Annual Review 2006

Faculty of Tropical Medicine
Mahidol University

Asia's Leader in Tropical Medicine
from the past to the present and into the future
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Compiler: Pornpimon Adams
Editorial Staff: Wanissara Chaiyabhandhu, Sivaporn Samung, Pitchapa Vutikes
Graphic Designer: Ronnachai Rarerng
Layout: Phaibul Vasanakomut
English Language Consultant: Paul Adams
Produced by Research and Academic Affairs Unit, Faculty of Tropical Medicine, Mahidol University, 420/6 Ratchawithi Road, Bangkok 10400, Thailand Tel: 66 (0) 2354-9100-19 ext. 1524, 1525 Fax: 66 (0) 2643-5578 E-mail: tmpww@mahidol.ac.th http://www.tmpubs.tm.mahidol.ac.th

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Foreword from the Dean

To commemorate His Majesty King Bhumibol Adulyadej’s 60th year of Accession to the Throne, the Faculty of Tropical Medicine is joining with Mahidol University and other government official sectors in dedicating their utmost efforts to improving the quality of life of the people, particularly those in tropical and developing countries. The Faculty of Tropical Medicine conducts three main activities: basic and clinical research in tropical medicine; provision of medical services; and postgraduate training through six international courses. The Faculty employs 98 academic staff, comprising 65 PhD and 33 Master degree graduates. The Faculty is currently affiliated with more than 20 leading institutes domestically and with more than 30 international academic institutes. The Faculty also conducts and supervises collaborative research on tropical diseases within the wider SE, South Asian regions, and worldwide. I myself, as Dean, and my colleagues, aim further to strengthen the Faculty as “Asia’s Leader in Tropical Medicine” through research, education, and services.

I wish to convey my sincere appreciation to all members of the Faculty, to our supporters and collaborators for their excellent work throughout the year 2005. I trust that the Faculty of Tropical Medicine Annual Review 2006 provides a comprehensive summary of the Faculty’s activities in 2005, and that any reader delving into it will find something of value and interest.

Pratap Singhasivanon
Dean
**Editor’s Note**

In the Year 2005 and the beginning of 2006, there was a lot of activity in the Faculty of Tropical Medicine. Particularly, the 46th Anniversary of the founding of the Faculty was symbolized by “Home-coming Day” for retired FTM members. It was the first time all five deans of the Faculty met on one day.

FTM staff no doubt realize how busy we were, and that delayed publication of this issue of the Annual Review. On behalf of the team, I wish to apologize for the delay. We will definitely try for a better and faster job next year.

The achievements in 2005 increased compared with the beginning of the transition period for the Dean, in 2004. From 2005, FTM granted 12 small research projects to young scientists, expecting that the published scientific papers of the Faculty in the 2007 Review will increase quantitively and qualitatively. This was also true for our training courses, with the number of tailored short courses higher than 2004. We hope that you find these facts pleasing, and enjoy reading this Review.

Assoc. Prof. Jitra Waikagul

*Editor*
Executive Summary

Research

Current research of the Faculty of Tropical Medicine ranges from molecular research to community studies, covering more than 20 diseases including malaria, melioidosis, soil-transmitted diseases, and mosquito-borne diseases. The current research programs include clinical trials, laboratory research, field and epidemiological studies, vaccine trials, assessment of future drugs for avian influenza, and assessment of the health effects of unpredicted natural hazards and disasters. The Faculty is a pioneer research hub in conducting HIV/AIDS and dengue vaccine trials, assessment of the efficacy of antiretroviral therapies, assessments of treatments for opportunistic infections, epidemiological surveys, and analyzing social risk factors. The Faculty is well placed to conduct high quality research, having a well-established Ethics Committee, Bioequivalence Unit, an extensive Data Management Unit, a board of research consultants, and the Research and Academic Affairs Unit. We encourage collaborative studies through both local and international linkages. The Faculty is currently affiliated with more than twenty leading research institutes from all continents of the globe. As part of our research activities, we provide international postgraduate education and training in tropical medicine for scientists, physicians and others from all nations.

In 2005, the Faculty published 129 international scientific papers, and 12 national or local scientific papers. There were 106 research projects, of which 49 were new, and 57 ongoing.

Seventy-four papers were presented at international conferences and 11 at national conferences. The Faculty remains the leader in Asia in publishing research on malaria and other tropical diseases. We will continue to encourage, support, and facilitate research in tropical disease and other related global health problems. The research activities of the Faculty will continue to strive to improve the education and health of the peoples in the region.

Education

The Bangkok School of Tropical Medicine offers six regular international postgraduate programs—the Diploma in Tropical Medicine and Hygiene, Master of Clinical Tropical Medicine, Master of Clinical Tropical Pediatrics, Master of Science in Tropical Medicine, Doctor of Philosophy in Tropical Medicine, and Doctor of Philosophy in Clinical Tropical Medicine. In the year 2005, we enrolled 29 new DTM&H students from 12 countries, 15 MSc students from 5 countries, and 11 PhD students from 2 countries. In total, 245 students were enrolled in the six programs (DTM&H: 29; MCTM: 7; MSc: 82; and PhD: 127) while 55 students graduated. To date, participants from more than 50 different countries have attended the Faculty’s international programs.

Joint International Tropical Medicine Meeting 2005

In 2005, the annual Joint International Tropical Medicine Meeting (JITMM 2005) was co-organized with the Parasitology and Tropical Medicine Association of Thailand, TROPMED Alumni Association, and SEAMEO TROPMED Network. The Meeting was held from 30 November to 2 December 2005, at the Grand Hotel, Bangkok, and attracted 586 delegates from 23 countries, with 106 oral and 96 poster presentations. Prof. Emeritus Mukda Trishnananda, President of the Thai Society of Travel Medicine, presented the 11th Chamlong-Tranakchit Harinasuta Lecture, entitled “Travel Medicine and Health”.

Collaborations

The Faculty has ongoing collaborative relationships in research and training with over 30 institutions internationally. Ten new Memoranda of Understanding were signed with international institutions, and eight with national institutions.

Finance

Total expenses amounted to 345.058 million Baht, of which 241.16 million Baht were supported by government budget, and 103.89 million Baht derived from Faculty revenues.

Personnel

In the year 2005, there were 771 staff in the Faculty, comprising 98 academic staff, 187 support staff, and 484 administrative staff. 67 staff (66%) had PhDs, while 31 (34%) had Master Degrees or comparable qualifications. Twenty-four staff were promoted to higher positions. The ratio of Professor : Assoc. Prof. : Assist. Prof. : Lecturer = 4 : 31 : 30 : 33, respectively. Twelve staff retired, and 4 took early retirement during the year.

The best-performing staff awards of the year 2005 were given to Mrs. Pornpimon Adams, Information Scientist Level 7; Mrs. Sureeporn Ratrungruengyos, Assistant Nurse Level 5; and Mrs. Pissamai Inkong, Janitor.

Staff development

Three staff have been continuing their education within Thailand, and 5 overseas. Seven staff were trained within Thailand and 6 overseas. Fifty-eight staff participated in international conferences and 364 in national conferences.

Construction and area development

Recent developments have included the construction of a new building on the main Phyathai campus, which includes the Executive and Administrative Office, Conference Room, Data Management Unit, and a Tropical Disease Reference Center and Museum. The building will be finished at the end of 2006.
Administrative Board

Assoc.Prof. Pratap Singhasivanon
Dean

Assoc.Prof. Jitra Waikagul
Deputy Dean for Academic Affairs and Special Projects

Prof. Sasithon Pukrittayakamee
Deputy Dean for Research

Assist.Prof. Usanee Suthisarnsuntorn
Deputy Dean for Educational Affairs

Assoc.Prof. Wattana Leowattana
Deputy Dean for Service and Hospital Director
Opening Ceremony and Orientation of the Collaborative Project to Produce Rural Doctors, Faculty of Tropical Medicine, Mahidol University, 19 December 2005


Opening Ceremony of the International Training Course on Management of Malaria, Faculty of Tropical Medicine, Mahidol University, 26 September 2005.
Special Events

Opening Ceremony D.T.M.&H., M.C.T.M. and M.C.T.P. Course for the Academic Year 2005
7 April 2005, Faculty of Tropical Medicine, Mahidol University.

Special Lecture on “Good Clinical Practice” By Prof. Juntra Karbwang, Clinical Coordinator, WHO/TDR, 23 September 2005, Faculty of Tropical Medicine, Mahidol University.

6 June 2005, Faculty of Tropical Medicine, Mahidol University.

Certificate Award Ceremony for Nurse Assistant Course 2005
Special Events

- Closing Ceremony of International Training Course in Partnership Building for Healthy Borders, 26 August 2005
- Welcome Ceremony for H.E. Prof. Dr. Nguyen Minh Hien, Minister of Education and Training of Vietnam and President of SEAMEO Council 2005, to SEAMEO/Faculty of Tropical Medicine, 20 August 2005.
- Signing Ceremony of Academic Exchange Agreement between Faculty of Tropical Medicine, Mahidol University and University of Shizuoka of Pharmaceutical Sciences, 8 August 2005.
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. Prof. Emeritus Sirivan Vanijjanonta
10. Lieut. Col. Dr. George Watt
11. Assoc. Prof. Supranee Changbumrung
12. Dr. Lalive Jitkarun
13. Dr. Manoch Uvutipong
14. Dr. Sunee Norasetthada
15. Dr. Somrueng Kanjanamatakul
16. Dr. Sakchai Atthavibul
17. Dr. Pipat Jiranairadul
18. Dr. Peerasak Pholpruksa
19. Dr. Suvich Thampapalo
20. Dr. Tienchai Kijsanayothin
21. Dr. Nithipat Siripan
22. Dr. Preecha Pinyopornpanich
23. Dr. Arun Sattayapisal
24. Dr. Sorakij Bhaeecheep
25. Dr. Piset Kiranantawat
26. Dr. Nattakorn Baisang

Visiting Professors 2005

Prof. Dr. Ma Sandra Bernado Tempongko
Dr. Peter Echeverria
Prof. David J.P. Ferguson
Dr. Stephen Wheeler King
Dr. Nicholas John Day

Faculty Board

1. Dean Chair
2. 11 Deputy Deans Members
3. 11 Heads of Department Members
4. 4 Lecturer Representatives Members (4-year term)
5. 1 Deputy Dean Member and Secretary

Faculty Senate

1. Assist. Prof. Achara Asavanich Chair
2. Assoc. Prof. Pornpit Petnitr Vice-Chair
3. Assoc. Prof. Punnee Pitsutitthum Lecturer Representative
4. Assist. Prof. Pongrama Ramasoota Lecturer Representative
5. Assoc. Prof. Narumon Komalamisra Representative, Department of Medical Entomology
6. Assist. Prof. Watcharee Chokejindachai Representative, Department of Tropical Pediatrics
7. Assist. Prof. Varee Wongchotigul Representative, Department of Microbiology and Immunology
8. Mr. Teera Kusolsuk Representative, Department of Helminthology
9. Miss Rachatawan Chiabchalar Representative, Department of Protozoology
10. Assist. Prof. Talabporn Harroongroj Representative, Department of Tropical Nutrition and Food Science
11. Dr. Duangkamol Viroonudomphol Representative, Department of Tropical Radioisotopes
12. Assist. Prof. Wanchai Phatihatakorn Representative, Department of Social and Environmental Medicine
13. Assist. Prof. Apichart Nonprasert Representative, Department of Clinical Tropical Medicine
14. Miss Pannamas Maneekan Representative, Department of Tropical Hygiene/Secretary
15. Assist. Prof. Urai Chaisri Representative, Department of Tropical Pathology/Assistant Secretary
Departments and Activities
Faculty of Tropical Medicine, Mahidol University
The Department of Clinical Tropical Medicine is comprised of 12 units: 1. Dermatology Unit, 2. Tropical Infectious Research Unit, 3. Nephrology Unit, 4. Clinical Infectious Disease Research Unit, 5. Gastroenterology Research Unit, 6. Traditional Chinese Medicine Unit, 7. Biochemistry Unit, 8. Clinical Pathophysiology Research Unit, 9. Liver Research Unit, 10. Tropical Medicine Laboratory Unit, 11. Critical Care Research Unit, 12. Clinical Pharmacology Unit.
Assist. Prof. Wirach Maek-a-nantawat
M.D.(1st Class honors), Dip in STDS & HIV/AIDS, D.T.M.&H. (Bangkok), Dip. Thai Board of Internal Medicine
Field of Expertise: Internal Medicine
E-mail: tmswma@mahidol.ac.th
Tel.: 0 2354 9168

Assist. Prof. Valai Bussaratid
M.D., M.Sc.(Dermatology)
Field of Expertise: Dermatology
E-mail: tmvb@mahidol.ac.th
Tel.: 0 2354 9168, 0 2354 9100-19 ext. 2065

Assist. Prof. Apichart Nontprasert
B.Sc.,(Biology), M.Sc.(Public Health), Ph.D.(Trop. Med.)
Field of Expertise: Neurotoxicity
E-mail: apichart@tropmedres.ac
Tel.: 0 2354 9100 ext. 1437

Assist. Prof. Mallika Imwong
B.Sc.,(Nursing), M.Sc.(Env.Sc.), Ph.D(Trop.Med.)
Field of Expertise: Molecular genetics of drug resistance in malaria
E-mail: noi@tropmedres.ac
Tel.: 0 2354 9100 ext. 1406

Assist. Prof. Weerapong Phumratanaprapin
M.D., Dip. Thai Board of Internal Medicine, Diplomate Thai Board of Nephrology, Diploma in The Specialty Family Medicine
Field of Expertise: Internal medicine/Nephrology
E-mail: tmwp@mahidol.ac.th
Tel.: 0 2354 9168, 0 2354 9100 ext. 1423

Assistant Prof. Udomsak Silachamroon
M.D. (Hons), Grad. Dip. in Clin. Sc.(Med.), M.Sc., Dip. Thai. Board of Internal Medicine, Diploma in Pulmonary Medicine, F.C.C.P.
Field of Expertise: Internal medicine/ Pulmonary medicine/ TB
E-mail: tmsuis@mahidol.ac.th
Tel.: 0 2354 9168, 0 2354 9100 ext. 1423

Assist. Prof. Dr. Kesinee Chotivanich
B.Sc. (Nursing Science), M.Sc.(Pathobiology), Ph.D. (Pathobiology)
Field of Expertise: Pathophysiology of malaria
E-mail: nok@tropmedres.ac
Tel.: 0 2354 9100 ext. 1427, 2036

Assist. Prof. Dr. Kesinee Chotivanich
B.Sc. (Nursing Science), M.Sc.(Pathobiology), Ph.D. (Pathobiology)
Field of Expertise: Pathophysiology of malaria
E-mail: nok@tropmedres.ac
Tel.: 0 2354 9100 ext. 1427, 2036

Dr. Jittima Dhitavat
M.D.(Hon.),M.Sc.,Dip Thai Board of Dermatology, D.Phil. (Clinical Medicine)
Field of Expertise: Dermatology, Mycology , Cell biology
E-mail: jittima_pu@yahoo.com
Tel.: 0 2354 9168, 0 2354 9100-19 ext. 2068

Dr. Wirongrong Chierakul
Field of Expertise: Tropical infectious disease esp. Melioidosis, Leptospirosis, Scrub typhus
E-mail: alwcr@diamond.mahidol.ac.th
Tel.: 0 2354 9100 ext 1427

Dr. Supat Chamnachanan
M.D., D.T.M.&H. (Bangkok)
E-mail: tmscc@mahidol.ac.th
Tel.: 0 2354 9168, 0 2354 9100-19 ext. 2068

Dr. Dr. Theeratus Jongboonyanuparp
M.D.
E-mail: theeratus@hotmail.com
Tel.: 0 2354 9168, 0 2354 9100-19 ext. 1423,1428, 0 1563 5354

Dr. Dr. Theeratus Jongboonyanuparp
M.D.
E-mail: theeratus@hotmail.com
Tel.: 0 2354 9168, 0 2354 9100-19 ext. 1423,1428, 0 1563 5354

Dr. Watcharapong Piyapane
M.D.(1st Class Honors), Dip Thai Board of Internal Medicine, Grad. Dip. Clin. Sc. (Internal Medicine)
Field of Expertise: Travel Medicine
E-mail: tewp@mahidol.ac.th
Tel.: 0 2354 9100-19 ext. 1428

Dr. Sant Muangnoicharoen
M.D., D.T.M.&H. (Bangkok)
Tel.: 0 2354 9168, 0 2354 9100 ext. 1243, 1428

Dr. Wichai Ekataksin
M.D., Ph.D.
Field of Expertise: Liver
Microcirculation, Computer-assisted 3D imaging
angioarchitectural morphology
E-mail: scwek@mahidol.ac.th
Tel.: 0 2354 9100 ext. 1691; Fax: 0 2354 9205

Mrs. Piengchan Sonthayanon
B.Sc.(Biology), M.Sc.(Biochemistry)
Field of Expertise: PCR-based diagnostic methods
E-mail: stprj@mahidol.ac.th, piengchan@tropmedres.ac
Tel.: 0 2354 9100-19 ext. 2025; 1426
Ms. Gedsuda Pattanapen
B.Sc. (Physical Therapy), M.Sc. (Anatomy)
Field of Expertise:
Hepatic stellate cells or arachnocytes in liver
E-mail: trgspt@mahidol.ac.th
Tel.: 0 2354 9100-19 ext. 1699; Fax: 0 2354 9205
Lecturer

Mr. Noppadon Tangpukdee
B.N.S., Dip. Med. Micro., M.Sc. (Toxicology)
Field of Expertise:
Clinical Study in toxicology and safety
E-mail: tmmnt@mahidol.ac.th
Tel.: 0 2354 9168, 0 2354 9100 ext. 1421
Lecturer

Ms. Borimas Hanboonkunupakarn
B.Sc. (Medical Science, First class honors)
Field of Expertise:
Hepatic ischemia – reperfusion injury
E-mail: borimash96@yahoo.com
Tel.: 0 2354 9100-19 ext. 1699; Fax: 0 2354 9205
(Scientist)

Ms. Sasikarn Phokham
(Researcher Associate)

Ms. Sirikorn Phokham
(Scientist)

Ms. Sujittra Inunchot
(Scientist)

Mr. Tritrar Pholcharoen
(Senior Medical Technologist)

Mrs. Sompong Mingmongkol
(Medical Technologist)

Mr. Surong Prasartpan
(Medical Science Associate)

Ms. Jantima Laegthaisong
(Scientist Assistant)

Mr. Kongpop Pupae
(Scientist Assistant)

Ms. Jariya Maharatchamongkol
(Researcher Associate)

Mrs. Chuanpit Preechawuthiwong
B.A. (Political Science)
Tel: 0 2354 9168, ext. 1429
General Affairs Officers
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 2,500 admitted cases of this disease. Most of the cases were falciparum malaria and vivax malaria and a few cases of mixed infections malariae malaria 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 alterations in malaria have been widely investigated. Interesting results were 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 efficacy of tetracycline, doxycycline, rifampicin and azithromycin was also studied.

Parasitic infestations have been studied, such as drug trials and investigations for gnathostomiasis and local drugs application parenterally for strongyloidiasis, opisthorchiasis, paragonimiasis and teniasis.

Research series are continuing, involving new applications of antifungal drugs for AIDS with fungal disease. Traditional medicines for the treatment of HIV/AIDS are 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, superficial fungal infections in normal and HIV patients, such as PPE, Dermatophytes, leucoplakia and PCP.
The titles of current departmental research activities are as follows:

1. 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

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 And A Study to Evaluate the Efficacy of Quadrivalent HPV V (Types 6,11,16, and 18) L1 Virus-Like Particle (VLP) Vaccine in Reducing the Incidence of HPV 6-11-and 18-Related CIN, and HPV16 and 18 Related external Genital Warts, VIN and VaIN, and HPV 16 and 18-Related Vulvar and Vaginal Cancer in 16-to 23 Year-Old Women----The F.U.T.U.R.E. Study

3. Safety and Immunogenicity Studies of WRSd1, a Live Attenuated Shigella dysenteriae type 1 Vaccine Candidate in Thai Adults

4. Safety, Immunogenicity, and Efficacy of Quadrivalent HPV (Types 6, 11, 16, 18) L1 Virus-Like Particle (VLP) vaccine in Mid-Adult Women----The FUTURE III (Females United to Unilaterally Reduce Endo/Ecto Cervical Cancer) Study

5. 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.

6. 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.


8. Efficacy and tolerability of ivermectin for gnathostomiasis.

9. Effect of drug accumulation in the neurotoxicity of arteseterm, dosing regimens with variable drug-free intervals in a mouse model.

10. Safety and therapeutic effects of Jin Huang Chinese medicine in uncomplicated HIV-1 patients.


13. Development of field methods and investigators of the molecular basis of sulfonamide resistance in Plasmodium vivax


15. Asexual and sexual stage antimalarial activities of artesunate and primaquine in falciparum malaria

16. Research and development for Thai people living at Thai-Myanmar border to free from tropical diseases.

17. Research and development on drugs and diagnostic tools for diagnosis and treatment of tropical diseases in Thailand.

18. Liver megaproject Phase 1: from basic research to education science and applied technology in clinical study.
AWARDS

**National Awards**

1. Dr. Wirongrong Chierakul “Young Investigator Award” (First Prize): In recognition of the outstanding research publication of the Annual Scientific Meeting of the Infectious Disease Association of Thailand 2005

2. Dr. Wirongrong Chierakul Research Award: In recognition of the outstanding research paper of the Annual Scientific Meeting of the Infectious Disease Association of Thailand 2005

3. Liver Research Unit “Micrograph Award” (First Prize) Micrograph Award 2005, Bioscience: LM 1st of Microscopy Society of Thailand XXIInd Annual Conference on Microscopy, 2-4 February 2005, Chonburi, Thailand.

**International Awards**


3. Ms. Naowarat Thanormsing “The Best Tropmed Student Presentation Award”.

**International Editorial Board**

Prof. Sornchai Looareesuwan 2005: Companion (Fourth Class) of the Most Admirable Order of the Direkgunabhorn.

- 1990-Present: Journal of Infectious Diseases and Antimicrobial Agents, Bangkok, Thailand.
- 1996-Present: Mahidol University Journal, Bangkok Thailand.
- 2000-Present: The Lancet Infectious Diseases, UK.
- 2001-Present: The Malaria Journal and Pubmed, Liverpool, UK.
- 2002-Present: International Medicine J. of Thailand
- 2005-Present: Journal of Molecular and Genetic Medicine
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- *Angiostrongylus cantonensis*: s-adenosyl methionine decarboxylase.
- Analysis of a protein expression from *Angiostrongylus cantonensis* DNA cloning for serodiagnosis of angiostrongyliasis.
- Detection of IgG-subclass for serodiagnosis of angiostrongyliasis.
- Experimental infection of freshwater fish in Thailand with infective stage of *Angiostrongylus*.

Cysticercosis & Taeniasis
- 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
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Echinococcosis
- Analysis of fluid antigens of Echinococcus cyst for diagnosis.
- Mitochondrial DNA sequence of protoscoleces of Echinococcus cysts from four patients.
- Serodiagnosis of suspected echinococcosis cases using native, partially-purified, and DNA recombinant antigens.

Filariasis
- Rare or unrecognized evidence of human dirofilariasis in Thailand: possible immunoblot diagnosis of one Thai patient.
- Study on prevalence of Wuchereria bancrofti infection in Kanchanaburi and Ratchaburi provinces.
- Urine ELISA for diagnosis of Bancroftian filariasis

Gnathostomiasis
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- Immunoblot-diagnostic specificity for gnathostomiasis.
- Prevalence of Gnathostoma spinigerum in cats and dogs in Buddhist Temples in Bangkok.

Opisthorchiasis
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- *Toxocara canis* larval antigens for serodiagnosis of human toxocariasis.

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Department of

MEDICAL ENTOMOLOGY

Assoc. Prof. Somjai Leemingsawat
Field of Expertise:
Medical entomology/Tick and mite-borne diseases/Filarial parasites and vectors
E-mail: tmslm@mahidol.ac.th
Tel: 1574
Head (to 30 Sep. 2005)

Assoc. Prof. Supattra Thongrungkiat
B.Sc., M.Sc.(Trop.Med.)
Field of Expertise:
Medical entomology/Mosquito colonization/Malaria parasite and vector/Dengue virus and vector/Mosquito inoculation
E-mail: tmtsr@mahidol.ac.th
Tel: 1574
Deputy Head

Assoc. Prof. Chammarn Apivathnasorn
Field of Expertise:
Medical entomology/Mosquito taxonomy/Ecology/Field study
E-mail: tmcaw@mahidol.ac.th
Tel: 1575
Head (from 1 Oct. 2005)

Assoc. Prof. Narumon Komalamisra
Field of Expertise:
Medical entomology/loenzyme of vectors/Vector genetics/Molecular entomology/Vector control
E-mail: tmnkm@mahidol.ac.th
Tel: 1843

Assist. Prof. Achara Asavanich
B.Sc., M.Sc.(Entomology), Ph.D.
Field of Expertise:
Malaria vector/Medical entomology
E-mail: tmaas@mahidol.ac.th
Tel: 1576

Assist. Prof. Chotechuang Panasoponkul
B.Sc., M.Sc., D.A.P.&E., Ph.D.
Field of Expertise:
Vector borne diseases eg. filariasis, malaria and field work
E-mail: tmcpn@mahidol.ac.th
Tel: 1530, 1578

Dr. Karnchana Pornpininworakij
M.D., D.T.M. & H., M.C.T.M.
E-mail: meyrek@yahoo.com
Tel: 1577
Lecturer

Ms. Yuwadee Trongtokit
Ph.D. (Trop. Med.)
Field of Expertise:
Medical Entomology, Vector control, Plant-based insecticides
E-mail: ytrongtokit@yahoo.com
Tel: 1577
Lecturer

Ms. Rutcharin Potiwat
B.Sc. (Biological), M.Sc. (Genetic Engineering)
Field of Expertise:
Molecular Biology, Protein purification, Isoenzyme of vector
E-mail: Kae_ruc@hotmail.com
Tel: 1577
Researcher

Mrs. Raweewan Srisawat
B.Sc., M.Sc., D.A.P.&E.
Field of Expertise:
Insecticide resistance
E-mail: tmsrs@mahidol.ac.th
Tel: 1844
Scientist

Mrs. Keawmala Palakul
B.Ed., D.A.P.&E., Traditional Pharmacy, Traditional Medicine
Field of Expertise:
Vector control by using medicinal plants
Tel: 1578, 1844
Scientist

Ms. Rutcharin Potiwat
B.Sc. (Biological), M.Sc. (Genetic Engineering)
Field of Expertise:
Molecular Biology, Protein purification, Isoenzyme of vector
E-mail: Kae_ruc@hotmail.com
Tel: 1577
Researcher

Mrs. Samereng Prummongkol
B.Ed., D.A.P.&E., Health Education
Field of Expertise:
Medical Entomology, Parasitology, Field study
Tel: 1578, 2109, 2100
Medical Science Associate

Office of the Department Telephone: 0 2354 9100 ext. 1571-8; Fax: 0-2643-5582
Laboratory Unit Telephone: 0 2354 9100 ext. 2109; Fax: 0-2643-5582
Insecticide Research Unit Telephone: 0 2354 9100 ext. 1843-5; Fax: 0-2643-5582
CURRENT RESEARCH ACTIVITIES

Research conducted by the staff of the Department of Medical Entomology involved both basic and applied knowledge applicable to controlling insects and arthropods that are vectors of tropical diseases, with an emphasis on mosquito-borne diseases.

The effective control of mosquito vectors directs both laboratory and field trials. Control of larvae of *Aedes aegypti* in the Faculty of Tropical Medicine premises, by Abate sand granules (temephos); studies on the efficacy of insect repellents extracted from various medicinal plants; and effective measures for preventing tropical disease infections in the population living at the Thai-Myanmar border are continuously conducted.

Inter-organizational projects on various aspects, such as, a construction of a key for the identification of *Anopheles aconitus* and the search for malaria transmission form(s), a search for effective herbal extracts for lice control, survey of malaria vectors in Sa Kaeo Province, and effective control measures of *Brugia malayi* in Narathiwat Province, are conducted.

Several research topics at the molecular level are performed, for example, DNA bank of mosquito vectors in Thailand, genetic diversity of *Anopheles barbirostris* group in Thailand for the control of tropical diseases, and specificity test of primers synthesized from DNA fragments of the *Anopheles minimus* mosquito. The effects of the heavy metals, lead and cadmium, on enzymes of *Culex quinquefasciatus* larvae are also studied.

HIGHLIGHT ACTIVITIES

Study on insecticidal activities of several species of Thai herbal extracts for controlling mosquito vectors. The promising oil extracts that showed mosquito repellency, such as qinghao (*Artemisia annua*), “may chang” (*Litsea cubeba*), clove (*Syzygium aromaticum*), and “makaen” (*Zanthoxylum limonella*), are formulated in forms of cream or gel. The extract of “thong pun chang” (*Rhinacanthus nasutus*) provided high larvicidal activity and is prepared in tablet form. The mosquito repellent formulation of the volatile oil mixture from *Artemisia annua* is in the process of patent application.
Laboratory colonies of different strains of mosquito vector species of *Anopheles, Aedes, Culex,* and *Mansonia* are continuously maintained in the insectarium for further use.

The Department of Medical Entomology also acts as a reference center on mosquito vectors in Thailand through the Mosquito Museum Annex. Academic consultation, especially on mosquito-borne diseases and their control measures, and also services for the detection of filarial parasites, identification of mosquitoes and other medically important insects and arthropods, are regularly provided.

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Prof. Srisin Khusmith
B.Sc., M.Sc., Doctorat D'Etat es Sciences
Field of Expertise: Immunology/molecular biology/malaria
E-mail: tmksm@mahidol.ac.th
Tel: 1594
Vice President for Research, Mahidol University

Assoc. Prof. Wipavee Jumpangern
B.Sc., M.Sc., Dr.Med.Sc.
Field of Expertise: Immunology of parasitic infections/immunology and molecular biology of dengue viruses
E-mail: tmwsu@mahidol.ac.th
Tel: 1595, 2098

Assist. Prof. Usanee Suthisarnsuntorn
M.D., Dip. American Board of Paediatrics, D.T.M. & H.
Field of Expertise: Clinical microbiology/bacteriology/pediatric infectious diseases
E-mail: tmus@mahidol.ac.th
Tel: 1592, 1671

Assoc. Prof. Yuvadee Mahakunkijcharoen
B.Sc., M.Sc., Ph.D.
Field of Expertise: Immunology/Aeromonas
E-mail: tmymh@mahidol.ac.th
Tel: 1596, 2094

Assist. Prof. Varee Wongchotigul
B.Sc., Ph.D.
Field of Expertise: Immunology, rickettsiology (scrub typhus)
E-mail: tmvw@mahidol.ac.th
Tel: 1595, 2097

Dr. Jintana Patarapotikul
B.Sc., M.Sc., Ph.D.
Field of Expertise: Immunology/molecular biology of malaria/human genetics
E-mail: tmjn@mahidol.ac.th
Tel: 1666, 1668
Lecturer

Dr. Pornsawan Leangsvutivong
Ph.D. (Tropical Medicine)
Field of Expertise: Medical Virology
E-mail: tmpam@mahidol.ac.th
Tel: 1597, 1591
Lecturer

Miss Akanitt Jittmittraphap
B.Sc., M.Sc.
Field of Expertise: Immunology Molecular biology of dengue viruses
E-mail: atanitt@yahoo.com,
tnajmr@mahidol.ac.th
Tel: 1597
Lecturer

Mrs. Teerarut Chanket
B.Sc., M.Sc.
Field of Expertise: Bacteriology, molecular biology
E-mail: Tel: 1673, 1671
Scientist

Miss Jarinee Panitchakorn
B.Sc., M.Sc.
Field of Expertise: Immunology/Malaria
E-mail: P.jarinee@hotmail.com
Tel: 2096, 1592
Researcher

Mr. Witawat Tunyong
B.Sc.
Field of Expertise: Bacterial identification
E-mail: Tel: 1671, 1673
Medical Technologist
CURRENT RESEARCH ACTIVITIES

1. Detection of dengue viral RNA in mosquitoes (Aedes aegypti) by nucleic acid sequence-based amplification (NASBA) and polymerase chain reaction (PCR).
2. Immunological studies on vector-borne disease of dengue hemorrhagic fever in Thailand.
4. Diagnosis of dengue virus infection by luminescence immunoprecipitation assay.
5. Serotypes of dengue virus infection in Petchaboon, Nakhon-Srithammaraj and Srisaket provinces.
7. Comparison of Salmo-Dot and PCR for the detection of Salmonella spp. in foods.
8. Molecular typing of leptospiral serovars based on genes of the rfb locus.
9. Study of the membrane protein antigen of Leptospira that react with leptospirosis patients’ serum.
10. An application of nested polymerase chain reaction in detecting scrub typhus DNA from clinical specimens.
11. Analyses of natural killer T (NK-T) cell subsets in patients with severe and uncomplicated falciparum malaria.
12. Indirect immunoperoxidase test for dual serodiagnosis of scrub typhus and leptospirosis.
13. Detection of Salmonella enterotoxin and enterotoxin in food and clinical isolates.
14. Detection of virulence factors from Aeromonas spp. in relation to diarrhea.
15. Antigenic recognition of Aeromonas antigens in mice.
17. Purification of a Vibrio cholerae O1 antigen by affinity chromatography using a killing active monoclonal antibody.

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Assoc. Prof. Yaowalark Sukthana
B.Sc., D.V.M., M.D.(Hons.), Dip. of Thai Board in Oto Rhino Laryngology, D.T.M.&H., M.C.T.M.
Field of Expertise:
Oto-rhino-laryngology/Toxoplasma gondii
E-mail: tmymv@mahidol.ac.th
Tel: 02-3549100 ext. 1833
Head

Assist. Prof. Waraporn Suphadtanaphongs
B.Sc., M.Sc., D.A.P&E.
Field of Expertise:
Cultivation and drug sensitivity test of P. falciparum
E-mail: tmwsp@mahidol.ac.th
Tel: 02-3549100 ext. 1830

Miss Rachatawan Chiabchalard
B.Sc.(Physical Therapy), M.Sc. (Biology)
E-mail: tmwcc@mahidol.ac.th
Tel: 02-3549100 ext. 1831
Lecturer

Assoc. Prof. Porntip Petmitr
Field of Expertise:
Biochemistry of malaria parasites/Cultivation of P. falciparum gametocytes and T. vaginalis
E-mail: tmppm@mahidol.ac.th
Tel: 02-3549100 ext. 1830

Miss Somri Kajorndechakait
Cert Medical Science Technology
Medical Science Associate
Tel: 02-3549100 ext. 1831

Miss Niramol Thima
Voc. Cert.
Medical Science Associate
Tel: 02-3549100 ext. 1831

Mr. Amorn Lekkla
B.Sc.(Health Education), M.Sc.(Public Health)
Tel: 02-3549100 ext. 1831
Researcher

Mr. Nuttpong Getmarchom
Voc. Cert.
Medical Science Associate
Tel: 02-3549100 ext. 1831

Miss Ruenruetai Udonsom
B.Sc.
Scientist
Tel: 02-3549100 ext. 1831

Miss Chantira Suthikornchai
B.Sc.(Biologiy), M.Sc.(Trop.Med.)
Researcher
Tel: 02-3549100 ext. 1831

Miss Chantira Suthikornchai
B.Sc.(Biologiy), M.Sc.(Trop.Med.)
E-mail: momotaro162@yahoo.com
Tel: 02-3549100 ext. 1831
Researcher

Mr. Ittisak Subrungruang
B.Sc.(Medical Technology), M.Sc.(Trop.Med.)
E-mail: pookkoong@hotmail.com
Tel: 02-3549100 ext. 1831
Researcher

Mrs. Nontiya Sensiriwattana
M.B.A.
E-mail: tmnsr@mahidol.ac.th
Tel: 02-3549100 ext. 1830
General Affairs Officer
HIGHLIGHT ACTIVITIES

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

CURRENT RESEARCH ACTIVITIES

1. Ultrastructure of acute and chronic toxoplasmosis after pyrimethamine and artesunate administration in vivo study
2. Dog and cat parasitic zoonoses
3. Biological contamination-free Thai frozen food
4. Molecular technique for diagnosis of toxoplasmosis and neosporosis in Thai dairy cows
5. Molecular and immunohistochemistry studies on stage interconversion of toxoplasmosis in immunocompromised hosts
6. Molecular diagnosis of malaria, amebiasis and cryptosporiosis
7. Purification and characterization of DNA topoisomerases from Trichomonas vaginalis
8. Effect of ultraviolet irradiation on viability of Cryptosporidium oocysts in water
9. Viability of Giardia cysts in water from Thai frozen food.
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Association of Members

Assoc. Prof. Wijitr Fungladda
B.Sc. (Med.Sc.), M.D., D.T.M. & H., M.P.H., Dr.P.H.
Field of Expertise: Social epidemiology of tropical diseases (malaria, opisthorchiasis, leptospirosis)
E-mail: tmvfd@mahidol.ac.th
Tel: 0 2354 9100-19 ext. 1565, 1890
Head

Assoc. Prof. Waranya Wongwit
B.Sc. (Biology), M.S. (Biological Sciences), Ph.D. (Biochemistry)
Field of Expertise: Biochemistry of parasites, Environmental toxicology
E-mail: tmwwg@mahidol.ac.th
Tel: ext 1567, 1890
Deputy Head

Assoc. Prof. Kamolnetr Okanurak
Field of Expertise: Community participation in disease control/ Treatment-seeking behavior
E-mail: tmkok@mahidol.ac.th
Tel: ext 1689

Assoc. Prof. Piyarat Butraporn
B.V.M., M.P.H., D.A.P. & E., M.P.H., Dr.P.H.
Field of Expertise: Social epidemiology in tropical diseases (malaria, DHF) and health impact assessment of water resource development
E-mail: mpmdb@mahidol.ac.th
Tel: ext 1681, 1689

Assoc. Prof. Voranuch Wangsuphachart
Field of Expertise: Environmental epidemiology/ Comparative risk assessment/Epidemiology and internet / Health Impact Assessment (HIA)
E-mail: tmvws@mahidol.ac.th
Tel: 0 2644 8837 ext 0 (direct), ext 1266, 1562-3

Assoc. Prof. Pongrama Ramasoota
D.V.M., M.P.H., M.Sc. (Molecular Biology), Ph.D. (Molecular Biology)
Field of Expertise: Molecular biology/Phage display technology/Vaccine design
E-mail: pongrama@yahoo.com
Tel: 1562-4

Dr. Prapin Tharnpoophasiam
B.Sc. (Med. Tech.), M.Sc. (Toxicology), Ph.D. (Trop. Med.)
Field of Expertise: Environmental toxicology
E-mail: torapin@hotmail.com
Tel: ext 1266, 1562-3
Lecturer

Mrs. Phunthira Pongsaskulchoti
B.Ed. (Biology)
Tel: ext 2107
Scientist

Mrs. Puwadee Siri-aaron
Field of Expertise: Brackish and Freshwater Malacology/Medical Malacology/Health Social Science/Health Impact Assessment of water resource development
E-mail: tmwps@mahidol.ac.th
Tel: ext 1266, 1562-3, 2106
Scientist

Mr. Wiwat Wanarangsikul
E-mail: tmwsl@mahidol.ac.th
Tel: ext 1688
Researcher

Dr. Suwalee Tantawiwat
B.N.S., M.Sc. (Technology of Environmental Management), Ph.D. (Trop. Med.)
Field of Expertise: Environmental toxicology
E-mail: minehoney@yahoo.com
Tel: ext 1266, 1562-3
Lecturer
The Department of Social and Environmental Medicine is responsible for teaching, research and academic services. In terms of teaching, the Department offers various postgraduate courses leading to the M.Sc. and Ph.D. in Tropical Medicine. Specialization is focused on three tracks, namely Social Medicine, Environmental Health, and Environmental Toxicology. Regarding research, activities involve both laboratory and field investigations. Efforts are concentrated on disease-oriented problems. In addition to laboratory studies, such as molecular biology of pathogenic organisms, leptospirosis vaccine design, and the biology of blood and liver flukes, activities expand to cover environmental epidemiology, environmental health, environmental toxicology, as well as social and behavioral factors influencing tropical diseases and public health problems of the country, including leptospirosis, DHF, TB, avian flu, and HIV (vaccine trial).

