% are male and 95% had completed at least primary education. Eighty-one percent of participants passed the TOU at first attempt with a median score of 19 correct answers; all participants passed after subsequent attempts. Risk behavior in terms of needle sharing declined from 33.0% at enrollment to 16.3% at 12-month follow-up ($p<0.001$). Most of the 32 reported social harms involved voluntary disclosure of trial participation and were related to personal relationships or employment. None were due to denial of health care, health or life insurance or housing problems. All harms have been resolved and could be categorized as having minimal impact. Of the nearly 200,000 CRFs transmitted, 97.7% were clean and 2.3% needed some data clarification. About 35% of the accompanying quality control notes pertained to missing values.

Conclusions: With appropriate training and resources, GCP can be established and conducted in clinical trials with HIV vaccines in developing countries. The data collected in this trial will meet international standards and can be used for licensing purposes. •

JOINT THAI-US PHASE III TRIAL OF HIV PRIME-BOOST VACCINES

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Purpose: To describe the plan for initiating and implementing a community-based, phase III efficacy trial of a prophylactic HIV candidate vaccine combination in Thailand. Methodology: *Trial objectives:* Determine whether this vaccine combination 1) reduces the HIV infection rate by at least 50%, and/or 2) results in decreased viral load and increased CD4 cell count in recipients who become infected with HIV, and 3) is safe and well tolerated. *Vaccines:* Designed specifically for the predominant circulating HIV of Thailand (CRF01_AE). Prime - recombinant canarypox ALVAC-HIV containing subtype B *Gag/Pro* and *Env-TM*, and subtype E *Env*(R5) gene insertions (vCP1521, Aventis Pasteur); Boost - monomeric gp120s B(X4) + E(R5) with alum (AIDSVAX B/E, VaxGen). *Study population:* 16,000 20-30 year old Thai citizens from the communities of Rayong and Chon Buri, Thailand. *Study design:* Randomized(vaccine:placebo = 1:1), placebo-controlled, double-blind, 3.5 year duration. *Endpoints:* Primary Efficacy - HIV infection based on serological and nucleic acid testing; Secondary Efficacy - HIV RNA and CD4 quantitation; Safety - Adverse events and HIV risk-relevant behaviors. *Projected start date:* December 2002 Discussion: Other than HIV vaccine candidates based on envelope subunit proteins, recombinant canarypox is the only candidate vaccine that has been assessed adequately to transition into phase III testing. Combining both strategies results in humoral and cellular immunity and increases the likelihood of vaccine protection. We describe the world's first efficacy trial of a HIV prime-boost vaccine combination. The predominance and relatively narrow diversity of HIV subtype E in Thailand provide an optimal setting for the test of this concept, utilizing vaccines derived from Thai primary isolates. An update of this phase III plan will be shared with the international community. •

SOCIAL HARM AND INCARCERATION AMONG INJECTING DRUG USERS PARTICIPATING IN THE AIDSVAX-B/E VACCINE EFFICACY TRIAL IN BANGKOK, THAILAND

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Background: A randomized, double blind, placebo-controlled HIV vaccine (AIDSVAX-B/E) efficacy trial was started in Thailand in March 1999 among 2,545 IDUs attending 17 drug treatment clinics of the Bangkok Metropolitan Administration. Methods were established for monitoring of trial-related social harms and episodes of incarceration while on study.

Methods: If a social harm was reported, a questionnaire was administered and follow-up interventions were made by study staff until the harm was resolved. Individual incarceration history was assessed at enrollment and at every 6 month follow-up visit using a standardized questionnaire. Clinic administration data were used to assess the number of study visits to incarcerated participants.

Results: Through November 2001, 36 social harms were reported. Most involved voluntary disclosure of trial participation and were related to personal relationships or employment. None were due to denial of health care, health or life insurance or housing problems. All harms have been resolved and could be categorized as having minimal impact. At enrollment, 78.5% of study participants reported a history of incarceration. At first follow-up 20.0% reported to have been incarcerated (jail and/or prison) during the last 6 months; at second and third follow-up these percentages were 25.7% and 26.2%, respectively. Through November 2001, 28,789 study visits were conducted; 27,115 were clinic visits and 1674 (5.8.%) were incarceration visits. In total, 650 incarcerated participants were visited in 47 different incarceration facilities, dispersed throughout the Bangkok metropolitan area.

