Faculty of Tropical Medicine
Mahidol University

Annual Report 2001

CONTENTS

Faculty of Tropical Medicine Mahidol University, Annual Report 2001

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Foreword

Every year the Faculty of Tropical Medicine has compiled its achievements in the past Fiscal Year. The Faculty's work in the period 1 October 2000 to 30 September 2001 has been compiled in this 2001 issue. All efforts have been made by the Faculty's staff to retain the image and standing of the Faculty as "Asia's Leader in Tropical Medicine".

This year, the Faculty of Tropical Medicine Self-Study Report (SSR) has been accredited by the committee appointed by Mahidol University and the committee appointed by the Ministry of University Affairs. The Faculty is now preparing for its Self-Assessment Report (SAR), a further step before becoming autonomous.

The Faculty of Tropical Medicine has always been dedicated to promoting research on tropical diseases. Every year, more than 100 papers are published by Faculty members. Multi-disciplinary and multi-national research is strongly encouraged and fully supported, and as a result, research collaboration between Faculty staff and members of the Communicable Disease Control Department of the Ministry of Public Health, Thailand, NASA, the Liverpool School of Tropical Medicine, Oxford University, UK, have been continuously carried out.

The Faculty of Tropical Medicine, as a regional centre - for both SEAMEO TROPMED and ACIPAC-JICA - provided short training courses and scholarships for the 10 SEAMEO member countries, especially the Greater Mekong Sub-region countries. These activities are fruitful in regional development and collaboration. The Joint International Meeting is also organized yearly to disseminate knowledge flowing from research and to promote co-operation between researchers. All of these activities are an essential part of the Faculty's strategic plan to retain and advance its status of international renown.

May I congratulate all staff for their outstanding performances in teaching, learning, research, services and administration. It is also very pleasing to acknowledge our productive cooperative and collaborative linkages with SEAMEO TROPMED, the Wellcome Unit, ACIPAC, the Bill and Melinda Gates Foundation, the Department of Communicable Disease Control, Ministry of Public Health, the World Health Organization, and other local, national and international organizations and institutes.

Sornchai Looareesuwan

Prof. Sornchai Looareesuwan
Dean

Editors' Note

The principal achievements of the Faculty of Tropical Medicine between 1 October 2000 and 30 September 2001 have been compiled and documented in this Annual Report. Being a Faculty of a University in Thailand, the Faculty has four major roles - teaching, research, academic services and culture-promoting activities. In teaching, we have five regular postgraduate programmes and in the Fiscal Year 2001, the number of students increased 8.43% over last year. Short training courses, seminars and workshops also increased by 50%. The number of visitors to the Faculty also increased.

In FY 2001, members of the Faculty of Tropical Medicine published 107 papers, and of them somewhat more than 90% were published in international medical/scientific journals. Several ongoing research undertakings are international collaboration projects; collaboration is not confined only to Asian, European and North American institutions, but extends to South American institutions, as well.

In December 6-8, 2000, we organized the 3rd Seminar on Food-Borne Parasitic Zoonoses (FBPZ3) concurrently with the Joint International Tropical Medicine Meeting 2000 (JITMM 2000), at the Royal River Hotel, Bangkok. There were 170 papers in symposia and oral presentations and 41 poster presentations. There was a total of 520 participants from 31 countries. On August 8-10, 2001, (JITMM 2001), there were 114 oral presentations and 68 posters and 850 participants, a pleasing increase of 330 on the previous year, came from 23 countries.

In November 2000, ACIPAC representatives visited countries in the Greater Mekong Sub-region (Cambodia, Lao PDR, Myanmar and Vietnam), to introduce the ACIPAC Project and gain govermental and institutional support. Then, in March 2001, we held the ACIPAC International Symposium: "Save Schoolchildren from Parasites", in Bangkok. In a significant milestone in the ACIPAC Project, on 17th September 2001, Their Excellencies Mr. Ryutaro Hashimoto, former Prime Minister of Japan, Mrs. Sudarat Keyuraphan, Minister for Public Health, Mr. Sutham Saengprathum, Minister for University Affairs, Dr. Somsong Rugpoa, Director-General CDC, and other dignitaries, kindly attended the Opening Ceremony of the first ACIPAC International Training Course on School-based Malaria and Soil-transmitted Helminthiases Control for Programme Managers. Training course participants came from Cambodia, Lao PDR, Myanmar, Thailand, Vietnam and Kenya.

On 9th March 2001, the Faculty was highly honored to have Her Royal Highness Princess Galayani Vadhana Krom Luang Naradhivas Rajanagarindra open the Faculty's malaria research station, "Rajanagarindra Tropical Diseases International Centre" at Suan Phung, Ratchaburi Province.

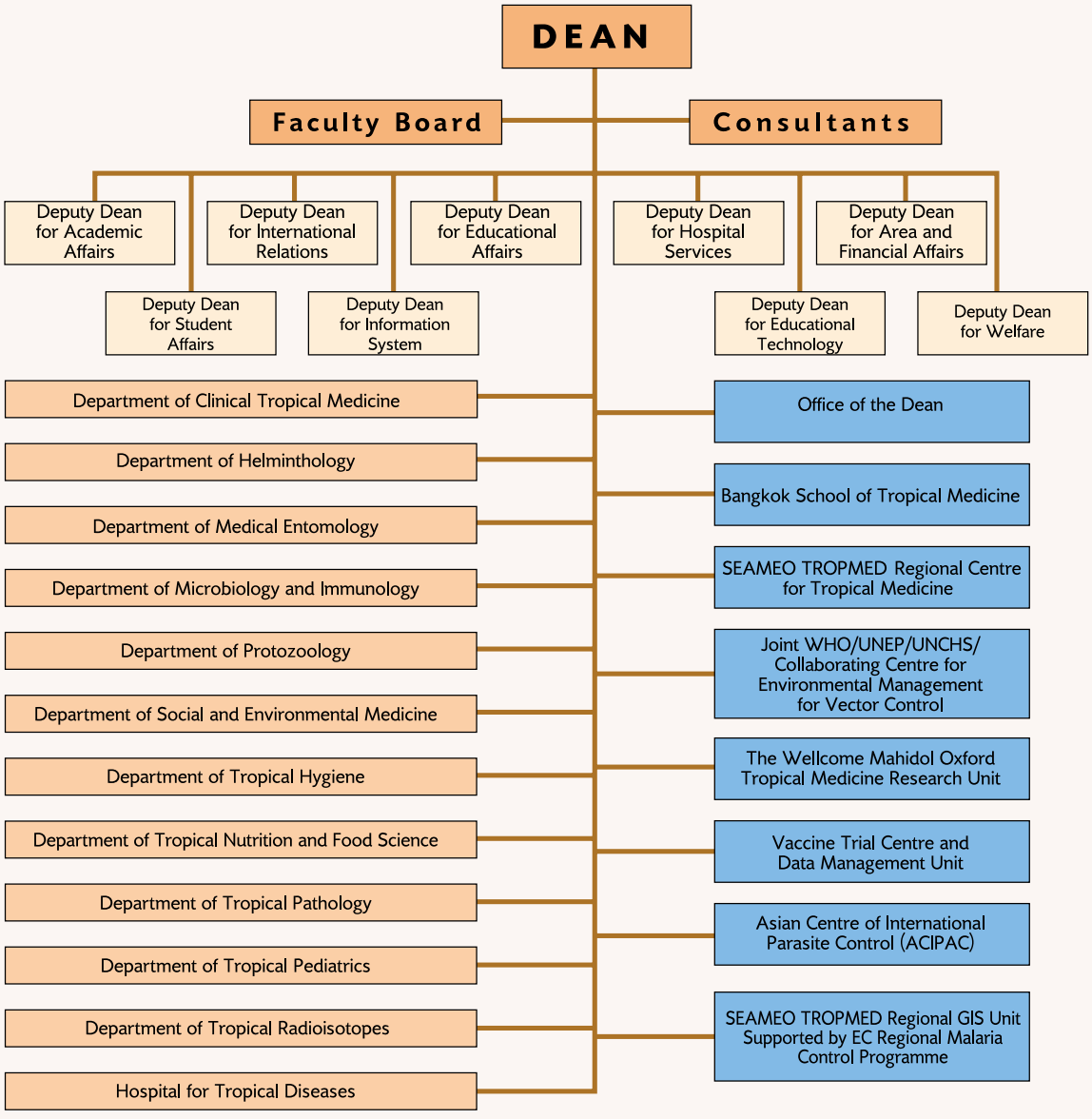
Another highlight of the reporting period was the Bill and Melinda Gates Foundation Grant, in November 2000, of U.S$ 4.72 million over 2 years for the Tak Malaria Initiative. This is a collaborative project of the Faculty, the CDC, Mahidol University, the University of Oxford, the Wellcome Unit and the Shoklo Research Unit in Tak Province. The Project aims to control malaria and prevent drug resistance along the Thai-Myanmar border area in Tak Province by systematic early diagnosis and early treatment with potent antimalarial combinations containing an artemisinin derivative.

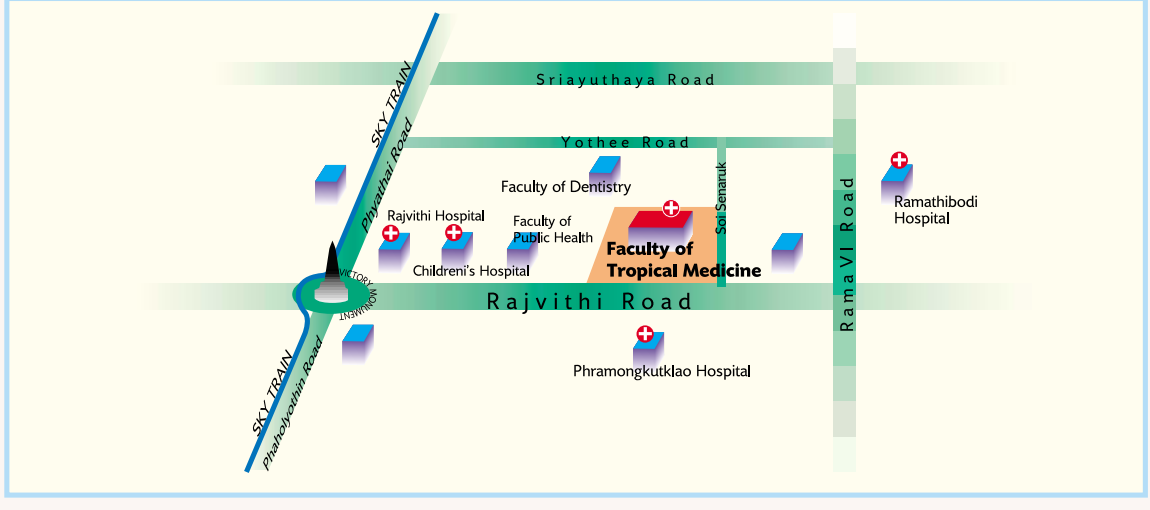
It is our great pleasure to present the Annual Report of the Faculty of Tropical Medicine, Mahidol University, for the Year 2000/2001.

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

ORGANIZATION AND ADMINISTRATION

THE FACULTY OF TROPICAL MEDICINE, MAHIDOL UNIVERSITY





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Dean

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Deputy Dean for
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Deputy Dean for
International Relations

Assoc. Prof. Jitra Waikagul
Deputy Dean for
Academic Affairs

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Deputy Dean for
Student Affairs

Associate Professor Kanjana Hongtong
Deputy Dean for
Welfare

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Deputy Dean for
Educational Technology

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

Miss Kobsiri Chalemrut
Assistant Dean for
Special Activities

DEAN, DEPUTY DEANS, ASSISTANT DEANS AND SECRETARY OF THE FACULTY

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Deputy Dean for
Area and Financial Affairs

Assist. Prof. Kasinee Buchachart
Deputy Dean for
Information System

Assist. Prof. Chukiat Sirivichayakul
Assistant Dean for
Educational Affairs

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

Assoc. Prof. Parnpen Viriyavejakul
Assistant Dean for
International Relations

Ms. Suparp Vannaphan
Assistant Dean for
Professional Development

Mrs. Vorapan Singhsilarak
Secretary of the Faculty








On 9 March 2001, the Faculty was highly honored to have her Royal Highness Princess Galayani Vadhana Krom Luang Naradhivas Rajanagarindra open the “Rajanagarindra Tropical Diseases International Centre” at Suan Phung, Ratchaburi

JITMM 2001

Joint International Tropical Medicine Meeting 2001, 8-10 August 2001, at the Century Park Hotel, Bangkok















Opening Ceremony of the first ACIPAC International Training Course on "School-based Malaria and Soil-transmitted Helminthiases Control for Programme Managers" on 17 September 2001, kindly attended by their Excellencies Mr. Ryutaro Hashimoto, Former Prime Minister of Japan, Mrs. Sudarat Keyuraphan, Minister for Public Health, and Mr. Sutham Saengprathum, Minister for University Affairs.




H.E. Professor C P Thakur, Minister of Health and Family Welfare of India, visited the Faculty of Tropical Medicine, Mahidol University, on 12 October 2001.

Wreath-laying to commemorate Mahidol Day, 24 September 2001.

Professor Sornchai Looareesuwan receives the 14th Khwarizmi International Award from the Iranian Research Organization for Science & Technology, on 5 February 2001.

Professor Sornchai Looareesuwan receives the Award for the Most Cited Author 1990-2001 in the field of Bioscience and Medicine from the Thailand Research Fund, on 2 August 2001.

Professor Polrat Wilairatana receives the Consolation prize of the Outstanding Dissertation Award from the National Research Council of Thailand, on 10 August 2001.

Retirement Day, 28 September 2001.

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 Echerverring (1 April - 30 September 2001)

VISITING PROFESSORS

No.	Name	Field	Department/University	Country
1.	Prof. Walther H. Wernsdorfer	Clinical Pharmacology	University of Vienna	Austria
2.	Dr. Chev Kidson	Immunology	SEAMEO TROPMED Network	Australia
3.	Prof. Ralf Clemens	Clinical Tropical Medicine	SmithKline Beecham Pharmaceutical	Belgium
4.	Dr. Frédérick Gay	Tropical Medicine	Regional Malaria Control Programme in Cambodia, Laos and Vietnam	France
5.	Prof. Frank P Schelp	Nutrition and Food Science	Freie Universität Berlin	Germany
6.	Dr.Gertrud Elise Schmidt-Ehry	Tropical Medicine	Cambodian-German Health System Development	Germany
7.	Prof. Gunther Wernsdorfer	Clinical Tropical Medicine	Tropical Medicine & Med. Parasitology Occupational Health	Germany
8.	Prof. Masamichi Aikawa	Tropical Pathology	Tokai University School of Medicine	Japan
9.	Prof. Shigeyuki Kano	Tropical Medicine	International Medical Center of Japan	Japan
10.	Prof. Somei Kojima	Tropical Medicine	The University of Tokyo	Japan
11.	Prof. Akira Ito	Tropical Medicine	Asahikawa Medical College	Japan
12.	Prof. C P Ramachandran	Parasitology	Universiti Putra Malaysia	Malaysia
13.	Datuk Dr. Manikavasagam Jegathesan	Tropical Medicine	Universiti Putra Malaysia	Malaysia
14.	Dr. P F Beales	Tropical Hygiene	WHO/Geneva	Switzerland
15.	Dr. David Warrell	Tropical Medicine	University of Oxford	UK
16.	Prof. Herbert M Gilles	Tropical Medicine	Liverpool School of Tropical Medicine	UK
17.	Prof. Gary M Brittenham	Tropical Medicine	Columbia University	USA
18.	Prof. John H Cross	Parasitology	Uniformed Services University of the Health Sciences	USA
19.	Dr. Stephen L Hoffman	Immunological Research for Vaccine Development	Naval Medical Research Institute	USA
20.	Prof. Myron Max Levine	Tropical Medicine	University of Maryland School of Medicine	USA
21.	Prof. James Carroll	Tropical Pediatrics	Medical College of Georgia	USA
22.	Prof. Victor R Gordeuk	Tropical Medicine	Howard University	USA
23.	Dr. Karl A Western	Tropical Medicine	National Institute of Health	USA

FACULTY BOARD

(1 October 2000 - 30 September 2001)

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

*	until 31 March 2001
**	from 16 August 2001

FACULTY SENATE

No.	Name	Position
1.	Assoc. Prof. Surang Tantivanich	Chairman
2.	Assist. Prof. Achara Asavanich	Vice Chairman
3.	Prof. Wanpen Chaicumpa	Lecturer Representative
4.	Assoc. Prof. Yupaporn Wattanagoon	Lecturer Representative
5.	Assist. Prof. Supatra Thongrungkiat	Representative, Department of Medical Entomology
6.	Dr. Kriengsak Limkittikul	Representative, Department of Tropical Pediatrics
7.	Dr. Wimol Nganthavee	Representative, Department of Tropical Pediatrics
8.	Assist. Prof. Porntip Petmitr	Representative, Department of Protozoology
9.	Assist. Prof. Yaowapa Maneerat	Representative, Department of Tropical Pathology
10.	Assist. Prof. Talabporn Harnroongroj	Representative, Department of Helminthology
11.	Assist. Prof. Petcharin Yamarat	Representative, Department of Tropical Radioisotopes
12.	Assist. Prof. Chantima Lohachit	Representative, Department of Social and Environmental Medicine
*13.	Dr. Nilarat Premmanisakul	Representative, Department of Tropical Hygiene
**14.	Dr. Apichai Tuanyok	Representative, Department of Tropical Hygiene
15.	Assist. Prof. Udomsak Silachamroon	Representative, Department of Clinical Tropical Medicine
***16.	Assist. Prof. Varee Wongchotigul	Representative, Dept. Microbiology and Immunology, Secretary General
****17.	Assist. Prof. Paron Dekumyoy	Representative, Dept. Helminthology, Secretary General

*	from 21 January 2000 - 21 May 2001
**	from 9 July 2001 - 30 September 2001
***	Secretary General from 19 January 2000 - 26 April 2001
****	Secretary General from 11 May 2001




Current Research Activities

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Medical Science Associate

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

CURRENT RESEARCH ACTIVITIES

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

Malaria research activities have focused on clinical trials, pathophysiology, clinical pharmacology and clinically related laboratory studies. Staff of the Department studied not fewer than 2,500 admitted cases of this disease. It was found that 45% were falciparum malaria, 52% were vivax malaria, 2% of mixed infections of the two above, a few cases of malariae malaria and occasionally cases of ovale malaria. The major focus is on clinical trials of multidrug resistant falciparum malaria

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

Besides extensive clinical studies, we also carried out interdepartmental and institutional collaborative studies of antigens in cerebral and non-cerebral malaria patients, of lymphocyte subpopulations during acute and convalescence phases of malaria, and qualitative and quantitative polymerase chain reaction to predict *Plasmodium falciparum* treatment failure. Pathophysiologic alteration in malaria has been widely investigated. Interesting results were the dynamic alteration in splenic function during acute falciparum malaria, in erythrocyte survival following clearance of malaria parasites, defective production of and response to IL-2 in acute falciparum malaria, cytoadherance 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 azithromycin was also studies.

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

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

Research on skin diseases in HIV patients is being conducted such as the epidemilogy of cutaneous manifestations in HIV patients in Thailand, fungal infection in leukoplakia patients, superficial fungal infections in normal and HIV patients.

The titles of current departmental research activities are as follows

1. Open-label, treatment protocol for the safety and efficacy of SCH 56592 (oral suspension form) in the treatment of invasive fungal infections.
2. Relationship of *Plasmodium* antigen and antibody profiles to therapeutic response in falciparum malaria.
3. PCR-RFLP detection of *Plasmodium vivax* dhfr mutations.
4. 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.
5. Neurotoxicity of artemether in animal model following intermittent intramuscular injections.
6. Safety and therapeutic effects of Jin Huang Chinese medicine in uncomplicated HIV-1 patients
7. Research and development of effective antimalarial drugs in combination for wide use in the treatment of malaria.
8. Safety, efficacy of DNP and artcom for uncomplicated *Plasmodium falciparum* malaria in Thailand.
9. Efficacy and tolerability of ivermectin on gnathostomiasis (pilot study).
10. Efficacy and tolerability of ivermectin on gnathostomiasis.
11. Effect of insecticide on female reproductive system.
12. Air pollution mitigation from the industrial sector.
13. Uses of CFC alternatives in Thailand.
14. Health risk from trihalomethane contamination of tap water in Bangkok Metropolitan area and boundary.
15. Development of genotyping technique for *Plasmodium vivax* parasite.
16. Study of auto-agglutination phenotype and disease severity in *P.falciparum* infection.
17. Assessment of the neurotoxicity of oral dihydroartemisinin in mice.
18. Association of gene mutations in *Plasmodium vivax* dhfr with resistance to sulphadoxine/pyrimethamine: geographical and clinical correlates.

International institutional linkages

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

Clinical Infectious Diseases Research Unit

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Secretary

FACILITIES

1. Clinical Trial facility for Outpatients, 7th Floor Chalerm Phrakiat Building

Current Research Activities:

1) Observational Probe Study of *In Vitro* Immune Response Parameters to the Candidate HIV-1 Vaccine Antigens Among Subjects From Brazil, Thailand, Malawi and Other Countries in Africa.

Objective: To estimate *in vitro* immune responses to the candidate HIV-1 Vaccine antigens and determine the involving CTL epitopes and the genetic sequence of HIV-1 genes from HIV-infected Thai Subjects: 50 asymptomatic HIV seropositive (17 males, 33 females) and 54 HIV negative (24 males, 30 females) were enrolled.

Protocol summary: 4-8 interval visits were scheduled for the HIV seropositive volunteers group. Blood drawn for Gramma IFN-ELISPOT (for CTLs producing cytokines), PCR for viral RNA detection and HIV sequencing with MHC-I/II typing have been performed.

2) Safety and Therapeutic Effects of Jin Huang Chinese Medicine in Uncomplicated HIV-1 Patients.

Objective: To assess the safety and efficacy of Jin Huang Ba Bao as an anti HIV-1 herbal medicine

Subjects: 21 asymptomatic HIV infected Thais (9 males, 12 females) voluntarily were enrolled.

Protocol summary: Phase I/II drug trial was conducted to assess safety, tolerability and preliminary efficacy of Jin Huang Medicine. 8.1 grams of Jin Huang capsules and 30 cc. of Jin Huang Oral were given daily to each volunteer for one week, then each volunteer was closely monitored for any adverse events. If there are no hypersensitivty reactions reported, the same doses are given at 2-week intervals for at least 6 months. Clinical and laboratory observations have been done monthly to assess the safety and efficacy of this drug by regular blood drawn for CD4 count and viral load.

3) Open-Label, Treatment Protocol for the Safety and Efficacy of Posaconazole (SCH 56592) in the Treatment of Invasive Fungal Infections

Objective: To evaluate the safety, tolerance and efficacy of Posaconazole under treatment protocol for invasive fungus infected patients which are resistant, refractory or intolerant to standard antifungal therapies.

Site: Bamrasnaradura Hospital

Protocol Summary: 20 HIV-infected patients with cryptococcal meningitis (14 males, 6 females) who were refractory to standard amphotericin B treatment were enrolled and treated with Posaconazole for at least 24 weeks (12 visits). Monitoring of clinical responses, microbiological response for safety and efficacy were performed regularly at intervals up to one month after stopping the drug. Mycological response was assessed from CSF culture for cryptococcus at intervals.

4) A Retrospective Study to Establish on Historical Database on the Efficacy of Standard Antifungal Therapy in Patients With Invasive Fungal Infection.

Objective: To assess the clinical efficacy of standard therapies in an historical group of cases with refractory invasive fungal infections or those intolerant of standard antifungal agents compared with the results observed in an open-label, non comparative study of posaconazole in a similar patient population.

Subjects: At least 1 year of retrospectively screened Thai AIDS patients who were infected with cryptococcal meningitis or disseminated fungal infections consistent with the inclusion criteria will be randomly enrolled for this study; at least 40 medical files.

Site: Bamrasnaradura Hospital (one of 30 sites around the world).

Protocol Summary: Medical data about clinical information and responses to regimen therapies from selected subjects will be recorded in the standard Case Record Files. These data will be reviewed by an independent Infectious Expert Committee. The results will be analyzed in terms of responses to drug therapies and survival analysis.

2. Immunology Lab

The current research activities are

1) Studies to develop improved methods to diagnose important tropical infections including penicilliosis and leptospirosis.

2) Studies to develop methods to improve prognosis of severe tropical infections including falciparum malaria and melioidosis.

Environmental and Industrial Toxicology Unit

The Environmental and Industrial Toxicology Unit is currently established at the Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University to strengthen knowledge and research in health risk assessment and hazard health impact from toxicant exposure in the environment and in industry. In addition, the Unit also provides graduate program and courses in clinical toxicology to study metabolism, toxicokinetics, pathways and targets for toxicity. The Unit is actively involved in health risk analysis and surveillance for volatile organic compounds (VOCs), heavy metals and hazardous waste. Several fundings are allocated from Mahidol University; Thailand Research Fund as well as foreign agencies such as DANCED; UNEP; University of Tokyo, Japan; University of Leicester, U.K. and Rutgers University, U.S.A.

Professor Sornchai Looareesuwan's Awards

5 Feburary 2001	The 14th Khwarizmi International Award from the Iranian Research Organization for Science & Technology.
2 August 2001	The Most Cited Author 1990-2001 in the field of Bioscience and Medicine from the Thailand Research Fund.

Professor Polrat Wilairatana's Award

10 August 2001	The Consolation Prize of the Outstanding Dissertation Award from the National Research Council of Thailand.

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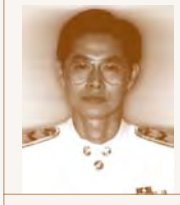

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DEPARTMENTAL ONGOING RESEARCH (2001)

1. A five-year retrospective evaluation of gnathostomiasis and diagnostic specificity by immunoblot.
2. Analysis of fluid antigens of *Echinococcus* cyst for diagnosis.
3. Angiostrongyliasis: partially purified antigens of *Angiostrongylus cantonensis* adult worms for diagnosis using immunoblot.
4. Angiostrongyliasis: potential fractionated antigens of *Angiostrongylus cantonensis* adult worms for diagnosis using ELISA.
5. *Angiostrongylus cantonensis*: s-adenosyl methionine decarboxylase.
6. Comparative studies on surface ultrastructure of adult worm of *Paragonimus* sp. in Thailand.
7. Current status of *Gnathostoma* infection in Nakhon Nayok and Prachin Buri.
8. Diagnosis of human opisthorchiasis with cocktail and eluted *Bithynia siamensis goniomphalos* snail antigen by ELISA.
9. Differentiation of fractionated larval antigens (*Cysticercus cellulosae*) responsible for antibody of neurocysticercosis patients.
10. Effect of ivermectin on *Gnathostoma spinigerum* morphology.
11. Effect of mebendazole on *Trichuris trichiura* morphology.
12. Efficacy of high dose mebendazole against trichuriasis in adult patients.
13. Experimental infection of freshwater fish in Thailand with infective stage of *Angiostrongylus*.
14. Fish as the natural second intermediate host of *Gnathostoma spinigerum*.
15. Fish-borne trematodes in Thailand.
16. *Gnathostoma* infection in fish caught for local consumption in Nakhon Nayok province.
17. Monoclonal antibody-based competitive ELISA and indirect ELISA for immunodiagnosis of trichinellosis.
18. Seasonal variation of *Gnathostoma* infection in swamp eels in Nakhon Nayok.

19. Soil-transmitted helminthiases control through school-based intervention.
20. Strongyloidiasis: crude, molecular weight cut-off and eluted antigens of third-stage larvae for immunodiagnosis.
21. Study on prevalence of *Wuchereria bancrofti* infection in Kanchanaburi and Ratchaburi provinces.
22. Studies on the efficacy of Thai traditional herbal medicines in the treatment of opisthorchiasis in hamsters.
23. *Toxocara canis* larval antigens for serodiagnosis of human toxocarosis.
24. *Trichinella* sp. in Thailand: differentiation of isolates by biological and molecular biological methods.

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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.

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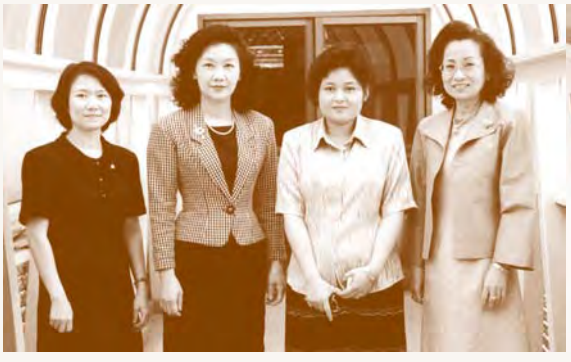
The main responsibilities of the Department of Microbiology and Immunology include teaching and training, research, laboratory services and academic consultation.

TEACHING AND TRAINING

Fourteen international courses at the postgraduate level in microbiology and immunology, including core subjects, elective and advanced courses are offered to the students of the D.T.M. & H. as well as the M.Sc. and Ph.D. in Tropical Medicine. The Department also shares some parts of teaching microbiology, immunology and molecular biology in other courses offered at the faculty, other faculties of Mahidol University, and other universities and institutions. As of September 2001, 45 students selected to work for their theses towards the M.Sc./Ph.D. degrees in various laboratories of the Department. Short courses on the subjects are given periodically.



CURRENT RESEARCH ACTIVITIES

The current research activities of the Department involve studies on biology, molecular biology and immunology of infectious agents/diseases, particularly those causing problems in tropical areas, with the ultimate aims at 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 epidemiologicas 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 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 the 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 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 the remote areas such as the conventional or dot-blot ELISA, immuno-colloidal gold and/or the dip-stick techniques as well as the use of immunomagnetic separation for higher sensitivity of detection of the pathogens, 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 are 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 both against *V. cholerae* O:1 for tolerability, 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 is 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, the 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 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; and the National Institute of Infectious Diseases, Tokyo, Japan; the London School of Hygiene and Tropical Medicine; International Vaccine Institute, Seoul, Korea; the Department of Microbiology and Immunology, Faculty of Medicine, Monash University, Melbourne Australia; the Department of Microbiology and Immunology, Faculty of Medicine, University of Adelaide, 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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The Department of Protozoology is one of the eleven departments within the Faculty of Tropical Medicine, Mahidol University. It was one of the first five departments established at the founding of the Faculty of Tropical Medicine in 1960. Its responsibilities are teaching, training, research and services in the field of medical protozoa.

CURRENT RESEARCH ACTIVITIES

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

TEACHING AND TRAINING

1. Regular courses
   - 1.1 Diploma in Tropical Medicine and Hygiene (D.T.M.&H.)
     - 1.1.1 Core subject TMPZ 501: Protozoology
     - 1.1.2 Elective subject TMID 505: Parasitology
   - 1.2 Master of Science in Tropical Medicine (M.Sc. (Trop. Med.)) and Doctor of Philosophy in Tropical Medicine (Ph.D. (Trop.Med.)).
     - 1.2.1 Core subject
       - TMID 512 : Tropical medicine
     - 1.2.2 Elective core subject
       - TMID 503 : Medical protozoology
       - TMID 516 : Practical parasitology
     - 1.2.3 Free elective
       - TMID 517 : Biochemistry of parasites
       - TMID 518 : Advanced parasitology
       - TMID 519 : Experimental techniques in parasitology
       - TMID 520 : Molecular biology of parasites
       - TMID 521 : Antiparasitic agents

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

TRAINING COURSES

1. Laboratory diagnosis of AIDS-related protozoa.
2. Workshop on clinicial and laboratory diagnostic parasitology.

SERVICES

The Department of Protozoology provides the following services:

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

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CURRENT RESEARCH ACTIVITIES

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

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

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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 related to tropical diseases are being conducted at Rajanagarindra Tropical Disease International Centre (RTIC) in Suan Phung, Ratchaburi Province. Rajanagarindra Tropical Disease International Centre, supported by Her Royal Highness Princess Fund, is one of the faculty's research stations for conducting research on tropical diseases. Various activities at the RTIC, such as the provision of health services for the local people and field epidemiology training for students, are conducted under the supervision of the personnel from the Department of Tropical Hygiene.

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

CURRENT RESEARCH ACTIVITIES

1. Epidemiology and control of malaria in Ratchaburi Province, Thailand.

2. Epidemiology and control of soil-transmitted helminthiasis in a rural community near the Thai-Burmese border.
3. Human genetics and malaria.
4. A multicentre, randomized, double-blind, parallel group study to assess the efficacy, safety and tolerability of a single 400 mg po dose of oxibendazole versus a single 500 mg po dose of mebendazole in the treatement of intestinal helminth infections in adults.

Teaching and Training Courses

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

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

CORE SUBJECTS :

TMHG 501 : Tropical Hygiene

ELECTIVE SUBJECTS :

TMHG 502 : Medical Statistics
TMHG 508 : Epidemiological Investigation
TMHG 509 : Computer Utilization

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

CORE SUBJECTS :

TMID 513 : Biostatistics
TMID 514 : Research Methodology and Design

ELECTIVE SUBJECTS :

TMHG 511 : Advanced Statistical Analysis In Biomedical Research
TMHG 512 : Modern Methods in Epidemiological Research
TMHG 513 : Use of Advanced Statistical Software in Epidemiological Analysis
TMHG 514 : Data Processing by Computer
TMHG 515 : Design and Analysis In Experimental Research
TMHG 601 : Special Topics in Epidemiology and Control of Communicable Diseases
TMHG 602 : Special Topics in Tropical Hygiene
TMHG 603 : Special Topics in Environmental Health

3. Master Degree in Primary Health Care Management
   ADPM 606 : Epidemiological Studies in Health System
4. M.Sc. (Medical Epidemiology)
   TMHG 668 : Epidemiologic Methods
   TMHG 676 : Epidemiology of Specific Health Problems
5. Ph.D. (Clinical Epidemiology)
   RACE 606 : Advanced Epidemiologic Methods

International Linkages

1. Research
   1.1. Clinica di Malattie Infetive e Tropicali, Universit Degli Studi Di Brescia
   1.2. Centre de Formation et de Recherche en Médecine et Santé Tropicales, Hôpital Felix Houphouet-Boigny, Marseille, France.
   1.3. Department des Maladies Infectieuses et Tropicales, Hôpital de la Salpêtrière, Paris, France.
   1.4. Association Santé Sud Medical Humanitarian French Association, Marseille, France.
   1.5. Freie Universität, Berlin, Germany.
2. International Training Courses
   2.1 SEAMEO-TROPMED Network
   2.2 Tropical Health Program, University of Queensland Medical School, Australia
   2.3 College of Public Health, University of the Phillipines, Manila
   2.4 Faculty of Public Health, University of Indonesia, Indonesia
   2.5 Institute for Medical Research, Malaysia
   2.6 Freie Universität Berlin

Training Courses

Second Regional Field-based Training Programme in Epidemiology and Control of Tropical Disease, May 14-August 3, 2001 (Supported by WHO/SEAMEO/EC)

Regional Advanced Training Course on Data Analysis, September 10-28, 2001 (Supported by EC Regional Malaria Control Programme in Cambodia, Laos and Vietnam)

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DEPARTMENT OF

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CURRENT RESEARCH ACTIVITIES

Research activities of the Department of Tropical Nutrition and Food Science are concerned with nutritional problems in Thailand, such as micronutrient deficiencies, lifestyle and dietary patterns of different age groups, the impact of overnutrition, oxidative stress and antioxidants in relation to health, especially dislipidemia and coronary heart disease, and the effect of smoking on work performance in

relation to the phenotype of α1-antitrypsin. Furthermore, molecular biology in cancers of the lung, liver, breast and cervix were investigated. Food and health relationship in populations of Asian countries are of interest to study and the data will be compared.

At the present time using food practice and food for disease prevention and treatment is particularly interested. This has led to the project for development of food and medicinal plants.

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

The topics of current research projects are as follows:

1. Food and health relationship in the Asian population.
2. Serum leptin concentration in obese subjects.
3. Micronutrients and oxidative stress in obese subjects.
4. Antioxidants and antioxidant enzymes, vitamins, trace elements in patients with dislipidemia and coronary heart disease.
5. The effect of smoking on work performance in relation to the phenotype of alpha-1-antitrypsin.
6. Relationship of folic acid and cervical cancer.
7. Identification of gene mutation in lung cancer cells of Thai patients.
8. Molecular biology of carcinogenesis in lung cancer.
9. Development of food and medicinal plants.
10. Medicinal plants for treatment of hookworm.
11. Medicinal plants against malaria.

Awards 2001

Third position award for research project presentation at the Third National Conference on Tobacco or Health held by the Institute of Tobacco Consumption Control, 13 July 2001, Asia Pattaya Hotel, Chon Buri Province.

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Assoc. Prof. Benjaluck Pholrat
Assoc. Prof. Niyomsri Vudhivai
Miss Duangkamol Viroonudomphol
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Title

'Tobacco smoking in relation to the phenotype of alpha-1-antitrypsin and serum vitamin C concentration'

Published in: *Journal of Nutritional & Environmental Medicine* 2001;11:169-75.

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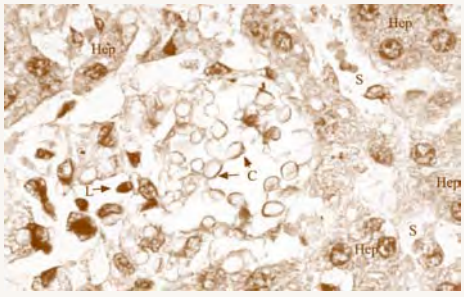

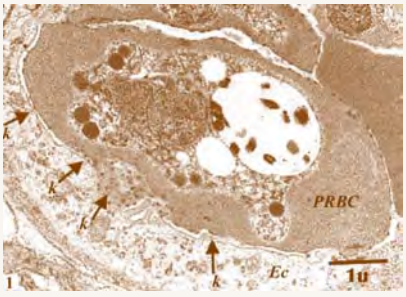

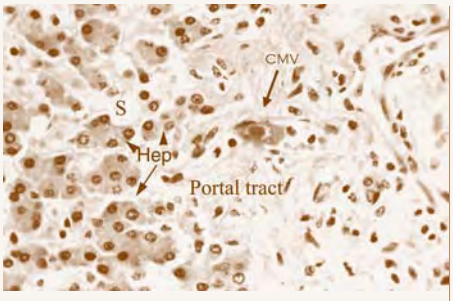

CURRENT RESEARCH ACTIVITIES

1. Malaria: histopathologic and electron-microscopic studies on various tissues and organs in humans.
2. Activation of endothelial cells activated by *Plasmodium falciparum*.
3. Tissue cytokines in AIDS.
4. Evaluation of stool samples in HIV infected patients.
5. Opportunistic infections in AIDS.

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Miss Udomluk Thangtaweewaroaj
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CURRENT RESEARCH ACTIVITIES

Vaccine

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

Dengue

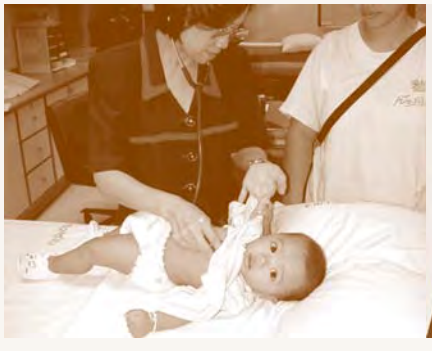
1. Dengue antibodies in Thai infants: age-specific seroprevalence and kinetics of transplacentally transferred dengue antibodies.
2. Follow-up with Thai schoolchildren immunized with live attenuated tetravalent dengue vaccine 3 to 8 years ago: current immunity response and history of serious medical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

Parasite

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

Allergy

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



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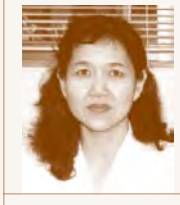

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CURRENT ACTIVITIES

Teaching

The Department is responsible for the Faculty's academic courses in teaching for the M.Sc. and Ph.D students.

1. Elective core subjects
   - TMRD 502 : Nuclear physics
   - TMRD 503 : Biological effects of radiation
   - TMRD 504 : Radioisotopes in medicine and biology
   - TMRD 505 : Radiation protection
2. Special topics
   - TMRD 601 : Special topics in tropical radioisotopes

These subjects have been cooperated with the Department of Radiological Science, Faculty of Medicine, Ramathibodi Hospital; the Department of Tropical Nutrition and Food Science, Faculty of Tropical Medicine; and the Office of Atomic Energy Commission for Peace, Ministry of Science, Technology and Environment.

The Department has provided teaching to M.Sc. students (Radiological Science); Faculty of Medicine, Siriraj Hospital in Practical Applications of Atomic Energy for Peaceful Uses in Environment and Nutritional Research (SIRA 609) on Nuclear Techniques in Parasite Infection. Moreover, the Department has

provided assistance and facilities to one M.Sc. student from the Faculty of Public Health, Mahidol Unviersity in folic acid determination.

Research

1. The Department's current research is as follows:
   - 1.1 Studies on erythrocyte glutathione peroxidase and plasma selenium in women with abnormalities of the uterine cervix.
   - 1.2 A clinical trial of modified bovine colostrum in HIV-infected Thai patients.
   - 1.3 Study on plasma copper and zinc level from women with abnormalities of the uterine cervix.
2. The Department has corperated with others, as follows:
   - 2.1 The correlation between folic status and cervical cytologic abnormalities in Thai women.
   - 2.2 Medicinal plants for treatment of hookworm.
   - 2.3 Determination of total folate analysis in food.

Services

The Department has two projects for services: (1) service for the measurement of folic acid; and (2) service for the measurement of vitamin B_{12}. Annual service usage is shown below.

1 October 2000 - 30 September 2001

	Vitamin B_{12} number	Serum folate number	Red cell folate number
Child	13	14	4
Woman	102	182	70
Man	117	212	69
Total	232	408	143

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Wellcome Unit

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Microbiologist

Mrs. Patchari Prakongpan
Administrator

Ms. Wantana Krisanarak
Accountant

Ms. Sujittra Sukhapiwat
Logistics

Ms. Kanchana Pongsaswat
Secretary

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

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

- in Mae Sot Provincial Hospital (studies of the pathophysiology and treatment of falciparum malaria),
- in the camps for displaced persons of the Karen 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 (study of melioidosis and fungal infections in patients with AIDS).

The current research activities of the Unit on malaria include studies of pathophysiological mechanisms

in severe malaria, descriptions of the pharmacokinetic and pharmacodynamic properties of antimalarial drugs, and studies of the epidemiology, prevention and treatment of malaria in the area of low or unstable transmission of the western border.

