

Faculty of Tropical Medicine
Mahidol University

Annual Review 2004

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Faculty of Tropical Medicine Mahidol University, Annual Review 2004

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Foreword

In the following Annual Review 2004, it is my great pleasure to report the activities undertaken by our staff in the period 1 October 2002-31 December 2003. All efforts have been made by members of the Faculty to maintain and improve the substance, image, and reputation of the Faculty as “Asia’s Leader In Tropical Medicine”.

Since its foundation, the Faculty of Tropical Medicine, Mahidol University, has been dedicated to promoting research into tropical diseases. Every year, more than 100 papers are published in peer-review journals. We also conduct international meetings, conferences, seminars and special training courses. Through the Bangkok School of Tropical Medicine, we offer six regular international postgraduate programs, which have attracted participants from 42 countries around the world.

Faculty collaborations located on-campus include the Wellcome-Mahidol University Oxford Tropical Medicine Research Programme (the Wellcome Unit), SEAMEO TROPMED Regional Centre for Tropical Medicine, ACIPAC (a cooperative regional parasite control project with JICA), Mahidol-Maryland University Tropical Medicine Research Program (TMRP), the Joint WHO/UNEP/UNCHS Collaborating Centre for Environmental Management for Vector Control, the Vaccine Trial Centre, and the SEAMEO TROPMED Regional GIS Unit (supported by the EC Regional Malaria Control Programme). The Faculty has ongoing collaborative relationships in research and training with over 30 institutions internationally. Our institution continues to work extremely well with our partners, including the Thai Ministry of Public Health, the World Health Organization (WHO), and Medicine for Malaria Vectors (MMV).

It is pleasing to mention that, during the reporting period, Prof. Sornchai Looareesuwan was presented with the Outstanding Student Award by the Faculty of Science Alumni, Mahidol University, and Assoc. Prof. Songsak Petmitr was presented with the Outstanding Lecturer Award by Mahidol University.

I wish to convey my sincere appreciation to all members of the Faculty, and to our supporters and collaborators, for their excellent work throughout the Year 2003. I trust that the Faculty of Tropical Medicine Annual Review 2004 provides a comprehensive summary of the Faculty’s activities in the reporting period, and will be interesting and useful for all those delving into it.



Sornchai Looareesuwan

Prof. Sornchai Looareesuwan

Dean

Editor's Note

Dear Readers,

In this issue, the title of the annual publication previously called the “Annual Report” has been changed to “Annual Review”. The “Annual Review” is a retrospective survey of the previous year’s activities. Previous issues of the Annual Report of the Faculty of Tropical Medicine had been compilations of activities and personnel for each Fiscal Year - from October to September of the following year. However, this year the policy has changed, and Annual Review 2004 covers activities according to the calendar year. Hence, this Annual Review covers activities from October 2002 to December 2003, and, since it compiles five quarter-years of achievements, it is larger than previous issues.



Some changes have also been made to the layout. The first half of this issue is comprised of Departmental, Center, Unit, and Office information. The personal information for each academic staff member is located under their photograph, so that it is convenient for those who would like to know their field of expertise and approach them directly for further collaboration. Lists of Ongoing Research, Publications and Abstracts are compiled in the latter part of the issue.

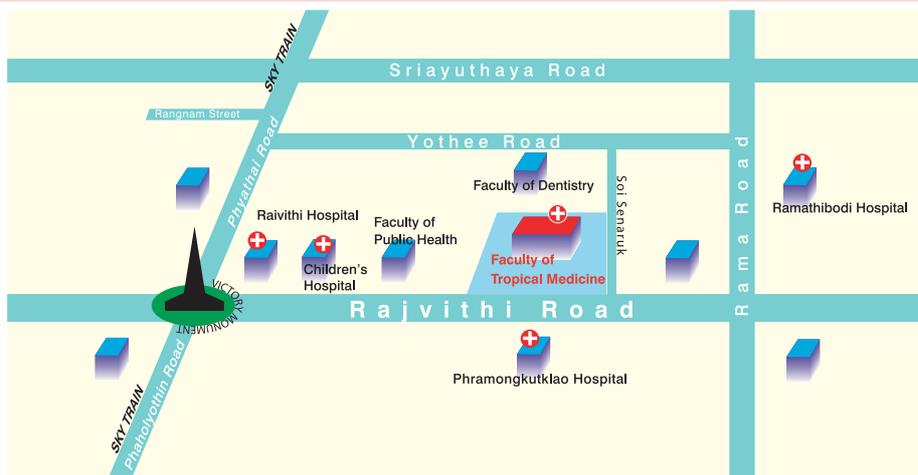
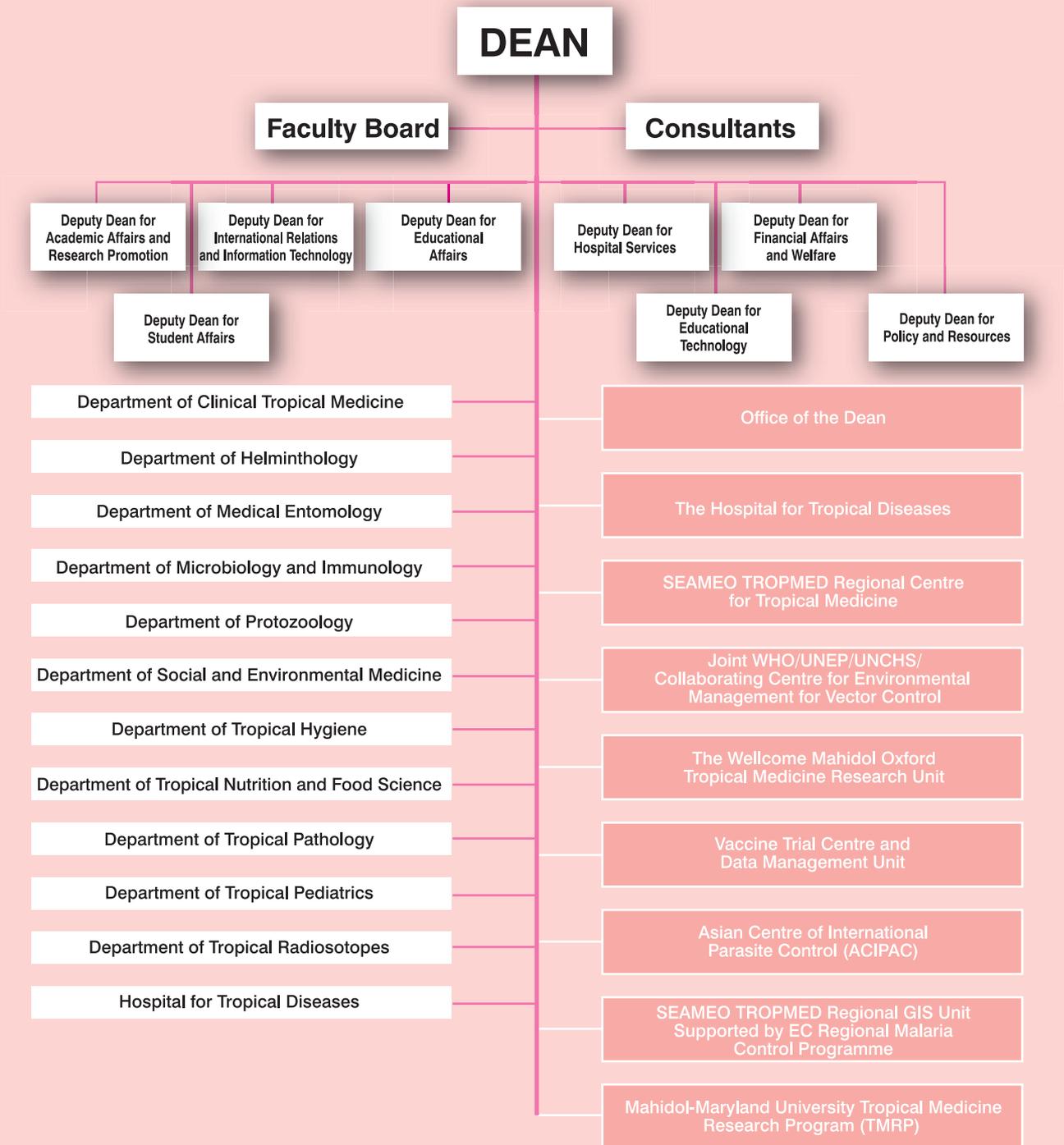
In 2003, a new research collaborating center was established, the Mahidol-Maryland University Tropical Medicine Research Program (TMRP). The Director is Assoc. Prof. George Watt. The goal of the TMRP is to establish a genuine, long-term collaboration between the Faculty of Tropical Medicine and the University of Maryland Medical School in Baltimore. More information about this Center is available in this Review.

I hope that you can find the information that you need to know about the Faculty of Tropical Medicine and enjoy reading it, as well. On behalf of the team, I anticipate that this Review is both informative and pleasing for all our readers. Your opinions, suggestions, criticisms and complaints, and also your praise, are welcome, to ensure that the next Annual Review is better than this one.

A handwritten signature in black ink that reads "Jitra Waikagul".

Jitra Waikagul
Editor

Organization Chart



Administrative Board

1 October 2002-30 September 2003



Prof. Sornchai Looareesuwan
Dean



Prof. Polrat Wilairatana
Deputy Dean for Hospital Services



Assoc. Prof. Jitra Waikagul
Deputy Dean for Academic Affairs



Assoc. Prof. Pratap Singhasivanon
Deputy Dean for International Relations and Information Technology



Assist. Prof. Chukiat Sirivichayakul
Deputy Dean for Educational Affairs



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



Assoc. Prof. Supraanee Changbumrung
Deputy Dean for Research Promotion



Dr. Chotechuang Panasonponkul
Deputy Dean for Student Affairs



Assoc. Prof. Kanjana Hongtong
Deputy Dean for Welfare



Assist. Prof. Chalit Komalamisra
Deputy Dean for Educational Technology



Assist. Prof. Varaporn Suphadtananphongs
Deputy Dean for Human Resource Development



Assoc. Prof. Emsri Pongponratn
Deputy Dean for Policy and Public Relation Affairs



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



Assoc. Prof. Parnpen Viriyavejakul
Assistant Dean for International Relations



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



Miss Kobsiri Chalermrut
Assistant Dean for Special Activities



Miss Suparp Vannaphan
Assistant Dean for Professional Development



Dr. Teerachai Kusolsuk
Assistant Dean for International Relations



Mrs. Vorapan Singhsilarak
Secretary of the Faculty

Administrative Board

1 October 2003 - the end of the reporting period



Prof. Sornchai Looareesuwan
Dean



Prof. Polrat Wilairatana
Deputy Dean for Hospital Service



Assoc. Prof. Jitra Waikagul
Deputy Dean for Academic Affairs and Research Promotion



Assoc. Prof. Pratap Singhasivanon
Deputy Dean for International Relations and Information Technology



Assist. Prof. Chukiat Sirivichayakul
Deputy Dean for Educational Affairs



Dr. Chotechuang Panasoponkul
Deputy Dean for Student Affairs



Assoc. Prof. Kanjana Hongtong
Deputy Dean for Financial Affairs and Welfare



Assist. Prof. Chalit Komalamisra
Deputy Dean for Educational Technology



Assist. Prof. Varaporn Suphadtanaphongs
Deputy Dean for Policy and Resources



Assist. Prof. Channarong Sanghirun
Assistant Dean for Area



Assist. Prof. Phanorsri Attanath
Assistant Dean for International Relations



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



Miss Kobsiri Chalermrut
Assistant Dean for Special Activities



Miss Suparp Vannaphan
Assistant Dean for Professional Development



Mrs. Vorapan Singhsilarak
Secretary of the Faculty



□ Celebration of the 80th Anniversary of Her Royal Highness Princess Galayani Vadhana Krom Luang Naradhivas Rajanagarindra
26 April 2003 - 10 May 2003





❑ 4th FBZ & JITMM 2003

4th Seminar on Food- and Water-borne Parasitic Zoonoses and Joint International Tropical Medicine Meeting 2003
2-4 December 2003, Siam City Hotel, Bangkok, Thailand

❑ Opening of the Kanchanaburi Research Centre (the new research station of the Faculty of Tropical Medicine) 1 August 2003



❑ ACIPAC International Course on School-Based Malaria and Soil-transmitted Helminthiasis Control for Program Managers, 7 July-26 September 2003, Bangkok, Thailand.



❑ Problem-based Learning Course, 9 December 2003



❑ International Training Course on Management of Malaria, 6-17 October 2003

Special Events 2003



Prof. Sornchai Looareesuwan was presented with the Outstanding Student Award by the Faculty of Science Alumni, Mahidol University, 29 October 2003



Assoc. Prof. Songsak Petmitr was presented with the Outstanding Lecturer Award by Mahidol University, 2 March 2004



Seminar on EQ and MQ, 18 September 2003



Seminar on Quality Assurance of the Office of the Dean, 16-17 August 2003, Siam Bayshore Resort, Thailand.



□ H.E. Dr. Edilberto C de Jesus, Secretary of Education, Philippines, and President of SEAMEO Council to SEAMEO TROPMED Network visited the Faculty of Tropical Medicine, Mahidol University, 7 August 2003.



□ Retirement Day,
18 September 2003



Consultants

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

Visiting Professors 2003

Name	Country
1. Prof. Walther H. Wernsdorfer	Austria
2. Prof. Chev Kidson	Australia
3. Prof. Frank P. Schelp	Germany
4. Prof. Gunther Wernsdorfer	Germany
5. Prof. Masamichi Aikawa	Japan
6. Prof. Dr. Shigeyuki Kano	Japan
7. Prof. Somei Kojima	Japan
8. Prof. Akira Ito	Japan
9. Prof. C.P. Ramachandran	Malaysia
10. Prof. Dr. Ma Sandra Bernardo Tempongko	Philippines
11. Prof. Peter F. Beales	Switzerland
12. Prof. David Warrell	UK
13. Prof. Herbert M. Gilles	UK
14. Prof. Victor R. Gordeuk	USA
15. Prof. Gary M. Brittenham	USA
16. Prof. John H. Cross	USA
17. Prof. James Carroll	USA
18. Lieut. Col. Dr. George Watt	USA
19. Dr. Brian Doberstyn	USA
20. Dr. Frederick Gay	France

Faculty Board

1. Dean Chairman
2. 11 Deputy Deans Members

Faculty Senate

1. Assoc. Prof. Surang Tantivanich Chairman/Lecturer Representative
2. Assist. Prof. Achara Asavanich Vice Chair/Lecturer Representative
3. Assoc. Prof. Porntip Petmitr Lecturer Representative
4. Assoc. Prof. Wipawee Usawattanakul Lecturer Representative
5. Assoc. Prof. Punnee Pitisuttithum Lecturer Representative
6. Assist. Prof. Talabporn Harnroongroj Representative, Department of Tropical Nutrition and Food Science
7. Dr. Wirach Maek-A-Nantawat Representative, Department of Clinical Tropical Medicine
8. Assist. Prof. Panyawut Hiranyachattada Representative, Department of Helminthology
9. Assist. Prof. Supatra Thongrungrat Representative, Department of Medical Entomology/Assistant Secretary
10. Assist. Prof. Yuvadee Mahakunkijcharoen Representative, Department of Microbiology and Immunology
11. Assist. Prof. Chutatip Siripanth Representative, Department of Protozoology
12. Assist. Prof. Chantima Lohachit Representative, Department of Social and Environmental Medicine
13. Assoc. Prof. Srivicha Krudsood Representative, Department of Tropical Hygiene
14. Assoc. Prof. Yaowapa Maneerat Representative, Department of Tropical Pathology/Secretary
15. Dr. Kriengsak Limkittikul Representative, Department of Tropical Pediatrics
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CURRENT RESEARCH ACTIVITIES

The Department has published more than 300 papers and has continued to pursue its mission in three major activities: teaching, research services, and social welfare. 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 about 2500 admitted cases of this disease. Most of the cases were falciparum malaria and vivax malaria and a few cases of mixed infections of malariae and ovale malaria. The major focus is on clinical trials of multidrug-resistant falciparum malaria in uncomplicated and complicated cases. Combinations of various antimalarial drugs were carried out continuously: halofantrine, mefloquine, quinidine, amodiaquine, artemether and artesunate in combination with mefloquine. We found that sequential treatment with artesunate or artemether followed by mefloquine is effective, well-tolerated and suitable as an alternative treatment for multidrug-resistant malaria.





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

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

Parasitic infestations have also been studied, such as drug trials and investigations for gnathostomiasis and local application of parenteral drugs, strongyloidiasis, opisthorchiasis, paragonimiasis, and taeniasis.

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

Research into skin diseases in HIV patients has been conducted in many aspects, the epidemiology of cutaneous manifestations in HIV patients in Thailand, fungal infection in leukoplakia patients, and superficial fungal infections in normal and HIV patients, (such as PPE, Dermatophytes, leukoplakia, and PCP).

The titles of current departmental research activities are as follows :

1. A multicenter, randomized, double-blind, phase II study to evaluate the safety, tolerance and efficacy of multiple doses of SCH 56592 versus fluconazole in the treatment of oropharyngeal candidiasis (OPC) in HIV-positive patients.
2. Neurotoxicity of oral artemether in an animal model following intermittent intramuscular injections.
3. Open-label, treatment protocol for the safety and efficacy of SCH 56592 (oral suspension) in the treatment of invasive fungal infections.
4. Efficacy and tolerability of ivermectin for gnathostomiasis.
5. Effect of insecticide on the female reproductive system.
6. Drug susceptibility of *P. vivax* & *in vitro*.
7. Search and development for Thai people living at Thai-Myanmar border, to be free from tropical diseases.
8. Effect of drug accumulation in the neurotoxicity of artemether, dosing regimens with variable drug-free intervals in a mouse model.
9. Safety and therapeutic effects of Jin Huang Chinese medicine in uncomplicated HIV-1 patients.
10. Observational probe study of *in vitro* immune response parameters to candidate HIV-1 vaccine antigens among subjects from Thailand.
12. Neuropathological toxicity of artemisinin derivatives in a mouse model.
13. Adverse effects of rifampicin on quinine efficacy in falciparum malaria.

14. Efficacy of the combination of antimalarial with ursodeoxycholic acid comparing to antimalaria and placebo in the prevention of acute renal failure in severely jaundiced falciparum malaria patients; a randomized controlled trial.
15. Development of field methods and investigators of the molecular basis of sulfonamide resistance in *Plasmodium vivax*.
16. Novel point mutations in the dihydrofolate reductase gene of *Plasmodium vivax*: evidence for sequential selection by drug pressure.
17. Quinine pharmacokinetic in uncomplicated falciparum malaria.
18. Asexual and sexual stage antimalarial activities of artesunate and primaquine in falciparum malaria.
19. A worldwide, phase I dose-escalating study of the safety tolerability and immunogenicity of a three-dose regimen of the MRKAd5- HIV-1 gag vaccine in healthy adults.
20. Immunogenicity and safety of quadrivalent HPV (Types 6, 11, 16, 18) L1 virus-like particle (VLP) vaccine in consistency lots for 16- to 23-year-old women with an additional immunogenicity bridge to the monovalent HPV 16 vaccine pilot manufacturing lot study - The F.U.T.U.R.E. Study (Females United to Unilaterally Reduce Endo/Ectocervical Disease) and A Study to Evaluate the Efficacy of Quadrivalent HPV (Types 6, 11, 16 and 18) L1 Virus-Like Particle (VLP) Vaccine in Reducing the Incidence of HPV 6/11-, 16-, and 18-Related CIN and VaIN, and HPV 6-11-, 16-, and 18-Related External Genital Warts and VIN in 16- to 23- Year Old Women - The F.U.T.U.R.E. Study (Females United to Unilaterally Reduce Endo/Ectocervical Disease).
21. Morphofunctional mechanism of ischemia/reperfusion injury in liver transplant.
22. Microcirculatory alteration and liver pathogenesis in congenital biliary atresia.
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Departmental On-going Research (2002)

Gnathostomiasis

- A seven-year retrospective evaluation of gnathostomiasis and diagnostic specificity by immunoblot.
- Effect of ivermectin on *Gnathostoma spinigerum* morphology.
- *Gnathostoma* infection in fish caught for local consumption in Nakhon Nayok Province.
- Seasonal variation of *Gnathostoma* infection in swamp eels in Nakhon Nayok.

Angiostrongyliasis

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

Toxocariasis

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

Trichinellosis

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

Cysticercosis

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

Echinococcosis

- Analysis of fluid antigens of *Echinococcus* cyst for diagnosis.

Opisthorchiasis

- Diagnosis of human opisthorchiasis with *Bithynia* snail antigen by ELISA.
- Studies on the efficacy of Thai traditional herbal medicines in the treatment of opisthorchiasis in hamsters.
- Research and development of an application to purify *Bithynia* snail antigen in serodiagnosis of opisthorchiasis.



Paragonimiasis

- Comparative studies on surface ultrastructure of adult worm of *Paragonimus* sp. in Thailand.
- Studies on *Paragonimus* populations: morphology, enzymology, molecular biology and epidemiology aspects.

Filariasis

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

Soil-transmitted helminthiasis

- Soil-transmitted helminthiasis control through school-based intervention.
- Effect of mebendazole on *Trichuris trichiura* morphology.
- Efficacy of high dose mebendazole against trichuriasis in adult patients.
- Epidemiology and treatment of strongyloidiasis with ivermectin.
- Impact on health and nutrition of deworming children and adolescence girls.

Other parasites

- Fish-borne trematodes in Thailand.
- Research and development of the integrated project on chemotherapy and control of malaria and parasitic infections.



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CURRENT RESEARCH ACTIVITIES

The Department of Medical Entomology has conducted research involving both basic and applied knowledge applicable in controlling insects and arthropods that are vectors of tropical diseases, with the emphasis on mosquito-borne diseases.

Study of the biology and ecology of fauna of medically important vectors at Kanchanaburi Campus Sai Yok District, a newly established campus of Mahidol University in Kanchanaburi Province, conducted. The infection rate of malaria parasites, vector capability, and susceptibility to insecticides are also studied in each mosquito vector species. The baseline data obtained from this study will be useful for malaria control in the study area.

Effective controls on mosquito vectors are directed at both laboratory and field trials. Control of larvae of *Aedes aegypti*, a main vector of dengue hemorrhagic fever, in the Faculty of Tropical Medicine premises, by Abate sand granules (temephos) is performed. The efficacy of mosquito repellents from medicinal plants, such as qinghao (*Artemisia annua*) are evaluated against the vectors. Effective measures for preventing the infection of tropical diseases in the population of people living at the Thai-Myanmar border are also introduced.

Several research topics in the molecular level are performed, for examples, DNA bank of mosquito vectors in Thailand, genetic diversity of *Anopheles barbirostris* group in Thailand for control of tropical diseases, and specificity



test of primers synthesized from DNA fragments of *Anopheles minimus* mosquito. Effect of heavy metals (lead and cadmium) on enzymes of *Culex quinquefasciatus* larvae is also studied.

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

Moreover, the Department of Medical Entomology acts as a reference center on mosquito vectors in Thailand through the establishment of the Mosquito Museum Annex. 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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CURRENT RESEARCH ACTIVITIES

▶ The current research activities of the Department involve studies on biology, molecular biology and immunology of infectious agents/diseases, particularly those causing problems in tropical areas, with the ultimate aims being 1) development of simple, rapid, specific, sensitive, cost-effective and practical diagnostic methods for use in remote areas and for the self-reliance of the country; 2) identification of potential protective antigens for vaccine development; 3) understanding of host responses and immunity; 4) understanding pathogenic mechanisms and virulence factors of pathogens and pathophysiology in hosts; and 5) acquisition of, and acquaintance with, modern technologies, e.g. genetic analysis of *Acanthamoeba*, amoeba and bacterial pathogens for epidemiological study, immunogenetic characteristics of severe malaria, *Acanthamoeba* spp., and invasive amebiasis, gene polymorphism of malaria parasitic and free-living amoebae parasites. Further details are given below:

Sodium dodecyl sulfate-polyacrylamide gel electrophoresis and immunoblotting have been used for the identification of the specific antigens of various pathogens, including *Opisthorchis viverrini*, *Paragonimus heterotremus*, *Trichinella spiralis*, *Strongyloides stercoralis*, *Gnathostoma spinigerum*, *Entamoeba histolytica*, *Plasmodium falciparum* and *P. vivax*, *Leptospira*, etc. Successful identifications of the specific antigens of these pathogens lead to the development of more simple, rapid, sensitive and specific immunodiagnostic methods for patients suffering from these diseases. For example, in human gnathostomiasis, a 24 kDa specific diagnostic component of *G. spinigerum* was further purified from crude extract by column chromatography. For affinity chromatography, the antigen used in the plate/membrane enzyme-linked immunosorbent assay (ELISA) gave 100% sensitivity and specificity for the disease. Attempts to produce the antigen, either by recombinant DNA technology or anti-idiotypic antibodies, are underway.



Specific polyclonal and/or monoclonal antibodies against various parasitic helminths, protozoa, bacteria and their toxins and viruses, including *Opisthorchis viverrini*, *Paragonimus heterotremus*, *Schistosoma mekongi*, *Trichinella spiralis*, *Gnathostoma spinigerum*, *Entamoeba histolytica*, *Plasmodium falciparum* and *P. vivax*; bacteria or their toxins including *Bordetella pertussis*, *Vibrio cholerae* O:1 and O:139, *Salmonella*, enterotoxigenic *E. coli*, enterohemorrhagic *E. coli*, verocytotoxins (VT-I and VT-II), *Leptospira*, *Shigella*, *Vibrio parahaemolyticus*, *Listeria*, *Campylobacter*, *Rickettsia*, Japanese encephalitis virus and respiratory syncytial virus have been produced in our laboratory for the detection of the pathogens/diagnosis of diseases caused by them in clinical specimens and/or contaminated food and environmental samples. The monoclonal antibodies produced against the whole cells, somatic and/or excretory-secretory antigens of these pathogens have been tested for their analytical, as well as diagnostic, sensitivities and specificities. Development of simple, specific, sensitive, rapid and cost-effective methods, which are practical for use in remote areas, such as the conventional or dot-blot ELISA, immuno-colloidal gold and/or dip-stick techniques, as well as the use of immunomagnetic separation for higher sensitivity of detection of the pathogens, have been carried out.

Additional work includes the application of DNA technology, e.g. development of DNA probes, PCR technology as well as other modern technologies for the detection of several pathogens, e.g. *Paragonimus*, *Entamoeba*, free-living amebae, *Plasmodium*, *Salmonella*, *Vibrio cholerae*, *Shigella*, *Bordetella pertussis*, *Leptospira*, viruses of national economic shrimps, 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*. The genetic polymorphisms of two noncoding loci (locus 1-2 and locus 5-6) and two protein-coding loci (chitinase and serine-rich *E. histolytica* protein [SREHP]) among *E. histolytica* isolates from different geographic regions have been studied *Acanthamoeba* spp. 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 virulence factors, have also been studied.

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

Other areas of research activity on bacterial infections include diarrhea caused by *Campylobacter jejuni* and *C. coli*, anaerobic bacterial infections, non-gonococcal urethritis and heparinase detection in facultative and anaerobic bacteria. Antimicrobial susceptibility test was done by modified Kirby-Bauer's method to suit the small number of pathogens isolated each day. Surveillance of nosocomial infections for the control of hospital infections is also being investigated.

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

Studies of *E. histolytica* revealed that its genome organization consisted of at least a circular supercoiled-like and a linear DNA molecule that behave like yeast chromosomes. There was no evidence of chromosome rearrangement in association with drug resistance. The mechanism of metronidazole resistance in *E. histolytica* involved a marked increase in superoxide dismutase, whereas pyruvate ferredoxin oxidoreductase was not decreased. Monoclonal antibody specific against *E. histolytica* conjugated with R-phycoerythrin (R-PE) and R-phycoyanin (R-PC) have been used successfully as antibody probes for the detection of trophozoites in human fecal samples. An immunotoxin (IT) consisting of a monoclonal antibody against pyruvate ferredoxin oxidoreductase of *E. histolytica* (EhPFOR MAb) and the toxic moiety of the plant toxin ricin A (RA) is potent in inhibiting proliferation of the organism. Therefore, IT would be one approach for future immunotherapy for invasive amebiasis. Moreover, some Thai medicinal plants used by AIDS patients may be able to kill amebae *in vitro*. X-ray crystallography of



R-PE, EhPFOR, Eh anti-PFOR MAb alone or in complexes are currently studied.

Research work on viral infections, especially the detection of cytomegalovirus (CMV) infection by 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 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; the National Institute of Infectious Diseases, and Keio University, 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 Institute for Hygiene and Social Medicine, University of Innsbruck, Austria; 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; Prince of Songkla University, University of Edinburgh, UK; University of Concepcion, Chile; and Institute de Biologie Structurale Jean-Pierre Ebel, CEA/CNRS, Grenoble, France, etc.

Specimen Statistics 2003																
Microbiology Unit, Department of Microbiology and Immunology																
Month	Hemo	Urine	CSF				Sputum			Stool	Other		IFA	Lepto	Total	
			AFB	GS	India ink	Culture	AFB	GS	Culture		GS	Culture				
Jan	-	-	-	-	-	-	-	-	-	-	-	-	15	3	18	
Feb	2	-	-	-	-	-	1	-	-	2	-	-	15	1	21	
Mar	11	11	-	-	-	-	17	5	2	6	2	2	12	11	79	
Apr	2	4	-	-	-	-	8	-	2	-	3	2	8	11	40	
May	1	-	-	-	-	-	7	-	-	-	1	1	3	12	25	
Jun	-	-	-	-	-	-	36	1	1	-	-	-	7	23	68	
Jul	-	-	-	-	-	-	19	-	1	-	-	2	10	16	48	
Aug	-	-	-	-	-	-	13	1	-	-	-	-	6	36	56	
Sept	-	-	-	-	-	-	17	2	-	-	-	-	7	17	43	
Oct	-	-	-	-	-	-	10	2	-	-	-	40*	10	53	115	
Nov	-	-	-	-	-	-	10	-	-	-	-	-	4	41	55	
Dec	-	-	-	-	-	-	4	-	-	-	-	-	3	38	45	
Total	16	15	0	0	0	0	142	11	6	8	6	47	100	262	613	

*Canal water examination project in Bangkok and circle area by the Department of Pollution Control (40 samples) for aerobic, anaerobic bacteria, fungi, protozoa.

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CURRENT RESEARCH ACTIVITIES

1. Study on DNA replication enzymes of *Plasmodium falciparum* as new chemotherapeutic targets against malaria.
2. Ultrastructure of acute and chronic toxoplasmosis after pyrimethamine and artesunate administration *in vivo* study.
3. Dog and cat parasitic zoonoses.
4. Inhibition of *Giardia intestinalis* and *Entamoeba histolytica* by medicinal plants.
5. Studies on ultrastructure of *Cryptosporidium* after exposure to drugs.
6. *Blastocystis hominis* in children with diarrhea in children hospitals.
7. *In vitro* cultivation for *Cryptosporidium* spp. and drug testing.
8. Rapid detection of *Entamoeba histolytica* antibody.
9. *In-vitro* sensitivities of *Plasmodium falciparum* to medicinal plant.
10. Study on antimalarial drug sensitivities to *Plasmodium falciparum* in community of Thailand.
11. Invention of Thai medicinal plant for treatment of coccidiosis.
12. Establish double antibody ELISA method (sandwich ELISA) for detection of *G. intestinalis*, *E. histolytica*, *B. hominis* in fecal specimens
13. Isolation and characterization of DNA helicase from *P. falciparum*.
14. Protozoal contamination in water used in food frozen industry.

15. Comparison study of indirect fluorescence antibody and the Sabin-Feldman dye test for *Toxoplasma gondii* antibody in Thai pregnant women.
16. PCR technique for detecting *Toxoplasma gondii* in animal amniotic fluid.
17. PCR technique for detecting *Toxoplasma gondii* in human clinical specimens.

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- A phase III trial of Aventis Pasteur live recombinant ALVAC-HIV (vCP1521) priming with VaxGen gp120 B/E (AIDSVAX™ B/E) boosting in HIV-uninfected Thai adults
- Socio-cultural and behavioral component for shigellosis disease burden studies in Kaeng Koi District, Saraburi Province, Thailand
- Socio-environmental management for sustainable dengue hemorrhagic fever control in Chaiyaphum Province
- Local wisdom in the treatment of herpes complex diseases: a case study on the treatment of herpes simplex by monk healer (Moh-Pra)
- Tuberculosis infection among household contacts under 15 years old in Bangkok, Thailand
- Hazardous substance management and development of computerized database inventory list on major hazardous substances used in the Faculty of Tropical Medicine



- Environmental health models for sustainable agriculture
- Distribution and genetic variations of the *Pila* snails
- Leptospirosis vaccine design using T7 phage display technique
- Control of soil-transmitted helminths in primary schools in Southern Thailand
- Detection of a possible specific serum marker in opisthorchiasis-associated cholangiocarcinoma patients
- Determination of zinc in soil and sludge from pig farm

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CURRENT RESEARCH ACTIVITIES

The Department of Tropical Hygiene was originally named the Tropical Hygiene Section. In 1960, upon the establishment of the Faculty of Tropical Medicine, the Tropical Hygiene Section was also founded. Since then, the section has been responsible for providing lectures and field training operations as part of the Diploma of Tropical Medicine and Hygiene (D.T.M. & H.) course. Epidemiologic research has also been one of the major activities of the section, responding to public health problems (i.e. scrub typhus and malaria) which afflicted the rural population during that time. In 1974, the Section was upgraded into the Department of Tropical Hygiene. At present, the department is responsible for providing instruction and training in the M.Sc. / Ph.D. degree programs in Tropical Medicine in addition to the existing D.T.M. & H. course. Most research activities being carried out at the moment are mainly in the field of epidemiology and in the application of Geographical Information System (GIS) to common tropical diseases. Furthermore, the department also has direct responsibility for managing the Rajanagarindra Tropical Disease International Centre (RTIC) to ensure the continuous delivery of quality and gratuitous health services, through its malaria clinic, to the people within the area. The RTIC is situated in a malaria-endemic rural community near the Thai-Myanmar border, in Suan Phung District, Ratchaburi Province.



The current research projects of the department are:

1. Epidemiology and Control of Malaria in Ratchaburi Province, Thailand.
2. Application of GIS in Monitoring Multi-drug Resistant Malaria in Greater Mekong Sub-Region of Southeast Asia.
3. Human Paragonimiasis in Ratchaburi Province, Thailand
4. Epidemiology and Drug Sensitivity of Enterobacteriaceae in a Rural Community near Thai-Myanmar border in Suan Phung, Ratchaburi Province.
5. Studies on the Water Quality of River Pachi at Tanawsri Sub-district, Suan Phung District, Ratchaburi Province.
6. Immunological Level of Scrub Typhus of People along Thai-Burmese Border in Suan Phung District, Ratchaburi Province.
7. A Survey of Metacercariae in Fresh Water Fishes in Small Reserviors in Suan Phung, Ratchaburi Province.
8. Study on the Ecology of Anopheline Larvae in Malaria Endemic Area.



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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, the effect of smoking on work performance in relation to homocysteine concentration. Furthermore, molecular biology in cancers of lung, liver, breast cholangiocarcinoma, colon and cervix were investigated. Food and health relationships in populations of Asian countries are of interest for study and the data will be compared.

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

The topics of the current research projects are as follows:

1. Relationship between alpha-2-macroglobulin, anthropometric parameters and lipid profiles in Thai overweight and obese in Bangkok
2. Serum concentration of vitamin A and E and lipid profiles in overweight and obese Thai
3. Serum homocysteine, B₁₂ and folic acid concentration in Thai overweight and obese subjects
4. Relationship of tobacco smoking with serum vitamin B₁₂, folic acid and hematological indices in healthy adults
5. Serum copper, zinc, ceruloplasmin and superoxide dismutase in Thai overweight and obese



6. Antioxidant enzyme level in the erythrocyte in riboflavin-deficient and *Trichinella spiralis*-infected rats
7. Relationship between soluble leptin receptor, leptin, lipid profiles and anthropometric parameters in overweight and obese Thai subjects
8. Platelet fatty acids in coronary heart disease, dyslipidemia, hypertension and healthy controls
9. Mutational analysis of ras gene family in lung cancer in Thai
10. Identification of genetic alterations in human cancers using arbitrarily primed PCR

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12. Mutational analysis of the PTEN gene localized at chromosome 10q23 in Thai patients with gliomas	188
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Awards 2003

No.	Title of Award	Award Recipient	Awarded by	Award Date
1.	<ul style="list-style-type: none"> • Best Student Presentation Award • Outstanding Student Presentation Award 	Miss Thanida Tangwanicharoen Mrs. Oranan Prommano Miss Souwanit Nakasiri	Joint International Tropical Medicine Meeting 2003	4 December 2003
2.	Professor Emeritus Khunying Tranakchit Harinasuta Award for the Most Outstanding Student of the Doctor of Philosophy in Tropical Medicine Class of 2002	Miss Pachuen Potup	Faculty of Tropical Medicine, Mahidol University	26 June 2003

CURRENT RESEARCH ACTIVITIES

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





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CURRENT RESEARCH ACTIVITIES

- Safety and immunogenicity of tetravalent dengue vaccine formulation in Thai adult volunteers: *eight-year antibody persistence*
- Safety and immunogenicity of tetravalent dengue vaccine formulations in healthy Thai children: *evaluation of a booster dose and five-year antibodies persistence*
- A phase II, pilot, randomized, open-label, single-center study to evaluate immunogenicity, safety and booster response of 3 full IM doses versus 3 half IM doses versus 3 ID doses versus 2 ID doses of PCEC rabies vaccine (Rabipur® administered concomitantly with JE vaccine as a pre-exposure regimen in 12-to 18-month-old toddlers in Thailand

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CURRENT RESEARCH ACTIVITIES

Research

1. The Department's current research has been carried out as follows:
 - 1.1 Comparison of non-radiological technique and ^{125}I -labeled method for measurement of folic acid in normal RBC and sera of patients with cervical dysplasia.
 - 1.2 Comparison of non-radiological technique and ^{125}I -labeled method for measurement of folic acid in patients with Alzheimer's disease.



- 1.3 Determination of total folate analysis in food.
2. The Department has cooperated with other departments, as follows :
 - 2.1 Treatment of hookworm with medicinal plants LD50
 - 2.2 The correlation between folic acid status and the cervical cytologic abnormality in Thai women.
 - 2.3 Established double antibody ELISA method for detection of pathogenic protozoal antigens in feces.
3. The Department has corporated with the Neuro-Behavioural Biology Center, Institute of Science and Technology for Research and Development in "Determination of Serum Vitamin B₁₂ and Folic Acid in Thai Alzheimer's Patients"
4. The Department has cooperated with the Department of Pediatrics, Faculty of Medicine Ramathibodi Hospital in "Homocysteinemia and Thrombosis in Thai Children Patients"

Services

The Department has two projects for services : (1) service for the measurement of folic acid in red blood cells and sera ; and (2) service for the measurement of vitamin B₁₂ in sera. Annual services are shown below.

The Department provided assistance and facilities to measure vitamin B₁₂ and folic acid levels of 530 serum samples for the Department of Clinical Tropical Medicine, Faculty of Tropical Medicine.

Two hundred and seventy serum samples were measured for vitamin B₁₂ and folic acid for the M.Sc. student of the Department of Tropical Nutrition and Food Science, Faculty of Tropical Medicine.

January 2003 - December 2003

	Serum vitamin B ₁₂ (number)	Serum folate (number)	Red cell folate (number)
Child	159	165	159
Man	60	186	97
Woman	78	155	90
Total	297	506	346

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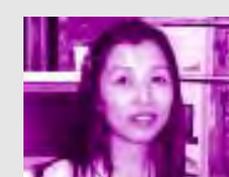
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CURRENT RESEARCH ACTIVITIES

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

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

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

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



The unit's work has provided the currently accepted dose regimens for chloroquine, quinine, artesunate, mefloquine, and artemether-lumefantrine. In the treatment of severe malaria, a major objective is to characterize the relative advantages of the artemisinin derivatives over current treatments. Studies are also underway to define the optimum treatment of vivax malaria, and the best methods of preventing and treating malaria in pregnancy. We have conducted studies of retinal capillary blood flow in severe malaria, comparative bioactivities of different artemisinin formulations, and mechanisms of parasite clearance. The Shoklo Malaria Research Unit conducted studies with artemether-lumefantrine and atovaquone-proguanil and large scale studies of malaria in pregnancy and young children.

Studies of melioidosis include a large prospective clinical description of the disease, and a series of clinical and microbiological investigations to improve diagnosis and management of this important infection.

Studies of fungal infections include a pharmacokinetic-pharmacodynamic evaluation of different treatment strategies in cryptococcal meningitis, and the development of improved methods to diagnose penicilliosis.



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Vaccine Trial Centre

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▶ The Vaccine Trial Centre is a clinical facility in the Faculty of Tropical Medicine, Mahidol University for testing newly developed vaccines that reach the stage where evaluation in human volunteers is needed. Individual scientists at any national or international institution may have their vaccines tested at this Centre. It is a joint responsibility of Mahidol University and the Ministry of Public Health, and operated by the Faculty of Tropical Medicine on their behalf. The establishment of the Centre was started in February 1984, however, full operation become possible in September 1986 and the first admission of volunteers into the ward was on the 3rd November 1986. The VTC Bangkok is the first and the only facility of its kind in Thailand, in the region, and perhaps also in the developing countries. The advantage of conducting vaccine trials at this Centre is that the studies will be on 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.

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.

Current Research

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



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Data Management Unit

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

The primary objective of the Unit is to provide data management and data analysis services to research projects, particularly clinical trials; meanwhile, its current commitment is put mainly into the Phase III Trial to determine the efficacy of AIDSVAX™ B/E vaccine in injecting drug users in Bangkok, Thailand. In September 2002, its Chief and Deputy Chief received technological transfer from VaxGen on preparation of data for the Data and Safety Monitoring Board (DSMB) meeting to consider interim efficacy analysis of this trial.

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

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

Clinical Trial Section



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CURRENT ACTIVITIES

1. A Phase III Trial of Aventis Pasteur Live Recombinant ALVAC-HIV (vCP1521) Priming with VaxGen gp120 B/E (AIDSVAX™ B/E) Boosting in HIV-uninfected Thai Adults.

OBJECTIVES:

Primary Objective

- To determine whether immunization with an integrated combination of ALVAC-HIV (vCP1521) boosted by AIDSVAX™ gp120 B/E prevent HIV infection in healthy Thai volunteers.

Secondary Objectives

- To determine whether immunization with this vaccine combination results in reduced HIV viral load.
- To determine whether immunization with this vaccine combination results in an increased CD4 count.
- To confirm the safety of vaccine combination in Thai volunteers.
- To evaluate whether participation is associated with behavior change.

Vaccines:

Prime:

- ALVAC-HIV (vCP1521) is a recombinant canarypox vector vaccine and HIV-1 gag and protease (subtype B).

Boost:

- AIDSVAX[®] B/E is a bivalent HIV gp 120 envelope glycoprotein vaccine containing a subtype E and a subtype B.

Study sites:

- 4 clinics in Chonburi Province and 4 clinics in Rayong Province.

2. Immunogenicity and Safety of Quadrivalent HPV (Type 6,11, 16,18)L1 Virus Like Particle (VLP) Vaccine in 16 to 23-Year-Old Women With an

Immunogenicity Bridge Between the HPV 16 component of the Quadrivalent Vaccine and the Monovalent HPV 16 Vaccine Pilot Manufacturing Material—The F.U.T.U.R.E. I Study (Females United to Unilaterally Reduce Endo/Ectocervical Disease)

OBJECTIVES:

- To demonstrate that quadrivalent HPV vaccine is generally well tolerated.

- To demonstrate that the Final Manufacturing Process (FMP) results in quadrivalent HPV vaccine

Study design:

- 2 groups: a quadrivalent HPV vaccine group and a placebo group.

- Randomized, double-blind, placebo-controlled, multicenter study.