Conclusions: Few social harms were reported, all of which were adequately resolved. Incarceration is common while on study, and retention of these individuals is critical to attain a successful follow-rate. •

LIVE RECOMBINANT ALVAC–HIV (VCP1521) PRIMING WITH AIDSVAX B/E BOOSTING IN THAILAND: SAFETY & IMMUNOGENICITY

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Background: A strategy to stimulate both HIV-specific cellular and humoral antibodies uses canarypox vector vaccine priming and protein subunit boosting. vCP1521 is a recombinant canarypox vector vaccine that has been genetically engineered to express subtype E HIV-1 gp120 (92TH023) linked to transmembrane anchoring portion of gp41 (strain LAI), and HIV-1 gag and protease (LAI strain). AIDSVAX B/E is a bivalent HIV gp120 envelope glycoprotein.

Methods: The study was a double–blind, randomized, placebo-controlled trial. Volunteers were enrolled and divided into two groups based on the dose of AIDSVAX B/E, as follows:

		Months			
Group	**Vaccinees/ Placebo**	**0**	**1**	**3**	**6**
I	45/15	vCP1521	vCP1521	vCP1521+ 200 mg of AIDSVAX B/E	vCP1521+ 200 mg of AIDSVAX B/E
II	45/15	vCP1521	vCP1521	vCP1521+ 600 mg of AIDSVAX B/E	vCP1521+ 600 mg of AIDSVAX B/E

Results: Most of observed reactogenicity was mild to moderate. There were no serious adverse events attributable to vaccine. Among recipients of the 600 mg dose of AIDSVAX B/E boost, 71% and 98% of vaccine recipient volunteers had neutralizing antibody to subtype E and B TCLA HIV strains, 71% had lymphocyte proliferation to gp120 CM244, while 49% had proliferation to gp120 MN.

Conclusions: Prime-boost vaccination with ALVAC-HIV and AIDSVAX B/E appears safe, well-tolerated and to induce both humoral and cellular HIV-specific immune responses. These results support the planning for the next phase III HIV vaccine trial in Thailand. •

THAILAND'S SUCCESS IN MOVING TO THE FIRST PHASE III HIV VACCINE EFFICACY TRIAL IN A DEVELOPING COUNTRY

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Background: In 1991, the World Health Organization initiated an HIV vaccine program to identify potential sites for vaccine evaluation in developing countries; Thailand, Brazil, Rwanda, and Uganda were selected as the most promising sites. In 1992, with international support, the Thai government made the development of a safe and effective HIV vaccine a national priority. A National Plan for HIV/AIDS Vaccine Development and Evaluation was drafted and the national AIDS Commission appointed a technical subcommittee on AIDS vaccine. This subcommittee plays a central role in coordinating and creating the scientific infrastructure to perform HIV vaccine studies, such as the creation of laboratory, data management and epidemiologic networks, as well as the establishment of a national HIV repository. A 1995-1998 Bangkok Metropolitan Administration (BMA) cohort study of 1,209 injecting drug users (IDUs) showed an annual HIV incidence rate

of 5.8 per 100 person years (21% subtype B, 79% subtype E), high rates of follow up and willingness to participate in HIV vaccine trials. In 1997, phase I and II studies of a bivalent B (MN)/E(A244) rgp 120 vaccine (AIDSVAX®B/E, VaxGen, Inc., USA) demonstated that this vaccine was safe and immunogenic in human volunteers. In March 1999, a phase III HIV vaccine trial of AIDSVAX ®B/E was initiated to test the protective efficacy of this vaccine among IDUs attending drug treatment clinics operated by the BMA. The protocol was approved by the National AIDS Commission scientific subcommittee; the Ethical Review Committees of Mahidol University, the Thai Ministry of Public Health, and the BMA; the Institutional Review Board of the U.S. Centers for Disease Control and Prevention; the U.S. Office of Protection of Research Risk; the U.S. Food and Drug Administration; and UNAIDS.