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

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

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

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Vaccine Trial Centre

Director

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Vaccine Trial Centre

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Data Management Unit

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General Affairs Officer

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VACCINE TRIAL CENTRE

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

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

The VTC is a clinical facility in the Faculty of Tropical Medicine, Mahidol University, for testing newly developed vaccines which reach the step where evaluation in human volunteers is needed. Individual scientists at any national or international institution may have their vaccines tested at this Centre. It is a joint responsibility of Mahidol University and the Ministry of Public Health, and is operated by the Faculty of Tropical Medicine on their behalf. The establishment of the Centre was started in February 1984, however, full operation was possible in September 1986 and the first admission of volunteers into the ward was on 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 persons residing in an area where the vaccines are going to be utilized most. The knowledge gained will benefit vaccine development and thus lead to effective control of infectious diseases in developing countries.

Physical facilities

The Centre occupies the 10th and 11th floors of the Chamlong Harinasuta Building of the Faculty of Tropical Medicine, with a total area of 648 square meters.

A. Self-contained clinical facilities on the 10th floor are comprised of:
   - Twenty-bed isolation ward
   - Sufficient space for recreational activities
   - Nursing section
   - Doctor's room and quarters
   - Laboratories

B. Outpatient unit on the 11th floor includes:
   - Lecture room
   - Recruitment and screening of volunteers
   - Follow-up facilities

C. Administrative office on the 11th floor

D. HIV Vaccine Trial Project on the 9th floor of the Anek Prasong Building
   - Registration and data entry room
   - Volunteer waiting area
   - Counselling rooms
   - Physical examination room
   - Vaccination room

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

Work scope

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

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

Types of studies planned

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

Data Management Unit

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Ms. Urairat Kerdmuangbua
Office Clerk

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 intravenous drug users in Bangkok, Thailand.

Vaccine Trial Project

Principal Investigator

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Miss Bussarin Thungmeephol CRA
Miss Pikul Kulchatchai CRA

CURRENT RESEARCH ACTIVITIES

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

Addendum#1

Two booster injections with a higher dose of Chiron vaccines HIV Thai E gp120 (200mg)/MF59 vaccine alone in volunteers previously immunized with Chiron vaccines HIV Thai E gp120 (100mg)/ MF59 vaccine or Thai E gp120 (100mg)+SF2 gp120 (25 or 50 mg)/MF59 vaccine.

Objectives:

- *Safety Objective:*

  To evaluate the safety of two additional booster doses (given three months apart) of Chiron vaccines human immunodeficiency virus (HIV) Thai E gp120 (200mg)/MF59 vaccine alone in previously immunized Thai volunteers.

- *Immunogenicity Objective:*

  To evaluate the immunogenicity of the two additional booster doses of the Chiron Vaccines Thai E gp120 (200mg)/MF59 vaccine alone in previously immunized Thai volunteers.

Study sites:

- *Two sites are involved:*

  Armed Forces Research Institute of Medical Sciences Royal Thai Army, Bangkok, 10400, Thailand

  Vaccine Trial Centre, Faculty of Tropical Medicine, Mahidol University, Bangkok, 10400, Thailand

Protocol summary:

- design: open trial.
- volunteers: 24 subjects previously received 3 doses of the vaccine. They are seronegative, and at low risk of HIV exposure.
- immunization: intramuscular injection at 18-36 months after the first vaccination as the first booster dose, then again 3 months after.
- Follow-up: volunteers will be followed up at 3 months after the last vaccination, and 1 year later, for HIV testing.

Measures of immunogenicity:

- Binding antibodies to Thai E gp120 antigens, measured by enzyme-linked immunosorbent assay (ELISA).
- Neutralizing antibodies to Thai E HIV-1, measured by TCLA or PBMC neutralization assays.
- Cellular T lymphocyte proliferation responses to Thai E gp120 & recall antigens & mitogen.

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

Objective:

- Phase I: Phase I (open label) description of the acute safety and tolerability of ALVAC-HIV (vCP1521:$10^{6,53}$ $CCID_{50}$)
- Phase II: Description of the safety and immunogenicity of ALVAC-HIV (vCP1521) priming with either 200 mg or 600 mg (100 or 300 mg) each B and E gp120) of the bivalent AIDSVAX™ B/E gp120 boosting.

Study sites:

- Two clinical sites situated within academic centers in Bangkok.

Study design:

- Group I: ALVAC-HIV (vCP1521:$10^{6,53}$$CCID_{50}$) will be tested for acute safety and tolerability in a group of 5 low risk, HIV seronegative Thai adults. If there are no serious vaccine-related adverse events or severe laboratory abnormalities after vaccination #2 in Phase I, Phase II will be initiated.
- Group II: 45 low-risk HIV seronegative Thai adults will be given ALVAC-HIV (vCP1521: $10^{6,53}$$CCID_{50}$) priming at weeks 0,4,12 and 24. At weeks 12 and 24, vCP1521 will be administered with 200 g of a bivalent AIDSVAX™ B/E gp120 (100 mg for each B and E gp120). Fifteen other subjects will receive a placebo.
- Group III: 45 low-risk HIV seronegative Thai adults will be given ALVAC-HIV (vCP1521: $10^{6,53}$$CCID_{50}$) at weeks 0, 4, 12 and 24. At weeks 12 and 24, vCP1521 will be administered with 600

g of a bivalent AIDSVAX™ B/E gp120 (300 mg for each B and E gp120). Fifteen other subjects will receive a placebo.

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

Primary objective:

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

Secondary objective:

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

Other objectives:

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

4. Plan for Phase III Vaccine Trial of HIV Prime-Boost Vaccine combination.

Purpose:

- To carry out a community-based, phase III efficacy trial of a prime-boost HIV vaccine combination.

Trial objectives:

- To determine if the vaccine combination
  1. prevents infection (50%-protection)
  2. is safe
  3. lowers viral load and/or increases CD4 cell count in recipients who become infected.

Vaccines:

- Designed specifically for the predominant circulating HIV of Thailand (CRF01-AE).

Prime:

A recombinant canarypox ALVAC-HIV (vCP1521) with a subtype B Gag/Pro and gp41, and subtype E gp120 (R5) gene insertions (Aventis Pasteur).

Boost:

One of the three subunit proteins below, currently under comparative evaluation in phase II trials, will be selected for the proposed phase III trial.

1. Monomers of gp120 B (X4) + gp120 E (R5) with MF59 (Chiron Vaccines)
2. Monomers of gp120 B (X4) + gp120 E (R5) with alum (AIDSVAX™ B/E, VaxGen)
3. Oligomer of gp160 E (R5) with polyphosphazene (PCPP, Aventis Pasteur)

Study population:

- Approximately 15,000 young adult Thai citizens from the general community, recruited through the health care system of the Ministry of Public Health.

Study design:

- Randomized, placebo-controlled, double-blind phase III trial comparing vaccine combination to placebo injection at a 1:1 ratio, immunization period of 6 months; prime to be given IM at 0, 1, 3 and 6 months, and boost to be given IM at 3 and 6 months. Follow-up period of 2 to 3 years depending on HIV incidence among trial population.

Study endpoints:

- HIV infection based on combined serologic and nucleic acid testing; HIV RNA and CD4 quantitation in volunteers developing HIV infection during trial and genetic characterization of infecting viruses for comparison with vaccine antigens.

Project start date: 2002

Study groups:

- CDC, MOPH Thailand
- Royal Thai Army Armed Forces Research Institute of Medical Sciences (AFRIMS)
- Vaccine Trial Centre, Mahidol University
- Walter Reed Army Institute of Research
- Aventis Pasteur, Vaxgen Inc.

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/menu/main.htm* 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.

Outstanding Students 2001

Prizewinners

1. Assoc. Prof. Kanjika Devakul Prize (Most Outstanding Student by Faculty and Student Vote)

DTM&H	
Dr. Supat Chamnachanan	Thailand
Dr. Abdinasir Ahmed Adem	Ethiopia

2. Professor Emeritus Khunying Tranakchit Harinasuta Prize (Highest Marks)

DTM&H			
TMCD 501	Tropical Medicine	Dr. Supat Chamnachanan	Thailand
TMID 507	Clinical Microscopy	Dr. Asif Harun	Bangladesh
MSc		Mr. Vongsavanh Pongsisay	Lao PDR
PhD		Miss Suwanna Chaorattanakawee	Thailand

Top Students by Programme

DTM&H	Dr. Raimund Helbok	Austria
MCTM	Dr. Siriluck Anunnatsiri	Thailand
MSc	Mr. Vongsavanh Pongsisay	Lao PDR
PhD	Miss Suwanna Chaorattanakawee	Thailand

D.T.M. & H. 2001

1.	Dr. Birgit Woitsch	Austria
2.	Dr. Raimund Helbok	Austria
3.	Dr. Asif Harun	Bangladesh
4.	Dr. Shahab Basit	Bangladesh
5.	Dr. M. Salim Uzzaman	Bangladesh
6.	Dr. Huy Rekol	Cambodia
7.	Dr. Lon Chan Thap	Cambodia
8.	Dr. Ung Sophal	Cambodia
9.	Dr. Abdinasir Ahmed Adem	Ethiopia
10.	Dr. Wolfgang Dent	Germany
11.	Dr. Hiroyuki Kato	Japan
12.	Dr. Tadao Hayakawa	Japan
13.	Dr. Yasutaka Mizuno	Japan
14.	Dr. Kenichiro Shimizu	Japan
15.	Dr. Piam Soukhanouvong	Lao PDR
16.	Dr. Viengthong Manivone	Lao PDR
17.	Dr. Thant Thwin	Myanmar
18.	Dr. Khin Thant Zin	Myanmar
19.	Dr. Hlaing Min Swe	Myanmar
20.	Dr. Robert Brands	Netherlands
21.	Dr. Opabola S. Babatunde	Nigeria
22.	Dr. Muneer Ahmed	Pakistan
23.	Dr. Johanna Irmgard Tesling	Sweden
24.	Dr. Supat Chamnachanan	Thailand
25.	Dr. Prakaykaew Tipmanee	Thailand
26.	Dr. Songpon Eiambootlop	Thailand
27.	Dr. Jane Li	USA
28.	Dr. Bui Duc Nguyen	Vietnam
29.	Dr. Duc Ai Quach	Vietnam
30.	Dr. Huynh Hong Quang	Vietnam
31.	Dr. Do Hung Son	Vietnam
32.	Dr. Nguyen Van Ky	Vietnam

M.C.T.M. 2001–2002

1.	Dr. Raimund Helbok	Austria
2.	Dr. Birgit Woitsch	Austria
3.	Dr. M. Salim Uzzaman	Bangladesh
4.	Dr. Abdinasir Ahmed Adem	Ethiopia
5.	Dr. Lon Chan Thap	Cambodia
6.	Dr. Wolfgang Dent	Germany
7.	Dr. Kenichiro Shimizu	Japan
8.	Dr. Piam Soukhanouvong	Lao PDR
9.	Dr. Khamphanh Prabouasone	Lao PDR
10.	Dr. Hlaing Min Swe	Myanmar

M.C.T.M. 2001–2002 (CONT)

11.	Dr. Robert Brands	Netherlands
12.	Dr. Muneer Ahmed	Pakistan
13.	Dr. Do Hung Son	Vietnam
14.	Dr. Nguyen Van Ky	Vietnam
15.	Dr. Duc Ai Quach	Vietnam
16.	Dr. Le Kien Ngai	Vietnam
17.	Dr. Prakaykaew Tipmanee	Thailand

M.C.T.M. (TROP.PED.) 2001–2002

1.	Dr. Ung Sophal	Cambodia

M.SC.(TROP.MED.) 2001

1st year students

1.	Miss Yoko Oshima	Japan
2.	Dr. Phonephouminh Simeuang	Lao PDR
3.	Miss Kanlaya Boonpen	Thailand
4.	Miss Kanchana Usuwanthim	Thailand
5.	Miss Kevalin Vongthoung	Thailand
6.	Miss Jaruwadee Rattanadakul	Thailand
7.	Lt. Jittima Hirunrussamee	Thailand
8.	Mr. Chalermpon Kaewjai	Thailand
9.	Lt. Chanakarn Kalambaheti	Thailand
10.	Mrs. Chamaiporn Suwanasophon	Thailand
11.	Miss Nattawan Rachapaew	Thailand
12.	Mr. Danai Sisuan	Thailand
13.	Mrs. Teerarut Chanket	Thailand
14.	Mr. Narin Hoisanks	Thailand
15.	Mr. Nitipon Ratanasetyuth	Thailand
16.	Mr. Nukool Limpairojn	Thailand
17.	Miss Natefa Uthaichotiwan	Thailand
18.	Miss Busakorn Promsarin	Thailand
19.	Mr. Preeda Wutthinuntiwong	Thailand
20.	Miss Pannumthip Pitaksajjakul	Thailand
21.	Miss Parichat Lapcharoen	Thailand
22.	Miss Potjamas Pansri	Thailand
23.	Miss Pimolrat Thongngarm	Thailand
24.	Miss Wijitporn Siriphapapun	Thailand
25.	Mr. Wichai Purisa	Thailand
26.	Mr. Weerapong Deumtan	Thailand
27.	Mr. Sompoj Chalermtaranukul	Thailand
28.	Mr. Santipong Sirikajorndachsakul	Thailand
29.	Miss Supawan Piyaratanavarasakul	Thailand
30.	Mr. Sangchai Yingsakmongkon	Thailand
31.	Mr. Amornthep Archawakulathep	Thailand

M.SC.(TROP.MED.) 2001 (CONT)

1st year students

32.	Miss Oranuch Kongpechsatit	Thailand
33.	Mr. Ittisak Subrungruang	Thailand
34.	Miss Uraiwan Krainara	Thailand
35.	Dr. Au Bich Thuy	Vietnam

2nd year students

1.	Mr. Vongsavanh Pongsisay	Lao PDR
2.	Dr. Manikip Outhayphone	Lao PDR
3.	Mr. Zulhainan bin Hamzah	Malaysia
4.	Mrs. Sira Ubwa Mamboya	Tanzania
5.	Mr. Krasae Kanakupt	Thailand
6.	Miss Tanyalak Khuntamoon	Thailand
7.	Pol.Capt.Natsuda Jamornthanyawat	Thailand
8.	Mr. Nitat Sookrung	Thailand
9.	Mr. Nirut Suwanna	Thailand
10.	Miss Busaba Tuntithavorn	Thailand
11.	Mr. Prasert Rukmanee	Thailand
12.	Miss Pitchapa Yungyuen	Thailand
13.	Mr. Phitsanu Tulayakul	Thailand
14.	Miss Penapa Yutayong	Thailand
15.	Miss Pensri Saelee	Thailand
16.	Mr. Panop Wilainam	Thailand
17.	Miss Matukorn Na Ubol	Thailand
18.	Miss Ladawan Vasinpiyamongcone	Thailand
19.	Mr. Sasipon Pumkumarn	Thailand
20.	Mr. Sith Premashthira	Thailand
21.	Miss Saichon Chimsumang	Thailand
22.	Miss Supranee Linthaworndee	Thailand
23.	Miss Charinthon Ngamamonpirat	Thailand
24.	Mr. Donald Edward Bryant	USA
25.	Dr. Nguyen Xuan Xa	Vietnam
26.	Dr. Ta Van Thong	Vietnam
27.	Dr. Tran Manh Ha	Vietnam

3rd year students

1.	Dr. Lek-Dysoley	Cambodia
2.	Miss Kanjana Sonji	Thailand
3.	Miss Gaysorn Bunyaraksyotin	Thailand
4.	Miss Junpen Suwimonteerabutr	Thailand
5.	Miss Nahathai Chulakarat	Thailand
6.	Lt. Tossapon Chaiyasith	Thailand
7.	Miss Piyaporn Suebtrakul	Thailand
8.	Mrs. Phimonsri Saengkar	Thailand

M.SC.(TROP.MED.) 2001 (CONT)

3rd year students

9.	Miss Malida Soontornruengyot	Thailand
10.	Miss Ratchanok Kumsiri	Thailand
11.	Miss Risara Jaksuwan	Thailand
12.	Mr. Sumate Aumpawong	Thailand
13.	Miss Suwanee Sungkawasee	Thailand
14.	Miss Souwanit Nakasiri	Thailand

4th year students

1.	Pol. Lt. Kitiyaporn Chaichana	Thailand
2.	Miss Chuthaporn Toonboonchoo	Thailand
3.	Miss Bunguorn Sermsart	Thailand
4.	Mr. Pornchai Kirdsiri	Thailand
5.	Miss Yupa Nakkinkun	Thailand
6.	Miss Akanitt Jittmittraphap	Thailand
7.	Miss Umaporn Pinyosirikul	Thailand

5th year students

1.	Miss Napa Onvimala	Thailand
2.	Miss Siriwan Tribanyatkul	Thailand
3.	Dr. Tran Do Hung	Vietnam

PH.D. (TROP.MED.) 2001

1st year students

	Dr. Kim Jung Ryong	Korea
	Miss Verena Ilona Carrara	Switzerland
	Dr. Kittipong Kongsomboon	Thailand
	Ms. Chomrach Sirigul	Thailand
	Mr. Tavorn Maton	Thailand
	Mr. Narisorn Na-ngam	Thailand
	Mr. Boonlue Chimbanrai	Thailand
	Miss Piyatida Tangteerawatana	Thailand
	Mrs. Panita Gosi	Thailand
	Miss Pornlada Nuchnoi	Thailand
	Miss Pruksa Nawtaisong	Thailand
	Ms. Phuangphet Waree	Thailand
	Mrs. Malee Geounuppakul	Thailand
	Dr. Sirinuch Rajchaiboon	Thailand
	Dr. Somyos Deerasamee	Thailand
	Mrs. Sirimon Chaikate	Thailand
	Miss Sirima Kitvatanachai	Thailand
	Miss Sukhontha Siri	Thailand
	Miss Sunanta Chariyalertsak	Thailand
	Mr. Surapon Tangvarasittichai	Thailand

PH.D. (TROP.MED.) 2001

1st year students

	Dr. Harald Noedl	Austria
	Dr. Sompong Srisaenpang	Thailand
	Miss Pannapa Susomboon	Thailand
	Miss Doungrat Riyong	Thailand
	MissYuwachat Wudthithumksusporn	Thailand
	Miss Siriporn Chanchay	Thailand
	Miss Kanjana Suriyaprom	Thailand

2nd year students

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

3rd year students

1.	Mr. Hari Har Joshi	Nepal
2.	Mr. Rajendra Kumar B.C.	Nepal
3.	Mr. Preecha Liangpunsakul	Thailand
4.	Miss Duangkamol Viroonudomphol	Thailand
5.	Mr. Kamon Foihirun	Thailand
6.	Miss Chutima Kamkhaek	Thailand
7.	Miss Nantika Panutdaporn	Thailand
8.	Miss Naowarut Dechkum	Thailand
9.	Mrs. Prapa Nunthawarasilp	Thailand

PH.D. (TROP.MED.) 2001 (CONT)

3rd year students

10.	Mr. Piyanan Taweethavonsawat	Thailand
11.	Mr. Panas Thumkiratiwong	Thailand
12.	Miss Pornphan Diraphat	Thailand
13.	Miss Pattra Suntornthiticharoen	Thailand
14.	Mr. Yuttana Sudjaroen	Thailand
15.	Mrs. Ratree Leelawongtawon	Thailand
16.	Miss Waraphon Phimpraphi	Thailand
17.	Miss Walairut Tuntaprasart	Thailand
18.	Miss Suwalee Tantawiwat	Thailand
19.	Mrs. Oranan Prommano	Thailand
20.	Miss Nitaya Poosanthanasarn	Thailand
21.	Miss Panee Chaksangchaichot	Thailand
22.	Miss Sirichit Wongkamchai	Thailand
23.	Dr. Aree Kantachuvessiri	Thailand

4th year students

1.	Miss Kriyaporn Songmuaeng	Thailand
2.	Miss Kleebkaew Pitasawad	Thailand
3.	Mrs. Prapin Tharnpoophasiam	Thailand
4.	Miss Pungasem Paeporn	Thailand
5.	Miss Mallika Imwong	Thailand
6.	Mr. Mana Vatakul	Thailand
7.	Mrs. Yupadee Sirissinsuk	Thailand
8.	Miss Wanida Pongstaporn	Thailand
9.	Miss Sawanee Tengrungsun	Thailand
10.	Miss Nitchakarn Noranate	Thailand
11.	Miss Pittayaporn Moungnoi	Thailand
12.	Miss Wannaporn Ittiprasert	Thailand
13.	Miss Yuwadee Trongtokit	Thailand

5th year students

1.	Mrs Kamolrat Silamut	Thailand
2.	Mrs. Kanjana Hongtong	Thailand
3.	Mrs. Chantima Lohachit	Thailand
4.	Mr. Chamnarn Apiwathnasorn	Thailand
5.	Mr. Paron Dekumyoy	Thailand
6.	Mrs. Patcharin Saengjaruk	Thailand
7.	Miss Siriwan Chancharoen	Thailand
8.	Mr. Apichart Nontprasert	Thailand
9.	Miss Thitima Wongsaroj	Thailand

6th year student

1.	Mr. Ruangyuth Chaiworaporn	Thailand

THESIS TITLES

M.C.T.M. 2001

Department	Name	Title of Thesis	Adviser
Clinical Tropical Medicine	Dr. Raimund Helbok	Sequential level of TNF alpha and clinical manifestations in severe, non-severe falciparum and vivax malaria	Dr. Sombat Treeprasertsuk
Clinical Tropical Medicine	Dr. Birgit Woitsch	Early clinical and laboratory response parameters including vital staining as predictors of therapeutic outcome in falciparum malaria	Prof. Polrat Wilairatana
Clinical Tropical Medicine	Dr. M. Salim Uzzaman	Fever of undetermined origin in Chonburi Hospital	Prof. Sasithon Pukrittayakamee
Clinical Tropical Medicine	Dr. Abdinasir Ahmed Adem	Clinical manifestations and short-term outcome of prolonged cough in HIV/AIDS patients at Bamrasnaradura Hospital	Assoc. Prof. Punnee Pitisuttithum
Clinical Tropical Medicine	Dr. Lon Chan Thap	The prevalence and clinical findings of scrub typhus infection with septic shock in Maharaj Hospital at Nakhon Ratchasima Province	Assoc. Prof. Wichai Supanaranond
Clinical Tropical Medicine	Dr. Wolfgang Dent	Sequential level of TNF alpha and clinical manifestations in severe, non-severe falciparum and vivax malaria	Prof. Sornchai Looareesuwan
Clinical Tropical Medicine	Dr. Kenichiro Shimizu	Fever with elevated alkaline phosphatase in HIV/AIDS patients at Chonburi Regional Hospital, Thailand	Assist. Prof. Udomsak Silachamroon
Clinical Tropical Medicine	Dr. Piam Soukhanouvong	Fever of undetermined origin in Chonburi Hospital	Prof. Sasithon Pukrittayakamee
Clinical Tropical Medicine	Dr. Khamphanh Prabouasone	Clinical manifestations and identified causes from stool examination of diarrhea among HIV/AIDS patients	Dr. Wirach Maek-A-Nantawat
Clinical Tropical Medicine	Dr. Hlaing Min Swe	Clinical manifestations and short-term outcome of prolonged cough in HIV/AIDS patients at Bamrasnaradura Hospital	Assoc. Prof. Punnee Pitisuttithum
Clinical Tropical Medicine	Dr. Robert Brands	Early clinical and laboratory response parameters including vital staining as predictors of therapeutic outcome in falciparum malaria	Dr. Thanawat Tosukhowong
Clinical Tropical Medicine	Dr. Muneer Ahmed	Fever with elevated alkaline phosphatase in HIV/AIDS patients at Chonburi Regional Hospital, Thailand	Assoc. Prof. Punnee Pitisuttithum
Clinical Tropical Medicine	Dr. Do Hung Son	Clinical manifestations and identified causes from stool examination of diarrhea among HIV/AIDS patients	Assoc. Prof. Punnee Pitisuttithum
Clinical Tropical Medicine	Dr. Nguyen Van Ky	Amoebic liver abscess in Ratchaburi Regional Hospital	Assist. Prof. Udomsak Silachamroon

M.C.T.M. 2001 *(Continued)*

Department	Name	Title of Thesis	Adviser
Clinical Tropical Medicine	Dr. Duc Ai Quach	Clinical manifestations and identified causes from stool examination of diarrhea among HIV/AIDS patients	Assoc. Prof. Wichai Supanaranond
Clinical Tropical Medicine	Dr. Le Kien Ngai	Amoebic liver abscess in Ratchaburi Regional Hospital	Assoc. Prof. Yupaporn Wattanagoon
Clinical Tropical Medicine	Dr. Prakaykaew Tipmanee	The prevalence and clinical findings of scrub typhus infection with septic shock in Maharaj Hospital at Nakhon Ratchasima Province	Dr. Sombat Treeprasertsuk

M.C.T.M. (TROP.PED.) 2001

Department	Name	Title of Thesis	Adviser
Tropical Pediatrics	Dr. Ung Sophal	The clinical diagnosis of dengue haemorrhagic fever in Thai children	Assoc. Prof. Pornthep Chanthavanich

M.Sc. (TROP.MED.)

Department	Name	Title of Thesis	Adviser
Clinical Tropical Medicine	Dr. Sira Ubwa Mamboya	Factors associated with poor compliance in pulmonary tuberculosis	Assist. Prof. Udomsak Silachamroon
Clinical Tropical Medicine	Dr. Donald Edward Bryant	Clinical manifestation and outcome of cryptococcal meningitis and AIDS	Assoc. Prof. Punnee Pitisuttithum
Helminthology	Col.Lt. Kitiyaporn Chaichana	Diagnosis of human opisthorchiasis with cocktail and eluted *Bithynia siamensis goniomphalos* snail antigens by ELISA	Assoc. Prof. Jitra Waikagul
Helminthology	Lt. Tossapon Chaiyasith	Gnathostomosis 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
Helminthology	Ms. Charinthon Ngamamonpirat	Sequence variation in *Gnathostoma spinigerum* mitochondrial DNA by single-strand conformation polymorphism analysis	Assoc. Prof. Jitra Waikagul
Helminthology	Dr. Ta Van Thong	Epidemiology of clonorchiasis in the Red River Delta of Vietnam	Assoc. Prof. Ponganant Nontasut
Medical Entomology	Ms. Ladawan Vasinpiyamongcone	Morphological variations for dengue virus susceptibility and transovarian transmission of *Aedes aegypti*	Assoc. Prof. Chamnarn Apiwathnasorn
Microbiology and Immunology	Dr. Tran Do Hung	Epidemiology study of Beta hemolytic streptococcus group A in the pharynx of school children in Cantho Province, Vietnam	Assist. Prof. Usanee Suthisarnsuntorn
Microbiology and Immunology	Miss Bunguorn Sermsart	Diagnosis of trichinellosis and gnathostomiasis using specific antigens purified from monoclonal antibody-based affinity chromatography	Prof. Wanpen Chaicumpa

M.Sc. (TROP.MED.) *(Continued)*

Department	Name	Title of Thesis	Adviser
Microbiology and Immunology	Miss Yupa Nakkinkun	Platelet dysfunction in immune thrombocytopenic disorder	Prof. Wanpen Chaicumpa
Microbiology and Immunology	Miss Akanitt Jittmittraphap	Detection of dengue viral RNA in patient's sera by nucleic acid sequence-based amplification (NASBA) and polymerase chain reaction (PCR)	Assoc. Prof. Wipawee Usawattanakul
Microbiology and Immunology	Miss Kanjana Sonji	Evaluation of salmonellosis and shigellosis diagnostic test kits in Prachomklao Hospital, Petchburi Province	Prof. Wanpen Chaicumpa
Microbiology and Immunology	Miss Gaysorn Bunyaraksyotin	Detection of pathogenic *Leptospira* spp. in urine	Prof. Wanpen Chaicumpa
Microbiology and Immunology	Miss Junpen Suwimonteerabutr	Detection of *Leptospira interrogans* in specimens of cattle	Prof. Wanpen Chaicumpa
Microbiology and Immunology	Miss Piyaporn Suebtrakul	-	Assist. Prof. Varee Wongchotikul
Microbiology and Immunology	Miss Suwanee Sungkawasee	Detection of *Vibrio parahaemolyticus* by monoclonal-antibody based immunoassay	Prof. Wanpen Chaicumpa
Microbiology and Immunology	Miss Saichon Chimsumang	Immunoperoxidase test for serodiagnosis of scrub typhus: comparative study with indirect immuno-fluorescent assay	Assist. Prof. Varee Wongchotikul
Microbiology and Immunology	Mr. Nitat Sookrung	Detection of cockroach allergen(s) by an MAb-based immunological method	Prof. Wanpen Chaicumpa
Microbiology and Immunology	Miss Pitchapa Yungyuen	Naturally acquired antibodies to *P. falciparum* merozoite surface protein-3 (MSP-3) and glutamate-rich protein (GLURP) in malaria endemic population in Thailand	Prof. Srisin Khusmiith
Microbiology and Immunology	Miss Matukorn Na Ubol	Detection of *Listeria* spp. in foods	Prof. Wanpen Chaicumpa
Microbiology and Immunology	Miss Supranee Linthaworndee	Immunodiagnosis of angiostrongyliasis by affinity-purified specific antigen	Prof. Wanpen Chaicumpa
Microbiology and Immunology	Mr. Vongsavanh Pongsisay	Monoclonal antibody-based detection of *Campylobacter* spp. in clinical samples	Prof. Wanpen Chaicumpa
Microbiology and Immunology	Mr. Nirut Suwanna	The application of flow cytometry and newly developed hemolysing solution for the detection of malaria	Assist. Prof. Varee Wongchotikul
Social and Environmental Medicine	Mr. Pornchai Kirdsiri	HIV/AIDS counselling service at hospitals in Kanchanaburi Province	Assist. Prof. Jaranit Kaewkungwal
Social and Environmental Medicine	Miss Umaporn Pinyosirikul	Biomarker of aniline exposure in rubber manufacture	Assist. Prof. Ladda Tangbanluekal

M.Sc. (TROP.MED.) *(Continued)*

Department	Name	Title of Thesis	Adviser
Social and Environmental Medicine	Miss Risara Jaksuwan	-	Assoc. Prof. Kamolnetr Okanurak
Social and Environmental Medicine	Mr. Phitsanu Tulayakul	-	Assist. Prof. Waranya Wongwit
Tropical Hygiene	Miss Nahathai Chulakavat	Sputum conversion among newly adult positive-smear pulmonary tuberculosis patients	Assoc. Prof. Pratap Singhasivanon
Tropical Hygiene	Mr. Sumate Aumpawong	Epizootiology of Japanese Encephalitis virus and West Nile virus: zoonosis of medical importance	Assoc. Prof. Pratap Singhasivanon
Tropical Hygiene	Dr. Lek Dysoley	Role of GIS in malaria and DHF control programme in Cambodia	Assoc. Prof. Pratap Singhasivanon
Tropical Nutrition and Food Science	Ms. Napa Onvimala	Application of reverse transcriptase polymerase chain reaction for identification of rotavirus serotypes	Assoc. Prof. Supranee Changbumrung
Tropical Nutrition and Food Science	Ms. Siriwan Tribanyatkul	Serum leptin concentrations in obese subjects and healthy controls	Assoc. Prof. Rungsunn Tungtrongchitr
Tropical Nutrition and Food Science	Miss Chuthaporn Toonboonchoo	Vitamin B_{12} folic acid and hematological parameters in overweight and obese Thais	Assoc. Prof. Rungsunn Tungtrongchitr
Tropical Nutrition and Food Science	Miss Phimonsri Saengkar	Vitamin B_{12} and folate status in cervical cytologic abnormalities in Thai women	Assist. Prof. Karunee Kwanbunjan
Tropical Nutrition and Food Science	Miss Malida Soontornruengyot	Relationships between smoking habits, hematological pattern, B_{12} and folic acid in Thai smokers	Assoc. Prof. Rungsunn Tungtrongchitr
Tropical Nutrition and Food Science	Miss Tanyalak Khuntamoon	Seasonal variation of fresh, sterilized and pasteurized cow milk	Assoc. Prof. Supranee Changbumrung
Tropical Nutrition and Food Science	Miss Busaba Tuntithavorn	Homocysteine, folic acid and cobalamin in subjects with dyslipidemia, coronary heart disease and healthy control	Assoc. Prof. Supranee Changbumrung
Tropical Nutrition and Food Science	Miss Pensri Saelee	-	Assoc. Prof. Songsak Petmitr
Tropical Nutrition and Food Science	Mr. Sasipon Pumkumarn	Antioxidant enzymes and trace elements in subjects with dyslipidemia, coronary heart disease and healthy controls	Assoc. Prof. Supranee Changbumrung
Tropical Pathology	Miss Ratchanok Kumsiri	Role of *Plasmodium falciparum* specific IgE in severity of *falciparum* malaria	Assoc. Prof. Yaowapa Maneerat
Tropical Pathology	Miss Souwanit Nakasiri	Light and electron microscopic correlation of knob proteins and staging *in vitro: Plasmodium falciparum*	Assoc. Prof. Emsri Pongponrat

Ph.D. (TROP.MED.)

Department	Name	Title of Thesis	Adviser
Clinical Tropical Medicine	Mrs. Kamolrat Silamut	Stage specific morphology of *Plasmodium falciparum in vitro* and *in vivo*	Prof. Sasithon Pukrittayakamee
Clinical Tropical Medicine	Mr. Apichart Nontprasert	Neurotoxicity of antimalarial drugs in animal model	Prof. Sasithon Pukrittayakamee
Clinical Tropical Medicine	Miss Waraphon Phimpraphi	-	Prof. Sornchai Looareesuwan
Clinical Tropical Medicine	Dr. Harald Noedl	*Plasmodium falciparum* histidine rich protein II: evidence of antimalarial drug action	Prof. Sornchai Looareesuwan
Helminthology	Mr. Paron Dekumyoy	Evaluation of metacestode antigens in serodiagnosis of neurocysticercosis	Assoc. Prof. Jitra Waikagul
Helminthology	Miss Kriyaporn Songmuaeng	-	Assist. Prof. Chalit Komalamisra
Helminthology	Miss Tippayarat Yoonuan	Life cycle of *Spirometra* spp. in Thailand	Assoc. Prof. Jitra Waikagul
Medical Entomology	Mr. Chamnarn Apiwathnasorn	Entomological study of *Anopheles campestris*, in relation to malaria transmission in Thailand	Assist. Prof. Achara Asavanich
Medical Entomology	Miss Yuwadee Trongtokit	Promising insecticidal and repellent activity of Thai phytochemical plants for control of mosquito vectors of diseases	Assist. Prof. Narumol Komalamisra
Medical Entomology	Miss Pungasem Paeporn	Study on vector potential of *Anopheles letifer* for *Brugia malayi* transmission in Narathiwat Province	Assoc. Prof. Chamnarn Apiwathnasorn
Medical Entomology	Miss Walairut Tuntaprasart	Study on critical indices related to dengue transmission	Assoc. Prof. Somjai Leemingsawat
Microbiology and Immunology	Ms. Patcharin Saengjaruk	Development of immunodiagnostic method for acute leptospirosis	Prof. Wanpen Chaicumpa
Microbiology and Immunology	Ms. Thitima Wongsaroj	Development of an immunodiagnostic method for Opisthorchiasis viverrini	Prof. Wanpen Chaicumpa
Microbiology and Immunology	Ms. Wannaporn Ittiprasert	Towards specific diagnosis of *Schistosoma mekongi* infection	Prof. Wanpen Chaicumpa
Microbiology and Immunology	Miss Nitchakarn Noranate	-	Dr. Jintana Pattarapotikul
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
Microbiology and Immunology	Miss Chutima Khamkhaek	Analysis of sequence polymorphism of T-cell epitope regions, Th 2 R and Th 3 R, *Plasmodium falciparum* circumsporozoite proteins in Thai isolates	Prof. Srisin Khusmith

Ph.D. (TROP.MED.) *(Continued)*

Department	Name	Title of Thesis	Adviser
Microbiology and Immunology	Mr. Piyanan Taweethavonsawat	Virulence factors of intestinal round worms and the host immune response(s)	Prof. Wanpen Chaicumpa
Microbiology and Immunology	Miss Pornphan Diraphat	-	Prof. Wanpen Chaicumpa
Microbiology and Immunology	Mrs. Ratree Leelawongtawon	Role of liposome and bacterial CpG DNA in immune response to oral cholera vaccine	Prof. Wanpen Chaicumpa
Microbiology and Immunology	Mr. Preecha Liangpunsakul	The development of luminescence immunoprecipitation assay for differential diagnosis of dengue infection	Assoc. Prof. Wipawee Usawattanakul
Microbiology and Immunology	Miss Sirichit Wongkamchai	Development of an immunodiagnostic assay for Brugian filariasis	Prof. Wanpen Chaicumpa
Microbiology and Immunology	Miss Naowarut Dechkum	-	Dr. Jintana Pattarapotikul
Microbiology and Immunology	Miss Nantika Panutdaporn	Genotypic and phenotypic analysis of clinical and environmental enterohemorrhagic *Escherichia coli* to identify pathogenic clones and their pathogenic	Prof. Wanpen Chaicumpa
Microbiology and Immunology	Mr. Apichai Srijan	-	Assist. Prof. Usanee Suthisarnsuntorn
Microbiology and Immunology	Mr. Adisak Bhumiratana	-	Dr. Jintana Pattarapotikul
Microbiology and Immunology	Mr. Parin Suwannaprapaha	-	Assist. Prof. Varee Wongchotigul
Microbiology and Immunology	Miss Petchara Tussana	Serogrouping of *Leptospira* spp. by DNA technology	Dr. Thareerat Kalambaheti
Microbiology and Immunology	Miss Suwanna Chaorattanakawee	-	Dr. Jintana Pattarapotikul
Microbiology and Immunology	Miss Onguma Natalang	-	Dr. Jintana Pattarapotikul
Microbiology and Immunology	Mr. Rongdej Tungtrakanpoung	-	Assist. Prof. Pongrama Ramasoota
Protozoology	Mrs. Prapa Nunthawarasilp	Purification and characterization of DNA polymerase b from *Plasmodium falciparum*	Assoc. Prof. Porntip Petmitr
Protozoology	Miss Pattra Suntornthiticharoen	Purification and characterization of DNA helicase from *Plasmodium falciparum*	Assoc. Prof. Porntip Petmitr
Protozoology	Mr. Somphong Sithiprom	-	Assoc. Prof. Porntip Petmitr
Protozoology	Mr. Zulhainan bin Hamzah	-	Assoc. Prof. Porntip Petmitr

Ph.D. (TROP.MED.) *(Continued)*

Department	Name	Title of Thesis	Adviser
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. Viroj Kitikoon
Social and Environmental Medicine	Mrs. Chantima Lohachitsnail	Ecological studies of *Bithynia goniomphalos* a intermediate host of *Opisthorchis viverrini* in Northeast Thailand.	Assoc. Prof. Viroj Kitikoon
Social and Environmental Medicine	Mrs. Prapin Tharnpoophasiam	Biomonitoring of occupational benzene exposure	Prof. Dwip Kitiyaporn
Social and Environmental Medicine	Mrs. Kleebkaew Pitasawad	Environmental health model towards pesticide utilization in sustainable agriculture in Bang Pae District, Ratchaburi Province	Assoc. Prof. Piyarat Butraporn
Social and Environmental Medicine	Miss Yupadee Sirisinsuk	Access and patterns of health services utilization among insured persons under the Social Security Act, 1990	Assoc. Prof. Wijitr Fungladda
Social and Environmental Medicine	Mr. Kamon Foihirun	-	Assist. Prof. Waranya Wongwit
Social and Environmental Medicine	Miss Suwalee Tantawiwat	-	Assist. Prof. Ladda Tangbanluekal
Social and Environmental Medicine	Dr. Aree Kantachuvessiri	-	Assoc. Prof. Kamolnetr Okanurak
Social and Environmental Medicine	Miss Nitaya Poosanthanasarn	-	Assoc. Prof. Wijitr Fungladda
Social and Environmental Medicine	Mr. Tawadchai Suppadit	Modification and development of broiler litter as a source of protein in mixed feed for fattening cattle to reduce environmental pollution and improve farmer's income	Assoc. Prof. Viroj Kitikoon
Social and Environmental Medicine	Miss Nantawan Kaewpoonsri	-	Assoc. Prof. Kamolnetr Okanurak
Social and Environmental Medicine	Mr. Songpol Tornee	-	Assoc. Prof. Kamolnetr Okanurak
Social and Environmental Medicine	Mrs. Pimsurang Taechaboonsermsak	-	Assoc. Prof. Kamolnetr Okanurak

Ph.D. (TROP.MED.) *(Continued)*

Department	Name	Title of Thesis	Adviser
Social and Environmental Medicine	Miss Anamai Thiravirojana	-	Assist. Prof. Ladda Tangbanluekal
Social and Environmental Medicine	Mrs. Sontaree Akawat	-	Assist. Prof. Ladda Tangbanluekal
Tropical Hygiene	Ms. Siriwan Chancharoen	-	Assoc. Prof. Pratap Singhasivanon
Tropical Hygiene	Miss Sawanee Tengrungsun	Survival analysis of Thai adult AIDS patients in the tertiary care hospital, Thailand	Assoc. Prof. Pratap Singhasivanon
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 Hygiene	Mr. Somchai Jadsri	-	Assoc. Prof. Pratap Singhasivanon
Tropical Hygiene	Miss Supawadee Konchom	Development of early detection system of system of malaria epidemics in Thailand	Assoc. Prof. Pratap Singhasivanon
Tropical Hygiene	Dr. M. Gias Uddin Ahsan	Gender differences in tuberculosis case detection, treatment seeking behavior and treatment compliance in rural Bangladesh	Assoc. Prof. Pratap Singhasivanon
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
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
Tropical Nutrition and Food Science	Miss Wanida Pongstaporn	Identification of genetic alterations in ovarial cancer by arbitrarily primed polymerase chain reaction and gene cloning	Assoc. Prof. Songsak Petmitr
Tropical Nutrition and Food Science	Miss Pittayaporn Moungnoi	-	Assoc. Prof. Supranee Changbumrung
Tropical Nutrition and Food Science	Miss Duangkamol Viroonudomphol	Levels of antioxidants for health determination in overweight and obese Thais	Assoc. Prof. Rungsunn Tungtrongchitr
Tropical Nutrition and Food Science	Mr. Panas Thumkiratiwong	The synergistic effects of riboflavin deficiency to trichnellosis in Wistar rat model	Assoc. Prof. Rungsunn Tungtrongchitr
Tropical Nutrition and Food Science	Mr. Yuttana Sudjaroen	-	Assoc. Prof. Supranee Changbumrung

Ph.D. (TROP.MED.) *(Continued)*

Department	Name	Title of Thesis	Adviser
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
Tropical Nutrition and Food Science	Miss Orntipa Sethabutr	-	Assoc. Prof. Songsak Petmitr
Tropical Nutrition and 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
Tropical Pathology	Mrs. Oranan Prommano	-	Assoc. Prof. Emsri Pongponrat
Tropical Pathology	Miss Thanida Tangwanicharoen	-	Assoc. Prof. Parnpen Viriyavejakul
Tropical Radioisotopes	Miss Waraporn Aumarm	-	Assist. Prof. Petcharindr Yamarat
Tropical Radioisotopes	Mr. Mana Vatakul	-	Prof. Polrat Walairatana

Ph.D. (CLIN.TROP.MED.)