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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 programs, from postgraduate diploma to PhD levels. English is the medium of instruction. The courses are open to students from all around the world. Details of the School's programs can be viewed on the Faculty's website at: <http://www.tm.mahidol.ac.th> or may be requested by e-mail from the School at e-mail address: tmedu@diamond.mahidol.ac.th

Regular Postgraduate Programs

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 Pediatrics

The M.C.T.M. program 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 program 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 program 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 program enables medical doctors to gain advanced knowledge, 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 Programs

Master of Science in Clinical Epidemiology

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

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6. Mrs. Raweevan Srisawat	Thailand
7. Mr. Aongart Mahittikor	Thailand
8. Miss Ubol Chuensumran	Thailand
9. Miss Waranee Boonchuaylier	Thailand
10. Pol.Capt. Jongkol Podang	Thailand
11. Mr. Tawee Saiwichai	Thailand
12. Mr. Trung Dac Nguyen	Vietnam
13. Mr. Tuc Phong Vu	Vietnam
14. Mrs. Tassanee Silawan	Thailand
15. Mr. Kittisak Thawnathom	Thailand
16. Mr. Apiwat Tawatsin	Thailand
17. Dr. Le Huu Tho	Vietnam

2nd year students

1. Miss Sudarat Nguansangiam	Thailand
2. Mr. Prasert Thavondunstid	Thailand
3. Miss Patchara Sriwichai	Thailand
4. Miss Pornsawan Amarapal	Thailand
5. Miss Pachuen Potup	Thailand
6. Miss Piyada Wongroongsarb	Thailand
7. Miss Piyanuch Preechapornkul	Thailand
8. Miss Supaluk Popruk	Thailand
9. Mrs. Urairat Singhanat	Thailand
10. Miss Doungdaw Nuntakomon	Thailand
11. Miss Chintana Phawong	Thailand
12. Mr. Narong Nitatpattana	Thailand
13. Miss Manirat Therawiwat	Thailand
14. Miss Naowarat Tanomsing	Thailand
15. Dr. Trinh Van Hung	Vietnam

3rd year students

1. Dr. Kittipong Kongsomboon	Thailand
2. Ms. Chomrach Sirigul	Thailand
3. Mr. Tavorn Maton	Thailand
4. Mr. Narisorn Na-ngam	Thailand
5. Mr. Boonlue Chimbanrai	Thailand
6. Miss Piyatida Tangteerawatana	Thailand
7. Mrs. Panita Gosi	Thailand
8. Miss Pornlada Nuchnoi	Thailand

3rd year students (Continued)

9. Miss Pruksa Nawtaisong	Thailand
10. Ms. Phuangphet Waree	Thailand
11. Mrs. Malee Geounuppakul	Thailand
12. Dr. Sirinuch Rajchaiboon	Thailand
13. Dr. Somyos Deerasamee	Thailand
14. Mrs. Sirimon Chaikate	Thailand
15. Miss Sirima Kitvatanachai	Thailand
16. Miss Sukhontha Siri	Thailand
17. Miss Sunanta Chariyalertsak	Thailand
18. Mr. Surapon Tangvarasittichai	Thailand
19. Ms. Verena Ilona Carrara	Switzerland
20. Dr. Kim Jung Ryong	Korea
21. Dr. Sompong Srisaenpang	Thailand
22. Miss Pannapa Susomboon	Thailand
23. Miss Dounggrat Riyong	Thailand
24. Miss Siriporn Chanchay	Thailand
25. Miss Kanjana Suriyaprom	Thailand

4th year students

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

5th year students

1. Mr. Kamon Foihirun	Thailand
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5th year students		5th year students (Continued)	
2. Miss Chutima Kamkhaek	Thailand	15. Mr. Hari Har Joshi	Nepal
3. Miss Naowarut Dechkum	Thailand	6th year students	
4. Mrs. Prapa Nunthawarasilp	Thailand	1. Miss Kriyaporn Songmuaeng	Thailand
5. Miss Pattra Suntornthiticharoen	Thailand	2. Mrs. Prapin Tharnpoophasiam	Thailand
6. Mr. Yuttana Sudjaroen	Thailand	3. Miss Wanida Pongstaporn	Thailand
7. Miss Waraphon Phimpraphi	Thailand	4. Miss Nitchakarn Noranate	Thailand
8. Mr. Panas Thumkiratiwong	Thailand	5. Miss Pittayaporn Moungrnoi	Thailand
9. Miss Suwalee Tantawiwat	Thailand	6. Miss Yuwadee Trongtokit	Thailand
10. Mrs. Oranan Prommano	Thailand	7. Miss Sawanee Tengrungrun	Thailand
11. Mr. Rajendra Kumar B.C.	Nepal	8th year student	
12. Miss Nitaya Poosanthanasarn	Thailand	1. Mr. Ruangyuth Chaiworaporn	Thailand
13. Miss Panee Chaksangchaichot	Thailand		
14. Dr. Aree Kantachuvessiri	Thailand		

Thesis Titles

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

Department	Name	Title of Thesis	Advisor
Clinical Tropical Medicine	Dr. Suprotik Ghagra	Clinical manifestation and treatment of non-severe falciparum malaria in Thai children	Assoc.Prof. Chukiat Sirivichayakul
Clinical Tropical Medicine	Dr. Huot Chantheany	Clinical manifestation of uncomplicated falciparum malaria and vivax malaria in Thai children	Assoc.Prof. Pornthep Chanthavanich
Clinical Tropical Medicine	Dr. Masri Sembiring Maha	Acute bacterial meningitis in adults at Chonburi Hospital	Assist.Prof. Udomsak Silachamroon
Clinical Tropical Medicine	Dr. Molina Choummanivong	Acute bacterial meningitis in adults at Chonburi Hospital	Assist.Prof. Weerapong Phumratanaprapin
Clinical Tropical Medicine	Dr. Ei Ei Tin	Efficacy and adverse effects of GPO vir cd4.T+3TC+NVP in HIV patients: follow up study	Assoc.Prof. Punnee Pitsuttithum

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

Department	Name	Title of Thesis	Advisor
Microbiology and Immunology	Dr. Do Hoang Long	Antibody recognition of Aeromonas antigens in mice	Assist.Prof. Yuvadee Mahakunkijcharoen
Protozoology	Miss Chantira Sutthikornchai	Protozoal contamination of water used in Thai frozen food industry	Assoc.Prof. Yaowalark Sukthana
Microbiology and Immunology	Miss Chanthanee Nitigaroon	PCR diagnosis of amebiasis	Assoc.Prof. Nittaya Thammapalerd

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

Department	Name	Title of Thesis	Advisor
Helminthology	Lt. Chanakarn Kalambaheti	ELISA values of serum antibodies from healthy Thai individuals against antigens of tissue helminths	Assoc.Prof. Wichit Rojekittikhun
Medical Entomology	Miss Parichat Lapcharoen	Three indigenous medical Thai plants for control of <i>Aedes aegypti</i> and <i>Culex quinquefasciatus</i>	Assoc.Prof. Chamnarn Apiwathnasorn
Microbiology and Immunology	Mr. Nitipon Ratanasyuth	Detection of dengue viral RNA in mosquitoes (<i>Aedes</i>) by nucleic acid sequence-based amplification (NASBA) and reverse transcriptase-polymerase chain reaction (RT-PCR)	Assoc.Prof. Wipawee Usawattanakul
Microbiology and Immunology	Miss Busakorn Promsarin	Detection of virulence factors from <i>Aeromonas</i> SOO in relation to diarrhea	Assist.Prof. Yuvadee Mahakunkijcharoen
Microbiology and Immunology	Miss Kanlaya Boonpen	Detection of anti-pyruvate: ferredoxin oxidoreductase (PFOR) antibody against <i>Entamoeba histolytica</i> in sera of amebiasis patients by using Western blotting	Assoc.Prof. Nittaya Thammapalerd
Microbiology and Immunology	Miss Oranuch Kongpechsatit	Characterization of rifampicin resistant <i>Mycobacterium avium</i> complex from Thailand using molecular techniques	Assist.Prof. Pongrama Ramasoota
Microbiology and Immunology	Mr. Chalermpon Kaewjai	Detection of <i>Acanthamoeba</i> spp. by using polymerase chain reaction (PCR) assays	Assoc.Prof. Nittaya Thammapalerd
Microbiology and Immunology	Miss Jaruwadee Rattanadakul	Analyses of natural killer T(NKT) cell subset in patients with severe and uncomplicated falciparum malaria	Assist.Prof. Varee Wongchotigul
Social and Environmental Medicine	Miss Pannumthip Pitaksajakul	Rapid detection of aerosol <i>Mycobacterium tuberculosis</i> and rifampicin resistant tuberculosis from hospitals using filtered air sampling and molecular techniques	Assist.Prof. Pongrama Ramasoota
Social and Environmental Medicine	Miss Yoko Oshima	Molecular epidemiology of <i>Aeromonas</i> spp. by using ERIC-PCR.	Assist.Prof. Pongrama Ramasoota

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

Department	Name	Title of Thesis	Advisor
Helminthology	Mr. Krasae Kanakupt	Evaluation of excretory-secretory and partially purified antigens of adult <i>Toxocara canis</i> against human toxocariasis by ELISA and immunoblot	Assoc. Prof. Malinee Thairungroj
Tropical Nutrition & Food Science	Miss Tanyalak Khuntamoon	Seasonal variation of fresh, sterilized and pasteurized cow milk	Assoc. Prof. Supranee Changbumrung
Tropical Nutrition & Food Science	Miss Busaba Tantithavorn	Homocysteine, folic acid and cobalamin in subjects with coronary heart disease and healthy controls	Assoc. Prof. Supranee Changbumrung
Helminthology	Miss Pennapa Yutayong	<i>Toxocara canis</i> larval antigens for serodiagnosis of human toxocarosis	Assoc. Prof. Wichit Rojekittikhun
Microbiology and Immunology	Miss Matukorn Na Ubol	Virulenced genes of <i>Vibrio cholerae</i> Thailand isolates	Prof. Wanpen Chaicumpa
Medical Entomology	Miss Ladawan Wasinpiyamongkol	Morphological variations for susceptibility and transovarial transmission of dengue virus in <i>Aedes aegypti</i>	Assoc. Prof. Chamnarn Apiwathnasorn
Tropical Nutrition & Food Science	Mr. Sasipon Pumkumarn	Antioxidant enzymes and trace elements in subjects with coronary heart disease and healthy controls	Assoc. Prof. Supranee Changbumrung
Microbiology and Immunology	Miss Saichon Chimsumang	Indirect immunoperoxidase test for dual serodiagnosis of scrub typhus and leptospirosis	Assist. Prof. Varee Wongchotikul

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

Department	Name	Title of Thesis	Advisor
Tropical Hygiene	Miss Nahathai Chulakavat	Sputum conversion among newly adult positive-smear pulmonary tuberculosis patients	Assoc. Prof. Pratap Singhasivanon
Helminthology	Lt. Tossapon Chaiyasith	Gnathostomiasis in Nakhon Nayok Province: prevalence and intensity of infection in fish caught for local consumption and the seasonal variation of infection in swamp eels	Assoc. Prof. Wichit Rojekittikhun
Microbiology and Immunology	Miss Piyaporn Suebtrakul	Seroprevalence of antibodies to <i>Orientia tsutsugamushi</i> in primary school children at Saiyoke District, Kanchanaburi	Assist. Prof. Varee Wongchotikul

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

Department	Name	Title of Thesis	Advisor
Medical Entomology	Mr. Norong Nitatpattana	Risk of Japanese encephalitis virus domestic transmission in Thailand: virological and entomological approach	Assoc.Prof. Chamnarn Apiwathnasorn
Microbiology and Immunology	Miss Piyada Wongroongsarb	Molecular characterization of Leptospira isolates in Thailand	Dr. Thareerat Kalambaheti

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

Department	Name	Title of Thesis	Advisor
Tropical Nutrition and Food science	Miss Siriporn Chanchay	Resistin and insulin in type II diabetes mellitus obese Thais	Assoc.Prof.Rungsun Tungtrongchitr
Tropical Medicine	Miss Pannapa Susomboon	Studying endothelial cell activation following <i>Plasmodium falciparum</i> infection erythrocyte binding <i>in vitro</i>	Prof. Sornchai Looareesuwan
Helminthology	Mrs. Dounggrat Riyong	Comparison of <i>Dirofilaria immitis</i> antigens for serodiagnosis of Bancroftian filariasis	Assoc.Prof. Jitra Waikagul
Tropical Nutrition and Food science	Mr. Surapon Tangvorasittichai	Mutagenicity and antimutagenicity of fractions of some plant extracts and their molecular formulas	Assoc.Prof. Supranee Changbumrung
Tropical Nutrition and Food science	Miss Sunanta Chariyalertsuk	Determination of genetic alterations in cholangiocarcinoma using arbitrarily primed polymerase chain reaction and gene cloning	Assoc.Prof. Songsak Petmitr
Tropical Hygiene	Dr. Sompong Srisaenpang	Burden and trend of infectious tuberculosis patients, their treatment outcomes and the associated factors for treatment success at Khon Kaen Medical School, 1997-2001	Assoc.Prof. Pratap Singhasivanon
Microbiology and Immunology	Miss Piyatida Tangteerawatana	Cytokine gene polymorphisms in severe malaria	Prof. Srisin Khusmith
Tropical Nutrition and Food Science	Mrs. Sirimon Chaikate	Serum C reactive protein, interleukin-6, tumour necrosis factor- α , lipid profiles and anthropometric assessment in overweight Thais and healthy controls	Assoc.Prof. Supranee Changbumrung
Medical Entomology	Miss Sirima Kitvatanachai	Laboratory determination of lead toxicity in <i>Culex quinquefasciatus</i>	Assoc.Prof. Chamnarn Apiwathanasorn

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

Department	Name	Title of Thesis	Advisor
Microbiology and Immunology	Mrs. Panita Gosi	Gene polymorphic analysis of <i>Plasmodium vivax</i> buffy binding protein of Thai isolates and their functional capacity in B and T cell activation	Prof. Srisin Khusmith
Medical Entomology	Miss Pruksa Nawtaisong	Analysis of ribozyme strategies for suppression of dengue virus in transgenic " <i>Aedes albopictus</i> "	Assist.Prof. Narumon Komalamisra

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

Department	Name	Title of Thesis	Advisor
Microbiology and Immunology	Miss Petchara Tussana	Serogrouping of <i>Leptospira</i> spp. by DNA technology	Assist.Prof. Thareerat Kalambaheti
Microbiology and Immunology	Mr. Rongdej Tungtrakanpoung	Leptospirosis vaccine designed using T7 phage display technique	Assist. Prof. Pongrama Ramasoota
Helminthology	Mrs. Tippayarat Yoonuan	<i>Paragonimus mexicanus</i> and its difference from some Asian species	Assoc. Prof. Jitra Waikagul
Tropical Nutrition & Food Science	Mr. Tanett Pakeetoot	Identification of genetic alterations in breast cancer by arbitrarily primed polymerase chain reaction and gene cloning	Assoc. Prof. Songsak Petmitr
Social and Environmental Medicine	Mr. Songpol Tornee	Tuberculosis infection among household contacts under 15 years old in Bangkok, Thailand	Assist. Prof. Jaranit Kaewkungwal
Microbiology and Immunology	Miss Sirichit Wongkamchai	Development of immunodiagnostic assay for Brugian filariasis	Prof. Wanpen Chaicumpa
Microbiology and Immunology	Miss Chutima Kamkhaek	Analysis of sequence polymorphism of T-cell epitope regions, Th 2R and Th 3, on <i>Plasmodium falciparum</i> circumsporozoite proteins in Thai isolates	Prof. Srisin Khusmith

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

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

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

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

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

Department	Name	Title of Thesis	Advisor
Social and Environmental Medicine	Mrs. Kleebkaew Pitasawad	Environmental health model of pesticide utilization for sustainable agriculture in Donka Subdistrict, Bang Pae District, Ratchaburi Province	Assoc. Prof. Piyarat Butraporn
Social and Environmental Medicine	Mrs. Prapin Tharnpoophasiam	Simultaneous determination of T, T-muonic acid and S-phenyl mercapturic acid and its application in monitoring of occupational benzene exposure	Prof. Dwip Kitayaporn
Medical Entomology	Miss Pungasem Paeporn	Temephos resistance in <i>Aedes aegypti</i> and its significance to the mechanism and dengue infection	Assist. Prof. Narumol Komalamisra
Social and Environmental Medicine	Mrs. Yupadee Sirisinsuk	Access and patterns of health service utilization among insured persons under the Social Security Act, 1990	Assoc. Prof. Wijitr Fungladda
Tropical Nutrition & Food Science	Miss Wanida Pongstaporn	Identification of genetic alterations in ovarian cancer by arbitrarily primed polymerase chain reaction and gene cloning	Assoc. Prof. Songsak Petmitr
Tropical Hygiene	Miss Sawanee Tengrungsun	Survival analysis of Thai adult AIDS patients in the tertiary care hospital, Thailand	Assoc. Prof. Pratap Singhasivanon
Medical Entomology	Miss Yuwadee Trongtokit	Promising insecticidal activity of Thai phytochemical plants for control of mosquito vectors of diseases	Assist. Prof. Narumol Komalamisra

Ph.D (Trop.Med) 8th year students

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

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

Department	Name	Title of Thesis	Advisor
Clinical Tropical Medicine	Dr. Yoshinari Moriyama	The clinical relevances of cytokines on severe malaria patients and effects of prostaglandin derivatives	Prof. Polrat Wilairatana

The Hospital for Tropical Diseases



Prof. Polrat Wilairatana
Director

Office Telephone: 0-2354-9154, 0-2354-9100-19 ext. 1624, 1625



Assoc. Prof. Srivicha Krudsood
Deputy-Director



Assist. Prof. Udomsak Silachamroon
Deputy-Director



Assist. Prof. Weerapong Phumratanaprapin
Deputy-Director



Dr. Wirach Maek-A-Nantawat
Assistant-Director



Dr. Teerachai Kusolsuk
Assistant-Director

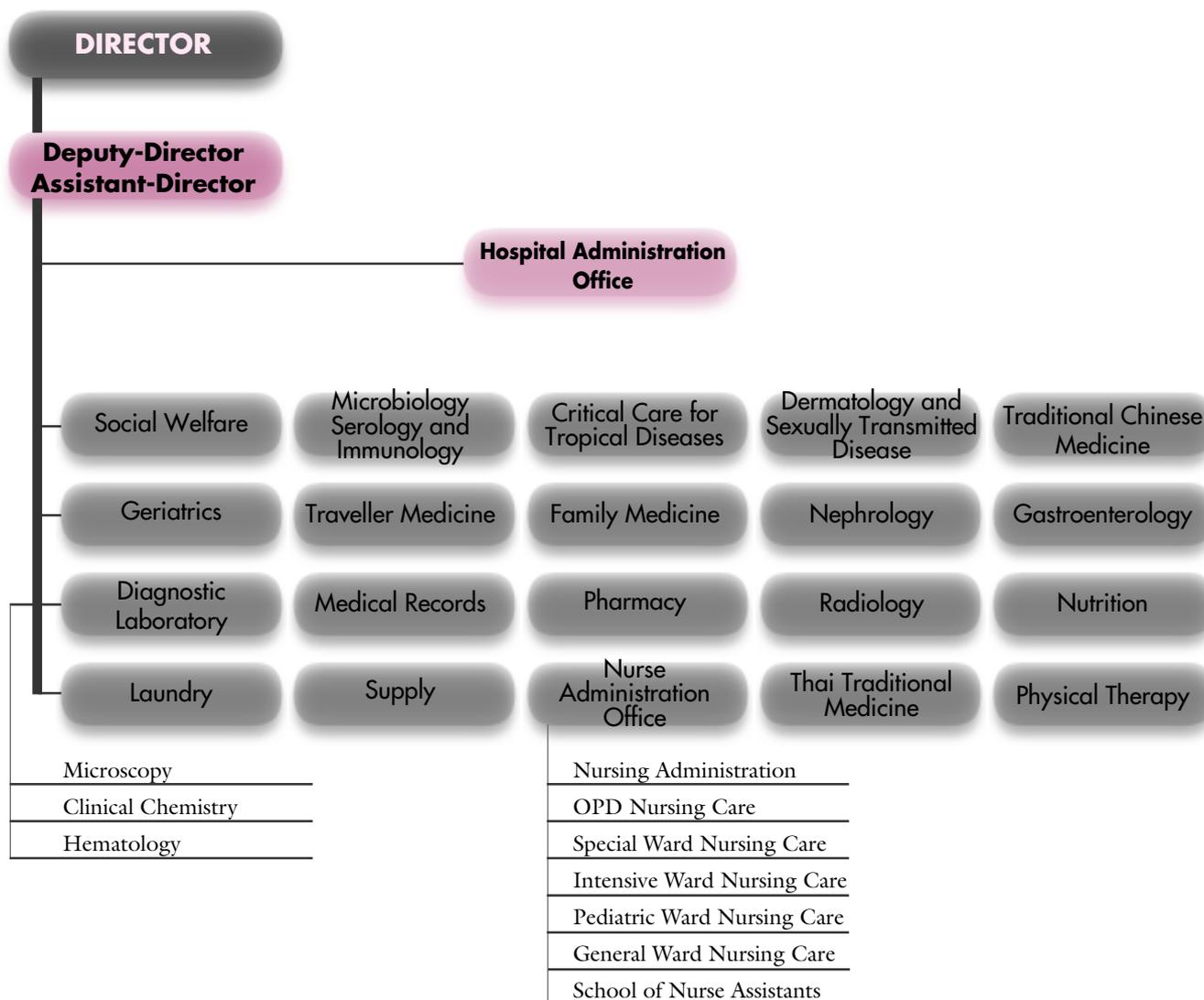
MEDICAL CARE SERVICES

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, a gastroenterology division, a dermatology division, and a sexually-transmitted diseases division.

Out-Patient Department services are as follows:

- General medicine: daily except public holidays, 8.00-16.00 hr.
- Malaria clinic: 24 hours daily.
- Health examination for immigrant 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.

Organization and Administration of the Hospital for Tropical Disease



- Electrocardiography (ECG).
- Spirometry.
- Audiogram.
- Visual acuity test and color blindness test.

Other Special Clinics are:

- Dermatology clinic: Monday - Thursday, 9.00-12.00 hr.
- Childrens clinic: Monday, Friday, 13.00-16.00 hr. and Wednesday, 9.00-12.00 hr.
- Chest clinic: Tuesday, 9.00-12.00 hr.
- Gastroenterology clinic: Tuesday, 9.00-12.00 hr.
- Geriatric clinic: Tuesday, 9.00-12.00 hr.
- Ear, nose, throat clinic: Tuesday, 9.00-12.00 hr.
- Gnathostomiasis clinic: Wednesday and Friday, 9.00-12.00 hr.
- Nephrology clinic: Monday and Wednesday, 9.00-12.00 hr.
- Thai Traditional massage: every day, 8.00-20.00 hr.
- Traditional Chinese acupuncture: Monday, Tuesday, Wednesday, 9.00-11.00 hr.

NURSING Unit



Mrs. Ladawun Supeeranuntha
Chief of Nursing Unit



Mrs. Wanna Plooksawasdi
Deputy Chief for Administration/Supervisor



Mrs. Yupin Rattanapong
Deputy Chief for Education/Supervisor



Miss Kobsiri Chalermrut
Deputy Chief for Service/Supervisor



Mrs. Rachanida Glanarongran
Director, School of Nurse Assistants



Mrs. Pinkaew Nipattasopone
Head of Ward OPD



Miss Suparp Vannaphan
Head of Ward ICU



Miss Arun Chanta
Head of Ward 2



Miss Sunee Chittamas
Head of Ward 3



Mrs. Kingkan A. Indravijit
Head of Ward 4



Mrs. Kingkaew Nakharutai
Head of Ward 5



Miss Aurathai Thanavibul
Head of Ward 7



Mrs. Siripan Srivilairit
Head of Ward 8



Mrs. Vipa Prariyanupharb
Head of Ward 9



Mrs. Monthira Ditta-in
Head of Ward 10



Mrs. Suwatana Siripiphat
Head of Ward 11



▶ In the fiscal year 2003 (October 2002-September 2003), the number of patients treated in the Hospital for Tropical Disease were classified by disease, as follows:

Diseases	No. of out-patients	No. of in-patients
1. Falciparum malaria	380	376
2. Vivax malaria	431	340
3. Mixed falciparum and vivax malaria	11	11
4. Malariae malaria	16	10
5. Unidentified infections	21	15
6. Scrub typhus	43	4
7. Typhoid	5	-
8. Diarrhea	151	19
9. Food poisoning	55	2
10. Hepatitis	798	50
11. Dengue hemorrhagic fever	152	132
12. Leptospirosis	2	2
13. Taeniasis	50	-
14. Hookworm	6	-
15. Ascariasis	2	-
16. Liver flukes	46	1
17. Pinworm	7	1
18. Strongyloidiasis	23	-
19. Trichuriasis	1	1
20. Gnathostomiasis	1,039	-
21. Dermatitis	2,237	4
22. Tuberculosis (pulmonary)	231	11
23. HIV infections	75	6
24. Hypertension	1,916	17
25. Diabetes mellitus	1,480	46
26. Hyperlipidemia	1,010	3
27. Diseases of oral cavity, salivary gland and jaw	164	158
28. Others	19,732 (66%)	499 (29%)
Total	30,081	1,707

Special Laboratory Services

Disease/Infection	Serological Test used	Specimen required	Time required (days)	Cost per test (Baht)	Place where specimen should be sent
Strongyloidosis	Immunoblot, ELISA	Serum 1-2 ml	2	200	Dept. Helminthology via OPD
Toxocariasis	Immunoblot, ELISA	Serum 1-2 ml	2	200	Dept. Helminthology via OPD
Angiostrongyliasis	Immunoblot	Serum 1-2 ml	2	200	Dept. Helminthology via OPD
Cysticercosis	Immunoblot	Serum 1-2 ml	2	200	Dept. Helminthology via OPD
Filariasis	ICT	Serum 1-2 ml	2	200	Dept. Helminthology via OPD
Gnathostomiasis	Immunoblot	Serum 1-2 ml	2	200	Dept. Helminthology via OPD
Paragonimiasis	Immunoblot	Serum 1-2 ml	2	200	Dept. Helminthology via OPD
Filariasis	Knotts concentration technique	Thick blood film, Mix blood 1-2 ml + 2% formalin 9 ml in 70% alcohol	1	120	Dept. Medical Entomology via OPD
Entomologic	Microscopy (insects + arthropods)	--	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	Serum 2 ml	7	450	Dept. Tropical Radioisotopes *
Serum folate	Microbiological assay (57 C°)	Serum 2 ml	7	250	Dept. Tropical Radioisotopes *
Red cell folate	Lactobacillus casei	Clot blood 2-3 cc	7	250	Dept. Tropical Radioisotopes *
Schistosomal 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 *
Pap smear-cervical, vaginal smear	Cytology	Vaginal smear, cervical smear	1	150/300	Dept. Pathology via OPD
Fluids	Cytology	Pleural effusion, ascites, urine	1	350/700	Dept. Pathology via OPD
Small pieces of biopsy	Histopathology	Small pieces of biopsy	3	300/600	Dept. Pathology via OPD
Organ	Histopathology	Organ	3	400/800	Dept. Pathology via OPD
Small pieces of biopsy	Frozen section	Small pieces of biopsy	3	300/600	Dept. Pathology via OPD
Organ	Frozen section	Organ	3	900/1,800	Dept. Pathology via OPD
Special stain		-	1	100	Dept. Pathology via OPD
Detection of heavy metals in whole blood	GFAAS	Heparinized whole blood 3 ml	2	250	Central Equipment Unit via OPD
Detection of heavy metal in urine		Urine 10 ml	2	250	Central Equipment Unit via OPD

* Send specimens directly to department

Disease/Infection	Serological Test used	Specimen required	Time required (days)	Cost per test (Baht)	Place where specimen should be sent
Alpha-fetoprotein	ELISA	Clotted blood 5 ml	2	200	Microbiology Serology & Immunology Unit via OPD
Anti DNA	Fluorescent	Clotted blood 5 ml	2	80	Microbiology Serology & Immunology Unit via OPD
Anti HAV IgM	EIA	Clotted blood 5 ml	1	250	Microbiology Serology & Immunology Unit via OPD
Anti HCV	EIA	Clotted blood 5 ml	1	250	Microbiology Serology & Immunology Unit via OPD
Anti HIV quick test	PHA + EIA	EDTA blood 2 ml	2hr.	300	Microbiology Serology & Immunology Unit via OPD
Anti HIV	PHA + EIA	Clotted blood 2 ml	1	150	Microbiology Serology & Immunology Unit via OPD
Cryptococcal/Ag	Agglutination	Clotted blood 5 ml	2	150	Microbiology Serology & Immunology Unit via OPD
Dengue IgG & IgM	HAI	Clotted blood 5 ml	1	250	Microbiology Serology & Immunology Unit via OPD
<i>E. histolytica</i> Ab	PHA	Clotted blood 5 ml	1	100	Microbiology Serology & Immunology Unit via OPD
HBs Ag	EIA	Clotted blood 5 ml	1	120	Microbiology Serology & Immunology Unit via OPD
HBs Ab	EIA	Clotted blood 5 ml	1	120	Microbiology Serology & Immunology Unit via OPD
HBc Ab	EIA	Clotted blood 5 ml	1	120	Microbiology Serology & Immunology Unit via OPD
VDRL	Agglutination	Clotted blood 5 ml	1	60	Microbiology Serology & Immunology Unit via OPD
Leptospiral Ab	Latex	Clotted blood 5 ml	1	150	Microbiology Serology & Immunology Unit via OPD
Mycoplasma Ab	Agglutination	Clotted blood 5 ml	1	200	Microbiology Serology & Immunology Unit via OPD
<i>P.pseudomallei</i> Ab	Agglutination	Clotted blood 5 ml	1	80	Microbiology Serology & Immunology Unit via OPD
Rheumatoid factor	Agglutination	Clotted blood 5 ml	1	100	Microbiology Serology & Immunology Unit via OPD
Widal test	Agglutination	Clotted blood 5 ml	1	100	Microbiology Serology & Immunology Unit via OPD
Weil Felix test	Agglutination	Clotted blood 5 ml	1	120	Microbiology Serology & Immunology Unit via OPD

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



Prof. Sornchai Looreesuwan
Director



Assoc. Prof. Pratap Singhasivanon
Deputy Director
1 October 2002 - 30 June 2003



Assoc. Prof. Suvanee Supavej
Consultant



Dr. Peter D. Echeverria
Consultant



Prof. Dr. Ma Sandra B. Tempongko
Deputy Coordinator



Ms. Vimolsri Panichyanon
Assistant Coordinator for Programme



Prof. Dr. Nelia P. Salazar
SEAMEO TROPMED Network
Consultant



Mr. Wim Duangdej
Administrative Officer



Mr. Prasasn Rujaphan
Accountant I



Mrs. Vimolpatana Indradat
Publication Officer



Ms. Pensri Chuenpradit
Program Officer



Mrs. Parinda Chomming
Accountant II



Ms. Jiraporn Kongtong
Publication Clerk



Ms. Arunkamol Desabaedya
Accountant Clerk



Mrs. Daosawan Kalayanamitr
Administrative Clerk



Mrs. Vandee Desabaedya
Clerk I



Ms. Rosario P. Vacal
Temporary Officer



Mrs. Payom Kaewbangkerd
Janitor



Mrs. Amnuay Sangkaram
Clerk II

▶ TROPMED/Thailand has 3 major functions, 1) teaching and training 2) research, and 3) services. Activities of the 3 functions are reported according to the 5 KEY RESULTS AREAS, as follows:

KRA1. ENHANCED PROGRAMME QUALITY AND RELEVANCE

1.1 Post-graduate regular courses. Five post-graduate, regular courses at the international level are offered by TROPMED/Thailand with a total of 217 students from 19 countries. There were 261 graduates in the academic year 2002/2003.

1.2 Undergraduate courses

TROPMED/Thailand also offers 2 undergraduate courses

- 1) Elective programme in tropical medicine with 23 medical students from 8 countries
- 2) Certificate in Nurse Assistant with 195 students.

In the FY 2002/2003, TROPMED/Thailand had 435 students from 19 countries among these, 20 were newly enrolled students in 7 courses offered by TROPMED/Thailand. Ninety-five percent of these students were fee-paying attendees and 261 (60.0%) 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)	20	11 (Austria, Bangladesh, Cambodia, Indonesia, Israel, Japan, Lao PDR, Switzerland, Germany, Thailand, USA)	17 (85%)	20 (100%)
MCTM (1-year course)	5	5 (Bangladesh, Cambodia, Indonesia Lao PDR, Myanmar)	2 (40%)	5 (100%)
MSc (TM)				
1 st year	19	3 (Japan, Thailand, Nepal)	73 (83.9%)	14 (16.0%)
2 nd year	21	2 (Vietnam, Thailand)		
3 rd year	31	2 (Thailand, Japan)		
4 th year	12	2 (Thailand, Lao PDR)		
5 th year	4	1 (Thailand)		
PhD (TM)				
1 st year	17	2 (Thailand, Vietnam)	103 (100%)	4 (3.8%)
2 nd year	15	2 (Thailand, Vietnam)		
3 rd year	25	3 (Thailand, Switzerland, Korea)		
4 th year	23	1 (Thailand, Malaysia)		
5 th year	15	1 (Thailand, Nepal)		
6 th year	7	1 (Thailand)		
8 th year	1	1 (Thailand)		
PhD (CTM)				
2 nd year	1	1 (Thailand)	1 (100%)	0
6 th year	1	1 (Japan)	1 (100%)	0
Subtotal	217		197 (90.7%)	43 (19.8%)

Course	Number	No. of nationalities	No. of fee-paying students	No. of graduates
Undergraduate				
Elective programme in Tropical Medicine	23	8 (Australia, USA, Canada, Japan, Austria, UK)	23 (100%)	23 (100%)
Certificate in Nurse Assistants	195	1 (Thailand)	195 (100%)	195 (100%)
Sub total	218		218 (100%)	218 (100%)
Grand Total	435	19	415 (95.4%)	261 (60.0%)

1.3 Training courses/Workshop/Meetings. Ten training courses at the regional level, eight at the international level, 1 international workshop and 1 international meeting were convened during FY 2002/2003, with a total number of 706 participants from 38 countries.

KRA2. INCREASED ACCESS TO MARKET

2.1 Active Marketing. One TV series and 5 news spots were broadcast, 15 news items were published in local newspapers, 8 radio announcements and 2 medical stories were published in a local journal.



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. Scientific and Ethical Review Group	Ethical Review	WHO	1	3 days

3.2 Visitors. Sixty-one visitors from 13 countries visited TROPMED/Thailand during FY 2002/2003.

KRA4. IMPROVED FINANCIAL STATUS

There were three sources of revenue for activities pertaining to the three major roles of TROPMED/Thailand: 1) Government budget, 2) Revenue from medical care fees, academic services and other activities, and 3) Research funds.

Table 3: Sources of revenue.

Sources of revenue	Amount in million Baht	% Increase / Decrease
1. Government budget	133.15	-14.78
2. Revenue from services and other activities	92.78	+04.25
3. Research funds from other organizations	168.25	+50.90

KRA5. ENHANCED QUALITY OF SEAMEO MANAGEMENT

TROPMED/Thailand has a total of 778 staff comprising 88 academic staff, 136 academic assistants and research staff, 103 administrative personnel, 69 university employees and 382 other employees. The qualifications and academic posts held by the 88 academic staff are shown in Table 4.

Table 4: Qualifications of 88 academic staff.

Qualification	No	%
PhD	59	67.0
Master	29	33.0
Bachelor	0	0.0
Total	88	100.0



The academic posts of 88 academic staff compared to those of Mahidol University are shown in Table 5.

Table 5: Academic posts of 88 staff of TROPMED/Thailand.

	Academic Posts			
	FTM staff		Mahidol University staff	
	No	(%)	No	(%)
Professor	5	(5.68%)	126	(5.28%)
Associate Professor	32	(36.38%)	780	(32.73%)
Assistant Professor	31	(35.22%)	817	(34.28%)
Lecturer	20	(22.72%)	660	(27.69%)
Total	88	(100.00%)	2,383	(100.00%)

5.1 Number of staff promoted or who obtained higher qualifications

Table 6: Number of staff promoted.

Academic rank	: Professor	= 2
	: Associate Professor	= 1
	: Assistant Professor	= 5
Career rank	: Higher rank	= 6
Higher qualification	: Higher degree	= 24
	Total	= 38



5.2 Number of research projects and publications. TROPMED/Thailand staff undertook 120 research projects with total research grants of 168.2 million Baht, and published research papers.

	New project	On-going	Accomplished
No. of research projects	23 (19%)	74 (62%)	23 (19%)
No. of published papers	= 55		

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

Sixteen staff (5.1%) took study leave for higher education. Thirty-eight (12%) attended training courses abroad. Six hundred and thirteen staff (78.79%) attended meetings, seminars, workshops. One staff may attend more than one meeting/seminar/workshop.

Table 8: Staff development through higher study, training courses, seminars/workshops.

Category of staff development	In country	Abroad	Total
Study leave	12 (2.0%)	4 (9.5%)	16 (2.5%)
Attending training courses	575 (97.9%)	38 (90.4%)	613 (97.4%)
Attending meetings/seminars/workshops			
No of staff	587 (75.4%)	42 (5.3 %)	629 (80.8%)

5.4 Special talks/lectures

To develop and/or improve knowledge of staff, 15 lunch talks/lectures on various topics for 578 attendees, 24 CME (Continuing Medical Education) lectures including information technology, were organized for 423 attendees.

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 28 medical doctors, 94 nurses and 80 nurse assistants. The total number of outpatients treated was 30,081, and the number of patients admitted to the Hospital was 1,707. 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 were opened for students/guests/visitors of TROPMED Thailand, in May 2000.

5.7 Number of staff awarded

1) Local Award:

Recipients	Awards
1. Prof. Sornchai Looareesuwan	1. Outstanding Alumnus Faculty of Science, Mahidol University

2) National Award:

Recipient	Awards
1. Mr.Ruangsak Prasobklin	1. Outstanding Government Employee Award From Office of the Prime Minister

The Asian Centre of International Parasite Control (ACIPAC)

Office Telephone: 66 (0) 2354-9100-19 ext. 1338, 1339; Fax: 66 (0) 2643-5616

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Prof. Sornchai Looreesuwan
Project Manager



Prof. Somei Kojima
Chief Advisor



Assoc. Prof. Jitra Waikagul
Assistant Project Manager



Dr. Jun Kobayashi
Expert on Parasite Control



Dr. Hironori Okabayashi
Expert on School Health



Mr. Usui Tetsuro
Project Coordinator



Ms. Pornpimol Chaivittayangkul
Secretary



Ms. Nichapat Na-Thalang
Assistant Secretary



Ms. Porntepini Sooksangprasit
Assistant Secretary

Asian Centre of International Parasite Control (ACIPAC)

▶ The aim of the Asian Centre of International Parasite Control (ACIPAC) is to strengthen parasite control in Southeast Asia through human resource development. In addition to being under threat of death due to malaria, a large proportion of schoolchildren in the Greater Mekong Sub-region (GMS) countries is still “wormy” (Stoll, 1947). Because of multiple infections with various species of parasites, schoolchildren are suffering from chronic disease burdens in terms of physical and mental disabilities caused by the infections. Therefore, we set up ACIPAC’s catchphrase “*Save Wormy Schoolchildren*”.

Based on successful Japanese experience in control of major parasitic diseases, including malaria, schistosomiasis and filariasis, as well as soil-transmitted helminthiasis (STH), all of which were serious public health problems just after the World War II, former Japanese Prime Minister Mr. Ryutaro Hashimoto emphasised the importance of parasitic disease control in improving public health, and proposed several steps necessary for effective international co-operation to overcome the hazard of parasitic diseases, through collaboration with WHO at the G8 countries’ summits in 1997, and 1998. The Japanese government decided to establish three centres for research and training, one in Asia and two in Africa, and ACIPAC became the first one established under the Hashimoto Initiative. The Hashimoto Initiative has been further strengthened by the Okinawa Infectious Diseases Initiative, which was announced at the Kyushu-Okinawa G8 Summit, in 2000. Thus, in Africa, two centres were launched; one (Eastern and Southern Africa Centre of International Parasite Control, ESACIPAC) in the Kenya Medical Research Institute, in 2001, and the other (West African Centre for International Parasite Control, WACIPAC) in the Noguchi Memorial Institute for Medical Research, University of Ghana, in January 2004. Because the establishment of ACIPAC “had a strong impact on promoting parasite control programs in the Greater Mekong Sub-region countries”, H.E. Mr. Hashimoto was conferred a degree of Doctor of Philosophy in Clinical Tropical Medicine, *honoris causa*, by Mahidol University in the year 2002 (*Spectrum* 2002;9(2)).

Toward its Overall Goal, ACIPAC has been holding an “International Training Course for School-based Malaria and Soil-transmitted Helminthiasis Control for Programme Managers” once a year since 2001. After finishing the Course, trainees were requested to start their pilot projects in respective countries, and pilot projects themselves should be utilised for further development of human resources through in-country training for health personnel, including laboratory technicians, health workers, teachers, etc.



To develop a new approach to school health, model activities have been carried out in selected schools in Suan Phung and Nakhon Si Thammarat with strong support from the Office of Basic Education Commission (OBEC), Ministry of Education. Teacher's manuals and textbooks for friendly learning prevention of malaria or STH were developed in collaboration with local teachers, and their English versions were distributed to partner countries and international agencies, as well.



Establishing the partnership with international organizations or agencies is also one of the most important roles of ACIPAC from the viewpoints of human resources/information networking in order to promote parasite control in partner countries. A typical example is that three participants were invited from Timor Leste to ACIPAC training course 2003, with the support of UNICEF, in collaboration with the local JICA representative office. ACIPAC also joined in publication of "Mapping Human Helminth Infections in Southeast Asia" which was supported by UNICEF and SEAMEO TROPMED. Another example is a partnership workshop on health-promoting schools or school health-based parasite control programmes jointly organized by WHO and JICA/KIDSMILE and ACIPAC held in Vientiane, Lao PDR. This kind of workshop became held periodically (once a year) under the initiative of the Government of Lao PDR, which has established a National Task Force for health-promoting schools and STH control in collaboration with WHO, UNICEF, WFP, JICA (ACIPAC and KIDSMILE) and JADDO (an NGO).

The first five years' activities of ACIPAC will end in March 2005, and all activities need to be evaluated before drawing up future plans, if any.

Mahidol - Maryland University Tropical Medicine Research Program (TMRP)

Tel. 0-2354-9100-19 ext. 2073, 0-2354-1754; Fax. 0-2354-1792



Assoc. Prof. George Watt
Director

Advisor

Prof. Sornchai Looareesuwan

Consultant

Prof. Dwip Kitayaporn

Assoc. Prof. Pratap Singhasivanon

Assoc. Prof. Wichai Supanaranond

Assoc. Prof. Pornthep Chanthavanich

Assoc. Prof. Punnee Pitisuttithum

Assoc. Prof. Jitra Waikagul

Assoc. Prof. Yupaporn Wattanagoon

Assoc. Prof. Srivicha Krudsood

Assist. Prof. Varee Wongchotigul

Assist. Prof. Udomsak Silachamroon

Assist. Prof. Varaporn Suphadanaphongs

Dr. Dorn Watthanakulpanich

Physician

Dr. Saranath Lawpoolsri

Dr. Benjaporn Tuntasood

Scientist

Ms. Pannamas Maneekarn

Ms. Tasawan Singhsilarak

Mr. Noppadon Tangpakdee

The Mahidol-Maryland Tropical Medicine Research Program (TMRP)

▶ **The** Mahidol-Maryland Tropical Medicine Research Project was formed in November, 2003. The goal of the TMRP is to establish genuine, long-term collaboration between the Faculty of Tropical Medicine and the University of Maryland Medical School in Baltimore. The TMRP will support research and training in fields of mutual interest to the two institutes, to advance knowledge in tropical medicine. Scientists from both universities will be involved in all aspects of the work performed by the TMRP—from conception, design, and planning, to execution and publication.

The burgeoning project will eventually have comprehensive laboratory and clinical components. Current laboratory efforts are focused on the use of real-time PCR to detect and quantify *Orientia tsutsugamushi* in clinical specimens from scrub-typhus-infected individuals. Plans are being made to explore the mechanisms by which scrub typhus inhibits HIV-1 in the TMRP laboratory.

The clinical efforts of the TMRP will focus on tropical infections of public health importance in Thailand and Southeast Asia. Prominent among these infections is HIV-1, and one area of active investigation involves interactions between the AIDS virus and a variety of tropical infections. The TMRP is involved in plans to develop and characterize a cohort of schoolchildren in Ratachaburi Province for possible phase 3 dengue vaccine trials. Studies are already underway at Takuapa District Hospital, Phang-nga to describe the causes of pyrexia of unknown origin. Similar investigations are planned at Chiangrai Regional Hospital.

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OFFICE of the Dean

Tel. 0-2354-9100-19 ext. 1326, 1328 Fax. 0-2354-9139



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

▶ **The Office of the Dean** is a support unit facilitating the major tasks of the Faculty, such as teaching, research, academic services, and hospital services, to meet the goals of the Faculty. The Office of the Dean is conducted under the authority and supervision of the Secretary of the Faculty and Deputy Deans with related duties. It can be differentiated into 10 major units, i.e., Administration and General Affairs Unit, Personnel Unit, Policy and Planning Unit, Financial and Procurement Unit, Educational Affairs Unit, Information Technology Unit, Educational Technology Unit, International Relations Unit, Area and Maintenance Unit, and Research and Academic Affairs Unit.

“ **Vision for the Office of the Dean**
Pleased to be of Service ”

Management Information

Personnel Management

In the year 2003, there were 778 staff in the Faculty; 88 academic staff, 265 support staff, and 425 administrative staff. 67% (59 staff) had Ph.Ds., while 33% (29 staff) had Master’s degrees or comparable qualifications. Two staff were promoted to Professor, one to Associate Professor, and 5 to Assistant Professor. The ratio of Professor: Assoc. Prof: Assist. Prof: Lecturer = 5 : 32 : 31 : 20, respectively, and 141 new staff were recruited, 77 staff resigned, and 10 staff retired during the year.

Staff Development

12 staff have been continuing their education inside the country, and 4 outside. 2 staff were trained inside the country, and 3 were trained overseas. 38 staff participated in international conferences, and 575 participated in national conferences. 4 staff were trained in management/administrative development.

Budget Management

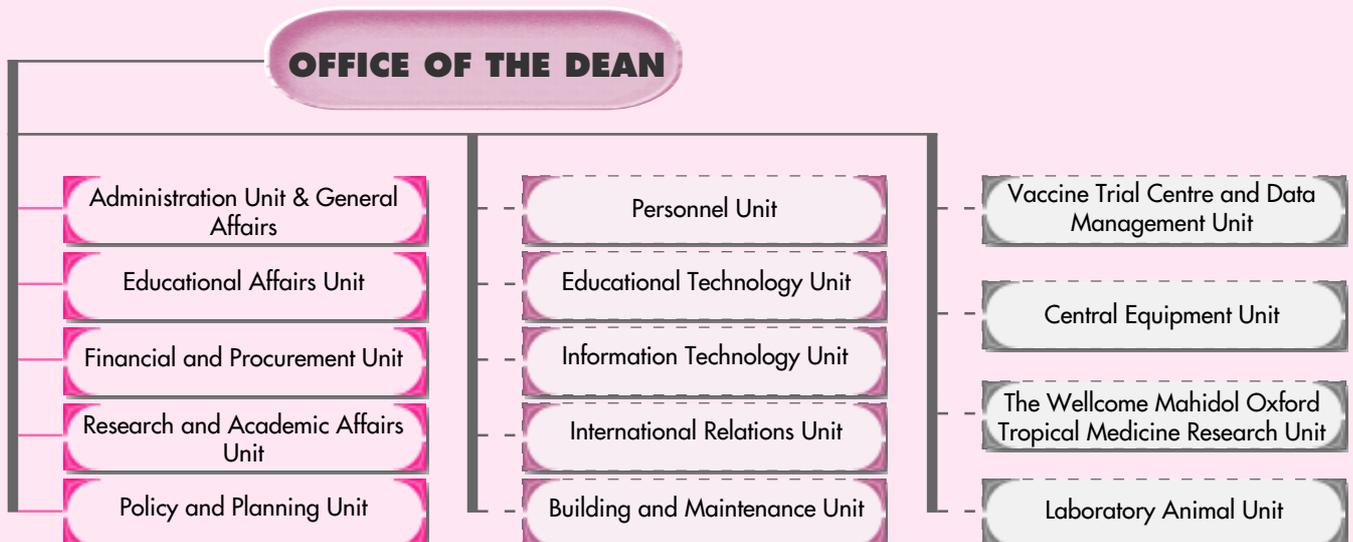
Total expenses were 225.93 million Baht, of which 133.15 million Baht were supported by government budget, and 92.78 million Baht was Faculty revenue, in a percentage ratio of 58.90 : 41.10. The expenditure can be broken down as follows:

Personnel Budget = 113.84 Million Baht (50.39%);
Operational Budget = 84.87 Million Baht (37.56%); Investment Budget = 27.22 Million baht (12.05%)

Construction and Area Development

The Kanchanaburi Research Centre building, which is the new research station of the Faculty, was completed and officially opened on 1 August 2003.

Organization Chart



Administrative and General Affairs Unit

Tel. 0-2354-9100 ext. 1302, 1304, 1801

The Unit is divided into 4 subunits, as follows:



Kannikarkaew Pinit

B.A. (General Management), B.A. (Business Education)

Head

Documentation Subunit

General Affairs Officer

Aree Masngammuang

B.A. (Political Science)

Maninthorn Phanumaphorn *M.B.A.*

Patra Kreekul

B.A. (General Management)

Nathaneeporn Panampai

B.A. (General Management)

Supavadee Yaowasang

B.A. (Lib.Info.Sc)

Sanchai Meeprom *B.A.*

Office Clerk

Pranee Kraisorn

Prachum Bauprasert

Operator

Chanpen Ronsuk

Data Input Clerk

Yupa Jarernrit



Public Relations Subunit

Public Relations Officer

Thitika Teeranetr *B.A., M.A. (Social Development)*

General Affairs Officer

Wandee Srasalee *B.A. (General Management)*

Varee Viriyarat *B.A. (General Management)*

Illustration Officer

Wasathum Phomngam *B.A. (Visual Comm. Design)*

Transportation Subunit

Driver

Prasarn Klamem

Area and Transportation Subunit

Security Guard

Somjai Promduang

Gardener

Sombat Khamthane

Dormitory Subunit

General Affairs Officer

Siriluke Kromwate

Boontarika Mungkung

Suchawadee Rohitratana

Tidarat Ekpatharapant



Educational Affairs Unit

Tel: 0-2354-9100-19 ext. 1532, 1533



Wanpen Putitanun

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Head

Educational Affairs Officer

Somporn Ngamsirisomsakul *B.B.A. (Marketing)*
Sivaporn Pisitsak *B.B.A. (Marketing)*
Wipada Eiamyaem *B.S.W. (Social Work)*

Scientist

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

General Affairs Officer

Wanida Onwan *B.A. (Thai&English)*
Chutarat Pradabprachr *B.Ed.*

General Affairs Officer Associate

Rangson Praevanit *Cert. Commercial*
Nutchantart Taewrob *Cert. Commercial*
Chiraporn Praevanit *Voc.Cert. Commercial*
Aree Buaprae *Voc.Cert. Commercial*
Rasamee Wongititakul *B.B.A. (Accounting)*

Staff

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

Specialist

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



Financial and Procurement Unit

Tel. 0-2354-9100 ext. 1204, 1305, 1323, 1325

The Unit is divided into 2 subunits, as follows:



Somkid Nima

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

Head

Financial and Accounting Subunit

Accountant Officer

Ketsinee Nima *B.B.A. (Accounting)*
Tham Chermkhuntod
B.A. (General Management), B.B.A. (Accounting)
Arayaporn Sawangrungrueng *B.A.*
Souvalak Medeepark
Sutira Paipong
Supakit Khachachai
Pornthiwa Senim *B.A.*
Aungkana Poolsawas

Accountant Staff

Jeeranat Kumseranee *B.A. (General Management)*
Prapaporn Krootmas
Nopadol Preechasunthorn *Voc. Cert.*
Vanthana Sreechiengsa *Voc. Cert.*
Prapussorn Sitisero
Nareerut Yossuksri
Chayan Muanom
Cert. in Commercial



Procurement Subunit

Procurement Officer

Prapaiporn Tiacharoen
B.B.A. (General Management)
Montree Noochan *B.B.A. (Econ)*
Wattana Korchasri
Jeranan Pansuebchuea *B.B.A.*
Nidaporn Klinmon

Procurement Staff

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

Officer Clerk

Oranart Supaka

Typist

Mongkol Bunchakorn

Photographer

Wattana Prechasunthorn



Policy and Planning Unit

Tel. 0-2354-9100-19 ext. 1303



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

The Unit is divided into 3 subunits

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

Policy and Planning Officer

Thanomsri Ketsuk *B.B.A. (Money & Banking)*
Jitra Suriya *B.B.A. (Money & Banking)*

Computer Scientist

Pramote Ketsuk
B.Sc. (Computer Science)



Personnel Unit

Tel. 0-2354-9100-19 ext. 1324, 1330



Sukanya Aung-aree
B.A. (Soc. Ant.)
Head

Personnel Officer

Phongsri Konthong *B.A. (General Management)*
Suphaporn Chotiwithin *Cert. Computer*
Chuleeporn Rummyarungsi

Business Associate

Surang Wattanakamolgul *Cert. Marketing*
Buarun Nilapa



Education Technology Unit

Tel. 0-2354-9100-19 ext. 1841, 1842; 0-2354-9152



Sompoch Thanuvathana

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

Head

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.

The Unit is comprised of 2 divisions:

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

Illustration Officer

Saranya Vongsngernyuang *B.Sc. (Med. Illus. & A.V. Tech.)*
Tawan Wathanakul *Voc. Cert., B.Ed. (Ed. Tech. Inn.)*
Vatcharin Nagpong *B.F.A. (Comm. Desi.)*
Sivaporn Kanchanamai *B.F.A. (Appli. Art)*

Illustration Associate

Chamnan Egasonth *Cert. Graphic Art*

General Affairs Officer

Kannika Petporee *B.A. (General Management)*



Information Technology Unit

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Duangjai Sahassananda

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Head

The Information Technology Unit provided information and Computer services throughout FY2002/2003 for the Faculty's staff, students and participants in short training courses, such as

I Teaching and Training

- 1.1 Teaching faculty students; MSc., PhD., DTM&H, MCTM, Assistant nurse
- 1.2 Training faculty staff;

Computer software training 8 times for 248 faculty staff which consist of:

Microsoft Office - Basic Knowledge on Computer/Windows 98/MS Word, MS Powerpoint, MS Excel, Statistic, SPSS progra, **Internet** - Information search via Internet: web and database, **Graphic** - Adobe Photoshop & Scanner, **Hospital Staff** - MS Office software for Hospital staff

- 1.3 Training for workshop, ACIPAC workshop

II General services

The unit provide services for the Faculty such as computer room, Network cabling, computer consulting/program installation, Antivirus update and clean, slide making, laser printer, computer scan image.