The Department offers various kinds of laboratory investigation, for example, circum-oval precipitation test (COPT) for blood fluke infection, identification of medically important mollusks, rapid diagnosis of multidrug-resistant Mycobacterium tuberculosis, etc. It is also home of the ‘Mollusk Museum’, where shell specimens of various medically important snail hosts are collected. This museum is considered one of the perfect mollusk museums in the region. The Department periodically offers training courses on various aspects of Socine and Environmental Medicine.
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</table>
Assist. Prof. Jaranit Kaewkungwal  
Field of Expertise: Research methodology/ Data management/ Statistics modeling  
E-mail: tmjkk@mahidol.ac.th  
Tel: ext.1682-4  
Head

Mr. Pitak Wuthisen  
B.Sc.(Biology), M.Sc.(Trop.Med.)  
Field of Expertise:  
Tropical Disease field works & Diagnostic parasitology  
E-mail: tmpwt@mahidol.ac.th  
Tel: ext.1682-3  
Deputy Head

Assist. Prof. Kasinee Buchachart  
B.Sc.(Microbiology), M.Sc.(Trop.Med.)  
Field of Expertise:  
Statistical analysis & Data processing of epidemiological research  
E-mail: tmkbc@mahidol.ac.th  
Tel: ext.1682-4  
Deputy Dean for Administration and Finance

Assoc. Prof. Pratap Singhasivanon  
M.B.B.S., D.T.M.&H., M.P.H., Dr.P.H. (Epidemiology)  
Field of Expertise:  
Epidemiology of tropical diseases/ Research methodology  
E-mail: tps@mahidol.ac.th  
Tel: ext.1680, 1682-3  
Dean

Dr. Nathanej Luplerdlop  
M.D., Ph.D. (Anatomy/ Molecular Immunovirology)  
Field of Expertise:  
Molecular immunovirology (Dengue), Molecular immunopathophysiology in malaria  
E-mail: tmnl@mahidol.ac.th  
Tel: ext.1684  
Lecturer

Miss Pannamas Maneekan  
B.Sc. (Nursing), M.Sc.(Community medicine)  
Field of Expertise:  
Community study  
E-mail: tmpmk@mahidol.ac.th  
Tel: ext.1682-3  
Lecturer

Assoc. Prof. Supalarp Puangsa-art  
B.Sc.(Agriculture), B.A.(Political Science), M.Sc.(Trop.Med.), M.Sc.(Biostatistics)  
Field of Expertise:  
Biostatistics, Data analysis, Ecology and Anopheles larva density  
E-mail: tmspa@mahidol.ac.th  
Tel: ext.1694  
Scientist

Dr. Saranath Lawpoolsri  
B.Sc.(Public Health), M.Sc.(Epidemiology)  
Field of Expertise:  
Epidemiology, Data analysis  
E-mail: friv@mahidol.ac.th  
Tel: ext.1695  
Lecturer

Mr. Irwin F. Chavez  
B.Sc.(Public Health), M.Sc.(Epidemiology)  
Field of Expertise:  
Epidemiology, Data analysis  
E-mail: friv@mahidol.ac.th  
Tel: ext.1695  
Lecturer

Mr. Nipon Thanyavanich  
Cert. Medical Science Technology, B.Ed.(Biology), M.Sc.(Infectious Disease)  
Field of Expertise:  
Diagnostic parasitology  
E-mail: tmnty@mahidol.ac.th  
Tel: ext.1686  
Researcher

Mr. Sirichai Chupraphawan  
B.Sc.(Agriculture), M.Sc.(Agriculture System)  
Field of Expertise:  
GIS & Remote sensing  
E-mail: tmscp@mahidol.ac.th  
Tel: ext.1695  
Researcher

Mr. Surapon Yimsamran  
Cert. Medical Science Technology, B.Ed.(Biology), M.Sc.(Epidemiology)  
Field of Expertise:  
Epidemiologist/ Research methodology/ Data management and analysis  
E-mail: tmhsy@mahidol.ac.th  
Tel: ext.1695  
Researcher
Mr. Wanchai Maneeboonyang
Cert. Medical Science Technology, B.Sc.(Education), M.Sc.(Infectious Disease)
Field of Expertise:
- Diagnostic parasitology/ Scrub typhus
E-mail: tmwmn@mahidol.ac.th
Tel: ext.1694
Researcher

Mr. Prasert Rukmanee
Cert. Medical Science Technology, B.Sc.(Environmental Sciences), M.Sc. (Trop. Med.)
Field of Expertise:
- Diagnostic parasitology/ General laboratory
Tel: ext.1682-3
Medical Science Associate

Mr. Seksan Sawatdiraksa
B.B.A.(Business Computer), M.Sc. MS-IED (Internet and E-Commerce Technology)
Field of Expertise: Computer System
E-mail: tswsd@mahidol.ac.th
Tel: ext.1694
Computer System Officer

Mrs. Natefa Rukmanee
Cert. Medical Science Technology, B.Sc.(Health Education)
Field of Expertise:
- General laboratory/ Computer data entry
Tel: ext.1686, 1682-3
Medical Science Associate

Mr. Sutthiporn Prommongkol
Cert. Medical Science Technology
Field of Expertise: Diagnostic parasitology
Tel: ext.1694
Medical Science Associate

Miss Muntana Nakmuan
Field of Expertise: Computer Data entry
Tel: ext.1682-3
Medical Science Associate

Miss Chotima Charusabha
B.Sc.(Computer)
Field of Expertise:
- Data Management and analysis
E-mail: tmcss@mahidol.ac.th
Tel: ext.1682-3
Research Officer

Mr. Wutthichai Chaimoongkun
B.A.(Business administration)
Field of Expertise:
- Malaria laboratory/ Computer data entry
Tel: ext.1682-3
Research Officer

Mr. Samarn Sonklom
Field of Expertise: Malaria laboratory
Tel: ext.1694

Mrs. Kamornwan Chaipakdee
B.Ed.(Social Study)
Field of Expertise: General administration
Tel: ext.1682-3
General Affairs Officer

Miss Ketsaraporn Thongpakdee
B.A.(Communication)
Field of Expertise:
- General administration/ Educational media
E-mail: ractd@mahidol.ac.th
Tel: ext.1682-3
General Affairs Officer
CURRENT RESEARCH ACTIVITIES

1. Application of GIS in monitoring multi-drug resistant malaria in the Greater Mekong Sub-Region of Southeast Asia III.
2. Epidemiological study of *Enterobius vermicularis* in preschool children in Tanowsri Subdistrict, Suan Phung, Ratchaburi Province.
3. Epidemiological study or asymptomatic malaria parasitemia in an endemic area.
4. Epidemiology and control of malaria in Ratchaburi Province, Thailand.
5. Epidemiology and health education program and treatment evaluation of *Pediculosis capitis* with Leech Lime cream in schoolchildren, Suan Phung District, Ratchaburi Province.
7. Field-based study of reappearance *Plasmodium vivax* malaria cases in the area near the Thai-Myanmar border, Suan Phung, Ratchaburi Province.
8. Geographic survey of health facilities and demographic data in Tsunami-affected area in Thailand.
9. GIS disease surveillance system in the Mekong region.

HIGHLIGHT 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. Epidemiological 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 epidemiological, and in the application of Geographical Information System (GIS) to common tropical diseases. Furthermore, the Department has direct responsibility for managing the Rajanagarindra Tropical Disease International Center (RTIC) to ensure the continuous delivery of quality and free 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.
12. Relationship of intestinal parasitic infections to malnutrition.
13. Search for genes susceptible to clinical malaria.
14. Seroprevalence of Rickettsia infection among Thai troops working along Thai-Myanmar border, Suan Phung, Ratchaburi Province.
15. Study of health behaviors and factors associated with intestinal parasite infections in the community and Air-Force unit in Ubolratchatani Province.
16. Study on the ecology of Anopheline larvae in malaria endemic area of 7 hamlets in Tanowsri Canton, Suan Phung District, Ratchaburi Province.

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Assoc. Prof. Songsak Petmitr
B.Ed.(Secondary School), M.S.(Chemistry Ed.), Ph.D.(Biochemistry)
Field of Expertise: Molecular biology/Molecular carcinogenesis of cancer
E-mail: tmspm@mahidol.ac.th, headtmnu@mahidol.ac.th
Tel: 2083; 0-2354-9100-19 ext 1581  Fax: 0-2644-7934
Head

Assoc. Prof. Rungsunn Tungtrongchitr
B.Sc.(Medical Technology), M.Sc.(Tropical Medicine), Ph.D.(Tropical Medicine)
Field of Expertise: Community nutrition/Nutritional epidemiology/Biochemical nutrition
E-mail: tmtbr@mahidol.ac.th
Tel: 2083; 0-2354-9100-19 ext. 1583-4  Fax: 0-2644-7934

Assist. Prof. Karunee Kwanbunjan
B.Sc.(Biology), M.Sc.(Tropical Medicine), Dr. oec. troph. (Nutrition and Food Sciences)
Field of Expertise: Biochemical nutrition/Nutritional epidemiology
E-mail: tmkkb@mahidol.ac.th
Tel: 2082; 0-2354-9100-19 ext. 1583-4  Fax: 0-2644-7934

Dr. Dumrongkiet Arthan
B.Sc. (Biochemistry), M.Sc. (Biochemistry) Ph.D. (Biochemistry)
E-mail: tedar@mahidol.ac.th
Tel: 2086; 0-2354-9100-19 ext. 1583-4  Fax: 0-2644-7934
Lecturer

Miss Anong Kitjaroentham
B.Sc.(Medical Technology), M.Sc.(Tropical Medicine)
E-mail: tmakj@mahidol.ac.th
Tel: 2088; 0-2354-9100-19 ext. 1583-4  Fax: 0-2644-7934
Researcher

Mrs. Yaovamarn Chantaranipapong
Cert.(Medical Science Laboratory Assistant)
Tel: 2086; 0-2354-9100-19 ext. 1583-4  Fax: 0-2644-7934
Medical Science Associate

Miss Saijai Paisiri
B.A.(General Management)
E-mail: tmsf@mahidol.ac.th
Tel: 2088; 0-2354-9100-19 ext. 1582  Fax: 0-2644-7934
General Affairs Officer

Dr. Sarunya Kaewprasert
B.Sc.(Biotechnology), M.Agr. (Nutritional Biochemistry), Ph.D. (Nutritional Biochemistry)
E-mail: tmkkf@mahidol.ac.th
Tel: 2088; 0-2354-9100-19 ext. 1583-4  Fax: 0-2644-7934
Lecturer

Miss Pornrutsami Jintaridhi
B.Sc.(Nursing), M.Sc.(Nutrition)
E-mail: tmpjt@mahidol.ac.th
Tel: 2082; 0-2354-9100-19 ext. 1583-4  Fax: 0-2644-7934
Scientist

Miss Apanchanid Thepouyporn
B.Sc.(Agriculture), M.Sc.(Biopharmaceutical Sciences)
E-mail: tmato@mahidol.ac.th, Apanchanid@hotmail.com
Tel: 2082; 0-2354-9100-19 ext. 1583-4  Fax: 0-2644-7934
Researcher

Mr. Somchai Puduang
B.N.S., M.Sc. (Technology of Environmental Management)
Tel: 2085; 0-2354-9100-19 ext. 1583-4  Fax: 0-2644-7934
Medical Science Associate
The 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 dyslipidemia and coronary heart disease, the effect of smoking on work performance in relation to homocysteine concentration. Furthermore, molecular biology in cancers of the lung, liver, breast, cholangiocarcinoma, colon and cervix, including the molecular biology of obesity, were investigated. Food and health relationships in the populations of Asian countries are of interest for study, and data will be compared.

The topics of the current research projects are as follows:

1. Novel DNA amplification on chromosomes 2p25.3 and 7q11.23 cholangiocarcinoma identified by arbitrarily primed polymerase chain reaction
2. Adiponectin/ACP30, a collagen-like plasma protein, in relation to anthropometric measurement in Thai overweight and obese subjects
3. Homocysteine and vitamin in healthy Thai smokers
4. Methylene tetrahydrofolate reductase (MTHFR) polymorphism (C677T) in relation to homocysteine concentration in overweight and obese Thai
5. Relationship between soluble leptin receptor, leptin, lipid profiles and anthropometric parameters in overweight and obese Thai subjects
6. Polymorphism of glutathione S-transferase omega gene and risk of cancer
7. Riboflavin-deficient and *Trichinella spiralis*-induced stresses on plasma corticosterone associated with spermatogenesis in male Wistar rats
8. Assessment of dietary patterns of Thais in Germany and Thailand
9. Low folate status as a risk factor for cervical dysplasia in Thai women
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2. *In vitro* model for studying pathogenesis of atherosclerosis.

3. Ig class switching induced by *Plasmodium falciparum*.

4. Endothelial cell activation by *Plasmodium falciparum*.

5. Ultrastructural study of malarial parasites and the infected red blood cells after drug treatment.

6. Cytokine expression in squamous cell carcinoma and HIV patients.
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<td>Joint International Tropical Medicine Meeting 2005</td>
<td>2 December 2005</td>
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<td>Miss Rungrat Nintasen</td>
<td>Faculty of Public Health and Faculty of Graduate Studies, Mahidol University</td>
<td>7 September 2005</td>
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Department of

TROPICAL PEDIATRICS

Assoc. Prof. Pornthep Chanthavanich
Field of Expertise: Chemotherapy of parasitic diseases, Chemotherapy of malaria in children, Vaccination in children
E-mail: tmpct@mahidol.ac.th
Head

Assoc. Prof. Krisana Pengsaa
M.D., Dip. Thai Board of Pediatrics, D.T.M.&H.
Field of Expertise: General pediatrics, Chemotherapy of parasitic diseases, Immunization in children/Neonatal infection
E-mail: tmkps@mahidol.ac.th

Assoc. Prof. Chukiat Sirivichayakul
M.D., Dip. Thai Board of Pediatrics, D.T.M.&H.
Field of Expertise: General pediatrics/Chemotherapy of childhood malaria/Parasitic infection in children/Childhood diarrhea
E-mail: tmcsn@mahidol.ac.th

Assoc. Prof. Phanorsri Attanath
Field of Expertise: In vitro sensitivity test to antimalarials, Pharmacokinetics of antimalarials
E-mail: tmpat@mahidol.ac.th

Assoc. Prof. Watcharee Chokejindachai
M.D., Dip. Thai Board of Pediatrics, D.T.M.&H.
Field of Expertise: Chemotherapy of malaria in children, Chemotherapy of parasitic diseases, Vaccine/General pediatrics
E-mail: watcharee_tm@yahoo.com

Dr. Keswadee Lapphra
M.D., Dip. Thai Board of Pediatrics, Cert. Pediatric Infectious Diseases
Field of Expertise: General pediatrics
E-mail: keswadee_j@yahoo.com
Lecturer

Mr. Chanathep Pojjaroen-anant
Field of Expertise: Cultivation and drug sensitivity test of P. falciparum
E-mail: tmpcp@mahidol.ac.th
Scientist

Mrs. Patraporn Wisetsing
Cert. On Medical Technology, B.Ed. (General Science)
Scientist

Miss Udomluk Thangtaweewaroaj
B.A. (Medical Secretary)
General Affairs Officer

Assoc. Prof. Emeritus Arunee Sabchareon
Field of Expertise:
E-mail: tmasc@mahidol.ac.th
Consultant

Prof. Emeritus Arunee Sabchareon
Field of Expertise:
E-mail: tmasc@mahidol.ac.th
Consultant

Assist. Prof. Kriengsak Limkittikul
M.D., Dip. Thai Board of Pediatrics, Dip. Virology
Field of Expertise: General pediatrics/Tropical virology
E-mail: tmek@mahidol.ac.th

Miss Udomluk Thangtaweewaroaj
B.A. (Medical Secretary)
General Affairs Officer

Faculty of Tropical Medicine, Mahidol University

Annual Review 2006
HIGHLIGHT ACTIVITIES

The major duties of the Department of Tropical Pediatrics are first, to disseminate medical knowledge, especially on tropical diseases in pediatrics, to health personnel and the people; second, to perform research and finally, to provide medical services.

The Master of Clinical Tropical Pediatrics program includes basic knowledge of tropical diseases, clinical tropical pediatric practices and a thematic paper, and is the major training course of the Department. The Department is involved in several training courses of the Faculty.

Each year, there is a one-month tropical pediatrics course for the fellowship in pediatric infectious diseases training program under the Pediatric Infectious Disease Society of Thailand.

Research topics of the Department are wide-spectrum, including clinical tropical pediatrics, infectious diseases, and vaccine trials.

CURRENT RESEARCH ACTIVITIES

1. Evaluation of long-term immunity against rabies in children vaccinated with Purified Chick Embryo Cell Rabies Vaccine (Rabipur®) in different pre-exposure regimens and boosted after one year (Extension of study M49P2)
2. Evaluation of long-term immunity against Japanese encephalitis in children vaccinated with Japanese encephalitis vaccine (Extension of study M49P2)
3. Accuracy assessment of using WHO criteria in diagnosis of dengue infection
4. Safety and immunogenicity of tetravalent dengue vaccine formulation in Thai adult volunteers: eight-year antibody persistence
5. Safety and immunogenicity of tetravalent dengue vaccine formulations in healthy Thai children: evaluation of a booster dose and five-year antibody persistence
6. Epidemiological study of dengue infection in children age 3-10 years in Ratchaburi Province (RAT0148)

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1. Early antibody response to multiple IM doses of purified Vero cell rabies vaccine
2. Kinetics of maternally transferred neutralizing dengue antibodies and wild-type dengue infections in the first two years of Thai infants
4. A comparison of pain scales in Thai children
5. Pre-exposure IM and ID regimens of rabies vaccine administered concomitantly with Japanese encephalitis vaccine in toddlers

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Assist. Prof. Channarong Sanghirun
D.V.M., M.PH.
Field of Expertise: Radioisotopes in medical science and biology, Monoclonal antibody for diagnosis of parasites
E-mail: headtmrd@mahidol.ac.th
Tel: 0 2643 5585, 2040, 2046
Acting Head

Miss Cheeraratana Cheeramakara
B.Ed., M.Sc. (Biology)
Field of Expertise: Radioisotopes in medical science and biology
E-mail: tmccr@mahidol.ac.th
Tel: 0 2643 5585, 2044, 2045
Acting Head

Dr. Voravannee Tolayon
M.D.
Field of Expertise: Radioisotopes in medical science and biology
E-mail: tmvty@mahidol.ac.th
Tel: 02 643 5585
Acting Head

Dr. Duangamol Viroonudomphol
Ph.D.
E-mail: tmdkv@mahidol.ac.th
Lecturer

Mrs. Korbkit Cherdchu
B.Sc., M.Sc.(Pharmacology)
Field of Expertise: Radioisotopes in medical science and biology
E-mail: tmkcr@mahidol.ac.th
Tel: 02 643 5585, 2042
Scientist

Mrs. Wanyarat Thanomsak
B.Sc., M.Sc.(Trop.Med.)
Field of Expertise: Radioisotopes in medical science and biology
E-mail: tmwtn@mahidol.ac.th
Tel: 02 643 5585, 2045
Scientist

Mrs. Suporn Paksanont
B.Sc., M.Sc.(Biology)
Field of Expertise: Radioisotopes in medical science and biology
E-mail: tmspn@mahidol.ac.th
Tel: 02 643 5585, 2042
Scientist

Miss Kriyaporn Songmuaeng
B.Sc., M.Sc.(Environmental Biology)
Field of Expertise: Radioisotopes in medical science and biology
E-mail: tmksv@mahidol.ac.th
Tel: 02 643 5585, 2043
Scientist

Mr. Naphachai Suthisai
Cert. Medical Science Technology
E-mail: tmsvn@mahidol.ac.th
Tel: 02 643 5585, 2043
Medical Science Associate

Mrs. Bangon Sukchart
Cert. Medical Science Technology
E-mail: tmvmsv@mahidol.ac.th
Tel: 02 643 5585, 2040
General Affairs Officer

Miss Duangduen Phienpicharn
B.Ed.(English)
E-mail: tmvd@mahidol.ac.th
Tel: 02 643 5585, 2040
Medical Science Associate
CURRENT RESEARCH ACTIVITIES

Research
1. Current research works :
   1.1 Distribution of C14-Labelled arteether after intramuscular injection in mouse kidney and liver.
   1.2 Studies of radiation effects on mouse macrophage cell line (RAW 264.7) and radio protective effect by various Thai medicinal plants.
   1.3 Comparison of non-radiological technique and 125I-labeled method for measurement of folic acid in normal sera.
   1.4 Determination of vitamin B12 and folic acid in Thai foods.
2. Collaborative research works :
   2.1 Studies on lethal dose LD50 of 4 Thai medicinal herbs in mice.
   2.2 Correlation between folic acid status and cervical cytologic abnormality in Thai women.

Award 2005
Second prize of the most attractive poster entitle “Study on serum transcobalamin II in patients with murine typhus” Joint International Tropical Medicine Meeting 2005.

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The Wellcome Trust-Mahidol University-Oxford Tropical Medicine Research Programme (the ‘Thailand Unit’) began in 1979 as a research collaboration between the Faculty of Tropical Medicine, Mahidol University and the University of Oxford. Our main administrative office and laboratories are embedded within the Faculty, though most of our clinical studies and much of our laboratory work takes place in ‘up-country’ study sites. Our main research interests are the epidemiology, diagnosis, pathophysiology and treatment of malaria, scrub typhus, melioidosis, leptospirosis and other tropical infections which impose a substantial disease burden on rural populations throughout this populous region. We have study sites in Ubon Ratchatani (melioidosis and cryptococcal
meningitis), Udon Thani (scrub typhus and leptospirosis), Mae Sod Hospital (malaria and microbiological support for SMRU), and Chittagong Medical College in Bangladesh (severe malaria). We also supervise severe malaria clinical trial sites in Burma and India.

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The Vaccine Trial Centre (VTC) was established in February 1984 and became a fully functioning centre in November 1986. The VTC is a joint responsibility of Mahidol University and the Ministry of Public Health, and is operated by the Faculty of Tropical Medicine on their behalf. The major purpose of the centre is testing newly developed vaccines that reach the clinical-trial stage; however, the centre is currently expanding its service to pharmaceutical drug development where evaluation in human participants is needed. The VTC has experience of conducting several Phase I/II and large Phase III trials for various infectious diseases, for example, diarrheal diseases, malaria, HIV, and other viral infections. Currently, the VTC is involved in the world’s largest HIV vaccine community trial, with 16,000 healthy informed consenting volunteers.

The VTC renders services in both the clinical and data management of the trial. The centre is the first and only facility of its kind in Thailand, in the region, and perhaps also in developing countries. The VTC has set its goal since establishment to ensure that all trials under its responsibility are conducted and documented in accordance with international standards and guidelines including the International Conference on Harmonisation (ICH) / WHO Good Clinical Practice standards. Each function would have pre-established systematic written procedures for the organization, conduct, data collection, data management, documentation and verification of the trial. The clinical trials carried out under VTC are entrusted with the validity of data and the ethical, scientific and technological quality of trials.

The VTC sets its mission to collaborate with scientists at any national and international institute as well as vaccine developers, pharmaceutical companies, and donor agencies. The centre provides the necessary infrastructure to enable multi-centre clinical trials and also epidemiological studies to be performed meeting international standards for design, conduct and reporting. The advantage of conducting the trials at VTC is that the centre is equipped with a validated system, technology and procedures, and that its professional staff are well-trained and have tremendous experience conduct in trial. The VTC collaborates with studies done in Thailand, the immediate region, or internationally. The centre accomplishes its mission by planning, implementing and evaluating study protocols or concepts with mutual cooperative agreements and contracts.

Current Research Activities:

- Screening and evaluation of potential volunteers for a trial in Thailand of a candidate Preventive HIV Vaccine
- 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
- Extended evaluation of the virologic, immunologic, and clinical course of volunteers who become HIV-1 infected during participation in a phase III vaccine trial of ALVAC-HIV and AIDSVAX® B/E.
The Data Management Unit (DMU) was officially established by the Executive Committee of the Faculty of Tropical Medicine, Mahidol University on 12 March 1999 to fulfill national requirements under the Thailand National AIDS Committee in conducting the first large-scale HIV vaccine trial in Thailand. Its establishment and early-year operations were sponsored by VaxGen Inc., Brisbane, CA, U.S.A. Currently, the DMU gets funding and personnel support from the Faculty as well as the national and international pharmaceutical product development industry.

The DMU is functionally under the VTC, the Dean’s Office, Faculty of Tropical Medicine. In 2002, DMU also rendered services in database development, consultation and training in data management and analysis for biomedical research through the Applied and Technological Service Centre of Mahidol University. The major objectives of the DMU include: (1) To establish a data management excellence centre in Thailand and serve as a reference centre for data management for vaccine and clinical trials in the region, (2) To serve as a collaborating centre for high-quality data management for vaccine and clinical trials within the Faculty and for other institutions, including international collaborators, (3) To provide training for Faculty staff and other institutions in clinical data management that complies with international standards and guidelines, and (4) To advise and/or develop data management and analysis for biomedical research and services.

The ultimate goal of the DMU is to provide data quality for a particular clinical trial or epidemiological study and, if required, data management in a regulatory compliance environment. Thus, the DMU has arranged its teams into three major areas. Besides the chief, administrative and secretarial staff, the data management personnel are divided into a “data quality group”, an “information-communication technology (ICT) group” and an “quality assurance group”. The number of personnel assigned to each group will depend on the complexity and amount of data and workload of the trial.

The DMU mission is accomplished through collaborative agreements, both academic and financial, among all parties involved. The Faculty renders all administrative and logistical support to facilitate the operation of the DMU to enable high-quality performance. The collaborator(s) enjoy the benefits of high-standard data management practices.

Currently, the DMU plays major roles in data management of the world’s largest HIV vaccine trial, conducted in Thailand. In this trial, all data management processes for over 25,000 volunteers during the 5-year study period are performed within the DMU; and, as this is the first trial in Thailand to maintain a primary database subject to audit by the US FDA, the DMU has utilized the highest quality data management technology ever used in the region. Besides this vast experience in data management in a regulated environment according to international standards, the DMU collaborates with other institutions in conducting research studies as well as consultation and database development, for example, database development for quality control and assurance processes for the Department of Medical Science, Ministry of Public Health.

### Staff

- **Dr. Jaranit Kaewkungwal**  
  Chief, Senior Investigator
- **Waranya Wongwit**  
  Deputy Chief, QA Co-ordinator
- **Amnat Khamspirwatchara**  
  Deputy Chief, Project Co-ordinator
- **Pongthep Miankaew**  
  IT Manager
- **Rungrawee Pawarana**  
  Data Manager 1
- **Soowaluk Thanawatharangkur**  
  Office Manager
- **Panpen Narusatpitich**  
  Document Control Administration
- **Klinsumon Sriratanitpon**  
  Data Manager 2
- **Yaowaluk Kitkungwal**  
  Administrative Assistant
- **Narong Cheepram**  
  System Manager
- **Jesada Hongto**  
  Database Programmer
- **Pawinee Jarujareet**  
  Data Manager 3
- **Nawarat Suntornwichakarn**  
  Clinical Data Associate 1
- **Somporn Kruarat**  
  Clinical Data Associate 2
- **Poramate Tirapichit**  
  Clinical Data Associate 3
- **Winita Suraphat**  
  Clinical Data Associate 4
- **Somjal Channgam**  
  Office Clerk
- **Suredej Luangaroon**  
  Driver
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 prevents 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 increased CD4 count.
• To confirm the safety of the 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 gp120 envelope glycoprotein vaccine containing a subtype E and a subtype B.

Study sites:
• 4 clinics in Chonburi Province and 4 clinics in Rayong Province.

Current updates:

Screening: 26,644 persons
Enrollment: 16,402 persons
Follow-up: continuing
Expected end date: 2009
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 HPV16 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.

Current updates:
- Screening 139 subjects
- Enrollment 134 subjects
- Completed vaccination (3 Doses) 130 subjects
- 3 subjects lost to follow-up
- 3 subjects personal problems
- Follow-up: continuing
- Expected end date: 2007

3. Safety, immunogenicity, and efficacy of Quadrivalent HPV (Types 6, 11, 16, 18) L1 Virus-Like Particle (VLP) Vaccine in mid-adult women—The FUTURE III (Females United To Unilaterally Reduce Endo-Ectocervical Cancer) Study.

Objectives:
- To demonstrate that a 3-dose regimen of Quadrivalent HPV (Type 6, 11, 16, 18) L1 VLP Vaccine is generally well tolerated in women 24 to 45 years of age.

Study design:
- 2 groups: a quadrivalent HPV vaccine group and a placebo group.
- Randomized, double-blind, placebo-controlled, multicenter study.

Current updates:
- Screening 269 subjects
- Enrollment 246 subjects
- Completed vaccination no.1 246 subjects
- Completed vaccination no.2 240 subjects
- Completed vaccination no.3 236 subjects
- Follow-up: continuing
- Expected end date: 2009

4. Establishment of a Shigella sonnei challenge model for evaluation of future vaccine candidates

Objectives:

Primary Objective
- To identify a challenge dose of *S. sonnei* 53G that will cause disease in 70% of Thai adults.

Secondary Objectives
- To assess the Shigella–specific immune response, both humoral and cellular, in shigellosis patients.

Study Subjects
- 36 subjects with 12 alternates
- 20-40 years old, male or female

5. Randomized, double blind HIV vaccine trial to evaluate the immune profile 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 identify the most sensitive validated cellular immune assays utilizing cryopreserved cells that retain specificity and correlate with the gold standard functional measurement of CD8 T-cell effector activity as measured by chromium (51Cr)-release cellular cytotoxicity assay for application to Phase III frozen samples. The primary objectives include:
- Clearly define the cellular immune profile of the ALVAC prime gp120 boost regimen being tested for efficacy in the RV144 trial;
- Technology transfer and validation of the PAVE ICC assay in Thailand on fresh and frozen samples during the conduct of the trial.
to allow application of the validated assay to exploring correlates of protection in the RV144 efficacy trial;

- Compare the ICC and ELISpot cellular immune response assays standardized by PAVE on cryopreserved PBMC to the Cr release cytotoxicity assays on fresh samples, for specificity and sensitivity at 6 months following the completion of vaccination (month 12), the prime time point of maximal cells collected in the Thai Phase III trial (RV144) and the original time points in the Phase II study RV135 (time 6, 9, 12 months), confirm the immunogenicity profile with the field’s new validated cellular assessment assays.

Secondary Objectives

- To compare cellular immune responses (CD4 and CD8) following receipt of two doses of ALVAC-HIV (vCP1521) versus a full vaccination regimen consisting of four doses of vCP1521 and two doses of AIDSVAX® B/E boosting.

Study Subjects

- 300 Thai participants, male or female, aged 18-30 years old
- 4 clinics in the Bangkok area
Philosophy
The program emphasizes producing graduates with an in-depth knowledge of tropical medicine and hygiene. Graduates will be able to manage, and provide consultation on, common health problems and diseases in the tropics.

Objectives
1. To produce graduates with a good level of knowledge of tropical health problems and diseases, including epidemiology, etiology, pathogenesis, pathology, nutritional aspects, risk factors, and clinical manifestations.
2. To produce graduates with the competency to manage common health problems and diseases in the tropics, including diagnosis, treatment, prevention, control, and providing consultation.

This program is fully accredited by the American Society of Tropical Medicine and Hygiene (A.S.T.M.H.), is offered in the English language, and is open to participants of all nationalities.

Admission Requirements
1. Students must hold a M.D., M.B.B.S., or other qualification as a qualified medical doctor accepted by Mahidol University.
2. Pass the English Proficiency Examination according to the requirements of the Faculty of Graduate Studies, Mahidol University.

Note 1: Applicants should have a TOEFL English language proficiency level of 500 or more or an IELTS score level of 5.5 or more.
Note 2: Exceptions may be made by the Program Committee and the Dean of the Faculty of Graduate Studies. Other categories of student may be permitted to attend, and be provided with a “Certificate of Attendance”.

Duration Of Study  6 months, April-September each year.
**MASTER OF CLINICAL TROPICAL MEDICINE**

**Introduction**

The Bangkok School of Tropical Medicine offers the international Master of Clinical Tropical Medicine program (M.C.T.M.) from the first week in April each year. The program is offered in English and is open to students of all nationalities.

**Objectives**

The M.C.T.M. was established to train medical graduates to be:

1. Well-versed and well-informed in tropical and endemic diseases with special reference to Southeast Asia in relation to their causes, epidemiology, pathogenic mechanisms, and prevention and control of diseases.
2. Able to efficiently examine, diagnose and treat the patients suffering from tropical and endemic diseases.
3. Able to provide consultation, and disseminate and impart knowledge of Tropical Medicine.
4. Able to conduct clinical research with special emphasis on problem solving that will lead to the autonomous initiation of new knowledge, and also to innovation and continuous academic advancement.

**Admission Requirements**

An applicant is required to:

1. Be a qualified, registered medical doctor, preferably with at least one year’s clinical experience.
2. Be physically and mentally healthy;
3. Be proficient in English (reading, writing, speaking, listening).

English language proficiency requirements are as follows: TOEFL score of at least 500 or an IELTS score of at least 6.0. If it is not possible to undergo TOEFL or IELTS testing before commencing the program, applicants will be enrolled as trial students, who will be required to pass the English Language Proficiency Examination of Mahidol University before graduation.

4. Persons who do not have the complete qualifications according to these regulations will be considered by the Postgraduate Committee of the Faculty of Tropical Medicine.

**Duration Of Study**

12 months, from the first week of April until the last week of March the following year.

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**MASTER OF CLINICAL TROPICAL PEDIATRICS**

**Introduction**

The Bangkok School of Tropical Medicine offers the international Master of Clinical Tropical Pediatrics (M.C.T.P) program every year, from the first week in April. The program is taught in English and open to students of all nationalities.

**Philosophy**

The program places its emphasis on training medical graduates to be able to understand the diseases related to tropical pediatrics, with reference to endemic diseases, particularly in Southeast Asia, including etiology, incidence, pathogenesis, clinical features, prevention and control, and to continuing their medical education, which is in accordance with the national education developmental plan.

**Objectives**

To train medical doctors who have basic knowledge in pediatrics, to be able to:

A. Plan appropriate investigations and manage common pediatric infectious diseases efficiently and effectively, with emphasis on tropical and endemic areas,
B. Be consultants and transfer their knowledge of tropical pediatrics to other health personnel,
C. Integrate curative services with preventive measures, including child health promotion,
D. Plan and conduct research according to the proposed methodology, data analysis and writing up of the thematic paper related to pediatric tropical diseases. Afterwards, students will be able to conduct research efficiently and effectively, to improve the health status of the people in their own countries,

E. Use and evaluate epidemiological data and medical biostatistics in solving child health problems,

F. Use information technology to locate and update knowledge for continuing medical education related to tropical pediatrics,

G. Possess responsibility, integrity, good morals and self-sacrifice for the welfare of the community.

Admission Requirements

Students must:

1. Hold a M.D., M.B.B.S. or other equivalent qualification that qualifies them to practice as a medical doctor, which is accepted by Mahidol University and have clinical experience in pediatrics of not less than 1 year.
2. Graduated in the D.T.M.&H., or equivalent, of which credit transfer may be considered by the Program Committee and the Dean of the Faculty of Graduate Studies.
3. Have good mental and physical health.
4. Pass the English Proficiency Examination offered by the Faculty of Graduate Studies, Mahidol University, or other qualified institutions, or have a TOEFL score of 500 or more.
5. For plan A(2) students should have a basic knowledge of clinical research by attending the research methodology and basic statistics for medical research.
6. Exceptions to the above items may be made by the Program Committee and the Dean of the Faculty of Graduate Studies.

Duration Of Study

12 months, from the first week of April until the last date of March the following year.

MASTER OF SCIENCE IN TROPICAL MEDICINE

DOCTOR OF PHILOSOPHY IN TROPICAL MEDICINE

Objectives

To build appropriate knowledge and skills for competency in research and the ability to deliver technical services related to tropical medicine, and, for the Ph.D., also to meet the urgent need to produce researchers who have in-depth knowledge and specialties in the field of tropical medicine and are capable of planning and undertaking research projects effectively.

Admission Requirements

For the M.Sc., applicants must hold an M.D., D.D.S., D.V.M., B. Pharmacy or B.Sc. degree.

For the Ph.D. Plan 1, applicants must hold:

1. M.Sc. in Tropical Medicine or related field, or
2. M.D., D.V.M., or D.D.S., and have at least 2 research publications, one as the first author, in a recognized journal.

For the Ph.D. Plan 2, applicants must hold:

1. M.Sc., M.D., D.V.M., or D.D.S., or
2. Be an M.Sc. (Trop.Med.) student who has completed the first year core subjects with a GPA of not less than 3.5, or hold a B.Sc. (Hon.).
3. Before enrolment into one of the above programs, an applicant must be accepted by an appropriate advisor.
4. Applicants should have a TOEFL English language proficiency level of 500 or more.
5. To graduate, all non-native English speakers must pass the English Language Proficiency Examination according to the requirements of the Faculty of Graduate Studies, Mahidol University.
6. Exceptions may be made by the Program Committee and the Dean of the Faculty of Graduate Studies.

Duration Of Study
For the M.Sc., a minimum of 2 years.
For the Ph.D. Plan 1, 3 year-course.
For the Ph.D. Plan 2, 3 year-course.

Commencement
Normally the first Monday of June each year. There is another intake in November each year, by arrangement.

DOCTOR OF PHILOSOPHY IN CLINICAL TROPICAL MEDICINE

Introduction
The Doctor of Philosophy in Clinical Tropical Medicine is offered by the Bangkok School of Tropical Medicine every year. The program is offered in English and is open to students of all nationalities. The aim of the course is to produce medical graduates at Ph.D. level who are competent in performing research leading to the solution of clinical problems in the Tropics, and to improving the quality of life of the people of tropical countries, particularly Thailand and Southeast Asia.

Objectives
To provide appropriate knowledge and skills for competency in research and the ability to deliver technical services related to tropical medicine and also to meet the urgent need for researchers who have in-depth knowledge and specialities in the field of tropical medicine and are capable of planning and undertaking research projects effectively.

Duration Of Study
Not more than 5 years.

Admission Requirements

A. Plan I
Candidates are required to:
1. Be certified in clinical specialties by the Board of the Thai Medicine Council, or its equivalent; and hold the Graduate Diploma in Tropical Medicine and Hygiene (D.T.M.&H.) from Mahidol University, or its equivalent;
2. Hold a license for general medicine (first class) in their domicile countries or in the countries where they graduated and held a license and have had a clinical appointment in a hospital for at least one year;
3. Have passed TOEFL with a score not less than 500 or have obtained an IELTS score of not less than 6.0 and not more than 2 years from the application date.

B. Plan II
1. Hold the Master of Clinical Tropical Medicine (M.C.T.M.) degree from Mahidol University, or its equivalent;
2. Hold a license for general medicine (first class) in their domicile countries or in the countries where they graduated and held a license and have had a clinical appointment in a hospital for at least one year;
3. Have passed TOEFL with a score not less than 500 or have obtained an IELTS score of not less than 6.0 and not more than 2 years from the application date.
## THESIS TITLES

**M. Sc. (Trop. Med.) 2005**

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<td>Miss Megumi Ishida</td>
<td>Discrimination of small liver and intestinal flukes eggs by ribosomal DNA-based PCR</td>
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<td>Medical Entomology</td>
<td>Miss Intira Pipitgool</td>
<td>Effectiveness of <em>Bacillus thuringiensis israelensis</em>, against temephos-resistant <em>Aedes aegypti</em> populations from Thailand, under laboratory conditions</td>
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<td>Helminthology</td>
<td>Mr. Panupong Sahaisook</td>
<td>Analysis of crude and excretory-secretory antigens of <em>Dirofilaria immitis</em> adult worms against antibody of Brugian filariasis by ELISA and immunoblot</td>
<td>Assist. Prof. Paron Dekumyoy</td>
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<td>Microbiology and Immunology</td>
<td>Miss Sunisa Malijunbo</td>
<td>Identification of genus-and/or species of <em>Aeromonas</em> by western blotting</td>
<td>Assist. Prof. Yuvadee Mahakhunkijchareon</td>
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<td>Miss Kulrat Chitcharoenrungrung</td>
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<td>Serodiagnosis of scrub typhus and melioidosis by dual immunoperoxidase test</td>
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<td>Clinical Tropical Medicine</td>
<td>Miss Juntima Sribabel</td>
<td>Effects of primaquine and its metabolites on the infectivity of <em>Plasmodium falciparum</em> gametocytes</td>
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<tr>
<td>Tropical Nutrition &amp; Food Science</td>
<td>Miss Sudaporn Kengkarn</td>
<td>Determination of DNA amplification in DNA fingerprinting amplified from AD 15 primer in colorectal cancer by gene cloning and DNA sequencing</td>
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<tr>
<td>Tropical Nutrition &amp; Food Science</td>
<td>Miss Tawiwnan Sareebot</td>
<td>Analysis of DNA amplification in colorectal cancer by AP-PCR using AB 19 primer, gene clonging and DNA sequencing</td>
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<tr>
<td>Microbiology and Immunology</td>
<td>Miss Ampai Tanganuchitcharnchai</td>
<td>Production of monoclonal antibodies against clinically important <em>Aeromonas</em> spp.</td>
<td>Assoc. Prof. Yuvadee Mahakhunkijchareon</td>
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<td>Protozoology</td>
<td>Mr. Nitisai Tantawivattananon</td>
<td>Viability of <em>Giardia</em> cysts in water from Thai frozen food industry</td>
<td>Assoc. Prof. Yaowalark Sukthana</td>
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<td>Miss Issariya Ieamsuwan</td>
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<td>Dr. Mohammad Jahirul Karim</td>
<td>Age-period-cohort analysis and spatial pattern of tuberculosis incidence in Bangladesh</td>
<td>Assoc. Prof. Pratap Singhasivanan</td>
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<td>Protozoology</td>
<td>Ms. Ruangrat Buddhhirongawat</td>
<td>Study of Toxoplasma gondii strain in Thai domestic and wild feldares</td>
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<td>Social and Environmental Medicine</td>
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<td>Construction of phage antibody library specific to H5N1 avian influenza virus</td>
<td>Assist. Prof. Pongrama Ramasoota</td>
</tr>
<tr>
<td>Medical Entomology</td>
<td>Miss Nuananong Jirankanjanakit</td>
<td>Morphometric analysis of wing geometry in the main dengue vector, Aedes aegypti</td>
<td>Assoc. Prof. Somjai Leemingsawat</td>
</tr>
<tr>
<td>Clinical Tropical Medicine</td>
<td>Dr. Srivicha Krudsood</td>
<td>New method for measurement of red blood cell destruction in malaria</td>
<td>Prof. Polrat Wilairatan</td>
</tr>
<tr>
<td>Tropical Hygiene</td>
<td>Dr. Md. Mushifiqur Rahman</td>
<td>The effect of adherence on the efficacy of artemether-lumefantrine (COARTEM) in the treatment of uncomplicated Plasmodium falciparum malaria in Bangladesh: a randomized controlled trial</td>
<td>Assoc. Prof. Pratap Singhawatin</td>
</tr>
<tr>
<td>Tropical Hygiene</td>
<td>Ms. Tippawan Sungkapong</td>
<td>Identification of antigenic proteins of the surface of P. vivax-infected erythrocytes</td>
<td>Assist. Prof. Kesinee Chotivanich</td>
</tr>
<tr>
<td>Tropical Pathology</td>
<td>Mr. Kraisorn Sappayatosok</td>
<td>Expression of NOS, VEGF, COX-2 and their clinicopathological correlation in oral and para-oral squamous cell carcinoma</td>
<td>Assist. Prof. Urai Chaisri</td>
</tr>
<tr>
<td>Microbiology and Immunology</td>
<td>Ms. Natharinee Horata</td>
<td>Polymorphism and function of PIEMP1 extracellular domains in Thai Plasmodium falciparum isolates causing severe and uncomplicated malaria</td>
<td>Prof. Srisin Khunits</td>
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<tr>
<td>Tropical Pathology</td>
<td>Ms. Navakanit Sachanonta</td>
<td>The effects of antimalarial drug-induced changes on Plasmodium falciparum and Pe-infected red blood cell ultrastructure</td>
<td>Assoc. Prof. Emnpongprat</td>
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<tr>
<td>Clinical Tropical Medicine</td>
<td>Mrs. Piengchan Sonthayanon</td>
<td>Molecular diagnosis and multi-locus sequence</td>
<td>Prof. Sasithon Pukrittiyakamee</td>
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<tr>
<td>Medical Entomology</td>
<td>Mrs. Raweewan Sirawat</td>
<td>The effect of gene mutations to the voltage gated sodium channel in resistant pyrethroid Aedes aegypti</td>
<td>Assoc. Prof. Narumon Komalamiisa</td>
</tr>
<tr>
<td>Protozoology</td>
<td>Mr. Aongart Mahittikorn</td>
<td>Molecular and immunohistochemistry studies on tachyzoite and bradyzoite stage conversion in toxoplasmosis</td>
<td>Assoc. Prof. Yaowalark Sukthana</td>
</tr>
<tr>
<td>Tropical Nutrition &amp; Food Science</td>
<td>Miss Ubol Chuensumran</td>
<td>Identification of genetic alterations in intrahepatic cholangiocarcinoma by arbitrarily primed-polymerase chain reaction (AP-PCR) and DNA sequencing</td>
<td>Assoc. Prof. Songsak Petmitr</td>
</tr>
<tr>
<td>Microbiology and Immunology</td>
<td>Mr. Trung Dac Nguyen</td>
<td>Molecular characterization of antibody resistance in clinical strains of Salmonella enterica serovar typhi from Vietnam</td>
<td>Assist. Prof. Usanee Suthisarnsuntorn</td>
</tr>
<tr>
<td>Microbiology and Immunology</td>
<td>Mr. Vu Phong Tuc</td>
<td>Impacts of pesticide exposure on sperm quality among male farmers in Thalibinh Province, Vietnam</td>
<td>Assoc. Prof. Voranuch Wangsupachart</td>
</tr>
<tr>
<td>Tropical Hygiene</td>
<td>Mrs. Tassanean Silawan</td>
<td>The spatio-temporal dynamics of dengue infection in Northeastern Thailand</td>
<td>Assoc. Prof. Pratap Singhawatin</td>
</tr>
<tr>
<td>Tropical Nutrition &amp; Food Science</td>
<td>Mr. Kittisak Thawnashom</td>
<td>Gene polymorphisms in homocysteine pathway in relation to homocysteine and vitamin status in overweight/obese Thais</td>
<td>Assoc. Prof. Rungsunn Tungtrongchitr</td>
</tr>
<tr>
<td>Medical Entomology</td>
<td>Mr. Apiwat Tawatkins</td>
<td>Novel repellents derived from phytochemicals against mosquito vectors and common cockroaches in Thailand</td>
<td>Assoc. Prof. Narumon Komalamiisa</td>
</tr>
<tr>
<td>Tropical Hygiene</td>
<td>Dr. Le Huu Tho</td>
<td>Alcohol consumption and sexual risk behaviors among adolescents and young adults in Nhatrang City, Vietnam: linear structural equation model</td>
<td>Assoc. Prof. Pratap Singhawatin</td>
</tr>
<tr>
<td>Tropical Pathology</td>
<td>Ms. Jaiaue Wongtanachai</td>
<td>Effects of antimalarial drugs on Plasmodium falciparum: morphology, viability and multiplication potential</td>
<td>Assoc. Prof. Urai Chaisri</td>
</tr>
</tbody>
</table>
The Hospital for Tropical Diseases (HTD), a specialized research hospital, is one of the three hospitals of Mahidol University, has operated since 1961. The HTD is an administrative structure at the Faculty of Tropical Medicine, Mahidol University that brings together a diverse group of faculty, staff, and students from several different specializations whose research and teaching is focused on human pathogens and their invertebrate and vertebrate vectors, the diseases caused by these organisms, and the impact of these diseases on human society. Members of HTD are concerned in particular with the impact of infectious diseases in less developed parts of the world, and research interests of center members range from biomedical science to issues of human rights. Center members also work on new and emerging infectious diseases of importance in the tropical countries, especially those like Severe Acute Respiratory Syndrome (SARS) and Avian flu disease whose public health impact is significantly influenced by human impacts on the environment. Among the diseases studied at HTD are malaria, toxoplasmosis, tuberculosis, lymphatic filariasis, leishmaniasis, dengue, leptospirosis, and scrub typhus. Many faculty work specifically on arthropod vectors, particularly mosquito vectors of arboviruses, filarial worms, and malarial parasites.
In the fiscal year 2005 the number of patients treated in the Hospital for Tropical Disease were classified by disease, as follows:

<table>
<thead>
<tr>
<th>Diseases</th>
<th>No. of out-patients</th>
<th>No. of in-patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Falciparum malaria</td>
<td>930</td>
<td>925</td>
</tr>
<tr>
<td>2. Vivax malaria</td>
<td>320</td>
<td>132</td>
</tr>
<tr>
<td>3. Mixed falciparum and vivax malaria</td>
<td>32</td>
<td>32</td>
</tr>
<tr>
<td>4. Malariae malaria</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>5. Unidentified infections</td>
<td>59</td>
<td>14</td>
</tr>
<tr>
<td>6. Scrub typhus</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>7. Typhoid</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>8. Diarrhea</td>
<td>150</td>
<td>28</td>
</tr>
<tr>
<td>9. Food poisoning</td>
<td>28</td>
<td>3</td>
</tr>
<tr>
<td>10. Hepatitis</td>
<td>846</td>
<td>15</td>
</tr>
<tr>
<td>11. Dengue hemorrhagic fever</td>
<td>138</td>
<td>101</td>
</tr>
<tr>
<td>12. Leptospirosis</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>13. Taeniasis</td>
<td>44</td>
<td>-</td>
</tr>
<tr>
<td>14. Hookworm</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td>15. Trichuris trichura</td>
<td>3</td>
<td>-</td>
</tr>
<tr>
<td>16. Liver fluke</td>
<td>29</td>
<td>-</td>
</tr>
<tr>
<td>17. Pinworm</td>
<td>4</td>
<td>-</td>
</tr>
<tr>
<td>18. Strongyloidiasis</td>
<td>15</td>
<td>-</td>
</tr>
<tr>
<td>19. Gnathostomiasis</td>
<td>485</td>
<td>1</td>
</tr>
<tr>
<td>20. Filariasis</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>21. Dermatitis</td>
<td>2,737</td>
<td>11</td>
</tr>
<tr>
<td>22. Tuberculosis (pulmonary)</td>
<td>158</td>
<td>14</td>
</tr>
<tr>
<td>23. HIV infections</td>
<td>60</td>
<td>7</td>
</tr>
<tr>
<td>24. Hypertension</td>
<td>2,377</td>
<td>41</td>
</tr>
<tr>
<td>25. Diabetes mellitus</td>
<td>1,726</td>
<td>52</td>
</tr>
<tr>
<td>26. Hyperlipidemia</td>
<td>1,456</td>
<td>1</td>
</tr>
<tr>
<td>27. Diseases of oral cavity, salivary glands and jaws</td>
<td>324</td>
<td>200</td>
</tr>
<tr>
<td>28. Others</td>
<td>21,236</td>
<td>692</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>33,173</strong></td>
<td><strong>2,279</strong></td>
</tr>
</tbody>
</table>

Other Special Clinics are:

- **Dermatology clinic:**
  Monday-Friday; 9.00-12.00 hr.
  (Assoc. Prof. Wichai Supanaranond and Dr. Jittima Dhitavat)

- **Childrens clinic:**
  Monday-Friday; 9.00-12.00 hr.
  (Assoc.Prof.Pornthep Chanthavanich, Assoc.Prof. Krisana Pengsaa, Assoc.Prof. Chukiat Sirivichayakul Dr.Keswadee Laphpra and Dr.Kriengsak Limkittikul)

- **Chest clinic:**
  Tuesday; 9.00-12.00 hr.
  (Assist.Prof. Udomsak Silachamroon)

- **Gastroenterology clinic:**
  Tuesday; 9.00-12.00 hr.
  (Prof. Polrat Wilairatana)

- **Liver clinic:**
  Monday; 9.00-12.00 hr.
  (Assoc. Prof. Wattana Leowattana, Dr.Sombat Treeprasertsuk, Dr.Wichai Ekataksin)
• **Ear, nose, Throat clinic:**  
  Tuesday; 9.00-12.00 hr.  
  (Assoc. Prof. Yaowalark Sukthana)

• **Gnathostomiasis clinic:**  
  Wednesday and Friday; 9.00-12.00 hr.  
  (Assoc. Prof. Mario Riganti and Assist. Prof. Valai Bussaratid)

• **Nephrology clinic:**  
  Monday and Wednesday; 9.00-12.00 hr.  
  (Assist. Prof. Weerapong Phumratanaprapin and Dr. Wipa Thanachartwet)

• **Thai Traditional Massage:**  
  every day; 8.00-20.00 hr.

• **Traditional Chinese Acupuncture:**  
  Monday- Friday; 9.00-12.00 hr.  
  (Assoc. Prof. Wichai Supanaranond)

---

**Central Laboratory Services**

<table>
<thead>
<tr>
<th>Test</th>
<th>No. of out-patients</th>
<th>No. of in-patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBC</td>
<td>7,327</td>
<td>8,037</td>
</tr>
<tr>
<td>Hb</td>
<td>7,214</td>
<td>8,379</td>
</tr>
<tr>
<td>Hct</td>
<td>7,266</td>
<td>12,004</td>
</tr>
<tr>
<td>Blood group</td>
<td>727</td>
<td>1,148</td>
</tr>
<tr>
<td>Reticulocyte count</td>
<td>360</td>
<td>1,573</td>
</tr>
<tr>
<td>ESR</td>
<td>408</td>
<td>529</td>
</tr>
<tr>
<td>HIV</td>
<td>-</td>
<td>8</td>
</tr>
<tr>
<td>Bleeding time</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>Malaria diagnosis</td>
<td>95</td>
<td>2,184</td>
</tr>
<tr>
<td>Urine</td>
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<td>4,757</td>
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<tr>
<td>Chloroquine</td>
<td>2</td>
<td>703</td>
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<tr>
<td>Stool examination</td>
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<td>1,355</td>
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<tr>
<td>Occult blood</td>
<td>69</td>
<td>429</td>
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<tr>
<td>Glucose</td>
<td>6,145</td>
<td>5,991</td>
</tr>
<tr>
<td>BUN</td>
<td>4,712</td>
<td>7,833</td>
</tr>
<tr>
<td>Creatinine</td>
<td>5,300</td>
<td>7,235</td>
</tr>
<tr>
<td>Direct-bilirubin</td>
<td>1,687</td>
<td>6,262</td>
</tr>
<tr>
<td>Total-bilirubin</td>
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<td>6,408</td>
</tr>
<tr>
<td>Total Protein</td>
<td>1,711</td>
<td>6,307</td>
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<tr>
<td>Albumin</td>
<td>1,985</td>
<td>7,171</td>
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<tr>
<td>ALP</td>
<td>4,767</td>
<td>6,796</td>
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<tr>
<td>AST</td>
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<td>7,699</td>
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<tr>
<td>GGT</td>
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<td>2,578</td>
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<tr>
<td>Cholesterol</td>
<td>7,464</td>
<td>4,819</td>
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<tr>
<td>Triglyceride</td>
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<td>1,229</td>
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<tr>
<td>HDL</td>
<td>4,434</td>
<td>576</td>
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<tr>
<td>Direct LDL</td>
<td>4,367</td>
<td>536</td>
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<tr>
<td>Sodium</td>
<td>1,125</td>
<td>7,889</td>
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<tr>
<td>Potassium</td>
<td>1,174</td>
<td>7,961</td>
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<tr>
<td>Chloride</td>
<td>1,117</td>
<td>7,785</td>
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<tr>
<td>CO2</td>
<td>1,118</td>
<td>7,751</td>
</tr>
<tr>
<td>Calcium</td>
<td>404</td>
<td>2,964</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Test</th>
<th>No. of out-patients</th>
<th>No. of in-patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phosphorus</td>
<td>169</td>
<td>1,967</td>
</tr>
<tr>
<td>Magnesium</td>
<td>53</td>
<td>839</td>
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<tr>
<td>Uric</td>
<td>3,009</td>
<td>1,782</td>
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<tr>
<td>LDH</td>
<td>74</td>
<td>1,629</td>
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<tr>
<td>CK</td>
<td>341</td>
<td>1,100</td>
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<tr>
<td>Amylase</td>
<td>19</td>
<td>515</td>
</tr>
<tr>
<td>C.S.F-Protein</td>
<td>1</td>
<td>27</td>
</tr>
<tr>
<td>Urine Micro TP</td>
<td>44</td>
<td>5</td>
</tr>
<tr>
<td>Estradiol</td>
<td>23</td>
<td>1</td>
</tr>
<tr>
<td>AFP</td>
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<td>13</td>
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<tr>
<td>CEA</td>
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<td>10</td>
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<tr>
<td>HBSAG</td>
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<tr>
<td>Anti-HBS</td>
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<td>42</td>
</tr>
<tr>
<td>Anti-HBE</td>
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<tr>
<td>HBEAG</td>
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</tr>
<tr>
<td>Anti-HBC</td>
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<td>39</td>
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<tr>
<td>HBV-DNA</td>
<td>196</td>
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<tr>
<td>Anti-HCV</td>
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<tr>
<td>HCG-BETA</td>
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</tr>
<tr>
<td>LH</td>
<td>17</td>
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<tr>
<td>Progesterone</td>
<td>21</td>
<td>-</td>
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<tr>
<td>Prolactin</td>
<td>36</td>
<td>2</td>
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<tr>
<td>Testosterone</td>
<td>13</td>
<td>-</td>
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<tr>
<td>FSH</td>
<td>41</td>
<td>-</td>
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<tr>
<td>G-6-PD</td>
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<td>506</td>
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<tr>
<td>PT+PTT</td>
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<td>648</td>
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<tr>
<td>Hb typing</td>
<td>242</td>
<td>366</td>
</tr>
<tr>
<td>CSF</td>
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<td>22</td>
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<td>Cross-match</td>
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<tr>
<td>HCT</td>
<td>76</td>
<td>1</td>
</tr>
<tr>
<td>Rh typing</td>
<td>-</td>
<td>10</td>
</tr>
</tbody>
</table>

**Total**           | 107,464             | 164,492            |
The Faculty of Tropical Medicine (FTM), Mahidol University, Bangkok, Thailand has been appointed by the Southeast Asian Ministers of Education Organization (SEAMEO) as the TROPMED National Centre for Tropical Medicine since 1967 and was later promoted as the SEAMEO TROPMED Regional Centre for Tropical Medicine (TROPMED/Thailand) since 1994. Its objectives are to provide 3 major functions namely: 1) Teaching and training, 2) Research, and 3) Services.

For teaching, the Bangkok School of Tropical Medicine offers five regular international postgraduate programs:

- Diploma in Tropical Medicine and Hygiene
- Master of Clinical Tropical Medicine
- Master of Clinical Tropical Pediatrics
- Master of Science in Tropical Medicine
- Doctor of Philosophy in Tropical Medicine
- Doctor of Philosophy in Clinical Tropical Medicine

For research, the FTM encourages basic and applied research that leads to the solution of clinical problems in the Tropics, to improve the quality of life of the people, particularly in tropical and developing countries. Research activities are focused on the development of new knowledge or innovations for the practice of tropical medicine. Several related organizations within the Faculty were organized to support facilitate, improve, and maintain research quality e.g. Ethics Committees, Board of Research Consultants, and the Research and Academic Affairs Unit. We encourage collaborative studies through both local and international linkages. As part of our research activities, the Faculty is currently affiliated with more than twenty leading research institutes from all continents of the globe. The current research...
programs include clinical trials in the Hospital for Tropical Diseases, laboratory research, field and epidemiology studies covering more than 20 diseases, including malaria, melioidosis, soil-transmitted diseases, and mosquito-borne diseases, HIV/AIDS, and the health effects of unpredicted natural hazards and disasters.

The FTM remains the leader in Asia in publishing research studies on malaria and other tropical diseases. We will continue to encourage, support, and facilitate research in tropical diseases and other related global health problems. The research activities of the Faculty of Tropical Medicine will continue to strive to improve the education and health of the people in this region.

For services, the Hospital for Tropical Diseases (HTD), a specialized research hospital, is one of the three hospitals of Mahidol University, has operated since 1961. The HTD is an administrative structure at the FTM, Mahidol University that brings together a diverse group of faculty, staff and students from several different specialists, whose research and teaching is focused on human pathogens and their invertebrate and vertebrate vectors, the diseases caused by these organisms, and the impact of these diseases on human society. Members of HTD are concerned in particular with the impact of infectious diseases in less developed parts of the world, and research interests of center members range from biomedical science to issues of human rights. Center members also work on new and emerging infectious diseases of importance in tropical countries, especially Severe Acute Respiratory Syndrome (SARS) and Avian flu, the public health impact of which is significantly influenced by human impacts on the environment. Among the diseases studied at HTD are malaria, toxoplasmosis, tuberculosis, lymphatic filariasis, leishmaniasis, dengue, leptospirosis, and scrub typhus. Many faculty members work specifically on arthropod vectors, particularly mosquito vectors of arboviruses, filarial worms, and malarial parasites.

Three functions of the TROPMEDE/Thailand’s activities are reported according to the 5 KEY RESULT AREAS, as follows:

**KRA 1 ENHANCED PROGRAMME QUALITY AND RELEVANCE**

1.1 Post-graduate regular courses. TROPMEDE/Thailand offers six post-graduate regular courses at the international level, with a total of 236 students from 23 countries.

1.2 Undergraduate courses.
   - TROPMEDE/Thailand also offers 2 undergraduate courses:
     1) Elective Program in Tropical Medicine with 32 both medical doctors and medical students from 5 countries.

   In FY 2004, TROPMEDE/Thailand had 470 students from 23 countries; among these, 322 were newly enrolled students. 452 of these students were fee-paying attendants.
Table 1: Number of students attending the 6 regular courses

<table>
<thead>
<tr>
<th>Courses</th>
<th>Number</th>
<th>No. (Nationality)</th>
<th>No. of fee-paying Students</th>
<th>No. of Graduates</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Postgraduate</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DTM&amp;H 6-month course</td>
<td>32</td>
<td>18 (Australia, Bangladesh, Cambodia, France, India, Indonesia, Japan, Lao PDR, Myanmar, Philippines, Spain, Sri Lanka, Switzerland, Thailand, United Kingdom, USA, United Arab Emirates)</td>
<td>29 (90.62%)</td>
<td>19 (59.37%)</td>
</tr>
<tr>
<td>MCTM 1 year course</td>
<td>7</td>
<td>7 (Ethiopia, India, Lao PDR, Myanmar, Somalia, Sri Lanka, Switzerland)</td>
<td>5 (71.42%)</td>
<td>6 (85.71%)</td>
</tr>
<tr>
<td>MSc (TM) 1st year</td>
<td>29</td>
<td>4 (Japan, Bangladesh, Nepal, Thailand)</td>
<td>72 (91.13%)</td>
<td>19 (24.05%)</td>
</tr>
<tr>
<td>MSc (TM) 2nd year</td>
<td>17</td>
<td>3 (Nepal, Japan, Thailand)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MSc (TM) 3rd year (onward)</td>
<td>33</td>
<td>3 (Lao PDR, Thailand)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MSc (TM) 4th-9th year</td>
<td>57</td>
<td>4 (Korea, Switzerland, Malaysia, Thailand)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>PhD (TM)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1st year</td>
<td>18</td>
<td>2 (Bangladesh, Thailand)</td>
<td>107 (95.53%)</td>
<td>13 (11.60%)</td>
</tr>
<tr>
<td>2nd year</td>
<td>19</td>
<td>2 (Thailand, Vietnam)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3rd year</td>
<td>18</td>
<td>2 (Thailand, Vietnam)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4th-9th year</td>
<td>57</td>
<td>4 (Korea, Switzerland, Malaysia, Thailand)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>PhD (Clin. Trop. Med)</strong></td>
<td>6</td>
<td>2 (Myanmar, Nepal)</td>
<td>5 (83.33%)</td>
<td>1 (16.66%)</td>
</tr>
<tr>
<td>1st year</td>
<td>2</td>
<td>2 (Myanmar, Nepal)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2nd year (Onward)</td>
<td>4</td>
<td>3 (Japan, Myanmar, Thailand)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Subtotal</strong></td>
<td>236</td>
<td></td>
<td>218 (92.37%)</td>
<td>58 (24.57%)</td>
</tr>
<tr>
<td><strong>Undergraduate</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elective Programme in Tropical Medicine</td>
<td>32</td>
<td>5 (Austria, Canada, Japan, Malaysia, USA)</td>
<td>32 (100%)</td>
<td>32 (100%)</td>
</tr>
<tr>
<td><strong>Nurse Assistant Certificate</strong></td>
<td>202</td>
<td>1 (Thailand)</td>
<td>202 (100%)</td>
<td>202 (100%)</td>
</tr>
<tr>
<td><strong>Sub Total</strong></td>
<td>234</td>
<td></td>
<td>234 (100%)</td>
<td>234 (100%)</td>
</tr>
<tr>
<td><strong>Grand Total</strong></td>
<td>470</td>
<td>23</td>
<td>452 (96.17%)</td>
<td>292 (62.12%)</td>
</tr>
</tbody>
</table>

1.3 Training Course/Workshop/Meeting. Nine international short training courses with 66 participants from 27 countries and 1 international meeting (Joint International Tropical Medicine Meeting 2004) were convened during FY 2004, with a total of 643 participants from 25 countries.
KRA 2  INCREASED ACCESS TO MARKET
2.1  Active Marketing. Thirty TV series were broadcast, 9 news items published in local newspapers, journals and magazines, 10 radio announcements. 5,000 copies of 6 tropical diseases/related fields information leaflets were produced and distributed to the public. 1,250 copies of centre’s internal journal were produced, and 92 news items announced on the Mahidol University website.

KRA 3  INCREASED LINKAGES
3.1  WHO Collaborating Centre: World Health Organization has designated the Faculty of Tropical Medicine a WHO Collaborating Centre for Environment of Disease Vector Control in Sustainable Development.
3.2  Visitors: Fifty-three visitors from 13 countries visited TROPMED/Thailand during FY 2004/2005, consisting of lecturers, assistant lecturers, academic staff, clinicians/medical doctors, medical students, public health personnel, scientists and researchers.

KRA 4  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 2: Sources of revenue

<table>
<thead>
<tr>
<th>Sources</th>
<th>Amount In million Baht</th>
<th>Percentage Increase/Decrease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Government budget</td>
<td>125.46</td>
<td>+ 2.56%</td>
</tr>
<tr>
<td>Revenue from services and other activities</td>
<td>94.20</td>
<td>N/A</td>
</tr>
<tr>
<td>Research funds from other organizations</td>
<td>167.21</td>
<td>- 0.62%</td>
</tr>
</tbody>
</table>

KRA 5  ENHANCED QUALITY OF SEAMEO MANAGEMENT
TROPMED/Thailand has a total of 788 staff comprising 101 academic staff, 179 academic assistants and research staff, 378 administrative personnel and employees, 130 university employees. The qualifications and academic posts by these 101 academic staff in the year under review are shown in Table 3.

Table 3: Qualifications of 244 academic and academic assistant staff

<table>
<thead>
<tr>
<th>Qualification</th>
<th>No</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PhD</td>
<td>65</td>
<td>64.35 %</td>
</tr>
<tr>
<td>Master</td>
<td>25</td>
<td>24.72 %</td>
</tr>
<tr>
<td>Bachelor</td>
<td>11</td>
<td>10.89 %</td>
</tr>
<tr>
<td>Total</td>
<td>101</td>
<td>100 %</td>
</tr>
</tbody>
</table>
The academic posts of 101 academic staff compared to those of Mahidol University are shown in Table 4.

Table 4: Academic posts of 101 staff of TROPMED/Thailand

<table>
<thead>
<tr>
<th>Academic Posts</th>
<th>Academic Posts Holding by FTM Staff No. (%)</th>
<th>Academic Posts Holding by Mahidol Staff No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Professors</td>
<td>5 (05.15%)</td>
<td>124 (04.46%)</td>
</tr>
<tr>
<td>Associate Professors</td>
<td>33 (34.02%)</td>
<td>780 (28.08%)</td>
</tr>
<tr>
<td>Assistant Professors</td>
<td>30 (29.70%)</td>
<td>821 (29.56%)</td>
</tr>
<tr>
<td>Lecturers</td>
<td>31 (30.69%)</td>
<td>1,052 (37.88%)</td>
</tr>
<tr>
<td>Total</td>
<td>101 (100.00%)</td>
<td>2,777 (100.00%)</td>
</tr>
</tbody>
</table>

5.1 Number of staff promoted or obtaining higher qualifications

Table 5: Number of staff promoted

- Academic rank:
  - Professors = 2
  - Associate Professors = 2
  - Assistant Professors = 3
  - Lecturers = 2
- Career rank:
  - Higher rank = 51
- Higher qualification:
  - Higher degree = 9
- Total = 69

5.2 Number of research projects and publication. TROPMED/Thailand staff undertook 118 research projects with total research grants of 167.21 million Baht and published 117 research papers.

Table 6: Number of research projects and publications

<table>
<thead>
<tr>
<th>New Project</th>
<th>On-going</th>
<th>Accomplished</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of research projects</td>
<td>17 (14.40%)</td>
<td>68 (57.62%)</td>
</tr>
<tr>
<td>Number of published papers</td>
<td>117</td>
<td></td>
</tr>
</tbody>
</table>

5.3 Number of staff taking study leave, attending training courses, and attending meetings/seminars/workshops.
Eleven staff (1.39%) took study leave for higher education. Seven hundred and twenty-five staff (92.00%) attended training, meetings, seminars, and workshops within country and abroad. One staff may attend more than one training/meeting/seminar/workshop.

Table 7: Staff development through higher study, training courses, seminars/workshops.

<table>
<thead>
<tr>
<th>Category of staff development</th>
<th>In country</th>
<th>Abroad</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study leave</td>
<td>6 (0.87%)</td>
<td>0 (0.0%)</td>
<td>6 (0.82%)</td>
</tr>
<tr>
<td>Attending training courses</td>
<td>682 (99.12%)</td>
<td>43 (100%)</td>
<td>725 (99.17%)</td>
</tr>
<tr>
<td>seminars, meetings</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>workshops</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of staff</td>
<td>688 (100%)</td>
<td>43 (100%)</td>
<td>731 (100%)</td>
</tr>
</tbody>
</table>

5.4 Special talks / lectures
To develop and/or improve knowledge of staff, 17 lunch talks/lectures on various topics for 780 attendees were organized, 22 CME lectures (Continuing Medical Education) including 8 information technology training courses were organized for 406 attendees. 54 academic staff were invited to give lectures within country on various topics.

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 31 medical doctors, 83 nurses, and 81 nurse assistants. The total number of outpatients treated was 28,432, and 1,502 patients were admitted to the Hospital. Routine and special laboratory services for diagnosis of tropical infections were also provided.

5.6 Improved infrastructure
1. Rajanagarindra Tropical Diseases International Centre (RTIC) is a centre for conducting field research on tropical diseases, and is located in Suan Phung district, Ratchaburi Province.
2. The Tropical Diseases Research Centre Kanchanaburi is one of the Faculty’s centres for conducting tropical disease research and is a field training center for students, located at the Kanchanaburi campus of Mahidol University.
3. Sixty computers were installed in the Computer Center for training and courses and administrative activities.
4. During FY 2004/2005, renovations of the Faculty were conducted, including the administrative building, the Hospital for Tropical Diseases, and the Bangkok School of Tropical Medicine, and some departments.
5. Since the International Guest House with 66 rooms was opened, 435 students/guests/visitors from 29 countries were served in FY 2004/2005.
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"

---

**Organization Chart**

- **OFFICE OF THE DEAN**
  - Administration Unit & General Affairs
  - Education Affairs Unit
  - Financial and Procurement Unit
  - Research and Academic Affairs Unit
  - Policy and Planning Unit
  - Personnel Unit
  - Education Technology Unit
  - Information Technology Unit
  - International Relations Unit
  - Building and Maintenance Unit
  - Vaccine Trial Centre and Data Management Unit
  - Central Equipment Unit
  - The Wellcome-Mahidol-Oxford Tropical Medicine Research Unit
  - Laboratory Animal Unit
# Training Programs

## Training Courses/Workshops, Faculty of Tropical Medicine, Mahidol University

**FY 2005**

<table>
<thead>
<tr>
<th>No.</th>
<th>Courses/Workshops</th>
<th>Duration</th>
<th>Number of Participants</th>
<th>Countries Participated</th>
<th>Organized by</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Training in Vector-borne Diseases Control and Pest Control Operation Who</td>
<td>4-14 Jan 2005</td>
<td>2</td>
<td>PR China</td>
<td>The Faculty</td>
</tr>
<tr>
<td>2.</td>
<td>Special Training on Tropical Diseases Management of HIV/AIDS</td>
<td>10 Jan-4 Feb 2005</td>
<td>2</td>
<td>Japan</td>
<td>The Faculty</td>
</tr>
<tr>
<td>4.</td>
<td>Application of GIS in Disease Surveillance with Special Reference to Spatial Analysis</td>
<td>18-25 April 2005</td>
<td>27</td>
<td>Cambodia, Lao PDR, Myanmar, PR China, Thai, Vietnam, Cambodia</td>
<td>Department of Tropical Hygiene</td>
</tr>
<tr>
<td>6.</td>
<td>Laboratory Diagnosis of Malaria I</td>
<td>22-23 August 2005</td>
<td>60</td>
<td>Thailand</td>
<td>Department of Protozoology</td>
</tr>
<tr>
<td>7.</td>
<td>Laboratory Diagnosis of Malaria II</td>
<td>25-26 August 2005</td>
<td>59</td>
<td>Thailand</td>
<td>Department of Protozoology</td>
</tr>
<tr>
<td>8.</td>
<td>Participants of Master of Primary Health Care Management Degree Program</td>
<td>26-27 August 2005</td>
<td>21</td>
<td>Bangladesh, Cambodia, China, Indonesia, Lao PDR, Nepal, Philippines, Sri Lanka, Thai, Vietnam</td>
<td>Department of Tropical Hygiene</td>
</tr>
<tr>
<td>9.</td>
<td>Refresher Course in Good Clinical Practice</td>
<td>4-5 September 2005</td>
<td>60</td>
<td>Thailand</td>
<td>Department of Tropical Pediatrics</td>
</tr>
<tr>
<td>10.</td>
<td>The International Training Course on Management of Malaria 2005</td>
<td>26-30 September 2005</td>
<td>19</td>
<td>Australia, Oman, Bhutan, Myanmar, Indonesia, Philippines, Solomon Islands, Japan</td>
<td>The Faculty</td>
</tr>
<tr>
<td>12.</td>
<td>Assessment and Research Methodology in Nutrition</td>
<td>25-27 October 2005</td>
<td>40</td>
<td>Thailand</td>
<td>Department of Tropical Nutrition &amp; Food Science</td>
</tr>
<tr>
<td>13.</td>
<td>Training Course on Molecular and Radioisotope-based Techniques Applied to Malaria Epidemiology</td>
<td>3 October-30 December 2005</td>
<td>1</td>
<td>Myanmar</td>
<td>The Faculty</td>
</tr>
</tbody>
</table>
## MOUS/Agreements

### between Faculty of Tropical Medicine and Oversea Institute

**FY 2005**

<table>
<thead>
<tr>
<th>No.</th>
<th>Institute</th>
<th>Duration</th>
<th>Start</th>
<th>Finish</th>
<th>Remarks</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>Chiangrai Regional Hospital, MoPH</td>
<td>5 yrs</td>
<td>15 June 2004</td>
<td>14 June 2009</td>
<td>MOU</td>
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<tr>
<td>2</td>
<td>Department of Medical Sciences, MoPH</td>
<td>5 yrs</td>
<td>28 May 2004</td>
<td>27 May 2009</td>
<td>MOU</td>
</tr>
<tr>
<td>3</td>
<td>Canadian Food Inspection Agency, Government of Canada, Saskatoon, Canada</td>
<td>5 yrs</td>
<td>3 Sep. 1998</td>
<td>Not specified</td>
<td>MOU</td>
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<tr>
<td>4</td>
<td>University of Leicester, United Kingdom</td>
<td>1 Apr 2002</td>
<td>present</td>
<td>MOU</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Freie Universitat at Berlin</td>
<td>30 May 1985</td>
<td>present</td>
<td>Agreement</td>
<td></td>
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<tr>
<td>6</td>
<td>The Swiss Tropical Institute, Basel, Switzerland</td>
<td>3 Jun 1998</td>
<td>present</td>
<td>MOU</td>
<td></td>
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<tr>
<td>7</td>
<td>University of Innsbruck, Austria</td>
<td>12 May 1992</td>
<td>present</td>
<td>Agreement</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Nagasaki University, Japan</td>
<td>5 yrs</td>
<td>1 Nov. 1999</td>
<td>Automatically extended every 5 yrs</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>University of Shizuoka School of Pharmaceutical Science</td>
<td>5 yrs</td>
<td>2005</td>
<td>3000</td>
<td>MOU</td>
</tr>
<tr>
<td>10</td>
<td>Department of Medical Sciences, MoPH</td>
<td>5 yrs</td>
<td>28 May 2004</td>
<td>2009</td>
<td>MOU</td>
</tr>
<tr>
<td>11</td>
<td>The Wellcome Trust-Mahidol University, Oxford Tropical Medicine Research Programme</td>
<td>5 yrs</td>
<td>Sep. 2004</td>
<td>Sep. 2010</td>
<td>MOU</td>
</tr>
<tr>
<td>12</td>
<td>Japan International Corporation of Welfare Services</td>
<td>1 month</td>
<td>Feb 2005</td>
<td>March 2005</td>
<td>MOU</td>
</tr>
<tr>
<td>13</td>
<td>Southeast Asian Ministers of Education Organization (SEAMEO) and the Government of Thailand</td>
<td>18 May 1971</td>
<td>MOU</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### INTERNATIONAL Linkages

1. Department of Immunology, University of Stockholm, Sweden  
(Prof. Dr. Martia Troye-Blomberg)

2. Department of Pharmacology and Therapeutics, Liverpool School of Tropical Medicine, United Kingdom  
(Dr. Alister Craig)

3. Department of Respiratory Diseases, Research Institute International Medical Center of Japan, Tokyo, Japan  
(Prof. Dr. Naoto Keicho)

4. University of Shizuoka School of Pharmaceutical Sciences, Japan  
(Prof. Dr. Yasuo Suzuki)

5. Institute of Tropical Medicine, Nagasaki University, Japan  
(Prof. Dr. Kouichi Morita)
### INTERNATIONAL Linkages (Continued)

<table>
<thead>
<tr>
<th>No.</th>
<th>Institution</th>
<th>Country</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.</td>
<td>Department of Human Genetics School of International Health Graduate School of Medicine, The University of Tokyo, Japan</td>
<td>Japan</td>
</tr>
<tr>
<td></td>
<td>(Prof. Dr. Katsushi Tokunaga and Dr. Jan Ohashi)</td>
<td></td>
</tr>
<tr>
<td>7.</td>
<td>Institute Pasteur Unit of Molecular Immunology Parasites, France</td>
<td>France</td>
</tr>
<tr>
<td></td>
<td>(Prof. Dr. Odile Pujilan and Dr. Peter H. Pavid)</td>
<td></td>
</tr>
<tr>
<td>8.</td>
<td>The University of Texas Health Science Center at Houston, U.S.A.</td>
<td>USA</td>
</tr>
<tr>
<td></td>
<td>(Prof. Dr. Herbert Dupont)</td>
<td></td>
</tr>
<tr>
<td>9.</td>
<td>Department of Microbiology Faculty of Medicine, Nursing and Health Sciences, Monash University, Australia</td>
<td>Australia</td>
</tr>
<tr>
<td></td>
<td>(Prof. Dr. Ben Adler)</td>
<td></td>
</tr>
<tr>
<td>10.</td>
<td>Oita University, Japan</td>
<td>Japan</td>
</tr>
<tr>
<td>11.</td>
<td>Liverpool School of Tropical Medicine, United Kingdom</td>
<td>United Kingdom</td>
</tr>
<tr>
<td>12.</td>
<td>Department of Parasitology, School of Veterinary Science, Murdoch University of South Street, Murdoch, Western Australia</td>
<td>Australia</td>
</tr>
<tr>
<td>13.</td>
<td>Nuffield Department of Pathology, University of Oxford, John Radcliffe Hospital, UK</td>
<td>United Kingdom</td>
</tr>
<tr>
<td>14.</td>
<td>Department of Parasitology and Tropical Hygiene, Heidelberg University, Germany</td>
<td>Germany</td>
</tr>
<tr>
<td>15.</td>
<td>Division of Electron Microscopy, Department of Cellular Pathology, The John Radcliffe Hospital, Oxford University, United Kingdom</td>
<td>United Kingdom</td>
</tr>
<tr>
<td>16.</td>
<td>Department of Medical Zoology, Kagawa Medical University, Japan</td>
<td>Japan</td>
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<tr>
<td>17.</td>
<td>Department of Immunology, The Wenner Gren Institute, Stockholm University, Sweden</td>
<td>Sweden</td>
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<td>18.</td>
<td>Radiation Safety Research Center, Redox Regulation Research Group, National Institute of Radiological Sciences (NIRS), Japan</td>
<td>Japan</td>
</tr>
<tr>
<td>19.</td>
<td>Department of Surgery, University of Heidelberg Medical School, Heidelberg, Germany</td>
<td>Germany</td>
</tr>
<tr>
<td>20.</td>
<td>Department of Cell Biology and Anatomy, College Medicine, University of Arizona Health Sciences Center, Tucson, Arizona, USA</td>
<td>USA</td>
</tr>
<tr>
<td>21.</td>
<td>Department of Anatomy Division I, Tokyo Medical and Dental University School of Medicine, Tokyo, Japan</td>
<td>Japan</td>
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<tr>
<td>22.</td>
<td>Department of Surgery, Nippon Medical College, Tokyo, Japan</td>
<td>Japan</td>
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</tbody>
</table>

### VISITORS 2005

<table>
<thead>
<tr>
<th>No.</th>
<th>Name</th>
<th>Country</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Dr. Hoang Trong Si</td>
<td>Vietnam</td>
</tr>
<tr>
<td>2.</td>
<td>Dr. Phan Than Hung</td>
<td>Vietnam</td>
</tr>
<tr>
<td>3.</td>
<td>Dr. Le Xuan Truong</td>
<td>Vietnam</td>
</tr>
<tr>
<td>4.</td>
<td>Dr. Nguyen Van Tam</td>
<td>Vietnam</td>
</tr>
<tr>
<td>5.</td>
<td>Dr. Tran Duc Quy</td>
<td>Vietnam</td>
</tr>
<tr>
<td>6.</td>
<td>Dr. Duong Thi Huong</td>
<td>Vietnam</td>
</tr>
<tr>
<td>7.</td>
<td>Dr. Pham Van Lai</td>
<td>Vietnam</td>
</tr>
<tr>
<td>8.</td>
<td>Dr. Le Thi Tuyet</td>
<td>Vietnam</td>
</tr>
<tr>
<td>9.</td>
<td>Dr. Pham Thien Dieu</td>
<td>Vietnam</td>
</tr>
<tr>
<td>10.</td>
<td>Dr. Nguyen Kim Nghia</td>
<td>Vietnam</td>
</tr>
<tr>
<td>11.</td>
<td>Dr. Tran Minh Thinh</td>
<td>Vietnam</td>
</tr>
<tr>
<td>12.</td>
<td>Dr. Nguyen Duy Luat</td>
<td>Vietnam</td>
</tr>
<tr>
<td>13.</td>
<td>Dr. Nguyen Thi Van Hong</td>
<td>Vietnam</td>
</tr>
<tr>
<td>14.</td>
<td>Prof. Nguyen Tran Thi Giang Huong</td>
<td>Vietnam</td>
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<td>15.</td>
<td>Prof. Ha Van Quyet</td>
<td>Vietnam</td>
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<td>16.</td>
<td>Ms. Le Thi Yen</td>
<td>Vietnam</td>
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<td>17.</td>
<td>Dr. Chu Van Loan</td>
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<td>18.</td>
<td>Dr. Nguyen Van Thai</td>
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<td>19.</td>
<td>Prof. Pham Van Than</td>
<td>Vietnam</td>
</tr>
<tr>
<td>20.</td>
<td>Ms. Cao Thi Hue Chi</td>
<td>Vietnam</td>
</tr>
</tbody>
</table>
### Elective Program in Tropical Medicine, FY 2005

#### 10 January – 4 February 2005
- Resident in Internal Medicine, U.S.A.  
  *Dr. Stephen Sethi*
- Lund University, Sweden  
  *Dr. Par Andersson*
- University of Toronto, Canada  
  *Dr. Alireza Zahirieh*

#### 4 – 29 April 2005
- Albert Einstein Medical, U.S.A.  
  *Dr. Margot Goodkin*
- St. George’s Hospital Medical School, UK  
  *Ms. Christina Bull*
  *Ms. Malathi Gunaratne*
  *Mr. Prithish Morar*
  *Mr. Nikunj Vadgama*
- Nagoya City University Medical School, Japan  
  *Mr. Keitaro Fukui*
  *Ms. Mayuka Oe*

#### 20 June – 22 July 2005
- Jikei University School of Medicine, Japan  
  *Mr. Hikaru Kobayashi*

---

### VISITORS 2005 (Continued)

<table>
<thead>
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<th>Name</th>
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<tr>
<td>21. Prof. Tohru Shimizu</td>
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<td>22. Dr. Katherine Bond</td>
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<td>23. H.E. Prof. Dr. Nguyen Minh Hien</td>
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<td>24. H.E. Mr. Khamhounge Huyangvongsy</td>
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<td>25. H.E. Dr. Carolyn Bennett</td>
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<td>26. Ms. Yasmin Ratansi</td>
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<td>27. Ms. Tricia Geddes</td>
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<td>28. Mr. David Yasui</td>
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<td>29. Ms. Chi Nguyen</td>
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<td>30. Ms. Alisa Udomweerakasem</td>
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<td>31. Ms. Cui Yili</td>
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<td>32. Mr. Shang Li</td>
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<td>33. Mr. Chu Lixi</td>
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<td>34. Ms. Guo Jinglei</td>
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<td>35. Dr. Md. Ridwanur Rahman</td>
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<tr>
<td>36. Dr. P.L.Joshi</td>
<td>India</td>
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<td>37. Dr. Sanjib Mohanty</td>
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<tr>
<td>38. Dr. Alan Roland Tumbelaka</td>
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<td>39. Dr. Bangkit Hutajulu</td>
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<td>40. Dr. Phyu Aye Aye</td>
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<td>41. Dr. Win Ni Aung</td>
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<td>42. Dr. Ronnatri Ruengveerayuth</td>
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<tr>
<td>43. Ms. Marion Mathibedi</td>
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<td>44. Ms. Thandi Sylvia Chaane</td>
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<td>45. Ms. Maphosa Ruth Gontsana</td>
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<td>46. Ms. Marie Oniwa</td>
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<td>47. Ms. Kaori Mizumoto</td>
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<td>48. Mr. Girindre Beeharry</td>
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<td>49. Mr. Dame Bridget Ogilvie</td>
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<td>51. Mr. Peter Potter-Lesage</td>
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<td>52. Mr. J carl Craft</td>
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<td>53. Prof. Robert W. Snow</td>
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<td>54. Dr. Mohammed bin Ali Al Shafae</td>
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<td>55. Dr. Satie Muqattash</td>
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<td>56. Dr. Shahina Daar</td>
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<td>57. Prof. Francesco Castelli</td>
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<td>58. Prof. Carlo Collivignarelli</td>
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<td>60. A. Lee Willingham</td>
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<td>62. Dr. Ms. Zheng Bin</td>
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<td>63. Prof. Glenn Morris</td>
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<tr>
<td>64. Dr. Azmi Mohd Tamil</td>
<td>Malaysia</td>
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SUMMARY OF DEPARTMENTAL RESEARCH PROJECTS, PUBLICATIONS, AND PRESENTATIONS

[Bar chart showing new projects, ongoing projects, publications, and presentations for different departments such as Clinical Tropical Medicine, Helminthology, Medical Entomology, Microbiology, and Immunology, Social and Environmental Medicine, Protozoology, Tropical Pediatrics, Tropical Pathology, Tropical Radiology, Office of the Dean, Vaccine Trial Centre, and Welcome Unit.]