Department	Name	Title of Thesis	Adviser
Clinical Tropical Medicine	Dr. Yoshinari Moriyama	The clinical relevances of cytokines on severe malaria patients and effects of prostagladin derivatives	Prof. Polrat Walairatana
Clinical Tropical Medicine	Dr. Hla Yin Mint	-	Prof. Sornchai Looareesuwan

The Hospital for Tropical Diseases

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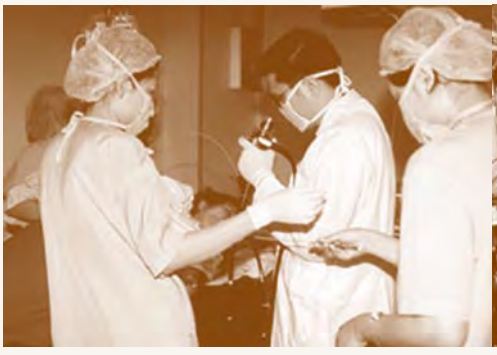
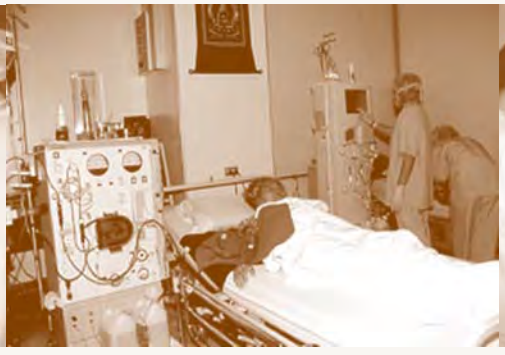
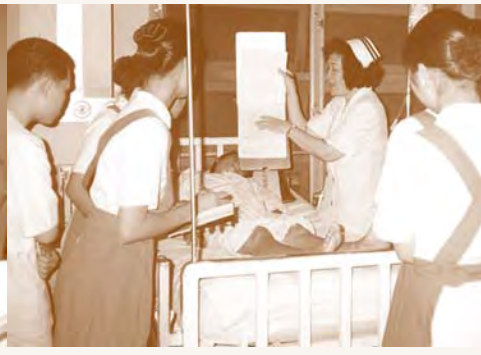
ext. 1624, 1625

MEDICAL CARE SERVICES

Medical care service is one of the main functions of the Faculty of Tropical Medicine. The Hospital for Tropical Diseases, a specialized hospital, provides medical care services for patients suffering from tropical diseases, as well as internal medicine. At present, the Hospital for Tropical Diseases can accommodate up to 250 in-patients. There are services for out-patients, 4 male and female general wards, a children's ward, 2 special care wards, a geriatric ward, an intensive care unit, an intensive care unit for tropical diseases, a gastroenterology division, a dermatology division, and a sexually-transmitted diseases division.

Out-Patient Department services are as follows:

- General medicine: daily except public holidays, 8.00-16.00 hr.
- Malaria clinic: 24 hours daily.
- Electrical stimulation health chair: daily from 6.30-16.00 hr.
- Health examination for emigrant workers: daily except public holidays, 8.00-16.00 hr.
- Laboratory diagnosis for helminthiasis: daily except public holidays, 8.00-10.00 hr.
- Consultation in traveler medicine.
- Center for diagnosis and detection of various specimens in cooperation with other departments and units of the Faculty.
- Medical care services to all Mahidol University students, staff and their families.
- Electrocardiography (ECG).
- Spirometry.
- Audiogram.
- Visual acuity test and color blindness test.

Organization and Administration of The Hospital for Tropical Diseases

Director
Prof. Polrat Wilairatana

Deputy Director
Dr.
Sombat Treeprasertsuk

Deputy Director
Assoc. Prof.
Srivicha Krudsood

Deputy Director
Assoc. Prof.
Parnpen Viriyavejakul

Deputy Director
Assist. Prof.
Udomsak Silachamroon

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.
- Traditional Thai massage: everyday, 8.00-20.00 hr.
- Acupuncture: Monday, Wednesday, 9.00-12.00 hr.

Nursing Unit

Chief of Nursing Unit
Mrs. Ladawun Supeeranuntha

Deputy Chief for Administration / Supervisor
Mrs. Wanna Plooksawasadi

Deputy Chief for Education / Supervisor
Mrs. Yupin Rattanapong

Deputy Chief for Service / Supervisor
Miss Kobsiri Chahermrut

Head of Ward 4
Mrs. Kingkan A. Indravijit

Head of Ward 9
Mrs. Vipa Prariyanupharb

Head of Ward 2
Miss Arun Chantra

Head of Ward 5
Mrs. Kingkaew Nakharutai

Head of Ward 10
Mrs. Monthira Ditta-in

Head of Ward 3
Miss Sunee Chittamas

Head of Ward 11
Mrs. Suwatana Siripiphat

Head of Ward ICU
Miss Suparp Vannaphan

Head of Ward 7
Miss Aurathai Thanavibul

Head of Ward OPD
Mrs. Pinkeaw Nipattasopone

Director School of Nurse Assistants
Mrs. Rachanida Glanarongran

Head of Ward 8
Mrs. Siripan Srivilairit

Special Laboratory Services

Disease / Infection/ Agent	Serological test used	Specimen required	Time required (days)	Cost per test (Baht)	Place where specimen should be sent
Strongyloidosis	Immunoblot	Serum 1-2 ml.	1	200	Dept. Helminthology via OPD
Toxocariasis	Immunoblot, ELISA	Serum 1-2 ml.	1	200	Dept. Helminthology via OPD
Angiostrongyliasis	Immunoblot	Serum 1-2 ml.	1	200	Dept. Helminthology via OPD
Cysticercosis	Immunoblot	Serum 1-2 ml.	1	200	Dept. Helminthology via OPD
Filariasis	ICT	Serum 1-2 ml.	1	200	Dept. Helminthology via OPD
Gnathostomiasis	Immunoblot	Serum 1-2 ml.	1	200	Dept. Helminthology via OPD
Paragonimiasis	Immunoblot	Serum 1-2 ml.	1	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	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 B_{12}	Dilution technique (57 C^{O})	Serum 2 ml.	7	450	Dept. Tropical Radioisotopes *
Serum folate	Microbiological assay	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 B_1	Enzymatic method	Heparinized blood 1-2 ml	7	400	Dept. Tropical Nutrition and Food Science *
Red blood cell Vitamin B_2	Enzymatic method	Heparinized blood 1-2 ml	7	400	Dept. Tropical Nutrition and Food Science *
Red blood cell Vitamin B_6	Enzymatic method	Heparinized blood 1-2 ml	7	400	Dept. Tropical Nutrition and Food Science *

* Specimens may be sent directly to the Department

Disease / Infection/ Agent	Serological test used	Specimen required	Time required (days)	Cost per test (Baht)	Place where specimen should be sent
Pap smear-cervical, vaginal smear	Cytology	vaginal smear, cervical smear	1	150 / 300	Dept. Trop. Pathology via OPD
Fluids	Cytology	Pleural effusion, Ascites, Urine	1	350 / 700	Dept. Trop. Pathology via OPD
Small pieces of biopsy	Histopathology	Small pieces of biopsy	3	300 / 600	Dept. Trop. Pathology via OPD
Organ	Histopathology	Organ	3	400 / 800	Dept. Trop. Pathology via OPD
Small pieces of biopsy	Frozen section	Small pieces of biopsy	3	300 / 600	Dept. Trop. Pathology via OPD
Organ	Frozen section	Organ	3	900 / 1,800	Dept. Trop. Pathology via OPD
Special stain		-	1	100	Dept. Trop. 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
Blood	Aerobic bacteria	Blood 5 ml. in T.S.B.	7	160	Div. of Bacteria via OPD
Urine	1) Culture 2) Gram stain	Urine 1	3	80	Div. of Bacteria via OPD
Stool	1) Culture 2) Gram stain	Stool 1	3-5	160	Div. of Bacteria via OPD
Sputum	1) Culture 2) Gram stain	Sputum 1	3-5	80	Div. of Bacteria via OPD
C.S.F.	1) Culture 2) Gram stain	C.S.F. 1	3	80	Div. of Bacteria via OPD
Wound, Fluid	1) Culture 2) Gram stain	Wound, Fluid 1	3	80	Div. of Bacteria via OPD
Fungus	KOH	All specimens	1	50	Div. of Bacteria via OPD
VDRL	Agglutination	Clot blood 3 ml	2	60	Div. of Serology via OPD
Widal	Agglutination	Clot blood 5 ml	4	100	Div. of Serology via OPD
Weil Felix	Agglutination	Clot blood 5 ml	4	120	Div. of Serology via OPD

Disease / Infection/ Agent	Serological test used	Specimen required	Time required (days)	Cost per test (Baht)	Place where specimen should be sent
Scrub typhus	Indirect immunofluorescent	Clot blood 5 ml		120	Div. of Serology via OPD
E. histolytica	Immunodiffusion	Clot blood 3 ml	7	150	Div. of Serology via OPD
Alpha-fetoprotein	Immunodiffusion	Clot blood 3 ml	7	200	Div. of Serology via OPD
HBs Ag	Enzyme immunoassay	Clot blood 5 ml	7	120	Div. of Serology via OPD
HBs Ab	Enzyme immunoassay	Clot blood 5 ml	7	120	Div. of Serology via OPD
HBc Ab	Enzyme immunoassay	Clot blood 5 ml	7	200	Div. of Serology via OPD
Anti HIV	Agglutination Enzyme immunoassay	Clot blood 3 ml	7	250	Div. of Serology via OPD
Anti HIV quick test	Enzyme immunoassay	Clot blood 3 ml	2 hr.	250	Div. of Serology via OPD
Leptospirosis	Microagglutination	Clot blood 5 ml	7	100	Leptospirosis Unit via OPD

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

Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

Director
Prof. Sornchai Looareesuwan

Deputy Director
Assoc. Prof. Suvanee Supavej

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 RESULT AREAS, as follows:

KRA1. Enhanced Programme Quality and Relevance

1.1 Post-graduate regular courses. Five regular post-graduate, courses at the international level are offered by TROPMED/Thailand with a total of 229 students from 18 countries. There were 66 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 13 medical students from 6 countries;

2) Certificate in Nurse Assistant with 172 students.

In the FY 2001/2002, TROPMED/Thailand had 414 students from 21 countries; among these, 291 were new students enrolments in 7 courses offered by TROPMED/Thailand. Ninety-six percent of these students were fee-paying attendants and 251 (60.6%) 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
Postgraduate				
DTM&H (6-month course)	32	16 (Austria, Bangladesh, Cambodia, Ethiopia, Germany, Japan, Lao PDR, Indonesia, Myanmar, Pakistan, Nigeria, Philippines, Thailand, Sweden, Vietnam, USA)	27 (84%)	32 (100%)
MCTM (1-year course)	15	10 (Bangladesh, Cambodia, Indonesia, Lao PDR, Myanmar, Sri Lanka Pakistan, Philippines, Thailand, Vietnam)	14 (93%)	15 (100%)
MSc (TM)				
1st year	35	3 (Japan, Nepal, Thailand)	31 (86%)	
2nd year	27	5 (Lao PDR, Malaysia, Tanzania, USA, Vietnam)		14 (26.9%)
3rd year	15	2 (Cambodia, Thailand)		
4th year and above	10	2 (Thailand, Vietnam)		
PhD (TM)	23	2 (Australia, Korea)	23 (100%)	
1st year	23	2 (Bangladesh, Thailand)		5 (7.1%)
2nd year	23	1 (Nepal)		
3rd year	24	1 (Thailand)		
PhD (CTM)				
1st year	1	1 (Myanmar)	1	0
4th year	1	1 (Japan)	0	0
Subtotal	**229**		**96 (90%)**	**66 (28.8%)**
Undergraduate				
Elective Programme in Tropical Medicine	13	6 (Austria, Australia, Canada, Germany, Poland, USA)	13 (100%)	13 (100%)
Certificate in Nurse Assistant	172	1 (Thailand)	172 (100%)	172 (100%)
Grand Total	**414**	**21**	**281 (96%)**	**251 (60.6%)**

1.3 Training Courses/Workshop/Meetings. One training course at the regional level, one at the international level, 1 international workshop and 2 international meetings were convened during FY 2000/2001, with the total number of 1,631 participants from 42 countries.

KRA2 Increased Access to Market

2.1 Active Marketing. Seven TV series and 5 news spots were broadcast, 14 news items were published in local newspapers.

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	2	1 weeks
2. Malaria Control in Cambodia, Laos and Vietnam	Malaria control	EC	2	2 weeks
3. Malaria Control	Data analysis	EC	2	10 days
4. Scientific and Ethical Review Group	Ethical review	WHO	1	3 days
5. Planning Workshop	Malaria control	EC	1	6 days
6. Roll Back Malaria	Malaria control	WHO	1	5 days

3.2 Visitors. One hundred and fifty-seven visitors from 18 countries visited TROPMED/Thailand during FY 2001/2002.

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 (million Baht)	% Increase / Decrease
1. Government budget	186.54	- 31.5
2. Revenue from services and other activities	74.68	+ 49.51
3. Research funds from other organizations	71.02	+ 1.17

KRA5. Enhanced Quality of SEAMEO Management

TROPMED/Thailand has a total of 738 staff comprising 80 academic staff, 141 academic assistants and research staff, 119 administrative personnel and 398 employees. The qualifications and academic posts held by these 90 academic staff are shown in Table 4.

Table 4: Qualifications of 80 academic staff.

Qualification	No	%
PhD	57	71.0
Master	22	28.0
Bachelor	1	1.0
Total	**80**	**100.0**

The academic posts of the 80 academic staff compared with those of Mahidol University are shown in Table 5.

Table 5: Academic posts of 89 staff of TROPMED/Thailand.

	Academic Posts			
	held by FTM staff		held by Mahidol University staff	
	No	(%)	No	(%)
Professor	7	(8.75%)	135	(4.8%)
Associate Professor	32	(40.0%)	753	(26.9%)
Assistant Professor	3	(38.8%)	871	(31.1%)
Lecturer	10	(12.5%)	1,044	(37.2%)
Total	**80**	**(100.0%)**	**2,803**	**(100.0%)**

5.1 Number of staff promoted or obtaining a higher qualification

Table 6: Number of staff promoted.

Academic rank	:	Professor	=	0
		Associate Professor	=	6
		Assistant Professor	=	8
Career rank	:	Higher rank	=	70
Higher qualification	:	Higher degree	=	15
Total			**=**	**99**

5.2 Number of research projects and publications. TROPMED/Thailand staff undertook 146 research projects with total research grants of 71.2 million Baht, and published research papers.

	New project	On-going	Accomplished
No. of research projects	39 (27%)	69 (47%)	38 (26%)
No. of published papers	= 126		

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

Thirty-one staff (4.3%) took study leave for higher education. Twenty-four (3.3%) attended training courses in Thailand and abroad. One hundred and thirty-three staff (32.6%) attended meetings, seminars, workshops. One staff member 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	19 (2.6%)	2. (0.3%)	21 (2.9%)
Attending training courses	71 (9.6%)	10 (1.4%)	8 (11.0%)
Attending meetings/ seminars/workshops			
No of staff	293 (39.7%)	29 (3.9 %)	327 (43.6%)
No of attendances	686	50	736

5.4 Special talks/lectures

To develop and/or improve the knowledge of staff, 10 special talks/lectures on various topics, including information technology, were organized for 367 attendants.

5.5 Patients treated for tropical diseases

The Hospital for Tropical Diseases offers medical care services to patients suffering from tropical and other diseases. The Hospital has 250 beds with 21 medical doctors, 93 nurses and 82 nurse assistants. The total number of outpatients treated was 34,286, and the number of patients admitted to the Hospital was 2,749. 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 was 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 from the Hospital for Tropical Diseases were given as 2001 Distinguished Staff Awards of the Faculty of Tropical Medicine.

2) National Awards:

Recipients	Awards
1. Prof. Sornchai Looareesuwan	1. The Most Cited Author of the Years 1990-1994 in the field of Bioscience and Medicine from the Thailand Research Fund
2. Prof. Polrat Wilairatana	1. The Consolation prize of the Outstanding Dissertation Award from the National Research Council of Thailand

The Asian Centre of International Parasite Control (ACIPAC)

Office Telephone: (662) 246-9000-12 ext. 1338, 1339
Fax: (662) 643-5616
E-mail: tmacipac@diamond.mahidol.ac.th

Project Manager
Prof. Sornchai Looareesuwan

Assistant Project Manager
Assoc. Prof. Jitra Waikagul

Chief Advisor
Prof. Somei Kojima

Dr. Nobuhiko Nagai
Expert on Parasite Control

Dr. Noriaki Tomono
Expert on School Health

Mr. Mitsuhiko Iwashita
JICA Coordinator

Ms. Wanida Onwan
Secretary

Ms. Ratanawadee Nanlar
Assistant Secretary

ACTIVITIES BETWEEN OCTOBER 1, 2000 TO SEPTEMBER 30, 2001

During the Thai Fiscal Year 2000, the main activities within ACIPAC were concerned with human resource development to establish networking between ACIPAC and partner countries in the Greater Mekong Sub-region - Cambodia, Lao PDR, Myanmar and Vietnam; creating understanding of the Hashimoto Initiative on Global Parasite Control Programme; and preparing the curriculum and materials for the training course on parasite control.

1) Introductory Visit

As introduction of the project during October and November 2000, ACIPAC members visited the Ministry of Health, Ministry of Foreign Affairs and Ministry of Education of the partner countries. Objectives and the scheme of ACIPAC were explained to all authorities concerned. Focal institutions and contact persons in each country were identified. Information on the current situations of parasite control programmes and school health curricula in primary schools were studied.

2) Curriculum Development Workshop

On December 19-20, 2000 the workshop on the curriculum of the training course on the school health approach to malaria and soil-transmitted helminthiases control for programme managers was held in the Chalermprakiet Building, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand. The 12-week tentative schedule of the training course, which included programme management, parasitology (emphasizing malaria and soil-transmitted helminths), epidemiology, primary health care, health education, project formulation and field practices, was discussed in detail. The former plan was re-scheduled, and the time allocations for management and health education sessions were increased. The new curriculum was adopted for the training course to be conducted in September-November 2001.

3). Filarial Workshop

On February 5-9, 2001, SEAMEO TROPMED, in collaboration with the WHO, organized a workshop on Mapping of Lymphatic Filariasis and Development of LF Information Network for the Mekong-plus countries. ACIPAC supported five participants from the ACIPAC partner countries to attend the workshop.

4). ACIPAC International Symposium

ACIPAC organized a symposium on the theme "Save schoolchildren from parasites" on March 19-20, 2001 at the Century Park Hotel, Bangkok, Thailand. Speakers were invited from WHO-Roll Back Malaria, Department of Control, Prevention and Eradication and

WHO Western Pacific Regional Office, Multilateral Initiative on Malaria (MIM), NIH-USA, Centers for Disease Control and Prevention, USA, School of Medicine, London, EC-RMCP, UNICEF, Chinese Academy of Preventive Medicine; Shanghai, Japanese Advisory Committee for Centers of International Parasite Control (CIPACs), representatives from each 'CIPAC' centre and representatives from partner countries. The topics of Global Malaria and Soil- transmitted Helminthiasis Control and the role of the Hashimoto Initiative and School Health Scheme in the Greater Mekong Subregion were discussed. Followed the symposium, some participants visited Rajanagarindra Tropical Disease International Centre, the field training and research station of the Faculty of Tropical Medicine in Ratchaburi Province.

5). Project Site Visit

During May 29-July 6, 2001, ACIPAC members visited partner countries to explain about the ACIPAC International Training Course and interview nominees, to discuss the plan for a small scale pilot project for school-based malaria and soil-transmitted helminth control, to observe pilot project sites and to discuss and identify the responsible institution for information networking for parasite control. School-based parasite control project managers of each country were identified, the project area was selected and a team of five participants of the international training course was formed. The institution responsible for information networking for parasite control in each country was also nominated by the Ministry of Health.

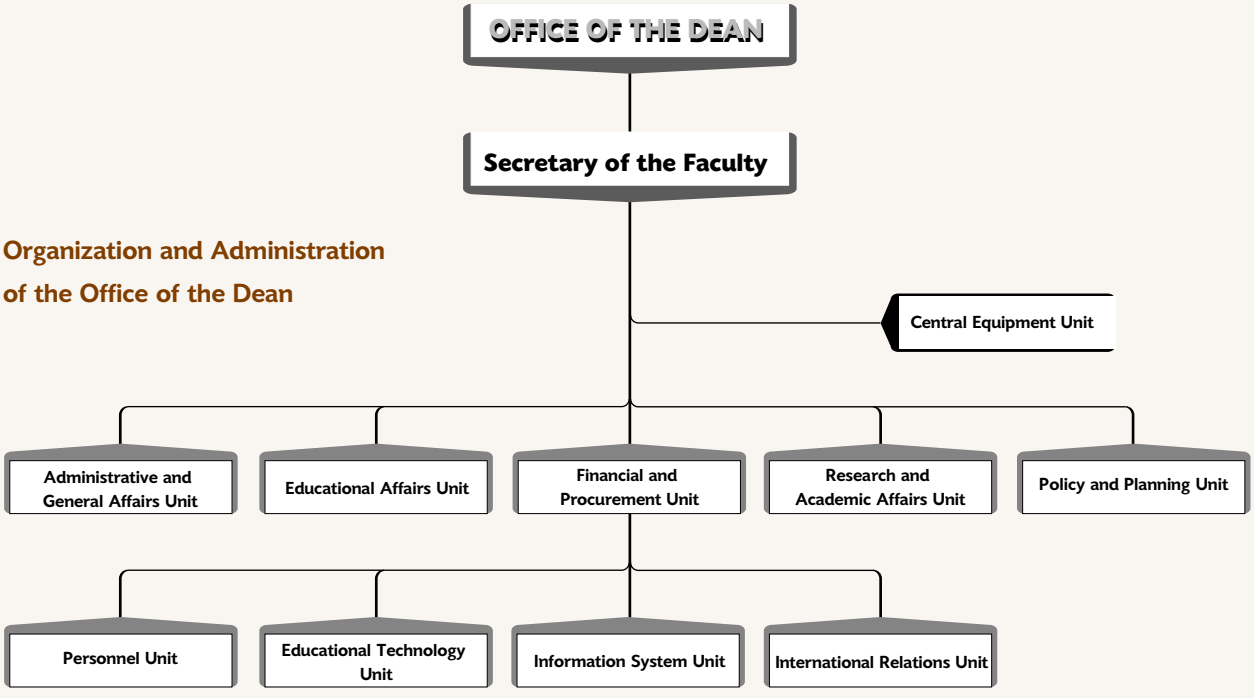
6). International Training Course

ACIPAC organized the international training course on School-based Malaria and Soil-transmitted Helminthiases Control for Programme Managers held between September 17-December 7, 2001 at the Faculty of Tropical Medicine. There were 26 participants; five trainees from each country Cambodia, Lao PDR, Myanmar, Thailand and Vietnam and one trainee from Kenya. Two observers from UNICEF Laos and Thailand Offices also participated for two weeks. The Course Opening Ceremony was attended by HE Mr. Ryutaro Hashimoto, Mr. Sutham Saengprathum, Minister for University Affairs and Mrs. Sudarat Keyuraphan, Minister for Public Health, Thailand. They also attended the Opening Ceremony for the Hashimoto Initiative Training Centre on the fourth floor of the Chamlong Harinasuta Building of the Faculty of Tropical Medicine.

Office of the Dean

Tel. 0-2246-9000 ext. 1322 Fax. 0-2246-8340

Organization and Administration of the Office of the Dean



Personnel Management

There are 738 staff, comprised of 340 government service staff, 26 University employees, 270 permanent employees and 93 temporary staff. In the fiscal year 2001, there were 116 new staff, 93 who transferred and resigned, and 16 who retired or retired early.

Budget Management

- Total expenses: 191.2 million Baht
- Operation statements (Operation budget): 169.6 million Baht
- Investment budget: 21.6 million Baht
- Government budget support: 137 million Baht, or 72%
- Expenditure of Faculty's revenue: 53.9 million Baht or 28%
- In the Fiscal Year 2001, the Faculty's revenue was 74.6 million Baht, from hospital services, educational fees and other academic service fees.

Building and Area Management

- In the year 2001, the Faculty opened the new 12-floor "Chalerm Phra Kiat" Building with an area of 24,000 m^2.

The area is divided into a laboratory section and Tropmed accommodation for students, doctors, nurses, and assistant nurses. In addition, there are patient wards and a car park. This new building has further developed the teaching, research and service facilities of the Faculty.

- In March 2001, the Faculty opened the Malaria Research Station, "Rajanagarindra Tropical Diseases International Centre" at Suan Phung, Ratchaburi Province.

Secretary of the Faculty
Mrs. Vorapan Singhsilarak
B.A.

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:

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

Administrative and General Affairs Unit

Tel. 0-2246-9000 ext. 1302, 1304, 1801

The Unit is divided into 4 subunits, as follows:

Documentation Subunit

Aree Masngammuang
B.A. (Political Science)
General Affairs Officer

Supavadee Yaowasang
B.A. (Lib.Info.Sc.)
Office Clerk

Maninthorn Phanumaphorn
M.B.A.
General Affairs Officer

Pranee Kraisorn
Office Clerk

Nathaneeporn Panampai
B.A. (General Management)
General Affairs Officer

Patra Kreekul
B.A. (General Management)
General Affairs Officer

Chanpen Ronsuk
Operator

Yupa Jarernrit
Data Input Clerk

Prachum Bauprasert
Office Clerk

Sanchai Meeprom
Office Clerk

Area and Transportation Subunit

Savek Chomming
B.En.
Civil Engineer

Thep Ngamnetr
B.Arch.
Architect

Prachuab Kitsupee
Steel Worker

Somjai Promduang
Security Guard

Sombat Khamthanee
Gardener

Kasem Kaewbangkerd
Driver

Public Relations Subunit

Thitika Teeranetr
B.A. (Communication Arts)
Public Relations Officer

Wandee Srasalee
B.A. (General Management)
General Affairs Officer

Varee Viriyarat
B.A. (General Management)
General Affairs Officer

Maintenance and Repairs Subunit

Nophadol Siriacharanond
B. En.
Electrical Engineer

Chaiyaporn Phoopan
Voc. Cert. (Electric)
Electrician

Panumas Tunritsa
Voc. Cert. (Electronics)

Tumrongsak Wimdsut

Educational Affairs Unit

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

Head
Wanpen Puttitanun
B.A. (General Management)

Benjarat Prompakdee
B.Ed., M.Ed.
Educational Affairs Officer

Somporn Ngamsirisomsakul
B.A.
Educational Affairs Officer

Chutamas Koomrungruang
B.Sc. (Biology), M.Sc.(Trop.Med.)
Scientist

Wannaporn Ittiprasert
B.Sc. (Med. Tech.)
Medical Scientist

Chiraporn Praevanit
Voc.Cert.Commercial
General Affairs Officer

Chutarat Pradabprachr
B.Ed.
General Affairs Officer

Aree Buaprae
Voc. Cert. Commercial
General Affairs Officer

Rangson Praevanit
Cert. Commercial
Office Clerk

Nutjanat Taiwrob
Cert. Commercial
Office Clerk

Nuljun Pochana
Cert. Commercial
Office Clerk

Anurat Kalasen
Cert. Commercial
Office Clerk

Srisuchart Monchonmu
Cert. Commercial
Laboratory Staff

Mr. Paul R. Adams
B.A., Grad.Dip.Lib., M.Mgt., AALIA, AFAIM, AAMI
Specialist

Financial and Procurement Unit

Tel. 0-2246-9000 ext. 1204, 1205, 1305, 1325

The Unit is divided into 2 subunits, as follows:

Head
Somkid Nima
B.B.A. (General Management), LL.B.

Financial and Accounting Subunit

Ketsinee Nima
B.B.A. (Accounting)
Accountant Officer

Tham Chermkhuntod
B.A. (General Management),
B.B.A. (Accounting)
Accountant Officer

Chuenboon Aimpraneet
B.A. (General Management)
Accountant Officer

Jeeranat Kumseranee
B.A. (General Management)
Accountant Staff

Arayaporn Sawangrungrueng
B.A.
Accountant Officer

Prapaporn Krusmas
Accountant Staff

Porntiva Sen-im
B.A.
Office Clerk

Vantana Theprod
Voc. Cert.
Accountant Staff

Chayan Muanom
Cert. In Commercial
Accountant Staff

Nopadol Preechasunthorn
Voc. Cert.
Accountant Staff

Procurement Subunit

Prapaiporn Tiacharoen
B.B.A. (General Management)
Procurement Officer

Montri Noochan
B.B.A. (Econ.)
Procurement Officer

Kanjanaporn Sukasem
B.B.A.
Procurement Staff

Thapana Khattiwong
B.B.A.
Procurement Officer

Inthira Pansuebchuea
B.B.A.
Procurement Officer

Rangsi Prathumrat
Cert. in Commerce
Procurement Staff

Tuenjai Ketanond
Voc. Cert.
Procurement Staff

Oranat Puchaka
Office Clerk

Mongkol Bunchakorn
Typist

Wattana Prechasunthorn
Photographer

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

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

Thanormsri Ketsuk
B.B.A. (Money & Banking)
Policy and Planning Officer

Jitra Suriya
B.B.A. (Money & Banking)
General Affairs Officer

Pramote Ketsuk
B.Sc. (Computer Science)
Office Clerk

Personnel Unit

Tel. 0-2246 9000 ext. 1324, 1330

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

Phongsri Konthong
B.A. (General Management)
Personnel Officer

Nathaporn Kotchasri
B.Ed.
Personnel Officer

Surang Wattanakamolgul
Cert.Marketing
Personnel Staff

Supaporn Chotivatin
Cert. Computer
Personnel Staff

Educational 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

Head

Sompoch Thanuvathana

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

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

Prastha Kidkian
Bachelor of Fine Art (Painting)
Illustration Staff

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

Vatcharin Nagpong
Illustration Officer

Kannika Petporee
B.A. (General Management)
Office Clerk

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

Tel. 0-2246 -9000 ext. 1521, 1526

Head
Duangjai Sahassananda
B.Sc. (Med.Tech.), M.Sc. (Information Technology in Business)

Krissada Boonruang
B.Sc. (Computer Science)
Computer Technician

Wimol Chotithammapiwat
B.Sc. (Computer Science)
System Administrator

Wuttichai Kitpremthaworn
B.Sc. (Computer Science)
Computer Technician

Shanon Hankiatkla
B.Sc. (Computer Science)
Programmer

Pongnatee Kingsawat
Dip. in Voc. Ed. (Electronic)
Electronic Associate

Anakanun Hinjiranan
B.A. (Visual Communication Design)
Illustration Officer

Jetsadaporn Chantachorn
B.A. (General Management)
Office Clerk

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. Lecture

Special lecture in information technology 4 times

II. IT visits

IT visits to other institutes 4 times

III. Teaching

- Computer software training 7 times for 141 faculty staff (20 terminals each time).
- Teaching computer solfware for faculty students

IV. General services

The Unit provide services for the Faculty such as computer room, UTP installations, consulting/program installation/virus scan, computer upgrades, slide making, laser print, color print, computer scan image and OCR.

V. Database projects

The Unit has 2 projects in information technology:

1. HEED-Net project

This project is a collaboration with the Ministry of Public Health; Faculty of Economics, Chulalongkorn University and Faculty of Tropical Medicine, Mahidol University to make health and economic information in GIS form.

2. SEAMEO TROPMED (Virtual Library, Homepage).

VI. Network and Application Development

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

- Network for 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; 0-02643-5614
Fax: 0-2246-9013
E-mail: tmknt@mahidol.ac.th

Head
Keeratiya Nontabutra
B.A.

Wanida Onwan
B.A. (Thai & Eng)
General Affairs Officer

Sethavudh Kaewviset
B.A.
General Affairs Officer

Ratanawadee Nanlar
B.A.
General Affairs Officer

Narumol Krudson
Office Clerk

Central Equipment Unit

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

Head
Yupa Chantachum
M.Eng. (Nuclear Tech.)

Hathairad Hananantachai
M.Sc. (Environment)
Scientist

Somchai Pooduang
Cert. Medical Science Technology
Medical Science Associate

Functions of the Unit

1. To provide scientific instrumentation and laboratory supplies for research and study within the Faculty
2. To offer assistance and guidance in the operation of on-site equipment to the Faculty's staff
3. To provide a general scientific consultancy service for members of the Faculty

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

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

Warissara Chaiyabhandhu
B.A. (General Management)
General Affairs Officer

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

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

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

Phaibul Vasanakomut
Illustration Staff

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 2001, the Unit provided the following services:

1. Circulated 22 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; 32 projects
5. Produced 4 volumes of the *Mosquito Borne Diseases Bulletin*, 2 volumes of the *Journal of Tropical Medicine and Parasitology*, 18 brochures and posters, 1 issue of the Annual Report, and 1 issue of JITMM/FBPZ abstract book
6. Provided publication services to external clients

Seminars, Workshops and Training Courses

1. Special Training on Tropical Diseases

9 October - 15 November 2000	
Republic of South Africa	1

2. Refresher Course on International Travel Medicine

30 - 31 October 2000	
Denmark	22

3. Special Training on Tropical Diseases

31 October - 11 November 2000	
Norway	1

4. Training on Information Exchange on Malaria Control in Thailand and Malaysia

11 - 22 December 2000	
Vietnam	10

5. WHO-SEAMEO TROPMED Workshop on Lymphatic Filariasis Situation Analysis and Mapping in Mekong-Plus Countries

5 - 9 February 2001			
Cambodia	3	Indonesia	2
Japan	1	Lao PDR	3
Malaysia	4	Myanmar	3
Philippines	2	Thailand	6
UK	6	Vietnam	3
WHO	7		

6. Training on Information Exchange on Malaria Control in Thailand and Malaysia

18 February - 2 March 2001	
Vietnam	11

7. Special Training on Tropical Diseases

11 - 19 March 2001	
Japan	4

8. Special Training on Tropical Diseases

30 March - 12 April 2001	
USA	1

9. Special Training on Tropical Diseases for Japanese Nurse

9 - 20 April 2001	
Japan	1

10. Special Training on Tropical Diseases

18 April - 15 June 2001	
Germany	1

11. Special Training on Tropical Diseases Management

30 April - 25 May 2001	
Japan	1

12. Special Training on Tropical Diseases

1 - 8 August 2001	
Japan	5

13. Special Training on Tropical Diseases

6 - 10 August 2001	
France	4

14. Special Training on Tropical Diseases

23 - 28 August 2001	
Japan	1

15. Regional Field-based Training Programme in Epidemiology and Control of Tropical Diseases

14 May - 3 August 2001			
Cambodia	7	Lao PDR	8
Vietnam	7		

16. Regional Advanced Training Course on Data Analysis

10 - 28 September 2001			
Cambodia	10	Lao PDR	10
Vietnam	11		

International Meetings

1. The 3rd Seminar on Food-Borne Parasitic Zoonoses

6 - 8 December 2000			
Australia	5	Austria	1
Belgium	1	Canada	3
Denmark	4	Egypt	1
England	1	Germany	1
India	1	Indonesia	4
Iran	1	Iraq	1
Italy	2	Japan	22
Korea	2	Lao PDR	3
Malaysia	2	Mexico	2
Myanmar	2	Nepal	3
Philippines	3	PR China	5
Singapore	1	Sri Lanka	1
Switzerland	1	Taiwan	1
Tanzania	1	Thailand	432
United Kingdom	3	USA	8
Vietnam	2	Zimbabwe	1
Total			**521**

2. Joint International Tropical Medicine Meeting 2001

8 - 10 August 2001			
Austria	3	Bangladesh	7
Cambodia	3	China	1
Ethiopia	1	France	8
Germany	1	Hong Kong	1
India	3	Indonesia	5
Japan	30	Lao PDR	2
Myanmar	3	Netherlands	1
Nigeria	1	Peru	3
Philippines	1	Poland	1
Singapore	3	Switzerland	2
Tanzania	1	Thailand	767
USA	4	Vietnam	1
Total			**851**

Elective students in Tropical Medicine

Name	Institute	Country	Duration
1. Ms.Nina Loughman	University of Newcastle	Australia	30 Oct-24 Nov 00
2. Mr.Erik Bertheussen	"	"	"
3. Ms.Mary Phylli Stevens	University of Sydney	"	6 Nov-1 Dec 00
4. Ms.Victoria Atkinson	University of Toronto	Canada	20 Feb-16 Mar 01
5. Ms.Joanna Holland	"	"	"
6. Ms.Christine M. Johnston	University of Minnesota Medical School	USA	1-30 Mar 01
7. Mr.William P. Harris	"	"	"
8. Ms.Ulrike Pellert	Humboldt University (Charite) Berlin	Germany	3-16 Mar 01
9. Ms.Agnieszka Wroczynska	Medical Academy of Gdansk	Poland	1-25 Aug 01
10. Mr.Schallenberg Ekkehard	University of Innsbruck	Austria	3-28 Sept 01
11. Mr.Max Rasp	"	"	"
12. Ms.Christina Grafl	University of Vienna	"	"
13. Ms.Gertraud Mayer	"	"	"

International Linkages

The Faculty of Tropical Medicine has ongoing collaborative activities in research and training with the following:

1. WHO/TDR Programme
2. Freie Universität Berlin, Germany, under the assistance of the German Agency for Technical Cooperation
3. Liverpool School of Tropical Medicine, UK
4. The University of Calgary, Canada
5. Nuffield Department of Medicine, University of Oxford, UK
6. Asian Parasite Control Organization (APCO), Japan
7. The Wellcome Trust, UK
8. International Development Research Centre (IDRC), Canada
9. Japanese Association for Parasite Control (JAPC)
10. SEAMEO TROPMED Regional Centres in Indonesia, the Philippines and Malaysia
11. University of Innsbruck, Austria
12. Queensland Institute of Medical Research, Australia
13. James Cook University of North Queensland, Australia
14. Deutsche Gesellschaft für Technische Zusammenarbeit (GTZ), Germany
15. Department des Maladies Infecteuse et Médicine Tropicale, Groupe Hospitalier Pitié Salpêtrière, France
16. Pasteur Institute, France
17. Chinese Academy of Preventive Medicine, PR China
18. Naval Medical Research Institute, Bethesda, Maryland, USA
19. University of Tsukuba, Japan
20. The Swiss Tropical Institute, Basel, Switzerland
21. The Australian Centre for International and Tropical Health and Nutrition (ACITHN) of the Queensland Institute of Medical Research and the University of Queensland
22. The Health of Animals Laboratory, Canadian Food Inspection Agency, Government of Canada, Saskatoon, Canada

The nature of these activities are: collaborative research work; consulting services; personnel exchange; specimen and information exchanges; joint training courses, seminars and conferences.