Methods: Following informed consent, HIV-seronegative IDUs meeting eligibility criteria were randomized to receive AIDSVAX®B/E (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. All participants are being followed for 3 years to detect a minimum 30% efficacy (1°endpoint, infection measured by ELISA and Western blot; 2 ° endpoint, reduced progression of disease as measured by RNA PCR viral load and CD4). Interim safety and efficacy analyses are conducted by as independent data safety monitoring board(DSMB)

Results: Recruitment and screening began on March 10, 1999. Recruitment methods included TV and radio spots, telephone hotline, posters, flyers, friend-help-friend referral program and extended clinic hours. Prior to enrollment, eligible participants were required to pass a knowledge test consisting of 20 true-false questions about study design, vaccine, informed consent etc. Enrollment of 2,545 IDUs was completed on August 31, 2000. Participants had a median age of 26 years and 93% were male. Through March 18,2001, follow-up has been excellent (0.3% lost to follow-up and 0.6% withdrew consent) and immunizations have been well tolerated. No vaccine-related serious adverse events have occurred, with pain and tenderness at the injection site (reported by 61% of subjects after 1 or more vaccinations) being the most commonly experienced side effect. Immunization compliance was 98%, with 2,513 (99%) subjects receiving the 2nd dose, 2,426 (97%) receiving the 3rd and 1,717 (96%) receiving the 4th dose, respectively. The DSMB advised trial continuation following safety reviews in September 1999, April and October 2000, and April 2001.

Conclusion: Thailand is the world's first developing country to initiate an HIV vaccine efficacy trial. Through March 18,2001, trial follow-up has been excellent (97.4%), and adverse effects have been unremarkable. Final results are expected in late 2003. •

RECRUITING VOLUNTEERS FOR A MULTISITE PHASE I/II HIV PREVENTIVE VACCINE TRIAL IN THAILAND

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Factors believed to be predictive of retention through the recruitment and screening processes for preventive HIV trials were investigated in a large multisite phase I/II HIV vaccine trial in Thailand. Retention through recruitment was equal to or greater than in previous smaller trials with similar populations. The data suggested that recruitment proceeded in a stepwise manner with different influences at each step. Demographic and motivational variables were most important in predicting retention in making and keeping screening appointments. Altruistic or mixed altruistic and nonaltruistic motives were associated with greater retention. Laboratory/medical variables appeared to be the main influence on retention during screening, although some volunteers withdrew for different reasons. The frequent presence of mixed (altruistic and nonaltruistic) motives at initial contact suggests that motivation for trials is more complex than has been previously acknowledged. •

CLINICAL AND MYCOLOGICAL IN HIV-INFECTED PATIENTS

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Introduction: OPC is a common opportunistic infection in HIV-infected patients. Although some patients are asymptomatic, progression of the disease may occur leading to esophageal candidiasis. Fluconazole resistant candidiasis has been reported in several international studies.

Objective: This study aimed to test the MICs (minimal inhibitory concentrations) to fluconazole of Candida species isolated from mouthwash specimens of 54 HIV positive patients with oral candidiasis. Clinical and mycological responses to fluconazole were also assessed in 16 patients. **Material and method**: This was a prospective study. Mouthwash specimens were cultured on sabouraud dextrose agar twice. Candida species identification was performed and MICs for fluconazole were obtained using NCCLS guidelines. Clinical and mycological responses were assessed on day 14 and 42 in 16 patients who received a 14-day course of fluconazole.