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Annual Review 2006
# Ongoing Research Projects of the Faculty of Tropical Medicine in Fiscal Year 2005

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<th>No.</th>
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<th>Principal Investigator</th>
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<tr>
<td></td>
<td><strong>Department of Clinical Tropical Medicine</strong></td>
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<tr>
<td>1</td>
<td>A multicenter, randomized, double-blind, phase II study to evaluate the safety,</td>
<td>Schering Plough Research Institute</td>
<td>Prof. Punnee Pitisuttithum</td>
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<td></td>
<td>tolerance and efficacy of multiple doses of SCH 56592 versus fluconazole in the</td>
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<td>treatment of oropharyngeal candidiasis (OPC) in HIV-positive patients</td>
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<td>2</td>
<td>Open-label, treatment protocol for the safety and efficacy of SCH 56592 (Oral</td>
<td>Schering Plough Research Institute</td>
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<td>Suspension) in the treatment of invasive fungal infections</td>
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<td>3</td>
<td>Observational probe study of in vitro immune response parameters to candidate</td>
<td>MERCK and Co., Inc</td>
<td>Prof. Punnee Pitisuttithum</td>
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<td></td>
<td>HIV-1 vaccine antigens among subject from Thailand</td>
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<td>*4</td>
<td>Safety, immunogenicity, and efficacy of quadrivalent HPV (Types 6, 11, 16, 18)</td>
<td>MERCK and Co., Inc</td>
<td>Prof. Punnee Pitisuttithum</td>
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<td>L1 Virus-Like Particle (VLP) vaccine in mid-adult women. The FUTURE III Study</td>
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<td>*5</td>
<td>A Phase III Trial of Aventis Pasteur Live Recombinant ALVAC-HIV (vCP1521)</td>
<td>The Henry M. Jackson Foundation for The Advancement of Military Medicine, Inc. and The Government of Thailand</td>
<td>Prof. Punnee Pitisuttithum</td>
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<td></td>
<td>priming with VaxGen gp120 B/E (AIDSVAX B/E) Boosting in HIV-uninfected Thai</td>
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<td>adults (Clinic)</td>
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<td>6</td>
<td>Research and development for Thai people living at Thai-Myanmar border to free</td>
<td>Government Budget</td>
<td>Prof. Sornchai Looareesuwan</td>
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<td></td>
<td>from tropical diseases</td>
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<td>7</td>
<td>Research and development on drugs and diagnostic tools for diagnosis and</td>
<td>Government Budget</td>
<td>Prof. Sornchai Looareesuwan</td>
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<td></td>
<td>treatment of tropical diseases in Thailand</td>
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<tr>
<td>8</td>
<td>Liver megaproject Phase I: from basic research to education science and applied</td>
<td>National Science and Technology Development</td>
<td>Dr. Wichai Ekatakpin</td>
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<td></td>
<td>technology in clinical study</td>
<td>Agency</td>
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<td>*9</td>
<td>Hospital based case-central study of leptospirosis</td>
<td>Government Budget</td>
<td>Assoc. Prof. Yupaporn Wattanagoon</td>
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<tr>
<td>10</td>
<td>Genotyping of <em>Plasmodium vivax</em>, development of field methods</td>
<td>Wellcome Trust of Great Britain</td>
<td>Assist. Prof. Mallika Imwong</td>
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<tr>
<td>11</td>
<td>Antimalarial drug susceptibility of <em>P. vivax</em> in Thailand</td>
<td>MMV</td>
<td>Assist. Prof. Kesinee Chotivanich</td>
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<td>12</td>
<td>Antimalarial drugs susceptibility of <em>P. vivax</em> in Korea and China</td>
<td>WHO</td>
<td>Assist. Prof. Kesinee Chotivanich</td>
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<tr>
<td>13</td>
<td>Cell-derived microparticles in malaria infection</td>
<td>Wellcome Trust of Great Britain</td>
<td>Assist. Prof. Kesinee Chotivanich</td>
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<tr>
<td>14</td>
<td>Development of field methods and investigators of the molecular basis of</td>
<td>Wellcome Trust of Great Britain</td>
<td>Assist. Prof. Mallika Imwong</td>
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<td></td>
<td>sulfonamide resistance in <em>Plasmodium vivax</em></td>
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<td>15</td>
<td>Novel point mutations in the dihydrofolate reductase gene of *Plasmodium</td>
<td>Wellcome Trust of Great Britain</td>
<td>Assist. Prof. Mallika Imwong</td>
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<td></td>
<td>vivax: evidence for sequential selection by drug pressure</td>
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* New project
### Ongoing Research Projects of the Faculty of Tropical Medicine in FY 2005

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<th>No.</th>
<th>Research Title</th>
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<tr>
<td></td>
<td><strong>Department of Helminthology</strong></td>
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<tr>
<td>16</td>
<td>Monoclonal antibody-based competitive ELISA and indirect ELISA for immunodiagnosis of trichinosis</td>
<td>Mahidol University</td>
<td>Mrs. Supaporn Nuamtanong</td>
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<tr>
<td>17</td>
<td>Angiostrongylus cantonensis: S-Adenosylmethionine decarboxylase</td>
<td>Government Budget</td>
<td>Mrs. Supaporn</td>
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<tr>
<td>18</td>
<td>Comparison of biochemical extract preparations of Cysticercus cellulosae by SDS – polyacrylamide gel electrophoresis and immunoblot technique</td>
<td>Mahidol University</td>
<td>Paron Dekumyoy</td>
</tr>
<tr>
<td>19</td>
<td>Experimental infection of freshwater fish in Thailand with the infective stage of Angiostrongylus cantonensis</td>
<td>Mahidol University</td>
<td>Assist. Prof. Chaith Komalamisra</td>
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<tr>
<td>20</td>
<td>Toxocara canis larval antigens for serodiagnosis of human toxocariasis</td>
<td>Mahidol University</td>
<td>Assoc. Prof. Wanna Maipanich</td>
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<tr>
<td>21</td>
<td>Helminthic infection in a tsunami-affected area: soil contamination and infection rates in the population</td>
<td>Brescia University, Italy</td>
<td>Assoc. Prof. Wanza Maipanich</td>
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<tr>
<td>22</td>
<td>Studies on the efficacy of Thai traditional herbal medicines in the treatment of opisthorchiasis in hamsters</td>
<td>Mahidol University</td>
<td>Assist. Prof. Panayaw Hiranyachattada</td>
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<tr>
<td>23</td>
<td>Research and development of the integrated project on chemotherapy and control of malaria and parasitic infections</td>
<td>Government Budget</td>
<td>Assoc. Prof. Jitra Waikagul</td>
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<td>24</td>
<td>Research and development of an application to purify Bithynia snail antigen in serodiagnosis of opisthorchiasis</td>
<td>Government Budget</td>
<td>Assoc. Prof. Jitra Waikagul</td>
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<td>25</td>
<td>Study on Paragonimus population: morphology, molecular biology, enzymology and epidemiology aspects</td>
<td>Ministry of Foreign Affairs</td>
<td>Assoc. Prof. Jitra Waikagul</td>
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<td>26</td>
<td>Control of soil-transmitted helminth through primary health care activities</td>
<td>Tropical Disease Trust</td>
<td>Assoc. Prof. Jitra Waikagul</td>
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<td>27</td>
<td>Molecular phylogenetics and biodiversity studies of Paragonimus spp. in Thailand using molecular biological approaches</td>
<td>Faculty of Tropical Medicine</td>
<td>Ms. Urusa Thaenkham</td>
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<td></td>
<td><strong>Department of Medical Entomology</strong></td>
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<td>28</td>
<td>Specificity of the synthetic primers from sequencing DNA fragments of Anopheles minimus</td>
<td>Faculty of Tropical Medicine</td>
<td>Assoc. Prof. Narumon Komalamisra</td>
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<td>29</td>
<td>Mosquito repellent from medicinal plants</td>
<td>Mahidol University</td>
<td>Assoc. Prof. Narumon Komalamisra</td>
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<td>30</td>
<td>Effect of heavy metals (Pb²⁺, Cd²⁺) on enzymes of Culex quinquefasciatus larvae</td>
<td>Mahidol University</td>
<td>Mrs. Raweewan Srisawat</td>
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<td>31</td>
<td>Study on fauna of medically important vectors at Kanchanaburi Campus Sai Yok District, Kanchanaburi Province</td>
<td>Mahidol University</td>
<td>Assoc. Prof. Somjai Leemingsawat</td>
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<td>32</td>
<td>DNA bank of mosquito vectors of Thailand</td>
<td>Government Budget</td>
<td>Assoc. Prof. Chamnarn Apiwathnasorn</td>
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<tr>
<td>*33</td>
<td>Efficacy of water dispersible granule formulation of Bacillus thuringiensis israelensis (VECTOBAC® WDG) and Bacillus sphaericus (VECTOLEX®WDG) to control Culex sitiens in brackish water ponds in Tsunami-affected areas of Phang-Nga Province, Southern Thailand</td>
<td>Brescia University, Italy</td>
<td>Dr. Yuwadee Trongtokit</td>
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<tr>
<td>*34</td>
<td>Field application of Bacillus thuringiensis (VECTOBAC® WDG) for the control of mosquito larvae in salt-marsh habitats in Tsunami-affected Areas, in Phang Nga Province, Thailand</td>
<td>Faculty of Tropical Medicine</td>
<td>Dr. Yuwadee Trongtokit</td>
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<tr>
<td>*35</td>
<td>Molecular study of Anopheles sundiacus in the coastal area of Andaman and the Gulf of Thailand</td>
<td>Faculty of Tropical Medicine</td>
<td>Ms. Peangpim Burivong</td>
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* New project
## Ongoing Research Projects of the Faculty of Tropical Medicine FY 2005

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<th>Research Title</th>
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<tr>
<td>36</td>
<td>Analysis of sequence polymorphism of T-cell epitope regions, Th2R and Th3R on Plasmodium falciparum circumsporozoite proteins in Thai isolates</td>
<td>The Thailand Research Fund</td>
<td>Prof. Srisin Khusmith</td>
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<td>37</td>
<td>Cytokine gene polymorphism in severe malaria</td>
<td>The Thailand Research Fund</td>
<td>Prof. Srisin Khusmith</td>
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<td>38</td>
<td>Relationship between cytokine gene polymorphism and severity of falciparum malaria</td>
<td>The Thailand Research Fund</td>
<td>Prof. Srisin Khusmith</td>
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<tr>
<td>39</td>
<td>Polymorphism of PfEMP1 extracellular domain in Thai isolates causes severe malaria uncomplicated P. falciparum malaria</td>
<td>The Thailand Research Fund</td>
<td>Prof. Srisin Khusmith</td>
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<td>40</td>
<td>Chemokine gene polymorphism and their susceptibility to tuberculosis</td>
<td>The Thailand Research Fund and Commission on Higher Education</td>
<td>Prof. Srisin Khusmith</td>
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<td>41</td>
<td>Dengue infection rates in Aedes related to environmental factors</td>
<td>Ministry of Public Health</td>
<td>Assoc. Prof. Wipawee Champangern</td>
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<td>42</td>
<td>Typing of Entamoeba histolytica isolates obtained from Southeast Asian countries</td>
<td>Japanese Health Sciences Foundation (JHSF)</td>
<td>Assoc. Prof. Nitaya Thammapalerd</td>
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<tr>
<td>43</td>
<td>HLA typing of amoebiasis</td>
<td>Japanese Health Sciences Foundation (JHSF)</td>
<td>Assoc. Prof. Nitaya Thammapalerd</td>
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<td>44</td>
<td>Study of the active site between the three-dimensional structure of R-PE-Mab complex</td>
<td>The Thailand Research Fund</td>
<td>Assoc. Prof. Nitaya Thammapalerd</td>
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<td>45</td>
<td>Development of strategies for serovar identification of Leptospira sp. based on specific gene sequences within rfb locus</td>
<td>Thailand-Tropical Diseases Research Programmes</td>
<td>Assist. Prof. Thareerat Kalambaheti</td>
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<td>46</td>
<td>Study of the immunoreactive membrane protein of leptospirosis</td>
<td>Vejodusit Foundation</td>
<td>Assist. Prof. Thareerat Kalambaheti</td>
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<tr>
<td>47</td>
<td>Development of dipstick assay technology using Plasmodium falciparum as model</td>
<td>Mahidol University</td>
<td>Miss Jarinee Panitchakorn</td>
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<td>48</td>
<td>Identification of genus- and species-specific antigens of Aeromonas spp. by Western blotting with mouse polyclonal antibodies</td>
<td>Faculty of Tropical Medicine</td>
<td>Assist. Prof. Yuvadee Mahakunkijcharoen</td>
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<td>49</td>
<td>Determination of the receptor binding specificity of the HSN1 viruses isolated from Thailand</td>
<td>Faculty of Tropical Medicine</td>
<td>Dr. Pornsawan Leaungwutiwong</td>
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<td>50</td>
<td>Comparison of Toxoplasma gondii antibody detection isolation and characterization of DNA helicase from Plasmodium falciparum</td>
<td>Thanad-Molee Choman Foundation</td>
<td>Assist. Prof. Varaporn Suphadtanapongs</td>
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<td>51</td>
<td>Detection of malaria parasites in after-drug treatment patients by using QBC method</td>
<td>Government Budget</td>
<td>Assist. Prof. Varaporn Suphadtanapongs</td>
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<td>52</td>
<td>Isolation and characterization of DNA topoisomerase I from Trichomonas vaginalis</td>
<td>Mahidol University</td>
<td>Assoc. Prof. Porntip Petmitr</td>
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<td>53</td>
<td>Purification and characterization of DNA polymerase B of Plasmodium falciparum and its role in base excision repair</td>
<td>Thailand-Tropical Diseases Research Programme</td>
<td>Assoc. Prof. Porntip Petmitr</td>
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<td>54</td>
<td>Ultrastructure effects on Toxoplasma gondii tachyzoites after pyrimethamine and artemisinin derivative administration in animal model</td>
<td>The Thailand Research Fund (Royal Golden Jubilee)</td>
<td>Assoc. Prof. Yaowalark Sukthana</td>
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<td>55</td>
<td>Dog and cat parasitic zoonoses</td>
<td>Tropical Disease Trust</td>
<td>Assoc. Prof. Yaowalark Sukthana</td>
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* New project
### ONGOING RESEARCH PROJECTS OF THE FACULTY OF TROPICAL MEDICINE FY 2005

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<td>*56</td>
<td>Viability study of <em>Giardia</em> cysts in water used in Thai frozen food industry</td>
<td>DAAD</td>
<td>Assoc. Prof. Yaowalark Sukthana</td>
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<td>*57.</td>
<td>Biological contamination-free Thai frozen food</td>
<td>National Research Council of Thailand</td>
<td>Assoc. Prof. Yaowalark Sukthana</td>
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<td>*58.</td>
<td>Development of differential diagnosis of <em>Entamoeba histolytica</em>, <em>Entamoeba dispar</em> and <em>Entamoeba histolytica</em> based on arbitrarily primed PCR and real time PCR</td>
<td>Government Budget</td>
<td>Assoc. Prof. Porntip Petmitr</td>
</tr>
<tr>
<td>*59.</td>
<td>PCR assays for detection of <em>Toxoplasma gondii</em> in Thai commercial meat products</td>
<td>Mahidol University</td>
<td>Ms. Rachatawan Chiabchalard</td>
</tr>
<tr>
<td>*60.</td>
<td>Detection of protozoal viability contamination of water used in Thai frozen food industry by cell culture PCR technique</td>
<td>Faculty of Tropical Medicine</td>
<td>Ms. Chantira Sutthikornchai</td>
</tr>
<tr>
<td>*61.</td>
<td>The development of differential characterization of <em>Plasmodium falciparum</em> strain based on Random Amplified Polymorphic DNA technique (RAPD)</td>
<td>Faculty of Tropical Medicine</td>
<td>Mr. Ittisak Subunruangruang</td>
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### Department of Social and Environmental Medicine

<table>
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<th>Principal Investigator</th>
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<tr>
<td>62</td>
<td>Intergated studies of human and animal heptospirosis in endemic areas of Nakhon Ratchasima, Thailand</td>
<td>Government Budget</td>
<td>Assoc. Prof. Wijitr Fungladda</td>
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<td>63</td>
<td>Collaborative study to evaluated operational programme of insecticide treated bednets for malaria control in Thailand</td>
<td>WHO</td>
<td>Assoc. Prof. Piyaarut Butraporn</td>
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<tr>
<td>*64</td>
<td>Modifying mosquito population age structure to eliminate dengue transmission</td>
<td>Gates Foundation</td>
<td>Assoc. Prof. Piyaarut Butraporn</td>
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**Local Publications 2006**


12. Current Issues in Dermatology 2005 สำนักการแพทย์ ภาควิชาวิทยาการสุขภาพสัตว์ คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย

**Tropmed’s new books**

1. HIV Vaccine Research and Development in Thailand. 
   Editors: Punnee Pitisutithum, Donald P. Francis, José Esparza, Prasert Thongcharoen

2. International Handbook of Foodborne Pathogens. 
   Editors: Marianne D. Miliptis, Jeffrey W. Bier
   - Opisthorchis viverrini. By Yupaporn Wattanagoon and Swangjai Pungpak
   - Incidence of Foodborne Illness in Southesat Asia. By Punnee Pitisutithum

3. ค้างวิภัยโรคชัน วั่นไวกิจชันรุ่นใหม่
   บรรณาธิการ พรณี ภิณฑ์ธิธรรม และชัยนันต์ พิเชษฐ์สุนทร
HEMATOPOIETIC FEATURES AND APOPTOSIS IN THE BONE MARROW OF SEVERE PLASMODIUM FALCIPARUM-INFECTED PATIENTS: PRELIMINARY STUDY


Department of Medical Science, National Institute of Health, Nonthaburi, Thailand.

The mechanism of anemia in severe falciparum malaria is still not completely understood. The purpose of this study was to determine whether apoptosis in the erythroid lineage causes anemia in falciparum malaria. Bone marrow aspirated from 8 severe falciparum malaria patients, 3 normal volunteers and 5 retrospective normal bone marrow smears were investigated. By light microscopic study, 5 of 8 hyperparasitemic patients had hypocellular bone marrows and erythroid hypoplasia, whereas the other 3 patients had normal cellularity. The mean myeloid:erythroid ratio of these 5 patients was significantly (p < or = 0.05) higher than normal. Apoptosis of bone marrow nucleated cells (BMNC) could be determined from the exposure of phosphatidylserine (PS) on the cell membrane but not DNA fragmentation (180-250 bp) or ultrastructural morphology. The percentages of apoptotic BMNC and apoptotic erythroid cells in bone marrow from each patient and controls varied from low to high, and were not associated with parasitemia. This study suggests that destruction of erythroid lineage, particularly through apoptosis regulation, cannot solely account for anemia in falciparum malaria.


RANDOMIZED, CONTROLLED DOSE-OPTIMIZATION STUDIES OF DIHYDROARTESMININ-PIPERAQUINE FOR THE TREATMENT OF UNCOMPlicated MULTIDRUG-RESISTANT FALCIPARUM MALARIA IN THAILAND

Elizabeth A Ashley,1,2,3 Srivicha Krudosood,1 Lucy Phaiphun,1 Siripan Srivilairit,2 Rose McGeary,1,2,3 Wattana Leowattana,2 Robert Hutagalung,1 Polrat Wilairatana,2 Alan Brockman,1,2,4 Somchais Looareesuwan,2 François Nosten,1,2,3 Nicholas J White2,3

1Shoklo Malaria Research Unit, Mae Sot, and 2Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; 3Centre for Clinical Vaccinology and Tropical Medicine, Churchill Hospital, Oxford, United Kingdom; 4Menzies School of Health Research, Charles Darwin University, Darwin, Australia

BACKGROUND Dihydroartesminin-piperaquine (DP) is a new and relatively inexpensive artemisinin-containing fixed-combination antimalarial treatment. An adult treatment course contained 6.4 mg/kg dihydroartesminin (DHA), which is >40% lower than the level in most artemisinin-containing combinations. This raised the possibility that the efficacy of the current formulation may not be optimal in the treatment of multidrug-resistant falciparum malaria.

Methods In 2 large randomized, controlled studies in Thailand, the recommended dose of DP was compared with a regimen with additional artemisinin derivative (12 mg/kg; DP+) and with mefloquine plus artesunate (MAS3).

Results A total of 731 patients were included: 201 in a hospital-based study and 530 in a community study. Day-28 cure rates in the hospital-based study were 100% (95% confidence interval [CI], 93.9%-100%) in the MAS3 and DP+ groups and 98.3% (95% CI, 91%-99.7%) in the DP group, with a single recrudescence on day 21. In the community study, polymerase chain reaction genotyping-adjusted cure rates on day 63 were 96.1% (95% CI, 92.6%-99.7%) in the DP group, 98.3% (95% CI, 96.1%-100%) in the DP+ group, and 94.9% (95% CI, 91.2%-98.6%) in the MAS3 group (P = 2). Adverse events were few, with an excess of mild abdominal pain in the DP group.

Conclusions The current dosage of DP (6.4 mg/kg DHA and 51.2 mg/kg piperaquine phosphate) given over the course of 48 h is highly effective, safe, and well tolerated for the treatment of multidrug-resistant falciparum malaria, and its efficacy is not improved by the addition of more DHA.

Published in: J Infect Dis 2004;190:1773-82.

TOLERABILITY OF IVERMECTIN IN GNATHOSTOMIASIS

Bussaratid V, Krudosood S, Silachamroon U, Looareesuwan S

Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, 420/6 Rajvithi Road, Bangkok 10400, Thailand.

At present, no universally-accepted effective treatment for cutaneous gnathostomiasis is available. At the Hospital for Tropical Diseases, Mahidol University, albendazole 400 mg twice a day for 14 days is commonly prescribed for patients diagnosed with cutaneous gnathostomiasis. The efficacy of albendazole to induce outward migration of the parasite was less than or around 20% in 2 studies. Research for alternative, more efficacious treatment, is needed. In this prospective open-labeled study, we assessed the safety of ivermectin in 20 Thai patients diagnosed with cutaneous gnathostomiasis. Ivermectin, one time only, at dosages of 50, 100, 150, or 200 microg/kg bodyweight,
The aim of this study was to compare the efficacy and time of 12 to 20 weeks. Drug side effects are common; laboratory abnormalities were found in 3 patients (15%). Transient microscopic hematuria, pyuria, and mildly elevated liver enzymes were found in 1 patient each. Ivermectin single dose, of 50, 100, 150, and 200 microg/kg bodyweight, is considered safe in Thai patients. Future trials of ivermectin on human gnathostomiasis may be performed using dosages up to 200 microg/kg bodyweight.

**OPEN-LABEL RANDOMIZED TRIAL OF ORAL TRIMETHOPRIM-SULFAMETHOXAZOLE, DOXYCYCLINE, AND CHLORAMPHENICOL COMPARED WITH TRIMETHOPRIM-SULFAMETHOXAZOLE AND DOXYCYCLINE FOR MAINTENANCE THERAPY OF MELIOIDOSIS**

Wipada Chaowagul,1 Wirotong Chierakul,2*, Andrew J Simpson,2,4 Jennifer M Short,2,4 Kasia Stepniewska,2,4 Bina Maharjan,2 Adul Rajchanuvong,1 Duangkaew Busarawong,1 Direk Limmathurotsakul,2 Allen C Cheng,2,4 Vanaporn Wuthiekanun,2 Paul N Newton,2,4 Nicholas J White,2,5 Nicholas PJ Day,2,4 Sharon J Peacock,2,4

Medical Department, Sappasithiprasong Hospital, Ubon Ratchathani,1 Faculty of Tropical Medicine, Mahidol University, Bangkok, 2Wellcome Trust-Mahidol University-Oxford Tropical Medicine Research Programme, Faculty of Tropical Medicine, Mahidol University, Bangkok, 3Department of Medicine, Faculty of Medicine, Khon Kaen University, Khon Kaen, and 4Centre for Clinical Vaccinology and Tropical Medicine, Nuffield Department of Clinical Medicine, University of Oxford, Oxford, Oxford, United Kingdom

**MELIOIDOSIS** (infection caused by *Burkholderia pseudomallei*) requires a prolonged course of oral antibiotics following initial intravenous therapy to reduce the risk of relapse after cessation of treatment. The current recommendation is a four-drug regimen (trimethoprim [TMP], sulfamethoxazole [SMX], doxycycline, and chloramphenicol) and a total treatment time of 12 to 20 weeks. Drug side effects are common: the aim of this study was to compare the efficacy and tolerance of the four-drug regimen with a three-drug regimen (TMP-SMX and doxycycline). An open-label, randomized trial was conducted in northeast Thailand. A total of 180 adult Thai patients were enrolled, of which 91 were allocated to the four-drug regimen and 89 to the three-drug regimen. The trial was terminated early due to poor drug tolerance, particularly of the four-drug regimen. The culture-confirmed relapse rates at 1 year were 6.6% and 5.6% for the four- and three-drug regimens, respectively (P = 0.79). The three-drug regimen was better tolerated than the four-drug regimen; 36% of patients receiving four drugs and 19% of patients receiving three drugs required a switch in therapy due to side effects (P = 0.01). The duration of oral therapy was significantly associated with relapse; after adjustment for confounders, patients receiving less than 12 weeks of oral therapy had a 5.7-fold increase of relapse or death. A combination of TMP-SMX and doxycycline is as effective as and better tolerated than the conventional four-drug regimen for the oral treatment phase of melioidosis.

**TWO RANDOMIZED CONTROLLED TRIALS OF CEFTAZIDIME ALONE VERSUS CEFTAZIDIME IN COMBINATION WITH TRIMETHOPRIM-SULFAMETHOXAZOLE FOR THE TREATMENT OF SEVERE MELIOIDOSIS**

Wirongrong Chierakul,1,2,4 Sriuluck Anunnatsiri,1,4 Jennifer M Short,2,5 Bina Maharjan,2 Proon Mootskapun,3 Andrew J Simpson,2,4 Direk Limmathurotsakul,2 Allen C Cheng,2,4 Vanaporn Wuthiekanun,2 Paul N Newton,2,5 Wipada Chaowagul,4 Nicholas J White,2,5 Sharon J Peacock,2,5 Nicholas P Day,2,5 Ploenchit Chotchotisakd

1Department of Clinical Tropical Medicine and 4Wellcome Trust-Mahidol University-Oxford Tropical Medicine Research Programme, Faculty of Tropical Medicine, Mahidol University, Bangkok, 2Department of Medicine, Faculty of Medicine, Khon Kaen University, Khon Kaen, and 5Medical Department, Sappasithiprasong Hospital, Ubon Ratchathani, Thailand; and 2Centre for Clinical Vaccinology and Tropical Medicine, Nuffield Department of Clinical Medicine, University of Oxford, Oxford, Oxford, United Kingdom

**BACKGROUND:** Two antibiotic regimens are used commonly in Thailand for the initial treatment of severe melioidosis: ceftazidime in combination with trimethoprim-sulfamethoxazole (TMP-SMX) and ceftazidime monotherapy. It is not known whether TMP-SMX provides an additional benefit.

**Methods:** Two prospective, randomized trials that compared these regimens for patients presenting with acute severe melioidosis were started independently at tertiary care hospitals in Ubon Ratchathani and Khon Kaen (in northeastern Thailand), and the results were analyzed together as a prospective, individual-patient data meta-analysis. The primary end point was in-hospital mortality rate.

**Results:** The in-hospital mortality rate among all enrolled patients (n = 449) was not significantly
MELIOIDOSIS IN 6 TSUNAMI SURVIVORS IN SOUTHERN THAILAND

Wirongrong Chierakul,1,2,4 Wut Winothai,3,4 Charunkij Wattanawatungrave,4 Vanaporn Wuthiekanun,2 Thaweesak Rugaetgaeng,1 Junairat Rattanalertnavee,3 Pornlert Jitpratoom,2 Wipada Chaowagul,2 Prapat Singhasivanon,2 Nicholas J White,2,5 Nicholas PJ Day,2,5 Sharon J Peacock2,5

1Department of Clinical Tropical Medicine and 2Wellcome Trust-Mahidol University-Oxford Tropical Medicine Research Programme, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; 3Takuapa General Hospital, Ubon Ratchathani, Thailand; Menzies School of Health Research, Charles Darwin University, Darwin, and The Geelong Hospital, Barwon Health, Geelong Australia; Center for Clinical Vaccinology and Tropical Medicine, Nuffield Department of Clinical Medicine, University of Oxford, Oxford, United Kingdom

ABSTRACTS

BACKGROUND: Six cases of melioidosis were identified in survivors of the 26 December 2004 tsunami who were admitted to Takuapa General Hospital in Phangnga, a region in southern Thailand where melioidosis is not endemic. All 6 cases were associated with aspiration, and 4 were also associated with laceration.

Methods: We compared the clinical, laboratory, and radiographic findings and the outcomes for these 6 patients with those for 22 patients with aspiration-related melioidosis acquired during 1987-2003 in a melioidosis-endemic region in northeast Thailand. Results of tests for detection of Burkholderia pseudomallei in soil specimens from Phangnga and from northeast Thailand were compared.

Results: The 6 patients (age range, 25-65 years) presented with signs and symptoms of pneumonia 3-38 days (median duration, 6.5 days) after the tsunami. Chest radiograph findings at the onset of pneumonia were abnormal in all cases; 1 patient developed a lung abscess. B. pseudomallei was grown in blood cultures in 3 cases and in cultures of respiratory secretions in 4 cases. Two patients required ventilation and inotropes; 1 patient died. Compared with tsunami survivors, patients with aspiration-related melioidosis in northeast Thailand had a shorter interval (median duration, 1 day) between aspiration and onset of pneumonia; were more likely to exhibit shock, respiratory failure, renal failure, and/or altered consciousness (P = .03); and had a higher in-hospital mortality (64% [14 of 22 patients]; P = .07). These differences may be related to the severity of the near-drowning episode, the inhalation of sea water versus fresh water, the size of bacterial inoculum, and the possible acquisition (among tsunami survivors) of B. pseudomallei via laceration. Only 3 (0.8%) of 360 soil samples from Phangnga were positive for B. pseudomallei, compared with 26 (20%) of 133 samples from northeast Thailand (P < .0001).

Conclusions: Tsunami survivors are at increased risk of melioidosis if they are injured in an environment containing B. pseudomallei.

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DISEASE SEVERITY AND OUTCOME OF MELIOIDOSIS IN HIV-COINFECTED INDIVIDUALS

Wirongrong Chierakul, Vanaporn Wuthiekanun, Wipada Chaowagul, Permit Amornchai, Allen C Cheng, Nicholas J White, Nicholas PJ Day, Sharon J Peacock

Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; Medical Department, Sappasithiprasong Hospital, Ubon Ratchathani, Thailand; Menzies School of Health Research, Charles Darwin University, Darwin, and The Geelong Hospital, Barwon Health, Geelong Australia; Center for Clinical Vaccinology and Tropical Medicine, Nuffield Department of Clinical Medicine, University of Oxford, Oxford, United Kingdom

T HIS study examined whether coinfection with HIV and Burkholderia pseudomallei leads to altered disease severity or outcome associated with melioidosis. Coinfection was detected in only 8 of 524 (1.5%) adults with melioidosis in northeast Thailand. Clinical presentation and acute outcome were similar in HIV-positive and HIV-negative patients.

HEPATOTOXIC EFFECT OF BARAKOL IN MICE

Watcharaporn Devakul Na Ayutthaya, Pornpen Pramyothin, Pawinee Pyachaturawat, Wichai Ekataksin, Praneet Chavalittumrong, Songphol Chivapat, Chaiyo Chaichantipyuth

Pharmacological Action of Natural Products Research Unit, Department of Pharmacology, Faculty of Pharmaceutical Sciences, Chulalongkorn University, Thailand. Department of Physiology, Faculty of Sciences, Mahidol University, Thailand. Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Thailand. Medicinal Plant Research Institute, Department of Medical Sciences, Ministry of Public Health, Thailand. Department of Pharmacognosy, Faculty of Pharmaceutical Sciences, Chulalongkorn University, Thailand.

A CUTE and subacute hepatotoxicity induced by barakol was investigated in mice. Blood clinical biochemistry parameters (serum AST, ALT, total bilirubin, cholesterol, triglyceride and glucose) and histopathological examination were used as criteria for liver injury. Mice were given barakol in a single dose (100, 200, 300 and 400 mg/kg, p.o.) and repeated doses (100, 200 and 300 mg/kg/day, p.o., 28 days) for acute and subacute toxicity studies, respectively. The acute and subacute hepatotoxic findings included the increase in total bilirubin, AST and ALT levels and the decrease in cholesterol, triglyceride and glucose concentrations which corresponded to the histopathological examination showing the hydropic swelling of hepatocytes, scattered degree of necrotic cells around central vein spreading to periportal zone and finally apoptotic cell death around centrilobular zone spreading to periportal area. The degree of the severity of barakol induced liver injury was dose and time dependent. The mechanism involved may be the induction of necrosis and apoptosis, resulting in the disturbance of normal liver cell function. The ultimate outcome of hepatotoxicity by barakol depended on the balance between the extent of liver cell damage and its repair. There were signs of liver regeneration and recovery in all doses of barakol treatment. Reduction of total cytochrome P450 content with unchanged protein expression of CYP3A1 and 2E1, inhibition of mitochondrial respiration and hemolysis of red blood cells may be involved in barakol induced hepatotoxicity.

ESTIMATION OF THE TOTAL PARASITE BIOMASS IN ACUTE FALCIPARUM MALARIA FROM PLASMA PFHRP2

Arjen M Dondorp1,2, Varunee Desakorn1, Winichada Pontavornpinyo1, Duangjai Sahassananda1, Kamolrat Silamut1, Kesinee Chotivanich1, Paul N Newton2,3, Punnee Pitisuttithum1, AM Smithyman4, Nicholas J White1,2*

1Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand, 2Centre for Clinical Vaccinology and Tropical Medicine, Churchill Hospital, Oxford, United Kingdom, 3Wellcome Trust–Mahosot Hospital, Vientiane, Lao People’s Democratic Republic, 4Cellabs, Brookvale, New South Wales, Australia

Background

Fallopia malariae sequestration of erythrocytes containing mature forms of Plasmodium falciparum in the microvasculature of vital organs is central to pathology, but quantification of this hidden sequestered parasite load in vivo has not previously been possible. The peripheral blood parasite count measures only the circulating, relatively non-pathogenic parasite numbers. P. falciparum releases a specific histidine-rich protein (PFHRP2) into plasma. Quantitative measurement of plasma PFHRP2 concentrations may reflect the total parasite biomass in falciparum malaria.

Methods and Findings

We measured plasma concentrations of PFHRP2, using a quantitative antigen-capture enzyme-linked immunosorbent assay, in 337 adult patients with falciparum malaria of varying severity hospitalised on the Thai–Burmese border. Based on in vitro production rates, we constructed a model to link this measure to the total parasite burden in the patient. The estimated geometric mean parasite burden was 7 × 1011 (95% confidence interval [CI] 5.8 × 1011 to 8.5 × 1011) parasites per body, and was over six times higher in severe malaria (geometric mean 1.7 × 1012, 95% CI 1.3 × 1012 to 2.3 × 1012) than in patients hospitalised without signs of severity (geometric mean 2.8 × 1011, 95% CI 2.3 × 1011 to 3.5 × 1011; p < 0.001). Parasite burden was highest in patients who died (geometric mean 3.4 × 1012, 95% CI 1.9 × 1012 to 6.3 × 1012; p = 0.03). The calculated number of sequestered parasites increased with disease severity and was higher in patients with late developmental stages of P. falciparum present on peripheral blood smears. Comparing model and laboratory estimates of the time of sequestration suggested that admission to hospital with uncomplicated malaria often follows schizogony—but in severe malaria is unrelated to stage of parasite development.

Conclusion

Plasma PFHRP2 concentrations may be used to estimate the total body parasite biomass in acute falciparum malaria. Severe malaria results from extensive sequestration of parasitised erythrocytes.


ATTENUATION OF CYTOADHERENCE OF PLASMODIUM FALCIPARUM TO MICROVASCULAR ENDOTHELIUM UNDER FLOW BY HEMODILUTION

Christine Flatt, Sheona Mitchell, Bryan Yipp, Sornchai Looaeresuwan, May Ho.

Department of Microbiology and Infectious Diseases and Immunology Research Group, University of Calgary, Calgary, Alberta, Canada; Hospital for Tropical Diseases, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

The cytoadherence of Plasmodium falciparum–infected erythrocytes (IRBCs) to endothelium is mediated by adhesion molecules within the physical constraints of a viscous fluid containing mostly erythrocytes. The volume fraction of erythrocytes (hematocrit) and their physical properties, such as deformability, are important properties of blood that affect cell recruitment to the vascular wall. In the present study, we examined the effect of hematocrit on IRBC rolling and adhesion on human microvascular endothelial cells in a flow chamber system in vitro. We found hematocrit to be a major determinant of IRBC/endothelial cell interactions. There was a 5-fold and 12-fold increase in IRBC rolling and adhesion, respectively, when hematocrit increased from 10% to 30%, as a result of changes in shear rate. Similar effects were seen in the presence of less deformable erythrocytes, serum proteins, and on endothelium stimulated with tumor necrosis factor-α. The results indicate that hemorheologic variations are an important determinant of the degree of cytoadherence.


TRENDS IN THE INJECTION OF MIDAZOLAM AND OTHER DRUGS AND NEEDLE SHARING AMONG INJECTION DRUG USERS ENROLLED IN THE AIDSVAX B/E HIV-1 VACCINE TRIAL IN BANGKOK, THAILAND

Frits Van Griensvena,Punnnee Pitisuttithum, Suphak Vanichsenid, Paula Wichienkuera, Jordan W Tappero, Udomsak Sangkumid, Dwip Kitayapom, Boonrawd Phasithiphoe, Karin Orelind e, Kachit Choopanya

Thailand Ministry of Public Health, US Centers for Disease Control and Prevention Collaboration. DDC 7 Building, Nonthaburi 11000, Thailand Centersfor Disease Control and Prevention, Atlanta, GA, USA C Mahidol University, Bangkok. Thailand d Bangkok Vaccine Evaluation Group, Bangkok. Thailand e VaxGen Inc., Brisbane, CA, USA
MIDAZOLAM injection may increase the hazards of drug use. Its ability to cause amnesia may be associated with increased HIV risk behaviour and its interaction with other licit and illicit drugs may cause overdose and death. We analysed midazolam injection among injecting drug users (IDUs) participating in the AIDSVAX BIE HIV-1 vaccine trial in Bangkok, Thailand. From March 1999 to August 2000, 2545 IDUs were enrolled and randomised to receive AIDSVAX BIE or placebo. An interviewer-administered questionnaire assessed demographics (at baseline) and drug use behaviour (every 6 months). Reports of midazolam injection were statistically evaluated. During 36 months of follow-up, injection of any drug decreased from 94 to 51% and needle sharing decreased from 33 to 16%. Among those who continued to inject, midazolam injection increased from 10 to 31% (all p<0.0001). Earlier study visit, lower education and less frequent injection were independently associated with less frequent midazolam injection; younger age, reports of needle sharing and receiving methadone treatment were independently associated with more frequent midazolam injection. Preventive interventions to educate IDUs and midazolam prescribers are urgently needed.

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NO EVIDENCE OF CARDIOTOXICITY OF ATOVAQUONE-PROGUANIL ALONE OR IN COMBINATION WITH ARTESUNATE

Ravindra K Gupta, Michele Van Vuig, Lucy Paiphun, Thra Slight, Sornchai Loaareesuwan, Nicholas J White, Francois Nosten

Department of Infection, St. Thomas’ Hospital, London, United Kingdom; Division of Infectious Diseases, Tropical Medicine and AIDS, Academic Medical Centre, University of Amsterdam, Amsterdam, The Netherlands; Shoklo Malaria Research Unit, Mae Sot, Thailand; Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; Centre for Vaccinology and Tropical Medicine, Nuffield Department of Clinical Medicine, John Radcliffe Hospital, Headington, Oxford, United Kingdom

Combinations are set to become the mainstay in treatment and prophylaxis of malaria due to Plasmodium falciparum. Various antimalarials have been implicated in cardiotoxicity via prolongation of the QTc interval. Atovaquone-proguanil is an effective and increasingly popular antimalarial choice when used alone or with artesunate in areas of drug resistance. We report the results of an investigation carried out on the Thai-Burmese border in 42 patients randomized to receive either atovaquone-proguanil or atovaquone-proguanil-artesunate for three days. Electrocardiographic recordings were made at baseline and one hour after each dose. There was no statistically significant change in QTc interval between baseline and any subsequent readings in either treatment group or the cohort as a whole. We conclude that atovaquone-proguanil shows no evidence of cardiotoxicity either alone or when combined with artesunate.


POLYMORPHISMS OF THE HLA-B AND HLA-DRB1 GENES IN THAI MALARIA PATIENTS

Hathairad Hananantachai, Jintana Patarapotikul, Jun Ohashi*, Izumi Naka*, Sornchai Looareesuwan and Katsushi Tokunaga

Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand and Department of Human Genetics, Graduate School of Medicine, The University of Tokyo, Tokyo 113-0033, Japan

SUMMARY: The high degree of polymorphism of human leukocyte antigen (HLA) genes has been suggested to result from natural selection against susceptibility to a variety of infectious pathogens, including malaria. HLA molecules are considered to play a crucial role in the defense of the host against malarial infection, and different HLA class I and class II alleles have been reported to be associated with reduced susceptibility to malaria or the severity of malaria in different populations. To test for associations between HLA alleles and the severity of malaria in a Thai population, polymorphisms of HLA-B and HLA-DRB1 genes were investigated in 472 adult patients in northwest Thailand with Plasmodium falciparum malaria. In this study, malaria patients were classified into three groups: mild malaria, non-cerebral severe malaria, and cerebral malaria. Our results revealed that the allele frequencies of HLA-B46, –B56, and –DRB1*1001 were statistically different between non-cerebral severe malaria and cerebral malaria (P = 0.005), between mild malaria and cerebral malaria (P = 0.032), and between mild malaria and non-cerebral malaria (P = 0.007). However, our results may be showing false positives due to multiple testing. Thus, further study with a larger sample size must be conducted to obtain conclusive evidence of the association of these HLA-B and DRB1 alleles with the severity of malaria in Thailand.

IN VITRO SUSCEPTIBILITY AND GENETIC VARIATIONS FOR CHLOROQUINE AND MEFLOQUINE IN PLASMODIUM FALCIPARUM ISOLATES FROM THAI – MYANMAR BORDER

Hatabu T, Kawazu S, Kojima S, Sato K, Singhhasivanon P, Looareesuwan S, Kano S

Research Institute, International Medical Center of Japan, Tokyo, Japan.

In vitro drug susceptibility to chloroquine (CQ) and mefloquine (MF) were assessed in 39 P. falciparum isolates from the Thai-Myanmar border area. To further characterize CQ- and MF-resistance profiles in this area, we also analyzed pfcrt K76T mutation that is critical for CQ resistance, and pfmdr1 polymorphism that has an association with MF resistance. Eighteen isolates were successfully examined by in vitro tests for CQ, and 17 of them had resistance to the drug. Geometric mean concentration of CQ that inhibited the growth of parasites at 50% (IC50) was 371 +/- 227 nM (105-971 nM). Sixteen isolates were successfully examined by in vitro tests for MF, and 8 of them were resistant to the drug. Geometric mean of IC50 for MF was 41 +/- 31 nM (4-125 nM). Genotypes of drug resistance, such as pfcr t and pfmdr1 mutations, were also analyzed. All the 39 isolates had the same haplotype (CVIET) for PfCRT at its 72-76th amino acids. A pfmdr1 Y86 mutation was found in 95% of isolates. A pfmdr1 D1042 mutation was also present in 7 isolates, while no pfmdr1 Y1246 mutation was observed. These results indicated a correlation between CQ resistance and the pfcr t T76 and pfmdr1 Y86 mutations.