Visitors

No.	Name	Country/Institute
1	Dr.Donald Burke	AFRIMS
2	Dr.Ruth Berkelman	AFRIMS
3	Dr.Ronald St.John	AFRIMS
4	Dr.Tim Straight	AFRIMS
5	Dr.Dimitri Cassimatis	AFRIMS
6	Mr.Heather M. Higgins	AFRIMS
7	Mr.Binh V. Vo	AFRIMS
8	Dr.Andy D Magnet	AFRIMS
9	Dr.Eric S Halsey	AFRIMS
10	Dr.Jason Wan	Australia
11	Ms.Gabriella Cerna	Austria
12	Dr.May Ho	Canada
13	Dr.Taj Jadavji	Canada
14	Dr.Clarence A. Guenter	Canada
15	Dr.Peter Harasym	Canada
16	Mrs.Marlyn Harasym	Canada
17	Miss Juliette Guitard	France
18	Miss Nadge Cotes	France
19	Miss Fanny Cagocle	France
20	Mr.A. Kumar	India
21	Mr.Sanjiv Sood	India
22	Lt.Gen.D.Raghunath	India
23	Dr.S. Hasnain	India
24	H.E.Dr.Yahya A Muhaimin	Indonesia
25	Mrs.Choifah Yahya Muhaimin	Indonesia
26	Mr.Dodon Hadi Permono	Indonesia
27	Dr.Arief S Sadiman	Indonesia
28	Mrs.Yun Widiati	Indonesia
29	Mr.Aris Munandar	Indonesia
30	Mr.Muhamad Yahya	Indonesia
31	Mr.Koh Asano	Japan
32	Ms.Maki Shiomi	Japan
33	Mr.Joji Tomioka	Japan
34	Ms.Ikumi Genka	Japan
35	Mr.Shinsaku Sakurada	Japan
36	Dr.Katsuro Tachibana	Japan
37	H.E.Hideyo Nakano	Japan
38	Mr.Iwai	Japan
39	Prof.Kiyoshi Kita	Japan

No.	Name	Country/Institute
40	Dr.Fumie Kobayashi	Japan
41	Dr.Katsuro Tachibana	Japan
42	Dr.Masaji Ono	Japan
43	Ms.Naomi Kurashige	Japan
44	Prof.Yusuke Wataya	Japan
45	Ms.Sachiko Baba	Japan
46	Mr.Norimama Shimizu	Japan
47	Ms.Erika Tokuhara	Japan
48	Mr.Homare Ito	Japan
49	Ms.Aina Arima	Japan
50	Mr.Daisuke Hatanaka	Japan
51	Ms.Yuji Miyoshi	Japan
52	Ms.Eri Aioi	Japan
53	Ms.Kei Mizuno	Japan
54	Ms.Onishi Naoko	Japan
55	Ms.Aoi Isohata	Japan
56	Mr.Ken Emoto	Japan
57	Mr.Toshiaki Kuwasaki	Japan
58	Dr.Seiki Tateno	Japan
59	Dr.Tsutomu Takeuchi	Japan
60	Ms.Fumiko Yamada	Japan
61	Dr.Atsuhiro Nishida	Japan
62	Mr.Koji Nakanishi	Japan
63	Mr.Masahiro Ohkubo	Japan
64	Ms.Suwa Koyama	Japan
65	Mr.Tomonori Arai	Japan
66	Mr.Satoshi Nanami	Japan
67	Dr.Toshiyuki Maruyama	Japan
68	Dr.Joseph Green	Japan
69	Dr.Kazuhiko Yamamoto	Japan
70	Dr.Chizuru Kato	Japan
71	Dr.Katsushi Tokunaga	Japan
72	Prof.Naoki Arizono	Japan
73	Asst.Prof.Mihoko Kikuchi	Japan
74	Asst.Prof.Jun Ohashi	Japan
75	Dr.Satoru Kawai	Japan
76	Mr.Arihiro Osanai	Japan
77	Dr.Hiroyuki Daida	Japan
78	Dr.Hiroshi Mokuno	Japan

No.	Name	Country/Institute
79	Mr.Teruyasu Nishino	Japan
80	Ms.Naoya Haibara	Japan
81	Ms.Amane Endo	Japan
82	Ms.Sachiko Ogawa	Japan
83	Mr.Kazuyo Terada	Japan
84	Ms.Emiko Sakurai	Japan
85	Mr.Satoshi Dohi	Japan
86	Prof.Keiko Masamura	Japan
87	Prof.Toshio Sei	Japan
88	Ms.Mayumi Kubo	Japan
89	Ms.Zushi Hiromi	Japan
90	Ms.Chigusa Yoshitake	Japan
91	Ms.Yoshiko Tsuneoka	Japan
92	Ms.Naoko Fujita	Japan
93	Ms.Ryoko Sakoda	Japan
94	Ms.Makiko Kashiwabara	Japan
95	Ms.Mari Tsuchiya	Japan
96	Ms.Chinami Tamehira	Japan
97	Dr.Bounsai Thovisouk	Lao PDR
98	Dr.Phoutone	Lao PDR
99	MA.Nona M. Avelina	Philippines
100	Dr.Tan Yi	PR China
101	Mrs.Zhong Gemai	PR China
102	Mr.Liao Guo Huo	PR China
103	Dr.Myo Myint	SEAMEO CHAT/ Myanmar
104	Ms.Khin Lay Soe	SEAMEO CHAT/ Myanmar
105	H.E.Tan Sri Dato Seri Musa bin Mohamad	SEAMEO Council President
106	Tan Sri Dr.Johari bin Mat	Malaysia
107	Hj Abdul Rafie bin Mahat	Malaysia
108	Faja Kamarudin bin Raja Ahmad	Malaysia
109	Dr.Basri bin Yusoff	Malaysia
110	Dr.Mohammad Khan	South Korea
111	Prof.Ju-Young Seoh	South Korea
112	Mr.Kornkrit Chaijenkij	Thailand
113	Miss Chalermkwan Klinphaka	Thailand
114	Mr.Natthawuth Supsinsoontorn	Thailand
115	Miss Ratama Pothisri	Thailand
116	Miss Ratanakarn Chaiprasitthikul	Thailand

No.	Name	Country/Institute
117	Miss Pongkwan Pradithanond	Thailand
118	Miss Uraporn Jaowattana	Thailand
119	Miss Areeda Hongsrichinda	Thailand
120	Miss Siritheera Srichanthapong	Thailand
121	Miss Duanthida Songdej	Thailand
122	Miss Arada Wongmek	Thailand
123	Prof.David Molyneux	United Kingdom
124	Prof.Dr.Martin Chapman	USA
125	Dr.David Murdoch	USA
126	Dr.David Murdoch	USA
127	Dr.Anne Riffle	USA
128	Dr.Richard Kiang	USA
129	Dr.Keattiyoat Wattanakit	USA
130	Mr.Andy Schmid	USA
131	Ms.Hlaphyu Aye	USA
132	Prof.Mir S. Mulla	USA
133	Dr.Marc Brodsky	USA
134	Ms.Victoria Wilkins	USA
135	Ms.Rabindra Watson	USA
136	Ms.Britta Lassman	USA
137	Ms.Porntip Duangploy	USA
138	Colonel Dale Vincent	USA
139	Colonel Banjamin Worth, Berg	USA
140	Mr.Don Hudson	USA
141	Mr.John Draude	USA
142	Dr.Andy D Magnet	USA
143	Dr.Eric S Halsey	USA
144	Dr.Allison Head	USA
145	LT (Dr.) Edie Lederman	USA
146	LT.Col.(Dr.) Gerry Brower	USA
147	LT (Dr.) Jeffrey O'Dell	USA
148	Dr.Tran Hung Bien	Vietnam
149	Dr.Tran Thi Gian Huong	Vietnam
150	Dr.Pham Hung	Vietnam
151	Dr.Nguyen Thi Pha	Vietnam
152	Dr.Truong Hoai Phong	Vietnam
153	Dr.Nguyen Xuan Thu	Vietnam
154	Dr.Hoang Ba Thuoc	Vietnam
155	Dr.Rob Ridley	WHO/Geneva
156	Dr.Francesco A. Rio	WHO/Geneva
157	Dr.Tom Kanyok	WHO/Geneva

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*
Chantima Lohachit	lohachitchantima@usa.net	Medical and freshwater malacology Limnology/Ecology/Spermatogenesis (TEM)/ Environmental Health
Chotechuang Panasoponkul	tmcpn@mahidol.ac.th	Vector borne diseases eg. filariasis, malaria and field work
Chukiat Sirivichayakul	chukiats@hotmail.com	General pediatrics/Chemotherapy of childhood malaria/Parasitic infection in children/ Childhood diarrhea
Chutatip Siripanth	tmcsr@mahidol.ac.th	Cultivation of *Giardia* and *E. histolytica*
Dwip Kitayaporn	tmdkt@mahidol.ac.th	Epidemiology of HIV/AIDS Research methodology
Emsri Pongponrat	headtmpa@mahidol.ac.th	Electronmicroscopy: pathology of malaria
Jaranit Kaewkungwal	tmjkk@mahidol.ac.th	Research methodology/Data management/ Statistics modeling
Jintana Pattarapotikul	tmjpt@mahidol.ac.th	Immunology and molecular biology of malaria
Jitra Waikagul	tmjwk@mahidol.ac.th	Taxonomy/Biology of helminths
Kamolnetr Okanurak	tmkok@mahidol.ac.th.	Community participation in disease control/ Treatment seeking behavior
Kanjana Hongthong	tmkht@mahidol.ac.th.	Biochemical nutrition/Nutritional epidemiology/Public health nutrition
Karunee Kwanbunjun	tmkkb@mahidol.ac.th.	Biochemical nutrition/Nutritional epidemiology
Kasinee Buchachart	tmkbc@mahidol.ac.th	Statistical analysis & data processing of epidemiological research
Kesinee Chotivanich	nokowellcome97@hotmail.com	Pathophysiology of malaria
Keswadee Lapphra	keswadee-j@mahidol.ac.th	General pediatrics
Krisana Pengsaa	tmkps@mahidol.ac.th	General pediatrics Chemotherapy of parasitic diseases Immunization in children/Neonatal infection

Lecturer	E-mail Address	Field of Specialization/Expertise
Kriengsak Limkittikul	tipgi@hotmail.com	General pediatics/Tropical virology
Ladda Tangbanluekal	grltb@mahidol.ac.th	Environmental and industrial toxicology Health risk assessment from toxicants
Lakana Leohirun	-	Biochemistry
Malinee Thairungroj	tmmtr@mahidol.ac.th	Medical helminthology/Immunodiagnosis
Manas Chongsa-nguan	tmmcs@mahidol.ac.th	Immunology of tropical infections Bacterial identification
Mario Riganti	-	Anatomical pathology/Gnathostomiasis/ Chemotherapy of gnathostomiasis/ Tropical pathology
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Parnpen Viriyavejakul	tmpvr@mahidol.ac.th	Anatomical pathology/Opportunistic infections in AIDS/Tissue cytokines in AIDS
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Petcharin Yamarat	tmpym@mahidol.ac.th	Rheology of malarial blood, blood of subjects digested garlic, cord blood
Phanorsri Attanath	tmpat@mahidol.ac.th	*In vitro* sensitivity test to antimalarials Pharmacokinetics of antimalarials
Piyarat Butraporn	tmpbt@mahidol.ac.th	Social epidemiology in tropical diseases Health impacts of water resource development
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Pornthep Chanthavanich	tmpct@mahidol.ac.th	Chemotherapy of parasitic diseases Chemotherapy of malaria in children Vaccination in children
Porntip Petmitr	tmppm@mahidol.ac.th	Biochemistry of malaria parasites/Cultivation of *P. falciparum* gametocytes and *T. vaginalis*
Pramuan Tapchaisri	tmpct@mahidol.ac.th	Immunology/Molecular biology of tropical infections
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Lecturer	E-mail Address	Field of Specialization/Expertise
Pravan Suntharasamai	tmpst@mahidol.ac.th	Clinical tropical medicine/ Vaccinology/Clinical epidemiology
Punnee Pitisuttithum	tmppt@mahidol.ac.th	Tropical diseases vaccine trial especially Phase I, II vaccine trial eg. Cholera vaccine, Rotavirus vaccine, AIDS vaccine, etc., Clinical studies of tropical diseases eg. cryptococcal meningitis in AIDS; chronic diarrhea in AIDS, etc. Drug trials in AIDS and opportunistic infection, especially oral candidiasis
Ratanaporn Kasemsuth	tmrks@mahidol.ac.th	Radioisotopes in medical science and biology RIA. (Radio immunoassay)
Rungsunn Tungtrongchitr	tmrtg@mahidol.ac.th	Community nutrition/Nutritional epidemiology/Biochemical nutrition
Sasithon Pukrittayakamee	Sasithon@hotmail.com	Tropical medicine
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Thongchai Deesin	-	Ecology/Mosquito-borne diseases/Field study
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Lecturer	E-mail Address	Field of Specialization/Expertise
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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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Voranuch Wangsuphachart	tmvws@mahidol.ac.th	Environmental epidemiology/ Comparative risk assessment/Epidemiology and internet
Wanchai Phatihatakorn	tmwpk@mahidol.ac.th	Environmental health impact assessment/ GRD Monitoring, evaluate and surveillance of parasitic diseases
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Yaowalark Sukthana	tmymv@mahidol.ac.th	Oto-rhino-laryngology/*Toxoplasma gondii*
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Ongoing Research Projects of the Faculty of Tropical Medicine in 2001

No.	Ongoing Research Projects in 2001	Grants	Principal Investigator
	Department of Clinical Tropical Medicine		
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	Schering Plough Research Institute	Assoc. Prof. Punnee Pitisuttithum
2	Neurotoxicity of artemether in animal model following intermittent intramuscular injections	Wellcome Trust of Great Britain and SEAMEO-TROPMED	Dr. Apichart Nontprasert
3	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
4	Efficacy and tolerability of ivermectin on gnathostomiasis (pilot study)	Mahidol University	Dr. Valai Bussaratid
5	Efficacy and tolerability of ivermectin on gnathostomiasis	Thailand - Tropical Diseases Research Programme (T-2)	Dr. Valai Bussaratid
6	Effect of insecticide on the female reproductive system	Tokyo University	Prof.Ryutaro (Assist. Prof. Ladda Tangbanluekal)
7	Health risk from trihalomethane contamination in tap water in Bangkok Metropolitan area and boundary	Mahidol University	Assist. Prof. Ladda Tangbanluekal
8	Development of genotyping technique for *Plasmodium vivax* parasite		Prof. Sasithon Pukrittayakamee
9	Association of genetic mutations in *Plasmodium vivax* dhfr with resistance to sulfadoxine/pyrimethamine geographical and clinical correlates	TRF and Wellcome-Trust of Great Britain	Miss Mallika Imwong
10	Assessment of the neurotoxicity of oral dihydroartemisinin in mice	Wellcome Trust of Great Britain	Mr. Apichart Nontprasert
11	Study of auto-agglutination phenotype and disease severity in *P. falciparum* infection	TRF and Wellcome-Trust of Great Britain	Dr. Kesinee Chotivanich
12	Research and development for Thai pople living at Thai-Myanmar border to be free from tropical diseases	Mahidol University	Prof. Sornchai Looareesuwan
13	Prevalence of important tropical diseases and treatment in Saiyok, Kanchanaburi, Thailand	Mahidol University	Prof. Polrat Wilairat

No.	Ongoing Research Projects in 2001	Grants	Principal Investigator
	Department of Clinical Tropical Medicine (continued)		
14	Observational probe study of *in vitro* immune response parameters to candidate HIV-1 vaccine antigens among subjects from Thailand	Merck Inc.	Assoc. Prof. Punnee Pitisuttithum
15	Safety and therapeutic effects of Jin Huang Chinese medicine in uncomplicated HIV-1 patients (Part II)	Huatai Pharmacy, Co., Ltd.	Assoc. Prof. Punnee Pitisuttithum
	Department of Helminthology		
16	The IFAT for human gnathostomiasis	Mahidol University	Miss Wattana Pahuchon
17	Monoclonal antibody-based competitive ELISA and indirect ELISA for immunodiagnosis of trichinosis	Mahidol University	Mrs. Supaporn Nuamtanong
18	Comparison of biochemical extract preparations of *Cysticercus cellulosae* by SDS-polyacrylamide gel electrophoresis and immunoblot technique	Mahidol University	Assist. Prof. Paron Dekumyoy
19	Experimental infection of freshwater fish in Thailand with the infective stage of *Angiostrongylus cantonensis*	Mahidol University	Assist. Prof. Chalit Komalamisra
20	*Toxocara canis* larval antigens for serodiagnosis of human toxocariasis	Mahidol University	Assoc. Prof. Wanna Maipanich
21	Comparative studies on surface ultrastructure of adult worm of *Paragonimus* sp. in Thailand	Mahidol University	Assist. Prof. Sanan Yaemput
22	Seasonal variation in the intensity of *Gnathostoma* larvae in eels in Nakhon Nayok Province	Mahidol University	Assoc. Prof. Wichit Rojekittikhun
23	Studies on the efficacy of Thai traditional herbal medicines in the treatment of opisthorchiasis in hamsters	Mahidol University	Assist. Prof. Panyawut Hiranyachattada
24	Epidemiology and prevention of trichinosis in Mae Hong Son	Mahidol University	Assoc. Prof. Ponganant Nontasut
25	*Angiostrongylus cantonensis*: S-Adenosylmethionine decarboxylase	Government Budget	Mrs. Supaporn Nuamtanong
26	Study on the killing effect of Thai medicinal plants against mosquito vectors and parasitic helminths	Mahidol University	Assoc. Prof. Jitra Waikagul
27	Reinfection of soil-transmitted helminthiases in village with one hundred percent latrine	Mahidol University	Mr. Chatree Muennoo
	Department of Medical Entomology		
28	Evaluation of certain chemical stimuli as attractants for sound trapping of *Culex tritaeniorhynchus*		Assoc. Prof. Vanida Deesin
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	Miss Raveewan Suvanich
32	Study on fauna of medically important vectors at Kanchanaburi Campus, Sai Yok District, Kanchanaburi Province	Mahidol University	Assoc. Prof. Somjai Leemingsawat

No.	Ongoing Research Projects in 2001	Grants	Principal Investigator
	Department of Microbiology and Immunology		
33	Anaerobic bacteria intraabdominal infection	Mahidol University	Assoc.Prof. Suvanee Supavej
34	Production of monoclonal antibodies for use in the diagnosis of scrub typhus	Faculty of Tropical Medicine	Assist. Prof. Varee Wongchotigul
35	Detection of dengue virus in mosquitoes (*Aedes aegypti*) by polymerase chain reaction compare with virus-cultivation	Mahidol University	Assoc. Prof. Wipawee Usawattanakul
36	Development of polymerase chain reaction for the diagnosis of vivax malaria	Mahidol University	Assoc. Prof. Pramuan Tapchaisri
37	Identification and characterization of T cell epitopes on *P. falciparum* sporozoite surface protein 2 recognized by human	Naval Medical Research Institute	Prof. Srisin Khusmith
38	The use of recombinant *Entamoeba histolytica* pyruvate: ferredoxin oxidoreductase (r PFOR) as a candidate vaccine against invasive amebiasis		Assoc. Prof. Nitaya Thammapalerd
39	Production of recombinant pyruvate: ferredoxin oxidoreductase of *Entamoeba histolytica* (Eh rPFOR) and its application for diagnosis of invasive amebiasis		Assoc. Prof. Nitaya Thammapalerd
40	Rapid diagnosis of salmonellosis using dip stick method	Mahidol University	Prof. Wanpen Chaicumpa
41	Development of opisthorchiasis by immunological method	MoPH, Faculty of Tropical Medicine and NRCT	Prof. Wanpen Chaicumpa
42	Production of monoclonal antibodies to *Bordetella pertussis* filamentous hemagglutinin	NSTDA, Faculty of Tropical Medicine and Tsukuba University, Japan	Assoc. Prof. Manas Chongsa-nguan
43	Antigenic analysis of *V. cholerae* isolated in Thailand for epidemic tracing	In cooperation with Japan and Tsukuba University	Assoc. Pramuan Tapchaisri
44	Production of allergenic components of cockroaches by genetic engineering	National Research Council of Thailand	Prof. Wanpen Chaicumpa
45	Studies on allergic components of cockroaches (*Blatta orientales*)	National Research Council of Thailand	Prof. Wanpen Chaicumpa
46	Diagnosis of gnathostomiasis using specifically purified antigen	NSTDA and TRF	Prof. Wanpen Chaicumpa
47	Development of rapid detection of *Vibrio cholerae* in immunomagnetic enriched samples by Mab-based dot-blot ELISA	Mahidol University	Assist. Prof. Yuvadee Mahakunkijcharoen
48	Efficacy testing of new vaccine adjuvant CpG DNA		Prof. Wanpen Chaicumpa
49	Development of molecular biological method for serotyping of *Leptospira*	NSTDA and TRF	Prof. Wanpen Chaicumpa
50	Development of a rapid test for detection of *Vibrio parahaemolyticus*		Prof. Wanpen Chaicumpa
51	Epidemiological survey of enterohemorrhagic *Escherchia*	Royal Golden Jubilee, TRF	Prof. Wanpen Chaicumpa
52	Towards the *Strongyloides stercoralis* Thai isolates	Royal Golden Jubilee, TRF	Prof. Wanpen Chaicumpa
53	Typing of *Entamoeba histolytica* isolates obtained from Southeast Asian countries	Japanese Health Sciences Foundation (JHSF)	Assoc. Prof. Nitaya Thammapalerd

No.	Ongoing Research Projects in 2001	Grants	Principal Investigator
	Department of Microbiology and Immunology (continued)		
54	Detection of *Leptospira* spp. in urine by polymerase chain reaction (PCR)	Thailand Research Fund	Dr. Thareerat Kalambaheti
55	Cloning and expression of fimbrial of *V. cholerae* o1 in the large scale as cholera vaccine candidate molecular biology & immunology	Thailand Research Fund	Dr. Thareerat Kalambaheti
56	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
57	A simple and rapid detection of scrub typhus	Mahidol University	Assist. Prof. Varee Wongchotigul
58	Genetic diversity of the CS protein as an epidemiological marker for the efficacy of pre-erythrocytic immunity	IRD French Ministry of Research	Prof. Srisin Khusmith
	Department of Protozoology		
59	Comparison of *Toxoplasma gondii* antibody detection between in-house latex agglutination and commercial test	Thanad-Molee Choman Foundation	Assist. Prof. Varaporn Suphadtanapongs
60	Isolation and characterization of DNA helicase from *Plasmodium falciparum*	Thailand Research Fund	Assoc. Prof. Pornthip Petmitr
61	Studies on the effect of Thai medicinal plants to *Cryptosporidium* and *Isopora in vitro*	Mahidol University	Assist. Prof. Chutatip Siripanth
62	Toxoplasmosis in population at risk in Thailand	Mahidol University	Assist. Prof. Yaowalark Sukthana
63	Study of association of *Toxoplasma gondii* antibody between cats and owners	Thanad-Molee Choman Foundation	Assist. Prof. Yaowalark Sukthana
64	Established Thai medicinal plants for treatment of coccidiosis in pig, poultry and cow	Ministry of University Affairs	Assist. Prof. Chutatip Siripanth
65	Established double antibody ELISA method for detection of pathogenic protozoal antigens in the feces	National Science and Technology Development Agency	Assist. Prof. Chutatip Siripanth
66	Detection of malaria parasites in after-drug treatment patients by using QBC method	Government Budget	Assist. Prof. Varaporn Suphadtanapongs
	Department of Social and Environmental Medicine		
67	Hazardous substance management and development of computerized database inventory list on major hazardous substances used at Faculty of Tropical Medicine, Mahidol University	Mahidol University	Assist. Prof. Voranuch Wangsuphachart
68	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)

No.	Ongoing Research Projects in 2001	Grants	Principal Investigator
	Department of Social and Environmental Medicine (Continued)		
69	Socio-cultural and behavioral factors of shigellosis burden studies in Kaeng Koi District	The International Vaccine Institute	Assoc. Prof. Piyarat Butraporn
70	Leptospirosis vaccine designed using T7 phage display technique	Thailand Research Fund	Assist. Prof. Pongrama Ramasoota
71	Development of an immunodiagnostic method for Opisthorchiosis viverrini: detection of *Opisthorchis viverrini* antigens in stool using a combination of specific monoclonal antibodies	Government Budget (CDC)	Dr. Praphasri Jongsuksuntigul (Assoc. Prof. Viroj Kitikoon)
72	Socio-environmental management for sustainable dengue haemorrhagic fever control in Chaiyaphum Province	Mahidol University	Mr. Pongsant Sitabutra
73	Local wisdom in the treatment of herpes simplex diseases. Case study: the treatment of herpes simples by monk healer (mor-pra)	Mahidol University	Mr. Wiwat Wanarangsikul
	Department of Tropical Hygiene		
74	Assessment of risk factors of mortality associated with vehicular crashes in a central province of Thailand: before and after enforcement of safety service law	SEAMEO-GTZ [M.Sc. Epidemiology (Public Health) Project]	Dr. Nilarat Premmanisakul
75	A comparative clinical trial of combinations of dihydroartemisinin plus azithromycin and dihydroartemisinin plus mefloquine for treatment of multidrug resistant falciparum malaria	Mahidol University	Assist. Prof. Srivicha Krudsood
	Department of Tropical Nutrition and Food Science		
76	Food and health relationship in Asian population	Palm Oil Research Institute of Malaysia	Assoc. Prof. Supranee Changbumrung
77	Development of food and medicinal plants	Government Budget FY 2001	Assoc. Prof. Supranee Changbumrung
78	Micronutrients and oxidative stress in obese subjects	Freie Universität, Berlin Germany	Assoc. Prof. Rungsunn Tungtrongchitr
79	Medicinal plants for treatment of hookworm	Government Budget FY 2001	Assoc. Prof. Supranee Changbumrung
80	Medicinal plants against malaria	Government Budget FY 2001	Assoc. Prof. Supranee Changbumrung
81	The correlation between folic acid status and cervical cytologic abnormalities in Thai women	Mahidol University	Assist. Prof. Karunee Kwanbunjan
	Department of Tropical Pathology		
82	Hematopoietic features of the bone marrow of *Plasmodium falciparum* infected patients	Mahidol University	Assoc. Prof. Yaowapa Maneerat
83	Pathology and immunohistochemistry of liver in AIDS: a necropsy study	Mahidol University	Assoc. Prof. Parnpen Viriyavejakul

No.	Ongoing Research Projects in 2001	Grants	Principal Investigator
	Department of Tropical Pathology (continued)		
84	Causes of diarrhea in HIV/AIDS patients	Mahidol University	Assoc. Prof. Parnpen Viriyavejakul
85	The effects of *Plasmodium falciparum*-induced cellular responses on activation of endothelial cells	Mahidol University	Assoc. Prof. Yaowapa Maneerat
	Department of Tropical Pediatrics		
86	Clinical efficacy and pharmacokinetics of suppositoried artesunate combined with mefloquine in the treatment of severe childhood falciparum malaria	Department of Tropical Pediatrics	Assoc. Prof. Krisana Pengsaa
87	Clinical efficacy and pharmacokinetics of suppositoried artesunate combined with mefloquine in the treatment of uncomplicated childhood falciparum malaria	Department of Tropical Pediatrics	Assist. Prof. Chukiat Sirivichayakul
88	The relationship of mixed infection and severity of falciparum malaria		Assist. Prof. Watcharee Chokejindachai
89	Safety and immunogenicity of tetravalent dengue vaccine formulations in Thai adult volunteers: evaluation of three-year persistence	Aventis Pasteur, France	Assoc. Prof. Pornthep Chanthavanich
90	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
91	Safety and immunogenicity of tetravalent dengue vaccine formulations in Thai children	Aventis Pasteur, France	Prof. Arunee Subchareon
92	Single dose therapy for treatment of *Giardia* infection in children	Mahidol University	Assoc. Prof. Krisana Pengsaa
93	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
94	Prevalence of intestinal parasitic infections among children with mental handicaps and recurrence rate at one year after chemotherapy	Mahidol University	Assist. Prof. Chukiat Sirivichayakul
95	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
96	Dengue antibodies in Thai infants: age-specific seroprevalence and kinetics of transplacentally transferred dengue antibodies (EPI 11)	Aventis Pasteur, France	Assoc. Prof. Krisana Pengsaa
97	Health problems, knowledge, attitudes and practices of children in Saiyok District, Kanchanaburi Province	Mahidol University	Assoc. Prof. Pornthep Chanthavanich
98	Prevalence and risk factors of atopic diseases in rural children in Saiyok District, Kanchanaburi Province	Mahidol University	Dr. Wimol Nganthavee

No.	Ongoing Research Projects in 2001	Grants	Principal Investigator
	Department of Tropical Radioisotopes		
99	Study of four Thai medicinal herbs as individuals and combinations for anti-snake venoms		Assist. Prof. Channarong Sanghirun
100	Viscosity of red cell ghosts and hemoglobin of red cells from patients with *Plasmodium falciparum* malaria	Mahidol University	Assist. Prof. Petcharin Yamarat
101	Effect of garlic on blood rheology and prevention of thrombolism	National Research Council of Thailand	Assist. Prof. Petcharin Yamarat
102	Studies on serum transcobalamin II in patients with pyrexia of unknown origin	Mahidol University	Miss Cheeraratana Cheeramakara
	Vaccine Trial Centre		
103	Development of new vaccines against cholera due to *Vibrio cholerae* O139 (Part I)	WHO	Assoc. Prof. Punnee Pitisuttithum
104	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	Assoc. Prof. Punnee Pitisuttithum
105	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
106	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)
107	Phase I/II trial of Pasteur Merieux Connaught (PMC) live recombinant ALVAC-HIV (VCP 1521) priming with Vaxgen gp 120 B/E (AIDVAXTM B/E) boost in Thai HIV-seronegative adults	Walter Reed Army Institute of Research	Assoc. Prof. Punnee Pitisuttithum

TROPMED'S Publications

(1 October 2000–30 September 2001)

1. Anderson TJ, Haubold B, Williams JT, Estrada-Franco JG, Richardson L, Mollinedo R, Bockarie M, Mokili J, Mharakurwa S, French N, Whitworth J, Velez ID, Brockman AH, Nosten F, Ferreira MU, Day KP. Microsatellite markers reveal a spectrum of population structures in the malaria parasite *Plasmodium falciparum*. *Mol Biol Evol* 2000;17:1467-82.

2. Angus BJ, Smith MD, Suputtamongkol Y, Mattie H, Walsh AL, Wuthiekanun V, Chaowagul W, White NJ. Pharmacokinetic-pharmacodynamic evaluation of ceftazidime continuous infusion versus intermittent bolus injection in septicaemic melioidosis *Brit J Clin Pharm*, 2000;50:184-91.

3. Anothay O, Pongvongsa T, Maharat N, Sirivichayakul C, Chantavanich P, Silachamroon U, Looareesuwan S. Clinical presentation of childhood malaria in Savannakhet Province, Lao PDR. *Southeast Asian J Trop Med Public Health* 2000;31 Suppl 1:85-90.

4. Anuntagool N, Aramsri P, Panichhakul T, Wuthiekanun V, Kinoshita R, White NJ, Sirisinha S. Antigenic heterogeneity of lipopolysaccharide among *Burkholderia pseudomallei* clinical isolates. *Southeast Asian J Trop Med Public Health* 2000;31:146-52.

5. Chaisri U, Nagata M, Kurazono H, Horie H, Tongtawe P, Hayashi H, Watanabe T, Tapchaisri P, Chongsa-nguan M, Chaicumpa W. Localization of Shiga toxins of enterohemorrhagic *Escherichia coli* in kidneys of pediatric and geriatric patients with fatal hemolytic uremic syndrome. *Microbial Pathogenesis* 2001;31:59-67.

6. Chandenier J, Husson J, Canaple S, Gondry-Jovet C, Dekumyoy P, Danis M, Riveau G, Henneqvin C, Rosa A, Raccurt CP. Medullary gnathostomiasis in a white patient: use of immunodiagnosis and magnetic resonance imaging. *Clin Infect Dis* 2001;32:154-7.

7. Changbumrung S, Jintaridhi P, Kwanbunjan K. Mutagenicity and antimutagenicity of some food plants. *Ann Nutr Metab* 2001;45(Suppl 1):543.

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ANTIMALARIAL ACTIVITY OF AZITHROMYCIN, ARTEMISININ AND DIHYDROARTEMISININ IN FRESH ISOLATES OF *PLASMODIUM FALCIPARUM* IN THAILAND

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Antibiotics with antimalarial activity may offer an interesting alternative for the treatment of multidrug-resistant falciparum malaria. Azithromycin, a relatively recent semisynthetic derivative of erythromycin, was tested for its *in vitro* activity against fresh isolates of *Plasmodium falciparum*. As the reportedly slow onset of action of azithromycin suggests its combination with fast-acting substances, such as artemisinin-derivatives, dihydroartemisinin (DHA) was tested in parallel as a possible combination partner. The effective concentrations found for azithromycin in this study (EC(50)=29.3&mgr;mol/l, EC(90)=77.1&mgr;mol/l blood medium mixture (BMM)) are comparable to those of other antimalarials in the antibiotics class and are considerably higher than those found for mefloquine or quinine. The absence of an activity correlation between azithromycin and chloroquine, quinine and artemisinin emphasises the independence of azithromycin drug response from the sensitivity to these drugs. A weak activity correlation (rho(EC90)=0.352; p=0.028), which could point to a potential cross-sensitivity, but is probably of little clinical importance, was found with mefloquine above the EC(50) level. Provided that further clinical trials support the combination of these drugs, DHA may offer an interesting combination partner for azithromycin owing to its rapid onset of action and the comparatively low effective concentrations (EC(50)=1.65nmol/l, EC(90)=7.10nmol/l BMM). This combination may serve as an interesting alternative to tetracycline and doxycycline, which cannot be used in pregnant women and children, and exhibit phototoxicity. Nevertheless, the relatively high cost of this combination, as well as the controversial reports of clinical efficacy, may limit the usefulness of azithromycin in malaria therapy and require an adjustment of previously used treatment regimens. ❑

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

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

2 capsules once daily for 1 day, 3 capsules daily for 3 days; and 4 capsules once daily on the first day followed by 3 capsules once daily for 2 days respectively. Two doses of mefloquine, 15 mg/kg/dose and 10 mg/kg/dose, were given at 72 hr and 84 hr, respectively. All patients were admitted for 28 days to the Hospital for Tropical Diseases to assess efficacy, tolerability, and delayed neuropsychiatric effects. The mean [SD] parasite clearance time and fever clearance time were 46.1+15.7 hr and 82.5+59.6 hr respectively. No deaths occurred. No patients had major adverse drug effects. The cure rate at 28 days of follow-up in patients was 95.0% (113 of 119 patients). Dihydroartemisinin suppository followed by mefloquine was well tolerated and effective. In severe malaria, sequential treatment is a suitable alternative treatment to parenteral drugs. Further studies in a larger number of patients under field conditions are required. ❑

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

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Malaria's pyrogenic threshold seems to depend on factors such as age and transmission patterns. We have studied the admission temperature of 200 mild malaria cases and observed after adjusting for body mass index, other helminths and other confounders, that only hookworm infected patients had less fever on admission that those without hookworm (37.5 ± 0.9/38 ± 0.8, $P<0.001$). Thus, we suggest the age dependence of the pyrogenic threshold could have been confounded by the epidemiology of iron deficiency. ❑

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

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Following an investigation suggesting a protective role for *Ascaris* against cerebral malaria, possibly through immunomodulation, we examined whether *Ascaris* had any impact on mixed *P. falciparum* and *P. vivax* infections. We studied a cross section of 928 patient files between 1991 and 1999. Forty patients had contemporaneous mixed infections and 40 patients had *P. falciparum* infections, followed by *P. vivax* infections. There was a significant association between *Ascaris* infection and the risk of having both contemporaneous or successive mixed *P. falciparum* and *P. vivax* infections (adjusted odds ratios respectively 6 [2-18] $P=0.001$ and 3.6 [1.2-11.1] $P=0.02$). There was a positive linear trend between the burden of *Ascaris* and the risk of mixed infections $P<0.0001$. These results suggested the possibility that pre-existing *Ascaris* infection may increase tolerance of the host to different *Plasmodium* spp., thus facilitating their co-existence. ❑

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

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Chloroquine-resistant *Plasmodium falciparum* is well documented in Thailand. Lao PDR, however, continues to use chloroquine as the first-line therapy for the treatment of falciparum malaria. The objective of this study was to determine the prevalence of *cg2, pfmdr1* and *pfcrt* allelic types that have previously been associated with chloroquine resistance in these two areas. *P. falciparum* isolates were collected from participants in ongoing treatment studies conducted near the Thai-Cambodian border and in Vang Vieng District of Lao PDR. *Pfmdr1* and *pfcrt* alleles were characterized by PCR-RFLP and mutations in *cg2* were characterized by PCR-SSCP. Of the 50 samples analyzed, 32% of Lao isolates (8/25) were found to contain the *pfmdr1* mutation N86Y, versus only 4% of Thai isolates (1/25;p = 0.02). The *cg2* polymorphism previously associated with chloroquine resistance was present in 40% of isolates from Lao PDR (10/25) compared to 96% of Thai isolates (24/25; p < 0.001). All samples from both countries (50/50) contained the *pfcrt* K76T mutant allele reported to confer resistance to chloroquine. The differences observed in the prevalence of Tyr86 and *cg2* alleles suggest that there is selective pressure for the maintenance of *pfmdr1* and *cg2* mutations. This drug pressure may be attributable to differences in malaria treatment policies between Thailand and Lao PDR. ❑

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

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To define the frequency of the early rising of parasitemia in falciparum malaria patients treated with artemisinin derivatives, a retrospective chart review of 497 patients admitted to the Hospital for Tropical Diseases, Bangkok in 1996 was carried out. Early rising parasitemia, which was defined as an increase in the parasite count over the baseline pretreatment level during the first 24 hours of treatment, was found in 59/229 episodes (25.8%) of uncomplicated, and 111/268 episodes (41.3%) of complicated, falciparum malaria. All uncomplicated cases were successfully treated without developing any complications. There were 2 deaths and 13 changes of drug regimen in the complicated group. Only one of these unfavorable responses was due to parasite response. Early rising parasitemia was very common in falciparum malaria treated with artemisinin derivatives, despite their ability to clear the parasitemia, and did not indicate failure of the drug used. ❑

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HELMINTH INFECTIONS ARE ASSOCIATED 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 relative to exposure to helminth infection in 2 separate groups of patients: 111 cerebral malaria cases and 180 mild *P. falciparum* malaria cases. Hookworm infections were excluded. Mean hemoglobin concentrations were significantly lower in helminth-infected patients relative to those without helminths both in the cerebral malaria group (10.1 ± 3 [n=47] vs 11.2 ± 2.4 g/dl [n=64], *P*=0.04) and the mild malaria group (11 ± 2.5 [n=89] vs 12.2 ± 2.7g/dl [n=91], *P*=0.004). Median reticulocyte counts, only available in the cerebral malaria group, were lower in helminth-infected patients relative to those without helminths (15340/23760 per ml, *P*=0.03). Adjustments for confounders such as body mass index did not alter these associations. Thus, we believe a nutritional pathogenesis was unlikely and favor a mechanism linked to differences in the immune response of helminth-infected patients during malaria. ❑

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CASE-CONTROL STUDIES ON HOST FACTORS IN SEVERE MALARIA

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Although molecular biology has illustrated the phenotypic heterogeneity of *P. falciparum*, there are still no specific markers of virulence. As parasite virulence is an important determinant of severe malaria, the choice of comparison groups in the study of host factors influencing severity is a delicate issue. Ignoring parasite factors in the selection of controls potentially leads to biased comparisons between a majority of cases with virulent parasites and a majority of controls with non-virulent parasites. We now discuss how to avoid this virulence bias in the absence of specific markers of virulence. ❑

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EVALUATION OF A NEWLY DEVELOPED DIPSTICK TEST FOR THE RAPID DIAGNOSIS OF SCRUB TYPHUS IN FEBRILE PATIENTS

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Scrub typhus is a potentially fatal, febrile disease prevalent in rural Asia. The etiological agent, *Orientia tsutsugamushi*, is transmitted to humans by the bite of a larval trombiculid mite. No current diagnostic test is sufficiently practical for use by physicians working in rural areas. A new dipstick test using a dot blot immunoassay format has been developed for the serodiagnosis of scrub typhus. We evaluated this test on 83 patients presenting with acute fever of unknown origin at Maharaj Hospital, a tertiary care medical center in Nakhon Ratchasima, Northeast Thailand. The diagnosis of scrub typhus was confirmed in 30 of these patients (36%) by the indirect immunoperoxidase test. The sensitivity of the test was 87% and its specificity was 94%. The dot blot immunoassay dipstick is accurate, rapid, easy to use, and relatively inexpensive. It appears to be the best currently available test for diagnosing scrub typhus in rural areas where this disease predominates. ❑

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LACK OF ASSOCIATION OF −308A/G *TNFA* PROMOTER AND 196R/M *TNFR2* POLYMORPHISMS WITH DISEASES SEVERITY IN ADULT THAI MALARIA PATIENTS

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It has been suggested that multiple host genetic factors are involved in the onset and progress of severe malaria. In order to detect the susceptibility of genes to severe malaria, a large number of candidate gene approaches have been performed to date. One of the candidate genes is that for tumor necrosis factor alpha (TNFa), because high levels of TNFa are considered to play an essential role in the pathogenesis of cerebral malaria. The association of the −308A homozygote with cerebral malaria was found in Gambian children [McGuire *et al*., 1994], and a similar tendency was observed in Kenyan children [Knight *et al*., 1999]. Recently, it was reported that the serum level of TNFa is particularly increased in Thai cerebral malaria patients [Chuncharunee *et al*., 1997], while an association of the −308A allele with cerebral malaria has never been studied in Thailand. ❑

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CLINICAL TRIAL OF HALOFANTRINE WITH MODIFIED DOSES FOR TREATMENT OF MALARIA IN THE HOSPITAL FOR TROPICAL DISEASES

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The spread of falciparum malaria resistant to chloroquine all over Southeast Asia has led to the increasing use of alternative antimalarial drugs. Halofantrine has been shown to be effective against multidrug resistant *Plasmodium falciparum*. One hundred and twenty falciparum malaria cases were randomly assigned to one of three different halofantrine regimes. Group I (HA1) received 500 mg three times daily for 3 days (total dose: 4,500 mg), group II (HA2) received 500 mg three times daily for the first and the third day (total dose: 3,000 mg) and group III (HA3) received 500 mg three times for one day followed by 500 mg once daily for 7 days (total dose: 4,500 mg). No significant difference in the cure rate was observed among the three regimes (cure rate: 89%, 73%, 97%, respectively). However, the cure rate was significantly higher in the HA3 group when compared to the HA2 group. There were no overt cardiac problems seen in this study. Thus, halofantrine has high efficacy in the recommended treatment dose of 500 mg three times after meals on the first day, followed by 500 mg once a day after a meal for 7 days (total dose: 4,500 mg). ❑

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A CLINICAL AND PHARMACOKINETIC TRIAL OF SIX DOSES OF ARTEMETHER-LUMEFANTRINE FOR MULTIDRUG-RESISTANT *PLASMODIUM FALCIPARUM* MALARIA IN THAILAND

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The efficacy, safety and pharmacokinetics of the six-dose regimen of artemether-lumefantrine (Coartem/Riamet; Novartis Pharma AG, Basel, Switzerland) were assessed in a randomized trial in 219 patients (> or = 12 years old) with acute, uncomplicated *Plasmodium falciparum* malaria in Thailand. One hundred and sixty-four patients received artemether-lumefantrine and 55 received the standard treatment combination of mefloquine-artesunate. Both drugs induced rapid clearance of parasites and malaria symptoms. The 28-day cure rates were 95.5% (90% confidence interval [CI] = 91.7, 97.9%) for artemether-lumefantrine and 100% (90% CI = 94.5, 100%) for mefloquine-artesunate. This high-dose regimen of artemether-lumefantrine was very well tolerated, with very good compliance. The most frequent adverse events were headache, dizziness, nausea, abdominal pain, dyspepsia, vomiting, and skin rash. Overall, only 2% of patients in both groups showed QTc prolongations but without any cardiac complication, and no differences were seen between patients with and without measurable baseline plasma levels of quinine or mefloquine. Plasma levels of artemether, dihydroartemisinin, and lumefantrine were consistent with historical data for the same dose regimen, and were higher, particularly for lumefantrine, than those previously observed with the four-dose regimen, explaining the greater efficacy of the six-dose regimen in a drug-resistant setting. These results confirm the excellent

safety and efficacy of the six-dose regimen of artemether-lumefantrine in the treatment of multidrug-resistant *P. falciparum* malaria. ❑

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LACK OF ASSOCIATION BETWEEN CSF NITRATE AND SERA NITRATE IN FALCIPARUM MALARIA INFECTION

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Nitrate levels in CSF and sera from 16 coma and 19 noncoma falciparum malaria patients were determined using nitric oxide colorometric assay. The medians (range lower, upper limits) of nitrate in sera of comatose and noncomatose patients were 0.28 (0.11, 1.24) and 0.23 (0.05, 0.87) microM, respectively. The medians of nitrate level in CSF of coma and noncoma cases were 0.09 (0.01, 0.28) and 0.15 (0, 1.18) microM, respectively. There was no difference of nitrate level in sera and CSF from comatose or noncomatose patients compared to that in normal sera and CSF. The amount of nitrate in sera and CSF of both groups was not significantly correlated with coma depth, parasitemia, parasite clearance time and time to recovery. Contrast to our *in vitro* study using immunoperoxidase staining, we found inducible nitric oside synthase production by brain endothelial cells during 4-24 hours of coculturing with late stage of *P. falciparum* infected red blood cells. These results suggests that malaria severity can not be differentiated by nitrate level in body fluid. ❑

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CAN TREATMENT OF *P. VIVAX* LEAD TO AN UNEXPECTED APPEARANCE OF FALCIPARUM MALARIA?