Results: 48/54 patients (88.89%) were found to carry pure C. albicans. The other 6 patients (11.11%) had mixed Candida species on cultures. Among these 6 patients, 5 patients had mixed C. albicans and C. glabrata, and 1 patient had C. albicans and C. krusei. Fluconazole MICs of C. albicans, C. glabrata, and C. krusei ranged from 0.125-32 (median=0.250), 4-64 (median=2), and 8 g/L respectively. This study showed that the MICs to fluconazole of oropharyngeal Candida was a good predictor of the therapeutic responses. •

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EFFECTS OF CIGARETTE SMOKING ON QUININE PHARMACOKINETICS IN MALARIA

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Objective: Quinine is an important antimalarial drug that is metabolised mainly by the hepatic mixed-function microsomal enzyme cytochrome P(450). Cigarette smoking in healthy volunteers has been reported to enhance quinine clearance. The present study evaluated the effects of smoking on quinine pharmacokinetics in patients with uncomplicated falciparum malaria treated with a 7-day course of oral quinine. Of 22 studied male patients, 10 were regular smokers and 12 were non-smokers.

Methods: All patients were treated with a 7-day oral regimen of quinine sulfate (10 mg salt/kg three times a day). Serial venous blood samples were taken for quinine levels before and during treatment at 12 h and 24 h and then daily until day 7. Plasma quinine and 3-hydroxyquinine concentrations were assayed using high-performance liquid chromatography. Quinine pharmacokinetics were evaluated using non-compartmental modelling.

RESULTS: All patients recovered, and there were no significant differences in clinical responses or cure rates between the two studied groups (P> or =0.32). The median (range) fever clearance time was 51 h (4-152 h) and mean (SD) parasite clearance time was 74+/-28 h. The overall median times to maximum concentrations of quinine and its main metabolite 3-hydroxyquinine were 1.5 days and 4.0 days, respectively. The maximum concentrations of quinine were approximately tenfold higher than 3-hydroxyquinine. There were no significant differences in any pharmacokinetic variables for the parent compound or metabolite between the two groups. The median area under the plasma drug concentration-time curve to day 7 (AUC(0-7)) of quinine in non-smokers was 67.0 micro g/ml/day and in smokers was 51.3 micro g/ml/day, and AUC(0-7) values of 3-hydroxyquinine were 6.2 micro g/ml/day and 4.8 micro g/ml/day, respectively.

CONCLUSION: These results indicated that cigarette smoking has no significant effects on quinine pharmacokinetics or the therapeutic response in patients with falciparum malaria. •

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DEVELOPMENT AND EVALUATION OF RAPID URINARY ANTIGEN DETECTION TESTS FOR DIAGNOSIS OF PENICILLIOSIS MARNEFFEI.

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Penicilliosis, caused by the dimorphic fungus Penicillium marneffei, is an important opportunistic systemic fungal infection affecting immunocompromised individuals living in areas where penicilliosis is endemic. We have demonstrated previously that a urinary enzyme-linked immunosorbent assay (ELISA) with purified rabbit polyclonal antibody against killed whole-fission-form arthroconidia of P. marneffei was specific and highly sensitive for the diagnosis of penicilliosis. In this study, a dot blot ELISA and a latex agglutination (LA) test were developed with the same polyclonal antibody and compared with the ELISA for the detection of P. marneffei urinary antigen. Urine specimens from 37 patients with culture-proven penicilliosis and 300 controls (52 healthy subjects and 248 hospitalized patients without penicilliosis) were tested. Antigen was detected in urine from all 37 (100%) penicilliosis patients by the LA test, 35 (94.6%) penicilliosis patients by the dot blot ELISA, and 36 (97.3%) penicilliosis patients by the ELISA. False-positive results were found by the three assays for 2 (0.7%), 8 (2.7%), and 6 (2%) of 300 controls, respectively. The overall sensitivities of the diagnostic tests were as follows: dot blot ELISA, 94.6%; ELISA, 97.3%; and LA test, 100% (specificities, 97.3, 98, and 99.3%, respectively). The LA test is simple, robust, rapid, and convenient and should prove to be an important addition to the existing diagnostic tests for penicilliosis. •

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MYCOBACTERIUM TUBERCULOSIS INFECTION AMONG HIV/AIDS PATIENTS IN THAILAND: CLINICAL MANIFESTATIONS AND OUTCOMES