CURDLAN SULPHATE IN HUMAN SEVERE/ CEREBRAL PLASMODIUM FALCIPARUM MALARIA

I Havlik1, S Looareesuwan2, S Vannaphan, P Wilairatana3, S Krudsood4, PE Thuma1, D Kozbor4, N Watanabe5

Y Kaneko6,7

1Department of Pharmacy and Pharmacology, University of the Witwatersrand, 7 York Road, Parktown, 2193, South Africa; 2Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, 4206 Rajavithi Road, Bangkok, 10400, Thailand; 3Macha Malaria Research Institute, Choma, Zambia; 4Department of Immunology, Roswell Park Cancer Institute, Elm and Carlton Streets, Buffalo, New York 14263, USA; 5Department of Tropical Medicine, Jikei University School of Medicine, 3-25-8 Nishi-Shinbash i, Minato-ku, Tokyo 105-8461, Japan; 6Ajinomoto Company Inc., 15-1, Kyobashi 1-chome, Chuo-ku, Tokyo 104-8315, Japan; 7Institute of Immunotherapy for Cancer, Kinki University, 377-2, Ohno-higashi, Osakaayamash i, Osaka 589-8511, Japan

Clinical Department of Neurology, Innsbruck Medical University, Innsbruck, Austria; Faculty of Tropical Medicine, Mahidol University, Hospital for Tropical Diseases, Bangkok, Thailand

The clinical presentation of Plasmodium falciparum malaria reflects a continuum from asymptomatic to multi-organ manifestation and death. Severe malaria is defined by the World Health Organization as a qualitative variable. We used the multi-organ dysfunction score (MODS) as a quantitative approach for severity in 29 patients with severe and complicated P. falciparum malaria to test its usefulness in discriminating different severity levels. The MODS on admission was highly correlated with the duration of symptoms after admission (r = 0.73, P < 0.001) and the serum level of tumor necrosis factor alpha (r = 0.41, P = 0.03). In addition, the simplified MODS, based mainly on clinical findings, was also correlated with liver dysfunction on admission.
ECTOPHOSPHORYLATION OF CD36 REGULATES CYTOADHRENCE OF PLASMODIUM FALCIPARUM TO MICROVASCULAR ENDOTHELIUM UNDER FLOW CONDITIONS

May Ho,1* Holly L Hoang,1 Kristine M Lee,1 Nalii Liu,1 Tara MacRae,1 Laura Montes,1 Christine L Flatt,1 Bryan G Yipp,1 Bradley J Berger,3 Laura Montes,1 Christine L Flatt,1 Bryan G Yipp,1 Bradley J Berger,3 Laura Montes,1 Christine L Flatt,1 Sornchai Looareesuwan,5 Stephen M Robbins2,3

Department of Microbiology and Infectious Diseases,1 Department of Oncology,2 Department of Biochemistry and Molecular Biology, University of Calgary, Calgary, Alberta, T2N 4N1 Canada,3 Chemical and Biological Defence Section, Defence R&D Canada, Suffield, Alberta, T1A BK6 Canada,4 Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand5

The adhesion of Plasmodium falciparum-infected erythrocytes (IRBCs) to human dermal microvascular endothelial cells (HDMECs) under flow conditions is regulated by a Src family kinase- and alkaline phosphatase (AP)-dependent mechanism. In this study, we showed that the target of the phosphatase activity is the ectodomain of CD36 at threonine-92 (Thr92). Mouse fibroblasts (NIH 3T3 cells) transfected with wild-type CD36 or a mutant protein in which Thr92 was substituted by Ala supported the rolling and adhesion of IRBCs. However, while the Src family kinase inhibitors PP1 and PP2 and the specific AP inhibitor levamisole significantly reduced IRBC adhesion to wild-type CD36 transfectants as with HDMECs, the inhibitors had no effect on IRBC adhesion to the mutant cells. Using a phosphospecific antibody directed at a 12-amino-acid peptide spanning Thr92, we demonstrated directly that CD36 was constitutively phosphorylated and could be dephosphorylated by exogenous AP. Endothelial CD36 was likewise constitutively phosphorylated. The phosphospecific antibody inhibited IRBC adhesion to HDMECs that could be reversed by preincubating the antibody with the phosphorylated but not the nonphosphorylated peptide. Pretreatment of HDMECs with AP abrogated the effect of PP1 on IRBC adhesion. Collectively, these results are consistent with a critical role for CD36 dephosphorylation through Src family kinase activation in regulating IRBC adhesion to vascular endothelium.


LIMITED POLYMORPHISM IN THE DIHYDROPTEROATE SYNTHETASE GENE(DHPS) OF PLASMODIUM VIVAX ISOLATES FROM THAILAND

Mallika Imwong,1 Sasithon Pukrittayakamee,1 Qin Cheng,2 Catrin Moore,1 Sornchai Looareesuwan,1 Georges Snounou,4 Nicholas J White,1,* Nicholas PJ Day1,3

Pneumonia is a common manifestation of melioidosis, the disease caused by Burkholderia pseudomallei. In this study, we defined the prognostic significance of a positive sputum culture. A total of 712 patients presenting to Sappasithiprasong Hospital, Ubon Ratchathani, Thailand, with melioidosis between January 1992 and December 2002 had a sputum culture performed during admission, which was positive for B. pseudomallei in 444 patients (62%). The median duration of sputum positivity was 9 days (range, 1 to 49 days). Sputum cultures were negative in 32% of patients with radiologic changes suggestive of pulmonary involvement. Overall in-hospital mortality was 48%. A positive sputum culture was associated with mortality (adjusted OR 2.8, 95% CI: 1.9, 4.0; P < 0.001). This was independent of renal disease, a prior history of melioidosis, positive blood cultures, and other potential confounders. The presence of B. pseudomallei in the sputum of patients with melioidosis is associated with a poorer prognosis.

ABSTRACTS

Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; Drug Resistance and Diagnostics Department, Australian Army Malaria Institute, Brisbane, Queensland, Australia; Centre for Clinical Vaccinology and Tropical Medicine, Churchill Hospital, Headington, Oxford OX3 7LJ, United Kingdom; Unité de Parasitologie Biomédicale, CNRS URA 2581, Institut Pasteur, Paris, France

The dhp sequences of 55 Plasmodium vivax isolates (39 from Thailand and 16 from elsewhere) revealed variant Pvdhps at codons 383 and/or 553 (A[T]G) in 33 isolates, all from Thailand. Mutations of Pvdhps and Pvdhfr were correlated. Multiple mutations were associated with high-grade sulfadoxine-pyrimethamine resistance.


Behavioral and Social Issues Maong Volunteers in a Preventive HIV Vaccine Trial in Thailand


ARTESUNATE–DAPSONE–PROGUNAIL TREATMENT OF FALCIPARUM MALARIA: GENOTYPIC DETERMINANTS OF THERAPEUTIC RESPONSE

Sivicha Krudsood1, Mallika Imwong2, Polrat Wilairatana3, Asithon Pukrittayakamee2, Apichart Nonprasert1, Georges Snounou3, Nicholas J White1-4, Sornchai Looareesuwan2

Antibody-dependent cell-mediated cytotoxicity (ADCC) was assessed in volunteers participating in an ALVAC-HIV (vCP1521)/AIDSVAX® B/E gp120 prime-boost vaccine trial in Thailand. ADCC activity was measured using chromium release from gp120 subtype B- and CRF01_AE-coated targets in 95 vaccinees and 28 placebo recipients. There was a significant difference in the magnitude of the ADCC response to both targets between vaccinees and placebo recipients. The frequency of responders to subtype B and to CRF01_AE was 96% and 84% in the vaccine group versus 11% and 7% in the placebo group. The results demonstrate that this HIV vaccine is a potent inducer of ADCC activity and may be an additional protection of this prime-boost vaccine in preventing HIV disease.


Artesunate–Dapsone–Proguanil Treatment of Falciparum Malaria: Genotypic Determinants of Therapeutic Response

Sivicha Krudsood1, Mallika Imwong2, Polrat Wilairatana3, Asithon Pukrittayakamee2, Apichart Nonprasert1, Georges Snounou3, Nicholas J White1-4, Sornchai Looareesuwan2

Antibody-dependent cell-mediated cytotoxicity (ADCC) was assessed in volunteers participating in an ALVAC-HIV/AIDSVAX® B/E prime-boost HIV-1 vaccine trial in Thailand.

Chitrarorn Karnasuta1, Robert M Paris1, Josephine H Cox2, Sorachai Nitayaphan1, Punnue Pitsutthithum3, Prasert Thongcharoen4, Arthur E Brown1, Sanjay Gurunathan3, Peter D Manisseri1, Elke M Schirmer1, Seth Silove1, James Tartaglia6, William L. Heyward7, John G. McNeil2, Deborah L. Binz, Mark S. de Souza2, Thai AIDS Vaccine Evaluation Group, Thailand TAVEG

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 multidrug-resistant falciparum malaria in Thailand failure rates were high. Proguanil is inexpensive, widely available and very similar to chlorproguanil. The safety and efficacy of artesunate–dapsone–proguanil (artesunate 4 mg/kg, dapsone 2.5 mg/kg, proguanil 8 mg/kg daily for three days), was studied prospectively in 48 Thai adult
patients with acute falciparum malaria followed daily for 28 days. Eleven of these had a recrudescence of their infection. Genotyping of *Plasmodium 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 insufficient for infections with parasites carrying the highly antifol-resistant *Pfdhfr* I164L mutation.

**Summary** This prospective study was conducted at Ramrasnaradura Hospital from November 11, 2002, until January 5, 2003, in order to describe the clinical manifestations and determine the aetiologies as well as to assess the short-term outcome of interstitial pneumonitis in HIV/AIDS patients. 59 patients with interstitial infiltrates on chest radiographs were included in the study. Tuberculosis (TB) was the most common diagnosis (44%), followed by Pneumocystis pneumonia (PCP) (25.4%), bacterial pneumonia (20.3%) and fungal pneumonia (10.2%). In TB, compared to other diagnoses, a mild cough (p = 0.031), pallor (p = 0.021), lymphadenopathy (p < 0.001), an absence of skin lesions (p = 0.003), a higher mean body temperature (p = 0.004) and an absence of dyspnoea on exertion (p = 0.042) were significant findings. In PCP, compared to other diagnoses, dyspnoea on exertion (p = 0.014), nonpurulent sputum production (p = 0.047), a higher mean respiratory rate (p < 0.001), and an absence of lymphadenopathy (p < 0.001) were significant factors. In bacterial pneumonia, compared to other diagnoses, production of purulent sputum (p = 0.014), haemoptysis (p = 0.006), skin lesions (p = 0.002) and severe cough (p = 0.040) were significantly associated factors. In fungal pneumonia, compared to other diagnoses, headache and papulonecrotic skin lesions were common findings, but no factor showed a significant association. After four weeks, 59.3% patients were alive and 13.6% had died. Among those alive, 88.6% had clinically improved. The cumulative survival after 28 days was highest among PCP patients, followed by bacterial pneumonia, TB and fungal pneumonia, but these differences were statistically not significant (p = 0.453).
Melioidosis is associated with significant mortality in countries in which it is endemic. Previous studies have demonstrated that quantitative *Burkholderia pseudomallei* counts in blood are predictive of mortality. Here we examine the relationship between outcomes and quantitative *B. pseudomallei* counts in urine. A total of 755 patients presenting to Sappasithiprasong Hospital, Ubon Ratchathani, northeast Thailand (in the northeast part of the country), with melioidosis between July 1993 and October 2003 had quantitative urine cultures performed within 72 h of admission. Urine culture results were divided into the following groups: (i) no growth of *B. pseudomallei* from a neat sample or pellet, (ii) positive result from a centrifuged pellet only (<10^3 CFU/ml), (iii) detection of between 10^3 and 10^5 CFU/ml from a neat sample, or (iv) detection of ≥10^5 CFU/ml from a neat sample. The overall in-hospital mortality rate was 45%. Patients with negative urine cultures had the lowest death rate (39%). Mortality rates rose with increasing *B. pseudomallei* counts in urine, from 58% for those with positive spum pellets only to 61% for those with between 10^3 CFU/ml and 10^5 CFU/ml and 71% for those with ≥10^5 CFU/ml. This was independent of age, presence of bacteremia, known risk factors for melioidosis such as diabetes, and the prior administration of antibiotics. The presence of *B. pseudomallei* in urine during systemic infection is associated with a poor prognosis.

**ABSTRACTS**

**ROLE AND SIGNIFICANCE OF QUANTITATIVE URINE CULTURES IN DIAGNOSIS OF MELIOIDOSIS**

Direk Limmathurotsakul,1 Vanaporn Wuthiekanun,1 Wirongrong Chierakul,1 Allen C Cheng,1,2 Bina Maharjan,1 Wipada Chaowagul,1 Nicholas J White,1,4 Nicholas PJ Day,1,4 Sharon J Peacock1,4

Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand;1 Menzies School of Health Research, Charles Darwin University and Northern Territory Clinical School, Flinlers University, Darwin, Australia;2 Medical Department, Sappasithiprasong Hospital, Ubon Ratchathani, Thailand;3 Centre for Clinical Vaccinology and Tropical Medicine, Nuffield Department of Clinical Medicine, University of Oxford, Churchill Hospital, Oxford OX3 7LJ, United Kingdom

**MELIOIDOSIS** is associated with significant mortality in countries in which it is endemic. Previous studies have demonstrated that quantitative *Burkholderia pseudomallei* counts in blood are predictive of mortality. Here we examine the relationship between outcomes and quantitative *B. pseudomallei* counts in urine. A total of 755 patients presenting to Sappasithiprasong Hospital, Ubon Ratchathani, northeast Thailand between July 1993 and October 2003 had quantitative urine cultures performed within 72 h of admission. Urine culture results were divided into the following groups: (i) no growth of *B. pseudomallei* from a neat sample or pellet, (ii) positive result from a centrifuged pellet only (<10^3 CFU/ml), (iii) detection of between 10^3 CFU/ml and 10^5 CFU/ml from a neat sample, or (iv) detection of ≥10^5 CFU/ml from a neat sample. The overall in-hospital mortality rate was 45%. Patients with negative urine cultures had the lowest death rate (39%). Mortality rates rose with increasing *B. pseudomallei* counts in urine, from 58% for those with positive spum pellets only to 61% for those with between 10^3 CFU/ml and 10^5 CFU/ml and 71% for those with ≥10^5 CFU/ml. This was independent of age, presence of bacteremia, known risk factors for melioidosis such as diabetes, and the prior administration of antibiotics. The presence of *B. pseudomallei* in urine during systemic infection is associated with a poor prognosis.

**RECURRENT MELIOIDOSIS IN PATIENTS IN NORTHEAST THAILAND IS FREQUENTLY DUE TO REINFECTION RATHER THAN RELAPSE**

Bina Maharjan,1 Narisara Chantratita,1 Mongkol Vesaratchavee,1 Allen Cheng,2 Vanaporn Wuthiekanun,1 Wirongrong Chierakul,1 Wipada Chaowagul,1 Nicholas P. J. Day,1,4 and Sharon J. Peacock1,4

Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand;1 Menzies School of Health Research, Charles Darwin University, and Geelong Hospital, Barwon Health, Geelong, Victoria, Australia;2 Medical Department, Sappasithiprasong Hospital, Ubon Ratchathani, Thailand;3 Centre for Clinical Vaccinology and Tropical Medicine, Nuffield Department of Clinical Medicine, University of Oxford, Churchill Hospital, Oxford OX3 7LJ, United Kingdom

**Hum**an melioidosis is associated with a high rate of recurrent disease, despite adequate antimicrobial treatment. Here, we define the rate of relapse versus the rate of reinfection in 116 patients with 123 episodes of recurrent melioidosis who were treated at Sappasithiprasong Hospital in Northeast Thailand between 1986 and 2005. Pulsed-field gel electrophoresis was performed on all isolates; isolates from primary and recurrent disease for a given patient different by one or more bands were examined by a sequence-based approach based on multilocus sequencing typing. Overall, 92 episodes (75%) of recurrent disease were caused by the same strain (relapse) and 31 episodes (25%) were due to infection with a new strain (reinfection). The interval to recurrence differed between patients with relapse and reinfection; those with relapses had a median time to relapse of 228 days (range, 15 to 3,757 days; interquartile range [IQR], 99.5 to 608 days), while those with reinfection had a median time to reinfection of 823 days (range, 17 to 2,931 days; IQR, 453 to 1,211 days) (P = 0.0001). A total of 64 episodes (52%) occurred within 12 months of the primary infection. Relapse was responsible for 57 of 64 (89%) episodes of recurrent infection within the first year after primary disease, whereas relapse was responsible for 35 of 59 (59%) episodes after 1 year (P < 0.0001). Our data indicate that in this setting of endemicity, reinfection is responsible for one-quarter of recurrent cases. This finding has important implications for the clinical management of melioidosis patients and for antibiotic treatment studies that use recurrent disease as a marker for treatment failure.


**A RANDOMIZED COMPARISON OF ARTEUNATE-ATOVAQUONE-PROGUANIL VERSUS QUININE IN TREATMENT FOR UNCOMPLICATED FALCIPARUM MALARIA DURING PREGNANCY**

Rose McGready,1,2,3 Elizabeth A. Ashley,1,2,3 Eh Moo,1 Thein Cho,1 Marion Barends,1,2 Robert Hutagalung,1,2 Sornchai Looareesuwan,1 Nicholas J. White,1,2,3 and François Nosten1,2,3

1 Shoklo Malaria Research Unit, Mae Sot, and 2 Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; 3 Centre for Vaccinology and Tropical Medicine, Churchill Hospital, Oxford, United Kingdom

**BACKGROUND:** There is no safe, practical, and effective treatment for pregnant women infected with multidrug-resistant *Plasmodium falciparum*. 

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THE PHARMACOKINETICS OF ORAL DOXYCYCLINE ADMINISTERED AT 200 mg EVERY 24 h WERE INVESTIGATED IN 17 PATIENTS RECOVERING FROM SEVERE PLASMODIUM FALCIPARUM MALARIA. THE DATA SUGGEST THAT THE DOSES OF DOXYCYCLINE CURRENTLY RECOMMENDED (CIRCA 3.5 mg/kg OF BODY WEIGHT DAILY) MAY NOT BE OPTIMAL.


A FUNCTIONAL POLYMORPHISM IN THE IL1B GENE PROMOTER, IL1B -31 C>T, IS NOT ASSOCIATED WITH CEREBRAL MALARIA IN THAILAND

Jun Ohashi1, Izumi Naka1, Akihiro Doi1, Jintana Patarapotikul2, Hathairad Hananantachai2, Noppadon Tangpukdee2, Sornchai Looareesuwan2, Katsushi Tokunaga1

1 Department of Human Genetics, Graduate School of Medicine, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-0033, Japan; 2 Faculty of Tropical Medicine, Mahidol University, 4206 Rajvithi Road, Bangkok, Thailand

BACKGROUND: IL-1beta and IL-1RA levels are higher in the serum of cerebral malaria patients than in patients with mild malaria. Recently, the level of IL1B expression was reported to be influenced by a polymorphism in the promoter of IL1, IL1B -31C>T.

METHODS: To examine whether polymorphisms in IL1B and IL1RA influence the susceptibility to cerebral malaria, IL1B -31C>T, IL1B 3953C>T, and IL1RA variable number of tandem repeat (VNTR) were analysed in 312 Thai patients with malaria (109 cerebral malaria and 203 mild malaria patients). RESULTS: In this population, IL1B -31C>T and IL1RA VNTR were detected, while IL1B 3953C>T (i.e., IL1B 3953T) was not observed in the polymorphism screening for 32 patients. Further analyses for IL1B -31C>T and IL1RA VNTR in 110 cerebral malaria and 206 mild malaria patients showed no significant association of these polymorphisms with cerebral malaria. CONCLUSION: The present results suggest that IL1B -31C>T and IL1RA VNTR polymorphisms do not play a crucial role in susceptibility or resistance to cerebral malaria.


STRONG LINKAGE DISEQUILIBRIUM OF A HBE VARIANT WITH THE (AT)9(T)5 REPEAT IN THE BP1 BINDING SITE UPSTREAM OF THE β-GLOBIN GENE IN THE THAI POPULATION

Jun Ohashi1,2, Izumi Naka1, Jintana Patarapotikul1, Hathairad Hananantachai2, Gary Brittenham3, Sornchai Looareesuwan4, Andrew G Clark2 and Katsushi Tokunaga1

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No Abstract

A gene
Nicholas PJ Day,1,2  Vanaporn Wuthiekanun1
(i.e., (AC) 3(AT)7(T)5) was found through the variation study, we investigated polymorphisms in the (AT) x(T)y alleles, thereby reducing the expression of HBB. In this study.

SHUTDOWN’S MEDIUM, Burkholderia pseudomallei selective agar (BPSA), and a commercial Burkholderia cepacia medium were compared for their abilities to grow B. pseudomallei from 155 clinical specimens that proved positive for this organism.

COMPARISON OF ASHDOWN’S MEDIUM, BURKHOLDERIA CEPACIA MEDIUM, AND BURKHOLDERIA PSEUDOMALLEI SELECTIVE AGER FOR CLINICAL ISOLATION OF BURKHOLDERIA PSEUDOMALLEI

Sharon J. Peacock,1,2  Grace Chieng,1,3  Allen C. Cheng,1,4  David AB Dance,1  Premjit Amornchai,1  Gumphol Wongsuvan,1  Nittaya Teerawattanasook,6  Wirongrong Chierakul,1  Nicholas PJ Day,1,2  Vanaporn Wuthiekanun1

Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand,1  Centre for Clinical Vaccinology and Tropical Medicine, Nuffield Department of Clinical Medicine, University of Oxford, Churchill Hospital, Oxford OX3 7JL, United Kingdom,2  Faculty of Medicine, University of Melbourne, Melbourne, Australia,3  Menzies School of Health Research, Charles Darwin University and Northern Territory Clinical School, Flinders University, Darwin, Australia,4  Health Protection Agency, Tamar Science Park, Plymouth, Devon, United Kingdom,5  Medical Department, Sappasithiprasong Hospital, Ubon Ratchathani, Thailand6

B. pseudomallei from 155 clinical specimens that proved positive for this organism.

The sensitivity of each was equivalent; the selectivity of BPSA was lower than that of Ashdown’s or B. cepacia medium.

HIV–1 PROPHYLACTIC VACCINE TRIALS IN THAILAND

Pitsuttithum P

Clinical Infectious Diseases Research Unit, Faculty of Tropical Medicine, Mahidol University, 420/6 Ratchawithi Road, Bangkok 10400, Thailand. tmppt@mahidol.ac.th

THE HIV epidemic has resulted in medical, social and economic consequences. There is general agreement that a safe, effective and affordable preventive HIV vaccine is urgently needed to control the epidemic. To date, over 60 phase I/II trials of about 30 candidate vaccines have been conducted worldwide. In 1991, Thailand was selected by WHO, UNAIDS as one of the countries for potential HIV vaccine evaluation sites, and 10 projects with HIV phase I, II and III trials have been conducted since 1994. Strong national commitment, collaboration both at national and international levels together with infrastructure strengthening and capacity building, are very important for success. The vaccine designs pursued included synthetic peptides, recombinant protein and recombinant viral vectors followed by or with boosting doses of recombinant proteins. All phase I/II trials indicated that the candidate vaccines were safe and produced binding and a certain level of neutralizing antibodies. The recombinant vector vaccines produced both humoral and cell-mediated responses. The AIDSVAX phase III trial conducted in 1999 was the first efficacy trial of HIV vaccine in Thailand that brought valuable information for further HIV vaccine development. Recently, a phase III trial of ALVAC-HIV priming with AIDSVAX B/E boosting was launched in 2003, and the findings of this trial will be shared with the international community. With committed parties in medical science, government, industry and the community, we hope that we can achieve success in developing a safe and effective HIV vaccine in the near future.
ACTIVITY OF POSACONAZOLE IN THE TREATMENT OF CENTRAL NERVOUS SYSTEM FUNGAL INFECTIONS

Punnee Pitisuttithum1,2, Ricardo Negroni3, John R Graybill4, Beatriz Bustamante5, Peter Pappas5, Stanley Chapman5, Roberta S Hare1, Catherine J Hardalo7

1Vaccine Trial Centre, Faculty of Tropical Medicine, Mahidol University, 420/6 Rajvithi Road, Bangkok 10400, Thailand; 2Hospital FJ Muniz, Buenos Aires, Argentina; 3University of Texas Health Sciences Center, San Antonio, TX, USA; 4Hospital Nacional Cayetano Heredia, Lima, Peru; 5University of Alabama at Birmingham, Birmingham, AL; 6University of Mississippi Medical Center Division of Infectious Diseases, Jackson, MS; 7Schering-Plough Research Institute, Kenilworth, NJ, USA

OBJECTIVES: A multinational, multicentre, open-label clinical trial was conducted to evaluate the safety and efficacy of posaconazole, an extended-spectrum triazole antifungal agent, in subjects with invasive fungal infections who had refractory disease or who were intolerant of standard antifungal therapy. In this subanalysis, we report on those subjects in this trial who had a fungal infection that involved the CNS.

Methods: Subjects received posaconazole oral suspension 800 mg/day in divided doses for up to 1 year; however, subjects could receive additional therapy as part of a treatment-use extension protocol. A blinded, third-party data review committee determined subject eligibility and outcome.

Results: Of the 330 subjects who enrolled in the study, 53 had infections of the CNS, of which 39 were considered evaluable for efficacy. Most had refractory disease (37 of 39) and underlying HIV infection (29 of 39). Twenty-nine subjects had cryptococcal meningitis, and 10 had infections caused by other fungal pathogens [Aspergillus spp. (four), Pseudallescheria boydii (two), Coccidioides immitis (one), Histoplasma capsulatum (one), Ramichloridium mackenziei (one), and Apophysomyces elegans plus a Basidiomycetes sp. (one)]. Successful outcomes were observed in 14 of 29 (48%) subjects with cryptococcal meningoitis and five of 10 (50%) subjects with CNS infections due to other fungal pathogens. Posaconazole was well tolerated.

Conclusions: These data suggest that posaconazole, as an oral medication, has clinical activity against fungal infections of the CNS and may provide a valuable alternative to parenteral therapy in patients failing existing antifungal agents.


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


Department of Tropical Nutrition and Food Science, Faculty of Tropical Medicine, Mahidol University, 420/6 Ratchawithi Rd, Bangkok 10400, Thailand.

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 (Body mass index (BMI) = 25.00-29.99 kg/m2) and obese (BMI > or = 30.00 kg/m2) Thai males and 166 overweight and obese Thai females, compared with 26 males and 81 females in a control group (BMI = 18.50-24.99 kg/m2), were determined The study subjects were persons who turned up regularly for physical check-ups at the Out-patient Department, General Practice Section, Ratchawithi Hospital, Bangkok, aged between 18-60 years. Serum leptin, triglyceride and low density lipoprotein cholesterol/high density lipoprotein cholesterol ratios (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 the 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 between weight, BMI, waist, hip and HDL-C, with leptin. Serum soluble leptin receptor levels were significantly negatively correlated with leptin and BMI. The results can elucidate the causes and consequences of obesity, and are expected to aid the provision of care for overweight and obese Thai people.

HEALTH STATUS: MALARIA, ANEMIA AND INTESTINAL PARASITIC ON THE THAI – MYANMAR BORDER

Nanthaporn Pothipak¹, Siripan Srivilairit, Chaweewan Perngruksa¹, Suparat Failhoug¹, Orohtai Haohan¹, Kobsin Chalclullut, Noppadon Tangpukdee¹, Pannamas Mancckan², Prayong Radoluyos³, Polrat Wilairatana², Sornchai Looareesuwan²

¹Hospital for Tropical Diseases, ²Department of Clinical Tropical Medicine, ³Department of Tropical Hygiene, ⁴Consultant to Faculty of Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

WEREPORTh a study of the health status of Sai Yok people living in Kanchanaburi Province, western Thailand, on the Thai-Myanmar border. Our report focused particularly on malaria, anemia, and intestinal parasitic infections. Falciparum malaria appeared not to be seasonal, with the prevalence in the dry month of February 2003 similar to the wet month of July 2003. In the first survey in February 2003, the prevalence of P. falciparum and P. vivax was 0.1 and 0.5%, respectively. A second survey was conducted in July 2003, when the prevalence of P. falciparum was 0.4% and P. vivax 0.6%. There was no difference in malaria prevalence between dry and rainy seasons. In February, anemia was found in one asymptomatic falciparum malaria patient (0.1%), whereas in July, anemia was not found in any malaria patient. Intestinal parasites were found in 398 (~7.8%) of 587 people presenting for stool examination in February. The three most frequently found intestinal parasites were Entamoeba coli (19.4%), Giardia lamblia (13.1%), and Endolimax nana (10.0%). One month later, after the results of stool examinations had been obtained, antiparasitic drugs and health education were given to the infected population. In July, a second survey was conducted, and intestinal parasites were found in 323 (25.8%) of people coming for stool examination (n = 1,252). The three most frequently found intestinal parasites were E. coli (10.4%), G. lamblia (4.1%), and hookworm (2.2%). The prevalence of intestinal parasitic infections was reduced markedly from 67.8% in the first survey to 25.8% in the second survey (p < 0.05).

In summary, the prevalence of malaria and anemia was low (< 2%) among the Sai Yok people. There was a high, but falling, rate of intestinal parasitic infections.


AN OPEN, RANDOMIZED TRIAL OF THREE-DAY TREATMENT WITH ARTESUNATE COMBINED WITH A STANDARD DOSE OF MEfloQUINE DIVIDED OVER EITHER TWO OR THREE DAYS, FOR ACUTE, UNCOMPlicated FALCIPARUM MALARIA


Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, 4206 Rajvithi Road, Bangkok 10400, Thailand. tmusl@mahidol.ac.th

THE combination of artesunate and mefloquine is currently one of the most effective treatments for multidrug-resistant Plasmodium falciparum malaria. Simultaneous, rather than sequential treatment with the two drugs, would allow better patient compliance. We therefore evaluated three-day treatment with artesunate combined with either 2 or 3 days of mefloquine co-administered once a day with artesunate. The study was an open, randomized trial for acute, uncomplicated falciparum malaria and was conducted at the Bangkok Hospital for Tropical Diseases. One hundred and twenty adult patients were randomized to two treatment groups. Group 1 patients received 4 mg/kg/day of artesunate for 3 days and 3 daily doses of 8.0 mg/kg/day mefloquine given with artesunate. Group 2 patients received the same dose of artesunate and the same total dose of mefloquine (25 mg/kg). However, the mefloquine was given as 15 mg/kg on the first day and 10 mg/kg on the second day, again with artesunate. The baseline demographic and clinical characteristics of the patients in the two groups were similar. The cure rates for the 3-day and 2-day mefloquine regimens were 100% and 99%, respectively. There were no significant differences in either median fever clearance times (group 1=32 hours; group 2=33 hours) or mean parasite clearance times (group 1=42.3 hours; group 2=43.3 hours). Both regimens were well tolerated and there were no significant differences in the incidence of adverse effects. Nausea or vomiting occurred in 3.8% of patients in both groups and transient dizziness occurred in 4% of group 1 and 9% of group 2 patients. These results suggest that a 3-day regimen of mefloquine administered with artesunate is effective and well tolerated. This practical regimen could improve patient compliance.

DETECTION OF ORIENTIA TSUTSUGAMUSHI IN CLINICAL SAMPLES BY QUANTITATIVE REAL-TIME POLYMERASE CHAIN REACTION

Tasawan Singsilarak, Wattana Leowattana, Sorndchai Looaresuwan, Varee Wongchoitigul, Ju Jiang, Allen L. Richards, George Watt

Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; Department of Microbiology, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; Rickettsial Diseases Department, Naval Medical Research Center, Silver Spring, Maryland; Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand and Department of Medicine, Hawaii AIDS Clinical Research Program, University of Hawaii, Manoa, Honolulu, Hawaii

Orientia tsutsugamushi infection causes scrub typhus, a common zoonosis of rural Asia. Orientia tsutsugamushi was recently detected by a real-time quantitative polymerase chain reaction (qPCR) assay in animal specimens. We evaluated the same qPCR assay in specimens obtained from patients with serologically proven scrub typhus infections. The 47-kDa qPCR assay was more sensitive than was mouse inoculation; it was reactive in whole blood specimens from all 10 isolate-positive patients and in 7 of 17 isolate-negative individuals (P = 0.003, Fisher’s two-tailed exact test). As few as 1,076 O. tsutsugamushi copies/μL were detected in whole blood. Four of 7 sera from isolate-proven scrub typhus infections were also reactive by qPCR. The assay was unreactive in all 12 individuals without scrub typhus infection. This is the first demonstration of a sensitive and specific real-time qPCR assay for human scrub typhus infection.


EVALUATION OF A REAL-TIME POLYMERASE CHAIN REACTION ASSAY FOR THE DIAGNOSIS OF MALARIA IN PATIENTS FROM THAILAND

Heather Swan, Lynne Sloan, Anthony Muyombwe, Pornthip Chavalitshewinkoon-petmitr, Srivicha Kruodood, Wattana Leowattana, Polrat Wilairatana, Sorndchai Looaresuwan, Jon Rosenblatt

Division of Clinical Microbiology, Mayo Clinic, Rochester, Minnesota; Department of Protozoology and Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

We compared the diagnosis of malaria in 297 patients from Thailand by a real-time polymerase chain reaction (PCR) assay using the LightCycler with conventional microscopy using Giemsa-stained thick and thin blood films. The PCR assay can be completed in one hour and has the potential to detect and identify four species of Plasmodium in a single reaction by use of melting temperature curve analysis (however, we did not detect Plasmodium ovale in this study). Blood was collected, stored, and transported on IsoCode STIX, which provide a stable matrix for the archiving and rapid simple extraction of DNA. A genus-specific primer set corresponding to the 18S ribosomal RNA was used to amplify the target sequence. Fluorescence resonance energy technology hybridization probes were designed for P. falciparum over a region containing basepair mismatches, which allowed differentiation of the other Plasmodium species. The PCR results correlated with the microscopic results in 282 (95%) of 297 patient specimens. Most of these were single-species infections caused by P. vivax (150) and P. falciparum (120), along with 5 P. malariae, 2 mixed infections (P. falciparum and P. vivax), and 5 negative specimens. No negative microscopy specimens were positive by PCR (100% specificity for detection of Plasmodium species).
MalariA remains a major cause of morbidity and mortality in tropical countries and subtropical regions in the world. Southeast Asia has the most resistant malaria parasites in the world, which has limited treatment options in this region. In response to this situation, short-course artemisinin-based combination therapies (ACTs) have been developed. The combination of dihydroartemisinin (DHA) and piperaquine (PQP) in the form of Artekin has been developed as an alternative to established treatments, such as artemesunate-mefloquine, primarily to reduce treatment costs and toxicity. We conducted a study comparing a standard treatment for acute uncomplicated falciparum malaria (artesunate 4 mg/kg/day together with mefloquine 8 mg/kg/day oral route once a day for 3 days) (Group A) and a combination of dihydroartemisinin 40 mg and piperaquine 320 mg in the form of Artekin given once a day for 3 days (Group B) to determine safety, efficacy, and tolerability. One hundred and eighty patients were randomly enrolled at the ratio of 1:2 into groups A:B. All patients had rapid parasite clearance once and could be used alternatively as the current treatment for multidrug-resistant P. falciparum malaria.

ABSTRACTS

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


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

RelAtionShip Between HyPerhomocysteinemIa and atheroSclerosis in chronic HEMODIALYSIS PATIENTS


Renal Division, Department of Medicine, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand.

BackGround: Hyperhomocysteinemia is an independent risk factor of coronary artery heart disease (CAHD) and atherosclerosis in a normal population. However, it is still controversial in end-stage kidney disease patients who underwent long-term dialysis. Carotid intima-media thickness (IMT) is the standard non-invasive measurement of atherosclerosis. The aims of the present study were to determine the homocysteine (Hcy) level, and to evaluate its role as a risk factor of atherosclerosis in hemodialysis (HD) patients.

Clinical data and blood chemistries were assayed in 62 HD patients. Atherosclerosis was defined by clinical presentations of CAHD, cerebrovascular or peripheral vascular diseases, or carotid plaque by ultrasound. IMT was also measured by ultrasound.

Plasma Hcy level in HD patients was significantly higher in HD patients than normal controls (28.3 +/- 8.3 vs 9.7 +/- 2.9 micromol/l, p < 0.001). Older age (p < 0.001), male sex (p = 0.05), longer duration of HD (p = 0.05), and higher plasma Hcy level (p = 0.01) correlated with atherosclerosis by univariate analysis, but plasma Hcy did not show significant correlation by multivariable analysis. There was also correlation between IMT and atherosclerosis in HD patients (p < 0.001) but no correlation was observed between plasma Hcy level and IMT.

Hyperhomocysteinemia is not an independent factor in the genesis of atherosclerosis in HD patients. Advanced age plays a major role of hyperhomocysteinemia and IMT is a useful marker of atherosclerosis in these patients.


 METHYLENETETRAHYDROFOLATE REDUCTASE (MTHFR) POLYMORPHISM (C677T) IN RELATION TO HOMOCYSTEINE CONCENTRATION IN OVERWEIGHT AND OBSE THAIS

Thawnasom K, Tungtrongchir R, Petmitr S, Pongpaew P, Phron B, Tungtrongchir A, Schelp FP

WE analyzed the association between MTHFR (C677T) gene polymorphism with serum concentrations of homocysteine, folate, and vitamin B12 in 37 male and 112 female overweight/obese Thai volunteers (BMI > or = 25.00 kg/m²), and compared them with 23 male and 90 female control subjects (BMI = 18.5-24.99 kg/m²). Statistically significant higher levels of serum homocysteine were found in the overweight/obese subjects than the control subjects (p < 0.05). Serum folic acid levels in the overweight/obese subjects were significantly lower than the control subjects (p < 0.05). When the data were grouped according to homocysteine concentration and MTHFR gene polymorphism, there were significantly higher homocysteine concentrations in the overweight/obese subjects than the control subjects in wild type gene polymorphism (CC) in the hyperhomocysteine group (homocysteine >10.0 mmol/l) (p < 0.05), but in genotype polymorphism (CC, CT, TT) there were lower folic acid and vitamin B12 concentrations in the overweight/obese subjects than in the control subjects. In the hyperhomocysteine groups, there was no significant difference in the frequencies of MTHFR (C677T) gene polymorphism between the overweight/obese subjects and the control subjects. Folic acid and gene polymorphism were found to be significantly related to the overweight/obese and control groups in logistic regression analysis (p < 0.05). The results support the supposition that folic acid is more important than vitamin B12.


THE EFFICACY AND ADVERSE EFFECTS OF GPO-VIR (STAVUDINE+LAMIVUDINE+NEVIRAPINE) IN TREATMENT-NAÏVE ADULT HIV PATIENTS

Tin EE, Bowonwatanuwong C, Desakorn V Wilairatana P, Krudsood S, Pitsuttithum P

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

A DESCRIPTIVE, combined retrospective and prospective study was conducted at the Anonymous Clinic, Chon Buri Hospital, Chon Buri Province, Thailand from November 10, 2003 to January 4, 2004. A total of 83 adult HIV-treatment-naïve patients undergoing treatment with GPO-VIR (stavudine, lamivudine, and nevirapine) for at least one year were studied. The objectives of the study were to assess the efficacy of GPO-VIR by evaluating body weight changes, CD4 T-cell count changes, the occurrence of opportunistic infections, and long-term side effects, such as lipodystrophy, during treatment. Of 83 studied patients, approximately half (52.3%) of them had a body weight increase > 10% of pre-treatment body weight after 12 months treatment. After taking GPO-VIR, CD4 T-cell counts increased rapidly, by a median of 78 x 10(6) cells/l during the first three months. 39.5% of the patients attained median CD4 counts > 200 x 10(6) cells/l, and 11.6% achieved > 500 x 10(6) cells/l after 2 years of treatment. The occurrence of opportunistic infections was significantly lower after treatment with GPO-VIR (p = 0.001). Subjective assessment of lipodystrophy by physicians and patients showed that 16.8% had symptoms of lipodystrophy within 2 years of GPO-VIR treatment. There was a significant association between older age group (40-49 years) and occurrence of lipodystrophy (p = 0.043). GPO-VIR is an inexpensive and effective antiretroviral drug regimen for initiating treatment of naive patients, but careful assessment for lipodystrophy is necessary, especially after one year of treatment.


ANTIBODIES FROM PATIENTS WITH MELIOIDOSIS RECOGNIZE BURKHOLDERIA MALLEI BUT NOT BURKHOLDERIA THAILANDENSIS ANTIGENS IN THE INDIRECT HEMAGGLUTINATION ASSAY

Rachaneeporn Tiyawisutsri,1,2,3 Sharon J Peacock,1,4* Sayan Langa,1 Direk Limmathurotsakul,1 Allen C Cheng,5 Wirongrong Chierakul,1 Wipada Chaowagul,6 Nicholas PJ Day,1,4* Vanaporn Wuthiekanun1

Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand,1 Faculty of Clinical Microbiology, Faculty of Medical Technology, Mahidol University, Bangkok, Thailand,2 Faculty of Allied Health Sciences, Chulalongkorn University, Bangkok, Thailand,3 Centre for Clinical Vaccinology and Tropical Medicine, Nuffield Department of Clinical Medicine, University of Oxford, Churchill Hospital, Oxford OX3 7LJ, United Kingdom,4* Menzies School of Health Research, Charles Darwin University, Darwin, and The Geelong Hospital, Barwon Health, Geelong, Australia,5 Medical Department, Sappasithiprasong Hospital, Ubon Ratchathani, Thailand6

The indirect hemagglutination assay routinely used to detect antibodies to Burkholderia pseudomallei was modified to detect cross-reactivity of antibodies to B. pseudomallei, B. mallei, and B. thailandensis antigens. We demonstrate a lack of cross-reactivity between B. pseudomallei and B. thailandensis but marked cross-reactivity between B. pseudomallei and B. mallei.

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IN VITRO STUDY OF MALARIA PARASITE INDUCED DISRUPTION OF BLOOD-BRAIN BARRIER

Lertyot Treeratanapiboon1,2, Katherina Psathaki3, Joachim Wegener1, Sornchai Looareesuwan4, Hans-Joachim Gall1, Rachanee Udomsangpetch1,2

1Department of Pathobiology, Faculty of Science, Mahidol University, Bangkok, Thailand; 2Department of Parasitology, Faculty of Medical Technology, Mahidol University, Bangkok, Thailand; 3Institute for Biochemistry, Westfälische Wilhelms University Muenster, Muenster, Germany; 4Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

The mechanism of blood–brain barrier breakdown in the complex pathogenesis of cerebral malaria is not well understood. In this study, primary cultures of porcine brain capillary endothelial cells (PBCEC) were used as in vitro model. Membrane-associated malaria antigens obtained from lysed Plasmodium falciparum schizont-infected erythrocytes stimulated human peripheral blood mononuclear cells (PBMC) to secrete tumor necrosis factor alpha. In co-cultivation with the brain endothelial cell model, the malaria-activated PBMC stimulated the expression of E-selectin and ICAM-1 on the PBCEC. Using electric cell–substrate impedance sensing, we detected a significant decrease of endothelial barrier function within 4 h of incubation with the malaria-activated PBMC. Correspondingly, immunocytochemical studies showed the disruption of tight junctional complexes. Combination of biochemical and biophysical techniques provides a promising tool to study changes in the blood–brain barrier function associated with cerebral malaria. Moreover, it is shown that the porcine endothelial model is able to respond to human inflammatory cells.