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Of 994 patients admitted to the Hospital for Tropical Diseases for *P. vivax* malaria, 104 (10.5%) experienced the appearance of *Plasmodium falciparum* following drug treatment for *P. vivax*. No *P. falciparum* parasites were found in any of the patients by microscopic examination upon admission. The mean time for *P. falciparum* appearance was 12.6 days after the commencement of chloroquine treatment. Patients experiencing the appearance of *P. falciparum* had significantly lower hematocrit, and greater initial *P. vivax* parasite counts. We use a mathematical model to explore the consequences of chloroquine treatment of such mixed infections. Both clinical results and features of the model suggest that such "hidden infections" may be quite common, and that the appearance of *P. falciparum* may be stimulated by treatment of *P. vivax*. ❑

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MALARIA IN SOUTHERN THAILAND: RELATIONSHIP BETWEEN PARASITAEMIA AND DISEASE

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The loose relationship between malaria parasitaemia and clinical symptoms has long been recognized, notably by Field and Niven (1973), who associated high *Plasmodium falciparum* density with increased mortality. More recently, several studies have elaborated the link between parasitaemia and non-severe malaria, particularly in an attempt to identify the pyrogenic density of the malaria parasites (Trape *et al*., 1985; Greenwood *et al*., 1987; Baudon *et al*., 1988; Marsh *et al*., 1989; Luxemburger *et al*., 1996). Other work had failed to find a correlation between clinical symptoms and levels of parasitaemia (Peterson *et al*., 1991) or even infection status (Bassett *et al*., 1991). One difficulty plaguing any attempt to link parasitaemia and disease is the often subjective rating of symptoms. To help control for such subjective measures, Cox, *et al* (1994) based their clinical assessment on whether patients self-reported to a clinic (passive case detection) or were identified by active surveillance; self-reported febrile patients had significantly higher parasitaemia than febrile patients identified in active survey, suggesting sequelae beyond fever in association with higher parasitaemia. Here we report an association between parasitaemia and fever, but an absence of association between parasitaemia and care-seeking behaviour. ❑

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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-2 (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 these, 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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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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SOCIO-ECONOMIC AND ENVIRONMENTAL PROTECTIVE/RISK FACTORS FOR SEVERE MALARIA IN THAILAND

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We conducted a cross-sectional study to identify the socio-economic and environmental protective/risk factors for severe malaria in Thailand. Forty-six cases of severe malaria, 72 cases of non-severe malaria with high parasite biomass and 40 mild malaria cases were included. When comparing severe malaria and non-severe malaria with high parasite biomass, specific logistic regression models showed a significant protective effect for helminths, adjusted odds ratio 0.24 (0.07-0.78) for low body mass index (BMI), adjusted odds ratio 0.11 (0.02-0.58). When comparing severe and mild malaria, a longer residence duration, adjusted odds ratio 0.36 (0.09-0.83), and the use of antimalarial self-medication, adjusted odds ratio 0.08 (0.009-0.84), were associated with protection from severe malaria. Using stepwise logistic regression with all the variables inserted in the model yielded similar results. These findings suggest that specific immunity and self-medication control parasite multiplication, whereas helminths and malnutrition more specifically affect the pathogenesis of severe malaria. ❑

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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 test 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 *Plasmodium falciparum* 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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CR1 DENSITY POLYMORPHISM ON ERYTHROCYTES OF FALCIPARUM MALARIA PATIENTS IN THAILAND

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Complement receptor type 1 (CR1) on erythrocytes shows an inherited numerical polymorphism which correlates with a HindIII-RFLP (restriction fragment length polymorphism) of the CR1 gene in various populations. To investigate the relationship between CR1 density polymorphism and disease severity, we typed 185 Thai patients with acute falciparum malaria (55 severe and 130 uncomplicated) for their genotypes of this polymorphism. The level of expression of erythrocyte CR1 from 42 randomly selected patients was measured by enzyme-linked immunosorbent assay (ELISA). We observed a significantly higher frequency of homozygotes of the CR1 low density allele (LL) among the severe group as compared to the uncomplicated group (P = 0.005). CR1 expression on erythrocytes from patients with the LL genotype was significantly lower than homozygotes with the high density allele (HH) (P < 0.0001) and heterozygotes (HL) (P = 0.013). The results suggest that a genetically-determined low CR1 density on erythrocytes may be a risk factor for developing a more severe form of malaria in Thai subjects. ❑

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ABSENCE OF ASSOCIATION BETWEEN THE ALLELE CODING METHIONINE AT POSITION 29 IN THE N-TERMINAL DOMAIN OF ICAM-1 (ICAM-1 (KILIFI)) AND SEVERE MALARIA IN THE NORTHWEST OF THAILAND

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Intercellular adhesion molecule 1 (ICAM-1) is known to be the endothelial receptor for *Plasmodium falciparum*-infected erythrocytes. Associations of the variant allele coding methionine at position 29 in the N-terminal domain of ICAM-1, ICAM-1(Kilifi), with severe malaria have been investigated in African populations, and the results of these investigations have varied widely. In this study, we investigated a possible association between the ICAM-1(Kilifi) and severe malaria in adult malaria patients living in northwest Thailand. The frequencies of the ICAM-1(Kilifi) among patients with mild malaria, with non-cerebral severe malaria, and with cerebral malaria were 1.7%, 2.7%, and 2.3%, respectively. This variant showed neither positive nor negative association with severe malaria in Thailand. ❑

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NATURAL HUMAN IgG SUBCLASS ANTIBODIES TO *PLASMODIUM FALCIPARUM* BLOOD STAGE ANTIGENS AND THEIR RELATION TO MALARIA RESISTANCE IN AN 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 a malaria endemic area in Kanchanaburi Province, western Thailand, were determined by enzyme-linked immunosorbent assay (ELISA). In this study, IgG_3 and IgG_1 were shown to be the predominant subclasses. Generally, IgG_2 was coexpressed with IgG_1 and IgG_3 while IgG_4 was found to coexpress with the other three IgG subclasses. The levels of specific IgG_1, IgG_2, and IgG_3 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 indicate that the higher antibody production required continuous stimulation under natural conditions. Furthermore, the levels of specific IgG_1, IgG_2 and IgG_3 increased in immune individuals without clinical malaria, reported in adolescents and adults, were associated with malaria resistance. Similar results were found in children with different patterns of IgG subclasses in which the specific IgG_2 and IgG_3, but not IgG_1 was related to resistance. ❑

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ANTIBODIES SPECIFIC FOR HEAT SHOCK PROTEINS IN HUMAN AND MURINE MALARIA

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Heat shock proteins (HSPs) are immunodominant antigens recognized by the host immune system in various infectious diseases. We analyzed HSP-specific antibodies, including immunoglobulin G (IgG), IgM and IgA, in sera from malaria patients in Thailand by using an enzyme-linked immunosorbent assay. All of the antibodies to HSP90 were remarkably increased in the patients compared with those in controls, while only IgM to HSP70 or IgA to IISP65 was significantly elevated. Further experiments showed that anti-HSP IgG was significantly increased in C57BL/6 mice infected with a non-lethal strain of *Plasmodium yoelii,* with anti-HSP90 IgG being the most elevated. These results suggest that the antigenic potential of HSP90 is higher than those of HSP70 and HSP65 in malaria infection. ❑

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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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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 =.0004), with a median ratio of 0.2:1.0 (range, 0.1-0.7). The estimated median percentage of parasite 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 =.036) and the subsequent RESA-RBC survival significantly shorter (P =.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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A STUDY OF ANEMIA IN PREGNANT WOMEN WITH *PLASMODIUM FALCIPARUM* AT DISTRICT HOSPITALS IN VIENTIANE, LAO PDR

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A descriptive cross-sectional study was carried out among pregnant women attending antenatal care at the district hospital, with suspected clinical manifestation

of malaria in order to determine the prevalence of anemia and malaria among pregnant women and to determine any correlation between degree of anemia and degree of malaria parasitemia in pregnancy with malaria infection. This is a quantitative research method using face-to-face questionnaire. This study was undertaken at the district hospitals of Vientiane Prefecture and Vientiane Province. Sixty-eight pregnant women with suspected malarial clinical manifestations attending the antenatal care at these hospitals were recruited between June-October, 1998. The subjects were asked about their sociodemographic, socio-economic characteristics, gravida and parity, gestational age, last pregnancy and past history of hematological diseases. Blood samples (dry smear for thick and thin blood films) were examined at the same time for *Plasmodium falciparum.* The study showed that the prevalence of anemia (Hb < 11 g/dl) and severe anemia (Hb 4-6.9 g/dl) in the total sample population was 48.5% and 8.8%, respectively. However, the prevalence of anemia among pregnant women with malaria was 68.75% compared to those without malaria infection (42.31%), but the difference was not statistically significant (p=0.117). A plausible explanation could be the small sample size. The prevalence of severe anemia in pregnancy with malaria parasitemia was 18.8% compared to those without parasitemia (5.8%). The difference was not statistically significant (p=0.102). The difference in the mean hemoglobin level in falciparum positive cases and falciparum negative cases was clinically and statistically significant (RR = 1.63 and p=0.00679). There was some evidence of a negative correlation between the degree of anemia and parasitemia count (r= -0.19 and r2= -0.04). In conclusion, this population had high prevalence of anemia in pregnant women and *P. falciparum* may be the main factor associated with anemia. There is a need to investigate other causes of anemia among pregnant women. Our results suggest that frequent and regular antenatal monitoring is necessary for pregnant women. They should be encouraged to attend antenatal clinics through health education, increased health personnel awareness of proper management for pregnant women with fever from malarial endemic areas. There is a need for further research in this area in order to obtain adequate sample size. ❑

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CLINICAL PRESENTATION OF CHILDHOOD MALARIA IN SAVANNAKHET PROVINCE, LAO PDR

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A descriptive study on the clinical presentation of childhood malaria was conducted in Savannakhet Province, Lao People's Democratic Republic. It aimed to describe the clinical features and to determine the association between the severity of malaria and the initiation or delay of treatment. A total number of 92 children 1-14 years of age with confirmed malaria diseases were enrolled in this study. Fifty-six cases (60.9%) had illness for less than 3 days before hospitalization and 36 cases (39.1%) for more than 3 days. Twenty-nine cases (31.5%) had self administered antimalarial medication before admission (9 cases of chloroquine, 16 cases of quinine and 4 cases of artesunate). Ten cases (10.9%) had abnormal consciousness, of whom 7 cases (7.6%) had confusion but responded to verbal command and 3 cases (3.3%) were in coma, did not respond to painful stimuli, but had reflex. Two cases 2.2%) had convulsions, 11 cases (12.0%) had dehydration, 47 cases (51.1%) had vomiting, 18 cases (19.6%) had hepatomegaly and 19 cases (20.7%) had splenomegaly. There was a statistically significant association between consciousness levels and the duration of illness before admission < or = 3 days and > 3 days (p = 0.01) while there was no significant difference between parasitemia density and the duration of illness before admission (p > 0.05). ❑

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

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

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IS THERE ANY ARTEMISININ RESISTANCE IN FALCIPARUM MALARIA?

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We reported two cases of complicated falciparum malaria who had poor response to artesunate with delayed parasite clearance times. They were splenectomized patients who were treated with high doses of artemisinin derivatives. Our cases showed the importance of the spleen in the clearance of malaria parasites and had different clinical outcome, one fatal and one recovery. The host factors, the parasitemia count, the quality of antimalarial chemotherapy and blood level of the antimalarial drugs must be considered in relation to the causes of the delayed clearance of parasitemia. ❑

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IgE DEPOSITION IN BRAIN MICROVESSELS AND ON PARASITIZED ERYTHROCYTES FROM CEREBRAL MALARIA PATIENTS

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Postmortem brain tissues of 21 cerebral malaria cases were obtained in Myanmar and Vietnam. The tissues were examined by light microscopy and by an immunohistochemical method. Brain microvessels (capillaries and venules) were examined for the presence of immunoglobulins IgE and IgG, *Plasmodium falciparum* antigen, and parasitized erythrocytes (PRBC). Deposition of IgE, IgG, and *P. falciparum* antigen was observed in the microvessels from all specimens examined. Sequestered PRBC in the microvessels were positive for IgG in all 21 cases and for IgE in six cases. In the latter cases, the percentage of microvessels with sequestered PRBC was > 50%, with the frequency of IgE-positive cells ranging from 42% to 52%. In contrast, in five cases that were only weakly positive for IgE, the percentage of microvessels with sequestered PRBC was remarkably low (< 1%). These data

indicate that the degree of deposition of IgE in microvessels and on PRBC from cerebral malaria patients correlated with that of PRBC sequestration. As IgE-containing immune complexes are known to induce local overproduction of tumor necrosis factor-alpha (TNF-alpha), a major pathogenic factor in cerebral malaria, IgE may contribute to the pathogenesis of this severe disease. ❑

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THERAPEUTIC RESPONSES TO QUININE AND CLINDAMYCIN IN MULTIDRUG-RESISTANT FALCIPARUM MALARIA

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Therapeutic responses to clindamycin in combination with quinine were assessed in adult Thai patients with uncomplicated multidrug-resistant *Plasmodium falciparum* malaria. In total, 204 patients were randomized to receive a 7-day oral treatment regimen of quinine (Q(7)) either alone (n = 68), in combination with clindamycin (Q(7)C(7); n = 68), or in combination with tetracycline (Q(7)T(7); n = 68). All patients had uncomplicated recoveries with no serious adverse effects. Fever clearance times for both of the two combination regimens (median of 47 h and range of 8 to 120 h for Q(7)C(7) and median of 36 h and range of 8 to 117 h for Q(7)T(7)) were significantly shorter than that for the Q(7)-only regimen (median, 56; range, 4 to 152 h) (P = 0.002). Parasite clearance times (overall mean ± standard deviation, 78 ± 23 h) were not significantly different between the three treatment groups (P = 0. 98). The cure rates assessed at 28 days of follow-up were 100% for Q(7)C(7) and 98% for Q(7)T(7), whereas the cure rate was 87% for the Q(7)-only regimen (P < or = 0.04). Clindamycin in combination with quinine is a safe and effective treatment for multidrug-resistant *P. falciparum* malaria. This combination may be of particular value in children and pregnant women, in whom tetracyclines are contraindicated. ❑

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INFLUENCE OF HEMOGLOBIN E TRAIT ON THE ANTIMALARIAL EFFECT OF ARTEMISININ DERIVATIVES

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To determine whether hemoglobin E trait influences the antimalarial effect of artemisinin derivatives, we retrospectively compared 32 case patients with hemoglobin E trait with 32 control patients who did not have hemoglobin E, beta-thalassemia, glucose-6-phosphate dehydrogenase deficiency, or alpha-thalassemia trait on the basis of a mean corpuscular volume > or =78 femtoliters. All patients were admitted to the Hospital for Tropical Diseases in Bangkok, Thailand, with acute falciparum malaria. Control patients were matched to case patients with hemoglobin E trait by treatment with artemisinin derivatives versus other antimalarial drugs, by ethnic group, and by parasite count. Among 38 patients treated with artemisinin derivatives, the presence of hemoglobin E trait was associated with significantly faster parasite clearance (2.9-fold; 95% confidence interval [CI], 1.4-6.3; P=.006). Among 26 patients treated only with other antimalarial drugs, hemoglobin E trait did not significantly enhance parasite clearance (hazards ratio, 1.1; 95% CI, 0.5-2.5; P=. 8). Hemoglobin E trait may potentiate the antimalarial effect of artemisinin derivatives. ❑

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THE COMBINED TREATMENT OF INTERFERON ALPHA-2A AND THYMOSIN ALPHA 1 FOR CHRONIC HEPATITIS C: THE 48 WEEKS END OF TREATMENT RESULTS

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The efficacy and safety of IFN alpha 2a and Thymosin alpha1 combination therapy in patients with chronic hepatitis C were determined. Twelve chronic hepatitis C patients (9 M, 3F), with positive HCV-RNA and histology compatible with chronic hepatitis C were included in this open, prospective study. Each patient received a combination therapy of IFN alpha 2a 3 mU s.c. TIW and Thymosin alpha1 1.6 mg s.c. twice a week for 52 weeks. Up to the present, 11 patients are still being followed-up after the end of 52 weeks' treatment. One patient dropped out after 32 weeks of follow-up due to noncompliance. Responses to treatment were evaluated by measuring serum HCV-RNA levels determined by RT-PCR. and serum amino transferases at the end of 48 weeks of treatment (end of treatment response: ETR). There were 8 naive and 4 previously IFN treated patients with partial response with a mean age of 45.0 +/- 10.1 (mean +/- SD). The mean duration from diagnosis until treatment was 25.1 +/- 22.9 months. The mean AST, ALT, and HCV-RNA levels before treatment were 79.5 +/- 36.8 U/L, 128.3 +/- 68.5 U/L, and 3.9+1.9 x 10(5) copies/ml respectively. Serum AST, ALT, and HCV-RNA levels were significantly lower at week 24 and 48 after treatment compared to before treatment ($p<0.05$). Of 11 cases, complete HCV-RNA clearance at week 24 was noted in 33.3 per cent, whereas, normal alanine aminotransferase values (ALT < 40 U/L) were observed in 41.7 per cent of patients. Complete HCV-RNA clearance and normal alanine aminotransferase at week 48 were seen in 45.5 per cent of the patients. At the end of week 48, complete response occurred in 4 of 5 naive patients. Minor side effects were observed during treatment with this combination therapy and these included myalgia (33.3%), a mild form of alopecia (33.3%), and weight loss (8.3%). In patients with chronic hepatitis C, Interferon alpha 2a and Thymosin alpha1 combination therapy produced a good response rate, especially in naive patients with an acceptable safety profile. The sustained response will be determined after the completion of follow-up for another 6 months. ❑

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PSEUDOMELANOSIS DUODENI: ASSOCIATION WITH HYPERTENSION AND CHRONIC RENAL FAILURE: CASE REPORT

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We present the first reported case with typical endoscopic and histological findings from Thailand. An 80-year-old man presented with chronic periumbilical abdominal pain for 3 months and melena for one week. He had had hypertension for 17 years, chronic renal failure for 4 years and gouty arthritis for 3 years. Panendoscopy was done and showed diffusely scattered small black and brown pigmentation over the stomach and duodenum. Tissue biopsies from the black pigmented lesions were taken for further microscopic and histochemical evaluation. Histological finding and special histochemical stains, Fontana stain, revealed mild chronic inflammation with accumulation of hemosiderin pigment in the lamina propria of the stomach and duodenal villi. This condition is called Pseudomelanosis duodeni. The literature of this condition was also reviewed. ❑

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ADENOCARCINOMA OF THE PANCREAS: THE CLINICAL EXPERIENCE OF 45 HISTOPATHOLOGICALLY PROVEN PATIENTS, A 6 YEARS STUDY

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A retrospective study of 45 cases of adenocarcinoma of the pancreas at Chulalongkorn University Hospital from 1993 to 1998 was reviewed by clinical and histopathological criteria. 55.6% of the patients were males and 44.4% were females. The mean age of the patients was 59.5 ± 10.0 years. The common presenting symptoms and signs were epigastric discomfort (80.0%), weight loss (60.0%) and jaundice (51.1%). 53.3% of the patients were screened for a tumor marker (CA 19-9) and 87.5% of these had high level of CA 19-9 (> 37 IU/ml). 35 of 45 patients had tumors located in the head of the pancreas. Most of the cases were investigated by using radiological imaging (ultrasonography or computerized tomography of the abdomen). 77.8% of the histopathological data were made by the operation, and the rest (22.2%) were performed by a fine needle aspiration from the pancreatic mass or liver metastasis. Whipple operation and bypass procedure were the most common surgical procedures in our studies. 55.6% of the patients had post-treatment complications from all modalities consisting of gastrointestinal bleeding, respiratory failure and infection. However, the mortality rate within 30 days postoperatively was 8.11%, which was due to blood loss during the operation and to infections. The post treatment mortality rate from all modalities was 33.3%. The average duration from diagnosis until death was 82.3 days. ❑

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STUDIES OF THE NEUROTOXICITY OF ORAL ARTEMISININ DERIVATIVES IN MICE

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Intramuscular injections of high doses of the oil soluble antimalarial artemisinin derivatives, artemether and arteether, produce an unusual pattern of selective damage to brain stem centers in experimental mammals, predominantly those involved in auditory processing and vestibular reflexes. We have shown recently in adult Swiss albino mice that parenteral artesunate, a water soluble derivative, is significantly less neurotoxic than intramuscular artemether in this murine model. Using the same model, in which the drugs were administered daily for 28 days, the neurotoxic potential of the oral drugs was assessed and compared with the parenteral routes of administration. The dose causing neurotoxicity or death in 50% of animals (ED_{50}) was approximately 300mg/kg/day of oral artemether and artesunate to 50mg/kg/day for intramuscular artemether. Doses of intramuscular artemether >100mg/kg/day were uniformly lethal. When oral artemether was given in peanut oil, there was an increase in neurotoxicity and mortality compared with the aqueous suspension (p=0.002), and when the food pellets were coated with artemether in oil, giving relatively constant oral intake, neurotoxicity was further increased; ED_{50} 150 mg/kg/day (p=0.017). These data indicate that once daily-oral administration of artesunate or artemether is relatively safe, presumably because the central nervous system is exposed transiently, whereas constant exposure either from depot intramuscular injection of oil-based drug, or constant oral intake carries relatively greater neurotoxic potential. ❑

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GENERAL CHEMOTHERAPY OF MALARIA

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Malaria kills approximately five people every minute. The increasing prevalence of *Plasmodium falciparum* malaria parasites resistant to the cheap, short-course, widely available drugs, such as chloroquine and pyrimethamine-sulfadoxine, is forcing changes in the strategy and cost of malaria treatment. In order to optimize the safe and efficient cure of malaria patients, many factors relating to the host (e.g. age, pregnancy, immunity) and the parasite (e.g. drug-resistant patterns) need to be considered. There is growing support for the use of antimalarials in combination to delay the development of clinically important resistance to the current generation of new drugs. ❑

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ALANINE METABOLISM IN ACUTE FALCIPARUM MALARIA

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Alanine disposition and liver blood flow, assessed by indocyanine green (ICG) clearance, were measured simultaneously in 10 patients with falciparum malaria (6 severe and 4 moderately severe malaria). The mean (SD) ICG clearance during acute malaria was not significantly lower than in convalescence (21.6 + 9.3 vs. 34.1 + 15.5 mL. min^{-1}. kg^{-1}, P = 0.25) although clearances were less than 15 mL. min^{-1}. kg^{-1} in the two fatal cases. Following intravenous infusion of alanine (0.3 g/kg), glucose increments ($AUC_{0\text{-}55\ min}$) were lower in patients with severe malaria compared to moderately severe patients (median = 508 vs. 808 mmol. min. L^{-1}; P = 0.055). There were no significant differences in the other metabolite increments (alanine, lactate, and pyruvate; P >0.27). The two fatal cases had markedly delayed alanine removal (larger $AUC_{0\text{-}55\ min}$), prolonged $T_{1/2}$ and slower clearance, P <0.007). Overall, the increments in blood alanine correlated directly with lactate increments (r_s = 0.84; P = 0.002) and inversely with glucose (r_s = -0.70; P = 0.025). The $AUC_{0\text{-}55\ min}$ of alanine, glucose, lactate and pyruvate and the ratio of lactate to pyruvate $AUC_{0\text{-}55\ min}$ were all lower in convalescence than in acute malaria (P = 0.07 for glucose and < 0.017 for lactate and pyruvate). There was a significant inverse correlation between ICG clearance and the post-infusion increments of lactate (r_s = -0.63, P = 0.049) and pyruvate (r_s = -0.74, P = 0.014). These studies suggest that alanine clearance is impaired in acute falciparum malaria in proportion to the severity of illness and suggest a pivotal role of anerobic glycolysis in the pathogenesis of hypoglycemia in severe malaria. ❑

NEUROPATHOLOGICAL TOXICITY OF ARTEMISININ DERIVATIVES IN A MOUSE MODEL

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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 results in more clinical abnormalities than other methods of drug administration. We have confirmed this clinical finding with microscopic examination of mouse brainstem. The neuropathological toxicity of the intramuscular artemisinin derivatives was examined and compared to the oral artemisinin derivatives. Intramuscular artemether given at a dose of 50-100 mg/kg/d for 28 days caused neuropathological damage to the brainstem. This abnormality is dose-dependent and occurred only in intramuscular artemether treated mice. There were no neuropathological abnormalities in either the same dose or higher doses (200-300 mg/kg/d) of artemether given by coated food pellet or gavage or following oral or intramuscular artesunate and in the control groups. The neurons in the Trapezoid nucleus, gigantocellular reticular nucleus and inferior cerebellar peduncle were found to be the most sensitive to damage by artemether. The neurons in the section level C had the most neuropathic damages when compared to other examined part of brainstem (mean ± SD neuropathic scores = 1.49 ± 0.858 VS 0.83 ± 0.287; p = 0.004). These data indicate that behavioural assessment of neurotoxicity is as sensitive and may be more sensitive than neuropathological assessment in this mouse model. ❑

NEUROPATHOLOGICAL TOXICITY OF ARTEMISININ AND ITS DERIVATIVES 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 clinical abnormalities than other methods of drug administration. We have confirmed this clinical finding with microscopic examination of mouse brainstem. The neuropathological toxicity of the intramuscular artemisinin derivatives was examined and compared to the oral artemisinin derivatives. Intramuscular artemether given at a dose of 100 mg/kg/d caused neuropathological damage to the brainstem. This abnormality is dose-dependent. There were no neuropathological abnormalities in the artemether coated food pellet, intramuscular artesunate, oral artemether, oral artemether in powder, oral artesunate and in the control groups. Trapezoid nucleus, gigantocellular reticular nucleus and inferior cerebellar peduncle were found the most sensitive to artemisinin derivatives in each section level of brainstem. The degenerative neurons in the hindbrain from hypoglossal nerve had the most neuropathic damages when compared to other part of brainstem. These data indicate that behavioural assessment of neurotoxicity is more sensitive than neuropathological assessment in a mouse model. ❑

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DOG GNATHOSTOMOSIS IN NAKHON NAYOK PROVINCE

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One thousand, one hundred and ninety-three fecal samples of stray and domesticated dogs were collected from 21 localities of four districts - Muang, Ongkharak, Ban Na and Pak Phli - in Nakhon Nayok Province, and examined especially for the presence of *Gnathostoma spinigerum* eggs. Seven of 490 samples (1.4%) from five areas of Muang District were positive for the helminth eggs. Two of 223 samples (0.9%) from two areas of Ongkharak District, and five of 264 samples (1.9%) from all four areas of Ban Na District were also positive, whereas those from all four areas of Pak Phli District were negative. The overall positive rate for gnathostome eggs was 1.2% with the highest rate of 4.2% being in Don Yo of Muang District.

Six other species of helminth eggs, including hookworm spp (73.0%), *Toxocara canis* (3.8%), *Trichuris vulpis* (1.8%), *Trichostrongylus*-like sp (0.2%), *Spirometra mansoni* (11.1%) and *Hymenolepis diminuta* (0.4%) were also encountered in these stool samples, resulting in an overall positve rate for all species of worm eggs of 73.8%. Multiple infections of up to four species of eggs per fecal sample were observed in two specimens (0.2%). Thirteen samples (1.1%) were triple infections, 179 samples (15.0%) were double infections, while 686 samples (57.5%) were single infection. The single infection of fecal specimens comprised 679 samples (56.9%) with hookworm, four samples (0.3%) with *T. canis* and three samples (0.2%) with *S. mansoni*. ❑

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PREVALENCE OF FILARIAL INFECTION IN SANGKHLA BURI AND SUAN PHUNG ASSESSED BY ICT CARD TEST, IGG4 ELISA WITH URINE AND OG4C3 ELISA

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In 24-26 March, 2001, 519 people in Sangkla Buri, Kanchanaburi Province were examined by ICT card test and IgG4 ELISA which used urine as samples (urine ELISA). Another group of 84 people in Suan Phung, Ratchaburi Province was examined by ICT test and urine ELISA in March-April, 2001. A total of 67 ICT positives from Sangkhla Buri were re-checked by Og4C3 and urine ELISAs in 4-8 June, 2001. Both ICT and Og4C3 tests detect circulating antigens of *Wuchereria bancrofti*, and the sensitivity and specificity of the methods have been reported to be very high. The urine ELISA is a new test which detects filaria-specific IgG4, and showed 95.6% sensitivity and 99.0% specificity. The prevalence by ICT test in Sangkla Buri was 16.8% (male 20.6%, female 13.3%), and that in Suan Phung 10.7%. The urine ELISA gave the prevalence of 21.2% (male 26.2%, female 16.6%) in the former and 7.1% in the latter. The ELISA in Sangkhla Buri revealed 10 positives in ages 7-15 years old, suggesting that filariasis transmission had been occurring in recent years.

In the study, we noticed that ICT resulted in a very high positive rate relative to the rate obtained by urine ELISA. Therefore, we re-examined known ICT positives by Og4C3 and urine ELISAs. Before this examination, the positives had been treated with a 12-day DEC regimen in early April. Of 67 ICT positives, 22 (32.8%) and 24 (35.8%) were positive with Og4C3 assay and urine ELISA, respectively. The difference between the two antigen assays was felt to be much bigger than expected even when the effect of DEC treatment was taken into account. We will discuss the reasons for the discrepancy. ❑

Presented at: Joint International Tropical Medicine Meeting, Bangkok, 2001.

BASELINE STUDY OF SOIL-TRANSMITTED HELMINTH INFECTIONS IN NAKHON SI THAMMARAT PROVINCE, THAILAND

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The study was conducted in Sichon and Chalerm Phrakiat Districts, Nakhon Si Thammarat Province. Health behavior relating to soil-transmitted helminthiasis was obtained by interviewing the parents of children who attended either one of the two selected schools in each of the Districts. The results revealed that about 85% and above of the population of both districts had perceptions about the transmission, prevention and control of the infection.

The infection rates with soil-transmitted helminths of schoolchildren in Wat Krou Chou Primary School, Sichon District and Wat Thangphoon Primary School, Chalerm Phrakiat District were 23.7% and 24.7%, respectively, with an overall infection rate of 24.1%. They were mainly infected by hookworm (21.1%), while *Trichuris* infection was less, only 5.4%. Light intensity infection was the most prominent, 85.7% for hookworm, 100% for *Trichuris* in Wat Krou Chou; 90.2% for hookworm and 96.3% for *Trichuris* in Wat Thangphoon.

The anemic status of schoolchildren aged 9-10 years was assessed by measuring hemoglobin and hematocrit values. There was no significant difference in hemoglobin values in children with and without hookworm infection. However, there was a significant difference in the hemoglobin of these schoolchildren after adjusting for school and age. ❑

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CONTROL OF SOIL-TRANSMITTED HELMINTHS IN PRIMARY SCHOOL SOUTHERN THAILAND

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In this investigation, we aim to study the model for control of soil transmitted helminths (hookworm) in school children, with the hypothesis that different geographic, demographic and occupational characteristics can influence beliefs, perceptions and behaviors in prevention and control of soil-transmitted helminthes in schoolchildren. Comparisons of control models between schoolchildren that have different characteristics were performed.

We evaluated knowledge, attitudes, and perceptions of prevention and control of soil-transmitted helminthes (hookworm) among school children before and after giving them the health education program. The prevalence of soil-transmitted helminths among children also performed (before and after giving health education) by using stool examination. We found that there is no clear evidence to conclude that different geographic, demographic and occupation al factors can influence the incidence of soil-transmitted helminths. Also, these characteristics did not clearly influence knowledge, attitudes, or behavior in prevention and control of soil-transmitted helminths among schoolchildren.

However, we can conclude that a health education program given by a schoolteacher can help to reduce the incidence of soil transmitted helminths in schoolchildren significantly. This health education program also can influence the knowledge, attitudes and behaviors in prevention and control of soil transmitted helminths among schoolchildren in a school that does not have any intervention program (health education). ❑

FACTORS AND HEALTH BEHAVIOR CONCERNING SOIL-TRANSMITTED HELMINTHIASES

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Soil-transmitted helminthiases are still an important public health problem in Thailand. The diseases directly affect the improvement of the quality of life of people, especially the people who live in remote areas of the country, and affect the country's economy indirectly. Investigation and control of the diseases have been continuously carried out for more than 80 years, since 1917, with emphases on different methodologies. This included, for example, the campaigns of latrine construction, mass chemotherapy and health education. However, until now, prevalence of the infections has still not decreased much. The reason for this is due to factors and health behaviors of most of the people, which do not change; for instance, defecation on the ground outside the latrine, eating unclean/unwashed food. Therefore, drug treatment and health education are still necessary to be implemented now and then to manage this issue. Moreover, it is also necessary to look for new control measures to reduce and eradicate these infections so as to bring about the better health and quality of life of the people, and also to improve the economy of the country. ❑

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PARASITIC CONTAMINANTS IN FOOD

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There is a wide variety of food and food products that may be contaminated with one or more parasites, enabling transmission to human beings. The prevalence of the specific parasites in food and food supplies varies between countries and regions. The reported sources of food and food product contamination with parasites are pigs, cattle, fish, crabs, crayfish, snails, frogs, snakes and aquatic plants. One of the major factors influencing the prevalence of parasitic infections in the population is the habit, and traditional popularity, of eating raw or inadequately cooked foods and their products. The parasites that may be acquired by eating these foods are helminths (in the group nematodes, trematodes, cestodes) and protozoa. The major parasites are *Trichinella, Gnathostoma, Angiostrongylus, Anisakis, Paragonimus, Clonorchis, Opisthorchis, Fasciola, Fasciolopsis, Echinostoma, Taenia, Sparganum* and *Toxoplasma*.

These food-borne parasitic infections are public health problems in many countries of the world. The contamination of food by parasites affects many areas concerning humans; these include the livestock industry, agriculture, and food manufacturing and processing. Unsafe foods must be condemned and destroyed.

Today there is increasing overseas travel and hence there is the risk of humans' acquiring food-borne parasitic infections through eating native food or raw food while travelling. Moreover, the consumption of imported livestock and foods, especially from endemic areas of food-borne parasitic zoonoses, can be the cause of acquiring infection. Awareness should be heightened wherever and whenever raw or inadequately cooked food may be consumed. ❑

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ANGIOSTRONGYLIASIS: ANALYSIS OF A CHROMATOGRAPHICALLY PURIFIED ANTIGEN OF *ANGIOSTRONGYLUS CANTONENSIS* ADULT WORMS BY IMMUNOBLOT

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A crude extract of female and male adult worms of *Angiostrongylus cantonensis* was partially purified through Sephacryl S-200 gel chromatography. The fraction peak 2 had been previously evaluated to be the best functional antigen among four peaks, with a sensitivity of 96.3% and a specificity of 96.53%, by indirect ELISA. In the present study, the antigen peak 2 was determined for its antigenicity by immunoblot for searching a diagnostic band. The detection of IgG from human angiostrongyliasis was responsible for the antigen of 31 kDa, not with negative controls and eighteen other helminthic infections. Unfortunately, it was crossreactive with toxocariasis (1/2) and hydatidosis (1/2) sera, but only one case of hydatidosis is proven and officially reported in Thailand. No toxocariasis case has ever been reported. The antigen was a glycoprotein analyzed by peroxidase-labelled Concanavalin A and Coomassie brilliant blue staining. It is necessary to study the specific antigenicity of the 31 kDa antigen by sophisticated technique and for it to be proven more with different kinds and numbers of other parasitic infections, including toxocariasis and hydatidosis. ❑

Presented at: Joint Internation Tropical Medicine Meeting, Bangkok, 2001.

STRONGYLOIDIASIS: IMPROVEMENT OF ANTIGEN PREPARATION FOR INCREASING THE SPECIFICITY OF IgG-ELISA

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Two preparations of antigens for diagnosis of strongyloidiasis were prepared by the extract of infective larvae of *Strongyloides stercoralis* designed as crude antigen (CA) and molecular weight cut-off antigen (MWCOA). Both antigens were analyzed by indirect ELISA against sera of strongyloidiasis (26 cases), other helminthiases (167) and normal controls (30). The larvae were obtained from fecal culture by some modification of the polyethylene tube technique after screening tests by simple smear technique had been done, in triples per case. The larvae were extracted with distilled water and further sonicated to obtain the supernatant, CA. A part of the CA was separated for an antigen containing molecules lower than 30 kDa by ultrafree-MC centrifugal filter tube (PLTK), designed as MWCOA. On analysis of the tests, CA gave 96.15% sensivity and 40.12% (67/167) specificity at cut-off value 0.980 (5SD); meanwhile, the false positives were 19 from 20 different kinds of helminthiases. Only paragonimiasis westermani infections showed true negative. The MWCOA showed 96.15% sensitivity at cut-off value 0.71 (4SD) and the specificity of the test was 79.04% (132/167), higher than that of CA. False positives also appeared with 15 kinds of helminthiases, but no cross reaction occurred with capillariasis, taeniasis, paragonimiasis heterotremus, paragonimiasis westermani or schistosomiasis. This study produced greater specificity for MWCOA than for CA. Due to the reduction of cross-reactivity, a purification of MWCOA will be done to gain particularly antigenic molecules for strongyloidiasis diagnosis. ❑

Presented at: Joint International Tropical Medicine Meeting, Bangkok, 2001.

COMPARISON OF ELISA AND GPAT IN DIAGNOSIS OF BOVINE FASCIOLOSIS USING EXCRETORY-SECRETORY ANTIGEN

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This study aimed to develop a sensitive and specific immunodiagnostic method for *Fasciola gigantica* infection using excretory-secretory (ES) antigen, from culturing living worms collected from the livers of naturally infected cattle at local slaughterhouses around Bangkok. The antigen was reacted with 269 cattle sera composed of 15 experimental fasciolosis sera, 15 calf sera, 119 heterologous sera, and 120 field-stool negative sera by indirect enzyme-linked immunosorbent assay (indirect ELISA) and gelatin particle indirect agglutination test (GPAT).

From ELISA, the sensitivity, specificity, positive predictive value, negative predictive value, and efficacy of the test were 100%, 23.4%, 23.4%, 100%, and 37%, respectively. When the antigen was applied with GPAT, sensitivity, specificity, positive predictive value, negative predictive value, and efficacy of the test were 100%, 11.1%, 25%, 100%, and 31.4%, respectively.

ELISA values and GPAT titers of cattle sera using ES antigen were moderately correlated, with a correlation coefficient of 0.57.

From this study, both ELISA and GPAT were highly sensitive but gave low specificity. It showed that these methods, using ES antigen, might not be suitable for the diagnosis of fasciolosis as they showed cross-reaction with many parasitic infections. ❑

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MEDULLARY GNATHOSTOMIASIS IN A WHITE PATIENT: USE OF IMMUNODIAGNOSIS AND MAGNETIC RESONANCE IMAGING

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A 48-year-old French diplomat presented with a sensory-motor paraparesis of rapid onset, leading to paraplegia. Successive magnetic resonance image scans showed lesions of the thoracic spinal cord that were at different levels from one examination to the next. Specific anti-gnathostome antibodies were detected by means of enzyme-linked immunosorbent assay and Western blot test in both plasma and cerebrospinal fluid. Albendazole treatment prevented disease progression, but only partial regression of the neurologic symptoms was obtained. ❑

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DIAGNOSIS OF HUMAN OPISTHORCHIASIS

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Opisthorchiasis *viverrini* is a liver fluke infection causing a serious public health problem in Thailand, Laos, Cambodia and South Vietnam because it acts as a strong promoter of cholangiocarcinoma. Diagnoses of human opisthorchiasis are based on four approaches due to clinical manifestations, parasitological, molecular biological, and immunological methods, which still have problems. Clinical manifestations of the patients are practically indistinguishable from other liver diseases. The features of the *O. viverrini* eggs using a light microscope as a parasitological method are difficult to differentiate from the minute intestinal flukes' eggs. Molecular biological methods, polymerase chain reaction (PCR) techniques are very complicated, expensive, and time-consuming, although they are highly sensitive and specific. PCR can detect a single egg in an experimental animal feces and a test has been proven in the field practice. At present, their applications for the detection of human specimens have never been reported. Actually, immunological tests are the choice of these approaches; the techniques can possibly be developed for routine work, field work, and epidemiological studies. Enzyme-linked immunosorbent assay (ELISA) and immunoelectrotransfer blot assays are the most published immunological tests in the detection of *O. viverrini*-specific antigens (coproantigens) and antibodies (IgM, IgG, IgA or IgE antibodies). The monoclonal antibodies are prepared to detect the coproantigens in stool specimens while the crude somatic and excretory-secretory antigens from the adult worm, metacercaria, eggs, and snail intermediate hosts are prepared to detect the antibodies in sera. The appropriate amount, type, and efficacy of antigen and antibody preparations are considered to prevent cross reactions between parasites. Advantages and disadvantages of these methods are discussed. ❑

Presented at: Joint International Tropical Medicine Meeting, Bangkok, 2001.

DIAGNOSIS OF HUMAN OPISTHORCHIASIS WITH COCKTAIL AND ELUTED *BITHYNIA GONIOMPHALOS* SNAIL ANTIGENS BY INDIRECT ELISA

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This study aimed to develop a sensitive and specific immunodiagnostic method for *Opisthorchis viverrini* infection using purified *Bithynia goniomphalos* snails as a cocktail antigen by gel filtration chromatography and an eluted antigen by SDS-polyacrylamide gel electrophoresis and electroelution method. Effectiveness and specificity in the serological diagnosis of opisthorchiasis using these two prepared antigens were tested by indirect ELISA against sera of 61 cases with opisthorchiasis, 125 cases with other parasitic infections and 30 normal healthy sera. The sensitivity, specificity, positive and negative predictive values of cocktail antigen were 95.1%, 79.4% 64.4% and 97.6%, respectively, at the cut off OD of 0.786. Cross reactions were observed with trichuriasis (1/7), trichinellosis (5/10), strongyloidiasis (5/10), hookworm infection (5/9), angiostrongyliasis (2/9), toxocariasis (1/5), ascariasis (1/8), filariasis (1/6), taeniasis (1/9), hymenolepiasis (1/4), hydatidosis (2/3) and gnathostomiasis (7/9). No cross-reacton was found with normal healthy sera. The sensitivity, specificity, positive and negative predictive values of eluted antigen (53 kDa) were 96.7%, 92.2%, 84.3% and 98.6%, respectively, at the cut off OD of 0.814. Cross reactions were observed with strongyloidiasis (4/10), angiostrongyliasis (1/9), gnathostomiasis (3/9), hymenolepiasis (1/4) and paragonimiasis (2/4). No cross-reaction was found with normal healthy sera. Further studies on improvement of cocktail and eluted antigen preparation may provide a better specific diagnosis of opisthorchiasis.