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A one year retrospective study, was conducted at Bamrasnaradura Hospital, Nonthaburi Province, Bangkok, Thailand, of 271 subjects with both TB and HIV/AIDS. Single males (median age group 31 to 40 years) were most likely to develop co-infection. The commonest clinical manifestations on initial presentation included a low grade fever, cough, weight loss, lymphadenopathy with pancytopenia, and lung infiltrates. Multi-drug resistant TB (MDR-TB) was found in 26.6% of the subjects which was significantly associated with a past history of anti-TB treatment ($p = 0.005$; OR=2.5); it was also significantly associated with disseminated TB ($p = 0.022$; OR=1.9) and mortality ($p= 0.013$; OR=2.8). Analysis of clinical outcomes showed that 46.7% were lost to follow-up and 13.3% had died by the time of follow-up. Among those who survived, only 11.4% had been successfully treated; the rest had not improved due to relapse (2.9%), therapeutic failure (8.8%), treatment in progress (5.9%), and failure to complete treatment (10.7%). •

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EVALUATION OF ATTITUDE, RISK BEHAVIOR AND EXPECTATIONS AMONG THAI PARTICIPANTS IN PHASE I/II HIV/AIDS VACCINE TRIALS

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Understanding among volunteers in vaccine trials about their roles as study participants and their voluntary commitment during study are always concerned as one of the important issues apart from evaluation of safety and efficacy, especially in HIV prophylactic vaccine trials. The apprehension of indirectly risky behavior encouragement and deviated expectations among volunteers should be concerned. This prospective cohort study was aimed to assess and monitor the changes of risk behavior, attitude and expectations among 164 volunteers from 2 different prophylactic HIV vaccines trials, the Chiron HIV Thai Egp 120/MF59 ± the Chiron HIV SF52 gp120 and Aventis Pasteur Live Recombinant ALVAC HIV (vCPI521) priming with VaxGen gp120B/E (AIDSVAX™ B/E) boosting. 113 males and 51 females with mean age (±SD) of 28.82±7.97 years old were enrolled during October 1997-December 1998 and February 2000-Apri12001. Education and risk reduction counseling were regularly performed at every visit and questionnaires about behavioral risks, knowledge, attitudes, social influences and expectations were asked at baseline, 4 month and 12 month of these study. No change of potentially HIV transmission related risky behavior was observed during the studies. There was statistically significant decrease of risky sexual practices from the beginning of .the trials (42.2% VS 1%, p<0.0001). While 35.2% from 62.2% at the beginning of studies continued sexual practice with identified single sexual partner at the end of studies (p<0.0001). All of volunteers expressed the beneficial expectations as knowledge gain, social contribution, meritorious commitment and self-benefits from health check-up. •

SAFETY AND EFFICACY OF JINHUANG "CHINESE HERBAL MEDICINE" AMONG ASYMPTOMATIC HIV INFECTED INDIVIDUALS

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Complementary remedies now have been widespread used for many chronic illnesses including HIV infection. Herbal medicine can be another choice of rumored alternative treatment of HIV infection for who unaffordable or undesirable to be treated with recommended antiretroviral therapy. This prospective study was done to evaluate the safety and efficacy in term of anti-HIV effects of Chinese herbal medicine named JinHuang that previously showed anti-HIV effects in vitro. 21 asymptomatic HIV infected Thais with mean age of 29.24±3.94 years old enrolled to this 1 year study. Regular visits for follow up as out patient basis was done with dose of JinHuang oral preparations, 6 capsules and 2 bottles of liquid formula three times a day. No serious adverse event related to JinHuang was detected during study. The common adverse effects included increased bowel movement (85.7%), intermittent diarrhea (62%) and vague taste and smell of the drug (57.1%). No significant change in term of log viral load reduction but the significant decrease of CD4 count was observed after 1-year period. There were inexplicit concurrent illnesses, asymptomatic urinary tract infection, mucocutaneous herpes simplex infections among 4 volunteers at 1-year evaluation. No change of body mass index among the volunteers was found. However, most of them subjectively mentioned about better quality of life (71.4%) as well being perceptions in physical (47.6%) and psychological (57.1 %) improvement after study participation and 66.7% agreed to continue this drug in the future. •