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tejct@mahidol.ac.th

III Network and Application development

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

- Network administration and monitoring
- Faculty website at <http://www.tm.mahidol.ac.th>
- ACIPAC website at <http://www.tmacipac.mahidol.ac.th>
- Hospital database system
- Database for student information (in progress)
- Intranet for the administrative section (in progress)



International Relations Unit

Tel: 0-2354-9100-19 ext. 1327, 1318; 0-2643-5614

Fax: 0-2354-9141, E-mail: tmknt@mahidol.ac.th



Keeratiya Nontabutra

B.A.

Head

The International Relations Unit is a coordinating office of the Faculty's abroad cooperation under the command of the Deputy Dean for International Relations and Information Technology. The Unit plays the following important roles :

1. International meetings, conferences, seminars, workshops, short course training
2. Elective students in tropical medicine
3. Visiting Professors
4. International linkages
5. Visa extensions for foreigners
6. English recommendation letter
7. Coordinating office of
 - Wellcome-Mahidol University Oxford Tropical Medicine Research Programme

Foreign Affairs Officer

Sethavudh Kaewwiset B.A.
tesvk@mahidol.ac.th

General Affairs Officer

Rattanawadee Nanlar B.A.
tikinan@hotmail.com



- SEAMEO TROPMED Regional Centre for Tropical Medicine (TROPMED/Thailand)
- The Asian Centre of International Parasite Control (ACIPAC)
- WHO Collaborating Centres for Environmental Management for Vector Control and for Management of Malaria, etc.
8. International Visitors

Buildings and Maintenance Unit



Sawek Chom-ming
B.En.
Head

Maintenance and Repairs Subunit

Somsak Lohpeung	Electrical Engineer
Phanumars Thunrittisa	Electronics Associate
Chaiporn Phuphan	Electrician Associate
Somsak Klompanuang	Janitor
Ruengsak Prasopklin	Janitor
Somsak Phongcharoen	Janitor
Krisada Kongrot	Janitor
Panom Auaon	Machine Associate
Kamol Thanasarnprasert	Machine Associate
Somporn Narint	Plumber's Assistant
Chinasup Malai	Plumber's Assistant
Sunun Boonraksa	Plumber's Assistant
Thepsathit Bunyaphuphasup	Electronics Associate
Vasan Nakthanram	Machine Associate
Sanya Maneeboonyang	Electrician Associate
Wantana Mee-r-sa	Business Associate

Area Subunit

Thap Ngamnat	Architect
Taywin Khaosanit	Draftman
Jatupong Toopbansao	Laboratory staff
Bunchan Kijsupee	Carpenter
Sutep Prempree	Carpenter
Amnauy Boonthana	Steel Worker
Chalad Naksit	Janitor
Kamol Songserm	Janitor

Thamrongsakdi Vimalasuta **Machine Associate**



Central Equipment Unit

Tel: 0-2354-9100-19 ext. 1291, 1662, 1664, 1668



Duangkamol Viroonudomphol
Ph.D.
Head

Scientist

Hathairad Hananantachai
Rachaneekorn Mingkhwan

General Affairs Officer

Nuttaporn Korchasri

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



Research and Academic Affairs Unit

Tel: 0 2354 9139-19 ext. 1524, 1525; Fax: 0 2643 5578

Homepage: <http://www.tmpubs.tm.mahidol.ac.th>

E-mail: tmpww@mahidol.ac.th



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

General Affairs Officer

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

Database Developer

Pitchapa Vutikes B.B.A. (*Business Computer*)

Illustration Officer

Ronnachai Rarerng B.Ed. (*Tech. Inn.*)

Illustration Staff

Phaibul Vasanakomutr



TRAINING Programs

During 1 October 2002 – 31 December 2003

1) 2 September 2002 – 11 October 2002

Regional Basic Course on Data Analysis for Epidemiological Research

India 8

Regional Advanced Course on Data Analysis for Epidemiological Research

India 8

2) 2 September – 22 November 2002

The ACIPAC International Training Course on School-Based Malaria and Soil-Transmitted Helminthiasis Control for Programme Managers

Cambodia	6	Lao PDR	7
Thailand	6	Vietnam	5
Ghana	1	Kenya	1

3) 7 October – 18 November 2002

Training Course in Tropical Medicine

USA 1

4) 20 October – 1 November 2002

Short Term Training on Laboratory Medical Skills

Vietnam 6

5) 4 – 15 November 2002

Training Course in Tropical Medicine

Taiwan	1	USA	1
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6) 18 – 28 November 2002

Asian Clinical Tropical Medicine Course

USA	16	Ireland	1
Israel	1	Taiwan	1
Mexico	1	Canada	4
Philippines	1		

7) 4 – 29 November 2002

Training Course in Global Infectious Diseases

Japan 6

8) 10 – 15 November 2002

Study Visit to Thailand of Community-oriented Teaching

Vietnam 9

9) 10 January – 28 February 2003

Training Course in Tropical Medicine

Japan 2

10) 20 – 28 February 2003

Refresher Course in Parasitology for Laboratory Technicians

Sweden 10

11) 3 – 28 March 2003

Thai Government Fellows (Pre-course Training Programme for DTM&H and MCTM)

Indonesia	1	Lao PDR	1
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12) 26 May – 6 June 2003

Training Course in Parasitology (WHO Fellow)

Bangladesh 1

13) 1 August – 30 October 2003

Training Course in Tropical Medicine

Philippines 1

14) 6 – 17 October 2003

International Training Course on Management of Malaria

Bangladesh	3	Bhutan	1
Myanmar	3	Indonesia	3
Nepal	4	Thailand	3
Pakistan	1	Sudan	3
Saudi Arabia	1	Sri Lanka	2
Japan	1	India	3

15) 23 – 26 November 2003

Workshop on Parasite Control in Latin America and the Caribbean

Argentina	1	Bolivia	1
Chile	1	El Salvador	1
Guatemala	1	Jamaica	2
Mexico	1	Nicaragua	1
Panama	2	Paraguay	1
Peru	1	Uruguay	2

16) 1 October – 30 November 2003

Training Course in Tropical Medicine

Austria 1

17) 17 November – 19 December 2003

Training Course in Tropical Medicine

Germany 1

18) Study Visits for Four Groups of Health Personnel from Bangladesh

23-29 November 2003

Short-term Training on Emergency Obstetrical Care (ECO) Services for Mid-Level Managers (15 Persons)

15-21 December 2003

Short-term Training on Orthopedics (6 persons)

Short-term Training on Traditional Medicine (6 persons)

Short-term Training on Cardiology (6 persons)

INTERNATIONAL Linkages

- Agreement between the Government of Thailand and the Southeast Asian Ministers of Education Organization (SEAMEO) (1967 - present).
- Memorandum of Agreement between the Faculty of Tropical Medicine, Mahidol University and the Faculty of Medicine, the University of Calgary, Canada (October 1991 - present)
- Agreement of Cooperation and Exchange between Mahidol University and the Free University Berlin, Germany (May 1985 - present).
- Memorandum of Understanding between the Nuffield Department of Medicine, University of Oxford, the Faculty of Tropical Medicine, Mahidol University and the Wellcome Trust, London, United Kingdom (1979 - present)
- Memorandum of Understanding between James Cook University of North Queensland, Australia and Mahidol University (May 1993 - present).
- Agreement on Cooperation and Joint Study Programme between the Faculty of Tropical Medicine, Mahidol University and the Faculty of Medicine, University of Innsbruck, Austria (May 1992 - present)
- Agreement for Academic Exchange and Cooperation between University of Tsukuba, Japan and Mahidol University, Kingdom of Thailand.
- Agreement between Deutsche Gesellschaft für Technische Zusammenarbeit (GTZ), Germany and Regional Tropical Medicine and Public Health Network of the Southeast Asian Ministers of Education Organization (SEAMEO-TROPMED Network) and the Faculty of Tropical Medicine, Mahidol University (June 1994 - present).
- Agreement of Cooperation between the Faculty of Tropical Medicine, Mahidol University and Department des Maladies Infectieuses Tropicales, Groupe Hospitalier Pitie Salpetriere, France (March 1995 - present).
- Memorandum of Understanding, Collaboration between The Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand, the SEAMEO TROPMED Network and the Swiss Tropical Institute, Basel, Switzerland.
- Agreement of Co-operation between the Tropical Medicine and Public Health Network of the Southeast Asian Ministers of Education Organization (SEAMEO TROPMED) and the Australian Centre for International and Tropical Health and Nutrition (ACTTHN) of the Queensland Institute of Medical Research and the University of Queensland.
- Memorandum of Understanding between the Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand and The Health of Animals Laboratory, Canadian Food Inspection Agency, Government of Canada, Saskatoon, Canada.
- Memorandum of Understanding between the Faculty of Tropical Medicine, Mahidol University and Liverpool School of Tropical Medicine, UK.
- Minutes of Meeting Between the Japanese Management Consultation Team and the Authorities Concerned of the Government of the Kingdom of Thailand on Japanese Technical Cooperation for the Project for the Asian Centre of International Parasite Control.

VISITORS

FY 2003

Name	Country	Name	Country
1. Mrs. Risa Yamamoto	Japan	34. 30 Indonesian visitors from Faculty of Public Health	Indonesia
2. Ms. Yoko Ogawa	Japan	35. Mr. Edward Wazer	U.S.A.
3. Ms. Fumihiko Kawamoto	Japan	36. 13 Japanese visitors from Asian Institute of Technology	Japan
4. Mr. Hideyuki Takahashi	Japan	37. Two Professors from Asian Institute of Technology	Thailand
5. Ms. Eiko Kaneda	Japan	38. Dr. Jonathan	England
6. Mr. Nobuaki Akao	Japan	39. Dr. April Truett	U.S.A.
7. Mr. Masamine Jimba	Japan	40. Dr. Robert Barthel	U.S.A.
8. Mr. Yoshifumi Kaji	Japan	41. Dr. Ute Schwarz	German
9. Mr. Tomohiro Kuroda	Japan	42. Dr. Tomas Jelinek	German
10. Mr. Shigeyuki Kano	Japan	43. 8 Vietnamese visitors from CDC	Vietnam
11. Dr. Irvan Afiandi	Indonesia	44. 9 Japanese visitors from Yamaguchi University	Japan
12. Dr. Guswan Wiwaha	Indonesia	45. 3 Visitors from Bormmaraj Chonni Nopparatvachira Nursing College	Thailand
13. Dr. Elsa Pudji Setiawati Sasongko	Indonesia	46. Prof. Gary M. Brittenham	U.S.A.
14. 8 Vietnamese officials from CDC	Vietnam	47. Dr. Robert Bos	Switzerland
15. Dr. Saito	Japan	48. Dr. Burkhard Fugmann	German
16. Ms. Aya Tanabe	Japan	49. 9 Medical Students from Ramathibodi Hospital	Thailand
17. Dr. Naoki Arizono	Japan	50. Ms. Terumi Kobayashi	Japan
18. Dr. Takahashi	Japan	51. Mr. Hironari Hamada	Japan
19. Pongpol Adireksarn	Thailand	52. Ms. Jun Shiraishi	Japan
20. 15 Indian visitors from Faculty of Public Health	India	53. Mr. Kei Sato	Japan
21. Mr. Khan Moududur Rahman	Bangladesh	54. Mr. Yuyuki Tateno	Japan
22. Mr. Faruk Ahmed	Bangladesh	55. Mr. Taku Yamamichi	Japan
23. Dr. Darwin Murrell	Denmark	56. Ms. Yoshiko Takeuchi	Japan
24. Dr. Fumie Kobayashi	Japan	57. Ms. Midori Takami	Japan
25. Prof. Hisami Watanabe	Japan	58. Ms. Imamura Wakana	Japan
26. Mr. Horoshi Takenaka	Japan	59. Ms. Kang Ji Ka	Japan
27. Mr. Yoshihido Terashima	Japan	60. Ms. Kanei Ayako	Japan
28. H.E. Dr. Edilberto C de Jesus	Philippines	61. Mr. Wakabayashi Hiroshi	Japan
29. Prof. Michael Wilson	Ghana		
30. Dr. Morinaka	Ghana		
31. Prof. H.M. Gilles	England		
32. Dr. Akihiko Yano	Japan		
33. Dr. Yuzo Takahashi	Japan		

Elective Programme in Tropical Medicine

1 Oct. 2002 – 31 Dec. 2003

Name	Institute	Country	Period
1. Ms. Sarah Lockley	University of Newcastle	Australia	2 Oct.-20 Nov.2002
2. Mr.Christopher Rallahbaker	University of Newcastle	Australia	2 Oct.-20 Nov.2002
3. Mr. Nareg Roubinian	University of Vermont	USA	13 – 24 Jan.2003
4. Ms. Erin Arthur	University of Vermont	USA	13 – 24 Jan.2003
5. Dr.Rocha Rocha	University of British Columbia	Canada	9 – 31 Jan.2003
6. Dr. Tristana Stein	University of British Columbia	Canada	9 – 31 Jan.2003
7. Ms.Alison Cheah	University of New South Wales	Australia	9 – 31 Jan.2003
8. Mr. Omeed Aziziras	Albert Einstein College of Medicine	USA	10 – 28 Feb.2003
9. Ms. Elaine Desnoyers	University of Calgary	Canada	16 Jun – 16 Jul 2003
10. Ms.Kelly Chu	University of Calgary	Canada	16 Jun – 16 Jul 2003
11. Ms.Melina Repka	University of Calgary	Canada	16 Jun – 16 Jul 2003
12. Mr.Sameer Chhibber	University of Calgary	Canada	16 Jun – 16 Jul 2003
13. Mr. Dareen Lorenz	University of Calgary	Canada	16 Jun – 16 Jul 2003
14. Mr. Hussein Kanji	University of Calgary	Canada	16 Jun – 16 Jul 2003
15. Mr. Keisuke Nishigaki	Miyazaki University School of Medicine	Japan	25 – 27 Aug.2003
16. Mr. Tomotaka Saitoh	Miyazaki University School of Medicine	Japan	25 – 27 Aug.2003
17. Ms. Nina Maehr	University of Innsbruck	Austria	1 – 26 Sept.2003
18. Ms.Kristin Kleewein	University of Innsbruck	Austria	1 – 26 Sept.2003
19. Ms.Julia Huemer	University of Vienna	Austria	1 – 26 Sept.2003
20. Mr.Emanuel Zitt	University of Innsbruck	Austria	1 – 26 Sept.2003
21. Ms.Aya Takai	Oita Medical University	Japan	24 Oct. – 20 Nov. 2003
22. Ms.Aya Yoshimatsu	Oita Medical University	Japan	24 Oct. – 20 Nov. 2003
23. Mr.Jason Biswas	Royal Free and University College University College London Medical School	UK	24 Oct. – 20 Nov. 2003

ONGOING RESEARCH PROJECTS of the Faculty of Tropical Medicine in 2003-2004

No.	Ongoing Research Projects	Grant	Principal Investigator
Department of Clinical Tropical Medicine			
1	Research and development for Thai people living at Thai-Myanmar border to free from tropical diseases	Mahidol University	Prof. Sornchai Looareesuwan
2	Research and development on drugs and diagnostic tools for diagnosis and treatment of tropical diseases in Thailand	Mahidol University	Prof. Sornchai Looareesuwan
3	Adverse effect of rifampicin on quinine efficacy in falciparum malaria	Wellcome Trust of Great Britain	Prof. Sasithon Pukrittayakamee
4	Asexual and sexual stage antimalarial activities of artesunate and primaquine in falciparum malaria	Wellcome Trust of Great Britain	Prof. Sasithon Pukrittayakamee
5	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
6	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
7	Safety and therapeutic effects of Jin Huang Chinese Medicine in uncomplicated HIV-1 patients	Huatai Pharmacy, Co., Ltd.	Assoc. Prof. Punnee Pitisuttithum
8	Observational probe study of <i>in vitro</i> immune response parameters to candidate HIV-1 vaccine antigens among subject from Thailand	MERCK and Co., Inc	Assoc. Prof. Punnee Pitisuttithum
9	Efficacy and tolerability of ivermectin on gnathostomiasis	Thailand - Tropical Diseases Research Programme (T-2)	Dr. Valai Bussaratid
10	Neurotoxicity of artemether in animal model following intermittent intramuscular injections	Wellcome Trust of Great Britain and SEAMEO-TROPED	Dr. Apichart Nontprasert
11	Effect of drug accumulation in the neurotoxicity of artemether, dosing regimens with variable drug-free intervals in a mouse model	Wellcome Research Unit	Dr. Apichart Nontprasert
12	Development of field methods and investigators of the molecular basis of Sulfonamide resistance in <i>Plasmodium vivax</i>	Wellcome Trust of Great Britain	Dr. Mallika Imwong
13	Novel point mutations in the dihydrofolate reductase gene of <i>Plasmodium vivax</i> : evidence for sequential selection by drug pressure	Wellcome Trust of Great Britain	Dr. Mallika Imwong
14	Liver megaproject phase I: from basic research to education science and applied technology in clinical study	NSTDA	Dr. Wichai Ekataksin
Department of Helminthology			
15	Research and development of the integrated project on chemotherapy and control of malaria and parasitic infections	Government Budget	Assoc. Prof. Jitra Waikagul
16	Research and development of an application to purify <i>Bithynia</i> snail antigen in serodiagnosis of opisthorchiasis	Government Budget	Assoc. Prof. Jitra Waikagul
17	Seasonal variation in the intensity of Gnathostoma larvae in eels in Nakhon Nayok Province	Mahidol University	Assoc. Prof. Wichit Rojekittikhun
18	Epidemiology of strongyloidiasis and treatment with ivermectin	Government Budget	Assoc. Prof. Pongnant Nontasut
19	Experimental infection of freshwater fish in Thailand with the infective stage of <i>Angiostrongylus cantonensis</i>	Mahidol University	Assist. Prof. Chalit Komalamisra
20	Comparison of biochemical extract preparations of <i>Cysticercus cellulosae</i> by SDS - polyacrylamide gel electrophoresis and immunoblot technique	Mahidol University	Assist. Prof. Paron Dekumyoy
21	Studies on the efficacy of Thai traditional herbal medicines in the treatment of opisthorchiasis in hamsters	Mahidol University	Assist. Prof. Panyawut Hiranyachattada

No.	Ongoing Research Projects	Grant	Principal Investigator
Department of Helminthology (Continued)			
22	<i>Toxocara canis</i> larval antigens for serodiagnosis of human toxocariasis	Mahidol University	Assoc. Prof. Wanna Maipanich
23	Comparative studies on surface ultrastructure of adult worm of <i>Paragonimus</i> sp. in Thailand	Mahidol University	Assist. Prof. Sanan Yaemput
24	Monoclonal antibody-based competitive ELISA and indirect ELISA for immunodiagnosis of trichinosis	Mahidol University	Mrs. Supaporn Nuamtanong
25	<i>Angiostrongylus cantonensis</i> : S-Adenosylmethionine decarboxylase	Government Budget	Mrs. Supaporn Nuamtanong
Department of Medical Entomology			
26	Study on fauna of medically important vectors at Kanchanaburi Campus Sai Yok District, Kanchanaburi Province	Mahidol University	Assoc. Prof. Somjai Leemingsawat
27	DNA bank of mosquito vectors of Thailand	Government Budget	Assoc. Prof. Chamnarn Apiwathnasorn
28	Specificity of the synthetic primers from sequencing DNA fragments of <i>Anopheles minimus</i>	Faculty of Tropical Medicine	Assist. Prof. Narumon Komalamisra
29	Mosquito repellent from medicinal plants	Mahidol University	Assist. Prof. Narumon Komalamisra
30	Development of mosquito repellent formulation of mixture of volatile oils from <i>Artemisia annua</i> and <i>Citrus lystrix</i> DC.	Tropical Disease Trust	Mrs. Keawmala Palakul
31	Effect of heavy metals (Pb ²⁺ , Cd ²⁺) on enzymes of <i>Culex quinquefasciatus</i> larvae	Mahidol University	Mrs. Raweevan Srisawat
Department of Microbiology and Immunology			
32	Analysis of sequence polymorphism of T-cell epitope regions, Th2R and Th3R on <i>Plasmodium falciparum</i> circumsporozoite proteins in Thai isolates	Royal Golden Jubilee, TRF	Prof. Srisin Khusmith
33	Genetic diversity of the CS protein as an epidemiological marker for the efficacy of pre-erythrocytic stage immunity	IRD (French Ministry of Research) and TRF	Prof. Srisin Khusmith
34	Cytokine gene polymorphism in severe malaria	Royal Golden Jubilee, TRF	Prof. Srisin Khusmith
35	Relationship between cytokine gene polymorphism and severity of falciparum malaria	TRF	Prof. Srisin Khusmith
36	Typing of <i>Entamoeba histolytica</i> isolates obtained from Southeast Asian countries	Japanese Health Sciences Foundation (JHSF)	Assoc. Prof. Nitaya Thammalard
37	Study of the active site between the three-dimensional structure of R-PE-Mab complex	Royal Golden Jubilee, TRF	Assoc. Prof. Nitaya Thammalard
38	Detection of dengue virus in mosquitoes (<i>Aedes</i> sp) by Nucleic Acid Based-Amplification (NASBA) and Polymerase Chain Reaction (PCR)	Mahidol University	Assoc. Prof. Wipawee Usawattanakul
39	Serotype of dengue and dengue-like illness in 3 hospitals along the Thai borderline	Mahidol University	Assoc. Prof. Wipawee Usawattanakul
40	Production of monoclonal antibodies for use in the diagnosis of scrub typhus	Faculty of Tropical Medicine	Assist. Prof. Varee Wongchotigul
41	Detection of <i>Leptospira</i> spp. in urine by Polymerase Chain Reaction (PCR)	Thailand-Tropical Diseases Research Programmes & Thailand Postdoctorate Research Fund	Assist. Prof. Thareerat Kalambaheti
42	Development of strategies for serovar identification of <i>Leptospira</i> sp. based on specific gene sequences within rfb locus	Thailand-Tropical Diseases Research Programmes	Assist. Prof. Thareerat Kalambaheti
43	Detection of enterotoxin gene and its product in salmonellae isolated from food and clinical samples	--	Assist. Prof. Yuvadee Mahakunkijcharoen
Department of Protozoology			
44	Ultrastructure effects on <i>Toxoplasma gondii</i> tachyzoites after pyrimethamine and artemisinin derivative administration in animal model	Royal Golden Jubilee, TRF	Assoc. Prof. Yaowalark Sukthana
45	Dog and cat parasitic zoonoses	Tropical Disease Trust	Assoc. Prof. Yaowalark Sukthana
46	Comparison of indirect immunofluorescent and the Sabin-Feldman dye test for detection of <i>Toxoplasma gondii</i> antibody	Faculty of Tropical Medicine, MU	Assoc. Prof. Yaowalark Sukthana
47	Isolation and characterization of DNA topoisomerase I from <i>Trichomonas vaginalis</i>	Mahidol University	Assoc. Prof. Pornthip Petmitr

No.	Ongoing Research Projects	Grant	Principal Investigator
Department of Protozoology (Continued)			
48	Purification and characterization of DNA polymerase B of <i>Plasmodium falciparum</i> and its role in base excision repair	Thailand-Tropical Diseases Research Programmes	Assoc. Prof. Pornthip Petmitr
49	Comparison of <i>Toxoplasma gondii</i> antibody detection between in-house latex agglutination and commercial test	Thanad-Molee Choman Foundation	Assist. Prof. Varaporn Suphadtanapongs
50	Detection of malaria parasites in after-drug treatment patients by using QBC method	Government Budget	Assist. Prof. Varaporn Suphadtanapongs
51	Established Thai medicinal plants for treatment of coccidiosis in pig poultry and cow	Ministry of University Affairs	Assist. Prof. Chutatip Siripanth
52	Established double antibody ELISA method for detection of pathogenic protozoal antigens in the feces	National Science and Technology Development Agency	Assist. Prof. Chutatip Siripanth
Department of Social and Environmental Medicine			
53	A phase III trial of Aventis Pasteur live recombinant ALVAC-HIV (vCP 1521) priming with VaxGen gp120 B/E (AIDSVAX® B/E) Boosting in HIV-uninfected Thai-Adults	The Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc.	Dr. Supachai Reukngam (Prof. Dwip Kitayaporn)
54	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)
55	Integrated studies of human and animal leptospirosis in endemic areas of Nakhon Ratchasima, Thailand	Government Budget	Assoc. Prof. Wijitr Fungladda
56	Collaborative study to evaluate operational programme of insecticide treated bednets for malaria control in Thailand	WHO	Assoc. Prof. Piyarat Butraporn
57	Factors associating with completion and default among DOTS and self-administered therapy (SAT) for treatment of TB	WHO	Assoc. Prof. Kamolnetr Okanurak
58	Rapid detection of rifampicin-resistant <i>M. tuberculosis</i> from indoor air	Thailand-Tropical Diseases Research Programmes	Assist. Prof. Pongrama Ramasoota
59	Development of serovar specific diagnostic test using phage antibody technique	The Thailand Research Fund	Assist. Prof. Pongrama Ramasoota
60	Early detection of quinolone-resistant <i>M. tuberculosis</i> from Thailand	Thailand-Tropical Diseases Research Programmes	Assist. Prof. Pongrama Ramasoota
61	Epitope mapping of monoclonal specific to <i>Burkholderia pseudomallei</i> using phage display technique	The Thailand Research Fund	Assist. Prof. Pongrama Ramasoota
Department of Tropical Hygiene			
62	Application of GIS in monitoring multi-drug resistant malaria in greater Mekong Subregion of Southeast Asia (II)	SEAMEO Trop. Med. and EC-Malaria	Assoc. Prof. Pratap Singhasivanon
63	Epidemiology and drug sensitivity of Enterobacteriaceae in a rural community near Thai-Myanmar border in Suan Phung, Ratchaburi Province, 2000-2002	Department of Tropical Hygiene	Assist. Prof. Kasinee Buchachart
64	A survey of metacercariae in fresh-water fishes in small reservoirs in Suanphung, Ratchaburi Province	-	Mr. Nipon Thanyavanich
65	Study on the ecology of anopheline larvae in malaria endemic area	Department of Tropical Hygiene	Mr. Supalarp Puangsa-art
Department of Tropical Nutrition and Food Science			
66	Food and health relationship in Asian population	Palm Oil Research Institute of Malaysia	Assoc. Prof. Supraneer Changbumrung
67	Development of food and medicinal plants	Government Budget	Assoc. Prof. Supraneer Changbumrung
68	Medicinal plants for treatment of hookworm	Government Budget	Assoc. Prof. Supraneer Changbumrung
69	Medicinal plants against malaria	Government Budget	Assoc. Prof. Supraneer Changbumrung
70	Identification of gene alterations in breast cancer	BIOTEC	Assoc. Prof. Songsak Petmitr
71	Determination of gene mutation in hMSH2 and hMSH6 in colon cancer	Government Budget	Assoc. Prof. Songsak Petmitr
72	Detection of serum alpha-2-macroglobulin and gene mutation in Thai obese subjects	Mahidol University	Assoc. Prof. Rungsun Tungtrongchitr
73	Detection of methylene tetrahydrofolate reductase (MTHFR 677T) polymorphism effect to hyperhomocysteinemia in Thai obese subjects: cardiovascular risk factors	Government Budget	Assoc. Prof. Rungsun Tungtrongchitr
74	Nutritional status and intervention in people living in Amphur Chalermprakiet, Nan Province	UNICEF	Assoc. Prof. Kanjana Hongtong

No.	Ongoing Research Projects	Grant	Principal Investigator
Department of Tropical Pathology			
75	Pathology and immunohistochemistry of liver in AIDS: a necropsy study	Mahidol University	Assoc. Prof. Parnpen Viriyavejakul
76	Causes of diarrhea in HIV/AIDS patients	Mahidol University	Assoc. Prof. Parnpen Viriyavejakul
77	Hematopoietic features of the bone marrow of <i>Plasmodium falciparum</i> -infected patients	Mahidol University	Assoc. Prof. Yaowapa Maneerat
78	The effects of <i>Plasmodium falciparum</i> - induced cellular responses on activation of endothelial cells	Mahidol University	Assoc. Prof. Yaowapa Maneerat
79	Role of nitric oxide in vascular pathologic changes in atherosclerosis: <i>in vitro</i> study	The Thailand Research Fund	Assoc. Prof. Yaowapa Maneerat
Department of Tropical Pediatrics			
80	A phase II, pilot, randomized, open-label, single-center study to evaluate immunogenicity and safety after PCECV rabies vaccine (Rabipur®) administered concomitantly with Japanese encephalitis vaccine as a pre-exposure regimen in 12 to 18 month old toddlers in Thailand	Chiron Vaccines, Co., Ltd., Italy	Prof. Arunee Sabchareon
81	Safety and immunogenicity of tetravalent dengue vaccine formulations in Thai adult volunteers: evaluation of three-year persistence	Aventis Pasteur (France)	Assoc. Prof. Pornthep Chanthavanich
82	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
83	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
84	Health problems, knowledge, attitudes and practices of children in Saiyok District, Kanchanaburi Province	Mahidol University	Assoc. Prof. Pornthep Chanthavanich
85	Early immune response to multi-site intramuscular injection of purified Vero cell rabies vaccine (PVRN) for rabies post-exposure treatment (RAB 24)	Aventis Pasteur (Thailand)	Assoc. Prof. Pornthep Chanthavanich
86	Dengue antibodies in Thai infants: age-specific seroprevalence and kinetics of transplacentally transferred dengue antibodies (EPI 11)	Aventis Pasteur (France)	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	Assoc. Prof. Chukiat Sirivichayakul
88	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
89	Prevalence and risk factors of atopic diseases in rural children in Saiyok District, Kanchanaburi Province	Mahidol University	Dr. Wimol Nganthavee
Vaccine Trial Centre			
90	Development of new vaccines against cholera due to <i>Vibrio cholerae</i> 0139 (Part III)	WHO	Assoc. Prof. Punnee Pitisuttithum
91	A phase I/II trial to evaluate the safety and immunogenicity of AIDS-VAX™ B/E vaccine in Bangkok, Thailand	VAXGEN Co, Ltd.	Assoc. Prof. Punnee Pitisuttithum
92	Phase I/II trial of Pasteur Merieux Connaught (PMC) live recombinant ALVAC-HIV (VCP 1521) Priming with Vaxgen gp 120 B/E (AIDVAX™ B/E) Boost in Thai HIV-seronegative adults	Walter Reed Army Institute of Research, USA	Assoc. Prof. Punnee Pitisuttithum
93	A phase III trial to determine the efficacy of AIDS-VAX™ B/E Vaccine in intravenous drug users in Bangkok, Thailand	AIDSVAX	Bangkok AIDS Vaccine Evaluation Group (Assoc. Prof. Punnee Pitisuttithum)
94	A phase III trial of Aventis Pasteur live recombinant ALVAC-HIV (VCP1521) priming with Vaxgen gp 120 B/E (AIDSVAX B/E) boosting in HIV-uninfected Thai adults	Walter Reed Army Institute of Research,	Dr. Supachai Ruekngam (Assoc. Prof. Punnee Pitisuttithum) USA

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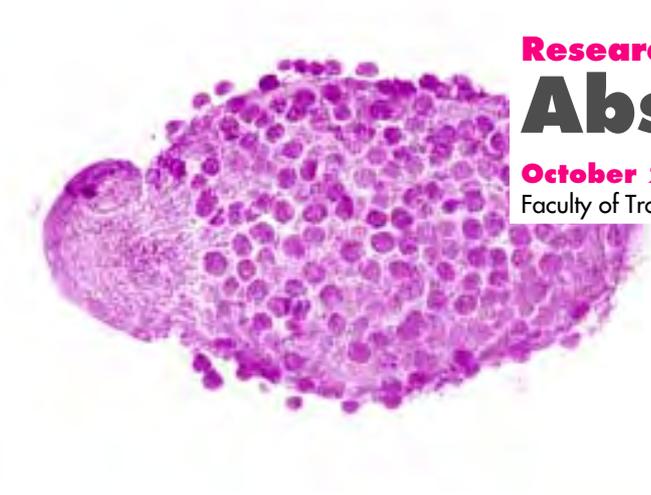
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NOVEL POINT MUTATIONS IN THE DIHYDROFOLATE REDUCTASE GENE OF *PLASMODIUM VIVAX*: EVIDENCE FOR SEQUENTIAL SELECTION BY DRUG PRESSURE

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Mutations in the dihydrofolate reductase (*dhfr*) genes of *Plasmodium falciparum* and *P. vivax* are associated with resistance to the antifolate antimalarial drugs. *P. vivax dhfr* sequences were obtained from 55 *P. vivax* isolates (isolates Belem and Sal 1, which are established lines originating from Latin America, and isolates from patient samples from Thailand [$n=44$], India [$n=5$], Iran [$n=2$], and Madagascar [$n=2$]) by direct sequencing of both strands of the purified PCR product and were compared to the *P. vivax dhfr* sequence from a *P. vivax* parasite isolated in Pakistan (isolate ARI/Pakistan), considered to represent the wild-type sequence. In total, 144

P. vivax dhfr mutations were found at only 12 positions, of which 4 have not been described previously. An F→L mutation at residue 57 had been observed previously, but a novel codon (TTA) resulted in a mutation in seven of the nine mutated variant sequences. A new mutation at residue 117 resulted in S→T (S→N has been described previously). These two variants are the same as those observed in the *P. falciparum dhfr* gene at residue 108, where they are associated with different levels of antifolate resistance. Two novel mutations, I3L at residue 13 and T→M at residue 61, appear to be unique to *P. vivax*. The clinical, epidemiological, and sequence data suggest a sequential pathway for the acquisition of the *P. vivax dhfr* mutations. Mutations at residues 117 and 58 arise first when drug pressure is applied. Highly mutated genes carry the S→T rather than the S→N mutation at residue 117. Mutations at residues 57 and 61 then occur, followed by a fifth mutation at residue 13. ■

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

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The Understanding of volunteers in vaccine trials about their role as study participants and their voluntary commitment during the study are always one of the important concerns apart from evaluation of safety and efficacy of vaccine trials, especially in HIV prophylactic vaccine trials. The apprehension of indirectly risky behavior encouragement and deviated expectations among volunteers should be of concern. The current prospective cohort study aimed to assess and monitor

the changes of risk behaviors, attitude and expectations among 164 volunteers from 2 studies of different prophylactic HIV vaccines, the Chiron HIV Thai E gp 120/MF59 ± the Chiron HIV SF52 gp 120 and Aventis Pasteur Live Recombinant ALVAC HIV (vCP1521) priming with VaxGen gp 120B/E (AIDSVAN™ B/E) boosting. 113 males and 51 females with a mean age (± SD) of 28.82 ± 7.97 years old were enrolled from October 1997 to December 1998 and February 2000 to April 2001. Education and risk reduction counseling were regularly performed at every visit and questionnaires about risk behaviors, knowledge, attitudes, social influences and expectations were asked at baseline, 4 months and 12 months.

No change of potentially HIV transmission related risk behavior was observed during the studies. There was a statistically significant decrease of risk sexual practices from the beginning of the trials (42.2% *vs* 1%, $p < 0.0001$). While 35.2 per cent from 62.2 per cent of the volunteers at the beginning of the study continued sexual practice with an identified single sexual

partner at the end of the study ($p < 0.0001$). All of the volunteers expressed the beneficial expectations as knowledge gain, social contribution, feelings of having gained merit and self-benefits from health check-ups. ■

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RECOMBINANT PfEMP1 PEPTIDE INHIBITS AND REVERSES CYTOADHERENCE OF CLINICAL PLASMODIUM FALCIPARUM ISOLATES IN VIVO

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▶ **The** parasite ligand *Plasmodium falciparum* erythrocyte membrane protein 1 (PfEMP1) and host endothelial receptors represent potential targets for antiadhesive therapy for cytoadherence. In the present study, the major host receptor CD36 was targeted *in vitro* and *in vivo* with a recombinant peptide, PpMC-179, corresponding to the minimal CD36-binding domain from the cysteine-rich interdomain region 1 (CIDR1) within the *MCvar1* PfEMP1. The *in vitro* inhibitory effect of PpMC-179 on human dermal microvascular endothelial cells (HDMECs) expressing multiple relevant adhesion molecules was investigated using a parallel-plate flow chamber. Pretreatment of endothelial monolayers with PpMC-179 (2 μM) inhibited the adhesion of infected erythrocytes

(IRBCs) from all clinical isolates tested by 84.4% on resting and 62.8% on tumor necrosis factor alpha (TNF-alpha)-stimulated monolayers. Adhesion to stimulated cells was further inhibited (90.4%) when PpMC-179 was administered with an inhibitory anti-intercellular adhesion molecule 1 (ICAM-1) monoclonal antibody 84H10 (5 $\mu\text{g}/\text{mL}$). To determine the *in vivo* effectiveness of PpMC-179, we used a human/severe combined immunodeficiency (SCID) mouse chimeric model that allowed direct visualization of cytoadherence on intact human microvasculature. In unstimulated skin grafts, PpMC-179 inhibited adhesion by 86.3% and by 84.6% in TNF-alpha-stimulated skin grafts. More importantly, PpMC-179 administration resulted in the detachment of already adherent IRBCs by 80.7% and 83.3% on resting and stimulated skin grafts, respectively. The antiadhesive effect of PpMC-179 was rapid and sustained *in vivo* for at least 30 minutes. Our data indicate that targeting cytoadhesion *in vivo* is feasible and may offer a rapid antimalarial therapy. ■

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GENETIC VARIANTS OF β -GLOBIN GENE IN THAI MALARIA PATIENTS

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▶ **Thalassemias** and hemoglobinopathies, caused by genetic variants of α - and β - globins, are commonly observed in parts of malaria endemic areas of Southeast Asia such as Cambodia, Thailand, and Myanmar, regardless of the

hematologic disadvantage. The plausible explanation for this is that heterozygotes of the causative variants have the advantage of protection from malarial infection of suggested by J.B.S. Haldane (e.g., Weatherall 1987). The overall prevalence of hemoglobinopathies has been reported to be 39% in Phitsanulok, a province in the southern part of northern Thailand, and the prevalence of hemoglobin E (Hb E; E26K variant of β -globin gene) in this province is 25% (Pravatmuang *et al*, 1995). If such a variant can be maintained by natural

selection due to the protection from malarial infection, there may be other variants causing thalassemias or hemoglobinopathies in malaria endemic areas of Thailand. In order to detect further variants, we performed variation

screening for exon 1 of b-globin gene in adult patients with malaria in northwest Thailand. ■

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INVOLVEMENT OF INTERLEUKIN-18 IN SEVERE *PLASMODIUM FALCIPARUM* MALARIA

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▶ **Serum** levels of IL-18, IFN- γ , and IgE were determined for 96 patients with falciparum malaria. They were divided into three groups, i.e., uncomplicated, severe, and cerebral malaria (CM) according to WHO criteria (2000). Elevation of IL-18 levels was observed in all of the groups, with a tendency of higher levels in cases with severe malaria throughout the course of the disease. Moreover, there was a significant correlation between IL-18 levels and the extent of

parasitemia among patients with severe malaria. However, IL-18 levels decreased more significantly in patients with CM compared to the other groups in the late stage of the disease. Elevated levels of IFN- γ were also observed in all groups of patients, especially in those with severe malaria or CM, and the levels in patients with CM remained significantly higher than in those with uncomplicated malaria during the time of day 4 to 7 post treatment, suggesting the involvement of IFN- γ in disease severity. Meanwhile, no significant difference was observed in IgE levels between severe and uncomplicated groups, although IgE levels were significantly higher in helminth-infected patients than uninfected patients. These results suggest that IL-18 plays a key role in inducing severe malaria through another pathway, such as elevation of IFN- γ , rather than its IgE inducing activity. ■

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

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

also contribute to hepatomegaly.

Nitric oxide (NO) is a key mediator of anti malarial immunity (Anstey *et al.*, 1996) but also has antiproliferative properties (Taylor-Robinson and Smith, 1999). Its generation requires the induction of the inducible NO synthase (iNOS), which can be achieved by a variety of immune mediators (Bogdan, 2001). Among these, the Fc ϵ R_{II}/CD23 receptor, upon ligation, can generate large quantities of NO (Dugas *et al.*, 1995). In the absence of ligands, CD23 is normally physiologically cleaved into soluble CD23 (sCD23) (Delespesse *et al.*, 1991), which has pleiotropic properties and is measurable in the plasma. On the contrary, upon ligation, the membrane CD23 receptor is

stabilized, and cleavage is reduced (Pritchard *et al.*, 1993). Recently, it was shown that helminth-infections were associated with protection from cerebral malaria. Adjustments for socioeconomic, nutritional factors and malaria history did not alter this association (Nacher *et al.*, 2001a). It was suggested that the CD23/NO pathway had a protective role against cytoadherence and severe complications of malaria (Nacher *et al.*, 2000; 2002). It was shown in Thailand that helminth-infected

patients had a lower incidence of renal failure and jaundice during malaria (Nacher *et al.*, 2001b), and that helminth-infected had higher reactive nitrogen intermediates concentrations (RNI), which correlated with IgE and sCD23 (Nacher *et al.*, 2002). Here, the objective was to look for a possible influence of helminthes and the CD23/NO pathway on liver size. ■

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

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▶ **In vitro** drug sensitivity tests were performed with mefloquine using blood samples collected from falciparum malaria patients followed the standard methodology for the assessment of the inhibition of schizont maturation. A total of

37 successful fresh isolates demonstrated mean IC₅₀, IC₉₀ and IC₉₉ (with 95% confidence intervals) of 0.036 (0.031-0.041), 0.118 (0.099-0.147) and 0.305 (0.230-0.449) μ M, respectively, indicating that all of them were sensitive to mefloquine. This result supports the current first line drug policy, by which the Ministry of Public Health, Thailand recommended mefloquine monotherapy in the southwestern area of Thailand. ■

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RECRUDESCENCE IN ARTESUNATE-TREATED PATIENTS WITH FALCIPARUM MALARIA IS DEPENDENT ON PARASITE BURDEN NOT ON PARASITE FACTORS

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▶ **Artemisinin** derivatives are first-line antimalarial drugs in Thailand. No firm evidence of clinically relevant artemisinin resistance exists. When used as monotherapy, artesunate has been associated with a high treatment failure (recrudescence) rate, which could be due to low-level artemisinin resistance. To understand the causes of recrudescence, we retrospectively

studied a cohort of 104 malaria patients treated with artesunate monotherapy, 32 of whom recrudesced. There was no difference in *in vitro* artesunate sensitivities between 6 nonrecrudescing isolates and 16 paired admission and recrudescing isolates. Paired admission and recrudescing isolates from 10 patients were genotyped; only 3 had *pfmdr1* mutations. Patients with admission parasitemias >10,000/ml had a 9-fold higher likelihood of recrudescence (adjusted odds ratio) compared with patients with lower parasitemias. This study suggests (1) recrudescence after treatment with artesunate is not the result of inherent parasite resistance, and (2) admission parasitemia may be useful in choosing therapeutic options. ■

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SRC-FAMILY KINASE SIGNALING MODULATES THE ADHESION OF *PLASMODIUM FALCIPARUM* ON HUMAN MICROVASCULAR ENDOTHELIUM UNDER FLOW

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► The pathogenicity of *Plasmodium falciparum* is due to the unique ability of infected erythrocytes (IRBCs) to adhere to vascular endothelium. We investigated whether adhesion of IRBCs to CD36, the major cytoadherence receptor on human dermal microvascular endothelial cells (HDMECs), induces intracellular signaling and regulates adhesion. A recombinant peptide corresponding to the minimal CD36-binding domain from *P. falciparum* erythrocyte membrane protein 1 (PfEMP1), as well as an anti-CD36 monoclonal antibody (mAb) that inhibits IRBC binding, activated the mitogen-activated protein (MAP) kinase pathway that was dependent on Src-family kinase activity. Treatment of HDMECs with a Src-family kinase-selective inhibitor (PP1) inhibited adhesion of IRBCs in a flow-chamber

assay by 72% ($P < .001$). More importantly, Src-family kinase activity was also required for cytoadherence to intact human microvessels in a human/severe combined immunodeficient (SCID) mouse model in vivo. The effect of PP1 could be mimicked by levamisole, a specific alkaline-phosphatase inhibitor. Firm adhesion to PP1-treated endothelium was restored by exogenous alkaline phosphatase. In contrast, inhibition of the extracellular signal-regulated kinase 1/2 (ERK 1/2) and p38 MAP kinase pathways had no immediate effect on IRBC adhesion. These results suggest a novel mechanism for the modulation of cytoadherence under flow conditions through a signaling pathway involving CD36, Src-family kinases, and an ectoalkaline phosphatase. Targeting endothelial ectoalkaline phosphatases and/or signaling molecules may constitute a novel therapeutic strategy against severe falciparum malaria. ■

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DISTRIBUTION OF TWO SPECIES OF MALARIA, *PLASMODIUM FALCIPARUM* AND *PLASMODIUM VIVAX*, ON LOMBOK ISLAND, INDONESIA

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► Medical and entomological surveys were conducted to determine the risk factors of *Plasmodium falciparum* and *P. vivax* infections on Lombok Island, Indonesia, to find the risk factors and the main mosquito vectors for each malaria. Multivariate longitudinal analysis demonstrated two significant risk factors for the infection with *P. falciparum*: disappearance

of *P. vivax* parasitemia ($P < 0.001$) and a specific study site ($P < 0.001$). In contrast, younger age ($P = 0.024$) and the interpolated virtual density of *An. subpictus* ($P = 0.041$) were significantly associated with increased risk of the infection with *P. vivax*. Thus it seems that the distribution of *P. vivax* was determined largely by the presence of *An. subpictus*, whilst that of *P. falciparum* was influenced by antagonism with *P. vivax*. This result shows the importance of the follow up of treated *P. vivax* patients to identify recrudescence of *P. falciparum* in this area. ■

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ADVERSE EFFECT OF RIFAMPIN ON QUININE EFFICACY IN UNCOMPLICATED FALCIPARUM MALARIA

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The effects of adding rifampin to quinine were assessed in adults with uncomplicated falciparum malaria. Patients were randomized to receive oral quinine either alone (n = 30) or in combination with rifampin (n = 29). Although parasite clearance times were shorter in the quinine-rifampin-treated patients (mean +/- standard deviation, 70 +/- 21 versus 82 +/- 18 h; P = 0.023), recrudescence rates were five times higher (n = 15 of 23; 65%) than those obtained with quinine alone (n

= 3 of 25; 12%), P < 0.001. Patients receiving rifampin had significantly greater conversion of quinine to 3-hydroxyquinine and consequently considerably lower concentrations of quinine in their plasma after the second day of treatment (median area under the plasma drug concentration-time curve from day zero to day 7 = 11.7 versus 47.5 micro g/ml. day, P < 0.001). Rifampin significantly increases the metabolic clearance of quinine and thereby reduces cure rates. Rifampin should not be combined with quinine for the treatment of malaria, and the doses of quinine should probably be increased in patients who are already receiving rifampin treatment. ■

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A POTENTIAL ROLE OF INTERLEUKIN 18 IN SEVERE FALCIPARUM MALARIA

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IL-18 is a potent proinflammatory cytokine that induces IFN-g production from Th1 cells, NK cells and activated macrophages, particularly in the presence of IL-12. However, it is also shown that without help from IL-12, IL-

18 is capable of inducing IL-4 and IL-13 production in T cells, NK cells, mast cells and basophils, and that administration of IL-18 in conjunction with an allergen increased serum IgE levels. In order to clarify the role of IL-18 in disease severity of falciparum malaria, we have examined serum levels of IL-18, IFN-g, and IgE for 96 patients with falciparum malaria (Nagamine et al., in press). Results suggested that IL-18 plays a key role in inducing severe malaria through a pathway of elevating IFN-g rather than its IgE inducing activity. Based on these results, the role of IL-18 in severe falciparum will be discussed in this review. ■

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HEPATOCELLULAR INJURY IN TROPICAL INFECTIOUS DISEASES COMMONLY FOUND IN THAILAND

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▶ **Common** tropical infectious diseases in Thailand and Southeast Asian countries include dengue fever, leptospirosis, malaria, scrub typhus and typhoid fever, usually presenting with acute febrile illness and various levels of clinical severity. Most of them are similar in clinical presentation, especially in the first week of onset, and have multiorgan involvement,

including renal insufficiency, respiratory failure and hepatocellular injury. Definite diagnosis of these diseases is based on clinical background and basic laboratory findings. However, the pattern of liver function tests correlated with clinical changes occurring each day may be another investigation used for making a diagnosis. We reviewed here the incidence, severity and time-course of hepatocellular injury in each tropical infectious disease which can be applied for clinical use for diagnosis and management. ■

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STRONGYLOIDIASIS: AN UPDATE

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▶ *Strongyloides stercoralis* is a common intestinal nematode, presenting gastrointestinal, cutaneous and pulmonary symptoms in accord with its life cycle. The diagnostic yield for *Strongyloides* detection from stool examination, stool culture and duodenal fluid are increasing

with the number of tests. Early diagnosis and prompt treatment can reduce the mortality rate and complications. In this era of increasing populations of immunocompromised persons, easier international travel and the shortage of available effective antiparasites, preventive methods, such as good personal hygiene and sanitation, are advised for the population at risk. ■

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ANTIMALARIAL DRUG RESEARCH AND DEVELOPMENT

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▶ **Malaria** remains one of important infectious diseases in the world. Many malaria control strategies exist, but none are appropriate and affordable in all contexts. Antimalarial drug resistance has emerged as one of the great challenges facing malaria control today. Drug resistance has been implicated in the spread of malaria where the disease had been eradicated. Drug resistance has also played significant role in the occurrence and severity of epidemics in some parts of the

world. The present approaches to new antimalarials include optimizing therapy with existing agents, evaluating compounds that are chemically related to existing agents, identifying the natural product and their relative compound for treatment, identifying agents that are developed or marketed as treatments for other diseases, identifying new targets, and subsequent discovery of compounds that act on these targets. Therefore, the continued control of malaria will likely require multiple new effective agents. ■