THE EPIDEMIOLOGY OF PATIENTS WITH SEVERE MALARIA WHO DIED AT THE HOSPITAL FOR TROPICAL DISEASES, 1991-2004


Intensive Care Unit, Hospital for Tropical Diseases, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

This study is a retrospective case series of the causes of death among patients with severe malaria. Data from the medical records of patients who were admitted to the Intensive Care Unit (ICU) of the Hospital for Tropical Diseases, Mahidol University, Bangkok, Thailand between 1991 and 2004 were analyzed. The overall hospital mortality rate was 0.2% and the ICU mortality rate was 1.8% for patients with malaria. Thirty-five patients died of malaria in the ICU during the study period, while a total of 1,866 patients were treated for malaria in the ICU during the study period. The most common complication of malaria was cerebral malaria (77.1%). The socioeconomic and demographic characteristics of those who died are examined here, as well as the cost of their treatment.

Efficacy of DB289 in Thai Patients with Plasmodium Vivax or Acute, Uncomplicated Plasmodium Falciparum Infections

Patrick Yeramian,1 Steven R Meshnick,2 Srivicha Krudsood,4 Kobssiri Chalermitr,4 Udomsak Silachamroom,4 Noppadon Tangpukdee,4 James Allen,1 Reto Brun,5 Jesse J Kwiek,2 Richard Tidwell,1 Sornchai Looareesuwan4

DB289 is the orally active prodrug of the diamidine DB75, which was developed for the treatment of human African trypanosomiasis.

Background: DB289 is the orally active prodrug of the diamidine DB75, which was developed for the treatment of human African trypanosomiasis.

Methods: We tested the safety and efficacy of DB289 for the treatment of Plasmodium vivax and acute, uncomplicated P. falciparum infections in an open-label pilot study at the Hospital for Tropical Diseases in Bangkok. Nine patients with P. vivax infections and 23 patients with P. falciparum infections were admitted and treated with 100 mg of DB289 given orally twice a day for 5 days and were followed for 28 days. Patients with P. vivax infections were also treated with primaquine on days 10-23.

Results: All patients cleared parasites by day 7, with a mean ± SD clearance time of 43 ± 41 h. One patient with a P. vivax infection had a recurrence of parasitemia on day 9. Of the 23 patients with P. falciparum infections, 3 had recurrences of parasitemia caused by P. vivax and 2 had recurrences of parasitemia caused by P. falciparum. In only 1 of 2 recurrences of parasitemia caused by P. falciparum were the parasites genotypically distinct from the infecting parasites the patient had at enrollment, which means there was a 96% cure rate.

Conclusions: DB289 is a promising new antimalarial compound that could become an important component of new antimalarial combinations.
MEDICAL TREATMENT OF MALARIA IN THAILAND
Pokrat Wilairatana, Srivicha Krudsood, Nonthaporn Pothisap, Sirapha Srivilai, Saowanat Vijayakdga, Chaiporn Rojanawatsirivej, Somneai Looareesuwun
Faculty of Tropical Medicine Mahidol University, Thailand; Malaria Division, Ministry of Public Health, Nonthabun, Thailand.

MALARIA is the most important parasitic infection in people, accounting for more than one million deaths a year'. Malaria has become a priority for the international health community, and it is now the focus of several new initiatives. Prevention and treatment of malaria could be greatly improved with existing methods if increased financial and labour resources were available. However, new approaches for prevention and treatment are needed. Several new drugs are under development, which are likely to be used in combinations to show the spread of resistance, but the high cost of treatments would make sustainability difficult. Malaria infection is caused by coccidian protozoan parasites of the genus Plasmodium carried by female Anopheles spp. mosquitoes. The clinical disease in humans may vary widely according to the species of the parasites -- Plasmodium falciparum, P. vivax, P. ovale or P. malariae -- and the genetics, immune status and the age of the host. These variables have a major influence on all aspects of the disease, including epidemiology, pathogenesis, clinical features and management.


SUBCUTANEOUS MYCOSES

Phothisap, Pothipak, Srivilairit, Vijaykada, Ronatari, Looareesuwun

SUBCUTANEOUS MYCOSES

LIVER DYSFUNCTION IN PATIENTS INFECTED WITH PLASMODIUM MALARIAE

Tangpukdee N¹, Wilairatana P¹, Krudsood S², Thanachartwet W³, Leowattana W⁴, Looareesuwun S¹
¹Department of Clinical Tropical Medicine, Faculty of Tropical, Mahidol University, Bangkok, Thailand; ²Department of Tropical Hygiene, Faculty of Tropical, Mahidol University, Bangkok, Thailand

We performed a prospective laboratory study on 54 patients with acute Plasmodium malariae infection admitted to Bangkok Hospital for Tropical Diseases between 1999 and 2004. The objective of the study was to document changes in hepatic biochemical indices after treatment with artemisinin derivatives. Thirteen patients (24%) were lost to follow up a median of 20 days after admission (range 14-21 days) for reasons not related to adverse effects. Forty-one patients (76%) completed the 28 day follow up period. On admission, 8 patients (15%) had slight increases in serum alkaline phosphatase and aminotransferase levels, and 20 patients (37%) had hypoalbuminemia. These minor abnormalities return to normal within two weeks after antimalarial drugs were administered.
CLINICAL TRIAL OF ARTESUNATE AND PRIMAQUINE FOR TREATMENT OF VIVAX MALARIA IN THAILAND

Krudsood S1, Tangpukdee N1, Chalearmrut K1, Wilairatana P1, Leowattana W1, Silachamroon U1, Brittenham G2, Looareesuwan S1

1Faculty of Tropical Medicine, Bangkok, Thailand; 2Columbia University, New York, U.S.A.


PRASMODIUM VIVAX, a common cause of malaria in Asia and South America, causes a clinically benign illness but relapse is frequent. Radical cure requires primaquine treatment but, in Thailand, 10-15% of vivax infections now seem refractory to standard doses (15 mg once daily for 14 days). Chloroquine-resistant P. vivax is found in the region and mixed infections with multidrug resistant P. falciparum may be present. Accordingly, new therapeutic regimens are needed that can be used in the absence of accurate microscopic diagnosis. We studied 399 Thai patients with acute, symptomatic P. vivax malaria to determine the efficacy, safety and tolerability of artesunate with selected regimens of primaquine. Patients were randomly assigned to one of six treatment groups: all patients received artesunate, 100 mg once daily for 5 days. Group 1 to 5 then received primaquine, 30 mg once daily for 5, 7, 9, 11 and 14 days, respectively. Group 6 received primaquine 30 mg twice a day for 7 days. The 28-day cure rates were 85%, 89%, 94%, 100%, 100%, 96%, respectively. Treatment of vivax malaria with artesunate for 5 days followed by high-dose primaquine is highly effective, well-tolerated and equivalent or superior to standard treatment with low-dose primaquine alone.
The relative balance between Th1 and Th2 cytokines appears important, since the role of cytokines has been reported in several studies by comparison of clinically heterogeneous groups of patients. This study is aimed to determine the role of interleukin-1 (IL-1), IL-2, IL-4, IL-6, IL-8, IL-10, gamma interferon (IFN-γ), and alpha-tumor necrosis factor (TNF-α) in a group of patients with uncomplicated Plasmodium falciparum malaria compared with severe cases. Levels of cytokine profile in serum for 40 patients with severe falciparum malaria (SFM), 36 patients with uncomplicated falciparum malaria (UFM), and 10 healthy volunteer subjects were determined by an Evidence Investigator Biochip Array (Randox, UK). Serum levels of IL-2 were not significantly different between SFM and UFM on admission and decreased rapidly 1 day later in both groups. After successful treatment, serum levels of IL-2 were slightly increased to the levels that higher than the levels on admission. Serum levels of IL-4, IL-6, IL-8, IL-10, IFN-γ and TNF-α were significantly different between SFM and UFM on admission and decreased rapidly in SFM group until the levels were normal at day 28 of hospitalization, but in UFM group, serum levels of IL-6 and IL-10 increased rapidly 1 day later and slightly decreased until touch the normal levels. In conclusion, the increase of serum IL-6, IFN-γ and TNF-α level (Cytokines that mediate natural immunity) during the acute phase of falciparum malaria may reflect and early and effective immune response. Moreover, the increase of serum IL-2, IL-4, IL-8, and IL-10 (Cytokines that regulate lymphocyte growth, activation and differentiation) may play a role in limiting progression from uncomplicated malaria to severe and life-threatening condition.


Screening and Baseline Epidemiologic Profile of Participants in the Phase I HIV Vaccine Trial in Thailand

Jittima Dhitavat, Punnee Pitsuttithum, Theeratus Jongboonyanoparp, Valai Bussaratid, Supa Naksrisok, Rungrapat Muanaum, Narumon Thantamnu, Wantanee Peonim, Vatcharachai Ngamdee, Darat Boonma

Vaccine Trial Center, Faculty of Tropical Medicine, Mahidol University. Thailand.

Background: Established the profile of potential participants in the HIV vaccine trials provides valuable guidance for conducting future trials. The aim of this study is to describe baseline epidemiologic characteristics of volunteers at the Vaccine Trial Center, as a part of the phase I, multicenter, double-blind, placebo-controlled study of an experimental HIV vaccine.

Methods: Fifty-seven healthy volunteers 18-50 years of age were screened. Recruitment strategies, demographics and risk behaviors were assessed. Baseline laboratory data were performed. HIV status was determined by using Sanofi and Abbott ELISA.

Results: From October 2003 through October 2004, 29 of 57 volunteers screened were enrolled. Nineteen were excluded on unacceptable laboratory results, including 1 with HIV infection; 3 with medical problems; 2 pregnancies; and 1 unable to turn up for enrollment. Three were eligible but the quota was full. Successful recruitment methods were referrals from volunteers and staff. Most volunteers were men (32/57), young (median, 27 years), single (38/57), Buddhism (56/57), employed (45/57) and had no risk for HIV during the past 6 months (56/57). The most common contraceptive method was abstinence and usage of male condoms.

Intramuscular administration of high doses of artemether and arteether to experimental animals produces selective damage to brain stem centres involved predominantly in auditory processing and vestibular reflexes. We investigated the distribution and accumulation of oil-soluble arteether intramuscularly (C14-labeled arteether, 20 µCi/kg body weight) in a mouse model. The results showed that the main localization of labeled arteether was found in the hind brain when compared to the other parts of the mouse brain (p = 0.001). Other organs where the drug accumulated included the intestine, heart, spleen, liver, lung, kidney. Cmax (mean ± SD) of arteether in whole blood was reached after 36 ± 8.215 minutes after injection. The terminal half-life of this labeled arteether was 1.8 hours. The blood / brain ratios at 4 hours after drug injection was 8 : 1. These findings suggest that labeled arteether can pass the blood-brain barrier of the mouse brain and accumulated mainly in the hind brain which is corresponding to our previous clinical and neuropathological findings of arteether toxicity.


 Autoradiography of Mouse Brain After Intramuscular Injection of C14-Labeled Arteether

Apichart Nontprasert¹, Sasithon Pukrittayakamee¹, Wichai Supanaranond², Arjen M. Dondorp¹, Nicholas J White¹, Nicholas PJ Day¹,²

¹Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, 10400, Thailand; ²Centre for Tropical Medicine, Nuffield Department of Clinical Medicine, John Radcliffe Hospital, Oxford, United Kingdom.

Intramuscular administration of high doses of artemether and arteether to experimental animals produces selective damage to brain stem centres involved predominantly in auditory processing and vestibular reflexes. We investigated the distribution and accumulation of oil-soluble arteether intramuscularly (C14-labeled arteether, 20 µCi/kg body weight) in a mouse model. The results showed that the main localization of labeled arteether was found in the hind brain when compared to the other parts of the mouse brain (p = 0.001). Other organs where the drug accumulated included the intestine, heart, spleen, liver, lung, kidney. Cmax (mean ± SD) of arteether in whole blood was reached after 36 ± 8.215 minutes after injection. The terminal half-life of this labeled arteether was 1.8 hours. The blood / brain ratios at 4 hours after drug injection was 8 : 1. These findings suggest that labeled arteether can pass the blood-brain barrier of the mouse brain and accumulated mainly in the hind brain which is corresponding to our previous clinical and neuropathological findings of arteether toxicity.

NEW antimalarial drugs that have been investigated at the Hospital for Tropical Diseases, Faculty of Tropical Medicine, Mahidol University, in recent years are as follows. atovaquone, a hydroxynaphthoquinone, was evaluated and it was found that atovaquone alone proved safe and effective. All patients treated had clinical cure, however, one third of patients had late recrudescence (RI). When it was combined with proguanil, the cure rate increased to 100%. This combination has now been developed into a fixed drug named Malarone. Artemisinine derivatives such as artesunate, artemether, arteether, and dihydroartemisinin are also tested at the Bangkok Hospital for Tropical Diseases. Artesunate and arteether alone at a total dose of 600 to 750 mg. given over 5-7 days produced cure rates of 80 to 95%. Artesunate or dihydroartemisinin suppositories at a dose of 10 mg/kg/day have been proved successful for the treatment of severe malaria. The artemisinin derivatives, (4 mg/kg/day) when used in combination with mefloquine (8 mg/kg/day) given once a day for 3 days gave improved cure rates, up to 95-100%. Dihydroartemisinin alone with a total dose of 480 mg given over 5 days gave a cure rate of 90%. Arteether, a WHO/TOR supported drug, has been evaluated in the Hospital and now has been registered for use (the same dose of arteether) in severe malaria under the name Artecom. – Other combinations (artemisinin derivatives combined with tetracycline or doxycycline and mefloquine combined with tetracycline or doxycycline) have also been evaluated with improvement in cure rates. Recently, a fixed drug (artemether plus lumefantrine) named Coartem© (six doses given over 72 hours) proved to be a safe and effective drug (cure rate over 95%) for the treatment of falciparum malaria and it has been registered for use in many western countries. At present, studies with combinations of artemisinin derivatives plus mefloquine (in various doses and durations of treatment) are being investigated. Recently we have finished the double-blind, randomized, comparative study of 200 patients (adults and children) with falciparum malaria treated by a pre-packed blister approach (4 mg/kg/day artesunate and 8 mg/kg/day given once a day for 3 days) and found that this approach proved safe and effective and this approach could translate clinically into a better patient compliance. Other fix-combinations (Artecom©, Artekin©) proved safe and efficacious (cure rate over 98%) and could be an alternative antimalarial drugs. In general, artemisinin derivatives (12 mg/kg total dose given in 3 days) combined with mefloquine (25 mg/kg total dose given in 3 days) have been a standard regimen for the treatment of multidrug resistant falciparum malaria in Thailand. Until proven otherwise, drug combinations are still recommended for all adult patients suffering from acute uncomplicated falciparum malaria contracted in multidrug resistant areas. The treatment for uncomplicated malaria is aimed at producing a radical cure using the combination of either (1) artesunate (4 mg/kg/day) plus mefloquine (8 mg/kg/day) for 3 days; (2) a fixed dose of artemether and lumefantrine (20/120 mg tablet) named Coartem (4 tablets twice a day for three days for adults weighing more than 35 kg); (3) quinine 10 mg/kg 8-hourly plus tetracycline 250 mg 6-hourly for 7 days (or doxycycline 200 mg once a day for 7 days as an alternative to tetracycline) in patients aged 8 years and over; and (4) a combination of atovaquone and proguanil called Malarone (in adult, 4 tablets given daily 3 days). In treating severe malaria, early diagnosis and early treatment with a potent antimalarial drug is recommended to save the patient’s life. The antimalarial drugs of choice are: intravenous quinine or a parenteral form of an artemisinin derivative (artesunate Lv./Lm. 2.4 mg/kg followed by 1.2 mg/kg injection at 12 and 24 hr and then daily for 5 days; arteether Lm. 3.2 mg/kg injection followed by 1.6 mg/kg at 12 and 24 hrs and then daily for 5 days; arteether Lm. (Artemotil©) with the same dose of arteether; artesunate suppository (5 mg/kg) given rectally 12 hourly for 3 days). Oral artemisinin derivatives (artesunate, arteether, dihydroartemisinin with the dose 4 mg/kg/day should replace parenteral forms when patients can tolerate oral medication. Oral mefloquine (25 mg/kg divided into two doses 8 hrs apart) should be given at the end of the artemisinin treatment course to reduce recrudescence. The treatment of vivax malaria in Thailand is still using chloroquine and primaquine. However with the ineffective to primaquine (15 mg/kg/day for 14 days with relapse rate of 15%) the higher dose (30 mg/kg/ day for 14 days) is recommended. The efficacy studies of primaquine in various regimen given together with Sulfadoxin/Pyrimethamine or artemisinin derivatives are in progress. Tefenoquine & phase III study in the planning stage for clinical trial in our setting in Thailand is in progress.

Conclusion: Healthy volunteers were successfully enrolled in the phase I HIV vaccine trial. Results of this dose-escalating study are expected in 2009.

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**THE EXTRALOBULAR ARACHNOCYTES: A HITHERTO UNRECOGNIZED VITAMIN A-STORING SITE IN MAMMALLIAN LIVER**

Narumon Chanwimalueang, Wichai Ekataksin, Gedsuda Pattanapen, Borimas Hanboonkunupakarn, Thamrong Chirachariyavei

Liver Research Unit Dept of Clinical Tropical Medicine. Faculty of Tropical Medicine, and Toxicopogy Unit Dept of Pathology, Faculty of Medicine Ramathibodi Hospital, Mahidol University. Bangkok; Dept of Anatomy and Cell Biology, Tokya Medical and Dental University School of Medicine, Tokyo, Japan.

**BACKGROUND** Recent reports show that vitamin A may have an immunological role in pathogenesis of malaria (Shankar et al, 1999; Serghides and Kain, 2001, 2002). Vitamin A is stored exclusively in the liver by hepatic stellate cells (Blomhoff and Wake, 1991), known also as Ito cells, retinol-storing cells, or arachnocytes (Ekataksin and Kaneda, 1999). The cells are located in the perisinusoidal spaces of Disse within the lobules (Wake. 1971, 1950, 1988; Wake and SaEO. 1993; Zou et al., 1995). In the course of our study to morphologically characterize liver store of vitamin A, we could identify a so-far-unreported mesenchymal cell type outside liver lobules with vitamin A-containing lipid droplets. Materials and Methods Fresh pig livers were flushed with saline and perfuse-fixed with cooled 1.5% glutaraldehyde in 0.062 M cacodylate buffer (pH 7.4) containing 1% sucrose. Sampled blocks were post-fixed in 0.1 M phosphate buffered (pH 7.4) 1% osmium tetroxide for 2 h at room temperature, dehydrated through alcohol series, and embedded in PolyBed 512. Semithin sections were prepared at 0.5-1.0 μm thickness, stained with toluidine blue, and carefully rinsed with 70% ethanol to create a differential stain pattern. Airdried specimens were mounted in Permound and examined under an ultrawide-field microscope (Olympus Provis AX80) with an ultrahigh-resolution digital camera (Olympus DP70). Panoramic reconstruction was applied and the mappings of 1.2-1.6 GB file size were outputted via an HP Designjet 500 large format printer. Unfixed livers were cut frozen section (Carl Zeiss, Microm K400) at 50 μm thickness, and observed by wide UV fluorescence (330-355 nm). Results Under toluidine blue preparation, liver lobules were demarcated with interlobular connective tissue. Hepatocytes appeared with a spectrum of bluish purple stains. From portal to central zones, sinusoids were well defined with endothelial cells, Kupffer cells, and arachnocytes. The latter were distinguished at every 40-60 μm interval by the presence of green lipid droplet(s), single or double, fully occupying each cell body. The droplets characteristically were very large, especially in the perportal areas, compressing deeply upon the nucleus. In the hepatocytes, fat vacuoles also stained greenish, but mostly were small in size and their profile did not deform the nuclei. In the septa, bundles of collagen fibrils/fibers crisscrossed through the honeycomb structure formed by fibroblasts (Ekataksin et al, 2000). Among them we identified occasional mesenchymal cells bearing a large, green lipid droplet tightly invaginating the nucleus; some were in the intralobular septum, others interlobular septa, but never found at the corner portal tract. They lay against the limiting plate in apposition with a sinusoid or capillary, or stayed surrounded by fibrous interstitium in the septum. Though sporadic, their entity was by no means rare; we encountered as many as 7 cells in one semithin toluidine blue section, or up to 2-4 cells per lobule. Under fluorescence microscopy, myriads of retinol-containing lipid droplets were glaringly luminescent, light blue or bright green, that faded within 20-200 seconds after exposure. Occasional fluorescent droplets could be confirmed inside the septum under objectives of high magnifications.

Discussion and Conclusions Findings are clear that capacity of vitamin A storage is responsible for by the retinol-storing arachnocytes in the lobules. This overwhelming abundance apparently masks the presence of retinol-containing lipid droplets in some mesenchymal cells residing in the interstitial spaces. With aid of supermegapixel digital microscopy and map reconstruction imaging visualized at ultrahigh resolution with large format printing, it becomes clear that the task of presenting rare structure as of extralobular arachnocytes is highly credible and convincing. The entity’s immediate impact is upon our understanding of hepatic fibrogenesis to not refuse the retinoid storage function. Supported by RBD Project Grant #4703 (to
TOTAL DEPLETION IN LIVER STORE OF VITAMIN A: A HITHERTO UNRECOGNIZED NATURE OF CEREBRAL MALARIA

Wichai Ekataksin, Narumon Chanwimalueang, Gedsuda Pattanapen, Borimas K Hanboon, Emsri Pongponratn, Mario Riganti, Thamrong Chirachariyavej, Ronnattrai Ruengweerayup

Liver Research Unit, Dept of Clinical Tropical Medicine; Dept of Tropical Pathology, Faculty of Tropical Medicine; Sororxicology and Forensic Unit, Dept of Pathology, Faculty of Medicine Ramathibodi, Mahidol University, Bangkok; Maesord Hospital, Maesord Dept of Anatomy and Cell Biology, Tokyo Medical and Dental University School of Medicine, Tokyo, Japan

ABSTRACTS


BACKGROUND Malaria accounts for more than one million deaths each year. We learn from textbook that Plasmodium falciparum sporozoites inoculated by Anophe-line mosquito proliferate into schizonts inside liver cells, followed by hepatocyte eruption, releasing matured merozoites into circulation to parasitize erythrocytes. Little is ever questioned about role of vitamin A-storing hepatic stellate cells.

Materials and Methods Fresh livers of patients (n=3) with cerebral malaria obtained from autopsy with informed consents were examined by fluorescence microscopy of 50 pm-thick frozen sections for retinol storage in hepatic stellate cells. This study represents the first of its kind to examine malarial livers with fluorescence microscopy. Earlier studies reported that malaria patients have decreased serum retinol levels (Thumham and Singkamani, 1991). Supplementation of vitamin A reduces morbidity due to P. falciparum (Shankar et al, 1999). Host resistance against malaria is potentiated with 9-cis-retinoic acid, a metabolite of vitamin A (Scherhides and Kain, 2002). Most recently, antimalaria effect of retinol has been demonstrated in vitro (Hamzah et al, 2004). The body could be utilizing retinol rapidly to produce plasma membrane of red blood cells. Our study suggests strongly that liver store of vitamin A is probably a prime indicator in determining the resistance or tendency to develop severe malaria. This also implies the prophylactic/therapeutic use of vitamin A to safeguard susceptible population in endemic areas is justified. (Supported by RBD Project #4703).

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THE DIVERSE PATHOLOGIES OF INFECTED LIVER WITH OPISTHORCHIS VIVERRIN

Mario Riganti, Vasant Khachonsaksumet, Wichai Ekataksin

J Department Unit , Tropical Pathology; Liver Research Unit, Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Thailand

O. viverrini (Liver fluke) is one of the causative agent of food-borne parasitic zoonoses, which infects animals or humans mainly in the North and the Northeast Thailand, Laos and Kampuchea. Transmission to humans occurs often from eating raw fish, raw crayfish, etc., containing viable metacercariae. We performed a retrospective study of the twenty-nine autopsy cases of patients from the Northeastern part of Thailand, aged from 7 to 68 years, whose fecal examination was positive for the O. viverrini eggs. By gross examination, the liver appeared with hepatomegaly (28 cases), dilation of the bile ducts (16 cases at intrahepatic, 13 cases at subcapsular), fibrosis (7 cases at portal area, 4 cases at periductal of the bile ducts), intrahepatic tumors (10 cases), and congestion of the either organ (5 cases). The adult worms were found in the bile ducts of all cases. The livers were processed for microscopic examination. The diverse pathologies were pericholangitis (28 cases), fibrous tissue infiltration at the wall of the bile ducts (27 cases), adenomatous formation (25 cases), dilatation of the bile ducts (24 cases), hyperplasia of epithelium (21 cases), desquamation of epithelium (20 cases), proliferation of epithelium 09 cases), dense fibrous tissue at portal areas (16 cases), cholestasis (12 cases), adenocarcinoma of the bile ducts (8 cases), hepatocellular carcinoma (2 cases), ruptured dilated bile duct with peritonitis (1 case) and perioval granuloma 0 case). The data presented in this
**THE DIVERSE PATHOLOGIES OF INFECTED LUNG WITH PARAGONIMUS HETEROTREMUS**

Vasant Khachonsaksunet, Mario Riganti, Ruchareka Asavisanu, Gedsuda Pattanapen, Borimas Hanboonkunupakam, Parkpoom Piyaman, Narumon Chanwimalueang, Wichai Ekataksin

Department of Tropical Pathology, Faculty of Tropical Medicine; Library and Information Center; Liver Research Unit, Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Thailand.

Paragonimus heterotremus (lung fluke) is one of the causative agents of food-borne parasitic zoonoses which infects animals and humans. More than 40 species of Paragonimus have been identified so far. Paragonimiasis is found mainly in Asia, part of West Africa and Central America. In Thailand, the first case of human paragonimiasis was reported from Petchaboon Province in 1928. Since then, the studies on paragonimiasis both epidemiological and taxonomic aspects have been carried out continuously. Six species of Paragonimus were found, among with P. heterotremus is of the etiologic significant in man. We performed an experimental study to examine the diverse pathologies of cat lung which was infected with P. heterotremus by feeding with infected mountain crab, harboring metacercaria. By gross examination, the cat lung appeared with small hemorrhagic spots. The worms were ably seen in the pleural cavity together with turbid pleural serosanguinous effusion. In the parenchyma were found miliary lung abscesses and cystic lesions containing adult worms with dense fibrous connective tissue around the cysts. The visceral pleura covering the cyst were thickened and inflamed. By microscopic examination, cross sections of the worm were located in the dilated bronchus which had already undergone squamous metaplasia. Surrounding the worm was a large granulomatous tissue containing yellowish brown operculated eggs with and without miracidium. The cystic lesions were surrounded by bands of thick fibroconnective tissue. The adjacent lung tissue showed marked diapedesis, congestion, atelectasis and pneumonia. Paragonimus can infect various kinds of mammalian hosts but the infection rate, the development of the worms and the pathology in their hosts may differ. In this study, we found the pathologies associated not only with the adult worms but also with the eggs. The irritation from the motility of the worms caused disruption of the bronchiolar mucosa which brought about the leakage of the eggs into the adjacent alveolar spaces and may form thereby granulomatous lesions.

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**LIVER STORE OF VITAMIN A WAS TOTALLY DEPLETED IN PATIENT WITH GEREbral MALARIA: A HITHERTO UNREPORTED HEPATIC INVOLVEMENT REVEALED BY FLUORESCENCE MICROSCOPY**

Wichai Ekataksin, Narumon Chanwimalueang, Gedsuda Pattanapen, Borimas Hanboonkunupakam, Thamrong Chiracharive, Prayong Radornyos, Mario Riganti, Emsri Pongponrat

Department of Tropical Pathology, Faculty of Tropical Medicine; Library and Information Center; Liver Research Unit, Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Thailand.

Because hepatic manifestation of malarial patient is generally minor, the study of liver in malariology has so far not received much attention. Despite its being the prime organ for parasite multiplication, still we know very little what role the liver plays in plasmodium infection and pathogenesis. The liver, 1410 g, was removed from a male patient, 22 ylo, with severe cerebral malaria at autopsy with informed consents. Brain smear revealed negative result for parasite load. The liver was challenged for an unprecedented investigation using fluorescence microscopy (Olympus Provis AX80) of frozen sections (50-100 J.1m thickness) and optical confocal digital microscopy with depth reconstruction at 12 megapixel resolution of Golgi-Kopsch silver preparations. Lipid droplet visualization was conducted with oil red 0 stain. Control liver was obtained from a forensic case of acute heart failure. Under wide UV (330-385 nm), normal human liver appeared with glowing spots densely and evenly distributed throughout the lobules, except for the portal and hepatic tract. The greenish fluorescence faded within 30-200 seconds after exposure. With higher magnification, each spot was found as composed of large and small lipid droplets closely grouped together, representing a single arachnocyte storing retinol in multiple lipid droplets in the cytoplasm (see also Chanwimalueang et al. in this issue). In malaria-infected liver, the fluorescence was null; we were startled at the complete lack of autofluorescence normally seen in any liver. Oil red 0 preparations demonstrated lipid droplets of arachnocytes in control liver, but failed to visualize so in the malarial liver. Golgi preparations showed the presence of arachnocytes with lipid...
droplets in normal liver (see also Pattanapen et al., in this issue), but without lipid droplets in the malaria liver. The latter exhibited arachnocytes that appeared with abundant cytoplasmic processes, contrasting strongly with that of normal human. There is little doubt that the lack of autofluorescence in liver of cerebral malaria patient reflects the absence of retinol storage in arachnocytes. This study represents the first of its kind to examine the liver affected by Plasmodium falciparum with fluorescence microscopy. It has been reported that patients with malaria have decreased serum retinol levels (Thumham and Singkamani, 1991). Supplementation of vitamin A reduces morbidity due to Plasmodium falciparum (Shankar et al., 1999). Host resistance against malaria is potentiated with 9-cis-retinoic acid, a metabolite of vitamin A (Serghides and Kain, 2002). Most recently, antimalaria effect of retinol has been demonstrated in vitro (Hamzah et al., 2004). It is not without support to think that liver store of vitamin A could be an important factor in determining the resistance or tendency to develop severe malaria. To state this with certainty, more studies are required.

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**VISUALIZATION OF HUMAN ARACHNOCYTES FOR THE FIRST TIME WITH GOLGI SILVER IMPREGNATION: MORPHOLOGICAL COMPARISON OF HEPATIC STELLATE CELLS FROM PIG AND MAN**

Pattanapen G, Ekataksin W, Hanboonkunupakarn B, Chanwimalueang N, Chirachariyavej T

Liver Research Unit, Dept of Clinical Tropical Medicine, Faculty of Tropical Medicine, Department of Anatomy, Tokyo Medical and Dental University School of Medicine, Tokyo, Japan; Toxicology Unit Dept of Pathology, Faculty of Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

In the previous report (Pattanapen et al., 2003), we distinguished the arachnocytes in pig liver into three major types, consolidated, typical, and liquefied arachnocytes with additional three intermediary forms, metaconsolidated, early typical, and preliquefied arachnocytes. In this study, the shape and form of typical arachnocytes of pig liver are compared with that of arachnocytes visualized for the first time of human liver. Liver samples obtained at autopsy cases free of liver disease from Ramathibodi Hospital, were subject to Golgi-Kopsch chromic silver method (pattanapen, 2004), and studied under light microscopy at oil-immersion objective. The impregnated arachnocytes were photographed under differential focuses for 5080 levels by an Olympus Provis AX80 with a microscopic digital camera DP70 at 4080 x 3072 pixels, using 2-3 gigabytes of disk spaces per one cell. Six series of cells were analyzed. The serial images were reconstructed precisely on Adobe Photoshop, and compared with the existing data of porcine arachnocytes. In human, arachnocytes contained multiple droplets of various sizes, unlike that of pig which stored vitamin A—n mono- or bi-lipid droplets. Typical arachnocytes of pig with full-blown and wide spread processes surrounded the sinusoids in a well-defined manner, but the processes of human arachnocytes were poorly organized. Their arms/legs and fingers were literally irregular, qualitatively and quantitatively, with uneven thicknesses and difficult-to-predict orientations. Their outline was characterized by frequent knobs and notches, making a “polygenu” profile with multiple angulations. Cell body was rather rich in cytoplasm. Hairs or microspines which were typical of pig arachnocyte, were very rare in human. This observation is the first of its kind to visualize the arachnocytes in human liver. Their processes were unexpectedly very irregular. The observed structures suggest little to support the idea that arachnocytes would actively contract “to control sinusoidal caliber. Rather the processes represent a passive reinforcement of the sinusoids. The multiple angulations in their processes with many knobs and notches suggest most likely that they are “collapsible” structure to accommodate the frequently-occurring collapse of the sinusoids. Supported by the Reverse Brain Drain (RBD) Project Grant #4703 (to WE), and NationScience and Technology Development Agency, Thailand.


**FLUORESCENCE MICROSCOPY: A HIHER UNOBSERVED NATURE OF ARACHNOCYTES**

Narumon Chunwimalueang, Wichai Ekataksin, Pawinee Pyachaturawat, Thamrong Chirachariyavet

Liver Research Unit Dept of Clinical Tropical Medicine, Faculty of Tropical Medicine Graduate Program. Dept of Physiology, Faculty of Science. Sarotoxology and Forensic Unit Dept of Pathology, Faculty of Medicine Ramathibodi, Mahidol University, Bangkok; Dept of Anatomy and Cell Biology, Tokyo Medical and Dental University School of Medicine, Tokyo, Japan.

The principal vitamin A compounds such as retinol and retinyl esters, can be found primarily in the hepatic stellate cells or arachnocytes (Ekataksin and Kaneda, 1 999). Under physiological conditions, arachnocytes store 80% of total vitamin A in the whole body as lipid droplets in the cytoplasm, and regulate...
both transport and storage of vitamin A. Parenchymal liver disease can interfere with hepatic store and metabolism of vitamin A. Chronic liver injury leading to collagen deposition has been found associated with altered retinol storing function of arachnocytes. Retinoid loss is a notable feature characteristic of fibrosis, and is assumed as a prerequisite in response to injury and subsequent fibrogenic pathogenesis. We applied the fluorescence microscopy to detect subtle changes in autofluorescence of retinyl esters; the latter serves as an indicator of vitamin A status. Livers of healthy subjects and alcoholics were obtained from Forensic Autopsy Unit with informed consents of Human Ethical Committee, Ramathibodi Hospital. The alcoholic patient had history of habitual drinking and the liver was documented as having a mild fatty change with a tan-yellowish appearance. After flushing with normal saline and perfusion-fixation with double strength formalin, frozen sections of liver tissue were performed at 50-μm thickness on a sliding microtome (Sakura, Pteratome CRM440) with an electronic freezing unit (Carl Zeiss, Microm K400) and immediately examined by DF fluorescence microscopy (Olympus Provis AX80). Frozen sections were also stained for oil red 0 with hematoxylin as counterstain. Routine liver preparations were stained for H&E and Masson trichrome. Under wide ultraviolet fluorescence, 330-385 nm excitation, morphological examination revealed heretofore undocumented patterns in the human liver. In normal liver, the autofluorescence from lipid droplets appeared with a homogeneous distribution in all zones, exhibiting a more or less tendency of higher intensity in the peripheral zone. However, in alcoholic patient, the fluorescence was inhomogeneous. Clusters of increased fluorescence brilliantly glaring were observed here and there; for every 5-20 lobules at least one cluster was encountered. The cluster assumed a round, ovoid or ill-defined shape. The diameter of a cluster ranged between 200-800 μm covering a good number, 20-70, of aggregated lipid droplets. Each of these aggregates represented an individual vitamin A-storing cell in which a few to dozens of various-sized droplets were closely packed together. A small cluster could be found in peripheral, intermediate, or central lobular zone, while a larger cluster could span over two or three zones. While the droplets of general arachnocytes had a dimension of 2-6 μm, that of the arachnocytes within the cluster were invariably noticed with extraordinarily sizes, measuring 12-20 μm in diameter. These gigantic droplets emitted accentuated fluorescence that lasted several minutes before fading. Occasionally, a gigantic droplet was present solitarily in an arachnocyte unassociated.

DEVELOPING A HISTOLOGY ATLAS LARGEST IN THE WORLD: PANORAMIC RECONSTRUCTION COMBINED
Borimas Hanboonkunupakarn, Wichai Ekataksin, Gedusa Pattanapen, Chokchai Ekataksin, Narumon Chanwimalueang, Kazuo Yamashita
Liver Research Unit Dept of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand. Dept of Anatomy, Tokyo Medical and Dental University School of Medicine, Tokyo, Japan Dept of Anatomy, Nippon Medical School, Tokyo, Japan

T HE education of histology is achieved through microscopic training. However, the field of visual perception under the lens is limited to the small area which will be further sacrificed at the higher magnification. During the course of medical school, many students have experienced a hard time identifying the structures assigned, due to the imperfection of specimens, quality and quantity; excellent specimens are precious and sometimes difficult to reproduce or unaffordable by the Course budget. With the advent of multimegapixel digital camera and high-resolution large-format printing technology, we now can produce a large-scale mapping of histological structures, which has proved as a powerful educative/illustrative medium to medical students and public alike. Preparations of different organ systems from Liver Research Unit collections were carefully selected and scrutinizingly evaluated. To create the large-scale map, i.e., a gigantic image, the specimens were photographed under appropriate magnification through an Olympus Provis AX80 with a microscopic digital camera DP70 at highest resolution 12 megapixels (4080 x 3072); a single image TIFF file was 35.7 MB in size. Serial images were taken in a matrical series, 50-700 shots per one mapping and 1.7-23.6 OB of hard disk spaces were required for raw TIFF files of one job series. Images were processed and reconstructed 1 on Apple computers Power Macintosh 04 or 05 and saved as a Photoshop ROB at 150-400 dpi. Using a ColorOate software, post RIP (Rasterized Image Processing) file sizes were expanded to 1.5-3.0 folds of the originals. The final files were outputted on a large-format inkjet printer (HP DesignJet 5500) using 6 colors at 600 dpi. Maps were laminated for anti-DV protection prior to public display. A usual finished dimension was 1-1.5 m in width and 1.2-3 m in height. We have generated more than thirty large-scale histology maps, about twenty of them were of hepatobiliary system in health and diseases. The extrahepatic organs included esophagogastric junction, stomach, cervix, testis, pituitary, and spinal cord. The printed work could be either placed flat on a large viewing table or hung vertical on a sliding rail. Each had been found with so-far unforeseen benefits with points of interest and artistic virtues. Liver maps well illustrated both familiar and unfamiliar structures in close vicinity, such as liver lobules and isolated arteries, respectively. Esophagogastric
junction and stomach maps clearly demonstrated the position and transition of different cell types and their relations. The tremendously dense venous sinus in the lamina propria was strikingly recognized in the map of cervix uteri with fornix vaginae. The honeycomb architecture was beautifully shown in testicular interstitium. The distribution of acidophils, basophils, and chromophobes in pituitary.


MICROCIRCULATORY IMPAIRMENT IN HEPATIC ISCHEMIA-REPERFUSION INJURY: A MORPHOLOGICAL STUDY OF PIG LIVER UNDER EXPERIMENTAL TRANSPLANTATION

Borimas Hanboonknupakarn, Wichai Ekataksin, Guido Alsfasser, Peter Schemme, Bernhard Urbanhek, Robert S McCuskey, Ernst Klar
Liver Resealth Unit Dept of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; Dept of Anatomy, Tokyo Medical and Dental University School of Medicine, Tokyo, Japan; Dept of Surgery, University of Heidelberg Medical School, Heidelberg, Germany; Dept of Medical Microbiology and Hygiene, Klinikum Mannheim, University of Heidelberg, Mannheim, Germany; Dept of Cell Biology and Anatomy, College of Medicine, University of Arizona Health Sciences Center, Tucson, Arizona, USA.

BACKGROUND: Liver transplantation is a treatment of choice for patients with end-stage liver diseases. However, the operation involves the state of ischemia followed by reperfusion (I/R) which worsens the results and exacerbates the complications. Among the recognized determinants of graft function during the early postoperative course after transplantation is the altered portal and arterial circulation (Klar et al, 1996). The microcirculatory impairment, which can be induced by I/R, is strongly associated with poor graft survival rate. Recently, it was reported that large amount of arterial blood escapes from parenchymal perfusion into systemic circulation, leading to organ failure (Mehrabi et al, 1998). To date, the morphofunctional mechanism(s), including the pathway that can account for circulatory redistribution, in the liver under I/R injury has not been identified.

Objectives: We aimed to characterize the structural changes that can account for the dramatic reduction in portal inflow and the drastic increase in hepatic arterial influx, and to identify the most-likely shunt pathway(s).

Materials and Methods: Experimental liver transplantation was prepared in pigs (n=6). Under general anesthesia, laparotomy was performed, followed by a dissection of porta hepatis. Portal vein and hepatic artery were clamped for 30 minutes, and then released (pringle’s maneuver). After 10 minutes of reperfusion, the livers were perfused with sterile saline until perfusate became clear. Vascular injection was done with colored-gelatin for examination under light microscopy (LM) and Batson #17 plastic mixture for microcorrosion casts studied under scanning electron microscopy (SEM). The gelatin-injected liver was cut perpendicular to the longitudinal axis into 12-14 segments and processed routinely.

Results: Under I/R, hydropic swelling was striking in parenchymal cells. In the lobules, hepatocytes assumed round-shaped cells mostly in the intermediate zone, whereas in the peripheral and centrilobular zones they formed rosette. White cell aggregations were frequently encountered along the narrowed sinusoids, forming chains and clusters. Endothelial cells showed varying degrees of swelling as evidenced by the thickened cytoplasm and enlarged nuclei. The lobular profiles were distinguished into two types, occluded lobules, recognized with diffusely collapsed sinusoids and distinctly shrunk central veins, and unoccluded lobules, recognized with open sinusoids and widened central veins. Morphoquantitative mapping revealed that the occluded lobules in different segments accounted for 80% rostrally and 60% caudally. In portal tracts, distended hepatic arteries and recoiled portal veins were common. The isolated arterioles were found with a prominent diameter. Hepatic vein’s wall was filled with dilated vasa varanum which emptied through the transintimal vasal outlets measuring 20-25 JLm in width. Under SEM, the dense plexus of vasa were observed. Their drainage through vasal outlets were found as plastic gloes sprouting into the luminal surface of hepatic vein, continuous with the venules of the vasa via a slender connector.

Discussion and Conclusions: The narrowing of sinusoids, white cell sequestration, endothelial cell swelling, hepatocyte ballooning, and rosette formation increased sinusoidal resistance. The recoil of portal vein and the shrinkage of central vein suggested the elevation of presinusoidal and postsinusoidal resistance, respectively. This reduces portal flow while increases arterial, resulting in a redistribution of intrahepatic circulation and a subsequent arterosystemic shunt. The data from SEM show an increased arterial circulation in the extraportal compartment, indicative of a functional arterosystemic shunt pathway. With the increasing practice of partial liver transplantation, the implication ofinhomogeneous injury in different organ segments, as revealed by the two lobular populations, would significantly influence the process of making decision in selecting donor grafts to best fit recipient individuals of years to come.