DEVELOPMENT OF *ISOSPORA BELLI* IN HCT-8, HEP-2, HUMAN FIBROBLAST, BEK AND VERO CULTURE CELLS

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The development of *Isospora belli*, a human coccidian parasite was studied in different cell lines. Merogony was observed in all kind of cells whereas microgametocyte was demonstrated only in Hct-8. It was shown that not only human cell line could be infected but also some kind of animal cell lines. The unizoites could be found in vero cell but human fibroblast could not be infected. The merozoites were transferred to a new culture cell and maintained for two weeks. However, the production of oocysts has not been observed in any culture cells during the cultivation. Trimetroprim-sulfamethoxazole combination was applied at concentration of 40 and 8 microgram per milliliter of culture medium and the abnormality of merozoites were detected under light microscope after staining. •

Present at:

DECREASED HEMOGLOBIN CONCENTRATIONS, HYPERPARASITEMIA, AND SEVERE MALARIA ARE ASSOCIATED WITH INCREASED PLASMODIUM FALCIPARUM GAMETOCYTE CARRIAGE

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To determine factors influencing gametocyte carriage, a cross-sectional study was conducted among 512 patients admitted for *Plasmodium falciparum* malaria. After adjustments for potential confounders, hemoglobin concentrations were lower in gametocyte carriers 10.5 (+/-2.5) than in patients without gametocytes 12.5 (+/-2.3) ($P < 0.0001$). Hemoglobin concentrations were negatively correlated with peak gametocyte counts (Spearman's $p = -0.37$, $P < 0.0001$) and gametocyte carriage durations (Spearman's $p = -(0.30$, $P < 0.0001$). Adjustments for the duration of the malaria episode and other potential confounders did not alter the association ($P < 0.0001$). After adjustment for potential confounders, the median asexual parasitemia was higher in patients with gametocytes than in patients without gametocytes ($P = 0.003$). Severe malaria cases were more likely to have gametocytes (65%) than malaria with hyperparasitemia (38%) or mild malaria (31%) ($P = 0.0001$). These findings suggest that events surrounding anemia and tissue hypoxia stimulate Plasmodium falciparum gametocytogenesis. •

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INTESTINAL HELMINTH INFECTIONS ARE ASSOCIATED WITH INCREASED INCIDENCE OF PLASMODIUM FALCIPARUM MALARIA IN THAILAND

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In a prospective study of the total population of 5 hamlets on the western border of Thailand, all subjects were screened for helminth infections; during the following year, the incidence of malaria was recorded. Patients were not treated for helminth infections. Among 731 villagers, helminth-infected subjects were more likely to develop falciparum malaria during the following year (adjusted risk ratio 2.24, range 1.4-3.6; $P = 0.001$). The risk of developing falciparum malaria increased with the number of helminth species ($P = 0.036$). Whereas in other studies helminths were associated with protection from severe complications of malaria, it seemed here that helminth-infected patients were more likely to develop malaria. It is suggested that a helminth-mediated Th2 shift may have complex consequences on malaria, decreasing antisporozoite immunity, but protecting against severe malaria. •

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MANAGEMENT OF MALARIA IN THAILAND

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The purpose of treatment for uncomplicated malaria is to produce a radical cure using the combination of: artesunate (4 mg/kg/day) plus mefloquine (8 mg/kg day) for 3 days: a fixed dose of artemether and lumefantrine (20/120 mg tablet) named Coartem (4 tablets twice a day for three days for adults weighing more than 35 kg): quinine 10 mg/kg 8-hourly plus tetracycline 250 mg 6-hourly for 7 days (or doxycycline 200 mg as an alternative to tetracycline once a day for 7 days) in patients aged 8 years and over: Malarone (in adult 4 tablets daily for 3 days). In treating severe malaria, early diagnosis and treatment with a potent antimalarial drug is recommended to save the patient's life. The antimalarial drugs of choice are: intravenous quinine or a parenteral form of an artemisinin derivative (artesunate i.v./i.m. for 2.4 mg/kg followed by 1.2 mg/kg injection at 12 and 24 hr and then daily for 5 days; artemether i.m. 3.2 mg/kg injection followed by 1.6 mg/kg at 12 and 24 hrs and then daily for 5 days; artemether i.m. (Artemotil) with the same dose of artemether or artesunate suppository (5 mg/kg) given rectally 12 hourly for 3 days. Oral artemisinin derivatives (artesunate, artemether, and dihydroartemisinin with 4 mg/kg/day) could replace parenteral forms when patients can tolerate oral medication. Oral mefloquine (25 mg/kg divided into two doses 8 hrs apart) should be given at the end of the artemisinin treatment course to reduce recrudescence. •