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ANTI-ADHESIVE EFFECT OF NITRIC OXIDE ON *PLASMODIUM FALCIPARUM* CYTOADHERENCE UNDER FLOW

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▶ **Nitric oxide** (NO) is widely known to inhibit platelet and leukocyte adhesion to endothelium through its regulatory effect on adhesion molecule expression. The objective of the present study was to investigate if NO affects the cytoadherence of *Plasmodium falciparum*-infected erythrocytes (IRBCs) to human microvascular endothelium (HDMECs) under flow conditions *in vitro*. The effect of endogenous NO was studied using the NO synthase inhibitor L-N(G)-nitro-arginine-methyl-ester (L-NAME). Treatment of HDMECs with 3 mmol/L of L-NAME for 4 hours significantly enhanced IRBC adhesion and the effect could be reversed by an anti-P-selectin but not an

anti-VCAM-1 antibody. The effect of exogenous NO on cytoadherence was studied by using the NO donor 3-(2-hydroxy-2-nitroso-1-propylhydrazino)-1-propanamine (PPN). PPN (300 micro mol/L) treatment reduced the number of adherent IRBCs on resting HDMECs by down-regulating basal ICAM-1 expression, and on tumor necrosis factor-alpha-stimulated HDMECs by inhibition of VCAM-1 induction and down-regulation of ICAM-1 expression. The inhibitory effect of PPN on tumor necrosis factor-alpha-induced VCAM-1 expression at 24 hours was evident when the NO donor was added for as short as 2 hours. These findings suggest that NO may be protective against *P. falciparum* infection by inhibiting cytoadherence, and underscore the therapeutic potential of NO in the treatment of severe falciparum malaria. ■

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THERAPEUTIC RESPONSES TO ANTIMALARIAL AND ANTIBACTERIAL DRUGS IN VIVAX MALARIA

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▶ **Plasmodium vivax** is the most prevalent malaria infection and is an important cause of morbidity in Central and South America and Asia. *P. vivax* is generally sensitive to the common antimalarial drugs but high level resistance to chloroquine and/or pyrimethamine has been documented in some geographic locations. In the studies reviewed here, the therapeutic responses to antimalarial and antibacterial drugs in vivax malaria has been assessed in the Bangkok Hospital for Tropical Diseases. The evaluated drugs consisted of the eight most widely used anti-malarial drugs and anti-bacterial drugs that possess antimalarial activities (tetracycline, doxycycline, clindamycin or azithromycin). The activities of these drugs in descending order of parasite clearance times were artesunate, artemether, chloroquine, mefloquine, quinine, halofantrine, primaquine, followed by the antibacterial drugs and lastly sulfadoxine-pyrimethamine. Clinical responses to sulfadoxine-pyrimethamine were also poor with evidence

of high grade resistance in 42% of the patients. Of the 4 antibacterial drugs, clindamycin was more effective than azithromycin and can be an alternative to the tetracyclines. Except for chloroquine and mefloquine which have long plasma half lives, the cumulative cure rates for the short acting antimalarial drugs were similar. Double infection with *P. falciparum* was common and usually manifested 3-4 weeks following clearance of vivax malaria. The prevalence of cryptic falciparum malaria was 8%-15% and was higher in patients treated with less potent antimalarial drugs. Follow-up studies have revealed that the time to relapse in Thai patient with vivax malaria is on average only 3 weeks, but can be suppressed by the slowly eliminated antimalarial drugs such as chloroquine and mefloquine. For accurate comparison of relapse/recrudescence rates in vivax malaria at least two month's follow-up is required. It can be concluded that in malarious areas of Thailand, double infection with *P. falciparum* and *P. vivax* is common affecting at least 25% of the patients and usually manifests as sequential illnesses. *P. vivax* in Thailand is sensitive to chloroquine but has acquired high grade resistance to sulfadoxine-pyrimethamine. ■

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HYPOKALEMIA IN SEVERE FALCIPARUM MALARIA

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To define the incidence of hypokalemia in severe falciparum malaria, a study was conducted in 234 consecutive patients in the Bangkok Hospital for Tropical Diseases. Eighty-six patients (36.8 %) had hypokalemia on admission and 134

patients (61.5 %) were normokalemic. In the latter group serum potassium dropped with mean (SD) of 0.26 (0.50) and 0.31 (0.48) mEq/L at the 24th and 48th hour respectively. The patients with metabolic acidosis on admission had more declining in serum potassium at the 48th hour compare to non-acidotic patients. ■

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USE OF TYMPANIC THERMOMETER IN A COMPLEX EMERGENCY SETTING

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In a prospective open study carried out on the northwest border of Thailand, 4 methods of temperature measurement were compared: tympanic, oral, axillary and rectal, using either infrared tympanic thermometer (ITT) or standard mercury glass thermometer. There were 818 persons accounted for overall analysis who had recording by tympanic, axillary plus oral or rectal methods. This included 162 persons aged five and younger in additional comparison analysis of tympanic/rectal temperature recordings as well as 656 persons aged six years or elder in comparison analysis of tympanic/oral temperature recordings. To assess whether the difference between recordings by the two different methods was related to the magnitude of the measurement, graphical techniques by plotting the differences between the measurements against their mean. To quantify the

limits of agreement, estimated by mean difference \pm 2 standard deviation of the differences. Although the mean differences in all comparisons were small, ITT temperature recordings could be expected to vary by more than 2 C from the actual temperature recordings as reported by other methods. The wide limits of agreement mean that tympanic temperature is not an exemplary approximation of rectal or oral temperature. The axillary measurements were closest to the tympanic recordings. Using the diagnostic testing, there would have been 3.0% of cases if compare to oral and 6.8% of cases if compare to rectal incorrectly reported. These numbers seem to be reasonable at very high specificity from over 95%. However, the sensitivity of 88% and 83% mean more than 10% of persons with fever would be missed by screening by tympanic thermometer temperatures with the likelihood to influence treatment. Based on these results and under given conditions in this setting, ITT is frequently unreliable and should be used with caution. ■

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PLATELET-INDUCED AUTOAGGLUTINATION OF *P. FALCIPARUM* INFECTED RED CELLS AND DISEASE SEVERITY IN THAILAND

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▶ **The** relationship of platelet mediated autoagglutination of *P. falciparum* infected red cells (IRBC) to disease severity was investigated in 182 Thai patients with falciparum malaria. Autoagglutination was evident in 43% of uncomplicated malaria

(N=63), 41% of severe malaria (N=104), and 100% of cerebral malaria patient isolates (P=0.001). Autoagglutination was reversed by heparin (EC₅₀; 50 units/ml) and EGTA (EC₅₀; 0.01 mM). The median (range) number of IRBC in agglutinates per 1000 IRBC was significantly higher in cerebral malaria (6; 3-42) compared to severe (0; 0-52) and uncomplicated malaria (0; 0-24) (P=0.01). In multivariate analyses, high parasitemia and cerebral malaria were associated independently with parasite agglutination. ■

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SIX YEARS MONITORING THE EFFICACY OF THE COMBINATION OF ARTESUNATE AND MEFLOQUINE FOR THE TREATMENT OF UNCOMPLICATED FALCIPARUM MALARIA

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▶ **Plasmodium falciparum** in Thailand is multi-drug resistant. In a previous study it was shown that artesunate and mefloquine were effective, as a follow up we therefore monitored the efficacy of this regiment for six years. During 1997-2002, 516 adult male volunteer patients in Chantaburi Province were enrolled (50 patients on the first year, 400 patients in 1998-2001 and 66 patients in 2002). The symptom complex and parasite count (thick blood film) were monitored on days 0, 1, 2, 7, 14, 21, 28, 35 and 42. The dosage used were artesunate (ATS) 150 mg and mefloquine (M) 750 mg at hour 0 and ATS 100 mg and M 500 mg at hour 24. Their ages ranged from 30-35 years and their mean body weights from 54-56 kg. The presenting symptoms were fever 100%, headache 97-100%, anorexia 78-90% and nausea 28-40%. The geometric mean of parasitaemia

ranged from 7,357-12,750/cumm.

Defervescence in one day was found in 42-76% of patients and 85-100% in 2 days. The sensitivity (S) ranged from 87-94% and RI resistance (recrudescence) ranged from 6-13%. Forty patients demonstrate RI type of response, thirty-seven were cured after being retreated with the same dosage and another 3 patients were cured after the third course of treatment. The aggravated adverse effects included vomiting (8-20%), anorexia (1-41%) and diarrhea (0-16%). These side effects were mild and transient. The efficacy of artesunate and mefloquine combination for treatment of uncomplicated falciparum malaria is high. RI type of response was due possibly to re-infection or multiple broods and possibly not to drug resistance. The adverse effects of anorexia, nausea, vomiting and diarrhea were mild and transient for mefloquine. The combination can be used as stand by treatment in areas of multi-drug resistant falciparum malaria. ■

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EVALUATION OF A NEW PLDH ASSAY (OPTIMAL-IT®) FOR DETECTION OF MALARIA

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▶ The performances of OptiMAL-IT® and Paracheck-Pf® malaria rapid tests were evaluated in symptomatic patients with uncomplicated falciparum malaria. The sensitivity, specificity, positive predictive and negative predictive values of the tests were calculated taking microscopy as the “gold standard”. The sensitivity and specificity of OptiMAL-IT® for the diagnosis of *Plasmodium falciparum* parasites were 88% and 92% respectively. For *Plasmodium non-falciparum*, the

sensitivity was 65% and specificity was 99%. The sensitivity and specificity of Paracheck-Pf® for *Plasmodium falciparum* was 90% and 96% respectively. For *Plasmodium falciparum* the sensitivity of both tests decreased markedly at parasitaemia <500 parasites/mL (0.01% of infected RBC). The sensitivity of OptiMAL-IT® for non-falciparum species decreased markedly at parasitaemia <5000 parasites/mL (0.1% IRBC) and was only 10% at the parasitaemia less than 100 parasites/mL (<0.002% IRBC). The performances of both tests for *Plasmodium falciparum* detection were not significantly different ($p>0.05$). ■

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EXTENDED LINKAGE DISEQUILIBRIUM OF THE HEMOGLOBIN E VARIANT DUE TO MALARIA SELECTION

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▶ The geographical distribution of the hemoglobin E variant (HbE; b26Glu->Lys) is concentrated in parts of malaria endemic areas of Southeast Asian, and the carriers of HbE have been shown to confer some protection against *Plasmodium falciparum* malaria. We analyzed biallelic markers surrounding the HbE variant in a Thai population to examine the effect of natural selection on the pattern of linkage disequilibrium (LD) and to infer the evolutionary history of

the HbE variant. The pairwise LD analysis of 44 markers revealed that LD between HbE and markers distal to HbE extended beyond 100 kb, whereas no LD was observed between non-HbE variants and the distal markers. The inferred haplotype network suggested that HbE had a single origin. Forward-in-time computer simulations under a variety of selection models indicated that the HbE variant arose within the past 1,240 to 4,440 years. These results support the conjecture that a mutation of HbE occurred recently, and the allele frequency had increased rapidly. Our study provides another clear demonstration that a high-resolution LD map across the human genome can detect recent variants that have been subjected to positive selection. ■

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THE EFFECTS OF P. FALCIPARUM AND P. VIVAX INFECTIONS ON PLACENTAL HISTOPATHOLOGY IN AN AREA OF LOW MALARIA TRANSMISSION

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P The histopathological features of the placenta were studied in a cohort of 204 women in an area of low transmission of both *P. falciparum* and *P. vivax*. Detection of malaria antenatally was active, by weekly peripheral blood smear, and all infections were treated. Presence of significant histopathological placental malaria changes: increased malaria pigment, cytotrophoblastic prominence and presence of

parasites; were found only in a minority of women who had *P. falciparum*. These changes were significantly increased in women with infection close to delivery and only at this time were inflammatory cells increased. *P. vivax* was only associated with presence of malaria pigment in the placenta. This study indicated that treatment of peripheral parasitaemias during pregnancy limits placental changes. The effect on birthweight reduction appears not to result from the physical presence of irreversible placental changes but from the acute insult of infection. These findings emphasize the importance of treating all pregnant women with effective antimalarials. ■

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FIELD EVALUATION OF A NOVEL COLORIMETRIC METHOD-DOUBLE-SITE ENZYME LINKED PLDH IMMUNODETECTION (DELI) ASSAY TO DETERMINE DRUG SUSCEPTIBILITIES OF *PLASMODIUM FALCIPARUM* ISOLATES FROM NORTHWESTERN THAILAND

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P A double-site enzyme linked lactate dehydrogenase enzyme immunodetection (DELI) assay has recently been developed for assessing the *in vitro* drug susceptibility of isolates of *Plasmodium falciparum* which relies on the detection of *P. falciparum*-specific lactate dehydrogenase (pLDH). The DELI assay offers two major advantages over currently used methods, it is non-isotopic and it is able to assay parasites even at extremely low densities.

To evaluate the potential of the DELI microtest for the monitoring of *in vitro* drug susceptibilities of field isolates in an area of multi-drug resistant *P. falciparum* in northwestern Thailand, we looked first at various parameters that might influence the measurement of pLDH and the drug dose-pLDH response, and then compared the DELI and isotopic microtest, initially in the K1 laboratory strain and then in 86 fresh clinical isolates to 8 antimalarial drugs (chloroquine, quinine,

mefloquine, lumefantrine, artesunate, dihydro-artemisinin, atovaquone and doxycycline). The DELI assay was able to determine *in vitro* susceptibilities at parasite densities from 0.2-0.005% but at the lowest levels the assay was less reliable. A higher degree of variability in repeated EC₅₀ measurements as determined by the DELI assay was observed (coefficient of variation [%] DELI *vs* isotopic assay for chloroquine 26.8 *vs* 4.4, quinine 23.8 *vs* 7.7, mefloquine 36.5 *vs* 13.8 and atovaquone 53.5 *vs* 17.5). When comparing the two assays in field isolates there were no significant differences in the geometric mean *in vitro* responses (EC₅₀ ng/mL [DELI *vs* Isotopic]) to (quinine 229.8 *vs* 208.7, mefloquine 22.7 *vs* 24.7 and doxycycline 5887 *vs* 5383), whereas small but significant differences were found for chloroquine 86.8 *vs* 78.0, lumefantrine 26.0 *vs* 21.6, artesunate 0.61 *vs* 0.96, dihydroartemisinin 0.69 *vs* 1.13 and atovaquone 2.39 *vs* 1.75. Divergence between the two assays increased with mean EC₅₀ values for all drugs tested except chloroquine. The DELI is an important advance in field testing of antimalarial drug susceptibility. ■

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LIVER FUNCTION TESTS AND CLINICAL SEVERITY OF DENGUE INFECTION IN ADULT PATIENTS

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Purpose: This study aims to describe the clinical manifestations of dengue infection in adult patients and to compare their severity between the group of dengue infection with and without abnormal liver function tests in adult patients.

Methods: A retro and prospective study of 127 cases of Dengue infection in adult (age ≥ 15 years) admitted at Hospital for Tropical Diseases from 2000 to 2002 and diagnosed by WHO clinical criteria with serological tests confirmed by using ELISA test or Rapid Immunochromatographic test was reviewed.

Results: Males and female were 1:1. The mean age of the patients was 26.4 ± 11.5 years. Classification of Dengue infection by WHO criteria were DF 3.1%, DHF gr.I 25.2%, DHF gr.II 65.4% and DHF gr.III 6.3%. Mean duration of fever clearance time was 6.0 ± 1.9 days but the fever last longer in cases of abnormal liver function tests (ALT > 10 times). The common presenting symptoms and signs were nausea and vomiting (87.7%), tourniquet test positive (77.2%), abdominal pain (42.7%), hepatomegaly (34.6%), bleeding (35.1%), skin rash (29.9%) and diarrhea (14.5%). Thirty six patients (28.3%)

had platelet count less than 20,000 cell/mm³. Abnormal AST and ALT were found in 88.2% and 69.3% of patients, respectively. The mean level of serum ALT was 129.3 ± 169.8 U/l in DF / DHF gr.I and 161.6 ± 230.6 U/l in DHF gr.II / DHF gr.III ($p > 0.05$). The ratio of AST and ALT, especially in the first 7 days of fever was 1.8:1. Ten fold greater than the normal limit of AST and ALT occurred in 11.0% and 7.0%, respectively. The dengue infected patients who had elevated ALT of greater than 4 times of upper normal limit present with lower white blood cells count, lower platelets count on admission than the patients who had elevated ALT of lower than 4 times ($p < 0.05$). However, their clinical severities, especially the bleeding tendency, were not significantly different in both group.

Conclusions: The clinical manifestations of dengue infection in adult patients were different from those in children in the aspect of the less prevalence of bleeding tendency, the more common of abnormal liver function tests. There was no any significant difference in their clinical severity between the group of normal and abnormal liver function tests in adult patients. ■

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QUININE PHARMACOKINETIC-PHARMACODYNAMIC RELATIONSHIPS IN UNCOMPLICATED FALCIPARUM MALARIA

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The relationships between the pharmacokinetic properties of quinine during a 7-day treatment course and the therapeutic response were studied in 30 adult patients with uncomplicated falciparum malaria monitored for $>$ or $= 28$ days. All patients received a 7-day oral quinine regimen either alone ($n = 22$) or in combination with rifampin ($n = 8$). The

median fever clearance time was 58.5 h, and the mean \pm standard deviation parasite clearance time was 73 ± 24 h. After recovery, six patients had recrudescences of Plasmodium falciparum malaria and seven had delayed appearances of P. vivax infection between days 16 and 23. Between the patients with and without recrudescences, there were no significant differences either in fever clearance time or parasite clearance time or in the overall pharmacokinetics of quinine and 3-hydroxyquinine. Patients for whom the area under the concentration-time curve from 3 to 7 days for quinine in plasma was < 20 microg.day/ml had a relative risk of 5.3 (95% confidence interval = 1.6 to 17.7) of having a subsequent

recrudescence of infection ($P = 0.016$). Modeling of these data suggested an average minimum parasitocidal concentration of quinine in plasma of 3.4 microg/ml and an MIC of 0.7 microg/ml for uncomplicated falciparum malaria in Thailand. To ensure a cure, the minimum parasitocidal concentration must

be exceeded during four asexual cycles (>6 days). ■

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ASEXUAL AND SEXUAL STAGE ANTIMALARIAL ACTIVITIES OF ARTESUNATE AND PRIMAQUINE IN FALCIPARUM MALARIA

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▶ **Asexual** and sexual stage antimalarial activities of Primaquine in combination with quinine or artesunate were assessed in 176 adult Thai patients with uncomplicated *P. falciparum* malaria. Patients were randomized to seven day oral-treatment regimens of quinine, quinine-tetracycline, quinine-primaquine (15 mg/day or 30 mg/day), artesunate or artesunate-primaquine. Clinical recovery occurred in all patients. There were no significant differences in fever clearance times, the rates of *P. falciparum* reappearances, or cryptic vivax malaria between the six treatment groups. Patients treated with artesunate alone or in combination with Primaquine had

significantly shorter parasite clearance times (mean \pm SD = 65 \pm 18 h. vs. 79 \pm 21 h.) and lower gametocyte carriage rates (40% vs. 62.7%) than those treated with quinine ($P \leq 0.007$). Primaquine did not affect the therapeutic response ($P > 0.2$). Gametocytemia was detected in 98 patients (56%; 22% before and 34% after treatment). Artesunate reduced the appearance of gametocytaemia (RR; 95%CI = 0.34; 0.17 to 0.70), whereas combinations containing Primaquine resulted in shorter gametocyte clearance times; median = 66 h. vs. 271 h. for quinine groups and 73 h vs. 137 h. for artesunate groups ($P \leq 0.038$). These results suggest that artesunate predominantly inhibits gametocyte development whereas Primaquine accelerates gametocyte clearance in *P. falciparum* malaria. ■

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APPLICATION OF REAL-TIME POLYMERASE CHAIN REACTION (PCR) ANALYSIS FOR DETECTION AND DISCRIMINATION OF MALARIA PARASITE SPECIES IN THAI PATIENTS

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▶ **A** TaqMan real-time PCR system was applied for the detection and discrimination of the 4 species of human malaria parasites in clinical blood samples. A 150-base pair (bp) region of the small subunit ribosomal RNA (SSU rRNA) gene of each malaria parasite, including species-specific sequences to be detected by TaqMan probe, was used as a target for PCR analysis. The PCR method use universal primers and species-specific TaqMan probes for *Plasmodium falciparum*, *P. vivax*,

P. ovale and *P. malariae*. The detection threshold for the method as determined with serial dilution of cultured *P. falciparum*-infected erythrocytes was 5 parasite-infected erythrocytes per reaction. Fifty blood samples of falciparum malaria and a second set of 50 samples of vivax malaria diagnosed by microscopic examination at the Hospital for Tropical Diseases, Mahidol University, Thailand, were analyzed with the real-time PCR method. In the 50 samples of microscopically diagnosed falciparum malaria, 40 were regarded as *P. falciparum* single infection, 7 were *P. falciparum* and *P. vivax* mixed infections and 3 were *P. vivax* single infection by real-time PCR. In the second set of 50 samples of microscopically diagnosed vivax malaria, all were considered

P. vivax single infection by PCR. Neither *P. ovale* nor *P. malariae* infection was identified in the 100 blood samples.

Real-time PCR analysis was shown to be more sensitive and accurate than routine diagnostic methods. Application

and extension of the PCR method reported here will provide a powerful tool for further studies of malaria. ■

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COMPLICATIONS OF PERCUTANEOUS LIVER BIOPSY BY ULTRASOUND-GUIDED IN CHRONIC VIRAL HEPATITIS

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Background: Liver biopsy is usually the specific tool to assess the severity of necroinflammation and degree of fibrosis in chronic viral hepatitis. It can be useful in confirmation of the diagnosis of non-viral chronic hepatitis. The different type of the procedure of liver biopsy, such as using ultrasound guided or not, percutaneous liver biopsy or fine needle liver biopsy, need to be assessed and compared for the risk of complication and benefit for the patients.

Objectives: To describe the risk of complication both minor and major type of percutaneous liver biopsy using ultrasound guided.

Patients and Methods: A prospective study of the patients of the Bangkok Hospital for Tropical Diseases, Bangkok, Thailand. The patients, aged between 18 and 65 years, were referred to the Liver clinic between tested positive with antiHbC, HBsAg, anti HCV. The patients' clinical data included demographic information, symptoms and signs related to liver disease, concurrent illnesses and current medication

were recorded. Percutaneous liver biopsies was carried out using ultrasonographic guidance and the number of passing needed was recorded. The size of liver specimen obtained was measured in centrimetre.

Results: Fifty-two patients of chronic viral hepatitis B and chronic viral hepatitis C were included. The laboratory findings including the mean ALT was about 3.5 times higher than the upper limit of normal. The mean interval from the detection of abnormal LFT until the liver biopsy was 12.9 ± 5.2 months. The ratio of mean AST to mean ALT in this group of patients was 0.7. The associated diseases including diabetes was found in 25% and hypertension in about 10%. For the minor and major complications recorded both immediately after the procedure and at 7 days of followed up were found in 50% and 4% respectively.

Conclusion: The complications of percutaneous liver biopsy in our reports had a higher detection rate than previous studies, however, most of them were minor complications which can be treated and controlled within 24 hours. ■

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MONITORING THE THERAPEUTIC EFFICACY OF ANTIMALARIALS AGAINST UNCOMPLICATED FALCIPARUM MALARIA IN THAILAND

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Increasing antimalarial drug-resistance is an important problem in Thailand. The results of monitoring the antimalarial efficacy are used in decision-making about using antimalarials to treat uncomplicated falciparum malaria in Thailand. In 2002, 552 patients with uncomplicated malaria were treated according

to the Thai National Drug Policy, with mefloquine 25 mg/kg plus artesunate 12 mg/kg and primaquine 30 mg in divided doses for 2 days in high-mefloquine-resistant areas; mefloquine 15 mg/kg plus primaquine 30 mg in non-or low-mefloquine-resistant areas; mefloquine 15 mg/kg plus artesunate 12 mg/kg and primaquine 30 mg in divided doses for 2 days or Coartem, (6-dose regimen for adult contains 480 mg artemether and 2880 mg lumefantrine) plus primaquine 30 mg given over 3 days in

moderate-mefloquine-resistant areas. The study shows that mefloquine, artesunate plus mefloquine, and artemether plus lumefantrine are effective in the treatment of uncomplicated malaria in most areas of Thailand except for Ranong and

Kanchanaburi, where the first-line treatment regimen should be revised. ■

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ARTESUNATE-DAPSONE-PROGUANIL TREATMENT OF FALCIPARUM MALARIA; GENOTYPIC DETERMINANTS OF THERAPEUTIC RESPONSE

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▶ The combination of chlorproguanil and dapsone is being considered as an alternative antimalarial to sulfadoxine-pyrimethamine in Africa, because of its greater efficacy against resistant parasites, and its shorter half-lives, which exert less selective pressure for the emergence of resistance. A triple artesunate-chlorproguanil-dapsone combination is under development. In a previous study of relatively low dose chlorproguanil-dapsone in multi-drug resistance falciparum malaria in Thailand failure rates were high. The safety and efficacy of artesunate-dapsone-proguanil (Artesunate 4 mg/kg, Dapsone 2.5 mg/kg, Proguanil 8 mg/kg daily for 3 days),

was studied prospectively in 48 Thai adult patients with acute falciparum malaria followed daily for 28 days. Proguanil is inexpensive and widely available, and is very similar to chlorproguanil. 11 (22%) of these patients had a recrudescence of their infection (RI). Genotyping of *P. falciparum* dihydrofolate reductase (*dhfr*) and dihydropteroate synthase (*dhps*) indicated that the *pfdhfr* I164L mutation was the main determinant of therapeutic outcome; all 11 failures carried this mutation (failure rate; 11/37; 30%) whereas none of the 11 infections with “wild type” 164 genotypes failed. The addition of artesunate considerably augments the antimalarial activity of the biguanide-dapsone combination, but this is not sufficient for infections with parasites carrying the highly antifol resistant *pfdhfr* I164L mutation. ■

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RISK FACTORS FOR PLASMODIUM VIVAX GAMETOCYTE CARRIAGE IN THAILAND

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▶ To study the risk factors for *P. vivax* gametocyte carriage, the presence or absence of gametocytes was determined in 2125 patients *P. vivax* malaria participating in clinical trials at the Hospital for Tropical Diseases in Thailand. Stepwise logistic regression models were used to sort which variables were significantly related to gametocyte carriage. On admission, 615 patients (29%) had detectable gametocytes (before treatment). After treatment had started an additional 245 patients (11%) developed patent gametocytemia. The variables retained by multivariate analysis

were: highest observed temperature adjusted odds ratio (AOR) 0.82 (95% CI = 0.71-0.94) per °C increase, $P = 0.006$; asexual parasitemia >9200 per ml AOR = 2.8 (95% CI = 1.9-4.2), $P < 0.0001$; erythrocyte counts AOR = 0.8 per million/ml increase (95% CI = 0.67-0.95), $P = 0.01$; monocyte percentage AOR = 0.93 per % increase (95% CI = 0.89-0.96), $P < 0.0001$; lymphocyte percentage AOR = 0.98 per % increase (95% CI = 0.97-0.99), $P = 0.006$; albumin AOR = 0.67 per 10 g/ml increase, (95% CI = 0.5-0.9), $P = 0.007$; and the anion gap AOR = 1.1 per unit increase (95% CI = 1.02-1.14), $P = 0.009$. The possible significance of these observations is discussed. ■

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ATOVAQUONE/PROGUANIL: A REVIEW OF ITS USE FOR THE PROPHYLAXIS OF *PLASMODIUM FALCIPARUM* MALARIA

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▶ Atovaquone/proguanil is a fixed-dose combination tablet of two antimalarial agents and is highly effective for the prevention of *Plasmodium falciparum* malaria. In combination with proguanil, the ability of atovaquone to inhibit parasitic mitochondrial electron transport is markedly enhanced. Both atovaquone and proguanil are active against hepatic (pre-erythrocytic) stages of *P. falciparum*, thereby providing causal prophylaxis and eliminating the need to continue post-travel treatment beyond 7 days. Both agents are also active against erythrocytic stages of *P. falciparum*, thereby providing suppressive prophylaxis. Atovaquone/proguanil is highly effective against drug-resistant strains of *P. falciparum*, and cross-resistance has not been observed between atovaquone and other antimalarial agents. In comparative, randomised clinical trials, there were no cases of *P. falciparum* malaria in nonimmune adults, adolescents and children (≥ 11 kg) visiting malaria-endemic regions for ≤ 28 days and receiving atovaquone/proguanil (250/100 mg in adults and dosage based on bodyweight in children < 40 kg) once daily. The efficacy for the prevention of *P. falciparum* malaria was estimated at 100% for atovaquone/proguanil and for mefloquine, and 70% for chloroquine plus proguanil. In individuals (≥ 11 kg) from

endemic regions who may carry some immunity to malaria (semi-immune), the prophylactic efficacy rating for atovaquone/proguanil based on placebo-controlled trials was 95-100%. Atovaquone/proguanil is generally well tolerated by both adults and children. The most common treatment-related adverse events in placebo-controlled trials were headache and abdominal pain, which occurred at a rate similar to that observed with placebo. Atovaquone/proguanil therapy was associated with significantly fewer gastrointestinal adverse events than chloroquine plus proguanil, and significantly fewer neuropsychiatric adverse events than mefloquine in nonimmune individuals. Significantly fewer recipients of atovaquone/proguanil discontinued treatment because of adverse events than individuals receiving chloroquine plus proguanil or mefloquine ($p < 0.05$).

CONCLUSION: Atovaquone/proguanil is a fixed-dose combination antimalarial tablet that provides effective prophylaxis of *P. falciparum* malaria, including drug-resistant strains. Both atovaquone and proguanil are effective against hepatic stages of *P. falciparum*, which means that treatment need only continue for 7 days after leaving a malaria-endemic region. Atovaquone/proguanil was generally well tolerated and was associated with fewer gastrointestinal adverse events than chloroquine plus proguanil, and fewer neuropsychiatric adverse events than mefloquine. Thus, atovaquone/proguanil provides effective prophylaxis of *P. falciparum* malaria and compared with other commonly used antimalarial agents has an improved tolerability profile, and, overall, a more convenient dosage regimen, particularly in the post-travel period. ■

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EVALUATION OF THE KAT™-QUICK MALARIA RAPID TEST FOR RAPID DIAGNOSIS OF *FALCIPARUM* MALARIA IN THAILAND

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► In recent years, several rapid diagnostic tests for falciparum malaria have been developed. KAT™ test results were compared with microscopy on 90 consecutive patients

hospitalized at the Hospital for Tropical Diseases, Bangkok, Thailand. Fifty one patients had *P. falciparum* infections while 49 had malaria due to other plasmodial species. For a geometric mean (range) parasitemia of $11,481 \pm 5.0$ (88-713,838), the sensitivity of the KAT test was 96% (95% CI=86-99.5), the specificity was 92% (95% CI=80-99), the accuracy was 94% and the reliability was 85%. These findings suggest that the KAT test is of potential interest in the diagnosis of *falciparum* malaria in Thailand. ■

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

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► The efficacy and safety of Artekin® were assessed in an open randomized trial in adults presenting with acute, uncomplicated *Plasmodium falciparum* malaria in Thailand. Two hundred and one Patients were randomly enrolled in to group A:B:C, the standard sequence of artesunate and mefloquine (group A), Artekin® (group B) and Artekin® plus

artesunate (group C). All patients had rapid initial clinical and parasitological responses. There were no significant differences in fever clearance time and parasite clearance time between both groups. The 28 day cure rates were high as 100%, 98% and 100% in the three groups respectively. Artekin® was effective and well-tolerated as artesunate-mefloquine, the current treatment in this area of multidrug-resistant *P. falciparum* malaria. ■

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

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► **Mechanism** of anaemia in severe falciparum malaria is incompletely understood. The purpose of this study was to determine whether apoptosis in erythroid lineage attributes

causing anaemia in falciparum malaria. Bone marrow aspirates from 8 severe falciparum malaria patients, 3 normal volunteers and 5 retrospective normal bone marrow smears were investigated. By light microscopic study, five of eight hyperparasitemia patients had hypocellular bone marrow and erythroid hypoplasia whereas the other three patients had normal cellularity. The mean myeloid: erythroid ratio of these 5 patients was significantly ($p < 0.05$) higher than that of normal. Apoptosis of bone marrow nucleated cells (BMNC) was determined from the exposure of phosphatidylserine (PS) on cell membrane, and DNA fragmentation. The mean percentage of apoptotic BMNC in the patients was significantly

($p < 0.05$) lower than that of normal. Whereas the mean percentage of apoptotic erythroid cells alone was neither different from that of normal ($p > 0.05$) nor associated with parasitemia. There was no DNA fragmentation (180-250 bp), confirmed by TUNEL and ultrastructural investigation, in BMNC of both patients and

control. This study suggested that destruction of erythroid lineage particularly through apoptosis regulation could not solely account for anaemia in falciparum malaria. ■

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EVIDENCE FOR CONTINUED TWO-BROOD REPLICATION OF *PLASMODIUM FALCIPARUM* IN VIVO DURING QUININE TREATMENT

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▶ **To** investigate the relationship between fever and parasite clearance in falciparum malaria, we studied 54 adults with *Plasmodium falciparum* infections who were all treated with quinine. The median oral temperature profile showed peaks at 24 h intervals during the first 3 days. Although there

was no equivalent pattern evident in the median parasite clearance curve, we hypothesize that small numbers of two distinct parasite broods continued to develop in antiphase through schizogony despite quinine therapy. These data are consistent with previous reports of two dominant broods in untreated humans and monkeys infected with *P. falciparum*, and highlight the need for an adequate duration of quinine treatment. ■

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HOOKWORM INFECTIONS OF SCHOOLCHILDREN IN SOUTHERN THAILAND

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▶ **A** study of hookworm infections of schoolchildren was conducted in Nakhon Si Thammarat Province, southern Thailand. Of the 2,940 hookworm that were recovered from the children, almost all (99.9%), were *Necator americanus*, only three (0.1%) were identified as *Ancylostoma duodenale*, and all were female worms. An estimation of the worm burden of and the worm expulsion from the schoolchildren indicated there were 17 cases of light intensity hookworm infection. Fifteen

cases (88.2%) expelled worms in numbers that corresponded with the worm burden that was estimated from the number of eggs per gram of feces. Two cases (11.8%) expelled more worms than predicted. In 16 moderate intensity cases, five (31.3%) expelled worms in a quantity that corresponding with the estimated worm burden. Eleven cases (68.7%) expelled fewer worms than predicted. All cases of heavy intensity infection expelled fewer worms than predicted. ■

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SCHOOL-BASED HELMINTHIASES CONTROL : I. A BASELINE STUDY OF SOIL-TRANSMITTED HELMINTHIASES IN NAKHON SI THAMMARAT PROVINCE, THAILAND

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▶ **A** baseline study of soil-transmitted helminthiasis was carried out in Nakhon Si Thammarat Province, southern Thailand. The study sites were Wat Krou Chou Primary School and nearby villages in Sichon district, and Wat Thang Phoon Primary School and nearby villages in Chalerm Phrakiat District. Surveys of the schoolchildren's stools were conducted by the Kato-Katz technique. The results showed that 23.7% of schoolchildren in Wat Krou Chou and 24.7% of those in Wat Thang Phoon were

infected with soil-transmitted helminths, with a 24.1% overall infection rate. The major infection was hookworm (22.2% and 19.6%) and the minor one was trichuriasis, (2.9% and 8.7% respectively). The intensity of infection was similar in both schools, 85.7% and 90.2% respectively for light intensity hookworm. Schoolchildren with hookworm infection were not anemic. The hemoglobin value of children with hookworm infection was not significantly different from that of uninfected children. Data regarding the health behavior of children's parents in both schools were reported. ■

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IMMUNODIAGNOSIS OF GNATHOSTOMIASIS

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▶ **Several** immunological methods for the diagnosis of gnathostomiasis have appeared in the literature. The oldest methods was the skin test, which was established initially by Japanese scientists in the 1960s. It was a convenient and relatively reliable diagnostic means in that period. During the 1980s, ELISA was evaluated by several investigators, and it was found that sensitivity varied from 56% to 100%. The antigen used in the assay was crude larval antigen of *Gnathostoma spinigerum*, crude adult antigen of *G. doloresi* or larval excretory-secretory antigen. The immunoblotting technique was studied during

the 1990s. The specific diagnostic band was the protein component with a molecular weight of 24 kDa. The routine current diagnostic method for human gnathostomiasis is the immunoblotting technique. Monoclonal antibodies (m Abs) to the crude soluble extract, 24 kDa protein component of *G. spinigerum* advanced third-stage larvae have been produced. Moreover, hybridoma cell lines, derived from spleen cells of an infected mouse, secreted antibodies that reacted with the cuticle of *GsAL3* sections by IFA. These mAbs were produced. However, the diagnostic value of these mAbs is not applicable for the diagnosis of human gnathostomiasis. ■

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THE FIRST HUMAN INFECTION WITH *BERTIELLA STUDERI* IN VIETNAM

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▶ **This** is the first case report of *Bertiella studeri* infection in Vietnam. The patient was a 4 year old boy in Cai Lay district of Tien Giang Province, noting some proglottids in his feces.

The time and mode of infection were unknown, but anorexia, weight loss, and intermittent diarrhea were noted. Niclosamide (Yomesan) 1 gram was prescribed, and then albendazole (Zentel) 400 mg daily for 3 days. Proglottids were found in the feces three months after the first treatment, and 1 month after the second course. ■

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UNEXPECTEDLY HIGH PREVALENCE OF WUCHERERIA BANCROFTI INFECTION OBTAINED BY ICT CARE TESTS IN COMPARISON WITH THAT DETERMINED BY IGG4 ELISA USING URINE SAMPLES. A POSSIBILITY OF FALSE POSITIVE REACTIONS WITH ICT CARD TESTS IN STUDY IN THAILAND

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▶ **With** the purposes of studying the recent prevalence of *Wuchereria bancrofti* infection in Thai-Myanmar border areas, and evaluating the usefulness of a new ELISA, which uses urine as samples (urine ELISA), 519 people in Sangkhla Buri and 84 people in Suan Phung were examined by ICT care test for filarial antigen and by urine ELISA for filaria-specific IgG4. In the former area, positive rates by ICT test and the ELISA were 16.8% and 21.2%, respectively; in the latter area, the respective

rates were 10.7% and 7.1%. These figures were unexpected, because the urine ELISA used to give much higher prevalence than antigenemia tests in our previous studies. In addition, only 37 of 96 ICT positives (38.5%) were urine ELISA positive. Our previous studies showed that the sensitivity of urine ELISA among the microfilaria and/or antigen positive individuals was more than 90%. Diethylcarbamazine treatment given to the known ICT positives at 300 mg/day for 12 days reduced antigenemia rate from 100% to 32.8%, which was determined 2 months after treatment by Og4C3 ELISA. The reduction of 67.2% seemed to be unusually high. These conflicting results could be explained by possible false positive reactions produced by ICT test. ■

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RISK FACTOR OF HELMINTHIASES AMONG SCHOOL CHILDREN IN SOUTHERN THAILAND

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▶ **School-age** children are particularly at risk of soil-transmitted helminthiasis (STH), which affects their growth and development. Hence, school-based helminthiasis control has been discussed and conducted as one of cost-effective ways in developing countries. A parasite control program is to be planned and conducted in an evidence based way as one of practical medical fields. However, a prevalence is likely to be influenced by various factors such as local environment and residents' behavior and so on. As few reports mentioning the relation of the prevalence and children's behavior and practice have been published, we conducted a survey to investigate such relation by asking children directly. Two hundred and

eighty pupils in grade 3 to grade 5 were enrolled, who were in the two schools in Nakhon Si Thammarat Province, southern Thailand. A cross-sectional study was conducted in February and in November 2001, on the relationship between helminthiasis and children's knowledge and practice by using Kato-Katz method and a questionnaire, respectively. Hookworm (Hw) was the most predominant helminth followed by *Trichuris*. Boys had more intensive Hw infection than girls ($p=0.022$), and wore shoes less frequently than girls ($p<0.001$). The pupils who nearly acquired Hw infection after the first stool examination had lower levels of the knowledge of STH comparing to those who did not ($p=0.011$). This study suggests that a prior survey can identify unique local factors as a part of diagnostic process, the results of which are useful for teachers to understand some point of health education at schools and can be applied as indicators for monitoring and evaluation. ■

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INTESTINAL HELMINTHIC INFECTIONS IN SCHOOL CHILDREN IN CAMBODIA

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▶ During the period January to December 1998, the National Malaria Center (CNM) carried out a parasitological survey of schoolchildren in rural and semi-urban areas, to assess intestinal helminthic infections in schoolchildren in the central parts of Cambodia. In the rural areas, there were four schools in Stung Treng Province (all situated along the Mekong River), five schools in Kratie Province (around rubber plantations), six schools in Kampong Chhnang Province (along Tonle Sap Lake); and in the semi-urban areas, three schools in Beng Tumpon Commune and five schools in Chbar Ampeou Commune (Mean Chey District) were selected for study. By

Kato-Katz technique, the prevalence of soil-transmitted helminthic infections in schoolchildren in both the rural and urban areas was high. The infection rate was between 10-40% for *Ascaris*, 2-17% for *Trichuris* and 5-65% for hookworm. Schistosomiasis and opisthorchiasis were found in the schoolchildren living along the Mekong River (Stung Treng Province); the infection rate of *S. mekongi* ranged from 12 to 43%. These infections in children were with hepatomegalies. An intervention in an urban area (Chraing Chamres) showed that after repeated treatment with mebendazole 500 mg single dose every 6 months, the prevalence of all parasites had dropped to about one third of the initial level. ■

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IMPROVED ANTIGENS FOR IGG-ELISA DIAGNOSIS OF STRONGYLOIDIASIS

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▶ Two preparations of antigens for the diagnosis of strongyloidiasis were prepared from an extract of the infective larvae of *Strongyloides stercoralis*: a crude antigen (CA) and a molecular weight cut-off antigen (MWCOA). Both antigens were analysed by indirect ELISA against the sera of strongyloidiasis (26 cases), other helminthiasis (167) and normal controls (30). The larvae were obtained from fecal culture by a modified polyethylene tube technique after screening tests by triple simple smears per case. The larvae were extracted with distilled water and further sonicated to obtain a

supernatant, the CA. A part of the CA was separated for an antigen containing molecules of lower than 30kDa by an ultrafree-MC centrifugal filter tube (PLTK): this was designed as the MWCOA. The CA gave 96.15% sensitivity and 40.12% (67/167) specificity at a cut-off value of 0.980 (5SD); false positives were produced by 19 of 20 different helminthiasis. The MWCOA produced 96.15% sensitivity at cut-off value of 0.71(4SD); the specificity of the test was 78.44% (131/167), higher than that of CA. False positives also appeared with 15 other helminthic infections. This study suggests that MWCOA is more specific than CA. A purified MWCOA will be necessary in order to reduce cross-reactivity and provide the suitable diagnosis of strongyloidiasis. ■

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GNATHOSTOMIASIS : AN EMERGING IMPORTED DISEASE

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▶ **As** the scope of international travel expands, an increasing number of travelers are coming into contact with helminthic parasites rarely seen outside the tropics. As a result, the occurrence of *Gnathostoma spinigerum* infection leading

to the clinical syndrome gnathostomiasis is increasing. In areas where *Gnathostoma* is not endemic, few clinicians are familiar with this disease. To highlight this underdiagnosed parasitic infection, we describe a case series of patients with gnathostomiasis who were treated during a 12-month period at the Hospital for Tropical Diseases, London. ■

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IMPORTED CUTANEOUS GNATHOSTOMIASIS : REPORT OF FIVE CASES

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▶ **Gnathostomiasis** has rarely been described outside endemic countries. We report on a series of 5 patients (4 females, 1 male, mean age 42.2 years) who returned to France from South-East Asia and presented with cutaneous gnathostomiasis. The cutaneous lesions appeared within a mean period of 62 d (range 10-150 d) after return. They consisted of creeping eruptions in 3 patients (in addition one also had papules, one had nodules and hepatitis and one had hepatitis; all 3 had profound asthenia) and recurring migratory swellings in 2 patients. The mean eosinophil count was 1546/

mm³ (range 398-3245/mm³). Diagnosis was based on positive serological tests in 2 patients and seroconversion in 2 patients and was confirmed by identification of *Gnathostoma hispidum* in a biopsy specimen from the fifth patient. Albendazole (1-4 courses) was given as treatment. On patient had recurring migratory swelling 20 months after apparent cure without reinfection. Gnathostomiasis should be considered when patients return from tropical countries and present with migratory swellings or creeping eruption that does not respond to the usual treatment for cutaneous larva migrans. Serological tests may be negative initially and thus need to be repeated to check for seroconversion. Treatment may require multiple course of albendazole and a prolonged period of follow-up is necessary. ■

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SOIL-TRANSMITTED HELMINTHIASES RE-INFECTION RATES IN A THAI VILLAGE WITH 100% LATRINE

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▶ **Five** hundred and eighty individuals in a village of houses having 100% latrine in Nakhon Si Thammarat Province were examined for soil-transmitted helminth infections by Katz's modified thick smear method. It was found that 74.0% (429/

580) were infected: 57.9% with hookworm, 62.9% with *Trichuris trichiura* and 10.2% with *Ascaris lumbricoides*. The infected cases were treated with 100 mg mebendazole twice daily for 3 consecutive days. Twenty-one days after administration, their stools were re-collected and examined. Uncured cases were treated again. Re-infection rates were assessed at 3, 6, 9 and 12 months after they had been cured by each treatment interval. The percent

infection rates of hookworm, *T. trichiura* and *A. lumbricoides* were 21.2, 15.6 and 3.0 after 3 months; 10.9, 12.0 and 4.5 after 6 months; 6.0, 11.5 and 2.1 after 9 months; 9.3, 12.9 and 1.5 after 12 months. The cumulative re-infection rates of hookworm, *T. trichiura* and *A. lumbricoides* were 47.4, 52.0 and 11.1, respectively. The prevalence of hookworm infection was highest

between October and December (rainy season) and lowest between April and June (Summer). The prevalences for *T. trichiura* and *A. lumbricoides* infections were similar in each 3-monthly period of the study. ■

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CONTROL OF HOOKWORM INFECTION IN PRIMARY SCHOOLS IN NAKHON SI THAMMARAT

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▶ **The** control program for hookworm infection in primary schools via school teachers was conducted in Nakhon Si Thammarat Province. Four schools, two experimental and two control, were selected for study. The first two schools are located in an area where most inhabitants are gardeners and Buddhist. These are Chumchon Ban Phut-hong (experimental) and Wat Thara Wong (control) schools, in Ron Phibun District. The other two schools are located in an area where most people are fishermen and Muslim. Wat Phisan Sathit School (experimental) is in Muang District and Ban Sa Bua School (control) is in Tha Sala District. A KAP survey was conducted by questionnairing the school children (grades 3-5).

Their fecal samples were collected and examined using Katz's modified thick smear technique. Stool-positive children

with hookworm or other soil-transmitted helminthes (eg, *Ascaris* and *Trichuris*) were given on tablet (100 mg) of mebendazole, twice daily for three consecutive days. Twenty-one days after the first treatment, fecal samples were recollected and examined. Infected cases were re-treated with the same regimen of mebendazole. All analyzed KAP data and fecal data were shown and explained to the teachers, who were involved in the programs at the two experimental schools, so as to gather concepts and make a control plan. One year later, the school children were interviewed again with the same set of questions. Their fecal samples were collected and examined. Although the children in the two experimental schools gained more knowledge and understanding of various aspects of hookworm infection, the highest (27.7%) and lowest (3.2%) reinfection rates were observed in Ban Sa Bua and Wat Thara Wong, which were both control schools. ■

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SOIL-TRANSMITTED HELMINTHIASES IN NAKHON SI THAMMARAT PROVINCE, 1991-2001

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▶ **Between** 1991-2001, a total of 8,569 fecal sample of primary school children and villagers in Muang, Chian Yai, Ron Phibun, Sichon and Tha Sala districts of Nakhon Si Thammarat Province were examined for eggs of soil-transmitted helminths using Katz's modified thick smear technique. The overall prevalence rates were 87.0% (1991), 81.4% (1993), 81.0% (1994), 55.4% (1995), 76.1% and 91.6% (1998), 46.8% (1999), 58.3% (2000) and 48.3% (2001). These included *Ascaris lumbricoides* 3.7% - 18.5%, *Trichuris trichiura*

28.5% - 66.9%, hookworm 18.0% - 80.0% and *Enterobius vermicularis* 0.7%. As for *Strongyloides stercoralis*, using a culture technique, the infection rates in 1991 and 1999 were 0.3% and 1.8%, respectively. High rates of infection were found in all schools in Muang, Chian Yai and Ron Phibun districts. In Muang District, a consistently high prevalence was found, especially in Islamic Thai who were fishermen and lived in villages with clustered housing. Decreasing prevalence rates, especially in hookworm infection, were found in villagers who earned their living by working in rubber plantations. ■

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FISH AS THE NATURAL SECOND INTERMEDIATE HOST OF *GNATHOSTOMA SPINIGERUM*

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▶ **Gnathostomiasis** is a helminthic disease most frequently occurring in Thailand. Human infections are usually found to be caused by *Gnathostoma spinigerum*, although five species of the genus *Gnathostoma* exist in Thailand, and three of these are capable of infecting man. In Thailand, 47 species of vertebrates – fish (19), amphibians (2), reptiles (11), avians (11) and mammals (4) – were reported to serve naturally as the second intermediate (and/or paratenic) hosts of *G. spinigerum*. Among these animals, fish, especially swamp eels

(*Monopterus albus*) were found to be the best second intermediate/paratenic hosts: they had the highest prevalence rate and the heaviest infection intensity. However, the scientific names of these fish have been revised and changed from time to time. Therefore, for clarity and consistency, we have summarized the current scientific names of these 19 species of fish, together with their illustrations. We also describe one additional fish species, *Systomus orphoides* (*Puntius orphoides*), which is first recorded as a naturally infected second intermediate host for *G. spinigerum*. ■

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GNATHOSTOMA INFECTION IN NAKHON NAYOK AND PRACHIN BURI, CENTRAL THAILAND

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▶ **Gnathostoma** infection in Nakhon Nayok and Prachin Buri Provinces, Central Thailand, was investigated. The prevalence and intensity of infection of swamp eels were determined; dog fecal samples and fresh-water copepods were examined for evidence of infection. The overall prevalence of eel infection was 38.1% (117/307) in Nakhon Nayok and 24.0% (74/308) in Prachin Buri – the former rate being significantly higher than the latter. Most of the positive Nakhon Nayok eels (53.8%) harbored only 1-9 larvae; only one eel bore more than 50 larvae. In Prachin Buri, 67.6% of the positive eels harbored 1-9 larvae; again, only one eel bore more than 50 larvae. The mean number of 11.0 ± 10.4 larvae/eel in Nakhon Nayok was not significantly different from that of Prachin Buri (9.3 ± 11.4).