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IMPACTS OF PERMETHRIN-IMPREGNATED BEDNETS ON *ANOPHELES DIRUS*

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Insecticide impregnated bednets have been introduced for use as a part of personal protection and malaria control. The reduction in mortality and morbidity is due to the effects of insecticide on the bednet through continuous use. The long term application of insecticide can lead to development of insecticide resistance in insect vectors as a result of selection pressure. Therefore, this study was conducted in the laboratory to observe the development of permethrin resistance in *Anopheles dirus*, the principal malaria vector in Thailand, since permethrin-impregnated bednets have been distributed to the population for malaria control. Other impacts of permethrin impregnated bednets on the mosquito, including body size, fecundity and longevity were also studied.

The results revealed the development of a low level of resistance in *An. dirus* after they had been selected by exposure to a permethrin impregnated bednet for 11 generations, with a resistance ratio of 4.88. The mosquitoes gradually decreased in susceptibility. This might be attributed to low selection pressure (6.25 mg./m^2); in addition, only females were exposed to insecticide. If the males inherited susceptible genes, the greater is the possibility that they can be transferred to the next generation, since the males were not exposed to selection. Hence, continuous segregation of susceptible genes could be expected.

The permethrin selection did not affect egg production, hatchability rate nor adult size based on body weight and wing length. However, adult longevity was reduced in permethrin-tolerant *An. dirus* when compared to that of 49 days in the normal strain. Reduced longevity will also reduce malaria transmitting capacity since the parasite needs at least 10-14 days of incubation to develop into its infective stage (sporozoite).

It was suggested, from this study, that the use of permethrin-impregnated bednets showed a tendency to induce resistance in *An. dirus*; however, the development was slow. If the use of permethrin-impregnated bednets is expected to continue for a prolonged pertod in malaria control programs, regular monitoring of the vector field population is needed to make sure of the susceptibility level. When resistant populations develop in the field, appropriate resistance management should be condurcted as soon as possible. ❑

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

MALARIA TRANSMISSION IN PA RAI (ARANYAPRATHET: SA KAEO PROVINCE) POTENTIAL BY *ANOPHELES CAMPESTRIS*

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In Pa Rai Subdistrict of Aranyaprathet, Sa Kaeo Province, member(s) *An. barbirostris* group particularly *An. barbirostris* and *An. campestris* has been implicated as a possible vector of *Plasmodium vivax*, based on field collections and laboratory studies. The isofemale colonizations for species confirmation and determination of life-cycle were established from wild caught mosquitoes captured by landing catches and cow-baited traps. Fourteen species of mosquitoes were found, but only *the An. barbirostris* group was dominant throughout the year. Pupal examinations indicated that all the suspected mosquitoes of the *barbitrostris* group were *An. campestris*. *An. campestris* comprised 78.59% of the total number of females captured by human landing catches but only 7.13% were collected from a cow-baited trap. The biting cycle showed an obvious peak during the period 2000-0100 hours, with highest density (17.6 bites per person-hour) at 23.00 hours. More *campestris* bit people indoors (9 bites/person-hour) than outdoors (4 bites/person-hour). The average development times from egg hatch to adult

were 18-47 days and 14-22 days under laboratory (25.0-27.0°C) and ambient (26-32 °C) conditions, respectively. The fecundity of *An. campestris* ranged from 173-311 eggs. Based on experimental infection trial, *An. campestris* was able to support sporogonic cycle with 76.2% and 23.8% *vivax* oocyst and sporozoite rate, respectively. *An. campestris* in Pa Rai, therefore, revealed high potential as a malaria vector by high biting density, anthropophilic habits, long survival and susceptibility to *vivax* parasites. Studies are underway to determine the possibility of using electrophoresis and karyotypes for identification of the adult *campestris* mosquitoes. ❑

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INTRASPECIFIC HYBRIDIZATION OF *ANOPHELES MINIMUS* (DIPTERA: CULICIDAE) SPECIES A AND C IN THAILAND

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Hybridization tests of laboratory-raised, isolined colonies of *Anopheles minimus,* species A and C, were done by induced copulation. The three isolined colonies were established based on three morphological variants of wild-caught, fully engorged females and two distinct types of metaphase chromosomes. They were *An. minimus* species A: V-Form (X_1Y_1), M-Form (X_2Y_1); species C: P-Form (X_3Y_2). The results of reciprocal and back crosses indicated that the two morphologically variant forms of species A were genetically compatible, providing viable progeny and completely synaptic salivary gland polytene chromosomes, whereas, they were genetically incompatible with species C and/or P-Form. Hybrid progeny were only obtained from both forms of species A females X species C males, but asynaptic salivary gland polytene chromsomes on 3L and partial development of ovarian follicles in females were recovered. Back crosses of F_1 hybrid males with parental species A females, providing viable progeny, while back crosses of F_1 hybrid females with parental species C males, providing low viable progeny and adult males with abnormal spermatozoa, suggesting partial reproductive isolation between *An. minimus* species A and C. ❑

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INTRASPECIFIC HYBRIDIZATION OF TWO KARYOTYPIC FORMS OF *ANOPHELES VAGUS* (DIPTERA: CULICIDAE), AND EGG SURFACE TOPOGRAPHY UNDER SCANNING ELECTRON MICROSCOPE

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Hybridization tests of the two karyotypic forms of laboratory-raised, isolined colonies of *Anopheles vagus* Form A and B were done by induced copulation. The results of reciprocal and back crosses indicated that they were genetically compatible, providing viable progeny. Comparative morphometry and morphology of eggs under a scanning electron microscope (SEM) revealed that the eggs of two karyotypic forms were morphometrically and morphologically similar. ❑

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INSECTICIDE STATUS OF MOSQUITOES AGAINST MALATHION AND PERMETHRIN

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Vector control programs in many parts of the world face the problem of insecticide resistance. Determination of vector resistance status is important to provide baseline data for program planning and control. The bioassay test recommended by the World Health Organization is a routine method that has many disadvantages. For example, it is expensive, needs a lot of mosquitoes and cannot detect resistance mechanisms. The biochemical microassay method is more simple and rapid and is able to detect resistance mechanisms in individual insects. Detoxification enzymes, non-specific esterases, mixed function oxidases and acetylcholinesterases are responsible for insecticide resistance mechanisms, especially when insects are exposed to organophosphorus and pyrethoids. In this study, the enzyme microassay was used to detect the resistance status of two common mosquito species.

The larvae and adults of *Culex quinquefasciatus* (4 strains: A, B, C, D) and *Aedes aegypti* (3 strains: E, F, G) were used in this study. The bioassay results, the LC_{50} of *Cx. quiquefaciatus* against malathion and permethrin ranged between 0.043-0.065 mg/l and 0.011-0.170 mg/l, respectively. For *Ae. aegypti*, the ranges of LC_{50} were 0.108-0.172 mg/l and 0.006-0.030 mg/l for malathion and permethrin, respectively.

The response of adult *Cx. quinquefasciatus* against 5% malathion and 0.75% permethrin showed the range of LT_{50} as 13.24-22.91 min and 18.04-46.83 min, respectively, while the results for *Ae. aegypti* were 16.40-18.56 min and 18.86-29.59 min.

The enzyme microassay showed no difference to the bioassay tests and showed correlation between the level of enzyme and insecticide status. ❑

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INTERSPECIFIC HYBRIDIZATION BETWEEN *ANOPHELES ACONITUS* AND *AN. PAMPANAI* (DIPTERA: CULICIDAE)

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Crossing experiments between two members of the *Anopheles minimus* species group, viz *An. aconitus* and *An. pampanai*, were carried out by artificial insemination in order to determine their genetic relationships. In comparing the F_1-hybrids with those of their parent species as the control, differences in embryonation, hatchability and viability were observed. The low embryonation, hatchability and high mortality of the hatched larve of F_1-hybrids indicated that these two morphological species exhibited complete reproductive isolation. ❑

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NATURAL HUMAN IgG SUBCLASS ANTIBODIES TO *PLASMODIUM FALCIPARUM* BLOOD STAGE ANTIGENS AND THEIR RELATION TO MALARIA RESISTANCE IN AN 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 indviduals living in a 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 the 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 higher antibody production required continuous stimulation under natural conditions. Furthermore, the levels of specific IgG1, IgG2 and IgG3 increases in immune individuals without clinical malaria, reported in adolescents and adults, were associated with malaria resistance. Similar results were found in children with different patterns 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 to be more diverse than those of V1/V2 of blood isolates. These findings suggested that the evolution of V1/V2 regions of CSF isolates seems to be advantageous for HIV-1 in CNS infection. In contrast, the genetic distance in V4 and V5 regions of CSF isolates showed less diverse suggesting that conservation in these regions might be necessary during the process of HIV-1 in CNS infection. ❑

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CHARACTERIZATION OF B-CELL EPITOPES IN HIV-1 SUBTYPE E

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Acquired immune deficiency syndrome (AIDS) is endemic worldwide and has become one of the most devastating infectious diseases in human history. To stop this pandemic, an effective AIDS vaccine is needed. Many candidate vaccines of subtype B have been studied intensively and some have even entered vaccine trials. However, neither T or B-cell defined epitopes for a vaccine for HIV-1 subtype E have been reported, despite the fact that the highest prevalence of HIV-1 in Thailand and Southeast Asian countries is subtype E which constitutes an immunologically distinct subtype. Therefore, to define the neutralizing epitopes of HIV-1 subtype E, the virus was isolated and its envelope gene was amplified, sequenced and aligned, based on the idea that the consensus sequence in each compartment might be different. In the Thai study, ten paired blood and CSF isolates of HIV-1 were investigated. Since no difference in the consensus sequence between blood and CSF isolates was observed using the MegAlign program, the consensus of envelope sequences of both gp 120 and gp41 were defined from both blood and CSF sequences. Moreover, all sequences were confirmed as HIV-1 subtype E by phylogenetic tree. The antigenic regions of the consensus sequence were then predicted by using a computer program (DNAstar). The peptides corresponding to the predicted regions were synthesized and their immunogenicity was confirmed by peptide ELISA. By using pooled sera from asymptomatic HIV-1 subtype E infected subjects, the peptides specifically reacting with pooled sera were considered to be the immunogenic epitopes. In this study, the order of potential immunogenicity domains in inducing antibodies in infected individuals was gp41 cluster I, V3, gp41 cluster II and V2 regions. The less antigenic domains were C1, C2 and C3 regions. In addition, two regions showed no reactivity to synthetic peptides, the C4 region and the N-terminal of gp41 region (gp41E3). All the immunogenic domains were further investigated for the purpose of identifying the neutralizing epitopes.

In identifying the neutralizing epitopes, the neutralizing activity of immune sera to both primary isolates and TCLA strains in the presence, and in the absence, of synthetic peptides was tested. The primary isolates, which were relatively sensitive to be neutralized, T-tropic (LP04), M-tropic (BB59) and Dual-tropic (BB40) were selected. Only peptides corresponding to the neutralizing epitopes could inhibit neutralization. Under this study, it was found that neutralizing epitopes of primary isolates were located in the C1, C2, V2 regions and gp41 clusters I and II. For TCLA viruses, the neutralizing epitopes were in the V3 region, gp41 clusters I and II.

The study suggests that the antibody response to HIV-1 subtype B might be different from subtype E. The level of neutralizing antibodies to gp41 cluster II in subtype E infected patients was relatively high when compared to patients infected with HIV-1 subtype B. In addition, two more neutralizing epitopes in constant region 1 (C1) and constant region 2 (C2) in subtype E were found, and which have never been reported elsewhere. Mapping the HIV-1 subtype E specificity of these neutralizing epitopes may have relevance for HIV vaccine studies in Thailand. ❑

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

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Competitive ELISA using a combination of monoclonal antibodies specific to vitellin subunits was used to monitor the fluctuation of hemolymph vitellogenin levels in *Penaeus monodon* during ovarian development induced by bilateral eye-ablation and to monitor the effect of eyestalk extract injection in prawns with developing ovary. The hemolymph vitellogenin levels were undetectable in the prawn with ovary at the resting stage but elevated sharply when the ovary began to develop. The hemolymph vitellogenin levels remained high during the ovary's development into the ripe stage and dropped down to low levels before spawning and the spent stage. The results from injection of eyestalk extract into prawns with developing ovary revealed that hemolyph vitellogenin levels elevated sharply within 2 hr, reached the maximal levels and remained high during 4-10 hr, then slightly declined at 24 hr. This response 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 was less effective, whereas the eyestalk extract from *Macrobrachium rosenbergii* did not cause any changes in hemolymph vitellogenin levels. Therefore, the assay is specific and indicative for use to determine the activity of putative gonad inhibiting hormone by monitoring the alteration of vitellogenin levels. ❑

CHARACTERIZATION OF VITELLIN AND VITELLOGENIN OF GIANT TIGER PRAWN *PENAEUS MONODON* USING MONOCLONAL ANTIBODIES SPECIFIC TO VITELLIN SUBUNITS

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Monoclonal antibodies specific to *Penaeus monodon* vitellin subunits were produced from mouse immunized with sodium dodecyl sulfate (SDS) treated ovarian extract prepared from gravid ovaries. After fusion of mouse spleen cells with P3X myeloma, hybridomas were selected by indirect immunoperoxidase ELISA against *P. monodon* ovarian extract. This was followed by dot-blotting against native and denatured proteins from ovarian extract, female hemolymph, and male hemolymph, then by dot-blotting against each vitellin subunit. Hybridoma clones producing antibodies specific to each of the vitellin subunits with a molecular mass of 83, 74, 104 and 58, 104 and 45 kD, antibodies specific to the 215 kD protein, an oocyte-specific protein, and one monoclonal antibody specific to hemocyanin were isolated. All monoclonal antibodies could bind to both native and denatured proteins. Western blot analysis of ovarian extract and female hemolymph from gravid ovary prawns separated by PAGE and SDS-PAGE revealed five vitellin subunits, molecular mass of 104, 83, 74, 58 and 45 kD in ovarian extract, and four vitellogenin related polypeptides, molecular mass of 200, 104, 83 and 74 kD in the female hemolymph. From the immunoreactive relationships among these proteins, it could be assumed that vitellogenin may be released into the hemolymph in two forms, 200 and 74 kD, then the 200 kD polypeptide was either processed into the 104 and 83 kD polypeptides, or directly taken up into the oocyte. In the oocyte, the 104 kD protein would be further cleaved into 58 and 45 kD polypeptides while

the 74 kD protein would undergo slight modification or remained unchanged. Western blot analysis of vitellin subunits at various stages of ovarian development revealed that the 200 kD protein appeared in the oocyte during early ovarian development and the 45 and 58 kD proteins appeared during the late development. ❑

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DIAGNOSIS OF AMEBIASIS USING IMMUNOLOGICAL AND MOLECULAR BIOLOGICAL METHODS

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Dedicated to the late Professor Emeritus Savanat Tharavanij and the late Professor Emeritus Khunying Tranakchit Harinasuta

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 AMEBAE AND THEIR MOLECULAR-BASED DIAGNOSIS

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At present, three genera of free-living amoebae capable of infecting the 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 amebic meningoencephalitis (PAM) and granulomatous acanthamebic encephalitis/meningoencephalitis (GAE/GAM) and chronic acanthamebic keratitis (CAK) with invasion of other tissues in man, respectively. A relatively large ameba *Balamuthia mandrillaris,* like *Acathamoeba* 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 a soil ameba; the other two may 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 acanthamebic infection of peptic ulcer and 2 cases of *Acanthamoeba* peluropneumonitits have been reported. Surveys in industrial plants and stagnant water revealed the prevalence of these free-living amebae. However, *Balamuthia* causing GAE has never been reported in this country, but has been reported elsewhere, in Peru 32 cases, in Brazil 1 case, and in the USA 4 cases, as well as 1 case in a mandrill baboon. There is good evidence supporting the motion that the facultative intracellular parasites, such as *Legionella pneumophila* and *Pseudomonas aeruginosa* are capable of growing inside a natural host; *Acanthamoeba castellanii* present in domestic water supplies, whirlpool bathes, and even in hot spring spas. The other ones, *Burkholderia cepacia* and *Candidatus Odyssella* thessalonicensis' gen.nov., sp.nov., are obligate intracellular bacteria of free-living amoeba *Acanthamoeba polyphagea*. Therefore, special attention should be paid to these potentially pathogeic 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 trest using specific polyclonal antibodies can serve a 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 IFA/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 antibodies (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 form. However, observations under conventional microscope, conventional staining with dyes (Giemsa, Hematoxylin and Eosin for trophozoites and fluorescent dye Calcofluor 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 lens etc., are 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

choices. 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. ❑

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

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There exist two species within what has been called *E. histolytica*, *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 is done using a light microscope, the cysts and trophozoites of the two species are morphologically indistinguishable and should be reported as *E. histolytical/ E. dispar.* Biochemical, immunological and genetic data now indicate their difference. Only *E. histolytica* is capable of causing invasive disease whereas *E. dispar,* or with asymptomatic *E. histolytica*, colonization never develop symptoms and spontaneously clears the infection. Therefore, amebiasis researchers have been trying in the 21st century to develop molecular-based diagnosis 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 antibodies (MAbs), small subunit rRNA (SSrRNA) genes and nested PCR using specific primers of these two species are 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, and cysteine proteinases in animal models. Protection against invasive amebiasis by a single monoclonal directed against a lipophosphoglycan antigen localized on the *E. histolytica* has been documented. Knowledge of the real prevalence of amebiasis will be useful for the control of parasite and amebiasis, as well as for testing of anti-amebic vaccine in an endemic area. ❑

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. histolytic* a to detect salivary IgA antibodies in intestinal amebiasis patients 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 was made between R-Phycocyanin-labeled monoclonal antibody (MAb) probes and R-phycoerythrin-labeled probes for the detection of the three standard reference strains of culture-derived *Entamoeba histolytica* trophozoites, namely HK-9, HM-1:IMSS and HTH-56:MUTM strains by using direct immuno-fluorescence 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 more and clearly 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 color. The sensitivity of both tests was 100%. Since this Eh208-C2-2MAb could recogize specifically *Entamoeba* pyruvate: ferredoxin oxidoreductase enzyme, therefore, our two antibody probes would be valuable for use as a rapid, easy and sensitive test for the diagnosis of invasive amoebiasis. ❑

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AMEBIASIS

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Particular highlights of research studies have included: 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 immunoperxidase test and to detect amebic antigens in circulation and in feces by MAb-PAb-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*. Ongoing researchs aim at surveillance and control of amebiasis,

and improved methods for specific diagnosis of *E. histolytica/E. dispar* with a simple test or technologies appropriate for Thailand, other developing and underdeveloped countries. ❑

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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 from August to October 1998 from blood donors at the blood bank of Rajvithi Hospital, Bangkok, Thailand. Their ages varied between 18-55 years. All specimens were tested by immunostaining and ELISA methods. Forty-seven specimens (10.66%) gave positive results by immunostaining. Among these, 20 cases were seropositive and 27 cases were seronegative. The age group 41-50 years had a high percentage of CMV infection as judged by the immunostaining method, more than the other age groups. By ELISA, 231 cases (52.38%) had positive IgG antibody to CMV, 42 cases (9.52%) were IgM antibody positive and 39 cases (8.84%) were positive for both IgG and IgM antibodies. The age group 36-40 years had a higher percentage of IgM antibody positives than the other age groups. Since the immunostaining method can detect early CMV infection, screening for the presence of antibodies alone is not enough to rule out CMV infection. Immunostaining along with ELISA detection of antibodies was useful for determining a decrease in CMV infection. ❑

RAPID DIAGNOSIS OF CYTOMEGALOVIRUS INFECTION IN CONGENITAL NEONATES

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Immunostaining was compared with PCR for the diagnosis of congenital CMV infection. IgM and IgG antibody assays were also performed in parallel. Immunostaining gave sensitivity and specificity of 60% and 97%, respectively. Correlations among immunostaining, PCR and the presence of IgM antibody was reported. Immunostaining can be used for early diagnosis of congenital CMV infection in parallel with detection of IgM antibody. ❑

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

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Hybridomas secreting specific monoclonal antibodies (MAb) to all members of the genus *Leptospira* (clone LF9) and those that are specific only to the pathogenic species (clones LD5 and LE1) were produced. MAbLF9, which were IgG1, reacted to a 38 kDa component of the SDS-PAGE separated whole cell lysates of all *Leptospira* spp., while MAbLD5 and MAbLE1, which were IgG1 and IgG2a respectively, reacted to the 35 to 36 kDa components of all serogroups of the pathogenic species of *Leptospira.* The MAbLD5 were used in a dot-ELISA for detecting *Leptospira* antigen in urine samples serially collected from two groups of patients diagnosed with leptospirosis, *i.e.*, 36 clinically diagnosed patients and 25 *Leptospira* culture-confirmed patients. Their serum samples were tested serologically by IgM Dipstick, indirect immunofluorescence (IFA) and/or microscopic agglutination test (MAT). Urine samples of 26 patients diagnosed for other illnesses and 120 healthy individuals served as controls. For the first group of patients who had been ill for an average of 3.4 days before hospitalization, the IgM dipstick, IFA and MAT were positive in 69.4%, 70.0% and 85.7% while the *Leptospira* antigenuria tested by the monoclonal antibody-based dot-ELISA was positive for 75.0%, 88.9%, 97.2%, 97.2%, and 100% on days 1, 2, 3, 7 and 14 of hospitalization, respectively. MAT was positive in 10 of 12 patients (83.3 %) of the 25 culture-positive *Leptospira* patients who had been ill for an average of 5.04 days before hospitalization; *Leptospira* antigen was found in 64.0%, 84.0%, 96.0%, 100%, 100%, 100% and 100% of the patients' urine samples collected on days 1, 2, 3, 4, 5, 6 and 7 of hospitalization, respectively. *Leptospira* antigenuria was found in 3 of the 26 patients diagnosed with other illnesses and 1 of 120 healthy controls. The reasons for this positivity are discussed. Urine antigen detection by monoclonal antibody-based dot-ELISA has high potential for rapid, sensitive and specific diagnosis of leptospirosis at a low cost. ❑

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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 uremic syndrome (HUS) is characterized by haemolytic anemia, thrombocytopenia and renal failure. Infection with enterohaemorrhagic *Escherichia coli* (EHEC), 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 EHEC-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. The 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 an infant case (21 months old). The Stx binding in the infant's glomeruli was at the podocytes, mesangial and endothelial cells. It has been known that young children are more susceptible than adults to HUS. One possibility exists that the more extensive binding of the Stx to the kidney tissue of the paediatric patient might be due to the higher synthesis and expression of Stx receptor, i.e. Gb_3, in infants and less so in aged individuals, which might account for the difference in susceptibility. However, other alternatives are possible, for example, the difference in stage of HUS in individual patients. Thus it is too early to draw any conclusion on this enigma and further investigation is required. ❑

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RAPID DETECTION OF *ESCHERICHIA COLI* O157 LPS AND SHIGA-LIKE TOXINS (Stxs) IN CLINICAL SPECIMENS USING MONOCLONAL ANTIBODIES

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Hybridomas secreting monoclonal antibodies (MAbs) to lipopolysaccharide (LPS) of *E. coli* O157 and A- and B-subunits of Shiga toxin-1 (Stx-1) and Shiga toxin-2 (Stx-2) were produced. The mono-epitope specificities of the MAbs were screened using individual homologous antigens and a wide range of heterologous antigens. The MAbs, namely MAb to O157 LPS and MAbs to A- and B-subunits of Stx-1 and Stx-2 were used in a dot-ELISA for the detection of their respective antigens in stool samples collected from patients with diarrhea. The MAb-based dot-ELISA, when performed in double-blinded manner, was positive for 9 samples (5 Japanese and 4 Thai samples) of 546 patients with diarrhea. Bacterial isolations from the

dot-ELISA positive samples revealed 1 sample with non-O157, Stx-1$^+$ Stx-2$^+$ *E. coli*, 2 samples with O157, Stx-1$^-$ Stx-2 *E. coli*, 1 sample with O157, Stx-1$^+$ Stx-2$^+$ *E. coli*, 1 sample with O157, Stx-1$^+$ Stx-2 *E. coli*, and 4 samples with untypeable *E. coli.* The dot-ELISA was negative for 537 samples. Among these dot-ELISA negative samples, 241 revealed other enteric pathogens which included 98 samples with *Shigella* spp., 67 samples with *Salmonella* spp., 42 samples with *Vibrio parahaemolyticus*, 9 samples with *Plesiomonas shigelloides*, 8 samples with enteropathogenic *E. coli* (EPEC), 7 samples with *Staphylococcus aureus*, 5 samples with mixed *Salmonella* spp. and *Shigella* spp., 2 samples with mixed *Salmonella* spp. and *Vibrio parahaemolyticus*, 2 samples with *Aeromonas hydrophila*, 1 sample with *Vibrio cholerae* Ogawa. No pathogenic bacteria were isolated from the remaining dot-ELISA negative 296 samples. The membrane ELISA is easy to perform and relatively inexpensive compared to the culture and DNA amplification methods. The procedure requires only 90 minutes; thus, the results are useful for treatment indication. The dot-ELISA provides for multi-sample testing at a single time without significant increase in the turnaround time. It does not require additional equipment and does not produce large quantities of contaminated waste. Most of all, the test using a cocktail of MAbs to the A- and B-subunits of both Stx even offers detection of the respective antigens in clinical specimens of patients infected with non-O157 Shiga toxin-producing bacteria. ❑

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AN OUTBREAK OF EOSINOPHILIC MENINGITIS CAUSED BY *ANGIOSTRONGYLUS CANTONENSIS* IN TRAVELERS RETURNING FROM THE CARIBBEAN

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Background Outbreaks of eosinophilic meningitis caused by *Angiostrongylus cantonensis* are rarely reported, even in Southeast Asia and the Pacific Basin, regions in which infection with this parasite traditionally has been considered endemic. We describe the largest reported outbreak of *A. cantonensis* meningitis in the Western Hemisphere outside of the Pacific Basin.

Methods We conducted a retrospective cohort study among 23 U.S. travelers returning from Jamaica using a clinical definition of eosinophilic meningitis that included headache onset within 35 days of the trip and at least one of the following symptoms: neck pain, altered cutaneous sensation or visual disturbance. We recorded clinical findings, treatment and outcome of the case-patients and tested acute- and convalescent-phase serum specimens for antibodies to *A. cantonensis* by Western blot analysis.

Results Twelve travelers met the case definition for eosinophilic meningitis, nine of whom were hospitalized and had lumbar punctures. The median time to symptom onset was 11 days (range 6 to 31) after return to the United States. Eosinophilia was eventually documented in all nine hospitalized case-patients, although it was present in the peripheral blood of only four (44%) and in the cerebrospinal fluid of five (55%) on initial evaluation. All patients recovered without anthelmintic therapy. Repeat lumbar punctures and corticosteroid therapy were effective in symptom control in two of three patients with severe headache, and intracranial pressure was lower during corticosteroid therapy in all three. In the cohort study, one shared meal (P= 0.001) and a Caesar salad eaten at that meal

(P= 0.007) were most strongly associated with eosinophilic meningitis. Antibodies to an *A. cantonensis*-specific 31 kDa antigen were present in only the convalescent-phase sera of 10 case-patients, in both the acute- and convalescent-phase sera of one case-patient, and in none of the sera from persons who did not meet the case definition.

Conclusions An outbreak of eosinophilic meningitis was associated with travel to Jamaica. Clinical and serologic data were most consistent with infection with *A. cantonensis*. Headache, raised intracranial pressure, and a non-neutrophilic cerebrospinal fluid pleocytosis, with or without eosinophilia, particularly in association with paresthesias or hyperesthesias, should alert clinicians to the possibility of *A. cantonensis* infection. ❑

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VALIDATION OF SALMONELLOSIS AND SHIGELLOSIS DIAGNOSTIC TEST KITS AT A PROVINCIAL HOSPITAL IN THAILAND

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Rapid diagnosis of salmonellosis and shigellosis was performed using six different diagnostic test kits which recently have been made available commercially. They were Salmo-Dot, Typhi-Dot, Shigel-Dot A, B, C, and D test kits for detection of *Salmonella* spp., group D Salmonellae, and groups A, B, C, and D *Shigella* spp., respectively. The principle of all test kits is a membrane (dot) ELISA using specific monoclonal antibodies to the respective pathogens as the detection reagents. The present study was designed to validate the accuracy of the test kits, at a laboratory in a provincial hospital in Thailand, in comparison with the conventional bacterial culture method alone or with the combined results of the culture and Western blot analysis (WB) for detecting the respective bacterial lipopolysaccharides (LPS) on specimens. Five hundred rectal swab samples of patients with diarrhea who sought treatment at the hospital, were evaluated. The diagnostic accuracy of the Salmo-Dot was 91.0% when compared with the conventional bacterial culture method alone, but was 100.0% in comparison with the combined results of the culture and the WB. The Typhi-Dot and the Shigel-Dot A, B, C, and D showed 100%, 99.2%, 95.0%, 94.0% and 96.4%, respectively, when compared with the culture alone and all were 100% in comparison with the combination of the results of the bacterial culture and the WB. The Shigel-Dot A revealed antigen of type 1 *Shigella dysenteriae* in several specimens in which the bacteria could not be recovered by the culture method. This difference is important as type 1 *Shigella dysenteriae* have high epidemic potential and often cause severe morbidity. Unawareness of their presence by the conventional culture may have a great impact on disease surveillance for public health. Pathogen detection using the six diagnostic test kits is sensitive, specific, rapid, and relatively simple and less expensive. Several specimens can be tested at the same time without much increase in turn around time. Moreover, these kits produce no contaminated waste as compared with the bacterial culture method. The test kits should be used for rapid screening of specimens of patients with diarrhea, especially in areas where culture facilities are inadequate. ❑

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IMMUNODIAGNOSIS OF FOODBORNE PARASITIC INFECTIONS: FROM RESEARCH EXPERIENCES TO PRACTICAL APPLICATIONS

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Over the past three decades, a wide range of immunological studies have been carried out in our laboratories on organisms responsible for parasitic and bacterial diseases in Thailand. In the area of parasitic diseases/infections, emphasis has been directed especially to inventing specific immunological methods to detect several food-borne helminthic infections, including gnathostomiasis, angiostrongyliasis, paragonimiasis, trichinellosis, opisthorchiasis, and others.

Although the most reliable means of diagnosing these food-borne parasitoses is to find the parasites and/or their products such as eggs or larvae in the host; however, this method is not sensitive and rather cumbersome. Immunological assays not only play a supplementary role to parasitological methods, but are often the only way to come to a diagnosis. Immunological assays for detecting host antibodies have become the most practical, useful and dependable methods, especially during the prepatent period of infections and for occult forms. However, reliability, accuracy and specificity of the antibody assays depend on the quality. *i.e.,* the purity of the antigenic preparation used in the tests. Parasites, especially the helminths and their products, are antigenically complex and they also exist in different developmental stages within their hosts. Thus, they express a certain degree of cross reactivity to antibodies incited by other parasites. Therefore, assays using crude parasite antigens have less diagnostic value. Because of this fact, extensive research has been carried out, not only to search for the specific antigens of the individual parasites, but also to prepare them in pure form (or pure enough to give no cross reaction with antibodies incited by other organisms). We have used two strategies in the development of these immunodiagnostic methods. One was to use pure antigen prepared by either the conventional method or by affinity chromatographies. The second strategy was the successful use of Westem blot analysis to reveal antibodies to the parasite antigenic components in patient's serum for diagnosis. Examples of our experiments have been published. ❑

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MOLECULAR EPIDEMIOLOGY OF ENTEROHEMORRHAGIC *ESCHERICHIA COLI* ISOLATED FROM HEALTHY CATTLE IN THAILAND

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Objective

To isolate and investigate genotypes and phenotypes of enterohemorrhagic *Escherichia coli,* which are known to cause human diarrhea, hemorrhagic colitis, or in some cases fetal renal failure, i.e. Hemolytic Uremic Syndrome (HUS), from cattle in Thailand.

Methods

Stool samples collected from healthy cattle in the outskirts of Bangkok were individually enriched overnight at 37°C in EC broth, diluted 1:10 in distilled water, boiled, centrifuged and the supernatants were used as DNA templates for multiplex PCR for amplification of *stx-I, stx-II* and their variants and O157 LPS gene.

The PCR positive samples were individually plated onto Sorbitol MacConkey agar and incubated at 37°C for 24 hours. About 20 to 40 colonies from individual plates were picked and re-screened for those genes. Positive colonies were subjected to phenotypic and hemolysis test. Determination of the phages carrying the respective genes, *i.e. hly*A, *etp*D and *kat*P were also performed.

Results

Among the 26 stool samples collected from 26 healthy cattle in the outskirts of Bangkok, 6 samples (23.1%) were positive for EHEC by PCR and 11 *E. coli* strains were established. Eight strains (72.7%) were genotypically and phenotypically positive for both toxins. One of them was a rough variant and the other 7 strains were untypable by the available typing sera. Two strains (18%) were positive for *stx-I* and *stx-II* and they were O15. One strain of *E. coli* isolates was O157. However, this strain lacked *stx* and was not verocytotoxic.

Conclusion

EHEC strains that could be isolated from healthy cattle in this study belonged to many serotypes. O157 strain, the serotype known to cause hemolytic uremic syndrome in humans, was also found among the isolates. However, the strain lacks *stx* gene. This is the first report of EHEC O157 isolate in Thailand. ❑

• The work was supported by the Thailand Research Fund (TRF) through a Senior Researcher Award to Professor Wanpen Chaicumpa, and the Royal Golden Jubilee Ph.D. Program; Japan Health Sciences Foundation, Japan.

Presented at: the RGJ-Ph. D. Congress II. 20-22 April, 2001, The Garden Beach Resort, Pattaya, Chonburi Province, Thailand and at the 4th International Symposium and Workshop on "Shiga-Toxin (Verocytotoxin)-Producing *Escherichia coli* Infections", October 29-November 2, 2000, Kyoto, Japan

A SEARCH FOR SPECIFIC ANTIGEN OF *STRONGYLOIDES STERCORALIS*

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Objective

To identify specific antigen of the *Strongyloides stercoralis* infective (filariform) larvae which do not cross-react with serum antibody from patients infected by other helminths.

Methods

Crude larval extracts of *S. stercoralis* (SSAg) were prepared from filariform larvae obtained from polyethylene-tube culture of stools of patients containing rhabditiform larvae of the parasite. The protein content of the prepartion was determined. The SSAg was used in Western blot (WB) for analysis of antibodies in 4 groups of individuals. These included 15 patients with *S. stercoralis* infection, 6 patients of mixed infection of *S. stercoralis* and other parasites, 21 patients infected with other parasites and 3 normal healthy, parasite-free individuals (groups I, 2, 3 and 4, respectively). Dot-ELISA, using a more refined, proteinase K treated-SSAg was also performed for differentiation of patients of groups 1 and 3.

Results

In WB, the SDS-PAGE-separated SSAg blotted onto NC were reacted individually with sera of patients of all groups. Ten sera from 15 (66.67%) of group I were positive. Three sera from group 2 (50%) and 1 serum of group 3 were also positive. The reaction appeared between 58.0 to 27.5 Kda as a diffuse smear which seemed atypical for reaction of protein. Thus, the SSAg was treated with proteinase K to destroy all proteins and the treated-SSAg retested in the WB as well as a dot-ELISA against the sera of pateints of groups 1 and 3. It was found that the protienasek treated-SSAg could differentiate patients with strongyloidiasis from patients with other parasitic infections.

Conclusion

Specific antigen of *S. stercoralis* is a carbohydrate which appears as a diffuse smear in WB against patient's serum between *Mr* 58.0 to 27.5 kDa. ❑

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RAPID DIAGNOSIS OF SHIGELLOSIS AND RAPID DETECTION OF *SHIGELLA* GROUPS A, B, C AND D BY A MONOCLONAL ANTIBODY BASED-DOT-ELISA

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To produce hybridomas secreting monoclonal antibodies against all serotypes of the four *Shigella* serogroups, several cell fusions have been carried out. Splenocytes used in the cell fusions were from Balb/C mice immunized with whole cell lysate(s) (Ly) of single or multiple serotypes of *Shigella*. In this study, 349 hybridomas producing specific MAbs to various serotypes of *Shigella* spp. were obtained. Among them, monoclonal antibodies secreted by thirteen hybridomas, namely: MAbSS1, MAbSS2, MAbSF1, MAbSF8, MAbSF11, MAbSF18, MAbSF19, MAbSF24, MAbSB2, MAbSB4, MAbSB5, MAbSB12 and MAbSD were selected for production of MAbs and the MAbs used as the detection reagents to detect *Shigella* spp. in clinical specimens by an MAb-based dot-ELISA. All secreted MAbs giving either a ladder appearance against Ly or diffused bands (smears) against LPS (typical reaction pattern of LPS and antibodies) of their respective immunogen(s) when tested in the Western blot analysis. The specificities of these MAbs were assessed by both indirect- and dot (membrane)-ELISA against Ly (and LPS) antigens of 44 strains of *Shigella* of all four groups and 114 strains of other bacteria and *E. histolytica*. The individually selected MAb reacted with Ly from the respective homologous *Shigella* serotype(s) but do not react with the bacteria other than *Shigella* serotypes and heterologous antigens. However, weak cross-reactivity of MAbSS1 and MAbSS2 (monoclonal antibody specific to *S. sonnei* phases I and II, respectively) to *S. boydii* types 2 and 4 were observed by dot-ELISA but not by indirect ELISA. The cross-reactivities among antibodies to *Shigella* spp. have been reported by several investigators.

The monoclonal antibodies secreted by the selected clones were used singly or appropriately combined into four sets of preparations. They were used in a dot-ELISA to detect individual serogroups of *Shigella* spp. rectal swabs/stool samples of patients with diarrhea in comparison with the conventional culture method and a Western blot analysis. The four sets of MAbs were MAbSD, MAbSF, MAbSB and MAbSS for detecting groups A, B, C, and D *Shigella* spp., respectively.

In the study, three batches of the patients's specimens were evaluated. The first batch included rectal swabs of 175 patients with diarrhea admitted to Prachom-kloa Hospital, Petchaburi province, Thailand. The rectal swabs were used in the conventional culture method at the hospital's laboratory and the samples were enriched overnight in buffered peptone water before subjecting them to the MAb-based dot-ELISA for *Shigella* antigen detection at the Department of Microbiology and Immunology, Bangkok. The second batch included 30 stool samples from children with diarrhea admitted to the Children's Hospita,l Bangkok. The bacterial cultures were performed at the Armed Forces Research Institute of Medical Sciences (AFRIMS), US Component, Bangkok. The MAb-based dot-ELISA for *Shigella* antigen detection was performed in Bangkok as for the first batch of specimens. The third batch of specimens was from 42 Vietnamese patients with diarrhea who sought treatment at the "108 Hospital" in Hanoi, Vietnam. They were rectal swabs in buffered glycerol saline. The samples were used for bacterial culture at the hospital in Vietnam and *Shigella* antigen detection in Bangkok. Specimens showing unconformed results by the two methods were subjected to a Western blot analysis (WB) for the detection of the respective *Shigella* lipopolysaccharide.

It was found that among the 175 samples of the first batch, the MAbSS dot-ELISA, MAbSF dot-ELISA and the MAbSB dot-ELISA had diagnostic sensitivity, diagnostic specificity and efficacy of 96.0%, 92.67% and 93.14%; 100%, 98.20% and 98.29% and 100%, 93.33% and 93.71%, respectively. There was no sample in the first batch from which *S. dysenteriae* could be isolated. Thus, the diagnostic sensitivity of the MAbSD dot-ELISA could not be calculated. Nevertheless, the MAbSD dot-ELISA showed 99.0% diagnostic specificity and efficacy.

The four sets of MAb preparations were assembled into "Ready-to-use test kits", namely Shigel-Dot A, Shigel-Dot B, Shigel-Dot C and Shigel-Dot D for rapid detection of *Shigella* of serogroups A, B, C and D, respectively. The test kits were sent for validation at Prachom-klao Hospital, Petchaburi Province, Thailand in comparison with the combined results of the conventional culture method and the Western blot analysis. It was found that the diagnostic sensitivity, diagnostic specificity, positive predictive value, negative predictive value and efficiency of all test kits were 100%.

Besides being sensitive, specific and accurate, the MAb-based antigen detection test kits for *Shigella* spp. in the form of the "Ready to use test kits" offer several other advantages which include rapid turn-around time and simplicity. The test kits are easily used following the instruction manual. They do not require special equipment or much technical skill. They are relatively inexpensive and do not cause an increase in contaminated waste. They are suitable for endemic areas of shigellosis and have high commercial potential. ❑

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- Submitted for Patent Right

DEVELOPMENT OF BROILER LITTER AS VALUABLE ANIMAL FEED INGREDIENT BY MIXING CASSAVA MEAL OR EFFECTIVE MICROORGANISM BY FERMENTATION METHOD

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This paper presents the results of research investigating the usefulness of fermented broiler litter as an ingredient for cattle feed rations. Broiler litter, mixed with cassava meal (0%, 10%, 20%) as well as Effective Microorganism (5%: BLEM) was allowed to ferment for 21 days. Before and after this period the nutritional value and extent of *Salmonella* spp. were assessed. Four types of broiler litter and two types of fermentation were used in this experiment. Broiler litter samples were collected from six farms, selected randomly, in Saraburi and Lopburi Provinces in Thailand. Each farm used rice hulls as the base litter material. The samples were mixed with cassava meal and Effective Microorganism (EM), as per the experimental design, packed into 50 kilogram plastic bags and allowed to anaerobically ferment. This process resulted in the general nutritional value of the broiler litter differing between the treatment ($P<0.05$), and decreasing significantly after fermentation ($P<0.05$), although energy levels did significantly increase ($P<0.05$) and interaction occurred between the 2 factors. *Salmonella* was evident in all samples prior to fermentation in weakened states, but none afterwards. ❑

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GENETIC ANALYSIS OF *VIBRIO CHOLERAE* ISOLATED IN THAILAND FOR EPIDEMIC TRACING

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Two hundred *V. cholerae* serogroup O:1 strains isolated from patients with severe diarrhea in seven provinces of Thailand, a Thai laboratory strain and ten standard strains of the organisms from India, Romania, the United States and Australia were characterized by pulsed-field gel electrophoresis (PFGE) for their genetic relatedness in an epidemiological study. It was found that genomic DNA of the bacteria cutting with *Not* I restriction enzyme yielded approximately 15 discrete DNA bands after PFGE. The cleavage patterns generated by *Not* I of the laboratory Thai strain isolated in 1990 and 10 other strains isolated from India, Peru, Romania, America and Australia were different in 2-4 DNA fragments, particularly the large molecules ranging from 194.0-390.0 kb. However, the strains which derived from the same country, *i.e.* 5 or six strains from India had an identical PFGE banding pattern. Additionally, the PFGE banding patterns of the laboratory strain and the 10 reference strains of *V. cholerae* were also different from the currently studied 200 *V. cholerae* O:1 strains isolated from various provinces in Thailand. The data indicated the genetic heterogeneity at the genomic level of *V. cholerae* O:1 isolated in various parts of the world.