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HIGH PERFORMANCE LIQUID CHROMATOGRAPHIC (HPLC) ANALYSIS OF SULPHADOXINE AND ITS DERIVATIVE AND PYRIMETHAMINE IN PLASMA OF FALCIPARUM MALARIA PATIENTS

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Objective: To investigate the level of sulphadoxine, its derivative and pyrimethamine by HPLC in the plasma of falciparum malaria patients after oral administration of a single dose of 1,500 mg and 75 mg of pyrimethamine. The levels are compared between the drug sensitive group and the drug resistant group. And to find the cause of failure in using this combination of drugs in the treatment of malaria might be by metabolic deviation of the host.

Background: In Thailand, a single dose of 1,000 mg of sulphadoxine plus 50 mg pyrimethamine is frequently used for the treatment of falciparum malaria. This combination has been recommended by World Health Organization, mainly has been used in Southeast Asia for treatment of the chloroquine-resistant strain. From 1975 to 199 the cure rate with this drugs combination dropped from 82% to 42%. If the failure is due to rapid acethylation of sulphadoxine one should find a lower level of active sulphadoxine in the plasma.

Methods: Blood specimens were collected from venous blood drown from each subject at administration and at 0.5,1.5, 3.0, 6.0, 8.0, 24.0, 32.0, 48.0, 2.0, 120.0, 168.0, and 288.0, hours after drug administration of single dose of 1,500 mg of sulphadoxine and 75 mg of pyrimethamine. The modified Edstein MD. Method was used for simultaneous HPLC analysis for sulphadoxine N_4-acetylsulphadoxine and pyrimethamine in plasma. Parallel counts for infected red blood cells were also performed. Standards were donated from F. Hoffman la Roche & Co.

Results: The results indicated that only five out of twelve with low average initial parasitemia (2<484 cell/µl) were cured with a single dose of 1,500 mg of sulphadoxine and 75 mg of pyrimethamine. Plasma sulphadoxine N_4-acetylsulphadoxine and pyrimethamine started from zero and gradually increased until reaching the highest concentration of 60.0 ± 23.4 µg/ml 4.5 ± 3.5 µg/ml and 0.2 ± 0.1 ng/ml respectively in the sensitive group at eight hours after medication began. The sensitive healthy control level (CS) were 49.4 ± 20.1 µg/ml 4.8 ± 34.0 µg/ml and 0.2 ± 0.2 ng/ml respectively, while in the resistant group the level were 74.3 ± 21.8 µg/ml, 2.7 ± 2.5 µg/ml and 0.2 ± 0.1 ng/ml respectively in the resistant type I group and 43.7 ± 13.2 µg/ml, 7.0 ±11.4 µg/ml and 0.2 ± 0.3 ng/ml, for the resistant type II group with resistant healthy controls (CR) at 59.8 ± 15.3 µg/ml, 9.0 ± 6.9 µg/ml and 0.2 ± 0.3 µg/ml, respectively.

Conclusion: The level of the drugs in each group were not significantly different statistically. The terminal half life of the drug in plasma for each patient group was also not significantly different. This study did not examine the relationship between the therapeutic response, acetylator phenotype and plasma concentration of sulphadoxine. The plasma levels of pyrimethamine in this study are consistent with previous studies on the combined uses of pyrimethamine and sulfalene. •

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