A total of 1,292 gnathostome larvae were recovered from 307 eels in Nakhon Nayok. Of these, 52.3% had accumulated in the liver and 47.7% had spread throughout the muscles. In eels from Prachin Buri, 50.6% and 49.4% of the total of 688 larvae (from 308 eels) were found in the liver

and muscles, respectively. The larvae preferred encysting in ventral rather than dorsal muscle; they also preferred the middle portion to the anterior and posterior portions. The average length of gnathostome larvae recovered from Nakhon Nayok eels was 4.0 ± 0.5 mm (range 2.5-5.1 mm) and the average body width was 0.40 ± 0.05 mm (range 0.29-0.51 mm). Those from eels in Prachin Buri were 3.9 ± 0.5 mm (range 2.2-5.1 mm) and 0.34 ± 0.05 mm (range 0.20-0.48 mm), respectively. The mean body length and width of the larvae from eels in Nakhon Nayok were significantly greater than those of the larvae from eels in Prachin Buri.

In Ban Phrao, Nakhon Nayok, none of the first 44 fecal specimens examined was positive. Of the second (68) and the third (70) specimens, one (1.5%) and two (2.9%) samples were found to be positive. However, six months after the third fecal collection, no eggs were found. In Tha Ngam, Prachin Buri, no eggs were found in all three batches (109, 115, and 100 fecal samples). A cyclops survey of 4,000-5,000 crustacea from each of two areas (Ban Phrao and Tha Ngam) found no evidence of natural cyclops infection. ■

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THE INFECTIVITY OF FROZEN *GNATHOSTOMA SPINIGERUM* ENCYSTED LARVAE IN MICE

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▶ **The** infectivity of encysted larvae of *Gnathostoma spinigerum* in mice, after being frozen in the freezer of a household refrigerator (about -4 °C), was evaluated. The larvae used in the experiment, which were obtained from laboratory-infected rats and mice, were 6 months old. Those recovered from naturally infected eels were of unknown age. Each group of larvae was placed in a blockglass containing physiological saline, kept in the freezer for 1, 6, 12, 18, 24, 30, 36 or 48 hours, and fed to clean mice, 5 larvae per mouse. Both the 6-

month-old and the unknown-age encysted larvae lost their infectivity completely after being frozen for 48 hours. When the larvae were rolled up inside the mice flesh and frozen at the same temperature for 48 hours, they could still infect clean mice, with an infectivity of 20.0%. It was concluded that although *G. spinigerum* encysted larvae could survive several days in the freezer of a household refrigerator they lost their infectivity only after 1-2 days. However, the mimetic infected meat containing encysted larvae resisted this freezing temperature for at least 48 hours. ■

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ON THE BIOLOGY OF *GNATHOSTOMA SPINIGERUM*

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▶ **Gnathostoma spinigerum**, the main causative agent of human gnathostomosis, is actually a nematode parasite of carnivores. The life cycle of the worm essentially involves 3 hosts: a definitive host, the first intermediate host and the second intermediate host. In Thailand, the natural definitive hosts of *G. spinigerum* are normally cats and dogs. Four species of cyclops serve experimentally as the first intermediate host. Forty-eight species of vertebrates serve naturally as the second intermediate (and/or paratenic) hosts. Among these animals, fish, especially swamp eels, have been found to be the best second intermediate/paratenic hosts of *G. spinigerum* on the basis of having the highest prevalence rate and the greatest

infection intensity. Swamp eels have also been found to harbor at least 4 species of *Gnathostoma*.

This paper reviews *G. spinigerum* natural definitive hosts; natural second intermediate hosts and paratenic hosts; the record numbers of *G. spinigerum* larvae in second intermediate/paratenic hosts; tissue distribution of the larvae in naturally infected swamp eels; experimental first intermediate hosts; experimental primary infection in vertebrate hosts; experimental secondary infection in vertebrate hosts; experimental infection in cats and dogs; infectivity of the larvae in mice; and the effects of temperature, chemicals, radiation and some native Thai foods upon the viability of the larvae. ■

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INTRAOCULAR GNATHOSTOMOSIS IN VIETNAM

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▶ **This** is the report of the first case of intraocular gnathostomosis observed in Vietnam. The disease progressed in two months in two distinct phases. In the first phase, the patient noted swollen nodes, which appeared at different times at different points on his face. This phase lasted around one month. The second phase was recognized by the embedding

of the parasite in the vitreous cavity of the right eye after an uveitis. Surgical extraction of the living *Gnathostoma* larva was carried out. Based on morphological aspects and other histological criteria, it could be an atypical third-stage larva of

Gnathostoma spinigerum. ■

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

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▶ A cross-sectional study of the prevalence of intestinal parasitic infections at eight schools in Bo Klau district and four schools in Chalerm Prakiet district, Nan Province, in January and February, 2001. A total of 1,010 fecal samples were examined using the formalin-ether sedimentation technique. Results revealed that the rate of helminthic infection was 60.0%, while protozoa accounted for 36.2% of infections; mixed infections were common, resulting in a total prevalence of both

parasites of 68.1%. Helminthic parasites, listed by frequency of infections, were *Ascaris lumbricoides* (21.7%), hookworm (18.5%), *Trichuris trichiura* (16.3%), *Opisthorchis viverrini* (1.7%), *Strongyloides stercoralis* (0.9%) and *Enterobius vermicularis* (0.9%). The protozoal infections were *Entamoeba coli* (25.8%), *Giardia lamblia* (5.3%), *Endolimax nana* (2.5%), *Entamoeba histolytica* (1.4%), *Blastocystis hominis* (0.8%), *Chilomastix mesnili* (0.3%) and *Iodamoeba b_tschlii* (0.1%).

This study emphasizes the need for improved environmental hygiene *ie* clean water supplies and enhanced sanitation, in affected communities. Health promotion, by means of a school-based educational approach is recommended; regular check-ups should be implemented, and a continuous program of treatment should be considered. ■

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SERODIAGNOSIS OF HUMAN OPISTHORCHIASIS USING COCKTAIL AND ELECTROELUTED BITHYNIA SNAIL ANTIGENS

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▶ **Cocktail** and electroeluted antigens from *Bithynia goniomphalos*, the snail intermediate host of *Opisthorchis viverrini*, were extracted and purified. The performance of these two antigens in the antibody detection of human opisthorchiasis was evaluated by indirect ELISA. Serum samples from people whose stool was either; (i) positive for *Opisthorchis* eggs (n = 61); or (ii) positive for at least one of 19 other species of parasite (n = 125); or (iii) clear of parasites (n = 30) were tested. The sensitivity, specificity, positive predictive value and negative

predictive value of ELISA using cocktail antigen were 88.5, 88, 78.2 and 94%, respectively; those of ELISA using eluted antigen (53 kDa) were 91.8, 98.4, 96.5 and 96.1%, respectively. Cross-reaction with the eluted antigen was seen in only one of four cases of hymenolepiasis and only one of 10 cases of stroglyoidiasis. The kappa coefficients for ELISA in relation to stool examination were 0.84 (cocktail antigen) and 0.87 (eluted antigen). This study showed that *Bithynia* snail antigen could be used to replace worm antigen in the antibody detection of human *O. viverrini* infection. ■

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SURVEILLANCE OF COMMENSAL RAT AND SHREW POPULATIONS IN THE BANGKOK AREA WITH REFERENCES TO FLEA INDEX AS THE RISK INDICATOR OF PLAGUE

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► **Commensal** rats and shrews were trapped from 47 fresh food markets in Bangkok during the two study periods in the same markets: 21st June to 28th December 1999 and 1st March to 31st May 2000. Trapping was performed using wire live traps on three consecutive nights in each period. The trapped animals were identified for taxonomic species and flea infestation. Fleas were collected, identified and counted. Four species of rodents: *Rattus norvegicus*, *Rattus rattus*, *Rattus*

exulans and *Mus musculus*, and one species of shrew: *Suncus murinus* were trapped in comparable numbers during the two study periods. Among the 1177 animals trapped, 84.3 per cent were *R. norvegicus*. Regarding sex prevalence, a higher number of female animals were trapped compared to males. Almost all the fleas collected were *Xenopsylla cheopis*, and there were very few *Ctenocephalides felis-felis*. Flea index based on the number of *X. cheopis* was 0.65 for all over Bangkok. Based on the geographical area of Bangkok, the inner area had the highest rodent population and the highest flea index of 0.86. Therefore, the inner region should be the priority for sanitation improvement. ■

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SUSCEPTIBILITY AND TRANSOVARIAL TRANSMISSION OF DENGUE VIRUS IN Aedes aegypti : A PRELIMINARY STUDY OF MORPHOLOGICAL VARIATIONS

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► **Two** types of morphological variants, the dark form and the pale form of *Aedes aegypti* were selected from wild-caught mosquitos. Ascertaining any differences between the two forms for susceptibility to dengue type 2 virus was performed by oral feeding. Transovarial transmission was further determined from the progenies of infected mosquitoes by tracing them to the third generation. Significant differences in oral infection were not observed between these two forms

of mosquitos. Transovarial transmission was found in the progenies of infected females of both forms, and the filial infection rates (FIRs) were also similar. However, there was a trend of declining FIR in the later generation. In order to achieve an accurate result, more tests are currently underway to obtain a larger number of progeny. Although the FIR was low in the present study under laboratory conditions, higher rates might occur under field conditions, which could have a significant impact on the maintenance of dengue viruses in nature. ■

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COMPARATIVE SUSCEPTIBILITY TO ORAL INFECTION WITH DENGUE VIRUSES AMONG LOCAL STRAINS OF Aedes aegypti (DIPTERA : CULICIDAE) COLLECTED AT DIFFERENT SEASONS OF THE YEAR

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▶ **The** vector competence of *Aedes aegypti* (L.) mosquitoes, collected during the hot, rainy and cool seasons from different localities in Thailand, was tested for a correlation with a seasonal cyclic pattern of dengue incidence. Under laboratory conditions, some groups of mosquitoes exhibited differences in susceptibility to oral infection but showed no correlation to dengue cases that peak during the rainy season.

Thus, the environmental conditions of each season, although they might affect a temporal change of mosquito vector competence, they might not have any direct effects on virus transmission patterns. Mosquito populations from different parts of Thailand were also likely to be homogeneous in their susceptibility to dengue virus during the study period. Other factors, such as characteristics of the virus, vector density and frequency of host-vector contact, should be considered for seasonal pattern of dengue diseases. ■

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EFFECTS OF CRUDE HERBAL EXTRACTS AGAINST ACANTHAMOEBA CASTELLANII TROPHOZOITE IN VITRO

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▶ **Acanthamoeba** is a free-living protozoa which is commonly found in the environment. However, several *Acanthamoeba* species have been found to cause diseases to human beings such as granulomatous amebic encephalitis and *Acanthamoeba* keratitis. This study was carried out to detect the effects of crude herbal extracts against trophozoite stage of *A. castellanii*. Three of the herbs; *Eurycoma longifolia* Jack, *Pisonia aculeata* Linn and *Suregada multiflorum* Baill showed capability to eradicate the *A. castellanii* trophozoite cells while the other two herbs; *Derris scandens* Benth and *Acacia concinna* did not give any effects to this amebae cells. *Eurycoma longifolia* Jack inhibits *A. castellanii* cell up to 90% in 5% (25 mg dried material/ml) concentration at day 7 compared to *Pisonia aculeata* Linn (87%) and *Suregada multiflorum* Baill (53%). Therefore the crude extract of *Eurycoma longifolia* Jack was selected for further investigation by increasing its

concentration as well as the combination of the snow mushroom extract. The increment at 10% concentration could cause dropping of the mean living cells/ml of *A. castellanii* to $0.05 \times 10^6 \pm 0.04$ on day 6 and 7, while the combination at 5% concentration of snow mushroom extracts could not give any effects in eradication of ameba cells. The snow mushroom extract was believed to have the capability to penetrate into the protozoan cell, but in this study, it did not show any reaction. In contrast, *Eurycoma longifolia* Jack could give better effect without any combination. The effectiveness of *Eurycoma longifolia* Jack was observed at 5% concentration (inhibited 90% of *A. castellanii* cells) while the standard drugs, itaconazole, gave eradication effect at 0.4 mg/ml (68% inhibition at day 7). Itraconazole eradicated the amebae cells up to 93% and 100% in 0.8 and 1.0 mg/ml concentration respectively. Therefore, further study against *Eurycoma longifolia* Jack is needed as an effort to detect the capability of this herb, which may have potential as an alternative treatment for *Acanthamoeba* infection. ■

IN VITRO SENSITIVITY OF BLASTOCYSTIS HOMINIS AGAINST HERBAL EXTRACT

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▶ **Blastocystis hominis** is an intestinal protozoa and the current treatment is metronidazole, although there are occurrences of parasite resistance and also development of

negative side effects have been noted, thus natural and slower approach treatment much recommended. In this study, five types of the cured herbal extracts that believed to have antiprotozoal compound were used as a test specimens, while metronidazole as a standard drug. The complete IMDM medium was included in each test to ensure the inhibition of

the parasite cells by monitoring in triplicate (1 ml culture test tubes) for 7 days. The eradication of viable cell detected by using the criteria of living cell counts (LCC) in aid of trypan blue staining. Out of the five crude herbal extracts (from *Acacia concinna* Merr., *Derris scandens* Benth., *Eurycoma longifolia* Jack, *Pisonia aculeate* Linn., and *Suregada multiflorum* Baill.), only two (*Suregada multiflorum* Baill. and *Eurycoma longifolia* Jack) were found to be effective, which showed decrement of *B. hominis* viable cells. The decrement of parasite cells were proportionate with the higher concentrations, which showed

up to $0.01 \times 10^6 \pm 0.00$ cells/ml on day 7th against the 5% (25 mg dried material/ml) crude of *Suregada multiflorum* Baill and *Eurycoma longifolia* Jack. Substantial concentrations of *Suregada multiflorum* Baill were selected to progress for 30% and 40% up to 15 days of monitoring. At these concentrations, there were fluctuation of eradication, where increment of the *B. hominis* young cells were obviously seen started from day 9th until day 12th. We believed that these young cells might appear from the cyst of the parasite. This has brought dubious where further test for *Eurycoma longifolia* Jack was suggested. ■

PRELIMINARY STUDY ON AN IDENTIFICATION OF ADULT ANOPHELES CAMPESTRIS BY ISOENZYME ELECTROPHORESIS

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▶ **Anopheles campestris** was found to be a potential vector of malaria in Sa Kaeo province, Thailand. Owing to difficulties in identification of adult females, the incrimination of this species as malaria vector remains an obstacle. The present study is an attempt to develop a tool for identification of the adult mosquitoes by electrophoresis. Several enzymes were used in a polyacrylamide gel electrophoresis. Phylogenetic dendrograms were produced by using the Biosys-1 program

based on UPGMA methods. The screening of 9 enzyme systems (*Ldh*, *Hk*, *Me*, *Est*, *Aldox*, *Xdh*, *Gpi*, *Odh*, *Lap*) were made on isofemale colonies of *An. campestris* collected from Pa Rai, Sa Kaeo province. Esterase was a promising isoenzyme for separating *An. campestris* from *An. barbirostris*. The enzyme revealed important markers to estimate variability and genetic divergence in natural populations of *An. campestris*. n

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

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▶ **The** biology of a hymenopteran parasitoid, *Pachycrepoideus vindemmiae* (Rondani), and its efficiency in the control of flies of medical importance was investigated in the laboratory. The life cycle study revealed that *Pachycrepoideus vindemmiae*, when developed in house fly puparia, the egg, the first, second, third, fourth and fifth instar larvae, and prepupa and pupal stages lasted 1-2, 1-2, 2-3, 1-2, 2-3, 3-4, 1-2 and 9-12 days respectively. The average development period from egg to adult emergence was 20.30 ± 1.43 days for males and 21.30 ± 1.16 days for females. The characteristics of each development stage of the parasitoid were

also described in this study. Adult longevity, when reared with 10% sugar solution, averaged 13.63 ± 4.06 days in males and 18.22 ± 2.93 in females. The mean fecundity was 112.18 ± 25.24 offspring per female. The sex ratio, female per male, of offspring produced by mated females was 1.58:1, while only males were obtained from unmated females. The parasitism rate in *Musca domestica* was $75.12 \pm 10.97\%$. Regarding the host preference in the laboratory, *Musca domestica* was the most preferred, followed by *Chrysomya megacephala* and *Parasarcophaga orchidae*, respectively. ■

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PYRETHROID RESISTANCE IN ASSOCIATION WITH THE USE OF INSECTICIDE IMPREGNATED BED NETS

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▶ **There** has been concern about whether pyrethroid tolerance or resistance will be selected in anophelines and other mosquitoes through the use of pyrethroid-impregnated bed nets. Pieces of nylon netting impregnated with different concentrations of lambda-cyhalothrin and permethrin were used for mosquito selection, to investigate the development of pyrethroid tolerance or resistance in adult *Aedes aegypti* and *Anopheles maculatus*. The WHO susceptibility test kits were lined inside with insecticide-impregnated nylon netting

and mosquitoes were exposed for periods of 30 seconds to 4 minutes. Mortality was scored after a 24-hour observation period. The LT_{50} values and the resistance ratio or increased tolerance in each generation were determined. The exposure of 9 generations of *Ae. aegypti* to 0.015 g/m² lambda-cyhalothrin, and 8 generations of *Ae. aegypti* to 0.15 g/m² permethrin produced 2.6-fold and 2.8-fold tolerance, respectively, whereas 5 generations of *An. maculatus* exposed to 0.1 g/m² permethrin showed 1.4-fold tolerance. The pattern of increased tolerance levels to lambda-cyhalothrin and permethrin by both mosquito species indicated no evidence for the development of pyrethroid resistance. ■

SUSCEPTIBILITY OF JAPANESE Aedes (STEGOMYIA) MOSQUITO TO DENGUE VIRUS

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▶ **Dengue** fever (DF), dengue hemorrhagic fever (DHF), and dengue shock syndrome (DSS) are medically important arthropod-borne virus diseases affecting humans in terms of morbidity. Although no domestic dengue virus infection has occurred recently, imported dengue cases have been reported frequently in Japan. Therefore, DF/DHF/DSS are still important infectious diseases in Japan. Since there is no specific cure for the disease and dengue vaccine is not available, prevention and control dengue relies solely on control of vector population. *Aedes (Stegomyia)* mosquitoes are an important vector of dengue virus. In Japan, there are several *Aedes (Stegomyia)* mosquito species, such as *Ae. flavopictus miyarai*, *Ae. albopictus*, *Ae. riversi*, *Ae. f. daitensis*, *Ae. f. downsi*, *Ae. flavopictus*, *Ae. wadai* and *Ae. galloisi*. Only *Ae. albopictus*, *Ae. flavopictus*, *Ae. riversi* and *Ochlerotatus dorsalis* were incriminated as vectors of the virus. Other species have not

yet been confirmed as susceptible vectors for the virus. The purpose of this study was to determine the susceptibility of *Ae. f. miyarai* to dengue type 2 virus.

Infection of *Ae. f. miyarai* by dengue type 2 virus was confirmed by RT-PCR 10 days' post-intrathoracic inoculation. Oral infection rates were also determined. *Ae. aegypti* mosquitoes that originated from Thailand were used as the control in both experiments. Infection rates of *Ae. f. miyarai* similar to *Ae. aegypti*, a principal vector of dengue in Thailand. In addition, there were no significant differences in mortality rates between the two species. Our data indicated that *Ae. f. miyarai* has sufficient potential to develop dengue virus in the body. So, it might be concluded that *Ae. f. miyarai* can act as a new putative member of the potential dengue vectors on Ishigaki Island, near Okinawa. ■

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A CURRENT STUDY OF *NAEGLERIA FOWLERI* IN THAILAND 2003

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Between 1988 and 2003 *Naegleria fowleri* was studied extensively in Thailand. The distribution of *N. fowleri* was studied in the following provinces: Sisa Ket, Ubol Rachathani (1988), Samut Prakarn, Lop Buri, Pathum Thani (1997), Bangkok (Taling Chan district) (2001). During 2002-2003, we received financial support from Mahidol University to survey pathogenic *Naegleria* spp. in water reservoirs in central, northern and western parts of Thailand. With these funds, research was conducted in Sara Buri, Nakhon Nayok, Nakhon Sawan, SuKho Thai, Prachuap Khirikhan, ChumPhon and SongKhla provinces. Studies indicated that pathogenic strains of *Naegleria* belong to the species *fowleri* and can be identified by external morphology, molecular weight, isoenzyme patterns and cytopathogenicity. Recent studies of the ultrastructure (1999), and of factors affecting the viability of pathogenic *Naegleria* spp. (1999) have indicated that there are similarities in the characteristics between the pathogenic reference control strain, *Naegleria fowleri* CDC VO3081 and strains isolated from Thai

patients who died from *Naegleria* infection. Since 1970 the effects of numerous drugs and chemical agents have been studied; there are continuing efforts to develop new drugs in *in vitro* and *in vivo* studies because the treatment of primary amoebic meningoencephalitis remains currently ineffective for most patients. A study of the *in vitro* effect of various antifungal drugs and the drug combination 5-fluorouracil and amphotericin B on pathogenic *Naegleria* spp. was published in 2002. It was concluded that amphotericin B in combination with ketoconazole was still the most effective treatment for pathogenic *Naegleria* spp. infection. In addition, the IC50 of this drug combination was significantly lower than that of amphotericin B and 5-fluorouracil alone ($t < 0.001$), and caused fewer side effects in patients. These results emphasize the need for prompt treatment at an adequate minimum dosage by the intrathecal route to the patient, in time to arrest the disease. Further studies using PCR to identify Thai strains of *Naegleria fowleri* are planned. ■

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STUDY ON FAUNA OF MEDICALLY IMPORTANT VECTORS AT KANCHANABURI CAMPUS, SAI YOK DISTRICT, KANCHANABURI PROVINCE

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The study was carried out throughout the year between October 2001 to September 2002 at Kanchanaburi Campus (Mahidol University) Sai Yok District, Kanchanaburi province. *Anopheles dirus* and *A. maculatus* groups, which are the main vectors of malaria in this province were caught by landing catch method. From animal (cow) bait traps, 3 species of malaria vectors were found (*A. dirus*, *A. maculatus* gr, *A. minimus*). However the breeding places of these mosquitoes were not found in the study area.

A total of 84 trapped rodents were examined for ectoparasites. Seventy percent of the trapped rodents were

Rattus rattus, and the dominant species of ectoparasites was *Lalaps nuttalli*. The majority of fly species present in the fly traps were *Chrysomya megacephala*. Among the 3 species of cockroaches collected from the trap, *P. eriplaneta americana* were more numerous than other species. More than 80% of the sand flies collected from the light trap were *Phlebotomus stantoni*.

The result shows that malaria vectors are found in the study area and near the campus there had also been reports of malaria cases every year. Further study is needed to identify the breeding places of the malaria vectors and effective methods to control the vectors at the campus. ■

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

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

revealed that the percentage reduction in mosquitoes landing at every distance increased corresponding to the increase in burning time. At 10 min, more than 60% mosquito landing reduction was found at 1 m and 2 m from the coil, while the same percentage reduction for 4 m and 7 m was observed at 15 min. When the coil had been alight for 60 min, 98% landing reduction could be achieved at every radial distance of the experiment. ■

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POLYMORPHISMS OF CD36 IN THAI MALARIA PATIENTS

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The human protein CD36 is a major endothelial receptor for *Plasmodium falciparum* parasitized erythrocytes. Several polymorphisms causing CD36 deficiency have been identified to date: T1264G in Kenyan and Gambian patients, and C478T, 539delAC, and 1159insA in Japanese patients. The T1264G polymorphism is reportedly associated with protection from severe malaria in Kenyans, although there is a contradictory report suggesting the susceptibility of T1264G to severe malaria. The polymorphism of CD36 has not been thoroughly studied in Asian malaria patients. In this study, nucleotide sequence variations in exons 4, 5, 6, and 10 of CD36 were investigated in mild and cerebral malaria patients living in northwest Thailand. A novel synonymous substitution T1168C was detected in exon 10, whereas no variation was

found in exons 4 and 6. The 539delAC allele in exon 5 was detected in Thai malaria patients, while T1264G, C478T, and 1159insA were not found. The 539delAC allele was observed in three cerebral malaria patients (3/107), but not in mild malaria patients (0/203). The frequency of 539delAC was significantly higher in cerebral malaria patients than in mild malaria patients ($p = 0.040$, Fisher's exact test). Although independent studies should be performed in order to confirm our findings, the 539delAC allele might be a high-risk variant for cerebral malaria in Thai. ■

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LACK OF ASSOCIATION BETWEEN INTERLEUKIN-10 GENE PROMOTER POLYMORPHISM, -1082G/A, AND SEVERE MALARIA IN THAILAND

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▶ **Interleukin-10** (IL-10) is an important cytokine in the down-regulation of inflammatory responses, and it has been reported that a low plasma concentration of IL-10 is associated with severe anemia and cerebral malaria in *Plasmodium falciparum* infections. The IL-10 gene is located on chromosome 1q31-32, and a promoter polymorphism (-1082G/A) is known to affect IL-10 protein production. In order to examine the possible association of the -1082G/A polymorphism with the severity of malaria, we studied 203 mild malaria, 164 non-cerebral severe malaria, and 109 cerebral

malaria patients living in northwest Thailand. The genotyping was performed by a fluorescence resonance energy transfer (FRET) method. The frequencies of a major allele -1082A in mild malaria, in non-cerebral severe malaria, and in cerebral malaria patients were 92.6%, 92.1%, and 92.7% respectively. Our results showed no significant association of the -1082G/A polymorphism with the severity of malaria. ■

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Fcγ RECEPTOR IIA AND IIIB POLYMORPHISMS ARE ASSOCIATED WITH SUSCEPTIBILITY TO CEREBRAL MALARIA

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▶ **Human** Fcγ₂RIIA and Fcγ₂RIIB exhibit genetic polymorphisms, Fcγ₂RIIA-131H/R and Fcγ₂RIIB-NA1/NA2, coding for different capacities for IgG binding and phagocytosis. Recently, Fcγ₂RIIA-131R was reported to be associated with protection against high-density *Plasmodium falciparum* infection in Kenya. Furthermore, Fcγ₂RIIB-NA1/NA2 polymorphism was shown to influence Fcγ₂RIIA function in an allele-specific manner. In this study, we examined a possible association of Fcγ₂RIIA-131H/R and Fcγ₂RIIB-NA1/NA2 polymorphisms with malaria severity in 107 cerebral malaria patients, 157 non-cerebral severe malaria patients, and 202

mild malaria controls living in northwest Thailand. This study reveals that, with the Fcγ₂RIIB-NA2 allele, the Fcγ₂RIIA-131H/H genotype is associated with susceptibility to cerebral malaria (OR 1.85, 95% CI 1.14-3.01; P=0.012), although these polymorphisms are not individually involved in the disease severity. Our results suggest that Fcγ₂RIIA-131H/R and Fcγ₂RIIB-NA1/NA2 polymorphisms have an interactive effect on host defense against malaria infection. ■

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ABSENCE OF ASSOCIATION BETWEEN THE Fc γ RECEPTOR IIIA-176F/V POLYMORPHISM AND THE SEVERITY OF MALARIA IN THAI

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▶ Human Fc γ receptor (Fc γ R) genes form a clustered gene family, which consists of Fc γ RIIA, IIB, IIC, IIIA, and IIIB genes, on chromosome 1q23. We previously reported that the Fc γ RIIA-131H/H genotype in combination with the Fc γ RIIIB-NA2 allele is associated with susceptibility to cerebral malaria, and that such an association can be caused by linkage disequilibrium (LD) between these polymorphisms and the primary associated gene(s) in this region. Fc γ RIIIA is known to exhibit the genetic polymorphism Fc γ RIIIA-176F/V coded for different affinity to IgG1 and IgG3. In this study, we examined a possible association between Fc γ RIIIA-176F/V polymorphism and severity of malaria in 462 adult Thai patients

with *Plasmodium falciparum* malaria. The frequencies of Fc γ RIIIA-176V among patients with mild malaria, with non-cerebral severe malaria, and with cerebral malaria were 32.7%, 29.9%, and 36.3%, respectively. This polymorphism showed neither positive nor negative association with the severity of malaria. Thus, we concluded that the association of Fc γ RIIA-131H/R and Fc γ RIIIB-NA1/NA2 polymorphisms with cerebral malaria in Thailand is not due to the LD caused by Fc γ RIIIA-176F/V. ■

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CD36 POLYMORPHISM IS ASSOCIATED WITH PROTECTION FROM CEREBRAL MALARIA

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▶ The human protein CD36 is a major receptor for *Plasmodium falciparum*-infected erythrocytes and contributes to the pathology of *P. falciparum* malaria. We performed variation screening of the CD36 gene and examined the possible association between CD36 polymorphisms and the severity of malaria in 475 adult Thai patients with *P. falciparum* malaria. Accordingly, we identified nine CD36 polymorphisms with a high-frequency (>15%) minor allele. Of these, the frequencies of the -14TÆC allele in the upstream promotor region and the -53GÆT allele in the downstream promotor region were significantly decreased in patients with cerebral malaria compared to those with mild malaria ($P = .016$ for -14TÆC and $P = .050$

for -53GÆT). The analysis of linkage disequilibrium (LD) between the nine common polymorphism revealed that there are two blocks with strong LD in the CD36 gene and that the -14TÆC and -53GÆT polymorphisms are within the upstream block of 35 kb from the upstream promotor to exon 8. Further association testing after the second variation screening in the upstream block indicated that the in3(TG)₁₂ (i.e., 12 TG repeats in intron 3) allele is most strongly associated with the reduction in the risk of cerebral malaria (odds ratio 0.59; 95% confidence interval 0.40-0.87; $P = .0069$). We found, by reverse-transcriptase PCR amplification, that in3(TG)₁₂ is involved in the nonproduction of the variant CD36 transcript that lacks exon 4 and 5. Since exon 5 of the gene is known to encode the ligand-binding domain for *P. falciparum*-infected erythrocytes, in3(TG)₁₂ itself or a primary variant on the haplotype with in3(TG)₁₂ may be responsible for protection from cerebral malaria in Thailand. Results of the present study suggest that

LD mapping has potential for detecting a disease-associated variant on the basis of haplotype blocks. ■

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A SINGLE NUCLEOTIDE SUBSTITUTION FROM C TO T AT POSITION -1055 IN THE *IL-13* PROMOTER IS ASSOCIATED WITH PROTECTION FROM SEVERE MALARIA IN THAILAND

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▶ **The** human chromosome 5q31-33 region contains a number of interleukin genes which play an important role in the host defense against malaria infection. We examined a possible association of single nucleotide polymorphisms (SNPs) in the promoters of *IL-3*, *IL-4* and *IL-13* genes on the 5q31-33, *IL-3*-16T>C, *IL-4*-590T>C and *IL-13*-1055C>T, with severity of malaria in 361 adult malaria patients in Thailand. The *IL-13*-1055T allele showed a significant association with protection from severe malaria (OR 0.51, 95% CI 0.32-0.80;

$p = 0.0032$ by a χ^2 test), while allele frequencies of *IL-3*-16T>C and *IL-4*-590T>C were not statistically different between mild and severe malaria patients. The *IL-13*-1055T has been reported to inhibit *IL-13* production. Thus, *IL-13*-1055T may show the resistance to severe malaria through the alteration of *IL-13* production. ■

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TRICHURIS TRICHIURA INFECTION IS ASSOCIATED WITH THE MULTIPLICITY OF *PLASMODIUM FALCIPARUM* INFECTIONS IN THAILAND

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▶ **The** cross-sectional study was performed to determine whether helminth infections had any influence on the multiplicity of *P. falciparum* (*P. f*) infection. Two hundreds and forty-seven consecutive patients who presented with microscopically confirmed *P. f* malaria were recruited. Blood samples could be investigated in a PCR-based assay to determine the multiplicity of *P. f* infection in each subject. Stool samples were collected and checked for intestinal helminth infections. There was a positive association between *Trichuris trichiura* and multiple infection of *P. f* and this association was statistically significant

even after adjusting for age and other helminths with adjusting odds ratio of 2.45 (1.14-5.22), $P = 0.014$. There also seemed to be a dose-effect trend between the intensity of the *Trichuris* infection and multiple *P. f* infection ($P = 0.06$). A linear trend between the number of *P. f* clones present in the infection and the presence of helminths was found ($P = 0.003$). It is conceivable that some immunological and/or haematological abnormality associated with *Trichuris* infection has impact on multiplicity of *P. f* infection. ■

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STORAGE DURATION AND POLYMERASE CHAIN REACTION DETECTION OF *PLASMODIUM FALCIPARUM* FROM BLOOD SPOTS ON FILTER PAPER

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▶ To evaluate the effect of long-term storage of sample filters on the sensitivity of polymerase chain reaction (PCR) detection of malaria, 252 blood spots from patients with microscopically confirmed *Plasmodium falciparum* malaria were analyzed and stratified by storage duration. The spots were collected between 1996 and 2000 on filter paper and stored at room temperature. A Chelex-based method was used to extract the DNA. Unexpectedly, after the first purification, the sensitivity of the PCR from the recently stored samples

was low and showed progressively increased with time storage, ($P=0.003$, by chi-square for linear trend). This suggested that PCR inhibitors were easier to dissolve from the more recent blood spots (<4 years old) than from blood spots 4 years old, thus leading to a time-dependent increase in PCR sensitivity. However, if DNA was purified again (when the first PCR result was negative), the cumulative sensitivity was not influenced by storage duration. This indicated that length of storage is not a critical issue providing purification is sufficient. ■

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INTRAGENIC POLYMORPHISMS OF MACROPHAGE INFLAMMATORY PROTEIN-1 ALPHA (MIP-1 α) DOES NOT CONTRIBUTE TO SEVERITY OF MALARIA IN THE THAI POPULATION

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▶ Human macrophage inflammatory protein-1 alpha (MIP-1 α) is a chemotactic cytokine, mainly produced by CD8⁺ T cells. MIP-1 α acts on chemokine receptor CCR1 and CCR5 that expressed on macrophage, T cells and B cells affecting their activation that involve in the immune response to malaria. Previously, MIP-1 α has been characterized and demonstrated to have 4 single nucleotide polymorphisms (SNPs) in Japanese population : C to T at position 954 in exon 2 ; A to G at position 1245 in intron 2 ; C to G at position 1728 and A to G at position 1771 in exon 3. In order to investigate the association of these SNPs with severity of malaria in Thai population, we performed typing of polymorphisms in MIP-1 α between 3 groups of adult Thai malaria patients; mild, non-cerebral severe malaria and cerebral malaria. As a result, we found no significant difference in the allele frequencies at all 4 position examined

among 3 groups of the patients by chi square test ($p > 0.05$). However, a novel type of polymorphism was found in Thai population. This polymorphism was due to a gene conversion of a new 10 bp sequence (CCCTGCCTG) replace the old 9 bp (ACCCCTACT) at position 1210 to 1219. Additionally, we also analyze frequencies of haplotype of MIP-1 α comprising these 5 polymorphic sites. There were no significant association of these haplotypes with severity of malaria. In conclusion, as far as 4 polymorphic SNPs and 1 polymorphic site conversion in MIP-1 α were analyzed, it seems that they were not associated and responsible for severe form of malaria. ■

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LACK OF ASSOCIATION OF +874T/A INTERFERON GAMMA GENE POLYMORPHISM AND SEVERE OR CEREBRAL MALARIA IN THAILAND

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▶ **Gamma** interferon (IFN- γ) is an important cytokine produced mainly by CD8⁺ and CD4⁺ T cells and its primary action is on the activation of macrophages involved in innate immune response to malaria. The *IFN-g* gene is located on chromosome 12q24.1 and a first intron polymorphism(+874T/A) is known to coincides with a putative NF-kappa B binding site which might have functional consequences for the transcription of the human *IFN-g* gene. In this study, single nucleotide polymorphism of *IFN-g* was investigated for possible association with severe or cerebral malaria in adult Thai patients infected with *P.falciparum*. Two hundred and two mild, 165 non-cerebral severe, and 108 cerebral malaria were recruited in the study. The genotyping was done by PCR-SSP method.

Consequently, frequencies of a major allele +874A in mild malaria, in non-cerebral severe malaria, and cerebral malaria patients were 62.9%, 63.6% and 66.7% respectively. Our results showed no significant association of the +874T/A polymorphism with the severity of malaria by chi-square test ($P>0.05$). Nonetheless, association of *IFN-g* gene with severe or cerebral malaria might be contributed by other polymorphic region of the gene. Analysis of polymorphism at the promoter region is now underway. ■

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POLYMORPHISMS IN β -GLOBIN GENE IN THAI MALARIA PATIENTS

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▶ **Hemoglobin E** (E26K) is commonly observed in parts of Southeast Asia such as Cambodia, Thailand, and Myanmar, regardless of the homozygote hematologic disadvantage. The plausible explanation for this is that the heterozygote individuals have the advantage of protection from malaria infection as suggested by J.B.S. Haldane. However, laboratory and epidemiologic studies have given contradictory results as for the protective role of E26K in malaria infection. Recently, E26K was reported to be protective against high parasitemias or severe *P.falciparum* malaria, suggesting that E26K is associated with protection from severe malaria rather than from malaria infection. In order to examine whether there are other polymorphisms associated with severe malaria, we performed variation screening

for exon 1 of β -globin gene in 64 adult *Plasmodium falciparum* malaria patients (32 mild malaria and 32 cerebral malaria), living in northwest Thailand. Accordingly, we identified 59C>T, E26K, 102A>T, and IVS+1G>T polymorphisms in Thai malaria patients. Of which, 59C>T, and IVS+1G>T are novel polymorphisms, and IVS+1G>T lies on the splice donor site. 102A>T is a stop mutation causing β -thalassemia. We will describe results from association test for these four polymorphisms in 197 mild and 108 cerebral malaria patients. ■

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A POSSIBLE ASSOCIATION BETWEEN FCG RECEPTOR POLYMORPHISMS AND SEVERITY OF MALARIA IN THAILAND

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▶ Human Fcγ receptor (FCGR) genes form a clustered gene family on chromosome 1q23, that consists of *FCGR1A*, *I1B*, *I1C*, *I1A*, and *I1B* genes. We previously reported that the *FCGR1A-131H/H* genotype with combination with the *FCGR11B-NA2* allele is associated with susceptibility to cerebral malaria, while such an association can be caused by linkage disequilibrium (LD) between these polymorphisms and the primary associated gene(s) in this region. *FCGR11A* is known to exhibit genetic polymorphism, *FCGR11A-176F/V*, coding for different affinity to IgG1 and IgG3. In this study, we examined a possible association of *FCGR11A-176F/V* polymorphism with the severity of malaria in 462 adult Thai

patients with *Plasmodium falciparum* malaria. The frequencies of the *FCGR11A-176V* among patients with mild malaria, with non-cerebral severe malaria, and with cerebral malaria were 32.7%, 29.9%, and 36.3% respectively. This polymorphism showed neither positive nor negative association with the severity of malaria. Thus, we concluded that the association of *FCGR11A-131H/R* and *FCGR11B-NA1/NA2* polymorphisms with cerebral malaria in Thailand is not due to the LD with *FCGR11A-176F/V*. ■

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PCR DIAGNOSIS OF LEPTOSPIROSIS BASED ON GENES FROM THE *rfb* LOCUS

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▶ In the PCR diagnosis of Leptospirosis, only a few oligoprimers have been published. The oligoprimers derived from the 5' end of Leptospiral 16S rRNA have been claimed to be specific for *Leptospira* species. When these primers were tested with other bacterial genomic DNA, they cross-reacted with other bacteria. Thus, the primers derived from 5' end 16S rRNA should not be used for diagnosis. The *rfb* genes are involved in LPS O-Antigen biosynthesis. These *orf*s are likely to be conserved among *Leptospira* spp. We designed nested-PCR primers from some unique genes that included the glycosyl transferase gene (*orf33*), putative transporter gene (*orf31*), the transmembrane protein gene (*orf14*) and *orf17* of unknown function. These genes possess less similarity to protein of other species in the genome database as determined by BLAST searches. Nested

PCR primers derived from all these selected *orf*s were shown to cross-react with a few bacteria. However, it was decided to work on *orf14* that encoded O-Ag polymerase and is reported to be the unique gene for each enteric bacteria. In addition, primers designed from *orf14* were able to detect most members of *Leptospira* spp. Attempts were made to adjust the PCR conditions to prevent cross-reaction with other bacteria. The first round PCR annealing temperature was set at 55°C, while the second round PCR, annealing temperature was increased from 55°C to 62°C. We used our assay to test paired serum from 27 patients who were MAT positive. Fifty-one serum specimens were used for extraction of DNA and this DNA was subjected to nested PCR and Southern Hybridization procedure. Comparison of MAT results as a gold standard comparator with our PCR assay demonstrated a sensitivity of 66.6%, with specificity was 25.0% when using Mc Nemar analysis. ■

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

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Competitive ELISA using a combination of monoclonal antibodies specific to vitellin subunits was used to monitor the fluctuation of haemolymph vitellogenin levels in *Penaeus monodon* during ovarian development induced by bilateral eyestalk-ablation and to monitor the effect of eyestalk extract injection in prawn with developing ovary. The haemolymph vitellogenin levels were undetectable in the prawn with ovary at the resting stage but elevated sharply when the ovary began to develop, remained high during the ovary developing into ripe stage then fell to the low

levels before spawning and spent stages. The result from injection of eyestalk extract into prawn with developing ovary revealed that haemolymph vitellogenin levels elevated sharply within 2 hr, reached the maximal levels and remained high during 4-10 hr, then declined slightly at 24 hr. This response directly depended on the amount of injected eyestalk extract and the response was species specific. The application of eyestalk extract from *Metapenaeus affinis* demonstrated the same stimulatory effect but was less potent whereas the eyestalk extract from *Macrobrachium rosenbergii* did not cause any changes in haemolymph vitellogenin levels. Therefore, the assay is specific and provides an indicator to monitor the activity of the putative gonad inhibiting hormone by assaying the alteration of vitellogenin levels. ■

GEOGRAPHIC DIVERSITY AMONG GENOTYPES OF *ENTAMOEBIA HISTOLYTICA* FIELD ISOLATES

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It has been known that only 5 to 10% of those infected with *Entamoeba histolytica* develop symptomatic disease. However, the parasite and the host factors that determine the onset of disease remain undetermined. Molecular typing by using polymorphic genetic loci has been proven to aid in the close examination of the population structure of *E. histolytica* field isolates in nature. In the present study, we analyzed the genetic polymorphisms of two noncoding loci (locus 1-2 and locus 5-6) and two protein-coding loci (chitinase and serine-rich *E. histolytica* protein [SREHP]) among 79 isolates obtained from different geographic regions, mainly Japan, Thailand, and Bangladesh. When the genotypes of the four loci were combined for all isolates that we have analyzed so far (overlapping isolates from mass infection events were excluded), a total of 53 different genotypes were observed

among 63 isolates. The most remarkable and extensive variations among the four loci was found in the SREHP locus; i.e., 34 different genotypes were observed among 52 isolates. These results demonstrate that *E. histolytica* has an extremely complex genetic structure independent of geographic location. Our results also show that, despite the proposed transmission of other sexually transmitted diseases, including human immunodeficiency virus infection, from Thailand to Japan, the spectra of the genotypes of the *E. histolytica* isolates from these two countries are distinct, suggesting that the major *E. histolytica* strains prevalent in Japan at present were likely introduced from countries other than Thailand. Although the genetic polymorphism of the SREHP locus was previously suggested to be closely associated with the clinical presentation, e.g., colitis or dysentery and liver abscess, no association between the clinical presentation and the SREHP genotype at either the nucleotide or the predicted amino acid level was demonstrated. ■

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IMMUNITY TO AMOEBIC INFECTIONS

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▶ **Amoebic** encephalitis is caused by at least five genera of amoeba including four genera of free-living amoeba (FLA), *Naegleria fowleri*, *Acanthamoeba* spp., *Balamuthia mandrillaris*, *Sappinia diploidea* and one genus of parasitic *Entamoeba histolytica*. In addition, contact lens wear is the leading risk factors for *Acanthamoeba* keratitis and *E. histolytica* also causes dysentery and amoebic liver abscess (ALA) in humans. Moreover, *Parachlamydia acantamoeba* as well as *E. gingivalis* are reported to be etiologic agents of pneumonia and periodontitis, respectively. Immunity to these amoebae is the subject of this review.

Immunity to *E. histolytica* is associated with the intestinal mucosal IgA response against the carbohydrate-recognition domain of the Gal/GalNAc lectin heavy subunit. The portion of cysteine-rich LC3, one main epitopes on the lectin is associated with the induction of humoral IgA and IgG immunity in asymptomatic as well as in ALA patients where acute disease is associated with suppression of cell-mediated immunity (CMI). The antibody responses to innate and acquired immunity indicates a role for CD4+ T cells in protection. Therefore, both innate and acquired immune responses limit infection.

In community, naturally acquired immunity to *N. fowleri*, *Acanthamoeba* spp. and *B. mandrillaris* plays an important role in restricting the number of cases of PAM and GAE. However, some healthy children may lack immunity to *B. mandrillaris*. Passive immunity in mice to *N. fowleri* infection shows a suppression of cell-mediated immunity during the acute course of meningoencephalitis and the transfer of splenocytes from immunized mice confers immunity against *N. fowleri*. Secretory IgA antibodies are able to inhibit amoeba adherence to collagen type I and pathogenic *N. fowleri* are resistant to lytic effects of serum complement. Innate immune elements, macrophages and neutrophils, are able to kill the cysts of *A. castellanii* by phagocytosis and by the secretion of myeloperoxidase (MPO), respectively. Anti-Acanthamoebic IgA antibodies inhibit amoeba adhesin i.e. mannose-binding protein (MBP) to host corneal epithelial cells as well as block the secretion of cytotoxic proteases and play a crucial role in macrophage-mediated complement lysis and providing protection against *Acanthamoeba* keratitis in *in vivo* model. So far, study of immunity to *Sappinia diploidea*, *Parachlamydia acantamoeba* and *E. gingivalis* are scanty. ■

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AMOEBIC ANTIGENS IN IMMUNODIAGNOSIS OF AMOEBIC LIVER ABSCESS

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▶ **An** enzyme immuno-assay for the rapid detection of the *Entamoeba histolytica* adhesin in liver human pus specimens was tested and the results were compared with the Drbohlar's Lock egg medium culture technique. There were 11

specimens from a total of 18 patients' pus (14 males and 4 females) which showed *Entamoeba histolytica* by culture. The adhesin of *E. histolytica* can be identified in 9 of these 11 positive cultivation specimens. The remaining 7 of 18 specimens in this study were negative by culture but there was one specimen of all the negative by culture gave positive by adhesin detection. Compared with culture analysis, the adhesin detection exhibits sensitivity and specificity of 81.8% and 100%, respectively. ■

RESTORATION AND LOSS OF VIRULENCE OF *ENTAMOEBIA HISTOLYTICA* AFTER PROLONGED CULTIVATION *IN VITRO*

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▶ It is generally accepted that originally virulent strains of *Entamoeba histolytica* on prolonged cultivation *in vitro*, become avirulent or noninvasive when inoculated into the ceca of rats and guinea pigs or into the livers of hamsters. Certain manipulations could restore the virulence of an attenuated strain in culture. Among these are cholesterol treatment and hamster liver passage. The present study aimed at restoring virulence after 5 years in axenic culture of *E. histolytica* strain HM-1:IMSS, 4+ years in axenic culture of *E. histolytica* strain HTH-56:MUTM and 1 month in monoxenic culture of strain HTH-68:MUTM by giving prednisolone orally to the animals and then followed by liver passage of amoebae, by liver passage

of amoebae together with *Crithidia luciliae*, and by liver passage of monoxenic amoebae to the hamsters, respectively. Results of our experiments clearly indicated that virulence could be revived by so doing with success rates of abscess formation of 52%, 100% and 100%, respectively. In contrast, the failure to restore the virulence of amoebae cultured *in vitro* for > 6 years in substrain HM-1:IMSS and in unmanipulated HTH-56:MUTM strain cultured *in vitro* for > 4 years occurred even by cholesterol treatment, liver passage in baby hamsters or splenectomy in the former and liver passage in the latter. The p15 line of *E. histolytica* strain HM-1:IMSS which had been periodically passed through the liver of hamsters to maintain its virulence served as positive control for abscess formation. To our knowledge, we suggest that periodic hamster liver passage offers the best method of restoring and maintaining the virulence of *E. histolytica* grown in axenic culture. ■

Presented at: EMBO Workshop on "Pathogenesis of amoebiasis from genomics to disease", Pasteur Institute, Paris, France, May 19-21, 2003. Program and Abstract p. 61.