The present study revealed that the differences in the PEGE banding patterns could be used for the epidemiological tracing of the organisms. Among 200 strains of *V. cholerae* isolated in Thailand, 11 different PFGE banding patterns could be found. Among these, patterns 1, 6 and 12 predominate. It was interesting, however, to note that certain provinces had limited numbers of pattern variation, whereas others had a wider pattern variation. These numbers of patterns found in the different provinces may reflect the transmission of different strains/clones of the organism.

In the present study, susceptibility to six different antibiotics of all the *V. cholerae* strains was carried out. It was found in the present study that there was no correlation between patterns and antibiotic sensitivity. The laboratory Thai strain isolated in 1990 and 10 reference strains of the bacterium isolated from India, Peru, Romania, America and Australia were susceptible to norfloxacin and tetracyline whereas those 200 recently isolated strains in Thailand were all susceptible to norfloxacin but had intermediate susceptible to tetracycline. Therefore, it can be concluded that norfloxacin is the main drug of choice for the treatment of cholera in Thailand.

In summary, among the 200 isolates of *V, cholerae* O:1 isolated from various provinces in Thailand in the present study, the PFGE bandings were very similar, but not identical. This indicated that PFGE has high discriminating power and that the technique can be used for the epidemiological study of the organisms. The result indicated that clinical cholerae in Thailand from time to time were caused by a single clone or very closely related clones as, shown by the similarity in PFGE banding patterns and cluster analysis. Additionally, the laboratory strain of *V. cholerae* isolated in 1990 revealed 2-4 different PFGE bands. This suggests a continuous evolutionary divergence of the bacterium, probably through the spontaneous mutation. Constant monitoring of the *V. cholerae* isolates in Thailand by PFGE over a period of time will provide useful information for following the progressing epidemic of cholera. ❑

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DNA AMPLIFICATION FOR *V. CHOLERAE* O:139 DETECTION

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Five hundred stool specimens were obtained between 1996-1997 from patients with severe diarrhea from Bamranaradura Infectious Hospital (390 cases), Bangkok Children's Hospital and Krung Thon Hospital (70 cases) and from Dr. G.B. Nair, India (40 cases). These samples were tested for presence of *V. cholerae* serogroups O:1 and O:139 by the conventional method, monoclonal antibody-based dot-blot enzyme-linked immunosorbent assay (dot-ELISA) and DNA amplification employing two sets of the oligonucleotide primers based on *rfb* and glycosyltransferase genes of *V. cholerae* serogroups O:1 and O:139, respectively.

It was found that the dot-ELISA employing two monoclonal antibodies, MAb27E10 and MAb12F5G11, was highly specific and sensitive for detection of *V. cholerae* serogroups O:1 and O:139, respectively. The sensitivity of the assay was 300 viable cells/dot or 1.5 ng of the whole cell lysate (WC)/dot for the serogroup O:1 and 300 viable cells/dot and 2.9 ng WC/dot for O:139.

Among the 500 stool samples, 185 (37%) were positive for *V. cholerae* O:1 and 10 (2%) were positive for *V. cholerae* O:139 by the culture method. One hundred and ninety-three samples (38.6%) were positive by dot-ELISA for *V. cholerae* O:1 and 20 samples (4%) were positive by dot-ELISA for *V. cholerae* O:139. The sensitivity, specificity and efficacy of dot-ELISA for detection of *V. cholerae* O:1, when compared with the culture method were 74.05%, 82.22% and 79.2%, respectively. The sensitivity, specificity and efficacy of the dot-ELISA for detection of *V. cholerae* O:139, when compared with the culture method were 100%, 97.97% and 98%, respectively.

It was found that the DNA amplification method for detection of *V. cholerae* O:1 and O:139 was highly specific. The sensitivity for detection by the method was 100 and 1,000 viable cells/reaction for *V. cholerae* O:1 and O:139, respectively. However, only 142 samples (104 samples with discrepancy results between dot-ELISA and culture method, 18 samples with positive results and 20 samples with negative results by both methods) were further selected for confirmation for the presence of *V. cholerae* O:1 by the DNA amplification method. Sixty-three cases were positive by both DNA amplification and dot-ELISA for *V. cholerae* O:1, 11 samples were positive by dot-ELISA alone and were negative by both methods. It was found that the sensitivity, specificity and efficacy of the DNA amplification, in comparison with the dot-ELISA, were 85.14%, 100% and 92.25%, respectively.

Twenty-one (10 positive for *V. cholerae* O:139 by the culture method and dot-ELISA, 10 with discrepant results and 1 with a negative result) were further confirmed for the presence of *V. cholerae* O:139 by the DNA amplification method. It was found that 12 samples were positive for *V. cholerae* O:139 by both DNA amplification method and dot-ELISA, 8 samples were positive by dot-ELISA only and 1 sample was negative by both methods. The sensitivity, specificity and efficacy of the DNA amplification method in comparison with the dot-ELISA were 60%, 100% and 61.9%, respectively. When compared with the culture method, the sensitivity, specificity and efficacy of the DNA amplification method were 60%, 45.45% and 52.38%, respectively.

It is concluded that the dot-ELISA employing the two monoclonal antibodies has the potential for detection of *V. cholerae* O:1 and O:139 in the standard laboratory or in remote areas because of its simplicity, rapidity, specificity and the low cost. ❑

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SPECIFIC ANTIBODY ASSAY USING AFFINITY-PURIFIED EGG ANTIGEN FOR DETERMINING *OPISTHORCHIS VIVERRINI* EXPOSURE IN AN ENDEMIC AREA

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A hybridoma (clone 3D6) secreting specific monoclonal antibodies (MAb) to *Opisthorchis viverrini* egg antigen was produced. The MAb from the clone 3D6 (g2al) were used to couple to CNBr-activated Sepharose CL-4B to create an MAb-affinity column. Crude extract of the *O. viverrini* adult parasite was applied to the column; the unbound antigens were washed away and the bound antigen was eluted out appropriately. The affinity purified egg antigen was used in a membrane ELISA to detect antibodies in sera of three groups of individuals. Group 1 included 30 parasitogically confirmed *O. viverrini* infected individuals. Not only their stool samples revealed *O. viverrini* eggs by a modified Kato-Katz method at the time of serum collection, but also the adult flukes were recovered from their stool after praziquantel treatment (40 mg per kg body weight) and saturated magnesium sulfate purgation (45 ml orally 3 hours after the praziquantel treatment). Group 2 were 377 individuals infected with parasites other than *O. viverrini.* They were 84 patients with trichinellosis (*Trichinella spiralis* larvae were found in nurse cells of muscle biopsies), 48 individuals with strongyloidiasis (filariform larvae of *Strongyloides stercoralis* could be cultured from their stool by a polyethylene tube method), 47 patients with gnathostomiasis (their serum samples contained antibodies to the 24 kDa specific antigen of *Gnathostoma spinigerum* infective larvae), 32 individuals with schistosomiasis mekongi (eggs of *Schistosoma mekongi* were found in stool specimens), 30 individuals with small intestinal fluke infections (eggs and the adult flukes were found in stool), 20 individuals with taeniasis (proglottids of the tape-worms were found in stool), 20 individuals each with echinostomiasis, trichuriasis, and ascariasis (eggs of the respective parasites were found in stool), 13 individuals with paragonimiasis (eggs of *Paragonimus heterotremus* were found in both sputum and stool), 13 individuals with filariasis (microfilaria in blood smears) and 10 individuals each with invasive amebiasis (antibody test positive) and angiostrongyliasis cantonensis (presence of antibodies to specific 31 kDa antigen in their sera). Group 3 included 82 normal, parasite-free individuals, 30 of whom were Swedes and 52 Thais. The membrane ELISA involved dotting 3 ml of the purified egg antigens (10 mg/ml PBS, pH 7.4) onto a nitrocellulose membrane (NCM), blocking the NCM with 3% bovine serum albumin and 0.01% gelatin in Tris buffer, pH 7.5 and 0.1% Tween-20, washed, reacted with 1:400 dilution of individual serum samples. The antigen-antibody reaction was revealed using rabbit anti-human immunonoglobulins labeled with horseradish peroxidase and substrate. A positive reaction appeared as a purplish-blue spot, while a negative reaction revealed a clear area on the NCM. The membrane (dot) ELISA gave a positive reaction to all serum samples of group 1 and negative to all samples of groups 2 and 3; thus there was 100% sensitivity, specificity and accuracy. It is worthwhile to evaluate this method for efficiency in detecting *O. viverrini* exposure, especially in a new endemic area in Thailand. ❑

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TOWARDS THE MOLONCLONAL ANTIBODIES TO FILAMENTOUS HEMAGGLUTININ OF *BORDETELLA PERTUSSIS*

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Specific mouse monoclonal antibodies against filamentous haemagglutinin of *B. pertussis* were produced from hybridomas derived from the fusion between P3-X63-Ag 8.653 myeloma cells with spleen cells from BALB/c mice immunized with filamentous hemagglutinin (FHA). The immunizations were performed by intra-peritoneally injecting 10 mg FHA in 0.2 ml normal saline solution (NSS) emulsified in an equal volume of Freund's complete adjuvant. The animals were reimmunized two more times at an interval of 2 weeks with the same dose of the antigen in Freund's incomplete adjuvant. Three days prior to cell fusion, the mouse was boosted intravenously with 10 mg FHA in 0.2 ml NSS. Spleen cells ($1.5x10^8$ cells) from the immunized mouse were then fused with $1.5x10^7$ P3-X63-Ag8.653 myeloma cells. The hybrids were screened for antibody specific to FHA by an indirect ELISA using homologous antigen. The positive hybrids were further tested for antigen specificity by Western blot analysis and monocloning by limiting dilution. Seven hybrids were selected and established as monoclones, namely, FHA12B3D10, FHA12B3E6, FHA15D10E8, FHA18E7E2, FHA21G5G10, FHA22D10G5 and FHA23G5G7. These seven monoclones were characterized for their antigen specificity, immunoglobulin classes and subclasses, and cross-reaction with the fourteen other respiratory tract microorganisms. The sensitivity of the monoclonal antibodies was also determined in the detection of FHA by dot ELISA. The monoclonal antibodies were used for the detection of FHA in artificially seeded normal nasopharyngeal secretion.

It was found that the monoclones FHA15D10E8, FHA18E7E2, FHA22D10G5 and FHA23G5G7 produced IgG1 subclass, FHA21G5G10 produced IgG2a and were highly specific to FHA and did not give any cross reaction to the eleven other microorganisms. All of them can detect FHA at 3.75 ng/dot by dot ELISA. The monoclones FHA15D10E8, FHA18E7E2, FHA21G5G10, FHA22D10G5 and FHA23G5G7, which showed no cross-reaction with the other tested microorganisms by both indirect and dot ELISAs, could be further used for the development of rapid detection of *B. pertussis*. ❑

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DIAGNOSIS OF PERTUSSIS USING MAb-BASED DOT-BLOT ELISA, INDIRECT ELISA AND DNA AMPLIFICATION

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Pertussis or whooping cough is an important disease of the human respiratory tract which continues to be one of the significant health problems in children worldwide. In Thailand, although the incidence has dramatically declined after introduction of pertussis vaccine, the disease still exists in the community as an important respiratory tract infection in children. Diagnosis based on only clinical picture in many pertussis cases may be difficult. Atypical symptoms resemble other respiratory tract infections and may be misdiagnosed. Thus, the development of a rapid, sensitive, specific and reliable method for detection of *B. pertussis* is needed. Presently, the culture method is used as a conventional method for detection of *B. pertussis*. Isolation of *B. pertussis* from various specimens provides a conclusive diagnosis, but this is cumbersome, time-consuming, and requires skilled personnel. Various rapid

techniques for detection of *B. pertussis* have been proposed, such as direct fluorescent antibody assay, enzyme immunoassay, and molecular biological techniques. However, these techniques can not be used as routine procedures because expensive equipment and/or highly skilled technicians are required.

In this study, PT5-2C11 and PT6-2G6 monoclonal antibodies (MAbs) specific to S1 subunit of pertussis toxin (PT) of *B. pertussis* were successfully used in the MAb-based dot-blot ELISA for detection of PT. It was found that as low as 0.94 ng and 1.88 ng of PT dissolved in DW and normal nasopharyngeal secretion, respectively, could be detected using this sysyem. The DNA amplification method using PTp1 and PTp2 specific primers for pertussis toxin operon was also optimized. The lowest number of *B. pertussis* which could be detected was 100 cells per reaction when the normal narspharyngeal samples artifically seeded with a known amount of *B. pertussis* were tested .

In this study, MAb-based dot-blot ELISA was used for detection of PT in nasopharyngeal specimens collected from pertussis suspected children at the Outpatients Department of the Children's Hospital in comparison with bacterial culture method and DNA amplification. Additionally, indirect ELISA for detection of IgA antibody to *B. pertussis* was also performed. Fifty-five nasopharyngeal secretion specimens were collected from the first group of children attending the Outpatient Department of the Children's Hospital, Bangkok according to the following criteria; 1) both males and females aged between 6 months to 12 years old; 2) more than a week with symptoms of URI; 3) treated with antibiotics for less than 5 days; 4) informed consent signed by either father or mother of the children. Nineteen children with other pertussis unrelated symptoms as control group were tested with the above-mentioned methods. The negative results of MAb-based dot-blot ELISA and DNA amplification methods were obtained from all NPs samples. It was found that these results corresponded with the bacterial culture method, that *B. pertussis* was not isolated from either group of children. However, it was found that the indirect ELISA could detect IgA antibody in 7 out of 55 (12.7%) samples as compared to the almost undetectable level of antibody in the control group.

In conclusion, the MAb-based dot-blot ELISA is more simple, sensitive, specific and more practical for detection of pertussis toxin of *B. pertussis* in clinical specimens, while the DNA amplification method could be applied for the detection of PT gene of *B. pertussis* in the well-equipped laboratory. Moreover, nasopharyngeal secretion samples from culture-proven cases are needed to consolidate the efficacy of both methods besides the reliable results obtained from experiments using artificial seeding specimens. ❑

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RICKETTSIAL INFECTIONS

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Rickettsial infections are prevalent throughout the world and cause serious diseases in humans. Most of the pathogenic rickettsiae are maintained in nature through a cycle involving reservoirs in mammals and are transmitted to humans by a diverse group of arthropod vectors. Humans are incidental hosts except for louse-borne typhus where humans are the principal reservoir and the human body-louse is the vector. At present, there are 4 medically important genera in the Rickettsiaceae family: *Rickettsia, Orientia, Coxiella* and the newly defined human pathogen, *Ehrlichia*.

Rickettsiae are small gram-negative coccobacilli that are obligate, intracellular organisms. Intracellular growth is slow with a doubling time of 9-12 weeks. Most patients with rickettsial diseases develop sudden onset of fever with headache and chills, which is similar to other febrile diseases such as leptospirosis, typhoid fever, dengue fever, malaria, etc.

In Thailand, as well as in other Southeast Asian countries, both scrub typhus and murine typhus are endemic, but the relatively important one is scrub typhus

caused by *Orientia tsutsugamushi*. A substantial number of people become infected while working in, or traveling to, areas where their activities expose them to the infected chiggers. Scrub typhus has been successfully treated with antibiotics. However, mild symptoms in delayed or improperly treated patients may proceed to severity that eventually becomes fatal. Death is usually due to pneumonitis, circulatory collapse, heart failure, renal failure and central nervous system involvement with coma.

Why are the diseases generally neglected and poorly recognized by physicians in many tropical and subtropical locations? The answer may be due to the lack of a convenient specific diagnostic test, coupled with a wide range of disease severity, and non-specific signs and symptoms. Therefore, a number of new generation diagnostic tests e.g., an antibody detection assay using specific rickettsial antigens, are currently being developed as a tool for early and specific diagnosis of this treatable disease. ❑

Presented at the Joint International Tropical Medicine Meeting, The Royal River Hotel, Bangkok, Thailand 6-8 December 2000.

RAPID DETECTION OF SALMONELLAE IN CONTAMINATED FOODS BY IMMUNOMAGNETIC ENRICHMENT AND ENZYME IMMUNOASSAY

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We established a method for rapid detection of Salmonellae in contaminated food by immunomagnetic enrichment (IME) in combination with enzyme immunoassay. Ab-reacted beads (goat anti-rabbit IgG coated superparamagnetic beads [BioMag] binding to *Salmonella*-specific rabbit immunoglobulins [RIg]) were used to capture the bacteria and/or their antigens in food samples. The antigen-capturing beads were collected using magnetic power and resuspended in a small volume of medium. MAb-based dot-blot ELISA was then used to detect the bacteria bound to the beads by using *Salmonella*-specific monoclonal antibody (MAb 102 B_2). The BioMag superparamagnetic beads were suitable for this study because of their superior ability to adsorb onto nitrocellulose membrane (NC). Our results showed that IME combining MAb-based dot-blot ELISA (IME/MAb-based dot-blot ELISA) was able to detect as little as 10^5 cfu/ml of Salmonellae in culture suspension. It should be noted that food samples should be cultured in tryptic soy broth (TSB) for at least 18 hours before the test. Although the sensitivity of the IME/MAb-based dot-blot ELISA was not significantly higher than that of the MAb-based dot-blot ELISA alone, the reaction of the former test observed on the NC was stronger. In comparison with the conventional culture method, the sensitivity and accuracy of IME/MAb-based dot-blot ELISA were between 72.81-96.55% and 58.33-68.29%, respectively, with no false positive results. The test was able to detect both live and dead bacteria or even antigens of the bacteria. Moreover, it took a total of 20-24 hours for the whole process with a much reduced amount of waste product. This method is thus useful for detection of the bacteria in food products before export. The less time consumed in the detection process is more advantageous not only in reducing the cost of food preservation, but also in maintaining food quality. ❑

Manuscript in preparation.

CYCLOSPORA CAYETANENSIS: CHARACTERIZATION OF OOCYSTS AND *IN VITRO* EXCYSTATION

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Cyclospora oocysts were detected from non-HIV and HIV infected patients in Thailand during 1999-2000 by formalin-ether concentration technique. Sporulation was performed by mixing in 2.5% potassium dichromate solution then sporulated oocysts were treated with various solutions before mechanical rupturing in order to establish the excystation. It was found that less than 10% of sporulated oocysts could be excysted. Our techniques provided a more distinct characteristic appearance of sporocysts and sporozoites within the oocysts by DMSO modified acid fast technique with some modification. The sporozoites were inoculated into the MDCK cell line but they could not be successfully cultivated. ❑

Presented at: Joint International Tropical Medicine Meeting 2001, Thailand, 8-10 August 2001.

PREDICTIVE VALUE OF LATEX AGGLUTINATION TEST IN SEROLOGICAL SCREENING FOR *TOXOPLASMA GONDII*

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The predictive value of a commercial latex agglutination kit (Toxo-screen DA, bioMerieux) was assessed for use as screening test for *Toxoplasma* IgG antibody. The sensivity and specificity were also compared with those of the reference standard Sabin-Feldman dye test. Five hundred serum samples were collected from 200 blood donors and 100 each from pregnant women, kidney recipients and HIV infected persons.

Eighty (16.0%) out of 500 subjects were positive for *Toxoplasma* IgG antibody by Toxo-Screen DA compared with 57 (11.4%) by Sabin-Feldman dye test. The sensitivity and specificity of Toxo-Screen DA were 100% and 94.8%, respectively, which were similar to previous reports from the area of high prevalence of *Toxoplasma* infection. In the present study, the positive predictive value of Toxo-Screen DA was only 71.3%.

The latex agglutination test should be considered as a screening test for *Toxoplasma* antibody, especially by small laboratories in remote areas due to its availability, simplicity, sensitivity and specificity. However, because of its moderate positive predictive value, the test should be used with caution in screening immunocompromised patients and pregnant women living in areas with a low prevalence of *Toxoplasma* infection. Since the number of false seropositive cases would be relatively higher than in a highly prevalent area, confirmation by the dye test would be needed. ❑

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PREVALENCE OF TOXOPLASMOSIS IN SELECTED POPULATIONS IN THAILAND

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Using the gold standard, the Sabin-Feldman dye test, we studied the prevalence of *Toxoplasma gondii* in 8,400 blood donors from various provinces of Thailand, 1,200 pregnant women with and without HIV infection, 500 newborn, as well as 190 HIV/AIDS patients and 200 kidney recipients.

The prevalence of *T.gondii* antibody in Thailand was 12.4% (95% CI = 11.7-13.1) in blood donors, 13.2% (95% CI = 11.3-15.2) in pregnant women, 0.8% (95% CI = 0.3-2.0) in newborns, 23.2% (95% CI = 17.6- 29.6) in HIV/AIDS patients, and 11.5% (95% CI = 7.2-16.0) in kidney recipients.

Health education concerning risk factors to prevent toxoplasmosis should be promoted among the population at risk. Cat ownership and a history of eating undercooked meat were found to be factors associated with this infection among pregnant women, whilst only the latter was found to be so among kidney recipients.

Though *Toxoplasma* prevalence is relatively low, its reactivation (43.2%) among Thai HIV/AIDS patients is high; thus *T.gondii* antibody detection is recommended for those patients. Proper chemoprophylaxis should be considered for HIV/AIDS patients as well as other immunocompromised subjects, such as kidney recipients with positive *Toxoplasma* antibody. ❑

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

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Two gametocyte-producing isolates of *Plasmodium falciparum*, KT1 and KT3 were cultivated *in vitro*. On day 11 of cultivation, pure gametocytes containing stage II, III and IV were used to test the gametocytocidal activity of 9-anilinoacridines that had previously demonstrated their activity against the asexual stage of the parasite. After drug exposure for 48 hours, gametocytes were maintained without drug for another two days before thin films were prepared for parasite counting. Gametocytocidal activities of 13 analogs of 9-anilinoacridine were observed with 50% inhibitory concentrations in the range of 0.6 M to greater than 100 M. The most active compound was 1'-CH_2NMe_2-9-anilinoacridine. Anilinoacridine derivatives with 3,6-diamino substitution had reduced gametocytocidal activity in contrast to their enhancing effect against the asexual forms. Morphological abnormalities of gametocytes were observed following drug exposure. ❑

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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 mid-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. ❑

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MULTIPLE MUTATIONS IN THE *rpoB* GENE OF RIFAMPICIN-RESISTANT *MYCOBACTERIUM TUBERCULOSIS* STRAINS FROM THAILAND

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

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

Presented in: The National Conference of Medical Sciences on 15th May, 2001 at BITEC Exhibition Hall, Bangkok, Thailand.

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

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Infections with atypical mycobacteria belonging to the *Mycobacterium avium*/intracellular complex (MAC) can occur in both animals and humans. Using a standardized-reagents commercial kit for random amplified polymorphic DNA (RAPD) analysis, 49 MAC strains isolated from 32 slaughtered pigs and 17 humans in Sweden were identified and sorted out, yielding 6 RAPD types. By combining the results of RAPD primers 4 and 5 and the primer IS1245A, we found that pigs and humans may be infected with the same types of MAC strains, since 14 strains from humans and 8 strains from pigs were essentially identical and together, comprised RAPD type 2, the largest group of strains (44.8% of strains). With respect to grouping of strains, serotype and RAPD type were uncorrelated, except for serotype 20 and RAPD type 6. Using standardized beads, RAPD analysis is a reproducible technique for typing MAC strains, as the indistinguishable banding patterns obtained with repeated analyses of two isolates from each strain in this study demonstrate. However, primer selection and DNA purity were crucial for differentiating closely related strains. ❑

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DIFFERENTIATION OF AVIAN PATHOGENIC *ESCHERICHIA COLI* (APEC) STRAINS BY RANDOM AMPLIFIED POLYMORPHIC DNA (RAPD) ANALYSIS

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Here we describe the application of a random amplified polymorphic DNA (RAPD) analysis for molecular genetic typing avian pathogenic *Escherichia coli* (APEC) strains. The RAPD technique was shown to be highly reproducible. Stable banding patterns with a high discriminatory capacity were obtained using two different primers. Overall, 55 *E. coli* strains were analyzed with a RAPD technique. The RAPD analysis showed that the *E. coli* strains isolated from poultry in Thailand and Sweden could be grouped into 50 RAPD types by using these two different primer sets. Most of these different *E. coli* RAPD types were not geographically restricted. There was, as expected, a tendency towards a higher genetic relationship among *E. coli* strains

isolated from the same farm. It is suggested that the RAPD technique may provide a rapid, low cost, simple and powerful tool to study the clonal epidemiology of avian *E. coli* infections. ❑

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HEALTH SURVEILLANCE AND MONITORING SYSTEM OF ENVIRONMENTAL POLLUTION

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National development in its socio-economic aspects and industrial, agricultural, services, and business development have been achieved at the expense of the environment and the country's natural resources. If such development gears towards raising the population's standard of living, promoting income generation, enhancing GNP without proper planning on systematic national resource usage, it will lead to impacts on humans and the environment. Degradation of the environment and natural resources are often caused by ineffective management systems, lack of sustainable/ irresponsible use of resources due to human activities, lack of preventive measures, low enforcement and good technologies. Principles of health surveillance and monitoring system for environmental pollution focus on key pollutants both point/non-point sources and the overall properties of those pollutants, which have potential adverse effects on human health - both acute and long term effects. The process employs a multi-disciplinary approach and environmental epidemiology to investigate causes and effects. Good models of health surveillance and environmental monitoring systems should be quick, convenient and simple to operate, sensitive to detect valid/invalid measurements, reliable, relevant to objectives of surveillance/monitoring, site-specific for hot spots, provide early detection of potential impacts/adverse effects and quick response/quick remediation to handle such potential impacts/adverse effects with existing technologies and local wisdom. Key factors pertinent to health surveillance and environmental monitoring are a) determination of risk areas/hot-spots of key pollutants likely to cause adverse health effects, including pollutant dispersal areas according to levels of concentration b) components relating to environmental and population health, including baseline information c) indicators/ parameters for surveillance and monitoring d) frequency of surveillance and monitoring. Establishment of sustainable environmental management and health surveillance/monitoring should be a holistic approach which links all relevant systems in all realms. ❑

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COMPARATIVE RISK ASSESSMENT: A CASE STUDY ON DIASTOLIC BLOOD PRESSURE AS RISK FACTOR FOR CORONARY HEART DISEASE

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Comparative risk assessment (CRA) is used to assess thorough estimation and total derivatives (attributable burden, attributable fractions) of potential risk factors (RFs) in the disease causal web of a specified population over a specified time. CRA not only indicates relative ranking of risks, but also signifies quantification of risks for the conduct of burden of disease (disability-adjusted life years, DALYs) in order to help establish evidence-based priorities for interventions. Results obtained from the CRA process would enable the evaluation of potential changes in the distribution of exposure of RFs in that specified population (feasible minimum risk, counterfactual), whereby resulting in risk reduction and avoidable burden of major diseases, disabilities and injuries through effective interventions or risk reduction strategies.

A case study to assess the risk estimation and the association of diastolic blood pressure (DBP), body mass index (BMI) and coronary heart disease (CHD) was conducted as a subset of key RFs in the causal web. Series of process and criteria had been used to ensure and sustain the success of the task.

The association of DBP and CHD mortality were investigated in nine major prospective observational studies conducted since 1965. Total 420,000 individuals, 843 strokes and 4856 CHD events, 6-25 years (mean=10) of follow-up were observed. The combined results demonstrated positive, continuous, and apparently independent associations, with no significant heterogeneity of effect among different studies. Among the nine studies, three long term follow-up studies with quintile distribution of DBP were used for this study, one in the UK-Whitehall study, two in the USA-MRFIT and Framingham studies. All of theses studies showed positive cumulative linear relationship between DBP and the risk/rate of CHD mortality, except for the Framingham study, which had both linear and exponential relationships. Age adjusted Standard Mortality Ratios (SMRs) or Relative Risks (RRs) across DBP distribution were estimated as summary measures of risk estimates and risk relationships to CHD. These RRs were then used for the calculation of attributable factions percent (AF%) for males using the true prevalence for all quintiles of DBP. The Whitehall study, carried out among 18,403 white male British civil servants aged 40-64 years old, indicated a linear trend of RRs of CHD mortality of, 1, 1.08, 1.42, 1.69 and 2.39.from the first to the fifth quintile of DBP accordingly. A similar linear trend was observed in MRFIT study, conducted among 350,977 white males, 35-57 years of age, with the RRs of 1, 1.2, 1.27, 1.66 and 2.32 across quintile distribution of DBP. Results of three successive 6-year follow-up periods from the Framingham study among 4,641 males aged 40-69 years old suggested a linear trend of CHD rate of 8, 9,10, 11 and 24 per 1000 across DBP quintile distribution. One study (Neaton *et al*, 1992) showed that DBP increased linearly with age in both males and females. The other (Schwarz *et al*, 1982) indicated a linear time-related trend between DBP and LDL-cholesterol level in both genders. The AF% calculated based on lowest risk category of DBP was 41.5 for both genders. Based on recommendations to reduce DBP by 2.5 mm Hg, population based, we estimated that a feasible minimum risk for CHD due to high DBP in the USA, as one possible counterfactual, would be that of 2.5 mm Hg among males. Application from the US population to other populations for this level of feasible minimum risk should be observed in different scenarios/settings. ❑

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A RANDOMIZED CLINICAL TRIAL OF COMBINATIONS OF ARTESUNATE AND AZITHROMYCIN FOR TREATMENT OF UNCOMPLICATED *PLASMODIUM FALCIPARUM* MALARIA IN THAILAND

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Recently, a combination of artesunate and mefloquine has proved effective, although it is contraindicated in early pregnancy and young children. Azithromycin, a widely used antibiotic that has antimalarial effects, replaces mefloquine as a new alternative antimalarial regimen. Two hundred and two uncomplicated falciparum malaria patients were randomly assigned to 1 of 3 regimens. Patients in group I (n = 68) received artesunate 200 mg once daily for 3 days, group II (n = 67) received artesunate 200 mg together with mefloquine 10 mg/kg on the first 2 days and artesunate 200 mg together with mefloquine 5 mg/kg on the third day, and group III (n = 67) received artesunate 200 mg together with azithromycin 50 mg once daily for 3 days. The 28-day cure rates were 44, 98 and 56%, respectively. The median time to recrudescence was significantly longer in group III. In conclusion, a combination of artesunate and azithromycin might be useful in treating children in whom bacterial and malarial infections may be concomitant. However, further work is required in order to enhance its clinical efficacy. ❑

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THE SITUATION OF MALARIA ALONG THE VIETNAM-LAO PDR BORDER AND SOME RELATED FACTORS

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This was a descriptive cross sectional study. It was done in 4 communes along the Vietnam-Lao PDR border of two mountainous provinces: Sonla and Nghean. The cluster multistage sampling technique was applied to choose the study sites. The results of the study show: among the 2,441 persons given blood tests to find malaria parasites, 0.7% of them carry malaria parasites, of whom 0.6% carry *P. falciparum* and 0.1% carry *P. vivax*. The malaria morbidity in the year was 6.9%. The mortality due to malaria is 1.59 per 100,000 population per year. Among the 106 hamlet motivators being interviewed, only 75.5% knew that malaria is transmitted by mosquitos, 71.7% knew that malaria patients are a source of transmission, over 50% of the motivators have mistaken understanding about the living environment of malaria mosquitos. Most of them have had mistakes in diagnosis, treatment of malaria, mosquito-killing spraying. Among the 729 adults being interviewed, 59.0% did not know about the causes of malaria, 30.7% did not take part in malaria control activities. Only 69.3% of the adults regularly sleep inside mosquito nets, 68% of adults buy medicine to cure malaria, 39.9% referred patients to health facilities for cure, and 25% use forest herbs to cure malaria. The factors that increased malaria morbidity in communes along the Vietnam-Lao PDR border have been identified. ❑

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LIFESTYLE AND HEALTH ASPECTS OF RAW FOOD EATERS

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Among a number of alternative dietary regimens, raw food diets are interesting and increasingly popular in western countries. A high proportion of raw foods in the diet is the general concept, while raw food eaters follow different raw food dietary recommendations. The subjects are composed of 230 male and 342 female raw food eaters between the ages of 25-74 years, having maintained raw food diets for 2.3 years on average. Health habits were investigated by means of a detailed questionnaire and food frequency questionnaire, which were used to estimate food intake and food habits of the subjects. The raw food eaters in this study had high awareness concerning health. Most of them refused smoking, alcohol and frequently exercised. Findings indicated that 29.5% of male and 24.9% of female raw food eaters were underweight according to their body mass indices (BMI). Underweight was more pronounced in the raw food eaters with a higher proportion of raw food intake. An obvious relationship between the proportion of raw food consumed and menstrual situation was observed. Most raw food eaters consumed vegetarian diets. The average amount of fruit and vegetables consumed by the study cohort was 1,836 g/d. The most favoured fluids among raw food eaters were water, mineral water, fruit juices and herbal tea. Some raw food eaters did not drink at all (3.0%) and 31.6% drank less than 500 ml/d. Raw food diets contain a lot of vitamins and minerals as well as phytochemicals, but the strict vegan group with a high proportion of raw food diets may pose nutritional problems. Antinutrients and toxic substances in some raw foods should be correspondingly considered. Moreover, food safety is another point for concern in the consumption of raw food diets due to possible contamination by parasites, bacteria and soil-transmitted pathogens. ❑

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IDENTIFICATION OF K-ras GENE MUTATION IN DIMETHYL NITROSAMINE INDUCED *OPISTHORCHIS VIVERRINI* INFECTED HAMSTER CHOLANGIOCARCINOMA

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The gene mutations in K-*ras*, H-*ras* and N-*ras* genes at codons 12, 13 and 61 of dimethylnitrosamine induced *Opisthorchis viverrini* infected hamster cholangiocarcinoma cell lines were studied using polymerase chain reaction and single stranded conformation polymorphism. Results showed that point mutations at these regions in K-*ras*, H-*ras* and N-*ras* oncogenes were not present in all samples. The results indicated that the mutations in *ras* gene family were not associated to the cholangiocarcinogenesis in dimethylnitrosamine induced *Opisthorchis viverrini* infected hamsters. ❑

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TOBACCO SMOKING IN RELATION TO THE PHENOTYPE OF ALPHA-1-ANTITRYPSIN AND SERUM VITAMIN C CONCENTRATION

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Objectives: To investigate the effects of tobacco smoking on serum alpha-1-antitrypsin (AT) concentrations in relation to the Pi types of AT (MM and non-MM phenotypes) and vitamin C concentration in serum of Thai smokers and non-smokers.

Design: Cross-sectional study of smokers and non-smokers in a military unit in Bangkok, Thailand.

Materials and Methods: 123 male smokers and 66 male nonsmokers were randomly selected from a military unit in Bangkok. Venous blood was analyzed by rocket immunoelectrophoresis for AT concentrations; AT phenotype and vitamin C status were determined by iso-electrofocusing (IEF) and spectrophotometric methods. Co-variance analysis was used to determine whether smoking directly influences AT levels.

Result: There were statistically significantly higher levels of serum alpha-1-antitryp sin (AT) and thiocyanate concentrations in smokers than in non-smokers.

The thiocyanate level correlated with the duration and quantity of cigarette smoking. However, vitamin C, an antioxidant, was found with statistically significantly lower concentrations in smokers compared with non-smokers.

Conclusions: The results of this study suggest that the increase of AT concentration in smokers is an immediate response of the organism to limit the damaging effect of smoking on the lung tissue, while the decrease of the antioxidant vitamin C relates to the long term risk of smokers' developing cancer. ❑

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MUTAGENICITY AND ANTIMUTAGENICITY OF SOME FOOD PLANTS

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Food plants have been traditionally consumed by humans. They have nutritive value, especially micronutrients, comprising vitamins and trace elements. They may also have preventive and treatment effects for some diseases. One interesting aspect of some food plants is their effects on currently incurable diseases, especially cancer and HIV. This study attempted to determine the mutagenicity and antimutagenicity of some spices commonly used in Thai food. Fresh specimens of garlic, onion, shallot, lemon grass, galangal, ginger, 'Kra-chaai' (*Boesenbergia pandurata*), 'Ma-krut' (Leech lime) and holy basil, were water extracted, freeze dried and analyzed for mutagenicity and antimutagenicity, using the Ames' test. The bacteria used were *Salmonella typhimurium* TA 98 and TA 100. The mutagens and carcinogens used for testing antimutagenicity were 4-nitroquinoline N-oxide, benzo(a)pyrene and aflatoxin B_1. The results showed that onion and shallot had mutagenic effects. Antimutagenic effects were found for garlic, galangal, ginger, 'Kra-chaai', 'Ma-krut', onion and holy basil. The results are of benefit for further study. ❑

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DETECTION OF A NOVEL POINT MUTATION IN THE *P53* GENE IN GRADE II ASTROCYTOMAS BY PCR-SSCP ANALYSIS WITH ADDITIONAL KLENOW TREATMENT

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Using polymerase chain reaction-single strand conformation polymorphism (PCR-SSCP) with additional Klenow treatment and direct sequencing, mutations in the *p53* tumor suppresors gene were analyzed from 21 cases of human astrocytomas. Three cases had *p53* gene mutation: two of them were glioblastomas showing a point mutation in exon 5 and the other in exon 6. The last one was a gemistocytic astrocytoma showing a point mutation in exon 5. The frequency of *p53* gene mutations in the astrocytomas examined was 14.3% (3 of 21). No SSCP alterations were observed in any of the *p53* fragments amplified from WHO grade I pilocytic astrocytomas and WHO grade III anaplastic astrocytomas. Further examination by direct sequencing showed that two mutations of glioblastomas had single base substitutions resulting in silent and missense mutations, whereas one of the gemistocytic astrocytomas had a double-base substitution resulting in a missense mutation. The present studies revealed that all mutations were located outside the hot-spots and, interestingly, one of them disclosed a missense mutation in exon 5 at codon 166, which was first detected in a grade II astrocytoma (gemistocytic type). It is possible that the missense mutation at this codon may be associated with special risk factors for the development of astrocytic tumors in Thai patients. ❑

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MICROSATELLITE ALTERATIONS IN NON-SMALL 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%) harbored 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 goiter rate of the women was 50.6%. In schoolchildren it was between 27 to 93%. The use of iodinated water was not successful. In the project area, iodinated fish sauce was favored over iodinated salt. This was because the local population mostly used fish sauce instead of salt in their cooking. The results of two independent intervention trials, one with females and another with schoolchildren, 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 goiter rate of females of reproductive age decreased to about 20%. ❑

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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 the

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

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The dynamic changes of socio-economics leading to the industrialization of countries are known to affect lifestyle and nutritional behaviors 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 hematological picture in 270 overweight and obese in Bangkok, Thailand, compared with 175 normal subjects. No statistically significant differences in hemoglobin and hematocrit were observed in the overweight compared with the control subjects. The prevalence of hypertension exhibited in both male and female overweight and obese subjects. The prevalence of anemia 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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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 serum 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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A QUANTITATIVE ULTRASTRUCTURAL STUDY OF THE PATHOLOGY OF MALARIA

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Death from severe *Plasmodium falciparum* malaria can result from a variety of syndromes including cerebral malaria and renal failure. Coma in severe malaria has been linked to sequestration of parasitized red blood cells (PRBC) in the cerebral microvessels. This study conducted a detailed electron microscopic study to examine ultrastructure in the kidneys and neuropathological features in the brains of fatal malaria in 65 patients who died of severe malaria in Thailand and Vietnam.

Quantitation of the amount of PRBC sequestration in the vasculature of the brains and the kidneys was performed, to see if this correlated with the clinical incidence of coma in cerebral malaria and acute renal failure. Parasite staging and PRBC sequestration in the brains and in the kidneys were compared with the peripheral blood, to calculate the sequestration index (S.I.). A number of different pathological features were identified, including PRBC sequestration, hemorrhages, endothelial cell changes, immune complex deposition and the interaction between PRBC and the host cells.

Rosette-'like' formation was observed in the lumen of a larger cerebral venule, intermixed with red blood cell aggregration. PRBC sequestration was significantly higher in the brains of patients with cerebral malaria (CM) compared to non-cerebral malaria (NCM) in all parts of the brain (cerebrum, cerebellum and medulla oblongata). There was a hierarchy of sequestration with the cerebrum and cerebellum showing higher sequestration than the medulla oblongata. PRBC sequestration in the brain was significantly higher than in the kidney. This implies that PRBC sequestration is more specific to the cerebral microvasculature.

Of the fatal cases with acute renal failure (ARF), it was found that, knob negative PRBC (K-PRBC) sequestration in the kidneys was significantly higher compared to those without renal failure (NARF). There was no deposition resembling immune complex at the basement membrane in the cerebral vessels. In the kidneys, only little evidence of the deposition was found in the basement membrane and in the mesangial areas. Leukocyte sequestration was a focal finding in the brains but more in the kidneys. Common to both the brains and the kidneys was the finding of mononuclear phagocytes containing phagocytosed malarial pigments. Little evidence of fibrin-platelet thrombus formation was seen. Similarly, changes of the endothelial cells in both CM and NCM group such as psuedopodia formation, vacuolation, cell swelling and intercellular gap of the endothelial cells were noted. Vacuolated, swollen pericytes were always found and sometimes filled in their cytoplasm with lipofuscin granules.

The overall sequestration index (S.I.) for patients showed 26.55 times more PRBC in the brain, and 2.82 times in the kidney microvasculature than the peripheral blood. The S.I. in the brain was significantly higher in

CM compared to NCM patients (CM, median=50.66, range 0-3660000; NCM, median=6.88, range 0- 29520; p= 0.042). There was no significant differentce in the S.I. in the kidneys comparing between different clinical groups (ARF, NARF, CM and NCM). Sequestration patterns were not affected by choice of drug treatment with either quinine or artemether or the time from treatment to death. There was no significant correlation of PRBC sequestration in the brains and the kidneys.

This research concludes that sequestration of PRBC undergoes extensive interaction in the same way with the host cells in the brains of CM or NCM groups and the kidneys, mostly with the endothelial cells and mononuclear phagocytes. K-PRBC sequestration in the kidneys is associated with acute renal failure. PRBC sequestration in the cerebral microvessels is associated with pre-mortem coma and cerebral malaria. ❑

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PLASMODIUM FALCIPARUM SPECIFIC CHIMERIC IgE: AN *IN VITRO* MODEL FOR STUDY OF *PLASMODIUM FALCIPARUM* ACTIVATED MONOCYTES

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Objective: To use a chimeric IgE, combining the $F(ab')_2$ part of *Plasmodium falciparum* (Pf) specific IgG and IgE myeloma, instead of natural falciparum specific IgE for study of Pf activated monocytes.