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NEUROTOXIC EFFECT OF THE INTERMITTENT INJECTION OF ARTEMETHER IN A MOUSE MODEL

A Nonprasert¹, S Pukrittayakamee¹, W Supanaranond¹, AM Dondorp¹,², N Day², NJ White¹,²

¹Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand; ²Centre for Tropical Medicine, Nuffield Department of Clinical Medicine, John Radcliffe Hospital, Oxford, United Kingdom

INTRAMUSCULAR administration of high doses of the oil soluble antimalarial artemisinin derivatives artemether and arteether to experimental mammals produce an unusual pattern of selective damage to brainstem centres predominantly involved in auditory processing and vestibular reflexes. We have shown recently in an adult Swiss albino mouse model that constant exposure either from depot intramuscular injection of artemether, or constant oral intake results in more neurological abnormalities and mortality than either artemether or artesunate given by any other route. The present study shows the neurotoxic effect depending on the total doses of intramuscular artemether injection in mice. Intramuscular artemether given at a total dose of 1400 - 2800 mg/kg caused dose-dependent neuropathological damage to the brainstem even in mice without behavioural change. There was no neurotoxicity in mice receiving at a total dose of equal or less than 700 mg/kg. The correlation between severity score of neuropathology and balance was observed in the experimental mice (p = 0.002). The neurons in the mid brain trapezoid nucleus and the pontine reticular nucleus were the most sensitive to the toxic effects of artemether. Most of the mice with neuropathological changes showed behavioural changes, whereas in some mice without gait disturbance, had neuropathological damage. There may be a reversible component to artemether neurotoxicity in a mouse model. This finding suggested that intramuscular artemether is neurotoxic even given spacing doses of 3, 6 or 8 weeks gap.

DOWN – REGULATION OF TIGHT JUNCTION MRNAS IN HUMAN ENDOTHELIAL CELLS CO – CULTURED WITH PLASMODIUM FALCIPARUM – INFECTED ERYTHROCYTES

Pannapa Susomboon¹,², Yaowapa Maneerat¹, Paron Dekumyoy¹, Thareerat Kalambaheti¹, Morintosh Iwagami¹, Kanako Komaki-Yasuda¹, Shin-ichiro Kawazu¹, Noppadon Tangpukdee¹, Sornchai Looareesuwan¹, Shigeyuki Kano³

¹Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, 420/6 Ratchavithi Road, Bangkok 10400, Thailand; ²Department of Tropical Pathology, Faculty of Tropical Medicine, Mahidol University, 420/6 Ratchavithi Road, Bangkok 10400, Thailand; ³Department of Helminthology, Faculty of Tropical Medicine, Mahidol University, 420/6 Ratchavithi Road, Bangkok 10400, Thailand; ⁴Department of Microbiology and Immunology, Faculty of Tropical Medicine, Mahidol University, 420/6 Ratchavithi Road, Bangkok 10400, Thailand; ⁵Department of Microbiology and Immunology, Faculty of Tropical Medicine, Mahidol University, 420/6 Ratchavithi Road, Bangkok 10400, Thailand; ⁶Department of Appropriate Technology Development and Transfer, Research Institute, International Medical Center of Japan, 1-21-1 Toyama, Shinjuku, Tokyo 162-8655, Japan

To understand the mechanism of sequestration in the microvasculature of patients with falciparum malaria, we examined the patterns of expression of mRNAs for adhesion molecules (ICAM-1, VCAM-1, and E-selectin) and tight junction molecules (occludin, vinculin, and ZO-1) in human umbilical vein endothelial cells (HUVECs) co-cultured with Plasmodium falciparum-parasitized red blood cells (PRBCs) in vitro. The PRBCs were collected from patients with uncomplicated, severe, or cerebral malaria (CM). Patterns of mRNA expression in HUVECs co-cultured with PRBCs were examined by real-time quantitative reverse transcription-polymerase chain reaction (RT-PCR). Levels of mRNAs for all the three adhesion molecules increased with increased culture time within 3 h, regardless of the source of the PRBCs. In contrast, the patterns of mRNA expression for the tight junction molecules varied between the different co-cultures. When HUVECs were cultured with PRBCs from uncomplicated malaria patients, levels of mRNAs for tight junction molecules increased according to the culture time. HUVECs co-cultured with PRBCs from severe malaria patients showed no change in the mRNAs levels during 3 h of observation. When HUVECs were cultured with PRBCs from CM patients, levels of mRNAs for tight junction proteins decreased according to the culture time. Although the mechanisms underlying these phenomena are not clear, our results suggest that PRBCs can alter expression of tight junction proteins in endothelial cells at the site of sequestration and thereby influence disease severity.

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EFFICACY OF BENZIMIDAZOLE CARBAMATE ON AN INTESTINAL FLUKE CO-INFECTED WITH NEMATODES

Jitra Waikagul, Dorn Watthanakulpanich, Chatree Muennoo, Wanna Maipanich, Surapol Sa-nguankiat, Somchit Phubampen

Department of Helminthology, Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand

The efficacy of a single dose of benzimidazole, drugs commonly used for the treatment of Ascaris and hookworm, was evaluated against one of the tiny-sized intestinal flukes, Haplorchis sp. in the endemic area where mixed infections of roundworms and flatworms existed. At day 7 after treatment, albendazole (400 mg) induced 42.5% cure rate, mebendazole (500 mg) a cure rate of 32.4%, on the other hand, praziquantel (40 mg/kg) gave 94.6% cure rate and the placebo at 15.9%. At the single dose, benzimidazole could not completely expelled the haplorchid; but could reduce one third to two fifth of the infection, similar to the drugs efficacy against Trichuris infection.


CUTANEOUS FASCIOLIASIS: A CASE REPORT IN VIETNAM

Le Thi Xuan1, Nguyen Thien Hung2, Jitra Waikagul3

1Department of Parasitology, Faculty of Medicine, University of Medicine and Pharmacy, Ho Chi Minh City; 2Medic Medical Center, Ho Chi Minh City, Vietnam; 3Department of Helminthology, Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand

A 40 year-old woman living in Gialai, Kontum, Vietnam, developed a red solid mass in the epigastric region. From ultrasound investigation, liver abscess and myositis of the intercostal muscle was diagnosed. Two weeks after treatment with antibiotics, the mass disappeared, but a migratory track developed in the right upper quadrant of the abdomen. An aspiration of the vesicular end of the serpiginous track showed a light brown, living worm that was later identified as an immature Fasciola sp. This is the first case report of cutaneous fascioliasis in the form similar to creeping eruption.


ANALYSIS OF SEQUENCE VARIATION IN GNATHOSTOMA SPINIGERUM MITOCHONDRIAL DNA BY SINGLE-STRAND CONFORMATION POLYMORPHISM ANALYSIS AND DNA SEQUENCE


*Department of Helminthology; *Department of Tropical Nutrition and Food Science, Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand

Morphological variations were observed in the advance third stage larvae of Gnathostoma spinigerum collected from swamp eel (Fluta alba), the second intermediate host. Larvae with typical and three atypical types were chosen for partial cytochrome c oxidase subunit I (COI) gene sequence analysis. A 450 bp polymerase chain reaction product of the COI gene was amplified from mitochondrial DNA. The variations were analyzed by single-strand conformation polymorphism and DNA sequencing. The nucleotide variations of the COI gene in the four types of larvae indicated the presence of an intra-specific variation of mitochondrial DNA in the G. spinigerum population.


THE CURRENT SITUATION REGARDING THE ESTABLISHMENT OF NATIONAL ETHICAL GUIDELINES FOR BIOMEDICAL RESEARCH IN THAILAND AND ITS NEIGHBORING COUNTRIES

Kojima S, Waikagul J, Rojekittikhun W, Keicho N

Asian Center of International Parasite Control, Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand

This study discusses the establishment of ethical guidelines for ethical review for biomedical research performed in Thailand, and to some extent, in neighboring countries. There are differences, from country to country, at national and institutional levels regarding guidelines for biomedical research. Only a handbook issued by Mahidol University describes guidelines for human genetic research and on research dealing with reproductive technology. Both these areas require special consideration to avoid violating human dignity, rights, and confidentiality. This indicates that further efforts should be made to establish research guidelines and/or principles dealing with the human genome.

DIAGNOSTIC VALUES OF IgG4 IN HUMAN GNATHOSTOMIASIS
Malinee T Anantaphruti, S Nuamtanong, P Dekumyoy
Department of Helminthology, Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand

The diagnostic values of immunoglobulin G subclass antibodies from patients with gnathostomiasis were assessed by immunoblot technique. Antigen was prepared from crude extracts of Gnathostoma spinigerum advanced third-stage larvae obtained from naturally infected eels. The sera were obtained from 14 parasite-confirmed gnathostomiasis cases, 63 patients with other helminthic infections and 13 healthy controls. Nine prominent IgG4 reactive bands appeared with molecular weights of 94, 51, 47, 43, 38, 24, 21, 20 and 15 kDa. The diagnostic sensitivity of each of the nine reactive bands ranged from 100% to 64.3% in 14 parasite-confirmed gnathostomiasis cases. All (100%) confirmed cases recognized the 21 kDa antigenic band, but not other helminthic infections or parasite-free control. Recognition of 21 kDa antigen in G. spinigerum advanced third-stage larvae crude extracts is the most specific diagnostic marker for human gnathostomiasis, with 100% sensitivity and specificity. The 20 and 24 kDa protein bands were additional diagnostic bands for confirming diagnosis of infection where the 21 kDa band was faint. No specific binding of IgG1, IgG2, or IgG3 antibodies was observed in any sera from confirmed gnathostomiasis cases.


PREVALENCE OF STRONGYLOIDES IN NORTHERN THAILAND AND TREATMENT WITHIVERMECTIN VS ALBENDAZOLE
Ponganant Nontasut¹, Chatree Muennoo¹, Surapol Sa-nguankiat¹, Sutep Fongsri², Adulsak Vichit³
¹Department of Helminthology, Faculty of Tropical Medicine, Mahidol University, Bangkok; ²Provincial Public Health Office, Chiang Mai; ³Division of Communicable Diseases Control, Ministry of Public Health, Region 10, Chiang Mai, Thailand

The stools of 697 cases were examined by agar plate technique at Tambon Makam Luang, Sun Pa Tong District, Chiang Mai; there were Strongyloides stercoralis 15.9%, Opisthorchis viverrini 5.1%, intestinal fluke 0.1%. Treatment with ivermectin 78 cases and albendazole 33 cases of strongyloidiasis gave cure rates at 98.7% and 78.7%, respectively. Alkaline phosphatase in some patients were increased at mild level after treatment. Side effects in ivermectin group were anorexia, nausea, diarrhea, diffuse itching and drowsiness; and in albendazole group were nausea and diarrhea. The efficacy of single dose and mild side effects suggest ivermectin as drug of choice for strongyloidiasis treatment.


LIVER FLUKE AND MINUTE INTESTINAL FLUKE INFECTIONS IN SA KAEO AND NAN PROVINCES, THAILAND
Department of Helminthology, Faculty of Tropical Medicine, Mahidol University 420/6 Ratchawithi Road, Bangkok 10400, Thailand

The prevalence of liver fluke infection (Opisthorchis viverrini) by Kato’s modified thick smear technique in Aranyaprathet District, Sa Kaeo province, eastern Thailand, in January 2004. Of the 545 stool samples collected, 261 (47.9%) contained small-sized eggs resembling O. viverrini eggs. The detected prevalence rate was higher than the prevalence in the same region reported by the Ministry of Public Health, at 5.3%. Fifty-nine infected cases were dewormed. After administration of praziquantel followed by laxative, whole-day stool samples were collected and washed by sedimentation method. Worms were collected under a stereomicroscope. O. viverrini adult worms were recovered in all 59 cases, and only 4 had mixed infections with minute intestinal flukes (Haplochis taichui). The same study was performed in Chaloem Phra Kiat and Ban Lung Districts, Nan Province, in northern Thailand, where the prevalence rate reported by the Ministry of Public Health was 20.6%. The result showed that the prevalence of O. viverrini/H. taichui in the 2 areas were 27.6% and 47.1% respectively. All 88 cases with small-sized eggs in Chaloem Phra Kiat District harbored H. taichui, while 16/84 cases in Ban Lung were mixed infection of O. viverrini and Haplochis sp.


PARAGONIMIASIS IN NAN PROVINCE, NORTHERN THAILAND
Watthanakulpanich D¹, Waikagul J¹, Dekumyoy P¹, Muangkhum P¹, Praevanit R¹, Mongkhonmu S²
¹Department of Helminthology, Faculty of Tropical Medicine, Mahidol University, Bangkok; ²Thung Chang Hospital, Thung Chang District, Nan Province; ³Bangkok School of Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

Two cases of paragonimiasis were identified within the hill-tribe population living on the Thai-Laotian border of Nan province, northern Thailand, where information on Paragonimus was then
showed Paragonimus populations. Nine enzymes tested from ten enzymes recovered from two species of these species. Twelve loci were obtained from these species. Key to the species of Thai Paragonimus should be used to differentiate these species. Isozyme patterns for acid phosphatase (Acph), a single monomorphic band, which was seen in both species. Isozyme patterns for acid phosphatase (Acph), dehydrogenase (Mdh), showed three banding patterns. Three of twelve loci in Paragonimus heterotremus and Japanese P. miyazakii were assayed using polyacrylamide gel electrophoresis to distinguish between the isolates. Twelve loci were obtained from ten enzymes recovered from two species of Paragonimus populations. Nine enzymes tested showed only a single band, whereas one enzyme, malic dehydrogenase (Mdh), showed three banding patterns. Three of twelve loci in Paragonimus heterotremus and one locus in P. miyazakii were polymorphic, whereas nine loci were a single monomorphic band, which was seen in both species. Isozyme patterns for acid phosphatase (Acph), adenylate kinase (Ak), hexokinase (Hk) and malic dehydrogenase (Mdh) were identical in all Paragonimus. Esterase (Est), phosphoglucomutase (Pgm) and 6-phosphogluconate dehydrogenase (6Pgd) showed slightly different patterns, while glucose phosphate isomerase (Gpi), glucose-6-phosphate dehydrogenase (G6pdh) and malic enzyme (Me) showed remarkable differentiations, indicating a species-specific marker between the two different populations.


CHAETOTAXY OF NEWLY EXCYSTED METACERCARIAE AMONG FIVE SPECIES OF THAI PARAGONIMUS

Chalit Komalamisra1, Supawadee Bunchuen2, Jitra Waikagul1, Emsri Pongponratn1

1Department of Helminthology; 2Department of Tropical Pathology, Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand

S CANNING electron microscopy was used to study the papillae distribution (chaetotaxy) among five species of newly excysted Paragonimus metacercariae (P. bangkokensis, P. harinasutai, P. heterotremus, P. siamensis, and P. westermani). Comparative data on the distribution of papillae in these species indicate considerable differences in the arrangement of papillae on the surfaces of the oral and ventral suckers. The numbers of papillae in the mouth of the oral sucker should be used to differentiate these species. Key to the species of Thai Paragonimus excysted metacercariae are given.


ISOZYME DISCRIMINATION BETWEEN PARAGONIMUS HETEROTREMUS AND P. MIYAZAKII

Chalit Komalamisra

Department of Helminthology, Faculty of Tropical Medicine, Mahidol University, 420/6 Ratchawithi Road, Bangkok 10400, Thailand

T HE lung flukes, Thai Paragonimus heterotremus and Japanese P. miyazakii were assayed using polyacrylamide gel electrophoresis to distinguish between the isolates. Twelve loci were obtained from ten enzymes recovered from two species of Paragonimus populations. Nine enzymes tested showed only a single band, whereas one enzyme, malic dehydrogenase (Mdh), showed three banding patterns. Three of twelve loci in Paragonimus heterotremus and one locus in P. miyazakii were polymorphic, whereas nine loci were a single monomorphic band, which was seen in both species. Isozyme patterns for acid phosphatase (Acph),...
Three-days water extract has larvicide effect against *Cx. quinquefasciatus* (LC$_{50}$ = 0.008% wet w/v) more than 1-day and 10-days extract, while the alcoholic extract of different maceration days gave similar larvicide effect (LC$_{50}$ = 0.006%, 0.005% and 0.005% wet w/v). However, longer exposure to every extracts will increase the percent of larval mortality. *Cx. quinquefasciatus* revealed more susceptible to alcoholic extract of *Piper retrofractum* than *Ae. aegypti* (for 1-day extract at 24 hours exposure LC$_{50}$ = 0.006%, LC$_{95}$ = 0.012% and LC$_{95}$ = 0.016%, LC$_{95}$ = 0.042% respectively). The high efficiency and ease preparation of the *Piper retrofractum* extract made it a method of choice for people to use as the household phytoinsecticide to control mosquito larvae.

**A NOTE ON DNA IDENTIFICATION OF MOSQUITO SPECIMENS FOR LONG-TERM PRESERVATION**

Peangpim Burivong, Chamnarn Apiwathnasorn, Yudthana Samung, Samrerng Prommongkol, Somjai Leemingsawat

Department of Medical Entomology, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

The cytochrome oxidase subunit I (COI) region of mitochondrial DNA (mtDNA) and internal transcriber spacer 2 (ITS2) ribonuclear DNA were used to amplify specific regions from total genomic DNA of preserved *Anopheles minimus* Theobald collected from Ratchaburi Province, Thailand. The universal primers were used to compare the techniques for long-term preservation. The experiments were conducted using the offspring of each individual mosquito. Mosquitoes were reared for F1 generation which then preserved as frozen and dried specimens. Frozen mosquitoes yielded amplified PCR product for both COI and ITS2 regions, whereas dried preserved mosquitoes yielded PCR product for only ITS2 region.

The comparison of DNA recovery by PCR amplification of preserved techniques for dried mosquitoes, stored for up to 22 years, showed that pin steel specimens were more efficient than paper-point specimens in the way that paper-point technique needed the nail polisher for attachment. This polisher might cause damage of DNA molecule. The ability to amplify mtDNA and ribonuclear DNA from different specimen preservations should be considerable in order to select the method of preservations for specific purposes and advance uses of these specimens in the future.

**PRELIMINARY ISOENZYME STUDY IN ANOPHELES SUNDAICUS FROM PHANG NGA, A TSUNAMI-AFFECTED AREA IN THAILAND**

Rutcharin Potiwat, Narumon Komalamisra, Chamnarn Apiwathnasorn, Yudthana Samung, Samrerng Prommongkol, Supatra Thongrungrukiat, Karnchana Pornpiminworakij, Somjai Leemingsawat, Achara Asavanich

Department of Medical Entomology, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

*A. sundaicus* has been known as a potential vector of human malaria parasites and is a primarily anthropophilic species along coastal Thailand. This species is attracting more attention from the Ministry of Public Health owing to its role as a malaria vector and its extensive post-tsunami breeding in coastline areas of Phang Nga Province. A comparative study was conducted to determine the dispersal and origin characteristics of the *A. sundaicus* population inhabiting both affected and unaffected areas, by electrophoresis technique. The screening of 16 enzyme systems--HK, ADK, 1-GPDH, FUM, XDH, EST, LDH, MDH, PGM, PGI, AOX, ME, MPI, AMY, ADH, and TO--comprising 20 loci, revealed allelic variation and genetic polymorphism among the *A. sundaicus* population. Sixteen--HK, 1-Gpdh, Xdh, Ldh, Pgm, Gpi, Aox, ME, Mpi, Amy, To, Est-1, Est-2, Est-3, Est-5 and Adh--presented a monomorphic locus, and 4 loci--Mdh, Adk, Fum and Est-4--showed multiple electromorphic locus in all of the studied populations. These results suggest that the characteristics of both mosquito populations were likely similar and possibly of the same origin.

**EFFICACY OF WATER DISPERSIBLE GRANULE FORMULATION OF BACILLUS THURINGIENSIS ISRAELENSIS (VECTOBAC®WDG) AND BACILLUS SPHAERICUS (VECTOLEX®WDG) TO CONTROL CULEX SITIENS IN BRACKISH WATER PONDS IN TSUNAMI-AFFECTED AREAS OF PHANG-NGA PROVINCE, SOUTHERN THAILAND**

Yuwadee Trongtokit1, Samrerng Prommongkol1, Yudthana Samung1, Theerawit Phanphoowong1, Chamnarn Apiwathnasorn1, Narumon Komalamisra1, Wanchai Nudda2, Paipat Pho-ngarn2, Panuwath Panpairoth2, Somjai Leemingsawat1


CULEX SITIENS is the predominant mosquito species in brackish water pools in Tsunami-affected areas in Phang-Nga province, Southern Thailand. Microbial control agents, Bacillus thuringiensis israelensis (VectoBac®) and B. shaericus (VectoLex®) in the form of water dispersible granule (WDG) formulations, were evaluated for their efficacy to control this mosquito species. The efficacy of VectoBac®WDG (500 g/ha), VectoLex®WDG (750 g/ha) and a mixture of VectoBac®WDG (500 g/ha) and VectoLex®WDG (750 g/ha) was evaluated 24, 48 and 72 hours post-treatment. All 3 treatments gave satisfactory control of 99-100% reduction within 72 hours post-treatment in the 3rd - 4th larval instar and pupae population. This pilot study, is first of such report, indicating that VectoBac®WDG and VectoLex®WDG were highly effective to control mosquito species in brackish-water habitats under field conditions in Thailand. In addition, these agents were observed to be safe to non-target organisms found in brackish-water environment.

Impact of Tsunami on Occurrence of Mosquito Vectors in the Affected Areas of Phang Nga Province

Chamnarn Apiwathnasorn, Yudthana Samung, Samrerng Prummongkol, Yuwadee Trongtokit, Theerawit Phanphoowong, Narumon Komalamisra, Somjai Leemingsawat, Achara Asavanich

Department of Medical Entomology, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

A earthquake in the Indian Ocean caused the Dec 26 tsunami, which killed more than 200,000 people and caused immense property damage. In Thailand, tsunami hit Andaman Coast (954 kilometres in length including six provinces, namely: Ranong, Phang Nga, Phuket, Krabi, Trang and Satun) and caused great loss of life and destruction to buildings and infrastructure with an estimation of 7.8 million dollars. 70% of the damages occurred in Phang Nga Province and 53,203 people of 12,293 families became its victims. The tsunami flooded the coastal areas up to two to three kilometers inland and contaminated surface waters in the inundated areas with seawater. The Department of Mineral Resources of MONRE carried out an assessment of the impact of sea water intrusion into surface water bodies and reported 96.7% of the sampled water bodies as of 1 February, 2005 were contaminated by seawater. It was estimated that 20,300 hectares of land on the mainland were inundated and about 1,505 hectares of agricultural land have been

RepeLent Activity of Products Containing Deet, HIPC, PMD and Plant Essential Oils Against Coastal Species of Mosquito in Phang-Nga Naval Base, Tsunami Affected Area

Kaewmala Palakul, Yuwadee Trongtokit, Narumon Komalamisra, Samrerng Prummongkol, Yudthana Samung, Theerawit Phanphoowong, Chamnarn Apiwathnasorn, Somjai Leemingsawat

Department of Medical Entomology, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

The efficacy of 5 commercial repellents (2 products contained synthetic chemical compound as active ingredient, and the other 3 products contained botanical extracts as active ingredient) and 4 laboratory prepared products which had plant essential oils as active ingredient were evaluated against coastal species of mosquito in the Phang-Nga naval base after tsunami. A 10x10x10 Latin square design was used to randomize the test subjects for possible individual difference for mosquito attraction. One gram of each product was applied to each volunteer’s leg (from knee to ankle). Mosquitoes attracted to treated areas of human baits were observed and collected from 1800 to 2200 hours. All 5 commercial products, which each contained active ingredient as deet (di-methyl benzamide), HIPC (hydroxyethyl isobutyl piperidine carboxylate), PMD (p-menthane diol), citronella oil, or tumeric oil and eucalyptus oil combination provided complete repellency throughout the observation periods of 4 hours. For the laboratory prepared products, each kind of plant essential oils (makaen oil, galangal oil and oil combination of qinghaosu, may chang and kaffir lime) was individually prepared as active ingredient in cream formulation. The preparation with oil combination was also formulated into ointment. All of the prepared repellents gave complete protection for 2-3 hours. The results indicate that the repellent activity of the commercial products was better than the laboratory formulated products; however, 2-3 hours of repellency would be sufficient to protect against evening mosquitoes if people use them before retiring to sleep under a bednet. Locally formulated repellents with these natural essential oils could be useful in where low cost alternatives are needed and in places where native aromatic plants are grown.
severely affected by salt water intrusion. The present study was conducted to determine an impact of tsunami on mosquito occurrence, abundance, distribution, and breeding places in the affected areas of Phang Nga Province, southern Thailand. We conducted mosquito surveys in tsunami-affected areas during February-April, 2005. The mosquitoes proliferated extensively in the available water sources contaminated with seawater within a month after tsunami occurrence. It was shown that the water logging with full sunlight provided excellent breeding places for Anopheles sundai cus and Culex sitiens. The former is considered as a potential vector of malaria along the coastal areas of Thailand and the latter is a biting nuisance mosquito species. It revealed that almost all sites along the coastline were positive for the presence of those mosquito larvae with maximum larval density of more than 150 larvae per dip. Their breeding places varied in size from small pits (1x2 m²) to large water reservoirs such as pit lakes and water collections of abandoned tin mines (220x730 m²) having a broad salinity ranging from 100 to 11,300 ppm, dissolved oxygen 1.3 to 24.8 mg/l, pH 6.4 to 8.6 and water temperature 29.5 to 34.0 °C. Stagnant water under full sunlit infested with filamentous green algae, Spirogyra sp. or floated pieces of dried leaves, particular grasses was most favourable breeding place of An. sundai cus where as Cx. sitiens preferred to breed in more putrefied water. A total of 4,948 mosquitoes belonging to six species was collected by human landing catches. The most abundant species was Cx. sitiens (81.6%). Only 430 (8.7%) An. sundai cus, 374 (7.6%) Cx. quinquefasciatus and 7 (0.1%) Ma. uniformis were caught. Regarding their biting cycles, An. sundai cus and Cx. sitiens showed nocturnal activity, with a single peak during 2000-2100 hours and 1900-2000 hours, respectively. The maximum biting rate of An. sundai cus was 35 mosquitoes per person-hour and 135 mosquitoes per person-hour for Cx. sitiens. Regarding malaria transmission, Anopheles sundai cus is of particular interest and its presence in this environment cannot be overlooked, irrespective of the tsunami event.

THE giant wave tsunami attacked six coastal provinces along the Andaman coast line of Thailand in the morning of December 26th, 2004. It caused remarkable damage, loss of life and change in large scale of the environmental areas. Several inland water sites became brackish water due to the filling of the seawater and became the suitable breeding site of Anopheles sundai cus and Culex sitiens. In order to control the mosquitoes, the insecticide susceptibility status of the field larvae and mosquitoes was performed under laboratory conditions. Larvae bioassay tests were conducted using WHO standard method. Three larvicides, the temephos, malathion, and plant extract (ethanolic extract of Piper retrofractum Vahl,) were used in the experiment. The results revealed that Culex sitiens was more susceptible to temephos than malathion and the plant extract, LC50 range from 0.0008-0.0014 ppm., 0.0046-0.0078 ppm., and 5.3180-10.1030 ppm., respectively. Culex quinquefasciatus showed more tolerate to every tested larvicides than Culex sitiens. Adults bioassay test using WHO test kit and diagnostic dose of 5% malathion, 0.75% permethrin and 0.05% deltamethrin and 4% DDT were conducted. The results revealed that Culex sitiens and Anopheles sundai cus were susceptible to all tested insecticides. The LT50 of 5%malathion were range from 25.7 – 26.0 min in Culex sitiens, and 44.7 min in Anopheles sundai cus. In addition Culex quinquefasciatus also showed susceptible to malathion with the LT50 of 19.7 min. However, it had high tolerate to both pyrethroid insecticides with LT50 of 33.1 min. for 0.75% permethrin and 19.6 min. for 0.05%deltamethrin and showed low percentage mortality after 24 hr pose-exposure, 48% and 32%respectively. In conclusion every tested larvicides could be used for control Culex sitiens larvae even in the brackish water, and malathion and pyrethroid insecticides for adult control of Culex sitiens and Anopheles sundai cus.


SUSCEPTIBILITY OF CULEX SITIENS TO SUBPERIODIC BRUGIA MALAYI

Samrerng Prummongkol, Yuwadee Trongtokit, Yudthana Samung, Chamnarn Apiwathanasorn, Somjai Leemingsawat, Chotechuang Panasoponkul

Department of Medical Entomology, Faculty of Tropical Medicine, Mahidol University

THE present study was carried out to determine the susceptibility of the most predominant species of mosquitoes, Culex sitiens, in Tsunami-affected areas of Phang Nga Province to subperiodic
**ABSTRACTS**

**DISTRIBUTION OF MEDICALLY IMPORTANT MOSQUITOES IN NAVA NAKORN INDUSTRIAL ESTATE, PATHUM THANI PROVINCE, THAILAND**

Sirima Kitvatanachai¹, Kritsana Janyapoon¹, Chamnarn Apiwathnasorn², Somjai Leemingsawat³

¹Faculty of Medical Technology, Rangsit University, Pathum Thani, Thailand; ²Department of Medical Entomology, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

A survey of the distribution of medically important mosquitoes was conducted in Nava Nakorn Industrial Estate, Pathum Thani Province from May to July, 2003. Mosquitoes were sampled bi-monthly by dipping, CO₂ light trap and human landing catch. Five species of mosquito larvae were found in breeding sites with Culex species potentially breeding in this area. Cx. quinquefasciatus was found to be breeding at a higher rate than other species in both sites of study, followed by Cx. gelidus. An estimated 47 larvae/dip were found at breeding site A and 36 larvae at breeding site B. By light trap method, Cx. tritaeniohrynchus was the main species found (53.1%) at site A, and Cx. vishnui (54.8%) at site B. An average of 25 mosquitoes/trap/night was recorded at site A, which was double that of site B. The mosquitoes attracted to humans were mainly Cx. gelidus (site A: 35.9%; site B: 52.3%) followed by Cx. quinquefasciatus and Cx. vishnui. The highest mosquito landing activity was found at 19.00-21.00 hr and 23.00-24.00 hr, and the highest mosquito landing density was 21 mosquitoes/hour.


**COMPARATIVE REPELLENCY OF 38 ESSENTIAL OILS AGAINST MOSQUITO BITES**

Yuwadee Trongtokit, Yupha Rongsriyam, Narumon Komalamisra, Chamnarn Apiwathnasorn

Department of Medical Entomology, Faculty of Tropical Medicine, Mahidol University. Email: ytrongtokit@yahoo.com

The mosquito repellent activity of 38 essential oils from plants at three concentrations was screened against the mosquito Aedes aegypti under laboratory conditions using human subjects. On a volunteer’s forearm, 0.1 ml of oil was applied per 30 cm² of exposed skin. When the tested oils were applied at a 10% or 50% concentration, none of them prevented mosquito bites for as long as 2 h, but the undiluted oils of Cymbopogon nardus (citronella), Pogostemon cablin (patchuli), Syzygium aromaticum (clove) and Zanthoxylum limonella (Thai name: makaen) were the most effective and provided 2 h of complete repellency.

From these initial results, three concentrations (10%, 50% and undiluted) of citronella, patchouli, clove and makaen were selected for repellency tests against Culex quinquefasciatus and Anopheles dirus. As expected, the undiluted oil showed the highest protection in each case. Clove oil gave the longest duration of 100% repellency (2-4 h) against all three species of mosquito. Copyright - 2005 John Wiley & Sons., Ltd.

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**DETERMINATION OF LEAD TOXICITY IN CULEX QUINQUEFASCIATUS MOSQUITOES IN THE LABORATORY**

Sirima Kitvatanachai¹, Chamnarn Apiwathnasorn¹, Somjai Leemingsawat², Waranya Wongwit³, Songpol Tornee³

¹Department of Medical Entomology, ²Department of Social and Environmental Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok; ³Department of Health Education, Srinakharinwirot University, Bangkok, Thailand

Laboratory investigations were carried out to study the effects of lead toxicity and lead uptake on Culex quinquefasciatus mosquitoes. Three different concentrations of lead nitrate were used in laboratory tests (0.05, 0.1, and 0.2 mg/l). An atomic absorption spectrometer (AAS) was used to determine lead concentrations. The results showed that lead significantly reduced hatching, egg-production, and emergence rates, compared with the unexposed groups (p<0.05). The ratio of female to male offspring was 3.64:1, which was observed in the second generation, after the parents were exposed to 0.2 mg/l lead. No effects where observed on oviposition


**Brugia malayi.** Female mosquitoes were raised under laboratory conditions from larvae collected from breeding places in the affected-areas. A laboratory stock colony of Aedes togoi was the susceptible control. Mosquitoes were allowed to feed when 3 to 5 days old on a microfilarial cat with a microfilarial density of 100-500 per 20 µl blood obtained from an endemic area in Surat Thani Province. Development of the microfilariae in the mosquitoes was detected by dissection 14 days after feeding. Cx. sitiens proved refractory. This is conclusive evidence that Cx. sitiens cannot naturally support the complete development of subperiodic *Brugia malayi.*
A population level, selection by immune pressure will play a critical role in immune protection against the asexual blood stages of *P. falciparum*, whereas the IgG2 and IgG4 do not and even are suggested to block protective mechanisms. In addition, anti- *P. falciparum* specific IgE could have a pathogenic role during malaria infection. Interleukin 4 is a Th2 type cytokine that induces Ig-class switching from IgM/IgG to IgE. Earlier data have shown that IL-4 producing T-cell subsets have been associated with the production of anti-Pf-RESA-specific IgG antibodies. The IL-4 –590 C/T transition in the IL-4 promoter has been reported to influence the promoter activity and to be associated with levels of total IgE. In addition, the T allele was found to be associated with elevated anti- *P. falciparum* IgG antibodies in the Fulani of west Africa. This suggests that anti- *P. falciparum* specific IgG subclasses might be influenced by host genetic factors. The aims of the study were to investigate whether the IL-4 –590 C/T polymorphism influences the production of anti- *P. falciparum* specific IgG, IgG subclasses, or IgE and whether this polymorphism and the antibodies were related to susceptible or resistance to severe malaria in people living in a malaria endemic area of Thailand.

**ANTI-Plasmodium falciparum** specific antibodies play a critical role in immune protection against the asexual blood stages of *P. falciparum*, whereas the IgG2 and IgG4 do not and even are suggested to block protective mechanisms. In addition, anti- *P. falciparum* specific IgE could have a pathogenic role during malaria infection. Interleukin 4 is a Th2 type cytokine that induces Ig-class switching from IgM/IgG to IgE. Earlier data have shown that IL-4 producing T-cell subsets have been associated with the production of anti-Pf-RESA-specific IgG antibodies. The IL-4 –590 C/T transition in the IL-4 promoter has been reported to influence the promoter activity and to be associated with levels of total IgE. In addition, the T allele was found to be associated with elevated anti- *P. falciparum* IgG antibodies in the Fulani of west Africa. This suggests that anti- *P. falciparum* specific IgG subclasses might be influenced by host genetic factors. The aims of the study were to investigate whether the IL-4 –590 C/T polymorphism influences the production of anti- *P. falciparum* specific IgG, IgG subclasses, or IgE and whether this polymorphism and the antibodies were related to susceptible or resistance to severe malaria in people living in a malaria endemic area of Thailand.

**Presented at:** The First Annual BioMalPar Conference on the Biology and Pathology of the Malaria Parasite, EMBL Heidelberg Germany, March 2-4, 2005.

**ANTI-BLOOD STAGE ANTIBODIES INDUCED BY NATURAL P. VIVAX INFECTION**

Santipong Sirikajomdachakul, Jarinee Panitchakorn, Yuvadee Mahakunkijcharoen, Srisin Khusmith

Department of Microbiology and Immunology, Faculty of Tropical Medicine, Mahidol University, Bangkok Thailand

**NTURALLY** acquired immunity to *P. vivax* blood stage antigens have been described in 211 vivax individuals living in malaria endemic area in Thailand. The specific IgG and IgG antibody response to *P. vivax* blood stage antigens was observed in 110 cases (52.13%) and 102 cases (48.34%), respectively. The majority of IgG responders had specific IgG1, IgG2, and IgG3 subclasses. In contrast, the specific IgG4 subclass...
was rarely detected. The IgG1 coexpressed with IgG2 showed the highest responders. The levels of either anti- P. vivax IgG or IgM antibodies seem not to be related with age of each individual \( r = 0.038, p = 0.474 \) for IgG2, \( r = 0.193, p = 0.052 \) for IgM). The levels of anti- P. vivax IgG subclasses were age independent since there were no significant correlation between the levels of each specific IgG subclass and age of each individual \( r = 0.100, p = 0.301 \) for IgG1, \( r = 0.069, p = 0.474 \) for IgG2, \( r = 0.004, p = 0.967 \) for IgG3, and \( r = 0.079, p = 0.414 \) for IgG4). There was no significant correlation between the number of malaria exposures and the levels of anti- P. vivax specific IgG, or IgM \( r = 0.044, p = 0.654 \) for IgG, \( r = 0.062, p = 0.537 \) for IgM). The levels of specific IgG1, IgG2 and IgG3 were higher in responders who had only IgG antibody and had more than one malaria attack. No significant correlation between the level of anti- P. vivax IgG, or IgM antibody and parasitemia was found \( r = 0.024, p = 0.728 \) for IgG, \( r = 0.016, p = 0.815 \) for IgM). Our results showed that individuals with naturally exposure to P. vivax malaria infection in endemic area in Thailand did develop the specific antibodies either IgG, or IgM both against stage antigens and the specific IgG1, IgG2, or IgG3 were the predominant subclasses.

Manuscript is preparing for publication

ANTIBODY RESPONSE PROFILE TO P. VIVAX MEROZOITE SURFACE PROTEIN1 (MSP1) IN NATURALLY EXPOSED MALARIA INDIVIDUALS IN THAILAND

Nada Pitabut1, Jarinee Panitchakorn1, Yuvadee Mahakunkijcharoen1, Chakrit Hirumpetcharat2, Srisin Khusmith1

1Department of Microbiology and Immunology; Department of Social Medicine, Mahidol University, Bangkok Thailand; Department of Microbiology, Faculty of Public Health, Mahidol University, Bangkok Thailand

OBJECTIVE: To evaluate the efficacy of a novel monoclonal antibody (MAb)-based dot-blot ELISA for detection of Leptospira antigens in urine samples of cattle.

Sample Population: Blood and urine samples of 45 test cattle from 5 farms in Chonburi province and 20 control cattle from 2 farms in Khon Kaen province in Thailand.

Procedure: Blood and urine samples were assayed (microscopic agglutination test and urine antigen test) for Leptospira infection by use of an MAb-based dot-blot ELISA, and results for the ELISA were compared with those for dark-field microscopy (DFM), microbial culture, and a polymerase chain reaction (PCR) assay.

Results: All urine samples with positive results for DFM, microbial culture, PCR assay, or > 1 of these tests also had positive results when tested by use of the MAb-based dot-blot ELISA, except for 1 sample that had positive results only for the PCR assay. Detection

The antibody responses to PvMSP1 (C-terminal) antigen were not correlated with age \( r = 0.035, p = 0.711 \) for IgG1; \( r = 0.600, p = 0.285 \) for IgG2; \( r = 0.077, p = 0.454 \) for IgG3; and \( r = 0.664, p = 0.051 \) for IgG4). There was no correlation between the number of malaria exposures and the levels of anti-PvMSP1 (C-terminal) IgM antibody \( r = -0.143, p = 0.225 \). While the levels of anti-PvMSP1 (C-terminal) IgG antibody were significantly correlated with the number of malaria exposures \( r = -0.208, p = 0.014 \). No correlation between the levels of either anti-PvMSP1 (C-terminal) IgG or IgM antibody and parasitemia was found \( r = -0.040, p = 0.639 \) for IgG; \( r = -0.060, p = 0.376 \) for IgM). Our finding indicated that individuals with naturally exposure to vivax malaria infection in some endemic areas in Thailand did develop the specific IgG and IgM antibodies to PvMSP1 (C-terminal) and the specific IgG1 and IgG3 were the predominant subclasses.

Manuscript is preparing for publication

EVALUATION OF A MONOCLONAL ANTIBODY –BASED DOT-BLOT ELISA FOR DETECTION OF LEPTOSPIRA SPP IN BOVINE URINE SAMPLES

Junpen Suwimonteerabutr1, Wanpen Chaicumpa2, Patcharin Saengjaruk3, Pramuang Tapchaisri2, Mansa Chongsu-nguan1, Thareerat Kalambaheti1, Pongrama Ramasoota1, Yuwapol Sakolvaree2, Prachin Virakul4

1Department of Microbiology and Immunology, Department of Social Medicine and Environment (Ramasoota), Faculty of Tropical Medicine, Mahidol University; 2Faculty of Medical Technology, Faculty of Allied Health Sciences, Thammasat University; 3Department of Pathology, Faculty of Medicine, Siriraj Medical Institute; 4Department of Obstetrics and Gynecology, Faculty of Veterinary Medicine, Chulalongkorn University.

OBJECTIVE: To evaluate the efficacy of a novel monoclonal antibody (MAb)-based dot-blot ELISA for detection of Leptospira antigens in urine samples of cattle.

Sample Population: Blood and urine samples of 45 test cattle from 5 farms in Chonburi province and 20 control cattle from 2 farms in Khon Kaen province in Thailand.

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Results: All urine samples with positive results for DFM, microbial culture, PCR assay, or > 1 of these tests also had positive results when tested by use of the MAb-based dot-blot ELISA, except for 1 sample that had positive results only for the PCR assay. Detection
limits of the dot-blot ELISA were 103 leptospires/mL of urine and 9.3 ng of *Leptospira* homogenate. Comparison revealed that the diagnostic sensitivity, specificity, efficacy (accuracy), positive predictive value, and negative predictive value for the ELISA were in agreement with results for DFM (100%, 72.72%, 80%, 57.14%, and 100%, respectively), microbial culture (100%, 61.54%, 66.62%, 28.57%, and 100%, respectively), and PCR assay (95.45%, 100%, 91.77%, 100%, and 95.83%, respectively).