ANTIAMOEBCIC ACTIVITY OF SOME MEDICINAL PLANTS USED BY AIDS PATIENTS IN SOUTHERN THAILAND

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▶ The antiamoebic activity of chloroform, methanol and water extracts from 12 Thai medicinal plants commonly used by AIDS patients in Southern Thailand were tested against *Entamoeba histolytica* strain HTH-56: MUTM *in vitro*. The extracts, at a concentration of 1,000 mg/ml, were incubated in triplicate with the trophozoites of *E. histolytica* for 24 hour

in 96 well plate and the results. were examined under inverted microscope. Chloroform extracts from *Piper retrofractum*, *Barleria lupulina*, *Murraya paniculata*, *Piper betle*, *Languas galanga* and *Zingiber zerumbet*, and chloroform and methanol extracts from *Boesenbergia rotunda* highly inhibited the growth of *E. histolytica*. The minimal inhibitory concentration (MIC) of a standard drug, metronidazole, against this strain of *E. histolytica* was 5 mg/ml. ■

Presented at: EMBO Workshop on "Pathogenesis of amoebiasis from genomics to disease", Pasteur Institute, Paris, France, May 19-21, 2003. Program and Abstract p. 69.

VIRULENCE GENES OF *VIBRIO CHOLERAE* THAILAND ISOLATES

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Background : Cholera, a severe diarrheal disease of man, is caused by a Gram-negative bacterium named *Vibrio cholerae*. The disease is endemic in Southern Asian countries including Thailand, parts of Africa and Latin America. Previous molecular analysis of epidemic isolates of *V. cholerae* revealed clonal diversity among strains during different epidemics. It was proposed that there had been a continual emergence of new clones of toxigenic *V. cholerae* which replaced existing clones, possibly through natural selection involving unidentified environmental factors and immunity of the host population.

Objective and Methodology : This study was aimed at determining the presence of virulence genes of *V. Cholerae* O1 strains isolated from patients with severe diarrhea from various endemic areas in Thailand during 2001-2002 and compare with those isolated during 1999-2000 by using the

specific primers in the polymerase chain reaction (PCR) or multiplex PCR. These genes included *ctxAB*, *zot*, *ace*, *toxR*, and *tcpA*. Eighty-five *V. cholerae* serogroup O1 strains were isolated during March 1999 to April 2000 and December 2001 to February 2002. Seventeen standard *V. cholerae* strains, *i.e.* a Thai O1 strain isolated in 1990 and a Thai O139 strain isolated in 1993 and fifteen O1 and O139 strains were also included. Additionally, the genetic heterogeneity among the two groups of the *V. cholerae* O1 isolates were studied and compared by pulse-field gel electrophoresis (PFGE.)

Results and conclusion : The present study revealed that most of organisms possessed the virulent determinants. Additionally, the differences in the PFGE banding patterns could be used for the epidemiological tracing of the organisms. It was interesting to note that certain provinces had limited number of the pattern variation whereas others had a wider pattern variation. These numbers of the patterns found in the different provinces may reflect the transmission of different strains/clones of the organism at certain period of time. ■

(Funded by: The work was financially supported by the Japan Health Science Foundation and the Thailand Research Fund (TRF)).

Published in: "The 10th Asian Conference on Diarrhoeal Diseases and Nutrition", (7-10 December 2003) Dhaka, Bangladesh.

RECOMBINANT AMERICAN COCKROACH COMPONENT, PER A 1, REACTIVE TO IGE OF ALLERGIC THAI PATIENTS

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Twelve similar recombinant Per a 1 clones were produced from an American cockroach (CR) cDNA library. The nucleotide sequence of a representative clone, *i.e.* clone A6, contained 579 base pairs (bp) and a 372 bp open reading frame (2-373) encoding 124 amino acids. A stop codon was found at position 374-376 followed by a 3' end untranslated region with an AATAAA polyadenylation signal and a poly (A) tail. The estimated molecular mass of the 24 amino acid residue protein was 13.8 kDa, with a predicted isoelectric point value of 4.74. Cysteine or N-linked glycosylation was not found. The deduced

amino acid sequence of the A6 revealed 84.68-95.97% identity to other previously reported Per a 1 clones and 65.87-69.60% homology to the previously reported Bla g 1 clones. However, while previously reported Per a 1 clones showed homology to ANG12, a precursor protein in the midgut of the female *Anopheles gambiae* secreted after the blood meal, the A6 DNA sequence was found to have homology (37.1 %) to DNA of G2, a putative protein in the midgut of *Aedes aegypti* (AY 050565). The deduced amino acid sequence of A6 contained a mitochondrial energy transfer protein signature, phosphorylation

sites for the cAMP- and cGMP-dependent protein kinase C and casein kinase II. Hydrophobic and hydrophilic characteristics of the A6 deduced peptide indicated that it was a transmembrane protein. This is the first report that Per a 1 is a transmembrane protein. The deduced amino acid sequence of the A6, which contained the sequence LIRSLFGLP, differed in one amino acid from two previously reported epitopes, i.e. LIRALFGL and IRSWFGLP, of Per a 1.0104 which bound 80% and 100%,

respectively, to IgE of the allergic patients tested. The A6 DNA sequence was deposited in the GenBank (Accession number AY 259514) and has been designated Per a 1.0105. The A6 expressed protein bound to monoclonal antibodies (MAb 3C2) specific to American cockroach and also bound to IgE of all (100%) of the 20 allergic Thai patients ■

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PLASMODIUM FALCIPARUM: EFFECT OF ANTI-MALARIAL DRUGS ON THE PRODUCTION AND SECRETION CHARACTERISTICS OF HISTIDINE-RICH PROTEIN II

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▶ **Plasmodium falciparum** histidine-rich protein II (HRP2) is one of the best documented malaria proteins. However, little is known about the development of HRP2 concentrations under the influence of anti-malarial drugs. HRP2 levels were determined in cell medium mixture, cellular compartment, and in culture supernatant using a double-site sandwich ELISA specific for HRP2. Characteristic increases in the overall HRP2 levels were found during the later ring and

the trophozoite stages. Throughout the later schizont development, rupture, and reinvasion, however, the HRP2 levels remained comparatively stable. When the cultures were exposed to serial dilutions of anti-malarial drugs, a distinct inhibition of HRP2 production was seen with increasing concentrations of drugs, resulting in sigmoid dose-response curves, similar to those obtained from conventional drug sensitivity assays. HRP2 therefore allows for a very accurate estimation of parasite development and its inhibition and may therefore be ideally suited for use in drug sensitivity or bioassays. ■

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

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

coding region at the 3' end of dengue viral RNA, and was used in the NASBA assay. The NASBA reaction product was then determined by agarose gel electrophoresis and electrochemiluminescence (ECL) signal count. The sensitivity of the NASBA assay was equal to 1 PFU/ml for all of four dengue virus serotypes. There was no false positive result with Japanese encephalitis virus. This method was used successfully to detect dengue virus in the infected tissue culture cell. This test will be useful for detection of dengue viruses in the clinical specimens. ■

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PREVALENCE OF LOWER GENITAL TRACT INFECTION AMONG WOMEN ATTENDING MATERNAL AND CHILD HEALTH AND FAMILY PLANNING CLINICS IN HANOI, VIETNAM

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To determine the prevalence of lower genital tract infection (LGTI) with *Candida* spp, *Trichomonas vaginalis*, *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, and bacterial vaginosis among symptomatic and asymptomatic women attending maternal and child health and family planning (MCH/FP) clinics in Hanoi, Vietnam. A multi-centered, cross-sectional descriptive study stratified by reported symptoms of vaginal discharge was carried out in three MCH/FP clinics among 1,000 women aged 18-44 years in 1998. Of these, 89.1% lived in Hanoi, 97.6% were currently married, and 99.2% had only one sexual partner in the past 12 months. Regarding

their contraceptive use, 28.2% did not use any contraception, 25.6% used an intrauterine device (IUD), 22.8% used condoms, and 23.4% used other methods. The overall prevalence of *Candida* spp was 11.1% (95% CI = 9.1-13.1 %); *T. vaginalis*, 1.3% (95% CI = 0.6-2.0%); no gonococcal infection was found; the prevalence of *C. trachomatis* was 4.4% (95% CI = 3.1-5.7%); and of bacterial vaginosis, 3.5% (95% CI = 2.4-4.6%). The presence of LGTI was not associated with reported symptom of vaginal discharge. LGTI was common among married and monogamous women attending MCH/FP clinics in Hanoi, of whom many used IUDs and may have an increased risk of complications in the presence of LGTI. The lack of association between symptoms and laboratory-confirmed infection underscores the challenge of diagnosing LGTI when laboratory testing is not available. ■

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THE USE OF FLOW CYTOMETRY AS A DIAGNOSTIC TEST FOR MALARIA PARASITES

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A total of 453 clinical blood samples were determined for malaria parasites by flow cytometric assay (FCM) and reagents from Sysmex Corporation, Japan. In this study, the FCM greatly simplified and accelerated parasite detection, with a sensitivity of 91.26%, specificity of 86.28% and accuracy of 87.42%. Overall, the parasite counts by flow cytometric measurement correlated well with the parasitemia measured by microscopic assay

(regression coefficient = 0.9409). The detection limit was 0.05-0.1% parasitemia. No evidence of malaria parasites in both blood donor volunteers or other disease patients groups was determined by FCM. However, there were 48 samples, who had been treated with antimalarial drugs and whose parasite microscopic counts were negative, who showed false-positive results. When the data of these 48 samples were analyzed, they were found to have high levels of reticulocytes, ranging from 2.0-18.9%. This finding suggested that a high reticulocyte concentration in the blood may interfere with the performance of the FCM. Further improvement, by eliminating this interference, will make the FCM one of the most promising tests for malaria diagnosis. ■

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

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Nucleic acid sequence-based amplification (NASBA) was employing a set of universal primers and probe based on the 3' non-coding region of dengue viral RNA sequence. NASBA was used for detection of the viral RNA in sera of patients clinically diagnosed of having dengue virus infection, and compared it with polymerase chain reaction (PCR). NASBA is an enzymatic amplification reaction, which using three enzymes: avian myeloblastosis virus-reverse transcriptase

(AMV-RT), RNase-H and T7-RNA polymerase for the continuous amplification of nucleic acids in a single mixture at isothermal temperature (usually at 41°C). Fifty-four acute sera were obtained from patients suspected of having dengue virus infection. There were 27 (50%) samples gave the positive result for both of NASBA and PCR, and 26 (48.15%) samples gave the negative result for both of NASBA and PCR. There was only one (1.85%) sample that gave false positive result with NASBA and no false negative result was found in this study. NASBA gave 100% sensitivity, 96.30% specificity and 98.15% efficacy, respectively. NASBA will be useful in early detection of acute dengue virus infection and the molecular study. ■

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

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Hybridomas secreting specific monoclonal antibodies (MAb) to all members of the genus *Leptospira* (clone LF9) and those that are specific only to the pathogenic species (clones LD5 and LEI) were produced. MAb LF9, which was immunoglobulin G1 (IgG1), reacted to a 38-kDa component of the sodium dodecyl sulfate-polyacrylamide gel electrophoresis-separated whole-cell lysates of all *Leptospira* spp., while MAb LD5 and MAb LEI,

which were IgG1 and IgG2a, respectively, reacted to the 35- to 36-kDa components of all serogroups of the pathogenic species of *Leptospira*. The MAb LD5 was used in a dot blot-enzyme-linked immunosorbent assay (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 assay, indirect immunofluorescence assay (IFA), and/or microscopic agglutination test (MAT). Urine samples of 26 patients diagnosed with 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 test, IFA, and MAT were positive for 69.4, 70.0, and 85.7% of patients, while the *Leptospira* antigenuria tested by the MAb-based dot-ELISA was positive for 75.0, 88.9, 97.2, 97.2, and 100% of patients on days 1, 2, 3, 7, and 14 of hospitalization, respectively. All but 1 of

11 patients whose serum samples collected on the first day of hospitalization were IgM seronegative, were positive by urine antigen test on day 1. This is strong evidence that detection of antigen in urine can provide diagnostic information that could be useful in directing early therapeutic intervention. The 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, and the *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 the 120 healthy controls. The reasons for this positivity are discussed. The detection of antigen in urine by the monoclonal antibody-based dot-ELISA has high potential for rapid, sensitive, and specific diagnosis of leptospirosis at a low cost. ■

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

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

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

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

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▶ **Experimental** longitudinal studies on intestinal protozoa infestation in 972 Thai school children were performed with the purpose of comparison the result of treatment between anti-parasitic drug alone and drug combined with health education. Infection rate before intervention was 6.4%. Proper anti-parasitic drugs were given to the positive cases in control group as well as drugs combined

with health education provided to children in the experimental group. The re-infection rate was 4.2% in control group, whilst it was 3.2% in experimental group. The result of treatment between the two groups was not statistically significantly different ($p=0.54$). ■

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HEALTH EDUCATION: AN ADJUVANT TREATMENT OF ENTEROBIASIS IN SCHOOL STUDENTS IN THAILAND

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▶ **Enterobiasis** infection is a worldwide epidemic, particularly prevalent in low-income areas, which re-infection is always determined. Health education as well as medical treatment was compared with medical treatment alone in 777 school children in suburb of Bangkok with the objective of whether health education could be an adjuvant treatment for reducing the re-infection rate of enterobiasis.

The students in schools which received supplemental education was shown to decrease from 18.03 % (77/427) to 8.66% (37/427) with an unre-infection rate of 80.5 % (62/77). The students in schools which received medical treatment

only were also examined. In these subjects the infection rate decreased from 21.42 % (75/350) to 19.43% (68/350) with an unre-infection rate of 50.7 % (38/75). As evident in this study there were significant differences between the two approaches. The study shows that education plays a key role in the prevention of infection. The Samut Prakan branch of Thailand's Ministry of Health conducted the first large-scale treatment for enterobiasis infections in school students. "Population health" that is able to target high risk individuals may be a cost effective way to allocate limited funds. Perhaps this type of approach and further study on the correlation of symptoms with infection may offer a comprehensive strategy to the enterobiasis dilemma. ■

Keywords: Education treatment, Enterobiasis, *Enterobius vermicularis*

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PATHOLOGIC STUDY OF ACUTE TOXOPLASMOSIS IN EXPERIMENTAL ANIMALS

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▶ **We** studied the pathology of acute toxoplasma in experimental mice inoculated with RH strain tachyzoites of *Toxoplasma gondii*. All died from severe disseminated toxoplasmosis involving the liver, spleen and pancreas.

Pathological features of acute toxoplasmosis in susceptible mice could be regarded as an excellent model for acute reactivation of toxoplasma in immunosuppressed host. ■

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TOXOPLASMA GONDII ANTIBODY IN THAI CATS AND THEIR OWNERS

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▶ **Humans** are thought to acquire *Toxoplasma* infection by three major routes; ingesting food and water contaminated

with oocysts from cat excreta, consumption of under-cooked infected meat, and transplacental transfer. Congenital clinical toxoplasmosis in the newborn indicating definite transplacental transmission had been reported in Thailand, whilst studies concerning infection due to other two routes were inconclusive. Since the way domestic cats live and eat and also the eating

behaviour of Thai people differ from those in the West, we conducted a sero-epidemiological study of *T. gondii* in cats and their owners in Bangkok metropolitan area. Among 327 humans, the prevalence of *Toxoplasma* antibody was 6.4 % and it was 7.3% in 315 cats. These relatively low prevalences may result from the predominantly well-cooked fish and rice diet of stray cats, which congregate in temples where they are fed. *Toxoplasma* antibody seropositivity was associated with living

in close proximity to seropositivity cats [OR (95% CI) = 5.43 (1.28-23.04); p=0.01]. Risks were increased in and around temples, particularly if courtyards were of earth or grass suggesting ground temperature was an important determinant of oocyst survival. ■

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CLINICAL TOXOPLASMOSIS: DIAGNOSTIC UPDATE

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▶ **Toxoplasma** infection is usually asymptomatic in the normal host, but life threatening clinical disorders, often due to central nervous system (CNS) involvement from reactivation of latent infection is common in immunocompromised individuals. Congenital toxoplasmosis, though rare, nevertheless is a health and economic burden. Early correct diagnosis is therefore important.

Laboratory diagnosis for congenital toxoplasmosis relies mainly on demonstrating serum specific antibodies and isolation of *T. gondii* DNA from amniotic fluid.

For suspected CNS toxoplasmosis in AIDS patients, computerized tomography (CT) and magnetic resonance imaging (MRI) are preliminary diagnostic tools for clinicians, although, neuroimaging often cannot differentiate cerebral toxoplasmosis from other tumors such as lymphoma. Positron emission tomography (PET) scanning, which could give more

exactly diagnosis, is costly and not readily available at present.

Serum and intrathecal *T. gondii* antibody is almost always low and parasite isolation from blood and cerebrospinal fluid (CSF) is successful in less than 40% of CNS toxoplasmosis cases. Brain biopsy is often impracticable, although, direct tissue staining with hematoxyline-eosin and enhanced by immunocytochemistry could apply.

DNA-amplification-based technique greatly contributes to the improvement of toxoplasmosis diagnosis. Polymerase chain reaction (PCR) on blood as a single test is not sensitive, but CSF PCR has a higher sensitivity (20-100%) and specificity (90-100%). Repeated testing and combining both CSF and blood PCR enhance the sensitivity. Stage-specific oligonucleotide primers provide an effective laboratory diagnosis of reactivation toxoplasmosis encephalitis in patient with AIDS. ■

Presented in: Joint International Tropical Medicine Meeting, Bangkok, 2-4 December 2003.

IDENTIFICATION OF HUMAN MALARIA PARASITES AND DETECTION OF MIXED INFECTION IN THAI PATIENTS BY NESTED PCR

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▶ **The** species-specific nested PCR previously described by Snounou and others for detecting the four species of human malaria parasites is evaluated in the current study testing 40 blood samples from malaria patients admitted during July-September, 2003 at the Hospital for Tropical Diseases, Faculty

of Tropical Medicine, Mahidol University, Thailand. Parasite DNA of each blood sample was extracted and purified by using QIAmp DNA blood kits. The nested PCR was performed by using genus-specific primers for the first PCR cycle and species-specific primers for the second cycle. Thin and thick smears were also made, stained with Giemsa and examined by expert microscopists. Only one out of 40 samples (2.5%) was identified as *Plasmodium malariae* infection by both microscopy and nested PCR. Twenty blood samples (50%) were identified as

Plasmodium falciparum infection by both methods. However, 19 blood samples (47.5%) were reported as *Plasmodium vivax* infections by microscopic method whereas nested PCR could detect a mixed infection of *Plasmodium vivax* and *Plasmodium falciparum* in one sample which taken from a young girl with 8 trophozoites of *P. vivax*/200 white blood cells. These results demonstrated that the nested PCR assay surpasses microscopy

and also offers a clear advantage in the detection of mixed infections, which is important not only for successful medical treatment but also for the study of malaria epidemiology. ■

Poster presentation in 4th Seminar on Food-and water-borne Parasitic Zoonoses 2nd International Meeting on Gnathostomiasis Joint International Tropical Medicine Meeting 2003.

METHOD FOR DETECTING PROTOZOAL CONTAMINATION OF WATER USED IN THAI FROZEN FOOD INDUSTRY

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▶ **Water** is involved in most food preparation and processing operations. Unsafe water, whether the result of direct contamination or improper treatment, may result in a contaminated food product. Protozoan cysts and oocysts occur in low numbers in the aquatic environment; therefore, large volume of water need to be analyzed.

We, proposed a method for detecting protozoan contamination of water used in the Thai frozen food industry. We collected 1,000 liters of both raw and treated water by filtration through a 1-micrometer nominal porosity activated

carbon block filter. Water samples were eluted by Tween 80 solution and sucrose concentration was accomplished. Identification of protozoa parasites was performed by specific monoclonal antibody to *Giardia*, *Cryptosporidium* and *Giardia/Cryptosporidium*, and then the fluorescence technique was applied. The results were accurate and easy to read. The advantage of this method is that it can detect low concentrations of protozoal contamination in several types of water, which can be used in the routine laboratory or frozen food industry. ■

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Presented as a Poster Presentations at Joint International Tropical Medicine Meeting, Bangkok, 2-4 December 2003.

COMPARISON OF INDIRECT IMMUNOFLOUORESCENT ANTIBODY TEST AND THE SABIN-FELDMAN DYE TEST FOR DETECTION OF *TOXOPLASMA GONDII* ANTIBODY IN THAI PREGNANT WOMEN

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▶ **Toxoplasmosis** is world-wide infection in human. It is usually asymptomatic in individuals, but it causes serious problems in fetus and immunocompromised host such as HIV infected person and organ transplant recipient, The Sabin-Feldman dye test is use to detect *Toxoplasma* antibodies. Although it is the gold standard test, but it needs the life parasites and accessory factor which is hard to perform. It is not common and easy to offer in a small laboratory. Alternative tests are needed, indirect fluorescent antibody test (IFAT) is the selective test in this study to determine the specific Ig G antibody for *Toxoplasma gondii* in Thai pregnant women.

Blood samples were collected from 300 Thai pregnant women, from March to May 2003, who come on the first visit at antenatal clinic of Rajavithi hospital.

The result of antibody measurement from indirect fluorescent test showed high sensitivity and high specificity and positive correlation when compared with the gold standard test, Sabin-Feldman dye test. IFAT is not time consuming, easy to perform and formalin-fixed whole antigens can keep for a long time. IFAT therefore, recommended as a selective test which used in laboratories that can not perform the Sabin-Feldman dye test. ■

Presented as a Poster Presentations at Joint International Tropical Medicine Meeting, Bangkok, 2-4 December 2003.

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

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▶ **The** study described development of *Cryptosporidium parvum* in MDCK, MA-104, Hep-2 and Vero cell lines. Differences of susceptibility, infectivity, and methodology of excystation were determined. Various solutions were adjusted to determine the factors, which enhanced the excystation *e.g.* with and without sodium hypochlorite, trypsin or sodium taurocholate. It was shown that the sporozoites could be excysted in media either with or without trypsin and sodium taurocholate but the number of sporozoites in the latter solution was less than the former one. Only digested oocysts by sodium hypochlorite and trypsin could enter the culture cells. Numerous meronts and oocysts were demonstrated and

persisted for 9 days. Asexual stages could not be observed in MA-104. Only few oocysts could be detected during 1-3 day post inoculations. There was a significant difference between the number of oocysts, which invaded MDCK, MA-104, and Hep-2 cells. MDCK gave the highest susceptibility to oocyst invasion among three cell lines and asexual stages were also found. Among 25 isolates, which had been cultivated, 23 isolates could be infected in MDCK and Hep-2. Only 2 isolates could not be infected in MDCK cell. These 2 isolates could be infected to Vero cell and yielded high numbers of trophozoites. PZQ, doxycycline and PRM were tested to the infected parasites. The drugs were added either with inoculum or 24 hours after inoculation. None of them was effective including PRM, which has been previously reported. ■

Presented as a Poster Presentations at Joint International Tropical Medicine Meeting, Bangkok, 2-4 December 2003.

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

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▶ **The** development of *Isoospora belli*, a human coccidian parasite, was studied in different cell lines. Merozoites were observed in all kinds of cells, whereas sporogony was demonstrated only in Hct-8. This implied that not only the

human cell line could be infected but also some kinds of animal cell lines. Unizoites could be found in Vero cells. The merozoites were transferred to a new culture cell for three passages and maintained for two weeks, but no oocyst production was observed in any culture cells during cultivation. ■

Presented in: Joint International Tropical Medicine Meeting, Bangkok, 2-4 December 2003.

IN VITRO STUDIES OF OPPORTUNISTIC PROTOZOA FROM STOOLS OF HIV-INFECTED PATIENTS IN THAILAND

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The studies involved the microscopic examination of spore-forming protozoa i.e. *Isospora belli*, *Cyclospora cayetanensis*, *Cryptosporidium parvum* and *Microsporidia* spp. which were collected from stools of HIV-infected patients. Oocysts from stools were detected by microscopic examination both fresh preparation and staining methods. Then they were processed and infected to culture cells for *in vitro* studies. The development of parasites in various cell lines was observed e.g. Infectivity, life cycle, host-parasite interaction including *in vitro* drug testing. *I. belli* showed distinct host specificity. Complete development of parasites was demonstrated in Hct-8 which is carcinoma cell of human intestine while *C. parvum* could infect most of cell lines. Only three cases of *C. cayetanensis* were collected but the number of oocysts was too small for *in vitro* study. However, it was found that oocysts in one case of *C. cayetanensis* appeared different characters from others by staining method therefore ultrastructural studies was performed

for comparison to typical *C. cayetanensis*. PCR technique was applied and found that the oocysts were not *C. cayetanensis*. Fifty isolates of *C. parvum* were cultivated. The parasite could infect all cell lines but numerous parasites including sexual cycle was observed in Hct-8 and severe apoptosis was distinct in this culture cell. Genotyping was studied and found that all isolates were human genotype or type one. The correlation of microscopic examination, serodiagnosis using commercial test kit and PCR detections were studied. Among 13 isolates of positive microscopic examination, only three isolates showed positive results from serodiagnosis, both before and after the process of excystation but 11 isolates showed positive results by PCR detection. Paromomycin and medicinal plants were tested but none of them could eliminate all stages of parasites from culture. Among 42 isolates of *C. parvum* cultivation, two isolates of *Microsporidia* were suspected in *C. parvum* culture. Typical characters of *Microsporidia* spores were demonstrated in culture medium after staining therefore transmission electron microscope was performed for ultrastructural study. ■

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PCR TECHNIQUE FOR DETECTING TOXOPLASMA GONDII IN ANIMAL AMNIOTIC FLUID

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The goal of diagnosing congenital toxoplasmosis is early detection of maternofetal transmission, for early treatment to prevent unwanted sequelae. Polymerase chain reaction (PCR) is a method used recently for detecting toxoplasmosis during pregnancy. The widely used clinical specimen is amniotic fluid, since it provides a rapid, simple and safe method to obtain accurate results. The advantages of the PCR technique are high sensitivity, specificity and positive predictive value compared with other laboratory methods. To determine the sensitivity,

specificity and lower detection limit in our laboratory, amplification of the B1 gene by nested PCR was performed to *T. gondii* tachyzoites added to companion animal amniotic fluid samples. From 20 samples, our technique could detect *T. gondii* in 12 samples out of 16 positive samples as well as all 4 negative samples. The sensitivity of this nested PCR technique is recommended as a diagnosis method for detecting *T. gondii* in suspected congenital toxoplasmosis animals. ■

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IN VITRO SENSITIVITY OF TRICHOMONAS VAGINALIS TO AT-SPECIFIC MINOR GROOVE BINDING DRUGS

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Trichomoniasis is one of the most common sexually transmitted diseases, with around 120 million worldwide suffering from *Trichomonas vaginalis*-induced vaginitis every year. Although trichomoniasis can be treated by metronidazole, the prevalence of metronidazole-resistant *Trichomonas vaginalis* seems to be increasing. Since the percentage of AT base pairs in *Trichomonas vaginalis* DNA (71%) is very much higher than in human cells, in this study a series of bisquaternary quinolinium salt compounds with high AT-binding specificity were tested for their antitrichomonal activities. Minimum

inhibitory concentrations (MICs) were determined for these compounds against a local strain of *Trichomonas vaginalis* in culture. Among 14 bisquaternary quinolinium compounds tested, an N-ethyl derivative was the most effective drug against *Trichomonas vaginalis*, being nearly as potent (MIC=0.16 mM) as metronidazole (MIC 0.096 mM), and with low toxicity towards human cells. The nature of the substitution at the quinolinium quaternary centre appears to be important in terms of effectiveness of bisquaternary compounds against the parasite. In contrast, no clear relationships could be seen for substituents on the quinolinium ring; Me and Cl substituted analogues showed higher activity against trichomonads, whereas OMe, NHMe and NH₂ substituents decreased activity. ■

This study was supported by a grant from Mahidol University.

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PAROXYSM SERUM FROM A CASE OF PLASMODIUM VIVAX MALARIA INHIBITS THE MATURATION OF P. FALCIPARUM SCHIZONTS IN VITRO

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In concurrent infections in vivo, the blood stages of *Plasmodium vivax* suppress those of *Plasmodium falciparum*. To see if the paroxysm (i.e. the periodic febrile episode) of *P. vivax* infection contributes to this suppression, sera from a *P. vivax*-infected volunteer were added to cultures of whole blood taken from cases of *P. falciparum* malaria. The crude rate of schizont generation from the ring forms, measured as the percentage of all asexual parasites that were schizonts after incubation for 24 h, was similar whether the cultures contained serum samples collected during paroxysms or those collected,

from the same volunteer, at other times (19.1% v. 18.9%; P=0.842). After a random-effect linear regression was used to adjust for disparities between the *P. falciparum* isolates, however, the degree of schizont maturation, measured as the mean number of nuclei per schizont, was significantly lower for the cultures with paroxysm serum than for those with non-paroxysm serum (4.8 v. 5.3; P=0.002). The proportion of schizonts considered mature was also significantly lower when paroxysm serum was used (3.7% v. 6.3%; P=0.03). This appears to be the first in-vitro study in which sera collected during a paroxysm of *P. vivax* have been shown to inhibit the maturation of *P. falciparum* schizonts. The role of this mechanism in intra- and inter-specific competition is discussed. ■

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PARTIAL PURIFICATION AND CHARACTERIZATION OF DNA HELICASE FROM *PLASMODIUM FALCIPARUM*

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P The malaria situation around the world is worsening and most of antimalarial drugs is rapidly losing their effectiveness. There is an urgent need for new antimalarial drugs and intensified investigation of potential target enzymes should be performed. Since, DNA helicases can catalyze the unwinding of double stranded DNA to provide single stranded templates for DNA replication, repair and recombination which are important processes for multiplication of malarial parasites so DNA helicases may serve as possible target enzymes combating malaria. In this study, DNA helicase from *Plasmodium falciparum* (K1 strain) were partially purified by fast protein liquid chromatography (FPLC). Nuclear extract of the parasites was loaded on Resource

Q column, Mono S column and single- stranded DNA column, respectively. DNA helicase activity was detected by measuring the unwinding of ³²P-labeled partial duplex DNA. The product was separated by 20% non-denaturing gel electrophoresis and visualized by auto-radiography. The directionality of unwinding reaction was 5' to 3' with respect to the single-stranded DNA to which the enzyme was bound. It could not unwind blunt-ended duplex DNA. DNA helicase inhibitors such as aclarubicin, daunorubicin, and doxorubicin, were tested against *P. falciparum* 5'-3' DNA helicase and IC₅₀ values were 4.0x10⁻⁶, 7.5x10⁻⁶ and 3.6x10⁻⁶ M, respectively. ■

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DNA HELICASES, ANTIMALARIAL DRUG TARGETS

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P In many parts of the world, *Plasmodium falciparum* has developed resistance to most currently employed antimalarials. Thus, there is an urgent need for new antimalarial drugs and intensive investigation of potential target enzymes at the biological and molecular level should be performed. Since, DNA helicases can catalyze the unwinding of double stranded DNA to provide single stranded templates for DNA replication, repair and recombination which are important processes for multiplication of malarial parasites therefore DNA helicases may serve as possible target enzymes combating malaria.

In our study, at least two types of DNA helicases were isolated and purified from *Plasmodium falciparum* strain K1. The 5'-3' DNA helicase of *P. falciparum* was partially purified by fast protein liquid chromatography (FPLC). Nuclear extract of the parasites was loaded on Resource Q column, Mono S column and single- stranded DNA column, respectively. DNA helicase activity was detected by measuring the unwinding of ³²P-labeled partial duplex DNA. The product was separated

by 20% non-denaturing gel electrophoresis and visualized by auto-radiography. The directionality of unwinding reaction was 5' to 3' with respect to the single-stranded DNA to which the enzyme was bound. It was able to use partial duplex DNA, fork-like DNA as substrates but could not unwind blunt-ended duplex DNA. The 3'-5' DNA helicase of *Plasmodium falciparum* was also isolated and purified by 80% ammonium sulfate precipitation. The protein was loaded onto Resource Q column and 2 peaks of DNA helicase activity were found; peak I (0.19-0.24 MKCl) and peak II (0.34-0.52 MKCl). Peak II enzyme was further purified by using Hitrap heparin, Mono S and ssDNA columns respectively. The directionality of unwinding reaction was 3' to 5'. It was able to unwind partial duplex DNA, fork-like DNA but could not unwind blunt-ended duplex DNA. DNA helicase inhibitors such as aclarubicin, daunorubicin, and doxorubicin were tested against both *P. falciparum* DNA helicases. ■

Oral Presentation in 4th Seminar on Food-and water-borne Parasitic Zoonoses 2nd International Meeting on Gnathostomiasis Joint International Tropical Medicine Meeting 2003.

This study was supported by the Thailand Research Fund.

IDENTIFICATION OF *CRYPTOSPORIDIUM PARVUM* GENOTYPE FROM HIV AND NON-HIV FECAL SAMPLES BY PCR

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▶ ***Cryptosporidium parvum*** is one of the important protozoal parasites associated with gastrointestinal disease world wide. Recent molecular studies show that *Cryptosporidium parvum* is composed of at least 8 genotypes. Studies and reports show that the most common genotypes of *Cryptosporidium parvum* that capable to establish and cause infection in humans are divided into two genotypes, *C. parvum* human genotype (genotype 1) and the *C. parvum* bovine genotype (genotype 2). Since routine microscopy examination is unable to identify the *C. parvum* genotypes, the genotyping by PCR technique is valuable in helping to elucidate sources and modes of transmission of this parasite.

In this study, specific primers of genotype 1 and 2 were used to identify the *C. parvum* genotypes in fecal samples. A

total number of 30 fecal HIV and non-HIV samples of *C. parvum* examined by microscopic method which comprised of 7 samples from non-HIV children, aged between 8 to 12 years, 11 fecal samples from adults with HIV positive and 12 purified oocysts of *C. parvum* from HIV patients were investigated. Within this group of infected children, 5 children were found to be infected with genotype 1 while 2 samples were unclassified. In the adult patients with HIV positive, 7 samples were found to be genotype 1, while 4 samples were unclassified. Of the 12 purified oocysts samples, 11 samples were found to be positive for genotype 1 while only 1 purified oocysts samples was unclassified. The unclassified samples observed in our study may belong to other the genotypes and there is no *C. parvum* genotype 2 were detected in our study group of population. ■

Presented in: 4th Seminar on Food-and water-borne Parasitic Zoonoses 2nd International Meeting on Gnathostomiasis Joint International Tropical Medicine Meeting 2003.

ASYMPTOMATIC ENTEROCYTOZOON BIENEUSI GENOTYPE A INFECTION IN THAI ORPHANS

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▶ ***E. bieneusi*** is a common causative agent of human microsporidial infection. It not only causes diarrhea in AIDS patients but also in patients with other immunosuppressive conditions and immunocompetent hosts. Transmission and sources of infection are still unclear. We reported *E. bieneusi* infection in children who lived in an orphanage, Bangkok, Thailand in 1999. Since then our surveys have always found that this organism was one of the common parasitic infections in these orphans. Although these children usually had no gastrointestinal symptoms, monitoring of the infection in these children will provide more epidemiological data. In the present study we conducted a cross-sectional survey of *E. bieneusi*

infection to determine epidemiological and clinical characteristics associated with *E. bieneusi* infection in this population in April 2003. Stool specimens were collected from 290 orphans and examined for microsporidia. By gram-chromotrope staining, *E. bieneusi* spores were detected in 12 specimens. The positive specimens were confirmed by PCR method specific for *E. bieneusi*. Unfortunately only 10 specimens were enough for PCR amplification. These 10 specimens were confirmed by PCR amplification specific for *E. bieneusi*. Sequence analyses revealed that these 10 isolates were *E. bieneusi* type A. Among 12 cases, only 1 child was HIV-positive. The prevalence of *E. bieneusi* infection was significantly different among age groups. All infected orphans had no gastrointestinal symptoms during the surveys.

Univariate and multivariate analysis showed that orphans aged between 13-24 months and living in one particular house had greater risk of acquiring *E. bieneusi* comparing to the others.

There was no significant association between *E. bienersi* infection and sex and HIV status. These data might indicate person-to-person transmission of *E. bienersi*. ■

Oral presentation in 4th Seminar on Food-and water-borne Parasitic Zoonoses 2nd International Meeting on Gnathostomiasis Joint International Tropical Medicine Meeting 2003.

EVALUATION OF PCR TECHNIQUE FOR THE DETECTION OF *ENTEROCYTOZOOM BIENEUSI* SPORES IN CLINICAL SPECIMENS

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▶ **Enterocytozoon bienersi**, an obligate intracellular organism, has been recognized as an opportunistic parasite causing persistent diarrhea in immunocompromised individuals, particularly AIDS patients. Gold standard for the detection of this organism is still electron microscopy. Because of the disadvantages of EM such as expensive cost and time consuming, other simple methods have been proposed. Light microscopy with special staining methods is rapid and inexpensive but well-trained technician is required. Thus PCR techniques have been developed to use as the diagnostic method. To date several techniques for DNA extraction and PCR amplification have been published, however there is no comparison among these methods in term of their sensitivities.

We evaluated the extraction methods using 2 commercial kits; FTA assay and QIAamp stool mini kit and conventional method in criterion of simplicity, time consuming and cost to increase the sensitivity of PCR. Our results showed

that both FTA and QIAamp stool mini kit could extract DNA from specimens containing *E. bienersi* as low as 1 spore. Because of its simplicity and low cost, FTA was chosen as our standard extraction method. From a serial dilution of *E. bienersi* spores, DNA was extracted by FTA method and used as template for PCR amplification using 5 specific primer pairs. The most sensitive primer pairs were both EBIER/EBIEF and MSP3/MSP4B. We have then chosen MSP3/MSP4B because of their usefulness for further study in term of genotypic characterization. We compared the sensitivities of PCR technique using this primer pair to that of the light microscopy. Our results showed that the sensitivities of PCR method and light microscopy were 100% and 86.7%, respectively. Specificities of both methods were 100%. In conclusion, PCR technique is useful for the detection of *E. bienersi* in clinical specimens. In addition, genotypic characterization can be determined. ■

Oral presentation in 4th Seminar on Food-and water-borne Parasitic Zoonoses 2nd International Meeting on Gnathostomiasis Joint International Tropical Medicine Meeting 2003.

PREVALENCE OF LOWER GENITAL TRACT INFECTION AMONG WOMEN ATTENDING MATERNAL AND CHILD HEALTH AND FAMILY PLANNING CLINICS IN HANOI, VIETNAM

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▶ To determine the prevalence of lower genital tract infection (LGTI) with *Candida* spp, *Trichomonas vaginalis*,

Neisseria gonorrhoeae, *Chlamydia trachomatis*, and bacterial vaginosis among symptomatic and asymptomatic women attending maternal and child health and family planning (MCH/FP) clinics in Hanoi, Vietnam. A multi-centered, cross-sectional descriptive study stratified by reported symptoms of vaginal discharge was carried out in three MCH/FP clinics among 1,000 women aged 18-44 years in 1998. Of these, 89.1% lived in Hanoi, 97.6% were currently married, and 99.2% had only one sexual partner in the past 12 months. Regarding their contraceptive use, 28.2% did not use any contraception,

25.6% used an intrauterine device (IUD), 22.8% used condoms, and 23.4% used other methods. The overall prevalence of *Candida* spp was 11.1% (95% CI = 9.1-13.1%); *T. vaginalis*, 1.3% (95% CI = 0.6-2.0%); no gonococcal infection was found; the prevalence of *C. trachomatis* was 4.4% (95% CI = 3.1-5.7%); and of bacterial vaginosis, 3.5% (95% CI = 2.4-4.6%). The presence of LGTI was not associated with reported symptom of vaginal discharge. LGTI was common among

married and monogamous women attending MCH/FP clinics in Hanoi, of whom many used IUDs and may have an increased risk of complications in the presence of LGTI. The lack of association between symptoms and laboratory-confirmed infection underscores the challenge of diagnosing LGTI when laboratory testing is not available. ■

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HIV TYPE 1 INCIDENCE ESTIMATES BY DETECTION OF RECENT INFECTION FROM A CROSS-SECTIONAL SAMPLING OF INJECTION DRUG USERS IN BANGKOK: USE OF THE IGG CAPTURE BED ENZYME IMMUNOASSAY

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► **Development** of serologic tests to detect recent HIV-1 infection has generated worldwide interest in applying this approach to estimate incidence. We previously devised an IgG-capture BED-EIA (or BED-CEIA) that detects increasing levels of anti-HIV IgG following seroconversion to identify recent infection and to estimate incidence among persons infected with diverse HIV-1 subtypes worldwide. Injection drug users (IDUs; n = 1969) were screened in 1996 for participation in a prospective cohort study. Serum specimens from 594 IDUs were HIV-1 seropositive (30.2%) and were tested with the BED-CEIA. The proportion of recent infections and estimated incidence by different epidemiological risk factors were compared with incidence data measured from the prospective cohort. Of 594

HIV-1-seropositive specimens, 113 (19%) were identified as recent infections. Overall, the estimated annual incidence among persons screened was 17.3%/year (95% CI, 12.8-24.2%/year) compared with 9.0%/year (95% CI, 6.7-11.9%/year) measured from the prospective cohort during the same time period. Estimated incidence was higher among younger aged and unemployed IDUs as well as among those who injected more frequently, confirming previously reported risk factors from this prospective cohort. As persons screened from a cross-sectional sampling probably have higher risk for HIV than selected uninfected individuals who choose to participate and receive risk reduction counseling in a longitudinal cohort study, use of this or other serologic testing strategies to identify populations with high incidence (such as for HIV vaccine trials) may overestimate incidence measured from prospective cohorts. ■

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DISTRIBUTION OF *PILA POLITA* IN A SOUTHERN PROVINCE OF THAILAND

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► **This** field study investigated the distribution of the freshwater snails of the family Ampullariidae in 18 provinces of Thailand. The introduced *Pomacea canaliculata* has wide distribution in the studied provinces. *Pila angelica*, *P.*

ampullacea and *P. pesmei* still have limited distribution. *Pila polita*, which is absent in the south, now can be found in Phangnga, a southern province of Thailand. Moreover, *P. polita* is currently used as a traditional medicine of the local people for the treatment of a skin disease. ■

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HIV RISK REDUCTION IN A COHORT OF INJECTING DRUG USERS IN BANGKOK, THAILAND

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▶ To determine changes in risk behavior in relation to study participation among injecting drug users (IDUs) in Bangkok, Thailand. **METHODS:** During 1995-1996, 1,209 HIV-seronegative IDUs were recruited from Bangkok Metropolitan Administration drug abuse treatment programs to participate in a prospective cohort study. Study visits occurred every 4 months, at which the participants underwent an interview to assess risk behavior and HIV counseling and testing. Eight hundred nine of the IDUs were considered “long-term” participants, who remained in the study through at least the first four scheduled follow-up visits (16 months). Injection risk behavior at each study visit was measured on a four-point scale strongly associated with incident HIV infections in the cohort. Individual regression slopes were used to assess changes in injection risk behavior (risk increase, no

change, or risk reduction). **RESULTS:** Of the 806 long-term study participants, 79% showed declines, 4% showed no change, and 17% showed increases in injection risk behavior. The percentage of participants in the highest-risk category (injecting daily or more frequently and sharing needles and syringes) declined from 42% at baseline to 3% at the final follow-up visit. Being in methadone maintenance treatment was associated with stable low rates of injection risk behavior, while recruitment from the 45-day detoxification treatment was associated with reductions in injection risk behavior. The risk reduction was independent of decline in risk behavior among IDUs in the community at large. **CONCLUSIONS:** Participation in this cohort study was associated with substantial declines in injection risk behavior. This information is important in the evaluation of possible adverse behavioral effects of participation in future preventive HIV vaccine trials including IDUs, particularly in developing country settings. ■

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DETECTION OF OPISTHORCHIS VIVERRINI IN EXPERIMENTALLY INFECTED BITHYRID SNAILS AND CYPRINOID FISHES BY A PCR-BASED METHOD

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▶ A PCR procedure for the detection of *Opisthorchis viverrini* in experimentally infected bithyrid snails and cyprinoid fishes was developed. This procedure was based on primers designed from a pOV-A6 specific probe sequence giving a 330 base-pair product. The detection was accomplished in host tissue homogenates to which a single cercaria or metacercaria

was introduced. PCR can detect as little as a single cercaria artificially inoculated in a snail or a single metacercaria artificially inoculated in a fish sample. The method gave a 100% positivity rate for all infected snails or fishes. The method did not yield a 330 base-pair amplified product with other digenean fluke DNAs such as *Haplorchis taichui*, *Centrocestus* spp., *Echinostoma malayanum*, *Fasciola gigantica*, animal schistosomes, *Paragonimus heterotremus* or *Haplorchoides* spp. The assay has great potential for application in epidemiological surveys of both snail and fish intermediate hosts as well as for investigation of foodborne parasites in freshwater fishes. ■

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SOCIAL AND BEHAVIORAL FACTORS ASSOCIATED WITH CLONORCHIS INFECTION IN ONE COMMUNE LOCATED IN THE RED RIVER DELTA OF VIETNAM

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Social behavioral factors associated with Clonorchis infection are needed for control measures. The population in Nga Tan commune were randomly sampled and questioned to determine knowledge, perception, and health behavioral factors associated with Clonorchis infection among heads of households. The cellophane thick smear method was applied to examine their stool samples. Seven hundred and seventy-one cases were examined, the positive rates were 17.2%, 66.9%,

78.7%, 15.9%, and 0.14% for Clonorchis sinensis, Ascaris lumbricoides, Trichuris trichiura, hookworm, and Dicrocoelium dendriticum respectively. There was no significant difference between the infection rate of clonorchiasis, education level, and family income groups ($p > 0.05$). But there was significance difference between the infection rate of clonorchiasis and people living in different family sizes ($p < 0.01$). Thirty-four clonorchiasis patients treated with praziquantel 25 mg/kg/day for three days showed a cure rate in 30 days of 97.1%. ■

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HEALTH SEEKING BEHAVIOR AMONG INSURED PERSONS UNDER THE SOCIAL SECURITY ACT, 1990

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Since having health insurance cannot guarantee access to care among the insured persons, their actual health seeking behavior should be evidence reflecting true access. Therefore, the study aimed to present the patterns of health seeking behavior among the insured persons who actually were able to get free services from their registered hospitals under the Security Scheme. Purposive sampling was done of 1,003 insured persons who were willing to participate in the study from small, medium and large establishments in the Huai Khwang district in Bangkok. A health diary was employed as one of the data collecting tools with a follow-up period of six months. The average illness rate found was 6.44 episodes/person/year. The characteristics of illnesses reported were described in terms of symptom groups, perceived severity, duration, work or non-work related cause.

No treatment or self care, seeking help from non-registered health facilities and seeking help from registered hospitals and clinics were the patterns of health seeking behaviors found in the study. The patterns of health seeking behaviors among the participants varied depending on the stage of treatment, perceived severity of illness and types of additional health benefits. Seeking care from registered hospitals and clinics was found among the illnesses with a higher level of perceived severity, among the participants with chronic diseases, and among the illnesses that were treated with higher stages. Therefore, health insurance might not be able to guarantee true access to needed care for people unless the comprehensive health care provider networks are designed to cover more types of services, be more convenient and have more accessible health care providers. ■

This study received financial support from The Social Security Office, Ministry of Labour.

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ENVIRONMENTAL HEALTH MODEL OF PESTICIDE UTILIZATION FOR SUSTAINABLE AGRICULTURE

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Pesticide utilization is considered to be serious environmental and health problems, and at least in terms of pesticide poisonings in Thailand. The quasi-experimental one group pretest-posttest study was designed to implement environmental health model (EHM) in a core group of 50 farmers in Donka Subdistrict, Bangpae District, Ratchaburi Province.

The objectives were to assess the EHM, that was modified from the WHO-SESAME Model, 1996, to be implemented in the farmer leaders and to evaluate the effectiveness of the EHM whether it could lead to a sustainable pesticide safe use in the agricultural program. An important tenet of the EHM is the process of establishment the environmental health team leaders (EHTL) of the farmers. The program implementation started from the planning stage with the community leaders, voluntarily selected EHTL, meetings set to the problem solution, training of the EHTL, data collecting and evaluating the program.

The establishment of the EHTL shows that 33 group members from 50 permanently jointed this environmental health team. This team would work as the leading farmers to

reduce risk of pesticide poisoning, to transfer technology received from the training to other neighboring farmers, and to promote this sustainable way of safe agriculture to their community. The training schedule consisted of ten sessions, for instance, the pesticide uses, problems and its impacts on health and environment, pesticide safe use guidelines, poisoning first aid, basic cardiac pulmonary resuscitation, alternative biotechnology agriculture, etc.

The evaluative results also showed that the scores of KAP toward pesticide uses, storage and prevention were significantly increased after the training. Blood cholinesterase enzyme levels were significantly increasingly different when compared between the pretest and posttest blood exams, respectively.