Methods: The concentration and specificity of the chimeric IgE were investigated by ELISA using plates coated with Pf Ag. The efficiency of chimeric IgE to stimulate monocyte activation was compared with that of LPS, soluble Pf antigen alone, chimeric IgE alone as well as with complexes of chimeric IgE and soluble Pf antigen. Monocytic response to Pf-chimeric IgE complexes through binding to monocytic CD23 was evaluated by determination of iNOS mRNA expression in stimulated monocyte (by RT-PCR) and TNF secretion in culture media (by ELISA) at various times.

Result: Complexes of chimeric IgE (20 pg/ml) and soluble Pf antigen (5 mg/ml) stimulated normal monocytes in 48 hr cultures to produce TNF-a as efficiently as LPS and much more than late stage Pf (10^6 parasites/ml) alone, soluble Pf Ag (5 mg/ml) or purified chimeric IgE (2-20 pg/ml) alone. The TNF-a level was maximal 24 hours after stimulation. The iNOS mRNA expression was increased within 2 hours after beginning of stimulation.

Conclusion: Complexes of soluble Pf Ag and IgE antibodies may contribute significantly to enhance the severity of *P. falciparum malaria.* ❑

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DOES HIV INFECTION ACCELERATE THE DEVELOPMENT OF HEPATOCELLULAR CARCINOMA? A CASE REPORT IN A YOUNG MAN

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Hepatocellular carcinoma (HCC) is an important cancer. It occurs more often in men than women, and occurs mostly in people 50 to 60 years old. HCC has not been previously reported in a young HIV-seropositive patient in Thailand. We documented a very rare case of HCC in a 33 year old man. He was diagnosed and treated as having salmonella septicemia and tuberculosis. However, additional diagnosis based on pathological study disclosed moderately differentiated HCC. Immunohistochemistry study of the liver tissue was positive for Hepatitis B surface antigen (HBsAg). The role of human immunodeficiency virus (HIV) infection in accelerating the development of hepatitis B-associated HCC is discussed. ❑

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CEREBROSPINAL FLUID ANALYSIS IN EOSINOPHILIC MENINGOENCEPHALITIS

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Eosinophilic meningoencephalitis (EME) remains one of the important neurological diseases and is widely distributed in Thailand. We collected and analyzed 56 EME cases from cytological submitted specimens. 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 in most patients. There was a clear seasonal occurrence between July to January. No specific treatment was given in this study. Supportive therapy, which included spinal taps, analgesics and corticosteroids were adequate. No fatal case was seen. The CSF specimens were classified in two categories, namely fresh CSF and the 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 ($p = 0.001$, $p = 0.001$, 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 yield of eosinophils, especially in the early course of the disease can readily be detected in the H&E stained centrifuged CSF sediment, wherein it was negative in the fresh specimen. However, a couple of tests may increase the sensitivity and specificity of EME diagnostic results. ❑

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VARIOUS MORPHOLOGIC FEATURES OF *GNATHOSTOMA SPINIGERUM* IN HISTOLOGIC SECTIONS: REPORT OF 3 CASES WITH REFERENCE TO TOPOGRAPHIC STUDY OF THE REFERENCE WORM

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Gnathostomiasis is common in Southeast Asian countries and can be found sporadically in other parts of the world mainly due to humen. The definitive diagnosis can be given either by identification of the parasite isolated from the patient or through histologic section of the lesion. It is therefore important for pathologists to be familiar with the morphology of parasitic larva which varies according to the levels of section-cuttings so that the diagnosis will not be misled. We presented three cases of gnathostomiasis with different features of parasitic morphology and compare with the reference adult worm. ❑

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NECROPSY IN HIV-INFECTED PATIENTS

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The increasing trend of human immunodeficiency virus (HIV) infection is usually followed by varieties of opportunistic infections, especially in the full-blown acquired immunodeficiency syndrome (AIDS). We studed the histopathological changes of different organs in relation to HIV infection, with special emphasis on the opportunistic infections. Various organs from seventeen cases of HIV-infected patients were collected by necropsy and analyzed for any histopathological changes. The major histopathological changes included cytomegalovirus infection, cryptococcosis, penicillosis, 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 are described and discussed in detail. ❑

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A COMPARATIVE TRIAL OF ALBENDAZOLE ALONE VERSUS COMBINATION OF ALBENDAZOLE AND PRAZIQUANTEL FOR TREATMENT OF *TRICHURIS TRICHIURA* INFECTION

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A randomized clinical trial was conducted to compare the effectiveness of albendazole alone and albendazole combined with praziquantel in the treatment of *Trichuris trichiura* infection. The drug regimens consisted of a single dose of albendazole 400 mg (A1, n=34X, 3 days of albendazole 400 mg daily (A3, n=34),

5 days of albendazole 400 mg daily (A5, n=35), a single dose of albendazole 400 mg plus praziquantel 40 mg/kg (A1P1, n=34), and 3 days of albendazole 400 mg plus praziquantel 40 mg/kg daily (A3P3, n=36). It was found that treatment with 3 or more consecutive days of albendazole with or without praziquantel resulted in significant reduction in density of *Trichuris* eggs in stool while a single dose of such drug did not. Praziquantel was not shown to have synergistic or antagonistic effects with albendazole. A regimen of 400 mg of albendazole daily for 3 days was found to be the most suitable therapy for *Trichuris* infection. ❑

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PLASMA RETINOL AND ALPHA-TOCOPHEROL LEVEL AND GROWTH INDICES OF 7 MONTHS OLD HEALTHY THAI INFANTS IN BANGKOK

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A cross-sectional study was conducted to measure plasma retinol and alpha-tocopherol status and the growth indices of 66 healthy Thai infants aged about 7 months old. The mean (SD) plasma retinol and alpha-tocopherol level were 1.59 (0.31) and 25.40 (7.01) ∝mol/L respectively. For their weight, height, and body mass index, the mean (SD) values were 7.96 (0.93) kg, 69.95 (2.42) cm, and 16.25 (1.43) respectively. There was a remarkable proportion of improper feeding. However there was no correlation between plasma retinol level, plasma alpha-tocopherol level, growth indices and duration of breast milk, formula milk, weaning food feeding, except for alpha-tocopherol level which has positively correlated with the duration of breastfeeding. ❑

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MICROSATELLITE MARKERS REVEAL A SPECTRUM OF POPULATION STRUCTURES IN THE MALARIA PARASITE *PLASMODIUM FALCIPARUM*

Anderson TJ, Haubold B, Williams JT, Estrada-Franco JG, Richardson L, Mollinedo R, Bockarie M, Mokili J, Mharakurwa S, French N, Whitworth J, Velez ID, Brockman AH, Nosten F, Ferreira MU, Day KP

Multilocus genotyping of microbial pathogens has revealed a range of population structures, with some bacteria showing extensive recombination and others showing almost complete clonality. The population structure of the protozoan parasite *Plasmodium falciparum* has been harder to evaluate, since most studies have used a limited number of antigen-encoding loci that are known to be under strong selection. We describe length variation at 12 microsatellite loci in 465 infections collected from 9 locations worldwide. These data reveal dramatic differences in parasite population structure in different locations. Strong linkage disequilibrium (LD) was observed in six of nine populations. Significant LD occurred in all locations with prevalence <1% and in only two of five of the populations from regions with higher transmission intensities. Where present, LD results largely from the presence of identical multilocus genotypes within populations, suggesting high levels of self-fertilization in populations with low levels of transmission. We also observed dramatic variation in diversity and geographical differentiation in different regions. Mean heterozygosities in South American countries (0.3-0.4) were less than half those observed in African locations (0. 76-0.8), with intermediate heterozygosities in the Southeast Asia/Pacific samples (0.51-0.65). Furthermore, variation was distributed among locations in South America (F: (ST) = 0.364) and within locations in Africa (F: (ST) =

0.007). The intraspecific patterns of diversity and genetic differentiation observed in *P. falciparum* are strikingly similar to those seen in interspecific comparisons of plants and animals with differing levels of outcrossing, suggesting that similar processes may be involved. The differences observed may also reflect the recent colonization of non-African populations from an African source, and the relative influences of epidemiology and population history are difficult to disentangle. These data reveal a range of population structures within a single pathogen species and suggest intimate links between patterns of epidemiology and genetic structure in this organism. ❑

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PHARMACOKINETIC–PHARMACODYNAMIC EVALUATION OF CEFTAZIDIME CONTINUOUS INFUSION *VS* INTERMITTENT BOLUS INJECTION IN SEPTICAEMIC MELIOIDOSIS

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Aims Experimental studies have suggested that constant intravenous infusion would be preferable to conventional intermittent bolus administration of beta-lactam antibiotics for serious Gram-negative infections. Severe melioidosis (*Burkholderia pseudomallei* infection) carries a mortality over 40% despite treatment with high dose ceftazidime. The aim of this study was to measure the pharmacokinetic and pharmacodynamic effects of continuous infusion of ceftazidime *vs* intermittent bolus dosing in septicaemic melioidosis.

Methods Patients with suspected septicaemic melioidosis were randomised to receive ceftazidime 40 mg kg^{-1} 8 hourly by bolus injection or 4 mg kg^{-1} h^{-1} by constant infusion following a 12 mg kg^{-1} priming dose and pharmacokinetic and phamacodynamic parameters were compared.

Results Of the 34 patients studied, 16 (59%) died. Twenty patients had cultures positive for *B. pseudomallei,* of whom 12 (60%) died. The median MIC_{90} of *B. pseudomallei* was 2 mg 1^{-1}, giving a minimum target concentration (4*MIC) of 8 mg 1^{-1}. The median (range) estimated total apparent volume of distribution, systemic clearance and terminal elimination half-lives of ceftazidime were 0.468 (0.241-0.573) 1 kg^{-1}, 0.058 (0.005-0.159) 1 kg^{-1} h^{-1} and 7.74 (1.95-44.71) h, respectively. Clearance of ceftazidime and creatinine clearance were closely correlated (r=0.71; P<0.001) and there was no evidence of significant nonrenal clearance.

Conclusion Simulations based on these data and the ceftazidime sensitivity of the *B. pseudomallei* isolates indicated that administration by constant infusion would allow significant dose reduction and cost saving. With conventional 8 h intermittent dosing to patients with normal renal function, plasma ceftazidime concentrations could fall below the target concentration but this would be unlikely with a constant infusion. Correction for renal failure, which is common in patients with meliodosis, is Clearance = k * creatinine clearance where *k*=0.72. Calculation of a loading dose gives median (range) values of loading dose, D_L of 18.7 mg kg^{-1} (9.5-23) and infusion rate I = 3.5 mg kg^{-1} h^{-1} (0.4-13) (which equals 84 mg kg^{-1} day^{-1}). A nomogram for adjustment in renal failure is given. ❑

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ANTIGENIC HETEROGENEITY OF LIPOPOLYSACCHARIDE AMONG *BURKHOLDERIA PSEUDOMALLEI* CLINICAL ISOLATES

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Burkholderia *pseudomallei* (BP) causes melioidosis, a potentially fatal human infection in the tropics. Clinical isolates from different geographical locations have similar morphological and biochemical characteristics. Although BP has been reported to possess 2 types of lipopolysaccharide (LPS) differing in the chemical structure of their O-polysaccharide (O-PS) component, an earlier report demonstrated that the clinical strains exhibited identical LPS moieties. Recently, we reported antigenic similarity between the pathogenic (Ara-) and nonpathogenic (Ara+) biotypes. However, a few clinical isolates showed atypical SDS-PAGE profiles. In this study, LPS from 739 BP isolated from patients and animals in different geographical areas were extracted by proteinase K digestion method. Their SDS-PAGE profiles and their immunoreactivities with patients' sera and monoclonal antibody (MAb) to LPS were analyzed. The isolates showed 3 LPS patterns differing in the number and electrical mobility of bands in silver-stained gel. A majority of BP (711) isolates exhibited an identical typical ladder pattern, 21 isolates showed an atypical ladder pattern and 7 isolates did not exhibit any ladder appearance. However, all LPS preparations exhibited similar endotoxic activity as determined by Limulus amebocyte lysate assay. On the other hand, there was no immunological cross reactivity between typical and atypical LPS, as judged from Western blot against homologous and heterologous sera from melioidosis patients from whom the typical and atypical LPS were isolated. Nevertheless, a Western blot profile of the typical LPS showed some variations when probed with MAb against BP LPS (9D5). Heat-killed bacteria from all LPS groups could similarly activate a mouse macrophage cell line to produce nitric oxide (NO) and inducible NO synthase (iNOS). ❑

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THE RESISTANCE TO PHYSIOLOGICAL SHEAR STRESSES OF THE ERYTHROCYTIC ROSETTES FORMED BY CELLS INFECTED WITH *PLASMODIUM FALCIPARUM*

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Rosetting forces are believed to be an important contributor to the microcirculatory obstruction that occurs in malaria caused by *Plasmodium falciparum.* In this study, rosettes of erythrocytes from cultures of this parasite were suspended in different media and exposed to shear stresses corresponding to those encountered on the arterial and venous sides of the human circulation. The rosettes formed by infected erythrocytes in malaria culture medium containing 10% AB serum were disrupted easily (approximately 50% being broken) when exposed to very low shear stresses of <0.5 Pa. However, use of higher concentrations of serum strengthened the rosetting binding forces considerably. Suspension of rosettes in a viscous colloid (e.g. dextran) increased the adherence forces between infected and uninfected red cells. The results indicate that rosettes do resist the physiological shear forces that are encountered in the venular side of the circulation and could thus contribute to microvascular obstruction in falciparum malaria. ❑

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PROGRESSION OF SKELETAL MUSCLE DAMAGE DURING TREATMENT OF SEVERE FALCIPARUM MALARIA

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To assess the relationship between severity of malaria and progression of skeletal muscle damage during initial treatment, we studied 28 Thai adults with slide-positive falciparum malaria. Six had uncomplicated malaria (Group 1), 12 had severe non-cerebral malaria (Group 2) and ten had cerebral malaria (Group 3). There were no significant differences between baseline serum creatine kinase (CK) levels in the three groups (P=0.071). There was no change in serum CK during the first 48 h of treatment in Group 1 cases. In Group 2 patients, the median peak serum CK was nine times that at baseline, while in Group 3, serum CK peaked at a median concentration 20 times that at presentation. In Groups 2 and 3, the peak serum CK occurred at least 24 h after presentation in more than half the patients, and was independent of intramuscular injections and convulsions during initial therapy. These longitudinal data suggest that: (i) severe falciparum malaria is associated with skeletal muscle damage that increases during initial therapy, especially in patients with coma; (ii) the effect of other major treatment or infection-specific factors that are associated with muscle damage does not diminish this relationship; and (iii) cerebral malaria in combination with a high baseline and rising serum CK should pre-empt monitoring and management strategies aimed at preserving renal function including renal dialysis. ❑

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THE CXC CHEMOKINES GAMMA INTERFERON (IFN-GAMMA)-INDUCIBLE PROTEIN 10 AND MONOKINE INDUCED BY IFN-GAMMA ARE RELEASED DURING SEVERE MELIOIDOSIS

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Gamma interferon (IFN-gamma)-inducible protein 10 (IP-10) and monokine induced by IFN-gamma (Mig) are related CXC chemokines which bind to the CXCR3 receptor and specifically target activated T lymphocytes and natural killer (NK) cells. The production of IP-10 and Mig by various cell types *in vitro* is strongly dependent on IFN-gamma. To determine whether IP-10 and Mig are released during bacterial infection in humans, we measured plasma levels of IP-10 and Mig in patients with melioidosis, a severe gram-negative infection caused by *Burkholderia pseudomallei*. IP-10 and Mig were markedly elevated in patients with melioidosis on admission, particularly in blood culture-positive patients, and remained elevated during the 72-h study period. Levels of IP-10 and Mig showed a positive correlation with IFN-gamma concentrations and also correlated with clinical outcome. In whole blood stimulated with heat-killed *B. pseudomallei*, neutralization of IFN-gamma and tumor necrosis factor alpha (TNF-alpha) partly attenuated IP-10 and Mig release, while anti-interleukin-12 (IL-12) and anti-IL-18 had a synergistic effect. Stimulation with other bacteria or endotoxin also induced strong secretion of IP-10 and Mig. These data suggest that IP-10 and Mig are part of the innate

immune response to bacterial infection. IP-10 and Mig may contribute to host defense in Th1-mediated host defense during infections by attracting CXCR3(+) Th1 cells to the site of inflammation. ❑

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NEONATAL NEUROLOGICAL TESTING IN RESOURCE-POOR SETTINGS

McGready R, Simpson J, Panyavudhikrai S, Loo S, Mercuri E, Haataja L, Kolatat T, Nosten F, Dubowitz L

The aim of the study was to design and test a neurological examination for newborns that could be performed reliably by paramedical staff in resource-poor settings. The examination was adapted from a method established by Dubowitz et al., the latest version of which includes an optimality score. The final items in the test were chosen because they were culturally acceptable, could be elicited according to strict but easily comprehensible instructions and because the expected responses could be scored by the descriptions given or by diagrams in the proforma. The shortened examination was easily taught to paramedical staff who achieved a high degree of inter-observer reliability. This shortened version of the examination was piloted by comparing newborns from a Karen refugee camp on the western border of Thailand and from a large maternity hospital in Bangkok with a standardized cohort of newborns in London. The modified shortened version of the test was sufficiently sensitive to identify a number of differences between the cohorts, notably the poor vision performance and markedly reduced tone of the Karen newborns. In conclusion, the test can be used very reliably by paramedical staff and is a useful, simple and portable tool for the neurological assessment of newborn babies where resources are limited. ❑

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RANDOMIZED COMPARISON OF MEFLOQUINE-ARTESUNATE VERSUS QUININE IN THE TREATMENT OF MULTIDRUG-RESISTANT FALCIPARUM MALARIA IN PREGNANCY

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Since no effective malaria prevention measures have been identified for pregnant women living on the western border of Thailand, prompt diagnosis and efficient treatment are paramount, although drug resistance in *Plasmodium falciparum* has narrowed the treatment options. An open randomized comparison of supervised quinine (10 mg salt/kg every 8 h) for 7 days (Q7) versus mefloquine 25 mg base/kg (total dose) plus artesunate 4 mg/kg per day for 3 days (MAS3) was conducted in 1995-97 in 108 Karen women with acute uncomplicated falciparum malaria in the second or third trimesters of pregnancy. The MAS3 regimen was more effective than the Q7 regimen: day 63 cure rates were 98.2% (95% CI 94.7-100) (n = 65) for MAS3 and 67.0% (95% CI 43.3-90.8) (n = 41) for Q7, P = 0.001. The MAS3 regimen was also associated with less gametocyte carriage; the average person-gametocyte-weeks for MAS3 was 2.3 (95% CI 0-11) and for Q7 was 46.9 (95% CI 26-78) per 1000 person-weeks, respectively (P < 0.001). MAS3 was significantly better tolerated. These evident advantages must be balanced against a possible increased risk of stillbirth with the use of mefloquine in pregnancy. Further

randomized studies assessing the safety and efficacy of other artemisinin-containing combination regimens in pregnancy are needed urgently. ❑

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ANTIMALARIAL BIOAVAILABILITY AND DISPOSITION OF ARTESUNATE IN ACUTE FALCIPARUM MALARIA

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The pharmacokinetic properties of oral and intravenous artesunate (2 mg/kg of body weight) were studied in 19 adult patients with acute uncomplicated *Plasmodium falciparum* malaria by using a randomized crossover artesunate and its principal metabolite, dihydroartemisinin. The oral study was repeated with 15 patients during convalescence. The mean absolute oral bioavailability of the antimalarial agent in patients with acute malaria was 61% (95% confidence interval [CI], 52 to 70%). The absorption and elimination of oral artesunate were rapid, with a mean elimination half-life of antimalarial activity of 43 min (95% CI, 33 to 53 min). Following oral administration to patients with acute falciparum malaria, peak antimalarial activity in plasma and the area under the plasma concentration-time curve were approximately double those during convalescence and the apparent volume of distribution and clearance were approximately half those during convalescence ($P < 0.005$). Acute malaria is associated with a significant reduction in the clearance of artesunate-associated antimalarial activity. ❑

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INTERACTION OF INSULIN WITH *BURKHOLDERIA PSEUDOMALLEI* MAY BE CAUSED BY A PRESERVATIVE

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Aim - To re-examine the previously reported *in vitro* interaction of insulin with *Burkholderia pseudomallei*, in the light of a suggestion that the interaction may have resulted from the presence of the preservative m-cresol in commercial preparations.

Methods - Broth culture studies of *B.pseudomallei* were performed with and without the addition of m-cresol and various preparations of insulin.

Results - Growth of *B.pseudomallei* was inhibited by m-cresol at the concentrations found in pharmaceutical insulin preparations, and by the insulin preparation Humulin R, but not by pure insulin.

Conclusions - The results of previous experiments may have been confounded by the presence of the preservative m-cresol. q

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DIFFERENTIAL ANTIBIOTIC-INDUCED ENDOTOXIN RELEASE IN SEVERE MELIOIDOSIS

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Severe melioidosis is a life-threatening, systemic bacterial infection caused by *Burkholderia pseudomallei*. A prospective, randomized treatment trial was conducted in northeast Thailand to compare ceftazidime (a penicillin-binding protein [PBP]-3-specific agent that causes release of large amounts of endotoxin *in vitro*) and imipenem (a PBP-2-specific agent that kills *B. pseudomallei* more rapidly but releases low amounts of endotoxin) in severe melioidosis over a 6-h time course after the first dose of antibiotic. Despite similar clinical, microbiological, endotoxin, and cytokine measures at study entry, ceftazidime-treated patients (n=34) had significantly greater systemic endotoxin (P<.001) than patients treated with imipenem (n=34) after the first dose of antibiotic. No overall difference in mortality was observed (35% in both groups [95% confidence interval, 20%-50%]). Differential antibiotic-induced endotoxin release is demonstrable in severe melioidosis. These differences in endotoxin release did not appear to have a significant impact on survival in this group of patients. ❑

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PROGNOSTIC VALUE OF CYTOKINE CONCENTRATIONS (TUMOR NECROSIS FACTOR-, INTERLEUKIN-6, AND INTERLEUKIN-10) AND CLINICAL PARAMETERS IN SEVERE MELIOIDOSIS

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Raised serum concentrations of tumore necrosis factor (TNF)-, interleukin (IL)-1, IL-6, or IL-10 are associated with mortality in patients with sepsis, but it is not known whether elevated cytokine levels are independently predictive of mortality. Cytokine assays (TNF-, IL-6 and IL-10) were performed on admission plasma samples from 172 adult Thai patients with severe melioidosis. Mortality was 31.4%. APACHE II score; septicemia; plasma lactate; TNF-, IL-6 and IL-10 concentrations; and IL-10/TNF- and IL-6/IL-10 ratios were each associated with outcome (P< .001 for all variables). Only the APACHE II score and either IL-6 or IL-10 concentration were independent predictors of mortality, as determined by use of multiple logistic regression (with cytokine concentrations and ratios entered separately). In a multivariate analysis, including both IL-6 and IL-10, concentration was no longer predictive. Therefore, APACHE II scores and either IL-6 or IL-10 concentration may be the most reliable parameters for stratification of patients in future studies of severe gram-negative sepsis. ❑

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SERUM BACTERICIDAL AND INHIBITORY TITRES IN THE MANAGEMENT OF MELIOIDOSIS

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A retrospective evaluation of the relationship between serum bactericidal and inhibitory titres and treatment outcome in 195 adult Thai patients with severe melioidosis was conducted. Drug regimens included ceftazidime (52% of patients), co-amoxiclav (24%), imipenem (11%) or the conventional four-drug combination (11%). Pre- and 1 h post-dose serum samples were collected after 48-72 h of therapy, and serum inhibitory and bactericidal titrations determined. Median post-dose titres were: bactericidal 1:8 (range 0-1:128) and inhibitory 1:16 (range 0-1:128). Overall mortality was 26% and outcome was not influenced by either inhibitory or bactericidal titres. Pre-dose titres correlated with renal function; renal function was the most important predictor of mortality. Determination of serum inhibitory or bactericidal titres is unhelpful in the management of severe melioidosis. ❑

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MEFLOQUINE PHARMACOKINETIC–PHARMACODYNAMIC MODELS: IMPLICATIONS FOR DOSING AND RESISTANCE

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Antimalarial resistance develops and spreads when spontaneously occurring mutant malaria parasites are selected by concentrations of antimalarial drug which are sufficient to eradicate the more sensitive parasites but not those with resistance mutation(s). Mefloquine, a slowly eliminated quinoline-methanol compound, is the most widely used drug for the treatment of multidrug-resistant falciparum malaria. It has been used at doses ranging between 15 and 25 mg of base/kg of body weight. Resistance to mefloquine has developed rapidly on the borders of Thailand, where the drug has been deployed since 1984. Mathematical modeling with population pharmacokinetic and *in vivo* and *in vitro* pharmacodynamic data from this region confirms that, early in the evolution of resistance, conventional assessments of the therapeutic response <28 days after treatment underestimate considerably the level of resistance. Longer follow-up is required. The model indicates that initial deployment of a lower (15-mg/kg) dose of mefloquine provides a greater opportunity for the selection of resistant mutants and would be expected to lead more rapidly to resistance than *de novo* use of the higher (25-mg/kg) dose. ❑

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THE TREATMENT OF THAI PATIENTS WITH HIV INFECTION: A CLINICAL TRIAL OF MODIFIED BOVINE COLOSTRUM (MDK 2000)

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A combination of protease inhibitors and nucleoside severse transcriptase inhibitors is now considered the standard antiretroviral treatment regimen. Although this regimen is usually well tolerated, the side-effects can be considerable. Moreover, the highly cost fo these drugs, together with uninterrupted long-term treatment in HIV-infected patients, leads to the need to develop a natural product that can be curative. MDK 2000, the mixture of bovine colostrum and biologically processed American Indian herbs was used in 10 human immunodeficiency virus (HIV)-positive patients with CD_4 cell count >50 x 10^6/l or HIV RNA >1,000 copies/m. Biochemical findings showed that this natural regimen had no effect on liver and kidney functions and no hematological disorder. Four patients had a reduction of HIV RNA >0.5 $\log_{10}$ copies/ml and three patients had an increase in the CD_4 cell counts >100 x 10^6/l. All patients gained weight, from 2 to 8 kg, while taking MDX 2000. They had shorter fever-effected periods and could recover without taking analgestics. None of them contracted opportunistic infection or pruritis. One case experienced a decrease in the size of enlarged cervical lymph nodes. ❑

SAFETY OF LIVE RECOMBINANT ALVAC-HIV (VCP1521) PRIMING WITH AIDSVAX™ B/E BOOSTING IN THAI HIV -1- NEGATIVE PARTICIPANTS: PRELIMINARY RESULTS

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Background: HIV -1 currently infects more than 33 million people (including 1.1 million children) worldwide and exists as multiple genetic subtypes (currently designated A - I and O). Data from antibody cross-reactivity studies demonstrate that binding and neutralizing antibodies from subtype B and E infected subjects react preferentially with viruses from the same subtype. These studies illustrate the technical limitations of the formal approach to the development of HIV-1 vaccine. A prime-boost combination of candidate vaccinesThe other empiric test products that elicit both humoral and cellular immune responses to viral strains prevalent within the region (subtypes E & B in Thailand), - ALVAC-HIV vaccine prime and AIDSVAX™ B/E boost, is evaluated.

Objective: To determine safety of live recombinant ALVAC-HIV (vCP1521) priming with two doses of AIDSVAX™ B/E boosting in Thai HIV-negative participants.

Methods: This phase I/II study is double-blind, randomized, and placebo-controlled. 122 volunteers were enrolled and divided into two groups based on dose of booster vaccine (61 volunteers each).

Group I: 45 low-risk, HIV -seronegativie Thai adults were given ALVAC-HIV (vCP1521,; $10^{6.53}$ $CCID_{50}$) priming at weeks 0, 4, 12, and 24. At weeks 12 and 24, ALVAC wasvCP1521 were administered with 200 mg of a bivalent AIDSVAX™ B/E gp120 (100 mg for each B (HIV MN) and E (HIV A244) gp120 antigen). 15 other subjects received placebo injections.

Group II: 45 low-risk, HIV-seronegativie Thai adults were given ALVAC-HIV (vCP1521;, $10^{6.53}$ $CCID_{50}$) at weeks 0, 4, 12, and 24. At weeks 12 and 24, vCP1521 ALVAC was administered with 600 ug of

bivalent AIDSVAX™ B/E gp120 (300 mg for each B and E gp120 antigen). 15 other subjects received placebo injections.

Results and Conclusions: Reactogenicity data were still blinded at writing of abstract. 57% and 67% of volunteers in Groups I and II, respectively, were males with median Group ages of 20-24 years. ALVAC vaccines priming with AIDSVAX™ boosting were safe (although including placebo participants in the analysis). The summary reactogenicity results are was shown in the table below (which include both vaccine and placebo recipients).

Group Over all Oral Temp >738.8°C ALVAC (n=61) or placebo AIDSVAX (n=61) or placebo

	Pain	Erythema	Induration	Pain	Erythema	Induration
Group I						
	(n=61)	4 (76.6%)	1118%	3 (54.9%)	5 (8.2%)	12%
				3 (5.3%)	25 (8.2%)	
Group II						
	(n=61)	6 (109.8%)	1321%	13 (21%)	8 (13%)	47%
				3 (5.0%)	8 (135%)	

There were no differentces in reactogenicities of ALVAC reported after successive immunization nor after administration concurrently with additional different doses of AIDSVAX™ B/E. Six participants reported serious adverse events; none were related to the study drug. Prime-boost vaccination with ALVAC-HIV and AIDSVAX™ B/E appears safe and well tolerated in Thai adults, and is an appropriate candidate for advancement to phase III evaluation. ❑

COMMUNITY CONSULTATION IN AN HIV VACCINE EFFICACY TRIAL AMONG INJECTING DRUG USERS (IDUs) IN BANGKOK, THAILAND

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Background: A phase III 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 (BMA) area. In Bangkok there are no non-governmental or community based organisations (NGOs or CBOs) representing the community of IDUs. To consult with members of the community and to address ethical concerns during the conduct of the trial, a community relations club (CRC) was established consisting of current and past IDUs.

Description: A community advisory working group was started in November 1998 to establish effective community consultation. Working group members were drug use counselors and social workers from the BMA clinics. Five focus group discussions were held among IDUs in methadone treatment to identify ways to foster mutual trust and understanding between the community and the investigators. In March 1999, the working group was transformed into a CRC, with its 11 members representing current and past IDUs. In October 2000, the CRC was revised to include more representatives of IDUs, including parents, community leaders, HIV-positive and HIV-negative IDUs and female IDUs. Since its inception, 14 bi-monthly meetings have been held in which issues such as confidentiality, benefits to participants, risk behavior changes in the community,

and access to antiretroviral and prophylactic treatment for HIV-infected IDUs in the trial were discussed and resolved with investigators.

Lessons learned: Community consultation for the design and conduct of the AIDSVAX™ B/E vaccine efficacy trial among Bangkok IDUs was hindered by the absence of NGOs and CBOs representing the interests of the drug using community. The establishment of a CRC initiated a platform to discuss and resolve issues related to trial participation and has been beneficial for both IDUs and investigators. ❑

DATA MANAGEMENT INFRASTRUCTURE DEVELOPMENT FOR AN HIV VACCINE TRIAL IN THAILAND

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Issues: Clinical trials of pharmaceutical products in developing countries pose significant challenges for the sponsor and host countries. Such trials should be conducted according to international standards and also benefit the host country with a better infrastructure.

Description: The AIDSVAX™ B/E candidate HIV vaccine efficacy trial was launched in March 1999 to enrol 2,545 IDUs in a randomized placebo-controlled trial. To strengthen the infrastructure of the country and to comply with the Good Clinical Practice (GCP) guidelines, a Data Management Unit (DMU) was established by VaxGen Inc. at the Vaccine Trial Centre, Faculty of Tropical Medicine, Mahidol University, using the DataFax (Clinical DataFax Systems Inc., Hamilton, Ontario, Canada) technology. This technology allows data-management quality control (QC) and quality assurance to be real-time, because the Case-Report Forms (CRF) are transmitted directly via facsimiles from the 17 participating drug treatment clinics instead of key-punching data. The DMU also serves as the off-site, encrypted back-up site for the HIV negative participants' laboratory data, which are blinded and transmitted monthly from the Bangkok Metropolitan Administration laboratory to VaxGen electronically as an attached, password-protected file. Data for participants who become HIV infected during the trial are also blinded and confidentially stored and backed up at the laboratory of The HIV/AIDS Collaboration, prior to monthly electronic password protected transmission to VaxGen. Through March 2001, the DMU had handled 181,022 CRF pages, with an average of 250 (0.1 %) QC problems per month delivered to 17 clinics on a weekly basis. The average turn-around time for the resolution of a QC problem has been approximately 11 days. In addition, more than 16,000 laboratory specimens were tested and these data were processed and transmitted to VaxGen.

Conclusions: This DMU is the first Thailand-established DMU for monitoring clinical trial data for licensing purposes. Its establishment is a model for collaborating sponsor and host countries, and it demonstrates that developing countries involved in clinical trials, with appropriate training, can perform this type of data management. The strengthened data management infrastructure in Thailand will be useful for future trials of HIV vaccines or other clinical trials. ❑

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 (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 an 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 excellent (0.4% 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 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 advized 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 2001 and final results are expected in late 2002. ❑

BASELINE DRUG USE, SEXUAL BEHAVIOR AND INCARCERATION PATTERNS AMONG 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 high rates of HIV infection. A 1995-1998 cohort study of Bangkok IDUs found an annual HIV incidence rate of 5.8 per 100 person-years, high rates of follow-up, and willingness to participate in HIV vaccine trials. In March 1999 a phase III trial was initiated to evaluate the protective efficacy of AIDSVAX™ B/E vaccine in this population.

Methods: Between March 1999 and August 2000, a total of 2,545 HIV seronegative IDUs with a history of injecting drug use in the preceding 12 months were enrolled in the trial. At baseline a standardized questionnaire was administered to assess demographic characteristics, sexual and drug use behaviors, and incarceration histories. Data were analyzed to evaluate HIV risk behavior patterns at enrollment.

Results: Study participants had a median age of 26 years, 93.4% were male and 99.8% had Thai nationality. At baseline, 93.8% reported to have injected drugs and 62.3% had received methadone detoxification treatment in the last 6 months. Heroin (98.5%) followed by stimulants (15.7%) were the preferred drugs injected, and daily injections (39.2%), needle sharing or re-use of needles (33.0%), and failure to always clean needles (33.1%) were reported by active users. In the 6 months prior to enrollment, 58.9% reported having had sexual intercourse, 57.4% reported living with a heterosexual partner, and 78.2% of these reported never using a condom when having intercourse with their live-in partners. Male to male sexual behavior was rarely reported (<1%). At baseline, a history of ever having been incarcerated (jail or prison) was common (78.5%); of those incarcerated in the last 6 months, 13.0% reported injection drug use while in jail or prison, and 1.1% reported anal sexual intercourse.

Conclusions: Bangkok IDUs enrolled in the AIDSVAX™ B/E vaccine trial reported high-risk injection drug use and sexual behaviors associated with transmission of HIV, confirming the need for a safe and effective HIV vaccine. Recruitment efforts to identify IDUs at highest risk of infection have been successful. Risk reduction counseling and monitoring are active components of the ongoing trial. ❑

INCARCERATION AMONG INJECTING DRUG USERS (IDUs) PARTICIPATING IN THE AIDSVAX™ B/E VACCINE EFFICACY TRIAL IN BANGKOK, THAILAND

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Background: In March 1999 a clinical trial to determine the protective efficacy of AIDSVAX™ B/E vaccine was started among 2,545 HIV seronegative IDUs in Bangkok, Thailand. HIV vaccine trial preparatory studies have shown incarceration to be a frequent occurence among Bangkok IDUs. We evaluate incarceration history at baseline and its frequency during follow-up among IDUs participating in the AIDSVAX™ B/E vaccine trial. No incarcerated IDUs were screened or enrolled in this trial.

Methods: 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: At enrollment, 78.5% of study participants reported a history of incarceration. At first follow-up, 20.2% reported to have been incarcerated during the last 6 months; at second and third follow-up these percentages were 24.3% and 24.5%, respectively. Through January 2001, a total of 16,835 study visits were conducted; 16,017 were clinic visits and 818 (4.9%) were prison visits. Each prison visit requires tracking of the participant and subsequent written permission of the Department of Corrections of the Ministry of Interior to visit the subject. In total, 363 incarcerated participants were visited in 21 different prisons, dispersed throughout the Bangkok metropolitan area. On 54 occasions 5 or more incarcerated participants were visited on 1 single day. Typically, a single prison visit takes half a day and requires the full-time presence of a doctor, a nurse, a councelor and a clinical research assistant (CRA) when vaccination is involved (n=414) and the full-time presence of a nurse, a counselor and a CRA for a standard follow up visit (n=404).

Conclusion: Incarceration is common among participants in the AIDSVAX™ B/E vaccine trial. Even though tracking of study subjects, permission requests, travel and time pose a serious logistical burden for study personnel, follow-up of participants becoming incarcerated during the trial has been successful. ❑

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 harm, 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 was 26 years (range 20 to 59), 93% were 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 was 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. ❑

RISK BEHAVIOR 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 were 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% ($p<0.001$), needle sharing to 16.3% ($p<0.001$) and injection drug use while being incarcerated to 8.6% ($p<0.01$). No significant changes were observed in condom use with steady or 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 reductions 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 indicated, risk reduction counseling will be adapted. ❑

RECRUITMENT OF INJECTING DRUG USERS (IDUs) IN THE AIDSVAX™ B/E VACCINE EFFICACY TRIAL IN BANGKOK, THAILAND: STRATEGIES AND LESSONS FOR HIV VACCINE STUDIES

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Issue: Recruitment of volunteers in large-scale clinical trials to test the efficacy of candidate HIV vaccines poses a serious challenge to investigators. We describe the modes of recruitment of volunteers enrolled in the AIDSVAX™ B/E vaccine trial in Bangkok, Thailand.

Description: Starting in 1988, IDUs in Thailand have experienced a severe HIV epidemic. The Bangkok Metropolitan Administration maintains a network of 17 drug treatment clinics, attended by some 16,000 IDUs annually. A 1995-1998 cohort study of 1,209 Bangkok IDUs showed an annual incidence rate of 5.8 per 100 person years, high rates of follow up and willingness to participate in HIV vaccine trials. In March 1999, a trial to test the efficacy of a bivalent rgp120 HIV vaccine (AIDSVAX™ B/E) was initiated in this population. During the first half-year of trial conduct, enrollment fell from 203 persons in May 1999 to 92 persons in October 1999. Activities to increase enrollment included: TV and radio spots, telephone hotline, posters, flyers (start: Sept. 1999); friend-help-friend referral program and extended clinic hours (Nov. 1999); recruitment and screening at mobile and suburban drug and health clinics (March 2000). During the remaining period an average of 157 persons were enrolled per month. Complete enrollment of 2,545 volunteers was achieved on August 31, 2000. Modes of recruitment of enrollees were: clinic attendee 1,105 (43.4%); friend-help-friend referral program 519 (20.4%); participant in the 1995-1998 cohort study 374 (14.7%); suburban health clinic 240 (9.4%); extended clinic hours 189 (7.4%); mobile clinic 72 (2.8%); others 50 (2%). Nineteen (0.8%) enrollees came forward after reading or hearing media messages (TV, radio, poster, flyer).

Conclusion: The majority of IDUs enrolled in this vaccine trial were recruited through personal contact. The most successful recruiting methods included contacts through the clinic, IDUs referring friends, and previous contact through the cohort study. Conventional recruiting methods through the media were not very productive. ❑

CUTANEOUS MANIFESTATIONS IN HIV POSITIVE PATIENTS

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Cutaneous manifestations are common clinical findings among HIV positive patients. The causes may be bacteria, viruses, fungi and other non-infectious agents. This study was conducted at the Pramongkutklao Hospital skin clinic to determine the frequency distribution of cutaneous manifestations in HiV positive patients. A total of 147 patients with HIV seropositivity were recruited and divided into a retropective group and a prospective study group. For the retrospective study, hospital records of 129 patients who attended from January 1995 to November 1998 were recruited. The prospective study was carried out from November 1998 to January 1999, and 18 patients were recruited. Cutaneous findings among patients in the two studies were evaluated. There were ten comon cutaneous manifestations observed in the retrospective and prospective study, including pruritic papular eruptions (PPE) (51.2%, 50%), oral candidiasis (16.7%, 21.7%), herpes zoster (10.9%,5.6%), oral hairy leukoplakia (10%, 5.6%), unclassified eczema (9%,

11.1%), urticaria (5.6%, 3.1%), seborrheic dermatitis (4.7%, 16.7%), folliculitis (4.7%, 5.6%), prurigo simplex (4.7%, 5.6%), and Steven-Johnson syndrome (3.9%, 0%). However, the distribution of cutaneous manifestations in the two studies were not significantly different. These findings may be useful as baseline data for common cutaneous manifestations in HIV positive patients. ❑

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KNOWLEDGE, BEHAVIORAL RISK AND PSYCHOLOGICAL ASSESSMENT OF THAI VOLUNTEERS PARTICIPATING IN PHASE I/II HIV/AIDS VACCINE TRIALS

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Background: The potential increase in risk behavior as a result of participation in prophylactic HIV vaccine studies was one of the major concerns. The few means to overcome this are education and monitoring of behavior attitudes though administration of questionnaires

Objective: This prospective cohort study was aimed to evaluate volunteers' knowledge, understanding and psychosocial reconciliation during vaccine trial.

Methods: 113 males and 51 females profiles from two phase I/II HIV vaccine studies at the Vaccine Trial Centre, Mahidol University, Bangkok: I Chiron Biocine HIV Thai E gp 120/MF59 +/- Chiron Biocine HIV SF52 gp 120 and II Aventis Pasteur Live Recombinant ALVAC HIV (vCP1521) Priming with VaxGen gp 120 B/E (AIDSVAX™ B/E) boosting, were enrolled during 1997-2001. They were regularly followed and interviewed by using questionnaires, from screening visits to 4 months after vaccination (total time = 6 months).

Results: Good knowledge about HIV and accepted understanding about each research were observed among these volunteers without statistically significant discrimination by age, sex and education. Lower, almost no, risky behavior with good protection was also demonstrated. History of having sex with a prostitute was significantly higher in the lower educational level ($p = 0.01$) and older groups; > 40 yrs ($p<0.001$). Volunteers with lower schooling level had more sexual experiences by history of sexual intercourse ($p<0.001$) and married status ($p<0.001$). Health problems and work/study stresses during studies can affect emotional responses in a few volunteers. 9.75% to 11.5% had concurrent health illness after vaccination. None blamed the relationship to vaccine. No psychological alteration could be detected in this period. 98-100% of the volunteers got precious virtue during participation in studies and would have been volunteers if they had the chance to do so again. ❑

Staff Index *(by first name)*

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