In conclusion, the EHM was successfully implemented and cooperated in the study setting between the farmers, the Agricultural Extension Office, and community leaders. Recommendations need to be addressed for future sustainable agriculture that the intersectoral coordination is necessary for the Agricultural Extension Office, Subdistrict Administrative Organization (SAO), community leaders and the EHTL group to get involved in community activities. ■

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SHIGELLOSIS IN THE VIEW OF COMMUNITY LEADERS: A QUALITATIVE STUDY

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There are four main species of *Shigella*, *S. dysenteriae*, *S. flexneri*, *S. boydii* and *S. sonnei*, which are able to cause diarrhea and/or dysentery. In Thailand, there are many reported shigellosis cases in each year. It means that they have many factors relating to persistence of the disease. This research conducted a qualitative study in 59 community leaders (health care providers, heads of community, women leaders and community teachers) who are living in rural and municipal areas in Kaeng Koi District, Saraburi Province. The study is based on community leader perceptions of symptoms, causes,

severity and risky group of *Shigella*, as well as its treatment, prevention, beliefs and health practices. The information was collected by indepth interview technique. The study shows that community leaders believed dysentery and diarrhea are not serious diseases because they can treat by themselves, either modern and herbal medicine. However, they also have a prevention program such as food, drinking water and garbage disposal, especially in school. Local explanation about names, symptoms, causes, severity and risky group of dysentery and diarrhea are benefit for health education messages, prevention and treatment program. ■

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SHIGELLOSIS IN THE VIEW OF PATIENT AND PATIENT'S CARETAKER

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▶ In Thailand, there are many reported shigellosis cases in each year. It implied the presence of many factors related to persistence of the disease. This research conducted a qualitative study in 21 shigella cases and patients' caretakers (17 female and 4 male) who were living in rural and municipal areas of Kaeng Koi District, Saraburi Province. The information was collected by indepth interview technique on patient and patient's caretaker perceptions of symptoms and

severity of *Shigella*, as well as its cause, treatment, prevention, beliefs and health practices. The results showed that the respondents knew well about symptoms and causes leading to shigella infection and believed that shigellosis in children was more serious than in adults. Treatment pattern in children and adults usually started up from an observation of illness symptoms and then self-treatment, either modern or herbal medicine, changed eating habits and lastly sought for health service at the near by health centers. ■

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SOCIO-CULTURAL AND BEHAVIORAL COMPONENT FOR SHIGELLOSIS DISEASE IN KAENG KOI DISTRICT, SARABURI PROVINCE, THAILAND

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▶ Shigellosis is the disease only in humans through the predominant mode of transmission by fecal-oral route. The estimation of annual cases worldwide are approximately 165 million infections and 1.1 million deaths, mostly in children. In Thailand, the number of deaths is even less, the number of cases are still high as 33,000 in a year. Probably, there are some attributable factors remain its transmission.

This report is a qualitative study of perceptions of the disease burden of shigella and the potential use of a vaccine against it that was conducted in Kaeng Koi District, Saraburi Province. It is based on community members' perceptions of the symptoms and severity of shigella, or bloody mucoid dysentery, as well as its causes, treatment and related preventive beliefs and practices. Data collection involved semi-structured interviews with 120 community residents.

The study shows that community residents recognize the symptoms of shigella. They perceive its causes to be the consumption of contaminated food and water, unhygienic personal behavior, and in a wider sense, domestic and

community sewage and garbage disposal problems that lead to flies and contaminated water. They also believe that eating overly spicy or raw food can lead to dysentery. Thus, they have an accurate understanding of the transmission of shigella, as well as adhere to beliefs about the need for balance in diet and body elements which are based on humoral theories of health and illness.

Approximately half of the community residents thought that dysentery, or bloody mucoid diarrhea, is severe because of the pain it causes, its economic burden and its potential fatal consequences. The other half of the respondents that did not think that shigella is severe believe that it is easily treatable and so poses no major threat. However, almost all respondents were interested in a vaccine against dysentery. Many said that everyone can contract it, but especially the elderly and children.

The methods of prevention they believe are awareness of foods and water, and vaccination when it is available in near future. Treatments usually start up from an observation of illness and then self-seeking for drugs, modern medicine or herbal medicine and lastly visiting the health service units. ■

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LOCAL WISDOM IN THE TREATMENT OF HERPES SIMPLEX DISEASES, CASE STUDY : THE TREATMENT OF HERPES SIMPLEX BY MONK HEALER (MOH-PRA)

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▶ The objectives of this study are: to identify an explanatory model of herpes simplex diseases in a monk healer and the herpes simplex patients, based on the concept of health belief systems, : to identify the process of treatment in monk healer and to study the health seeking and decision-making behaviors that treated by monk healer in herpes simplex patients.

Qualitative methods were used to obtain the data from observation and in-dept interviews, identified the explanatory model of herpes simplex diseases by Kleinman, A's model and classified the health seeking and decision-making behaviors by the theories of Chrisman, N.J. and Young, J.C. The cases of this study were 1 monk healer and 12 herpes simplex patients.

The result showed that the explanatory model of herpes simplex diseases in monk healer based on 2 beliefs : belived in the folk or local medicines and belived in the magic (supernatural).

The process of treatment in monk healer composed of 3 main methods : monk healer chewed the herbs and splinkled them on the wounds, the patients took the herbal medicine and anointed the wounds by herbal liquid. However, the

process of treatment just conducted by the rituals.

The explanatory model about herpes simplex diseases in the herpes simplex patients. They did not sure about the characteristics or the causes of diseases. In addition, the explanatory model of the patients were involved by the social network.

The result of health seeking and decision-making behaviors of the patients were 3 types : 1. treated the diseases by themselves, 2. treated the diseases by the cosmopolitant medicines and 3. treated the diseases by monk healer at first. Moreover, the health seeking and decision-making behaviors of patients just related to the social network in the main.

Recommendations : A state should continue to encourage people for self health care in their local wisdom, to disseminate information or knowledge about many kinds of ethnomedicine, to praise and to resuscitate the ethnomedicine in the role of helper for communities, to assemble the local wisdom in term of ethnomedicine from several communities by means of complete system. ■

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CHOLINESTERASE SCREENING TEST AMONG ORGANOPHOSPHATE EXPOSURE OF RICE FARMERS IN SOUTHERN VIETNAM

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▶ A cross-sectional study was carried out among rice farmers in My Huong commune, Southern Vietnam to assess the effects of occupational exposure to organophosphates (OPs) on cholinesterase (pChE) enzyme activity. US-CDC questionnaire with face-to-face interview was used to identify exposure patterns of 325 subjects. Blood from the finger prick of each subject was collected after the interview to measure cholinesterase enzyme level by Reactive Paper. STATA software was used to analyze the correlation between occupational exposure and cholinesterase enzyme activity with $\mu = 0.05$.

The results showed that 99.6% of the farmers were male. 59% of them were under 35 years of age. 85% reported of being farmers more than 5-10 years up. 65% owned less than 2 hectares of land and about 50% admitted of having direct contact with OP use. Only 30.5% had a training of pesticide safe use. 62.5% and 40% admitted of always/frequently drinking and smoking during PO use respectively. 80% informed of mixing more than one pesticides use. Personal protective equipment (PPE) was almost ignored by the farmers. The most common working clothes were ordinary clothes with long sleeved shirt, long trousers and cloth hats. Regarding Cholinesterase enzyme level, 44% were normal and 56% were below normal. In our study, clinical symptoms were not

associated with ChE enzyme level. The odds ratio of farmers with pChE below normal and exposed to OP use more than 10 times within the last two months was 5.2 at higher risk than those used only once (95% CI = 2-13.5). Those farmers with pChE below normal and with a history of washing spray can after use had the odds ratio of 2.5 (95% CI = 1.5-4.1). The odds ratios of farmers with pChE below normal and with reporting a history of always drinking and smoking were 2.1 (95% CI = 1.3-3.9) and 2.2 (95% CI = 1.2-3.8) respectively.

These findings suggest that health education and training of pesticide safe use to change the farmers' practice

are very important. PPE which is suitable for the hot weather should be available to promote its use among farmers without suffering their inconvenience. The study also found that the snail epidemic had led the farmers to overuse of pesticides. Proper assessment on the impacts of this matter is necessary for effective management of the problem in this locality. ■

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MAPPING SOIL-TRANSMITTED HELMINTHS IN SOUTHEAST ASIA AND IMPLICATIONS FOR PARASITE CONTROL

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▶ **Establishing** the current status and distribution of soil-transmitted helminths is essential for developing and implementing parasite control. Although Southeast Asia is known to have a high prevalence of infection, a precise estimate of the total disease burden has not been fully described. Here, we use Geographical Information Systems (GIS) to collate and map recent published surveys on soil-transmitted helminth epidemiology and distribution for this region. Distinct geographical variation was observed, which is suggested to

reflect climatic variation, as well as behavioral differences. However, for much of the region few data are available, and therefore it proved necessary to generate predictions of the distribution of soil-transmitted helminths using remotely sensed (RS) satellite sensor environmental variables. A significant finding was the importance of land surface temperature in influencing the distribution of *Ascaris lumbricoides* and *Trichuris trichiura*. Spatial analyses using RS satellite sensor data were then used to generate predictive maps of infection risk. This information provided the basis for an estimate of the population at risk of infection and the numbers requiring treatment. These applications of GIS and remote sensing provide a good basis for developing control of soil-transmitted helminths in the region. ■

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N-ACETYL-CYSTEINE IN SEVERE FALCIPARUM MALARIA IN THAILAND

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▶ **One** hundred and eight patients with severe falciparum

malaria underwent a placebo controlled trial with the antioxidant, N-acetylcysteine (NAC), as an adjunctive therapy along with standard intravenous artesunate therapy. Three NAC dosage regimens were used: an intravenous loading dose of 140 mg/kg followed by 70 mg/kg every four hours intravenously for up to 18 doses (Group 1); a single intravenous

loading dose followed by oral NAC in the same amount as for Group 1 (Group 2); a regimen identical to Group 1 except that oral NAC was administered after the first 24 hours (Group 3). Fifty-four patients received placebo plus artesunate. Two critically ill patients died in Group 1. No patient sustained an adverse reaction to the NAC other than vomiting, and the deaths were attributed to severe disease with multiple organ

involvement. The excellent results with NAC, the lack of adverse effects, and the rationale for NAC benefit supports the need for a large, double blind trial of NAC as an adjunctive therapy for severe malaria. ■

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CLINICAL EXPERIENCE WITH INTRAVENOUS QUININE, INTRAMUSCULAR ARTEMETHER AND INTRAVENOUS ARTESUNATE FOR THE TREATMENT OF SEVERE MALARIA IN THAILAND

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► **We** prospectively studied 803 Thai patients admitted to the Bangkok Hospital for Tropical Diseases to assess the safety, tolerability and effectiveness of treatments for strictly defined *P. falciparum* malaria. Patients were assigned to one of five treatment groups: (i) a 5-day course of intravenous artesunate in a total dose of 600 mg, Group Aiv; (ii) intravenous artesunate as in Group Aiv followed by mefloquine, 25 mg/kg, Group Aiv+M; (iii) a 3-day course of intramuscular artemether in a total dose of 480 mg, Group Aim; (iv) intramuscular artemether as in Group Aim followed by mefloquine, 25 mg/kg, Group Aim+M, and (v) intravenous quinine, 200 mg/kg given in divided doses over seven days followed by oral tetracycline, 10 mg/kg, for 7 days. When patients could take oral medications, the parenteral antimalarials were administered as oral agents.

There were no major adverse effects observed with any of the five treatment regimens. With all regimens, 95 to 100% of the patients survived. Mean parasite clearance times were more rapid with the artemisinin regimens (53 to 62 hours) than with quinine (92 hours). The mean fever clearance times with intravenous artesunate (80 to 82 hours) were about a day shorter than those with intramuscular artemether (108 hours) or intravenous quinine (107 hours). Mefloquine reduced the recrudescence rate from 24 to 5% with intravenous artesunate but from 45 to 20% with intramuscular artemether; recrudescence was 4% with quinine and tetracycline. A dose and duration of therapy greater than those in this study are needed for optimal therapy with intramuscular artemether. Effective therapy for severe falciparum malaria can be provided by either intravenous artesunate followed by mefloquine or by intravenous quinine followed by tetracycline. ■

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MOLECULAR CHARACTERIZATION OF HEREDITARY PERSISTENCE OF FETAL HEMOGLOBIN IN THE KAREN PEOPLE OF THAILAND

Trachoo O, Sura T, Sakuntabhai A, Singhasivanon P, Krudsood S, Phimpraphi W, Krasaesub S, Chanjarunee S, Loareesuwan S

► **Hereditary** persistence of fetal hemoglobin (HPFH) is the condition whereby a continuously active gamma-globin gene expression leads to elevated fetal hemoglobin (Hb F) levels in adult life [Stamatoyannopoulos G, Grosfeld F. Hemoglobin switching. In: Stamatoyannopoulos G, Majerus PW, Perlmutter RM, Varmus H, eds. *The Molecular Basis of Blood Diseases*. Philadelphia: W.B. Saunders, 2001:135-182; Wood WG.

Hereditary persistence of fetal hemoglobin and delta(beta) thalassemia. In: Steinberg MH, Forget BG, Higgs DR, Nagel RL, eds. *Disorders of Hemoglobin: Genetics, Pathophysiology, and Clinical Management*. Cambridge: Cambridge University Press, 2001:356-388; and Weatherall DJ, Clegg JB. Hereditary persistence of fetal hemoglobin. In: Weatherall DJ, Clegg JB, eds. *The Thalassemia Syndromes*. Oxford: Blackwell Scientific

Publishers, 1981:450-507]. The condition is caused either by mutation of the beta- and gamma-globin genes, or the gamma-gene controlled region on other chromosomes. Several families with this condition have been reported from Vietnam, Cambodia and China, and the Southeast Asian mutation (or HPFH-6), a 27 kb deletion, was demonstrated. Here we report on a mother and her daughter of the Karen ethnic group with high levels of Hb F, living in the Suan Pueng District on the border of Thailand and Myanmar. Genotyping showed a heterozygosity for the 27 kb deletion of the beta-globin gene. Their conditions have been confirmed by gap polymerase chain reaction (PCR) with three oligonucleotide primers recently developed by Xu et al. [Xu X-M, Li Z-Q, Liu Z-Y, Zhong X-L, Zhao Y-Z, Mo Q-H. *Molecular*

characterization and PCR detection of a deletional HPFH: application to rapid prenatal diagnosis for compound heterozygotes of this defect with beta-thalassemia in a Chinese family. Am J Hematol 2000; 65:183-188.], and a DNA sequencing method. Thus far there has been no official report of the HPFH-6 anomaly from Thailand. The compound heterozygosity of beta-thalassemia (thal) and hereditary persistence of Hb F causes the phenotype of thalassemia intermedia; in contrast, homozygotes for this anomaly show only mild microcytic anemia. Hence, genetic counseling for hereditary persistence of Hb F carriers is needed for family planning. ■

Hemoglobin 2003 May;27(2):97-104.

COMPARATIVE CLINICAL TRIAL OF TWO-FIXED COMBINATIONS, DIHYDROARTEMISININ-NAPHTHOQUINE-TRIMETHOPRIM (DNP) AND ARTEMETHER LUMEFANTRINE (COARTEM/RIAMET) IN THE TREATMENT OF ACUTE UNCOMPLICATED FALCIPARUM MALARIA IN THAILAND

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▶ An open randomized comparison of two-fixed dose artemisinin derivative-containing combination regimens was conducted in adults with acute uncomplicated multidrug resistant falciparum malaria in Thailand. DNP, a combination of dihydroartemisinin with naphthoquine and trimethoprim developed recently in China, has been evaluated in China, Vietnam, Cambodia and Thailand. This study was performed

to compare the safety, tolerability and efficacy of DNP and artemether-lumefantrine/Coartem. One hundred and thirty eligible uncomplicated falciparum malaria patients were enrolled into the study. Patients were randomly assigned in a 2:1 ratio into group A, which received DNP one tablet twice a day for one day; and group B, which received Coartem/Riamet four tablets twice a day for 3 days. The cure rates at 28-day were 99% and 97% in group A and group B, respectively. No serious adverse events occurred. We concluded that both DNP and Coartem/Riamet were safe, well tolerated and highly efficacious in the treatment of acute uncomplicated falciparum malaria in Thailand.

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

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▶ We studied prospectively 801 Thai patients admitted to the Bangkok Hospital for Tropical Diseases with acute, symptomatic Plasmodium vivax malaria to determine the optimum duration of treatment with oral artesunate and the safety, tolerability, and effectiveness of a high dose of primaquine in prevention of relapse. Patients were randomly assigned to one of four treatment groups: 1) a five-day course of artesunate

(Group A5); 2) a seven-day course of artesunate (Group A7); 3) a five-day course of artesunate plus a 14-day course of high-dose primaquine (0.6 mg/kg, maximum dose = 30 mg) (Group A5 + P); and 4) a seven-day course of artesunate plus a 14-day course of high-dose primaquine (Group A7 + P). During 28 days of observation, *P. vivax* reappeared in the blood of 50% of those who received artesunate alone (Groups A5 and A7), compared with none of those who received primaquine (Groups A5 + P and A7 + P; $P < 0.0001$). Adverse effects were confined

to the 13 patients with a deficiency for glucose-6-phosphate dehydrogenase; high-dose primaquine (0.6 mg/kg of base a day) had to be stopped in four (31%) patients because of a significant decrease in the hematocrit. The combination of five days of artesunate and 14 days of primaquine is a highly effective and generally well-tolerated treatment regimen for vivax malaria in Thailand. ■

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USE OF GIS-BASED SPATIAL MODELING APPROACH TO CHARACTERIZE THE SPATIAL PATTERNS OF MALARIA MOSQUITO VECTOR BREEDING HABITATS IN NORTHWESTERN THAILAND

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► **We** sampled 291 bodies of water for *Anopheles* larvae around three malaria-endemic villages of Ban Huay, Ban Pa Dae, and Ban Tham Seau, Mae Sot district, Tak Province, Thailand during August 2001-December 2002 and collected 4,387 larvae from 12 categories of breeding habitat types. We modeled surface slope and wetness indices to identify the extent and spatial pattern of potential mosquito breeding habitats by digitizing base topographical maps of the study site and overlaying them with coordinates for each larval habitat.

Topographical contours and streamlines were incorporated into the Geographical Information System (GIS). We used Global Positioning System (GPS) instruments to locate accurately each field observed breeding habitat, and produced a 30-m spatial resolution Digital Elevation Model (DEM). The slope (of less than 12 degrees) and wetness (more than 8 units) derived from spatial modeling were positively associated with the abundance of major malaria vectors *An. dirus*, *An. maculatus*, *An. minimus*, and *An. sawadwongporni*. These associations permit real-time monitoring and possibly forecasting of the distributions of these four species, enabling public health agencies to institute control measures before the mosquitoes emerge as adults and transmit disease. ■

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TREND OF MALARIA INCIDENCE IN HIGHLY ENDEMIC PROVINCES ALONG THE THAI BORDERS, 1991-2001

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► **The** intercountry border areas of Thailand have high malaria receptivity and vulnerability that present numerous problems in the control of malaria transmission. This study focused on the 30 provinces of Thailand situated next to

neighboring countries, which can be divided into 4 groups: the Thai-Myanmar border (10 provinces), the Thai-Cambodia border (6 provinces), the Thai-Lao border (10 provinces) and the Thai-Malaysia border (4 provinces). The purpose of the present study was to describe the pattern and trend of malaria incidence in the highly endemic provinces along the Thai borders for the 11 years from 1991 to 2001. Analysis of trends showed the distribution of malaria parasites to have shifted from a

prapponderance of *Plasmodium falciparum* to *Plasmodium vivax* along the western border with Myanmar, the northern border with Lao PDR and along the eastern border with Cambodia whereas the southern border with Malaysia the pattern changed from a preponderance of *P. vivax* to *P. falciparum*, since 1997. There was a significant difference in annual parasite incidence between borders and non-border districts, especially along the Thai-Myanmar and Thai-Cambodia borders. It is thus evident that all border districts, especially along the Thai-Myanmar and

Thai-Cambodia borders. It is thus evident that all border districts should pay more attention to control of malaria transmission and the activities of the malaria surveillance system, and that monitoring and evaluation of the Thai Malaria Control Program needs to be performed consistently, including some areas where a few malaria cases were found as well as in malaria free areas. ■

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SOME ENTOMOLOGICAL OBSERVATIONS ON TEMPORAL AND SPATIAL DISTRIBUTION OF MALARIA VECTORS IN THREE VILLAGES IN NORTHWESTERN THAILAND USING A GEOGRAPHIC INFORMATION SYSTEM

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► **This** spatial and temporal heterogeneity in the distribution of *Anopheles* mosquitoes were studied during August 2001 to December 2002 in three villages Ban Khun Huay, Ban Pa Dae, and Ban Tham Seau, in northwestern Thailand in Mae Sot district, Tak province. The three Karen villages are located about 20 km east of the city of Mae Sot near the Myanmar border. Twenty-one species were collected on human collections during 68 nights of 17 months. *Anopheles minimus* comprised of 86% of the specimens biting man. *An. Minimus* was implicated as a vector based on the detection of sporozoite infections using

enzyme-linked immunosorbent assays for *Plasmodium falciparum* and *P. vivax*. Seasonal comparison of vectorial capacity and entomological inoculation rate was calculated. *An.dirus* was rarely encountered and probably played little part in transmission in these three villages during the period of study. Information is provided on nightly biting activity, parity rate, infectivity, and adult and larval bionomics. Spatial and temporal comparisons among the collections were displayed on different satellite images including the Normalized Difference Vegetation Index data from on the National Oceanographic and Atmospheric Administration satellites (NOAA/NDVI), the LANDSAT satellite Thematic Mapper (spatial resolution 30x30 m) and the IKONOS satellite (spatial resolution 1x1 m) in a Geographical Information System (GIS). ■

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

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► **The** aim of this study was to assess anthropometric variables and the lipid pattern in relation to alpha-2-macroglobulin in normal- and over-nourished Thai individuals, to further support the hypothesis that alpha-2-macroglobulin plays a beneficial role in the determination of nutritional status. The study sample comprised of 48 male and 166 female

overweight and obese Thai volunteers and 26 male and 81 female normal subjects. The overweight individuals had statistically significant lower alpha-2-macroglobulin (A2M) serum levels. The total serum cholesterol, low density lipoprotein-cholesterol (LDL-C) and triglycerides were significantly higher and high density lipoprotein-cholesterol (HDL-C) lower in the over-nourished group as compared with the normal subjects. The LDL/HDL ratio was slightly but significantly higher in the over-nourished group, but still well below the value of 5 for both groups. In using a stepwise multiple linear regression, the model, which best explained the variation of A2M for all individuals including age, HDL-C, BMI, and gender. The relationship of A2M to the variables under study differed between males and

females. For males, a model which includes cholesterol and BMI explained best the variation of the proteinase inhibitor. For the females, the best model includes age, HDL-C and BMI. The role of protease inhibitors has hardly been explored in human epidemiological studies despite its relationship to important public health issues including nutrition, smoking, cancer and cardiovascular diseases. The results of this study further support the hypothesis, that A2M might play a role in the interrelationship of the nutritional status with the occurrence and the prevention of diseases. ■

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SERUM CONCENTRATION OF VITAMIN A AND E AND LIPID PROFILES IN OVERWEIGHT AND OBESE THAI

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► **The** weight, height, body mass index (BMI), waist/hip ratio, serum retinol and -tocopherol and lipid profiles of 16 overweight (BMI 25.0 kg/m²) Thai males and 56 overweight females, compared with 14 males and 58 females in a control group (BMI 18.5-24.9 kg/m²), were investigated. Subjects for the study were those persons who turned up regularly for physical check-up at the Outpatient Department, General Practice Section of Rajvithi Hospital, Bangkok. The study was conducted between December 2000-March 2001. Higher levels of cholesterol, LDL-C, LDL-C/HDL-C ratio were found in the overweight compared with the control subjects. Statistically significantly higher triglyceride levels were found in the overweight compared with the control subjects. The median serum retinol concentration in overweight subjects was 2.80 mol/L (range 0.53-4.62 mol/L) compared with 2.97 mol/L (range 1.21-4.12 mol/L) in control subjects ($p=0.0736$). The median serum -tocopherol concentration in overweight subjects was 17.30 mol/L (range 6.29-28.65 mol/L) compared with 18.75 mol/L (range 5.30-

30.28 mol/L) in control subjects ($p<0.05$). The median values of retinol and -tocopherol serum concentrations in the overweight and obese males were lower than those of the overweight and obese females. A total of 6.3% (1 out of 16) and 12.5% (2 out of 16) of the overweight/obese males had decreased retinol and -tocopherol levels, while the overweight/obese females had decreased retinol and -tocopherol level of 1.8% (1 out of 56) and 10.7% (6 out of 56), respectively. A total of 12.5% and 39.3% of the overweight/obese males and females had cholesterol concentrations of 6.48 mmol/l. However, the prevalence of low HDL-C (HDL-C 0.91 mmol/l) was found to be 50% in the overweight and obese males and 10.7% of the overweight and obese females. Statistically significant associations were found between age, cholesterol, LDL-C, and serum -tocopherol in the overweight and obese male and female subjects. A negative correlation was found between weight, BMI, AC, MAMC, hip circumference and serum retinol in both the overweight and obese subjects. A negative correlation was found between weight, BMI, MAMC, waist, hip circumferences and serum -tocopherol in both the overweight and obese subjects. ■

(Graduate, Faculty of Tropical Medicine, Mahidol University & Free University of Berlin).

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SERUM HOMOCYSTEINE, B12 AND FOLIC ACID CONCENTRATION IN THAI OVERWEIGHT AND OBESE SUBJECTS

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▶ This study investigated serum homocysteine, vitamin B12, folic acid, vitamin B6 and vitamin C, including anthropometric measurements and waist/hip ratios, of 37 male and 112 female overweight and obese Thai volunteers (BMI 25.00), as well as 23 male and 90 female normal Thai volunteers, who came for a physical check-up at the Out-patient Department, General Practice Section, Rajvithi Hospital, Bangkok during the period March-October, 2000. All of the anthropometric variables, except the height of the overweight group, were significantly higher than the normal subjects. There were statistically significantly higher levels of serum homocysteine in the overweight than in the control subjects and serum homocysteine concentrations in overweight and obese males were significantly

higher than in overweight and obese females. Serum folic acid and vitamin C in the overweight and obese were found to be statistically significantly lower than control subjects. No statistically significant difference in vitamin B12 was found in overweight and obese subjects compared with normal control subjects. The medians of serum folic acid and vitamin C concentrations in overweight and obese males were significantly lower than those of overweight and obese females. A negative correlation was found between serum folic acid and homocysteine concentrations in all overweight and obese subjects. There was a significant negative correlation between serum folic acid and vitamin B6 in both male and female overweight and obese subjects. It has been suggested that hyperhomocysteine in overweight and obese subjects seems to be caused by insufficient dietary folic acid intake and might not be induced by B12 deficiency. ■

(Mahidol University & Free University of Berlin)

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RELATIONSHIP OF TOBACCO SMOKING WITH SERUM VITAMIN B12, FOLIC ACID AND HAEMATOLOGICAL INDICES IN HEALTHY ADULTS

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▶ Objectives: To investigate the effects of tobacco smoking on serum vitamin B12, folic acid and haematological parameters in healthy Thai smokers and non-smokers.

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

Setting: A military unit in Thailand.

Subjects: One hundred and twenty-three male smokers from a military unit in Bangkok, who participated voluntarily in the study, were investigated. Sixty-six male non-smokers from the same unit were selected as controls. Fasting blood samples were collected for investigation of vitamin B12, folic acid and

haematological variables.

Results: The serum folic acid concentration of smokers was lower than the non-smokers, but not statistically significantly different. The haemoglobin in the smokers was lower than in the non-smokers, 16.3% of smokers were anemic, compared with only 3.0% of non-smokers. Anaemia was not related to folate deficiency. The white blood cell count in the smokers was found to be higher than non-smokers.

Conclusion: The results of this study suggest that there were low serum folic acid concentrations in smokers compared with non-smokers, which might contribute to the development of vascular and cardiovascular diseases. The higher white blood cell might be indicative alterations in the immune functions of smokers. ■

(Free University of Berlin)

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SERUM COPPER, ZINC, CERULOPLASMIN AND SUPEROXIDE DISMUTASE IN THAI OVERWEIGHT AND OBESE

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The serum copper, selenium, ceruloplasmin, superoxide dismutase (SOD) (specific activities of antioxidant enzymes), anthropometric measurements, including waist/hip ratio 51 male and 190 female overweight (body mass index (BMI) 25.0 kg/m²) compared with a 26 male and 83 female control group (BMI = 18.5-24.9 kg/m²) Thai volunteers who attended the Out-patient Department, General Practice Section, Rajvithi Hospital, Bangkok, for a physical check-up during March-October, 1998, were investigated. There was no age difference between overweights and controls. All of the anthropometric variables, except the height of the overweight group, were

significantly higher than those of normal subjects. The medians of weight and waist/hip ratio of overweight and obese males were significantly higher than those of overweight and obese females. Serum ceruloplasmin, copper were statistically significantly higher in overweight subject than in controls. While, serum zinc and superoxide dismutase activity in overweight were found to be lower than in control group. Higher serum cerulo-plasmin, copper, zinc and superoxide dismutase activity were shown in male overweight than in female. Ceruloplasmin was found to be positively correlate with copper concentration but negatively related with superoxide dismutase enzyme activity. A negative correlation was found between serum copper and zinc concentrations in both sexes of overweight and obese subjects. Low SOD activity found in overweight and obese subjects might cause by low zinc intake. ■

(Tropical Medicine, Mahidol University & Free University of Berlin)

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ANTIOXIDANT ENZYME LEVEL IN THE ERYTHROCYTE IN RIBOFLAVIN DEFICIENT AND TRICHINELLA SPIRALIS-INFECTED RATS

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The objective of this study was to investigate certain important erythrocyte antioxidant enzyme level and hepatic histology in the riboflavin-deficient and *Trichinella spiralis*-infected rats. The rats were deprived of riboflavin at 8th weeks of the experiment with the erythrocyte glutathione reductase activity coefficient (EGR AC) values ≥ 1.30 while as there was no biochemical sign of riboflavin deficiency appeared in rats infected with *T. spiralis*. At the 12th week of the experiment, the level of catalase, superoxide dismutase (SOD) and glutathione peroxidase

(GSH-Px) was significantly lowered in the riboflavin-deficient, *T. spiralis*-infected and combined riboflavin-deficient and *T. spiralis*-infected rats as compared to the control group. This may be due to more free oxygen radicals as a consequence of riboflavin deficiency. However, in the group with combined administration of riboflavin deficiency and *T. spiralis* infection the level of three antioxidant enzymes tended to be insignificantly higher than that of in the rats fed only riboflavin-deficient diet or *T. spiralis* infection alone. It was probably implicated in more *T. spiralis*-produced antioxidant enzyme per se, especially SOD and GSH-Px. It was probable that *T. spiralis* itself may have to cope with more additional free oxidants that underlying by stress from the riboflavin deficiency and *T. spiralis* infection. ■

(Graduate from Free University of Berlin)

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MUTATIONAL ANALYSIS OF RAS GENE FAMILY IN LUNG CANCER IN THAI

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▶ **H-, K- and N-*ras*** gene mutations were analyzed in lung cancer from Thai patients. Thirteen out of 58 cases (22%) harbored the mutations. Ten cases showed K-*ras* gene mutations at codon 12, 1 case presented a mutation at codon 13 and another

case exhibited a mutation at codon 63. Silent mutations of N-*ras* gene in codons 57 and 62 were seen in one patient, whilst no H-*ras* mutation was found in these patients. Bases change in K-*ras* gene were G T transversion (62%), G A transition (15%) and G C transition (15%), whereas T G transversion and A G transition were detected in N-*ras* mutant gene. ■

(The China Medical Board of New York, Inc. (USA)

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RELATIONSHIP BETWEEN SOLUBLE LEPTIN RECEPTOR, LEPTIN, LIPID PROFILES AND ANTHROPOMETRIC PARAMETERS IN OVERWEIGHT AND OBESE THAI SUBJECTS

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▶ **Median**, range and 95% confidence interval (CI) for median of age, anthropometric variables, soluble leptin receptor, serum leptin and lipid profile levels of 48 overweight (BMI 25.00 kg/m²) Thai males and 166 overweight Thai females, compared with 26 males and 81 females in a control group (BMI = 18.50-24.99 kg/m²), were determined. Subjects for the study were those persons who turned up regularly for physical check-ups at the Out-patient Department, General Practice Section of Rajvithi Hospital, Bangkok. Serum leptin, triglyceride and low density lipoprotein cholesterol/high density lipoprotein cholesterol ratio (LDL-C/HDL-C ratio) were significantly higher in the overweight and obese males and females. Soluble leptin receptor and HDL-C were

significantly lower in the overweight and obese males and females. Cholesterol and LDL-C were significantly higher in overweight and obese females but there was no significant difference in the overweight and obese males when compared with the control males. Low soluble leptin receptor levels were found in 38.1% (8/21) of the overweight and obese males, while 31.5% (29/92) were found in the overweight and obese females. Elevated leptin levels were found in 66.7% (32/48) and 89.8% (149/166) of the overweight and obese males and females, respectively. Both low soluble leptin receptor levels and elevated leptin levels were found in 9.5% (2/21) and 29.4% (27/92) of the overweight and obese males and females, respectively. A significant positive correlation was found between soluble leptin receptor and cholesterol, and also between weight, BMI, waist, hip and HDL-C with leptin. Serum soluble leptin receptor levels were significantly negatively correlated with leptin and BMI in all subjects. ■

(Mahidol University Research & Free University of Berlin)

Submitted to: *Nutr Res* 2003.

IDENTIFICATION OF GENETIC ALTERATIONS IN HUMAN CANCERS USING ARBITRARILY PRIMED PCR

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Development of human cancers caused by accumulation of genes abnormality. In many cancers, saturated genetic alterations are not available.

The arbitrarily primed PCR is a gene amplification based DNA fingerprinting technique that use single primer of random nucleotide sequences and several PCR cycles of low stringency. Comparison of the PCR fingerprints from matched tumor and normal tissues allows the detection of allelic losses and gains in tumor cells by the reduction or increase in intensity

of tumor fingerprint bands, respectively.

By using the arbitrarily primed PCR with a set of 60 single primers followed by gene cloning and nucleotide sequencing, we are able to identified a novel tumor markers DNA in several human cancers in Thai patients such as ovary, breast, cervix, lung, liver cancers and cholangiocarcinoma. ■

Presented at: National Cancer Conference in Celebration of the Auspicious Occasion of Her Majesty the Queen's 6th Cycle Birthday Anniversary on the 12th August 2004, Oncology II after 2000, Imperial Queen's Park Hotel, November 12-14, 2003, Bangkok, Thailand. p.46.

PLATELET FATTY ACIDS IN CORONARY HEART DISEASE, DYSLIPIDEMIA, HYPERTENSION AND HEALTHY CONTROLS

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A cross-sectional study was performed to investigate 250 volunteers from Pramongkutklo Hospital, Samphanthawong district, Wat Chaiyapreukmala and Wat Pradoo in Taling Chan districts. They were divided into groups of 35 apparently healthy males, 16 males with coronary heart disease, 37 males with dyslipidemia and 9 males with hypertension with age ranges of 24-62, 56-69, 25-69 and 26-75 years, respectively. The female groups were composed of 55 apparently healthy females, 10 females with coronary heart disease, 73 females with dyslipidemia and 15 females with hypertension with age ranges of 27-65, 33-67, 22-73 and 38-70 years, respectively. Platelet fatty acids levels were found to have no significant difference between the different male

groups. In the female group, the -linolenic acid (ALA) level in hypertension was significantly higher than in coronary heart disease (CHD) ($p < 0.05$), whereas the arachidonic acid (AA) level in hypertension was significantly higher than in the apparently healthy females ($p < 0.05$). No correlation was found between platelet fatty acids and age or anthropometric parameters, which indicate that platelet fatty acids may not depend on either age or anthropometric parameters. Positive correlations were shown between ALA and cicosapentaenoic acid (EPA), AA and docosahexaenoic acid (DHA), ALA and the diastolic blood pressure, DHA and total cholesterol (TC), and between low density lipoprotein cholesterol (LDL-C) and plasma glucose. Negative correlations were shown between LA and EPA, AA and EPA, EPA and DHA, EPA and the systolic blood pressure, and AA and the diastolic blood pressure. ■

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THE ASSOCIATION OF FOLATE STATUS AND CERVICAL DYSPLASIA IN THAI WOMEN

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The relationship between folate status and incidence of cervical dysplasia was studied among Thai women that identified from National Cancer Institute, Bangkok Metropolitan Administration Medical College, Vajira Hospital and Chonburi Cancer Center. Fasting blood samples were collected from 134 women with mild, moderate, severe cervical dysplasia and 95 women with cytological normal as a control group for this serum vitamin analysis by radioassay. Cervical smears cytology obtained for histological diagnosis and colposcopy directed biopsy investigated as a confirmation. The polymerase chain reaction (PCR) method was used to define the presence or absence of genital HPV DNA. The socioeconomic background, gynecologic history and others

possible risk factors were also performed by personal interview and the daily intakes of folate was investigated by 24-hours recall.

Serum folate of the women with cervical dysplasia indicated statistical significant less than that of the control group ($p < 0.001$), whereas the daily folate intake in both groups had no difference. The median daily folate consume in all studied groups were less than daily recommendation from Thai committee of daily nutrients intake recommendation and Dietary Reference Intake, Food and Nutrition Board of America and Canada (DRIs). Serum folate was strong inverse correlated with the severity of dysplasia ($r = -0.37$; $p < 0.001$). Using the logistic regression individuals whose serum folate was in the lower two tertiles had nearly ten-fold risk for dysplasia than did those in the upper tertile. This finding supported that the state of folate deficiencies increase risk of cervical change in women in this study. ■

(Abstracts, the IX Asian Congress of Nutrition, New Delhi, India, February 23-27, 2003; 349)

MUTATIONAL ANALYSIS OF THE PTEN GENE LOCALIZED AT CHROMOSOME 10Q23 IN THAI PATIENTS WITH GLIOMAS

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Phosphatase and tensin homologue deleted on chromosome 10 (*PTEN*), a tumor suppressor gene located on chromosome 10q23, has recently been shown to act as a phosphatidylinositol 3,4,5-triphosphate phosphatase and to modulate cell growth and apoptosis. Genetic alterations in the *PTEN* tumor suppressor gene occur in several types of human cancers including glioblastoma, prostate, and breast. We examined

genetic alterations of the *PTEN* gene in human gliomas. We screened 28 astrocytic tumors for mutations throughout the *PTEN* coding regions using polymerase chain reaction-single strand conformation polymorphism (PCR-SSCP), Klenow treatment and direct DNA sequencing of aberrantly migrating PCR products. We found nucleotide changes in introns but no mutations that caused amino acid alterations. Interestingly, the intronic mutations accompanying silent mutations were found only in patients with glioblastomas. In conclusion, the majority of astrocytic tumors do not carry mutations of the *PTEN* gene, which suggests that there may be other genes on chromosome 10 which are important in the tumorigenesis of gliomas. ■

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AFLATOXINS M₁ AND M₂ IN HUMAN BREAST MILK

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▶ **Aflatoxin** concentrations were investigated in the breast milk of 124 lactating women whose ages ranged from 16-42 years. Sixty-four mothers were from Bangkok metropolitan area and 60 were from Khon Kaen, in northeastern Thailand. The nutritional status of the mothers in both groups, assessed by anthropometric measurements i.e. body mass index (BMI) and mid-upper arm circumference (MUAC) were similar. The triceps skin-fold thickness (TSK) of the mothers in Bangkok was overall significantly higher than those of the mothers from Khon Kaen, resulting in significantly lower mid-upper arm muscle circumference (MUAMC) of the mothers from Bangkok, compared with the mothers from Khon Kaen. Only aflatoxins M₁ and M₂ were found in the breast milk samples investigated. Aflatoxin M₁ (AFM₁) was most frequently detected as it was

found in 10 (15.6%) and 14 (23.3%) breast milk samples of the mothers from Bangkok and Khon Kaen, respectively. Aflatoxin M₁ was detected at a median concentration of 20 ng/L (range: 5-409 ng/L) for mothers from Bangkok, and 23 ng/L (range: 4-6,372 ng/L) for mothers from Khon Kaen. Aflatoxin M₂ (AFM₂) was detected in 2(3.1%) and 13(21.7%) breast milk samples for mothers from Bangkok and Khon Kaen, respectively. The median concentration of aflatoxin M₂ in milk samples of mothers from Bangkok was 10 ng/L (range: 5-15 ng/L), and 63 ng/L (range: 4-1,140 ng/L) for milk samples of mothers from Khon Kaen. Among these, AFM₁ and AFM₂-contaminated milk samples, a mixture of AFM₁ and AFM₂ was found in 1.6% breast milk samples from Bangkok and 13.3% from Khon Kaen. It could be extrapolated that mothers from Khon Kaen were at higher risk of consuming aflatoxin-contaminated food than mothers from Bangkok. ■

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AN ULTRASTRUCTURAL STUDY OF THE BRAIN IN FATAL PLASMODIUM FALCIPARUM MALARIA

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▶ **Cerebral** malaria (CM) is a major cause of death in severe *Plasmodium falciparum* malaria. We present quantitative electron microscopic findings of the neuropathologic features in a prospective clinicopathologic study of 65 patients who died of severe malaria in Thailand and Vietnam. Sequestration of parasitized red blood cells (PRBCs) in cerebral microvessels was significantly higher in the brains of patients with CM compared with those with non-cerebral malaria (NCM) in all parts of the brain (cerebrum, cerebellum, and medulla oblongata). There was a hierarchy of sequestration

with more in the cerebrum and cerebellum than the brain stem. When cerebral sequestration was compared with the peripheral parasitemia pre mortem, there were 26.6 times more PRBCs in the brain microvasculature than in the peripheral blood. The sequestration index was significantly higher in CM patients (median = 50.7) than in NCM patients (median = 6.9) ($P = 0.042$). The degree of sequestration of *P. falciparum*-infected erythrocytes in cerebral microvessels is quantitatively associated with pre-mortem coma. ■

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PATHOLOGIC STUDY OF ACUTE TOXOPLASMOSIS IN EXPERIMENTAL ANIMALS

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▶ We studied the pathology of acute toxoplasmosis in experimental mice inoculated with RH strain tachyzoites of *Toxoplasma gondii*. All died from severe disseminated toxoplasmosis involving the liver, spleen and pancreas.

Pathological features of acute toxoplasmosis in susceptible mice could be regarded as an excellent model for acute reactivation of *Toxoplasma* in the immunosuppressed host. ■

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SPECIFIC MONOCLONAL ANTIBODIES TO STRONGYLOIDES STERCORALIS: A POTENTIAL DIAGNOSTIC REAGENT FOR STRONGYLOIDIASIS

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▶ In this study, specific hybridomas secreting monoclonal antibodies (MAb) to antigen of *Strongyloides stercoralis* filariform larvae were produced. Specific epitopes targeted by the MAb were protein in nature and located *in situ* in the internal content of the filariform larvae of the parasite but not in the esophagus. The MAb reacted to the homologous antigen in an indirect ELISA but did not reveal any reaction to the SDS-PAGE separated-homologous antigen in a Western blot analysis (WB) suggesting a conformational epitope specificity. The MAb were of IgG1 isotype which is the isotype known to have high affinity to this epitope so they were used

in a dot - ELISA to detect the antigen of the parasite. The assay could detect the epitopes in 78 ng or more of the crude filariform larval extract but did not reveal any positive result when applied to detect antigen in stool samples of parasitologically confirmed strongyloidiasis patients. The negative antigen test results can be explained as follows. Either the MAb were filariform stage-specific and thus did not recognize the rhabditiform larval antigen mainly contained in the patient's stool or the amounts of antigen in the stool samples were too small and/or unevenly dispersed. In the latter instance, the MAb developed in this study would have a diagnostic potential if used in an immunological test design where more volume of fresh stool sample could be accommodated in the test, e.g. a sandwich plate ELISA. ■

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

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▶ Many species of the genus *Leishmania* cause many diseases in tropics and subtropics. There are many ways to detect each of those diseases. We present one of the laboratory detection

for the confirmation diagnosis of cutaneous leishmaniasis (be caused by *L. tropica*) by the examination of a skin ulcer smear that is stained with a modified method of Wright staining of blood (*ie* that used for routine hematological). ■

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TYPING OF DENGUE VIRUSES IN CLINICAL SPECIMENS FROM CENTRAL THAILAND

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► **Dengue** virus infection is a very old disease that had a widespread distribution in the tropics and subtropics with all four dengue serotypes co-circulating epidemic in the large urban centers of most countries. We performed the serotyping of dengue viruses in the specimens from a total of 136 patients

(children under 15 years old) suspected of having dengue virus infections and who had been admitted to Pathumthani Provincial Hospital, Thailand, during the period May, 1999 to April, 2000. Altogether 44 strains were isolated (isolation rate : 32.4%); consisting of 18 DEN-1, 18 DEN-2, 7 DEN-3 and 1 DEN-4. The isolation rate decreased according to the number of days after the onset of disease, from day 4 to day 8. ■

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THE CAUSES OF REDUCED MICROCIRCULATORY FLOW IN SEVERE FALCIPARUM MALARIA: AN ELECTRON MICROSCOPIC STUDY

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► **One** of the most important features of the biology of *Plasmodium falciparum* is its ability to cause infected red blood cells to adhere to the endothelium of blood vessels. The adherence is mediated by contacts between electron dense knobs on the infected cell surfaces and the endothelial membrane. This process is termed “sequestration”.

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

to traverse the capillary and, when erythrocytes are unusually rigid, obstruction may occur.

In larger vessels, erythrocytes contain mature parasites formed a layer along the endothelium (margination). A number of young parasites infected red cells and normal red cells were seen in the center of the lumen. Aggregation of normal red cells were observed. When infected cells were seen in the aggregation, special observation was performed in attempt to find out whether there is any rosette formation. Occasionally, an infected cell was found enclosed by red blood cells which may represent rosette formation. The infected red cells appeared attach to the other infected cells. It was suggested that these cells stuck together and had difficulty passing through the capillary bed and could further slow down microcirculatory flow.

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

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

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THE CAUSES OF REDUCED MICROCIRCULATORY FLOW IN SEVERE FALCIPARUM MALARIA AND THEIR PATHOPHYSIOLOGIC SIGNIFICANCE

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The pathophysiology of severe falciparum malaria is complex, but evidence is mounting that its central feature is the old concept of a mechanical microcirculatory obstruction. The principal cause for this is cytoadherence of erythrocytes containing the mature forms of the parasite to the vascular endothelium, leading to sequestration and obstruction of small vessels. In post-mortem brain biopsies capillaries clogged up by parasitised red cells blocking cues of unparasitised red cells can be clearly demonstrated. However, this sequestered parasite biomass is difficult to assess during life from the peripheral blood film of a patient, although the presence of late stages in the film is an indicator for a larger proportion of sequestered parasites. Besides their ability to sequester, parasitised red cells also become rigid, compromising their flow through capillaries that often have smaller midline diameters than their own. This rigidification is due to changes in the red cell membrane, like the incorporation of knob associated histidine rich protein, increase of the internal viscosity of the red cell by the presence of the relatively undeformable parasite and an unfavorable, more spherical, surface to volume ratio. Moreover, the uninfected erythrocytes can become rigid in severe malaria. This lack of deformability may be particularly important in areas of intense sequestration where the lumen is reduced below a critical threshold of around 5 mm (inversion of the Fåhrus Lindqvist phenomenon). Reduction in the overall red cell deformability has proven to be

a strong predictor for a fatal outcome in severe malaria.

Finally, adhesive forces between infected red cells (auto-agglutination), between infected and uninfected red cells (rosetting) and between uninfected erythrocytes (aggregation) could further slow down microcirculatory flow, but their contribution will depend on their ability to resist shear forces present in the microcirculation.

Until recently there was no direct evidence *in vivo* to what extent the microcirculation in severe malaria is indeed disturbed, although there was strong circumstantial evidence. Lactic acidosis, due to increased anaerobic glycolysis, is an important feature of severe malaria and has a strong prognostic value. Moreover, it can be derived from measurements of cerebral blood flow in severe malaria that vascular resistance is increased. However, a new technique enables us to directly visualize the microcirculation on mucosal surfaces in patients with severe malaria. The Orthogonal Polarisation Spectral imaging device is a small, hand-held, microscope giving clear intravital images of red blood cells flowing through the microcirculation. A video will be shown, demonstrating obstruction of capillaries by sequestered red cells *in vivo*. Microcirculatory flow appears to be very inhomogeneous, with hyperdynamically perfused capillaries adjacent to obstructed microvessels. ■

Presented at: International Conference on “Malaria: Current Status and Future Trends”. February 16-19, 2003. The Convention Center, Chulabhorn Research Institute, Bangkok, Thailand.

PATHOLOGICAL CHANGES IN SEVERE MALARIA

Isabelle M Medana, Nicholas PJ Day, Tran Tinh Hien, Emsri Pongponratn, David Ferguson, Nguyen Thi Hoan Mai, Nicholas J White, Gareth DH Turner

Cerebral malaria is still a major killer in the developing world, but we know very little about the causes of this disease.

How does *Plasmodium falciparum* cause such a devastating neurological disease while it remains in the brain vasculature?

Why do some patients die, whereas others survive? What processes contribute to disease in the brain, and can we reverse them?

The talk will summarise the major pathological changes that occur in severe malaria, using autopsy data from clinicopathological studies of fatal and severe malaria in south East Asia. The major neuropathological features of disease will be reviewed, including parasitised erythrocyte sequestration, haemorrhages, cellular and glial immune responses, cerebral oedema and pigment deposition. In addition a summary of possible pathophysiological mechanisms will be discussed, which might contribute to coma and cerebral dysfunction in severe malaria. This will concentrate on several potential mechanisms identified by our research in the past 10 years, which might be targets for therapeutic intervention as

secondary neuroprotective therapy in severe malarial coma. These include

- i) Axonal Injury
- ii) Hypoxia-inducible proteins
- iii) Blood-brain barrier function
- iv) Soluble neurotoxic metabolites of the Kynurenine pathway

These results will be put in the context of a potential model, where the role of parasite induced cerebral endothelial cell signaling allows transduction of pathogenic stimuli into the brain parenchyma. ■

Presented at: 4th Seminar on Food-and Water-borne Parasitic Zoonoses 2nd International Meeting on Gnathostomiasis Joint International Tropical Medicine Meeting 2003, 2-4 December 2003, Siam City Hotel, Bangkok, Thailand.

CRYPTOCOCCAL MENINGITIS IN HUMAN IMMUNODEFICIENCY VIRUS (HIV)-POSITIVE AND HIV-NEGATIVE PATIENTS

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This study compared clinical manifestation, blood biochemistry and cerebrospinal fluid (CSF) results in patients with cryptococcal meningitis between HIV-positive and HIV-negative patients. We collected 57 cases of cryptococcal meningitis from the cytological specimens submitted to the Department of Tropical Pathology. Pertinent clinical data were analyzed retrospectively in 47 cases and compared with the clinical manifestations, laboratory features and outcome in 38 HIV-positive and 9 HIV-negative patients. Headache was the commonest symptom seen in all cases of which 70.2% occurred with fever. CSF examination of HIV-positive and HIV-negative cases revealed an elevated opening pressure. An increased in CSF protein and depressed CSF glucose were seen in HIV-negative cases.

This differs from HIV-positive cases where slight change was noted in those parameters. CSF pleocytosis in HIV-positive was variable. Forty eight percent of HIV-positive patients had CSF leucocytes count below 20 cells-mm³. None was found in HIV-negative patient. The depressed in immune response may be accounted for. Specific treatment of amphotericin B, fluconazole and itraconazole were given in this study. Five fatal cases of cryptococcal meningitis were noted. All of which were HIV-positive. There were statistically significant difference between HIV-positive and HIV-negative patients of blood neutrophils, blood eosinophils, CSF leucocytes count, CSF neutrophils, CSF lymphocytes, CSF glucose and CSF total protein. ($p = 0.050$, $p = 0.022$, $p = 0.002$, $p = 0.016$, $p = 0.047$, $p = 0.031$, $p = 0.009$, respectively). ■

Presented at: 4th Seminar on Food-and Water-borne Parasitic Zoonoses, 2nd International Meeting on Gnathostomiasis, Joint International Tropical Medicine Meeting 2003, 2-4 December 2003, Siam City Hotel, Bangkok, Thailand.

LIGHT AND ELECTRON MICROSCOPY OF KNOB PROTEINS AND STAGING IN VITRO: *PLASMODIUM FALCIPARUM*

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Knobs are structures found on the membrane of *Plasmodium falciparum*-infected red blood cell (PRBC) when the parasites mature to trophozoite and schizont stages. These knobs form focal junctions with the endothelial cell membrane or with the knobs of other infected red blood cells, resulting in the sequestration of these PRBC along the vascular endothelium, leading to vascular obstruction. Various studies have reported that microvascular sequestration of PRBC is considered to play a central role in the pathogenesis of organ failure in severe falciparum malaria, especially in cerebral malaria. This study was proposed to examine the time and parasite stage of knob appearance on PRBC membrane using transmission electron microscopy (TEM). Three to five ml of blood from 3 *P. falciparum* infected patients with more than 3% parasitemia were taken (isolate AQ 846, AQ 933 and NAC 105). Two laboratory strains (A4 and C10) were also included in the study. Synchronous cultures were performed and erythrocytes were collected in every 4 hours until one intraerythrocytic cycle was completed. The number of PRBC examined under light microscope of isolate AQ 846 and laboratory strain A4 was not statistically significant difference

between light microscopy and TEM ($p = 0.51$ and $p = 0.36$, respectively). In contrast, the number of PRBC isolates AQ 933, NAC 105 and laboratory strain C10 observed under TEM were statistically higher than observation by light microscope ($p < 0.05$). Ultrastructural study using TEM showed that the appearance of knobs on the surface of PRBC was first revealed at 16 hours for two patients (isolate AQ 933 and NAC 105), and one laboratory strain (C10). The other clinical isolate (AQ 846) and one laboratory strain (A4) showed knobs which appeared at 20 hr. The parasite stages at which the knobs first appear were large ring stage and growing trophozoite. The knobs were found on PRBC from large ring stage to schizont stage. An increasing of a number of knobs was associated with the maturation of the parasites. The result of this study contributes to the understanding of PRBC sequestration in the microcirculation. The time of knob appearance may correlate to parasites sequestration in deep visceral organ which influences the severity of malaria. ■

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QUANTITATIVE ULTRASTRUCTURAL STUDY OF LIVER AND SPLEEN IN FATAL *FALCIPARUM* MALARIA

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Enlargement of the liver and spleen are common findings in falciparum malaria. This enlargement may associate with sequestration of parasitized red blood cells (PRBC) and premature destruction of red blood cells (RBC). In order to demonstrate this effect, quantitation of the amount of RBC, PRBC and phagocytes that show phagocytosed PRBC or malarial pigments in hepatic and splenic sinusoids of fatal falciparum malaria was performed using transmission electron microscopy. PRBC

sequestration in the liver and the spleen were compared with PRBC in the peripheral blood, to calculate sequestration index (S.I.). The sequestration index was not significantly different for PRBC sequestered in the liver and the spleen of the same patient. However the number of RBC and PRBC including knob positive PRBC (K⁺ PRBC) and knob negative PRBC (K⁻ PRBC) were significant higher in the spleen than the liver ($p = 0.012$, 0.012 , 0.018 and 0.012 , respectively). The number of phagocytic cells in the spleen was significantly higher than in the liver of the same patient ($p = 0.012$). This implies that spleen is the major organ of culling abnormal red blood cells. To determine whether the

pathological features of the liver and the spleen was associated with the complications in falciparum malaria, the pathological features of each organ were compared between different clinical groups. Statistically results showed that the parameters examined in the liver and the spleen were almost similar between cerebral malaria (CM) and non-cerebral malaria (NCM) patients. There was no significant different in most of counting parameters in the liver and spleen between acute renal failure (ARF) and non-acute renal failure (NARF) cases except the number of K⁺PRBC in the liver. The number of K⁺PRBC in the liver was significant higher in ARF patients than NARF patients ($p = 0.026$). Of the fatal

cases with jaundice, it was found that K⁺PRBC and phagocytic cells in the liver were significantly higher compared to those cases without jaundice ($p = 0.05$ and 0.05 , respectively). ■

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NITRIC OXIDE INVOLVEMENT IN PATHOGENESIS OF KIDNEY IN FALCIPARUM MALARIA

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▶ **The** role of nitric oxide (NO) in renal diseases including renal failure in falciparum malaria is still controversial. The objective of this study was to determine the association between severity of renal injuries and amount of NO in kidney. Kidney sections from thirty severe falciparum malaria patients autopsied during 1969-2001 were examined 1) histopathologic changes by standard hematoxylin and eosin staining, and 2) amount of inducible nitric oxide synthase (iNOS), the important NO synthesized enzyme during infection, by immunostaining. The degrees of renal histopathologic changes observed in glomeruli, tubules, blood vessels and interstitial tissues were recorded. Glomerular changes included sequestration, mesangial cell proliferation, mesangial thickening and proteinaceous material

in Bowman's space; tubular changes included cloudy swelling, hydropic degeneration, coagulative necrosis, acute tubular necrosis, proteinaceous material in the lumens; inflammatory cell infiltration in interstitium were graded. The expression of iNOS was found in mesangial cells, glomerular epithelium, tubules, mononuclear cells, endothelium and smooth muscle of blood vessels. The intensity of immunostaining referred to amount of iNOS and NO was vary in each case. The correlation between severity of renal injuries and amount of iNOS will be discussed in detail. ■

Presented at: International Conference on Malaria: Current Status and Future Trends. February 16-19, 2003. Convention Center, Chulabhorn Research Institute, Bangkok, Thailand.

COMPARISON OF THE FIRST FIND MATURE FEMALE ADULT AND THE THIRD STAGE LARVA OF G. SPINIGERUM REMOVED FROM THAI PATIENTS

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▶ **Many** species of the genus gnathostoma causing human gnathostomiasis which was found in many countries in the world. In Thailand, the disease causes by eating the inappropriately cooked food harboring advanced third stage of the gnathostome larvae. Man is the accidental host of the worm. We studies the morphology of the first find female adult

and compared with the third stage larva which recovered from Thai patients by the size and the external morphology. There are apparent distinguishable features in size, cuticle and reproductive system. ■

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GNATHOSTOMIASIS IN THAILAND : A REVIEW

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▶ In Thailand, human gnathostomiasis is caused by eating the inappropriately cooked food harboring advanced third stage of the Gnathostome larvae. The prevalence of *Gnathostoma spp.* infections in animals were found in almost every province; whereas most of the cases were from the central of Thailand.

Nowadays, there are many ways to confirm the diagnosis. Few drugs are used to treat this disease; however, the results of the treatments have not been concluded. ■

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THE DIVERSE PATHOLOGICS OF 41 FATAL MALARIA CASES IN THAILAND

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▶ In Thailand, *Plasmodium falciparum* is the cause of cerebral malaria (CM) in human which is fatal. This is the study of the significant pathological differences from 41 autopsies of falciparum malaria; 25 cases with CM and 26 cases with non-CM. All of the cases had petechial hemorrhages; congested with parasitized and non-parasitized red blood cells

in the capillaries of the brains and the interstitial vessels congested in the kidneys too. Nineteen cases were pulmonary edema and 21 cases were pneumonia. Twenty cases were clinical respiratory failure. Farther more, falciparum malaria involved the other internal organs. One case was cerebral malaria which mixed infection with *P. vivax* and *P. falciparum*. ■

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REDUCED MICROCIRCULATORY FLOW IN SEVERE FALCIPARUM MALARIA: PATHOPHYSIOLOGY AND ELECTRON-MICROSCOPIC PATHOLOGY.

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▶ The pathophysiology of severe falciparum malaria is complex, but evidence is mounting that its central feature is the old concept of a mechanical microcirculatory obstruction. Autopsy studies, but also *in vivo* observations of the microcirculation, demonstrate inhomogeneous distributed obstruction of the microcirculation in severe malaria. The principal cause for this is cytoadherence to the vascular endothelium of erythrocytes containing the mature forms of the parasite, leading to sequestration and obstruction of small vessels. Besides, parasitized red cells become rigid, compromising their flow through capillaries whose lumen has

been reduced by sequestered erythrocytes. Adhesive forces between infected red cells (auto-agglutination), between infected and uninfected red cells (rosetting) and between uninfected erythrocytes (aggregation) could further slow down microcirculatory flow. A more recent finding is that uninfected erythrocytes can also become rigid in severe malaria. Reduction in the overall red cell deformability has a strong predictive value for a fatal outcome. Rigidity is presumably caused by oxidative damage to the red blood cell membrane by malaria pigment released at the moment of schizont rupture. Antioxidants like N-acetylcysteine can reverse this effect and are promising as adjunctive treatment in severe malaria. ■

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THE EFFECTIVENESS OF 3, 5 OR 7 DAYS OF ALBENDAZOLE FOR THE TREATMENT OF *TRICHURIS TRICHIURA* INFECTION

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▶ A randomized clinical trial was carried out to study the relationship between the duration of albendazole therapy, at 400 mg/day, and its effectiveness in the treatment of *Trichuris trichiura* infection. The 168 patients were treated for three ($N = 56$), five ($N = 56$) or seven ($N = 56$) consecutive days. Compared with both of the shorter regimens, treatment for 7

days resulted in a significantly higher cure rate and significantly greater reductions in the level of egg excretion. The advantage of using the longer (5- or 7-day) regimens was most apparent among the patients who had heavy infections (at least 1000 *Trichuris* eggs/g faeces) when treated. It is therefore suggested that albendazole be given for at least 3 days to those with light infections and for 5-7 days to patients with heavy infections. ■

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PREVALENCE OF INTESTINAL PARASITIC INFECTION AMONG THAI PEOPLE WITH MENTAL HANDICAPS

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The prevalence of intestinal parasitic infection was studied by stool examination in institutionalized and non-institutionalized Thai people with mental handicaps. It was found that the prevalence of infection was much higher in institutionalized (57.6%) than in non-institutionalized people (7.5%). The common parasites found in institutionalized people

were *Trichuris trichiura* (29.7%), *Entamoeba coli* (23.1%), *Giardia intestinalis* (8.0%), *Hymenolepis nana* (7.8%), and *Entamoeba histolytica/dispar* (7.1%). Institutionalized mentally handicapped people should be considered as a high risk group for intestinal parasitic infection and a parasitic control measure should be emphasized. ■

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MATERNALLY TRANSFERRED NEUTRALISING DENGUE ANTIBODIES IN THAI INFANTS: A PILOT STUDY

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▶ In a dengue-endemic area, sera from 42 mother-infant pairs and sera collected from the infants at follow-up at the ages of 3 months ($n=27$), 6 months ($n=34$), 9 months ($n=23$) and 12 months ($n=8$) were tested for antibodies to four dengue serotypes using a plaque reduction neutralisation test (PRNT50), IgG ELISA and haemagglutination inhibition assay (HAI). The IgG ELISA and HAI tests were less sensitive than PRNT50 in detecting low levels of antibodies. Levels of maternally transferred dengue neutralising antibodies in the

cord sera were very high and identical to those in the mothers. Neutralising antibody prevalences in the newborns were 95% to dengue serotype 1 (DEN-1), 93% to DEN-2 and DEN-3 and 91% to DEN-4. The antibodies decreased with increasing age. At least one dengue serotype neutralising antibody persisted in the infants at ages 3, 6 and 9 months in 92%, 69% and 13%, respectively. No maternally transferred antibody was observed in 12-month-old infants. In endemic areas therefore, where most infants have maternally transferred dengue antibodies, interference with dengue vaccine is likely to be less after 12 months of age than before then. ■

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PREVALENCE OF INTESTINAL PARASITIC INFECTION AMONG PEOPLE WITH MENTAL HANDICAPS AND THE PREVALENCE AT ONE YEAR AFTER CHEMOTHERAPY

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The prevalence of intestinal parasitic infection among people with mental handicaps was studied in Thai institutionalized and non-institutionalized people. It was found that the prevalence of infection was much higher in institutionalized than in non-institutionalized people (prevalence 57.6 and 7.5% respectively). The common parasites found in institutionalized people were *Trichuris trichiura*, *Entamoeba coli*, *Giardia intestinalis*, *Hymenolepis nana*, and *Entamoeba histolytica/dispar* (prevalence 29.7, 23.1, 8.0, 7.8 and 7.1% respectively). Very crowded

environment, poor food and water hygiene, as well as improper health behavior may be predisposing factors.

A single dose treatment with tinidazole for *Giardia* infection in institutionalized people did not affect its prevalence one year later. On the other hand, a single dose of albendazole decreased the prevalence of *Trichuris* and hookworm infection significantly. However, the prevalence of these infections one year after the treatment was still high. Further studies for appropriate medication, including dosing interval, and other controlling measures are recommended. ■

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

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

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

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

one month after the third dose for JE neutralizing antibody response using the corresponding JE virus strain.

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

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

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

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

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

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

Materials & Methods: A randomized controlled trial was carried out in children aged 7-15 years old with giardial infection. Fifty-eight children were allocated into 2 regimens, group 1 (n = 31) albendazole 400 mg combined with

praziquantel 20 mg/kg and group 2 (n = 27) tinidazole 50 mg/kg single dose. The treatment was considered as a cure when *Giardia* was not found in two consecutive stool samples.

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

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

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

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

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

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

Materials & Methods: Twenty children with giardia infection were randomly allocated for 400 mg albendazole combined with 20 mg/kg praziquantel group (n=10) or albendazole 400 mg group (n=10) alone. Blood samples were

collected through a 24-hour period of drug administration. Concentrations of albendazole/albendazole sulphoxide in plasma were quantified by using high performance liquid chromatography.

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

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

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

HOW MANY POLYMORPHIC MARKERS ARE REQUIRED TO IDENTIFY VIRULENCE LOCI BY ALLELIC ASSOCIATION WITH SEVERE FALCIPARUM MALARIA?

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Parasite genetic determinants of virulence in human malaria have not clearly been identified. Microsatellite markers are very abundant in the *Plasmodium falciparum* genome, suggesting that case-control studies might be able to use a genome-wide allelic association approach to find virulence loci. The magnitude of linkage disequilibrium (LD) between linked sites declines with increasing molecular map distance, and it is necessary to know the rate of this decline to estimate the minimum density of markers required. In a sample of 100 *P.*

falciparum isolates from Thailand, Among 16 linked microsatellites spanning a distance of ~135 kb on chromosome 2, significant LD was only rarely seen beyond distance of 10 kb. The *P. falciparum* genome is 23 Mb, so this implies that a minimum of 2300 polymorphic markers either microsatellite loci or SNPs will be required for whole-genome studies to identify allelic association in *P. falciparum* in Thailand. Therefore, genome-wide allelic association is not feasible to identify the virulence loci of severe falciparum malaria. ■

(Presented at International Conference on Malaria: Current Status and Future Trends, 16-19 February 2003).

ASSESSMENT OF PAIN IN CHILDREN WITH HIV/AIDS: A PILOT STUDY

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Background: Children with human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) are believed to experience a significant amount of pain. This may significantly interfere with their quality of life. The prevalence and characteristics of pain were investigated in a group of Thai children with HIV infection.

Materials & Methods: We developed a child and a caregiver questionnaire to determine the overall occurrence, the characteristics and the impact of pain. Three commonly used pain scales, the visual analogue scale, the Wong-Baker Faces Pain Scale, and the Faces Pain Scale Revised were administered alongside the child questionnaire. We interviewed 61 patients attending HIV clinic, Queen Sirikit National Institute of Child Health, and an equal number of age-matched, healthy children with their caregivers.

Results: Forty-four percent of HIV-infected children reported significant pain compared to 13 percent of healthy children ($p < 0.01$). Seven percent of the infected children

experienced chronic pain. Children with HIV disease stages B and C reported more pain than children in stages N and A ($p = 0.02$). Wasted children tended to report more pain. Pain in infected children tended to be in the abdomen, lower limbs or head. Only 44 percent of the infected children experiencing pain received analgesic medication and only 44 percent of them were successfully relieved of their pain by medication or other pain relief techniques. The results of the 3 pain scales were significantly correlated. The intensity of pain was significantly higher in infected children than in healthy children.

Conclusions: Pain is a common experience in HIV-infected children and can adversely impact on their quality of life. Pain is insufficiently taken into account and treated in these patients. Therefore, adequate pain identification, assessment and management should be systematically considered in their routine care. ■

Presented at: 7th Annual Meeting of Pediatric Infectious Disease Society of Thailand. 8-9 May 2003. Regent-Cha Am Hotel, Phetchaburi Province, Thailand.

DENGUE ANTIBODIES IN THAI INFANTS: AGE-SPECIFIC SEROPREVALENCE

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Background: Dengue infection is the most important mosquito-borne viral disease in tropical areas. Live attenuated tetravalent dengue vaccines are being developed with promising results, and dengue-endemic countries are considered a priority. However, maternally transferred dengue antibodies might interfere with dengue vaccine when given in infancy.

Objectives: To study age-specific and serotype-specific seroprevalence of dengue antibodies in infants living in an area of high endemicity.

Materials & Methods: A cross-sectional survey of dengue antibodies was performed in 450 healthy infants aged 9, 12 and 18 months who attended the well baby clinic at Queen Sirikit National Institute of Child Health, Bangkok, Thailand from November 2000 to March 2001. Two ml. of blood was drawn from each child, dengue antibodies were performed using Hemagglutination inhibition assay (HI), Enzyme-linked immunosorbent assay (ELISA) for IgG/IgM antibody and Plaque reduction neutralization test (PRNT).

Results: There was a good correlation among the three

tests. Neutralizing dengue antibody was demonstrated in 23% of the 9-month-age group while only 9% dengue antibody observed in the 12-month-age group. Dengue antibody prevalence increased to 17% in the 18-month infants.

Dengue serotype 1 (DEN-1) was the most prevalent antibody, detected in 20.3%, 6.0% and 14.7% of 9-, 12- and 18- month infants, respectively. The same pattern was observed in DEN-2, DEN-3 and DEN-4. These proportion indicated a lower spread of DEN-4 compared with other serotype in Thailand.

The proportions of infants with at least 1 serotype were highest and the proportions of infants with 4 serotypes were lowest in each age group. Three percent of the studied infants acquired natural dengue infection.

Conclusions: This epidemiological survey found that the nadir of dengue antibody was at 12-month-old infants. Therefore, in dengue endemic area, dengue vaccines are to be more effective when giving to infants aged 12-months or more.

Presented at: Pre-congress Workshop on Pediatric AIDS, Special Symposium on Dengue and Dengue Hemorrhagic Fever, The 11th Asian Congress of Pediatrics & The 1st Asian Congress on Pediatric Nursing, 2–7 November 2003, Sofitel Central Plaza Hotel and Bangkok Convention Center, Bangkok, Thailand.

FOLLOW-UP OF THAI SCHOOL CHILDREN IMMUNIZED WITH LIVE ATTENUATED TETRAVALENT DENGUE THAI-MAHIDOL STRAINS 3-8 YEARS AGO: CURRENT IMMUNITY RESPONSE AND OCCURRENCE OF DF/DHF

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Dengue is the most important emergent arboviral disease in humans in terms of both morbidity and mortality. Prevention by vector control is impractical and there is no effective treatment. The physiopathology of severe disease (1% of children in Asia) is not well known and is most probably

multifactorial. Secondary infection with heterologous type has been reported as an important risk of severe disease. From 1992 to 1997, 140 children aged between 4 and 15 years old received one dose of the Mahidol live-attenuated tetravalent dengue strains. In 2001, we conducted a descriptive epidemiological study in these vaccinees. The objectives of the study were (1) to evaluate humoral immunity in Thai children 3-8 years after single immunization with the Mahidol

live-attenuated tetravalent dengue strains, and (2) to describe retrospectively severe dengue cases in vaccinees and age-matched controls. Among 140 immunized children, 113 cases were included in the study. The mean age was 15.8 years old and the mean follow-up year was 6.8 at the point of study. The percentages of the vaccinees who had neutralizing antibody titers of 10 or higher against at least three dengue serotypes varied between 38% and 83% at 6 months, according to the formulation. After 3-8 years, these percentages had increased in all formulation groups, varying from 50 to 96%. The percentages of vaccinees who had neutralizing antibody titers of 10 or higher against each of four serotypes were little lower than the age-matched controls. The percentage of vaccinees who had neutralizing antibody titers of 10 or higher against

2, 3 and 4 serotypes were little lower than the age-matched controls. In 113 vaccinees, one developed DF and three developed DHF, while 13 DHF cases were recorded in 226 controls. These results suggest that (1) neutralizing antibody titers were boosted by wild dengue virus infection, and (2) there was no major increase in DF/DHF cases in vaccinees. Prevalence of neutralizing antibodies was different between the vaccinees and the control groups. This was probably due to the selection of flavivirus-naïve subjects for immunization of tetravalent vaccine. ■

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SAFETY AND IMMUNOGENICITY OF A THREE DOSE REGIMEN OF TWO TETRAVALENT LIVE-ATTENUATED DENGUE VACCINES IN FIVE- TO TWELVE-YEAR-OLD THAI CHILDREN

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Objective: The safety and immunogenicity of tetravalent live-attenuated dengue vaccines after a three dose vaccination series were evaluated in Thai children.

Methods: One hundred three healthy flavivirus-seronegative schoolchildren ages 5 to 12 years were randomized to receive either dengue vaccine containing 3, 2, 1 and 2 log₁₀ of the 50% cell culture infective dose, respectively, of the live-attenuated dengue vaccine serotypes 1, 2, 3 and 4 per dose (F3212; *n* = 40) or 3, 3, 1 and 3 log₁₀ of the 50% cell culture infective dose (F3313; *n* = 42) or purified Vero cell rabies vaccine (control group; *n* = 21) given in a two dose schedule (3 to 5 months apart). A third dose was administered 8 to 12 months after the second dose to 90 subjects. Safety and immunogenicity were evaluated within 28 days after each injection.

Results: No serious adverse event related to the vaccines occurred. Most children experienced mild to moderate fever, rash, headache and myalgia occurring within 12 days after Dose 1 and generally lasting 3 days or less. One subject in Group F3212 had a 1-week dengue-like fever. Reactogenicity was minimal after Doses 2 and 3. Transient mild variations in liver enzymes and hematologic indices were noted mainly after Dose 1. After the third dose 89% of the subjects in Group F3212 seroconverted (neutralizing antibody response, ≥10) to all four serotypes, and all children in Group F3313 seroconverted.

Conclusions: This study demonstrates a moderate although improvable reactogenicity and high seroconversion rates against the four serotypes of dengue after a three dose schedule of tetravalent live-attenuated dengue vaccine in children. ■

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DISAPPEARANCE OF NUCLEAR BINDING PROTEINS SPECIFICALLY BOUND TO THE UPSTREAM REGION OF THE INTERLEUKIN-1B GENE IMMEDIATELY AFTER IRRADIATION OF MOUSE MACROPHAGES

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▶ Immediately after X-irradiation, monocytic cells can express the gene for interleukin (IL)-1b, which enhances inflammation and contributes to radioprotection in mice. In order to analyze the mechanism(s) for the immediate-early induction of IL-1b after X-irradiation at 20 Gy in cultured murine macrophages, we examined the molecules that bound to the DNA fragments corresponding to the upstream region of 10 kb of the mouse IL-1b gene using an electrophoretic

mobility-shift assay. Three DNA fragments corresponding to the 8,500, 8,000 and 2,500 bases upstream of the gene showed a unique binding site with the nuclear extract. Specific binding activity with these DNA fragments was observed in the nuclear extract from non-irradiated cells, and disappeared upon a pretreatment of the extract with proteinase K. The binding activity was not detected in the nuclear extract from irradiated cells. This shows that protein(s) specifically binding to the far-upstream regions of the IL-1b gene disappear immediately after X-irradiation in the nuclei of macrophage cells, and that the event is potentially related to the immediate-early response of IL-1b gene expression. ■

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THE ASSOCIATION OF FOLATE STATUS AND CERVICAL DYSPLASIA IN THAI WOMEN

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▶ The relationship between folate status and incidence of cervical dysplasia was studied among Thai women that identified from National Cancer Institute, Bangkok Metropolitan Administration Medical College, Vajira Hospital and Chonburi Cancer Center. Fasting blood samples were collected from 134 women with mild, moderate, severe cervical dysplasia and 95 women with cytological normal as a control group for this serum vitamin analysis by radioassay. Cervical smears cytology obtained for histological diagnosis and colposcopy directed biopsy investigated as a confirmation. The polymerase chain reaction (PCR) method was used to define the presence or absence of genital HPV DNA. The socioeconomic background, gynecologic history and other

possible risk factors were also studied by personal interview and the daily intakes of folate were investigated by 24-hours recall. Serum folate of the women with cervical dysplasia were statistically significant less than that of the control group ($p < 0.001$), whereas the daily folate intake in both groups had no difference. The median daily folate consumption in all studied groups was less than daily recommendation from Thai committee of daily nutrients intake recommendation and Dietary Reference Intake, Food and Nutrition Board of America and Canada (DRIs). Serum folate showed strong inverse correlation with the severity of dysplasia ($r = -0.37$; $p < 0.001$). Logistic regression revealed that individuals whose serum folate was in the lower two tertiles had nearly ten-fold risk for dysplasia than did those in the upper tertile. This finding supported that the state of folate deficiencies increase risk of cervical change in women in this study. ■

Presented at: the IX Asian Congress of Nutrition, New Delhi, India February 2003;23-27:349.

DETERMINATION OF SERUM VITAMIN B12 AND FOLIC ACID IN THAI ALZHEIMER'S PATIENTS

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▶ Low serum vitamin B12 levels and folic acid deficiencies are frequently found in the elderly. Many studies shown a relationship between vitamin B12 and folic acid deficiency with Alzheimer's disease (AD) but in Thai Alzheimer's patients has not been defined. The objective of this study was to determine the serum vitamin B12 and folic acid in probable AD and non-AD demented patients. We studied in 67 subjects aged 50 years and over. Probable AD group was 16 cases, non-AD demented group was 29 cases, and age-matched controls was 22 cases. The serum vitamin B12 and folic acid levels were determined by radioimmunoassay technique. We used vitamin B12 < 200 pg/ml and folic acid < 5 ng/ml to define low levels of vitamin B12 and folic acid. One case of probable AD group, 6 cases of non-

AD demented patients, and 1 case of age-matched controls group had vitamin B12 deficiencies. Four cases of probable AD group, 13 cases of non-AD demented group, and 8 cases of age-matched controls group had folic acid deficiencies. The levels of serum vitamin B12 and folic acid were expressed as means \pm SEM and using Student's *t* test to analyze them. There were significant differences in the probable AD group when compared to age-matched controls, and non-AD demented group when compared to age matched controls in the serum vitamin B12 level ($P=0.01$ and $P < 0.01$). There was a significant difference between non-AD demented group and age-matched controls in serum folic acid level ($P < 0.05$). A regression analysis indicated that there was a decrease in the vitamin B12 level during the duration of disease. This study suggests that serum vitamin B12 and folic acid may be involved in the development of AD. More numbers of subjects should be studied for statistical significances. ■

Presented at: The Sixth IBRO World Congress of Neuroscience, Prague, Czech Republic, July 10-15, 2003.

TRIAL CONDUCT AND LESSONS LEARNED IN THE FIRST PHASE III EFFICACY TRIAL OF AN HIV VACCINE (AIDSVAX® B/E, VAXGEN, INC.) IN AN INTERNATIONAL SETTING

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▶ **Background:** A phase III efficacy trial of candidate bivalent B/E rgp120 HIV vaccine (AIDSVAX, B/E) was initiated in Bangkok, Thailand in March 1999.

Methods: The trial is a randomized, double blind, placebo-controlled trial to determine the vaccine's safety and protective efficacy among 2545 injecting drug users (IDUs). Volunteers received intensive education/counseling every 6 months and 7 injections over 36-months follow-up.

Results: Thus far, volunteer loss to follow has been minimal (<5%), few have withdrawn consent (1%),

reactogenicity has been mild-moderate in most (99%) with pain and tenderness at the injection site being the most common (22%), and few (1.5%) have reported trial-related social harms (all later resolved). No vaccine-related SAEs have been reported. Periodic education/counseling was successful in reducing overall high risk behavior among volunteers. Lessons learned include: IDUs can be recruited and successfully followed over time, counseling can effectively reduce high risk behavior, and trials in international settings can be conducted under Good Clinical Practices with minimal social harms.

Conclusions: The first international HIV vaccine efficacy trial has been successfully conducted and will conclude in late 2003. With proper research infrastructure strengthening and support, other vaccine trials should be possible in international settings where an effective HIV vaccine is most needed. ■

PHASE III TRIAL OF HIV PRIME-BOOST VACCINE COMBINATION IN THAILAND

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Background: This abstract provides an update of the preparations for the community - based, phase III efficacy trial of a prime - boost HIV vaccine combination in Thailand.

Methods: Objectives: determine if this prime-boost vaccine strategy 1) prevents infection, 2) alters disease course in vaccinees who become infected, and 3) is safe. Vaccines were designed specifically for the predominant circulating HIVs in Thailand (subtypes E and B). Prime: a recombinant canarypox ALVAC-HIV (vCP 1521) with a subtype B *gag/pro* and gp41,

and subtype E gp120 (R5) gene insertions (Aventis Pasteur). Boost: AIDSVAX gp120 B/E, monomers of gp 120 B (X4) +gp120 E (R5) with alum (VaxGen). Subjects: 16,000 adult Thais, recruited through the health care system of the Ministry of Public Health. Study design: randomized, Placebo-controlled, double - blind phase III trial. Immunization will be intramuscular over 6 months with a 3 year follow up period.

Discussion: The world's first efficacy testing of a prime-boost HIV vaccine combination is targeted for start in late 2003. This vaccine combination stimulates both humoral and cellular immunity and, thus, should maximize the likelihood of inducing protection. With focus on a low-incidence, Community-based population, the trial size is large, logistics very demanding and community engagement crucial. ■

EFFICACY OF AIDSVAX® B/E VACCINE IN INJECTING DRUG USERS

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Background: As a result of HIV/AIDS epidemic in Thailand, a National Plan for HIV/AIDS Vaccine Development and Evaluation was written in 1993. Since then several vaccine studies have been conducted including the phase III trial of the AIDSVAX® B/E vaccine that began in 1999.

Method: Following informed consent, 2546 HIV-seronegative IDUs meeting the eligibility criteria were randomized to receive AIDSVAX® B/E (300µg 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 were followed for 3 years. The primary end-point was HIV infection. Efficacy and safety analyses were conducted by an independent data analysis group and data safety monitoring board.

Results: 2546 IDUs were enrolled with excellent

follow-up rate. There were no significant differences in baseline characteristics or risk behaviors between vaccine and placebo participants. The drop out rate was 10% for both vaccine and placebo. In the ITT analysis, 106 of 1267 (8.4%) vaccine and 105 of 1260 (8.3%) placebo participants became infected with HIV-1 during the trial. The annualized HIV incidence rate was 3.4 per 100 person-years, 95% CI= 2.8-4.1, for both arms. Vaccine efficacies for all strain, subtype E and subtype B were 0.001 (0.308-0.238), -0.014 (-0.377-0.254) and 0.175 (-0.637-0.584), respectively. There were no statistically significant differences in age, gender or baseline risk behavior between the two groups. Vaccine Efficacy on infection and composite endpoint for ITT cohort were 1.1% and 0.6% respectively.

Conclusion: IDU(s) were successfully enrolled in the phase III HIV vaccine trial. The study was well conducted, risk reduction was achieved during the trial. AIDSVAX® B/E provides no protection against HIV infection. ■

EARLY ORIGIN AND RECENT EXPANSION OF *PLASMODIUM FALCIPARUM*

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The emergence of virulent *Plasmodium falciparum* in Africa within the past 6000 years as a result of a cascade of changes in human behavior and mosquito transmission has

recently been hypothesized. Here, we provide genetic evidence for a sudden increase in the African malaria parasite population about 10,000 years ago, followed by migration to other regions on the basis of variation in 100 worldwide mitochondrial DNA sequences. However, both the world and some regional populations appear to be older (50,000 to 100,000 years old), suggesting an earlier wave of migration out of Africa, perhaps during the Pleistocene migration of human beings. ■

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BERI-BERI: THE MAJOR CAUSE OF INFANT MORTALITY IN KAREN REFUGEES

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During a prospective evaluation of malaria prophylaxis in pregnancy in a refugee population on the north-western border of Thailand from 1987 to 1990, an extremely high infant mortality rate (18%) was documented despite good access to health care. Infantile beri-beri was recognized as the main cause of death accounting for 40% of all infant mortality. Thereafter, severe vitamin B1 deficiency in infants was diagnosed and treated promptly. The impact of this was assessed prospectively from 1993 to 1996 in a second cohort study. The case fatality of infantile beri-beri fell from almost 100% to 7%. The overall infant mortality rates declined from 183 to 78

per 1000 live births. Post-neonatal deaths fell by 79% (95% CI 65-87%) while neonatal mortality remained unchanged. Mortality resulting from acute respiratory infections did not change (15 and 11 per 1000, respectively), whereas mortality attributable to beri-beri decreased from 73 to 5 per 1000 ($P < 0.0001$). Before its recognition approximately 7% of all infants in this population died from infantile beri-beri. This lethal but preventable syndrome may be more common than hitherto recognized, particularly in refugee populations, in this populous region. ■

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THE PHARMACOKINETICS OF ATOVAQUONE AND PROGUANIL IN PREGNANT WOMEN WITH ACUTE FALCIPARUM MALARIA

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OBJECTIVE: To determine the pharmacokinetic properties of atovaquone, proguanil, and the triazine metabolite cycloguanil in women with recrudescing multi-drug resistant falciparum malaria during the second and third trimesters of pregnancy treated by artesunate-atovaquone-proguanil.

METHODS: Serial plasma concentrations of atovaquone, proguanil and cycloguanil were measured in 24 women at baseline and after the final dose of the 3-day treatment with atovaquone (20 mg/kg/day) plus proguanil (8 mg/kg/day) plus artesunate (4 mg/kg/day) daily.

RESULTS: The triple combination was well tolerated and highly effective. The outcomes of pregnancy were all

normal. Population mean (\pm SEM) oral clearance (Cl/F) estimates were 313 ± 33 ml/h/kg and 1109 ± 43 ml/h/kg, total apparent volume of distribution (Vd/F) 13.0 ± 1.3 l/kg and 22.9 ± 1.4 l/kg, and terminal elimination half-life; 29.1 h and 14.3 h, for atovaquone and proguanil, respectively. Using conventional and population pharmacokinetic analyses, Cl/F and Vd/F estimates for both drugs were approximately twice, and plasma concentrations less than half those reported previously in healthy subjects and patients with acute malaria.

CONCLUSION: Artesunate-atovaquone-proguanil is a promising treatment for multi-drug resistant falciparum malaria during pregnancy, but the dose of atovaquone-proguanil may need to be increased. ■

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PREGNANCY AND USE OF ORAL CONTRACEPTIVES REDUCES THE BIOTRANSFORMATION OF PROGUANIL TO CYCLOGUANIL

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OBJECTIVE: To determine the effects of late pregnancy and also oestrogen supplementation on the CYP2C19-mediated biotransformation of proguanil (PG) to its active antifolate triazine metabolite cycloguanil (CG).

METHODS. Case control study conducted on the NW border of Thailand; a single dose of PG (4 mg/kg) was administered to Karen women in late pregnancy and a single blood and urine sample taken 6 h later. Women were studied in late pregnancy (>36 weeks) and restudied 2 months after delivery. A separate cohort of Karen women newly attending a birth-control clinic were studied before and 3 weeks into their first course of oral contraceptives (OCP: levonorgestrel 0.15 mg and ethinyloestradiol 0.03 mg). Forty-five pregnant women and forty-two healthy OCP users were studied.

RESULTS. The results were similar in both groups; pregnancy and OCP use were both associated with reduced formation of cycloguanil (CG). Impaired PG biotransformation was seen in women with the extensive metaboliser phenotype (urine PG/CG ratio <10). CG levels, adjusted for dose, were a median (range) 73% (-59 to 420%) higher following the pregnancy than during the pregnancy in women characterised as extensive metabolisers ($P < 0.001$). CG levels in women characterised as extensive metabolisers were 34% (-54 to 323%) higher before than while taking the OCP ($P < 0.01$).

CONCLUSION. Late pregnancy and OCP use impair biotransformation of the active antimalarial metabolite CG from the parent PG. This may be mediated by oestrogen inhibition of CYP2C19 activity. The dose of PG should be increased by 50% in these groups. ■

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MALARIA AND AMPHETAMINE "HORSE TABLETS" IN THAILAND

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▶ During recent clinical malaria research in Thailand we found a high frequency of amphetamine misuse and withdrawal

amongst patients admitted to hospital with *Plasmodium falciparum* malaria. This comorbidity may cause diagnostic confusion, alter malaria pathophysiology and lead to drug interactions. ■

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RANDOMIZED COMPARISON OF ARTESUNATE AND QUININE IN THE TREATMENT OF SEVERE FALCIPARUM MALARIA

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▶ A randomized, open-label comparison of artesunate and quinine was conducted in 113 adults with clinically severe falciparum malaria in western Thailand. Mortality was 12% with artesunate and 22% with quinine treatment (relative risk, 0.53; 95% confidence interval, 0.23-1.26; $P=0.22$). Multiple logistic regression analysis found admission plasma lactate level, Glasgow Coma Scale score, and total serum bilirubin level to be independent risk factors for death. Coma recovery and times

to normalize plasma lactate levels were similar, but the parasite clearance time was much shorter among artesunate-treated patients ($P=0.019$). Fewer patients became hypoglycemic during artesunate therapy (10%) than during quinine therapy (28%) ($P=0.03$). Artesunate is at least as effective as quinine in the treatment of adults with severe malaria. Larger trials are required to determine whether mortality is reduced among patients treated with artesunate. ■

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MATERNAL MALARIA: TIME FOR ACTION

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▶ Among human parasitic diseases, malaria remains the world's most important cause of morbidity and mortality. The impact of malaria on health and on development is huge and, because of the spread of drug resistance in *P.falciparum*, it is worsening. In all endemic regions, children and pregnant

women are the two groups mostly at risk of severe disease and death. The true magnitude of the burden of maternal malaria is unknown, but recent reports indicate that it may be much higher than previously thought. ■

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

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P We studied prospectively 801 Thai patients admitted to the Bangkok Hospital for Tropical Diseases with acute, symptomatic *Plasmodium vivax* malaria to determine the optimum duration of treatment with oral artesunate and the safety, tolerability, and effectiveness of a high dose of primaquine in prevention of relapse. Patients were randomly assigned to one of four treatment groups: 1) a five-day course of artesunate (Group A5); 2) a seven-day course of artesunate (Group A7); 3) a five-day course of artesunate plus a 14-day course of high-dose primaquine (0.6 mg/kg, maximum dose = 30 mg) (Group A5 +

P); and 4) a seven-day course of artesunate plus a 14-day course of high-dose primaquine (Group A7 + P). During 28 days of observation, *P. vivax* reappeared in the blood of 50% of those who received artesunate alone (Groups A5 and A7), compared with none of those who received primaquine (Groups A5 + P and A7 + P; $P < 0.0001$). Adverse effects were confined to the 13 patients with a deficiency for glucose-6-phosphate dehydrogenase; high-dose primaquine (0.6 mg/kg of base a day) had to be stopped in four (31%) patients because of a significant decrease in the hematocrit. The combination of five days of artesunate and 14 days of primaquine is a highly effective and generally well-tolerated treatment regimen for vivax malaria in Thailand. ■

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Published in: *Am J Trop Med Hyg* 2003;69:14-8.

ARTEMETHER BIOAVAILABILITY AFTER ORAL OR INTRAMUSCULAR ADMINISTRATION IN UNCOMPLICATED FALCIPARUM MALARIA

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P The antimalarial activity of artemether following oral or intramuscular administration in the plasma of 15 adults with acute uncomplicated *Plasmodium falciparum* malaria was measured by bioassay. The peak concentrations in plasma following oral administration were higher in patients with acute illness (median, 1,905 mmol of dihydroartemisinin [DHA] equivalents per liter; range, 955 to 3,358 mmol of DHA equivalents per liter) than in patients in the convalescent phase (median, 955 mmol of DHA equivalents per liter; range, 576 to 1,363 mmol of DHA equivalents per liter), and clearance (CL/F) was lower in patients in the acute phase (1.11 liters/kg/h; range, 0.21 to 3.08 liters/kg/h) than in patients in the

convalescent phase (median, 2.76 liters/kg/h; range, 1.56 to 5.74 liters/kg/h) ($P < 0.008$). Antimalarial activity in terms of the peak concentration in plasma (C_{max}) after oral administration was a median of 16 times higher than that after intramuscular administration. The ratio of the area under the plasma concentration-time curve during the first 24 h (AUC_{0-24}) after oral administration of artemether to the AUC_{0-24} after intramuscular administration was a median of 3.3 (range, 1 to 11) ($P = 0.0001$). In the acute phase, the time to C_{max} was significantly shorter after oral administration (median, 1 h; range, 0.5 to 3.0 h) than after intramuscular administration (median, 8 h; range, 4 to 24 h) ($P = 0.001$). Intramuscular artemether is absorbed very slowly in patients with acute malaria. ■

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DIABETES MELLITUS, INSULIN, AND MELIOIDOSIS IN THAILAND

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▶ **A** review of case records for 1817 Thai patients with melioidosis revealed that <10% of the 382 patients with diabetes mellitus were insulin dependent. This provides

evidence against the hypothesis that insulin deficiency contributes to the known susceptibility to melioidosis in patients with diabetes mellitus. ■

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Published in: *Clin Infect Dis* 2003;36:e71-2.

THE DE NOVO SELECTION OF DRUG-RESISTANT MALARIA PARASITES

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▶ **Antimalarial** drug resistance emerges *de novo* predominantly in areas of low malaria transmission. Because of the logarithmic distribution of parasite numbers in human malaria infections, inadequately treated high biomass infections are a major source of *de novo* antimalarial resistance, whereas use of antimalarial prophylaxis provides a low resistance selection risk. Slowly eliminated antimalarials encourage resistance largely by providing a selective filter for resistant

parasites acquired from others, and not by selecting resistance *de novo*. The *de novo* emergence of resistance can be prevented by use of antimalarial combinations. Artemisinin derivative combinations are particularly effective. Ensuring adequate treatment of the relatively few heavily infected patients would slow the emergence of resistance. ■

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Published in: *Proc R Soc London B Biol Sci* 2003;270:545-54.

MELIOIDOSIS

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▶ **Melioidosis**, which is infection with the gram-negative bacterium *Burkholderia pseudomallei*, is an important cause of sepsis in east Asia and northern Australia. In northeastern Thailand, melioidosis accounts for 20% of all community-acquired septicaemias, and causes death in 40% of treated patients. *B. pseudomallei* is an environmental saprophyte found in wet soils. It mostly infects adults with an underlying predisposing condition, mainly diabetes mellitus. Melioidosis is characterised by formation of abscesses, especially in the lungs, liver, spleen, skeletal muscle, and prostate. In a third of paediatric cases in southeast Asia, the disease presents as parotid abscess. In northern Australia, 4% of patients present with brain

stem encephalitis. Ceftazidime is the treatment of choice for severe melioidosis, but response to high dose parenteral treatment is slow (median time to abatement of fever 9 days). Maintenance antibiotic treatment is with a four-drug regimen of chloramphenicol, doxycycline, and trimethoprim-sulfamethoxazole, or with amoxicillin-clavulanate in children and pregnant women. However, even with 20 weeks' antibiotic treatment, 10% of patients relapse. With improvements in health care and diagnostic microbiology in endemic areas of Asia, and increased travel, melioidosis will probably be recognised increasingly during the next decade. ■

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

Published in: *Lancet* 2003;361:1715-22.

THE MANAGEMENT OF SEVERE FALCIPARUM MALARIA

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▶ *Plasmodium falciparum* malaria kills over 5,000 people every day. Most of these deaths are in African children but many are in nonimmune adults. With an incubation period of approximately 2 weeks, and ever increasing air travel, malaria

in travelers may present to medical attention in temperate non-endemic countries. The diagnosis is often delayed, increasing the probability of progression to severe malaria and death. ■

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Published in: *Am J Respir Crit Care Med* 2003;167:673-7.

AREAS OF UNCERTAINTY IN THE MANAGEMENT OF HUMAN TRICHINELLOSIS – A CLINICAL PERSPECTIVE

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▶ **There** is disagreement among authorities on most facets of trichinellosis therapy. The most controversial issues are when to use corticosteroids and what antihelminthic drug should be administered, for how long and at what dose. These issues are particularly important in the treatment of severe, potentially fatal infections. A major reason for the lack of

consensus about trichinellosis management is that there have been very few prospective, controlled clinical trials of this infection. After a brief review of pertinent epidemiological and clinical features of the disease, we will review selected treatment concerns and highlight areas where more information is urgently required. ■

Expert Review of Anti-Infective Therapy (in press).

COINFECTION BY HIV-1 AND SCRUB TYPHUS MAY LEAD TO DECREASED VIRAL LOAD AND PREFERENTIAL SUPPRESSION OF X4 VIRUSES

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▶ **Background:** Scrub typhus (*O. tsutsugamushi*) infection of HIV-positive patients can be accompanied by a decrease in HIV load. Transfer of plasma from scrub typhus patients to HIV-infected individuals also results in a drop in viral load. The mechanism of suppression is unclear but may involve induction of inhibitory substances like chemokines or cross-reactive antibodies.

Methods: We tested sera from HIV-negative scrub typhus patients for its ability to inhibit replication of CCR5-(R5) and CXCR4-specific (X4) strains of HIV *in vitro*. We

performed genotypic analyses to determine the coreceptor usage of virus obtained from HIV-infected individuals infused with plasma from scrub typhus patients. A mathematical model was used to quantitate the proportion of HIV using each coreceptor and mixed-effects analyses were used to examine the relationship between viral load, coreceptor usage, and chemokine concentration.

Results: *In vitro* replication of HIV was inhibited 2 to 10-fold by addition of sera from scrub typhus patients; this effect was limited to X4 strains. Although depletion of chemokines had no impact on HIV replication, depletion of antibody abrogated the serum's inhibitory effect. *In vivo*, passive transfer of plasma from scrub typhus-infected patients into HIV-infected individuals caused a statistically significant drop in viral load for 7 of 10 recipients. This reduction in HIV

RNA level was accompanied by a shift in the viral population from X4 to R5 strains ($p=0.0008$). Patients who showed no drop in HIV load were infected by virus that solely used CCR5. No association was seen between changes in viral load and serum chemokines. Viral load and coreceptor usage did not change in 3 patients who received infusions of normal plasma.

Conclusions: These data suggest that scrub typhus

infection may induce antibodies or other soluble molecules that inhibit X4 strains of HIV. Elucidating the mechanism of suppression of X4 virus is relevant to treatment and vaccine design. ■

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