**Conclusions and Clinical Relevance:** The MAb-based dot-blot ELISA is suitable as a tool for detecting leptospires in urine samples of cattle. (Am J Vet Res 2005;66:762-766)


**COMPARISON BETWEEN SALMO-DOT, PCR, AND BACTERIAL CULTURE FOR DETECTION OF SALMONELLA SPP. IN FOOD SAMPLES**

Amonrattana Roobthaisong¹, Manas Chongsa-nguan¹, Pramuan Taphaisri², Pongsi Tongtawe², Patavee Soisangwan², Wanpen Chaicumpa²

¹Department of Microbiology and Immunology, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; ²Faculty of Allied Health Sciences, Thammasat University, Rangsit Center, Pathumthani 12121, Thailand; ³Department of Medical Sciences, Ministry of Public Health, Nonthaburi 11000, Thailand

**ALMONELLOSIS continues to be a major foodborne infection of humans worldwide.** Contamination of *Salmonella* spp. in foods can cause problems in food industries especially the export of chicken meat and other food products because processed foods are expected to be *Salmonella*-free. Standard culture method is reliable and has been widely accepted as a gold standard procedure for determination of *Salmonella* spp. in food. Nevertheless, bacterial culture takes 4-5 days before the results are known. It is laborious and expensive. Besides, it produces large amount of contaminated waste. At present, several alternative and rapid methods for detection of *Salmonella* spp. in food have been developed. In this study, an immunological test using a test kit namely “Salmo-Dot” which is an MAb-based antigen detection test (MAb specific to lipopolysaccharide of *Salmonella* spp.) and polymerase chain reaction (PCR) to detect *stn* and *invA* genes were compared with the standard culture method for detection of *Salmonella* in food samples. Among the 50 chicken meat samples tested, 15 samples (30%) were positive by all methods, i.e. Salmo-Dot, PCR amplification of *stn* gene, PCR amplification of *invA* gene and the culture method. One strain of *Salmonella* was isolated from each of the positive sample, and 15 *Salmonella* isolates have been established. Although, the results of Salmo-Dot and PCR were conformed, with 100% sensitivity and 100% specificity, to the standard culture method, the Salmo-Dot is the better alternative of the conventional culture method than PCR for detection of *Salmonella* in naturally contaminated food samples because it requires shorter time for completing the process, less expensive and more simple.

**Presented at:** Joint International Tropical Medicine Meeting, 30 November - 2 December 2005, The Grand Hotel, Bangkok, Thailand.

**CLINICAL DIFFERENCES AMONG PCR-PROVEN DENGUE SEROTYPE INFECTIONS**

Kriengsak Limkittikul¹, Sangchai Yingsakmongkon², Akanitt Jittmittraphap¹, Somchai Chuananon³, Wiroon Supakul⁴, Surasak Kowasupath⁴, Chaiyaporn Rojanawatsirivit⁴, Wiwatee Usawattanakul¹,*

¹Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; ²Faculty of Veterinary Medicine, Kasetsart University, Bangkok, Thailand; ³Ministry of Public Health, Nonthaburi, Thailand

**The objective of this study was to compare the clinical spectra of dengue serotypes proven by PCR technique.** The retrospective study reviewed the clinical information of dengue-infected patients who were admitted to northeastern provincial hospitals in Thailand from June to September 2002. Dengue infection and viral serotype were confirmed by polymerase chain reaction (PCR). Pair anti-dengue immunoglobulin G (IgG) and Ig M from paired sera were analyzed by enzyme-linked immunosorbent assay (ELISA). Ninety-nine PCR-proven dengue-infected Thai patients were studied. Their ages ranged from 3-30 years. They were infected with DEN1, DEN2, DEN3, and DEN4 in 21, 55, 12 and 12%, respectively. Twenty-two percent had primary, and 78% had secondary infections. Dengue fever was the most common presentation for both primary (77.2%) and secondary infections (46.7%). The ratio of dengue fever:dengue hemorrhagic fever (DF:DHF) and non-dengue shock syndrome:dengue shock syndrome (non-DSS:DSS) for DEN2 was the lowest of the dengue serotypes. There was no difference in the duration of fever, percentage of hepatomegaly and bleeding among the serotypes in both DF and DHF. The trend of white blood cell, lymphocyte and atypical lymphocyte counts of DEN3 were the highest, while those of DEN1 were the lowest among the dengue serotypes.

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IDENTIFICATION OF RECEPTOR MOLECULE FOR DENGUE VIRUS FROM MOSQUITO CELL LINE

Wipawee Usawattanagul1, Sineewanlaya Wichit1, Akanitt Jimittiraphap1, Songsak Peimitr1, Sukathida Ubol1, Butsaya Thaisomboonsuk2, Yasuo Suzuki1

1Faculty of Tropical Medicine, Mahidol University, 2Faculty of Science, Mahidol University, 1Armed Forces Research Institute of Medical Sciences, 2University of Shizuoka, Japan

DENGUE viruses (DENV) infect cells by attaching to a surface receptor, probably through the envelope (E) glycoprotein, located on the surface of the viral membrane. However, the host cell receptors remain unknown. This study sought to identify dengue virus binding receptors on the surface of AP-61 and LLC-MK2 cells, from mosquito and mammalian cells, respectively. These cells were extracted by chloroform/methanol system, then separated into neutral and acidic glycolipids by Q-sepharose column. Next, neutral lipid fractions were purified by latex bead and HPLC column. In order to identify the putative receptor molecules, TLC/virus binding assay, TLC/immunostaining, cell surface staining, enzyme β-N-acetyl-hexosaminidase treatment and MALDI-TOF/MS structure analysis were performed. In the neutral lipid fractions, L-3 (GlcNAc1-3Man β-Glc1-1Cer) and L-4 (GalNAc1-4GlcNAc1-3Man β-Glc1-1Cer) were found in AP-61 cells, while GA2 (GalNAc1-4Gal1-4Glc1-1Cer) and PG (Gal1-4GlcNAc1-3Gal1-4Glc1-1Cer) were found on the LLC-MK2 cell. All of these glycosphingolipids can react with DENV-2. Interestingly, in the acidic fractions of both cells contained the sulfatide, similarly to the heparan sulfate (HS) that have the sulfate group and also strongly reacted with DENV. This study strongly suggests that L-3, L-4, GA2, PG and sulfatide are the putative receptor of DENV-2. Moreover, L-3, L-4, GA2, PG contain β-HexNAc in the reducing end, which may play an important role in DENV binding.


DEVELOPMENT AND EVALUATION OF A LATEX AGGLUTINATION TEST FOR THE RAPID DIAGNOSIS OF SCRUB TYPHUS

Varee Wongchotigul1, Sunthareeya Waicharoen2, Searmsap Riengrod3, Saichon Chimsungsan1, Jaruawadee Rattanadakul4 and Soonthareeya Waicharoen2

1Department of Social and Environmental Medicine, Faculty of Tropical Medicine, Mahidol University; 2Department of Microbiology, Faculty of Public Health, Mahidol University; 3Department of Microbiology and Immunology, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

The purpose of this research was to develop a simple and rapid diagnostic test for scrub typhus using a latex agglutination test (LAT) to detect antibodies against Orientia tsutsugamushi. Five strains of O. tsutsugamushi were propagated in L929 cells. The rickettsiae were purified and concentrated with percoll density gradient centrifugation. A suitable concentration of O. tsutsugamushi soluble antigen was used to sensitize latex to prepare the latex antigen. The specificity, sensitivity, and accuracy of the latex antigen were assessed. The LAT, indirect immunofluorescent antibody test (IFA), and Weil-Felix agglutination test (WF) were compared by testing 109 acute febrile illness cases and 100 confirmed non-scrub typhus cases (50 other febrile disease cases and 50 healthy controls). By using the IFA as the standard reference method, the overall sensitivity, specificity, and accuracy of the LAT were 89.1, 98.2, and 93.6%, respectively. By contrast, the sensitivity of the WF, compared with the IFA, was only 47.3%, while the specificity and accuracy were 92.6 and 69.7% respectively. Thus, The LAT described here is another important alternative test for the diagnosis of scrub typhus.


DEVELOPMENT OF MULTIPLEX PCR FOR THE DETECTION OF TOTAL COLIFORM BACTERIA FOR ESCHERICHIA COLI AND CLOSTRIDIUM PERFRINGENS IN DRINKING WATER

Suwalee Tantawiwat1, Unchalee Tansuphasiri2, Warany Wongsit1, Varee Wongchotigul3 and Dwi Kitayaporn4

1Department of Microbiology and Immunology, Faculty of Tropical Medicine, Mahidol University; 2Department of Microbiology, Faculty of Public Health, Mahidol University; 3Department of Microbiology and Immunology, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

MULTIPLEX PCR amplification of lacZ, uidA and plc genes was developed for the simultaneous detection of total coliform bacteria for Escherichia coli and Clostridium perfringens, in drinking water. Detection by agarose gel electrophoresis yielded a band of 876 bp for the lacZ gene of all coliform bacteria; a band of 147 bp for the uidA gene and a band of 876 bp for the lacZ gene of all strains of E. coli; a band of 280 bp for the plc gene for all strains of C. perfringens; and a negative result for all three genes when tested with other bacteria. The detection limit was 100 pg for E. coli and C. perfringens, and 1 ng for coliform bacteria when measured with purified DNA. This assay was applied to the detection of these bacteria in spiked water samples. Spiked water samples with 0-1,000 CFU/ml of coliform bacteria and/or E. coli and/or C. perfringens were detected by this multiplex PCR after a pre-enrichment step to increase the sensitivity.
and to ensure that the detection was based on the presence of cultivable bacteria. The result of bacterial detection from the multiplex PCR was comparable with that of a standard plate count on selective medium (p=0.62). When using standard plate counts as a gold standard, the sensitivity for this test was 99.1% (95% CI 95.33, 99.98) and the specificity was 90.9% (95% CI 75.67, 98.08). Multiplex PCR amplification with a pre-enrichment step was shown to be an effective, sensitive and rapid method for the simultaneous detection of these three microbiological parameters in drinking water.


INDIRECT IMMUNOPEROXIDASE TEST FOR THE DIAGNOSIS OF LEPTOSPIROSIS

Saichon Chimsumang¹, Siriporn Chettanadee¹, Somchai Jirathai² and Varee Wongchotigul¹

¹Department of Microbiology and Immunology, Faculty of Tropical Medicine, Mahidol University, Bangkok; ²Buri Ram General Hospital, Buri Ram Province. Thailand

Leptospirosis is a widespread zoonotic disease that affects all mammals, including humans, in different parts of the world. Clinical recognition of leptospirosis is challenging, and the definitive serologic diagnosis assay, the microscopic agglutination test (MAT), is time-consuming and difficult to conduct. In this study, an indirect immunoperoxidase (IIP) test to detect Leptospira-specific antibodies in human serum samples was developed. The efficacy of the IIP was compared with the indirect immunofluorescent assay (IFA) and MAT. A total of 368 human serum samples were analyzed by MAT, IFA, and IIP. Using a MAT titer of >1:100 as the gold standard, the sensitivities for the detection of Leptospiral antibodies at a titer of 1:200 were 94.7% by IFA and 93.6% by IIP; specificities were 95.3% by IFA and 94.9% by IIP; and accuracies were 95.1% by IFA and 94.6% by IIP. With a titer of 1:400, the sensitivity, specificity and accuracy were 86.2%, 98.9%, and 95.7% by IFA, respectively; whereas, for the IIP, the sensitivity was 85.1%, specificity 98.5%, and accuracy 95.1%. A further evaluation of this test with 80 unknown-febrile-disease sera was also included. We found that the sensitivity and specificity of this test were 100% and 76.8%, respectively. Therefore, the IIP test is a potentially valuable tool for the diagnosis of leptospirosis.


SHORT REPORT: DETECTION OF ORIENTIA TSUTSUGAMUSHI IN CLINICAL SAMPLES BY QUANTITATIVE REAL-TIME POLYMERASE CHAIN REACTION

Tasawan Singhilsarak¹, Wattana Leowattana¹, Sornchai Looaresuwan¹, Varee Wongchotigul¹, Ju Jiang³, Allen L. Richards³, And George Watt⁴

¹Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; ²Department of Microbiology, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; ³Rickettsial Diseases Department, Naval Medical Research Center, Silver Spring Maryland; ⁴Department of Medicine, Hawaii AIDS Clinical Research Program, University of Hawaii, Manoa, Honolulu, Hawaii

Orientia tsutsugamushi infection causes scrub typhus, a common zoonosis of rural Asia. Orientia tsutsugamushi was recently detected by a real-time quantitative polymerase chain reaction (qPCR) assay in animal specimens. We evaluated the same qPCR assay in specimens obtained from patients with serologically proven scrub typhus infections. The 47-kDa qPCR assay was more sensitive than was mouse inoculation; it was reactive in whole blood specimens from all 10 isolate-positive patients and in 7 of 17 isolate-negative individuals (P=0.003, Fisher’s two-tailed exact test). As few as 1,076 O. tsutsugamushi copies/µL were detected in whole blood. Four of 7 sera from isolate-proven scrub typhus infections were also reactive by qPCR. The assay was unreactive in all 12 individuals without scrub typhus infection. This is the first demonstration of a sensitive and specific real-time qPCR assay for human scrub typhus infection.


ANALYSIS OF NATURAL KILLER T CELL SUBSETS IN PATIENTS WITH SEVERE AND UNCOMPlicated FALCIPARUM MALARIA IN THAILAND

Watanabe H¹, Kobayashi P¹, Wongchotigul V¹, Kita K¹, Looaresuwan S²


There is limited evidence about the roles of natural killer T (NKT) cells coexpressing NK marker and T cell receptors in the immunological status of malaria patients. The analysis of NKT cell subsets may disclose the roles of innate immune responses during falciparum malaria infection and provide insights in...

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Faculty of Tropical Medicine, Mahidol University
vaccine development or therapeutic approaches to severe malaria. We aimed to examine the relationships between NKT cell subsets and the severity in falciparum malaria patients. The case definition of severe falciparum malaria was based on that recommended by WHO. The peripheral blood lymphocytes from 11 severe malaria patients (SMP), 22 uncomplicated malaria patients (UMP) and 30 healthy controls (HC) were used to analyze the proportion of NKT cell subsets (CD16+, CD56+, CD57+ and CD161+T cells) during the course of malaria illness by flow cytometry. A dynamic alteration in NKT cell subsets during malaria infection was observed. On admission day, CD16+T cells expanded in the peripheral blood of the UMP when compared with the HC while the level of CD57+T cells in the SMP was lower than in the HC. In addition, there were higher levels of CD56+ and CD161+T cells in the SMP than the UMP on day 7 after treatment. These results indicated that each NKT cell subset might have functional properties relating to severity of falciparum malaria or immunoregulatory function.

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A CHOICE BETWEEN BLOOD CLOT AND EDTA BLOOD FOR NESTED POLYMERASE CHAIN REACTION IN DETECTING SCRUB TYPHUS DNA

Montrakul P1, Chimsumang S2, Kalambaheti T1, Mayurasakorn S2, Jitrathai S1 and Wongchotigul V1

1Department of Microbiology and Immunology, Faculty of Tropical Medicine, Mahidol University, Bangkok; 2Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok; 1Buriram Hospital, Buriram, Thailand.

To determine whether blood clot or EDTA blood is more accurate for nested polymerase chain reaction (PCR) in detecting scrub typhus DNA, thirty pairs (acute and convalescent) unknown specimens from pyrexia of unknown origin (PUO) patients, 30 healthy controls and 15 other diseases patients were used to detect scrub typhus DNA by nested PCR, and then were compared with the indirect immunofluorescent antibody (IFA) test as the gold standard. At the acute stage, there were no significant differences between the results of the nested PCR from blood clot, EDTA blood and the IFA test (p=0.157). However, there were significant differences between the results of the nested PCR from blood clot and the IFA test (p=0.021) at the convalescent stage. At the acute stage, the sensitivity, specificity and accuracy of the nested PCR for blood clot were 26.3, 85.7, 70.7% and for the EDTA blood 52.6, 87.5, 78.7%, respectively. In addition, at the convalescent stage, the sensitivity, specificity and accuracy of blood clot and EDTA blood specimens increased to 52.6, 94.6, 84%, and 73.7, 96.4, 90.7%, respectively. These results suggest that an EDTA blood specimen is better than a blood clot specimen for diagnosing scrub typhus by nested PCR, especially in the convalescent stage.


A SINGLE DOSE OF PLASMODIUM YOELII MSP119 IMMUNIZATION FORMULATED WITH MONTANIDE ISA51 AND CPG OLIGODEOXYNUCLEOTIDE IS ENOUGH TO INDUCE PROTECTION AGAINST P. YOELII INFECTION

Pimmada Jeamwattanalert1, Yuvadee Mahakunkijcharoen2, Leera Kittigul1, Pakpimol Mahannop3, Sathit Pitchyangkul1, Chakit Hirunpetcharatk1

1Department of Microbiology, Faculty of Public Health, Mahidol University; 2Department of Microbiology and Immunology, Faculty of Tropical Medicine, Mahidol University; 3Department of Parasitology, Faculty of Public Health, Mahidol University; 4Department of Immunology and Medicine, US Armed Forces Research Institute of Medical Science, Bangkok, Thailand.

*Author correspondence.

The carboxy-terminal 19kDa-fragment of merozoite surface protein 1 (MSP119), is highly conserved and effective in induction of protective immune response against malaria infection. Our previous studies in mice based on using complete/incomplete Freund’s adjuvant demonstrated that a four-dose immunization was able to induce complete protection. However, the kinetics of MSP119-specific antibody response induced by a single dose-immunization has not been investigated. In this study, we then singly immunized BALB/c mice subcutaneously with MSP119 in the mixture of Montanide ISA51 and CpG oligonucleotide (ODN) and monitored the antibody level. The MSP119-specific antibody reached maximum level by 28 days post immunization. At that day, the IgG or its isotype (IgG1 and IgG2a) levels were comparable to those of mice with four-dose immunization. However, the longevity of the IgG antibody response is shorter, or which the higher IgG1 level decreased rapidly which the lower IgG2a level still persisted over 22 weeks of study period. All immunized mice survived. P. yoelii infection post challenge with little patent parasitemia occurring during the first 2 weeks and then being cleared. These findings suggest that one-dose immunization is enough to induce MSP119-specific immunity against parasite infection, and that leaving time longer than three weeks post the first immunization may be helpful in generating more complete memory response.

LONG-TERM, PROTECTIVE IMMUNE RESPONSE OF MICE FOLLOWING IMMUNIZATION WITH THE CARBOXY-TERMINAL 19KDA-FRAGMENT OF P. YOELII (MSP119) FORMULATED WITH MONTANIDE ISA51 AND CpG OLGODEOXYNUCLEOTIDE

Pimmada Jeamwattanalert1, Yuavadee Mahakunkijcharoen2, Leera Kittigul1, Pakpimol Mahannop1, Sathit Pitchyangkul3, Chakrit Hirunpetcharat1

1Department of Microbiology, Faculty of Public Health, Mahidol University; 2Department of Microbiology and Immunology, Faculty of Tropical Medicine, Mahidol University; 3Department of Parasitology, Faculty of Public Health, Mahidol University; 4Department of Immunology and Medicine, US Armed Forces Research Institute of Medical Science, Bangkok, Thailand

*Author correspondence.

MSP1 is the major protein on the surface of plasmodial merozoite and its carboxy-terminus, the 19kDa-fragment (MSP119), is highly conserved and effective in induction of protective immune response against malaria parasite infection as demonstrated in mice and monkeys but its longevity has not been elucidated. We then investigated this immune response against malaria parasite infection as demonstrated in mice and monkeys but its longevity has not been elucidated. We then investigated this immune response against malaria parasite infection as demonstrated in mice and monkeys but its longevity has not been elucidated. We then investigated this immune response against malaria parasite infection as demonstrated in mice and monkeys but its longevity has not been elucidated. We then investigated this immune response against malaria parasite infection as demonstrated in mice and monkeys but its longevity has not been elucidated.


GENETIC CHARACTERIZATION ORIENTIA TSUTSUGAMUSHI ISOLATED IN THAILAND DURING 2003-2005

Rungnapa Luksameetanasan1,2, Daniel H Paris1, Thareerat Kalambaheti1, Vanaporn Wutheikanun1, Wirongrong Cheirakul1, Sunee Chueasawanchai1, Rose McGready1, Sharon Peacock1,3, Nicholas PJ Day1,3, Stuart D Blacksell1,3

1Wellcome Trust-Mahidol University-Oxford Tropical Medicine Programme, Faculty of Tropical Medicine, Mahidol University, Bangkok, 10400, Thailand; 2Department of Microbiology and Immunology, Faculty of Tropical Medicine, Mahidol University, Bangkok, 10400, Thailand; 3Centre for Tropical Medicine, Nuffield Department of Clinical Medicine, John Radcliffe Hospital, Oxford, United Kingdom

O. tsutsugamushi is the causative agent of scrub typhus infection and relationships with prototype strain of O. tsutsugamushi isolated from scrub typhus patients at two sites in Thailand and their genetic characterization.

Patients were recruited from two clinical investigation sites located in Udorn Thani in north-eastern Thailand and Mae Sot on the Thai-Burma border. Samples were collected between November 2003 to February 2005 from patients with those of suspected scrub typhus infection using the framework of two ongoing acute febrile illness studies. Isolation of O. tsutsugamushi in mammalian cell culture was performed and isolates were characterized by PCR amplification and nucleotide sequencing of the entire 56 kDa gene. DNA sequence of the 56 kDa gene were compared with reference and prototype strains of O. tsutsugamushi. A dendrogram that demonstrated phylogenetic relationships was constructed using Kimura 2-parameter and Neighbor-Joining algorithms.

Seventeen O. tsutsugamushi isolates were propagated from the patient samples with 14 (82%) and 3 (18%) originating from Udorn Thani and Tak provinces, respectively. The majority of the isolates (11/17) grouped with the Karp reference strain and formed distinct clusters. The Tak isolate, FPW2031, belonged to the Karp group and demonstrated relatedness to a group of Udorn Thani isolates. Four isolates grouped with the Gilliam strain. Isolate FPW1038 grouped with Kato strain and was very similar to the historical Thai isolate TA716 (100% homology). Isolate UT302 was distinct from the Karp, Kato and Gilliam genogroups and demonstrated relatedness to the historical Thai isolate TA763 (96% homology).

Tsutsugamushi is the causative agent of scrub typhus infection and relationships with prototype strains. It also demonstrates the need for ongoing surveillance and isolation of O. tsutsugamushi from scrub typhus
patients in order to understand the natural history and ecology of contemporary strains of O. tsutsugamushi in a locality, understand the diagnostic implications of genetic and antigenic variation in contemporary isolates. These can be used to produce or design new diagnostic tools, characterise antibiotic susceptibility of O. tsutsugamushi isolates.


STRONG LINKAGE DISEQUILIBRIUM OF A HbE VARIANT THE (AT)\(^9\)(T)\(^5\) REPEAT IN THE BP1 BINDING SITE UPSTREAM OF THE BETA-GLOBIN GENE IN THE THAI POPULATION


Department of Human Genetics, Graduate School of Medicine, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, 113-0033, Japan. Juno-ty@umin.ac.jp

A binding site for the repressor protein BP1, which contains a tandem (AT)x(T)y repeat, is located approximately 530 bp 5’ to the human beta-globin gene (HBB). There is accumulating evidence that BP1 binds to the (AT)\(^9\)(T)\(^5\) allele more strongly than to other alleles, thereby reducing the expression of HBB. In this study, we investigated polymorphisms in the (AT)x(T)y repeat in 57 individuals living in Thailand, including three homozygotes for the hemoglobin E variant (HbE; beta26Glu \(\rightarrow\) Lys), 22 heterozygotes, and 32 normal homozygotes. We found that (AT)\(^9\)(T)\(^5\) and (AT)\(^7\)(T)\(^7\) alleles were predominant in the studied population and that the HbE variant is in strong linkage disequilibrium with the (AT)\(^9\)(T)\(^5\) allele, which can explain why the betaE chain is inefficiently synthesized compared to the normal betaA chain. Moreover, the mildness of the HbE disease compared to other hemoglobinopathies in Thai may be due to, in part to the presence of the (AT)\(^9\)(T)\(^5\) repeat on the HbE chromosome. In addition, a novel (AC)n polymorphism adjacent to the (AT)x(T)y repeat (i.e., (AC)\(^3\)) was found through the variation screening in this study.


POLYMORPHISM OF THE HLA-B AND HLA-DRB1 GENES IN THAI MALARIA PATIENTS

Hananantachai H, Patarapotikul J, Ohashi J, Naka I, Looareesuwan S, Tokunaga K

Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand. Juno-ty@umin.ac.jp

The high degree of polymorphism of human leukocyte antigen (HLA) genes has been suggested to result from natural selection against susceptibility to a variety of infectious pathogens, including malaria. HLA molecules are considered to play a crucial role in the defense of the host against malarial infection, and different HLA class I and class II alleles have been reported to be associated with reduced susceptibility to malaria or the severity of malaria in different populations. To test for associations between HLA alleles and the severity of malaria in a Thai population, polymorphisms of HLA-B and HLA-DRB1 genes were investigated in 472 adult patients in northwest Thailand with Plasmodium falciparum malaria. In this study, malaria patients were classified into three groups: mild malaria, non-cerebral severe malaria, and cerebral malaria. Our results revealed that the allele frequencies of HLA-B46, -B56, and –DRB1*1001 were statistically different between non-cerebral severe malaria and cerebral malaria (P = 0.005), between mild malaria and cerebral malaria (P = 0.032), and between mild malaria and non-cerebral malaria (P = 0.007). However, our results may by showing false positives due to multiple testing. This, further study with a larger sample size must be conducted to obtain conclusive evidence of the association of these HLA-B and DRB1 alleles with the severity of malaria in Thailand.


A FUNCTIONAL POLYMORPHISM IN THE IL1B GENE PROMOTER, IL1B-31C>T, IS NOT ASSOCIATED WITH CEREBRAL MALARIA IN THAILAND

Ohashi J, Naka I, Doi A, Patarapotikul J, Hananantachai H, Tangpukdee N, Looareesuwan S, Tokunaga K

Department of Human Genetics, Graduate School of Medicine, The University of Tokyo, 7-3-1 Hongo, Tokyo 113-0033, Japan. Juno-ty@umin.ac.jp

BACKGROUND: IL-1beta and IL-1RA levels are higher in the serum of cerebral malaria patients than in patients with mild malaria. Recently, the level of IL1B expression was reported to be influenced by a polymorphism in the promoter of IL-1, IL1B-31C>T.

METHODS: To examine whether polymorphisms in IL1B and IL1RA influence the susceptibility to cerebral
malaria, IL1B-31C>T, IL1B 3953C>T, and IL1RA variable number of tandem repeat (VNTR) were analysed in 312 Thai patients with malaria (109 cerebral malaria and 203 mild malaria patients). RESULTS: In this population, IL1B –31C>T and IL1RA VNTR were detected, while IL1B 3953C>T (i.e., IL1B 3953T) was not observed in the polymorphism screening for 32 patients. Further analyses for IL1B-31C>T and IL1RA VNTR in 110 cerebral malaria and 206 mild malaria patients showed no significant association of these polymorphisms with cerebral malaria. CONCLUSION: The present results suggest that IL1B-31C>T and IL1RA VNTR polymorphisms do not play a crucial role in susceptibility or resistance to cerebral malaria.

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THE ROLE OF THE TAT GENE IN THE PATHOGENESIS OF HIV INFECTION

Pornsawan Amarapal1, Surang Tantivanich1, Kruavon Balachandraa, Kazuhiro Matsuo4, Punnee Pitsutthum4 and Manus Chongsa-nguan1

1Department of Microbiology and Immunology, Faculty of Tropical Medicine, Mahidol University, Bangkok; 2Medical Biotechnology Center, National Institute of Health, Department of Medical Sciences, Ministry of Public Health, Nonthaburi, Thailand; 3AIDS Research Center, National Institute of Infectious Diseases, Japan; 4Vaccine Trial Center, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

The human immunodeficiency virus Tat regulatory protein is essential for virus replication and for the efficient transcription of HIV-1 provirus, and in the pathogenesis of AIDS. The role of the tat gene was investigated in 300 samples. It was found that 71.7% were subtype CRF_01AE, 9.3% were subtype B, while 11.7 and 7.3% of them were cross-reactive and non-typeable, respectively. Moreover, the results from peptide ELISA also showed that a low CD4 cell count was related to low anti-Tat antibody (p<0.05), which may be due to the progression of HIV-1, which can be found predominantly in AIDS patients. The results of nested PCR showed that the second Tat exon might also play a role in T-cell activation. Reverse transcription polymerase chain reaction (RT-PCR) was used to measure HIV-1 mRNA expression in PBMC. RT-PCR negative results were found mostly in the asymptomatic HIV-seropositive group (88%). HIV-1 mRNA expression was found to correlate with current immunologic status. The differences in Tat protein sequences from DNA sequencing between the patients who had anti-Tat antibody positive and anti-Tat antibody negative, were not significant (p>0.05). These results suggested that the Tat amino acid sequences were conserved among each group of samples and did not change significantly compared with the consensus sequence in previous studies. Several factors make Tat an attractive target for vaccine design.


AN EXOTIC SINUSITIS

Sukthana Y1, Rigunti M2, Siripanth C1, Kusolsuk T1, Chintrakarn C1, Kulpaditharom B1

1Department of Protozoology, Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand; 2Department of Tropical Pathology, Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand; 3Department of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand; 4Department of Oto-Rhino-Laryngology, Faculty of Medicine, Mahidol University, Mahidol, Thailand, Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand

We report a case of sinusitis caused by mixed free-living amoebae, Acanthamoeba and Naegleria, in an immunocompetent host; this has not been documented before. Free-living amoebae should be considered in the differential diagnosis of pathogens that cause sinusitis with or without central nervous system involvement, especially when bacteria or fungi are not found by smear, biopsy or culture.


SPA, SPRINGS AND SAFETY

Sukthana Y1, Lekka A1, Suthikornchai C1, Wanapongse P2, Vejjajiva A3, BovornkittiS3

1Department of Protozoology, Faculty of Tropical Medicine, Mahidol University, 420/6 Rajvithi Road, Bangkok, Thailand; 2Office of Atoms for Peace, Ministry of Science and Technology, Bangkok, Thailand; 3The Academy of Science, The Royal Institute, Bangkok, Thailand

Natural mineral water has long been used worldwide for bathing and health purposes. At present, Thailand is famous for health spas and natural hot springs among local people and tourists. Due to possible risks of exposure to harmful agents, we studied hazardous pollutants at 57 natural hot springs in 11 provinces in northern, central, eastern and southern Thailand. Pathogenic, free-living amebae of the genera *Naegleria* and *Acanthamoeba*, which can cause central nervous system infection, were found in 26.3% (15/57) and 15.8% (9/57), respectively. Dissolved radon, a soil gas with carcinogenic properties, was present in nearly all hot springs sites, with concentration ranging from 0.87-76,527 Becquerels/m³. There were 5 water samples in which radon concentration exceeded the safety limit for drinking. *Legionella pneumophila* (serogroups 1, 3, 5, 6, 7 10 and 13) were found in samples from 71.9% (41/57) of studied sites. Because spas and natural springs are popular tourist attractions, health authorities should be aware of possible hazards and provide tactful measures and guidelines to ensure safety without causing undue alarm to foreign and Thai tourists.

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PROTOZOAL CONTAMINATION OF WATER USED IN THAI FROZEN FOOD INDUSTRY.

Sutthikornchai C1, Jantanavivat C1, Thongrungkiat S2, Harroongroj T1, Sukthana Y1

1Department of Protozoology, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; 2Department of Medical Entomology, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; 3Department of Food Science, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand.

This study evaluated the prevalence of contamination of water that was used for food preparation. Since protozoal cysts can be found in small numbers in water, 1,000 liters of either untreated or treated water were filtered through activated carbon block filters (1 microm nominal porosity). Identification of protozoa was performed using specific monoclonal antibodies against Giardia and Cryptosporidium parasites followed by fluorescence microscopy. Twelve of 20 untreated water samples (60%) were found to be contaminated by Giardia cysts, with an average of 53.33 cysts/1,000 liters (geometric mean 39.43), whilst 7 samples (35%) were contaminated by Cryptosporidium oocysts, with an average of 28.57 oocysts/1,000 liters (geometric mean 26.92). Three samples of untreated water (15%) were positive for both organisms. In contrast, none of the treated water samples were contaminated.

FREE-LIVING AMEBA CONTAMINATION IN NATURAL HOT SPRINGS IN THAILAND

Lekkla A1, Sutthikornchai C1, Bovornkiti S2, Sukthana Y1

1Department of Protozoology, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; 2The Academy of Science, The Royal Institute, Bangkok, Thailand.

This study carried out the contamination of free-living ameba, Naegleria spp and Acanthamoeba spp contamination in natural hot springs in Thailand from 13 provinces. The temperature of hot springs water varied from 28 degrees-65 degrees C and pH from 6-8. We found that 38.2% (26/68) of water samples were positive, Acanthamoeba was 13.2% (9/68) whilst Naegleria was 35.3% (24/68). Contamination by free-living ameba in natural hot springs may pose a significant health risk to people who use such water for recreation activities.

IMPACT OF HEALTH EDUCATIONAL PROGRAMMES ON THE PREVALENCE OF ENTEROBIAISIS IN SCHOOLCHILDREN IN THAILAND

Nithikathkul C1, Akarachantachote N2, Wannapinyosheep S3, Pumdonming W4, Brodsky M5, Sukthana Y6

1Department of Biological Science, Faculty of Science and Technology, Huachiew Chalermprakiet University, Samut Prakan Province, Thailand; 2Dept. of Mathematic and Statistics, Faculty of Science and Technology, Huachiew Chalermprakiet University, Samut Prakan Province, Thailand; 3Department of Basic Medical Science, Faculty of Science and Technology, Huachiew Chalermprakiet University, Samut Prakan Province, Thailand; 4Dept. of Mathematic and Statistics, Faculty of Science and Technology, Huachiew Chalermprakiet University, Samut Prakan Province, Thailand; 5United States Naval Hospital, United States; 6Department of Protozoology, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand.

Enterobiasis is a worldwide prevalent disease particularly in low income areas. The budget needed for the prevention, treatment and eradication of the disease has thus far frustrated the limited budgets of global public health systems. A study was undertaken to determine if education in addition to medical treatment of enterobiasis could make a difference to the rates of infection. A total of 777 children (399 male and 378 female) from 11 elementary schools in five districts of Samut Prakan Province, Thailand were examined between December 2000 and
A large variety of species of free-living amoebae (FLA) caused an indefinite form of these protozoa. Non-fixed form, as indicated by amoeboid movement and possessed the bacteria to survive in nature. Two species of pathogenic FLA: Naegleria fowleri and Acanthamoeba spp. were identified as the causative agents of Primary Amoebic Meningoencephalitis (PAM) and Granulomatous Amoebic Encephalitis (GAE) respectively. They were suggested to amphizoic protozoa, capable of living as parasites or as free-living and were also considered to be distributed worldwide. These amoebae were detected in lakes, rivers and ponds. The first case of meningoencephalitis was observed in 1961 by Fowler. Many cases were reported later on and the pathogenicity was tested by nasal inoculation of mice. In fact, quite a number of FLA were isolated but only a few species were pathogenic to humans. The three typical features which allow recognition of Naegleria spp. flagellate stage, round cyst and promitotic trophozoite. This promitosis distinguishes the Naegleria genus from Acanthamoeba spp. The disease caused by PAM usually occurs with acute onset, whereas chronic for GAE. The GAE cases mentioned are mostly in debilitated patients, chronic alcoholics or patients under treatment with immunosuppressive methods. About 6 cases of PAM were reported in Thailand during 1982-1997. Four cases of GAE were reported in 1994 and two isolated cases of Acanthamoeba from keratitis patients were reported in 2000. Finally one case of PAM and one case of GAE were reported in 2001. The surveys of FLA were set up to study the distribution of these pathogenic amoebae and determine the prevalence of amoebae in aquatic habitats of human environments. About 40% were identified as Acanthamoeba spp., 30% were Naegleria spp., 20% were Hartmanella and 10% were Vahlkampfia. Only 10% of Naegleria spp. belonged to Naegleria fowleri.

**Early Detection and Identification of Amphizoic Amoebae from Nasal Exudates of a Symptomatic Case**

A man visited the Out Patient Department of the hospital for Tropical Diseases in February 2004 with low grade fever and severe headache for a week. He had the history of diving in a natural pond 2-3 days before the onset of the disease. A thick bloody mucous was observed from the nasal discharge. Fresh microscopic observation of the exudates in 0.85% sodium chloride revealed numerous active amoeba trophozoites. Two groups of the trophozoites were observed. The first group was 10 ì sized amoeba with active directional movement by lobopodia and the second group was 15-30 ì sized amoeba with active multiprogressive movement by filopodia. Few flagellate forms were observed after exflagellation in distilled water and some polygonal cysts were also found. Giemsa stain was used to differentiate the amoeba trophozoites from the leukocytes. It was concluded that this patient was infected by both Naegleria spp. and Acanthamoeba spp. This is the first report of double infection of free-living amoeba in a symptomatic and non-fatal patient.

**The In Vitro Anti-Giardial Activity of Extracts from Plants that are Used for Self-Medication by AIDS Patients in Southern Thailand**

Sawagjaroen N1, Subhadhirasakul S2, Phongpaicit S1, Siripanth C1, Jamjaroen K1, Sawangjaroen K4

1Department of Microbiology, Faculty of Science, Prince of Songkla University, Hat Yai, 90112 Songkhla, Thailand; 2Dept. Pharmacog. Pharmaceutical Bot., Faculty of Pharmaceutical Sciences, Prince of Songkla University, Hat Yai, 90112 Songkhla, Thailand; 3Department of Protozoology, Faculty of Tropical Medicine, Mahidol University, 10400 Bangkok, Thailand; 4Department of Pharmacology, Faculty of Science, Prince of Songkla University, Hat Yai, 90112 Songkhla, Thailand
This study evaluated the anti-giardial activity of chloroform, methanol and water extracts of 12 medicinal plants (39 extracts), commonly used as self medication by AIDS patients in southern Thailand. The plant extracts and a standard drug, metronidazole, were incubated with 2×10⁵ trophozoites of *Giardia intestinalis* per millilitre of growth medium in 96-well tissue culture plates under anaerobic conditions for 24 h. The cultures were examined with an inverted microscope and the minimum inhibitory concentration (MIC) value for each extract was determined. The chloroform extracts from *Alpinia galanga*, *Boesenbergia pandurata*, *Eclipta prostrata*, *Piper betle*, *Piper chaba*, *Zingiber zerumbet*, and the methanol extracts from *B. pandurata* and *E. prostrata* were classified as "active", i.e. with an IC₅₀ of < 100 µg/ml, whereas the chloroform extracts from *Murraya paniculata* was classified as being "moderately active". This study shows that extracts from some medicinal plants have potential for use as therapeutic agents against *G. intestinalis* infections.

**COMPARISON OF FIVE DNA EXTRACTION METHODS AND OPTIMIZATION OF A B1 GENE NESTED PCR (N-PCR) FOR DETECTION OF TOXOPLASMA GONDII TISSUE CYSTS IN MOUSE BRAINS**

Aongart Mahittikorn¹, Hannes Wickert H², Yaowalark Sukthana¹

¹Department of Protozoology, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; ²Department of Parasitology, Hygiene Institute, Heidelberg University, Germany

Oxoplasmosis, caused by *Toxoplasma gondii*, is an important parasitic disease worldwide. Different techniques have been developed for *T. gondii* detection. At present, Polymerase chain reaction (PCR) has been widely used. However, the PCR for identifying *T. gondii* remains unsatisfactory in many laboratories because of lack of standardization and variations in efficiency. In the present study, we optimized a nested PCR protocol (n-PCR) in order to compare the amplification of *T. gondii* DNA, after being extracted from mouse brains by five different DNA extraction methods including phenol chloroform, QiAamp DNA minikit, Genomic DNA purification kit and Chelex with or without proteinase K. All DNA extraction methods used in our experiment were able to extract DNA from a single tissue cyst from mouse brains. However, among our five DNA extraction methods, the Chelex without proteinase K appeared to be the most rapid and easiest one.

This study was financially supported by Royal Golden Jubilee-PhD Programme.)

**IMMUNOHISTOCHEMICAL STUDY OF ACUTE TOXOPLASMOSIS IN THE LIVER, SPLEEN AND BRAIN INEXPERIMENTALLY INFECTED MICE**

Phuangphet Waree¹³, David Ferguson¹, Emsri Pongponratn³, Urai Chaisri³, Yaowalark Sukthana¹

¹Department of Protozoology, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; ³Nuffield Department of Pathology, University of Oxford, John Radcliffe Hospital, Oxford, United Kingdom; ²Department of Tropical Medicine, Mahidol University, Bangkok, Thailand; ³Department of Microbiology and Parasitology, Faculty of Medical Science, Naresuan University, Phitsanulok, Thailand

In this study, immunohistochemical technique was used to enhance visualization of the pathological lesion in the liver, spleen and brain in experimentally infected mice. ICR mice were infected with RH strain *Toxoplasma gondii*. By histology, the structure of the liver was affected and showed several areas of necrosis, which increased with the period post-inoculation. They were observed at the surface of the liver and then invaded deep into the tissue. Similar results were observed for the spleen. In contrast, only a few organism were seen in the brain, however, it was only immunohistochemistry that the number and distribution of *Toxoplasma gondii* organisms could be identified.

(This study was financially supported by Royal Golden Jubilee-PhD Programme.)

**COST-EFFECTIVENESS OF PERINATAL SCREENING OF TOXOPLASMA GONDII ANTIBODY IN PREGNANT THAI WOMEN**

Yaowalark Sukthana¹, Rachatawan Cheabchalard¹, Krisana Pengsaa¹, Sukawadee Khanganawat¹, Ruenruetai Udonsom¹, Amorn Lekkla¹

¹Department of Protozoology, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; ²Department of Obstetric and Gynecology, Queen Sirikit Children’s Hospital, Bangkok, Thailand

**ABSTRACTS**

T HIS study evaluated the anti-giardial activity of chloroform, methanol and water extracts of 12 medicinal plants (39 extracts), commonly used as self medication by AIDS patients in southern Thailand. The plant extracts and a standard drug, metronidazole, were incubated with 2×10⁵ trophozoites of *Giardia intestinalis* per millilitre of growth medium in 96-well tissue culture plates under anaerobic conditions for 24 h. The cultures were examined with an inverted microscope and the minimum inhibitory concentration (MIC) value for each extract was determined. The chloroform extracts from *Alpinia galanga*, *Boesenbergia pandurata*, *Eclipta prostrata*, *Piper betle*, *Piper chaba*, *Zingiber zerumbet*, and the methanol extracts from *B. pandurata* and *E. prostrata* were classified as "active", i.e. with an IC₅₀ of < 100 µg/ml, whereas the chloroform extract from *Murraya paniculata* was classified as being "moderately active". This study shows that extracts from some medicinal plants have potential for use as therapeutic agents against *G. intestinalis* infections. © Springer-Verlag 2004.

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Aongart Mahittikorn¹, Hannes Wickert H², Yaowalark Sukthana¹

¹Department of Protozoology, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; ²Department of Parasitology, Hygiene Institute, Heidelberg University, Germany

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Phuangphet Waree¹³, David Ferguson¹, Emsri Pongponratn³, Urai Chaisri³, Yaowalark Sukthana¹

¹Department of Protozoology, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; ³Nuffield Department of Pathology, University of Oxford, John Radcliffe Hospital, Oxford, United Kingdom; ²Department of Tropical Medicine, Mahidol University, Bangkok, Thailand; ³Department of Microbiology and Parasitology, Faculty of Medical Science, Naresuan University, Phitsanulok, Thailand

In this study, immunohistochemical technique was used to enhance visualization of the pathological lesion in the liver, spleen and brain in experimentally infected mice. ICR mice were infected with RH strain *Toxoplasma gondii*. By histology, the structure of the liver was affected and showed several areas of necrosis, which increased with the period post-inoculation. They were observed at the surface of the liver and then invaded deep into the tissue. Similar results were observed for the spleen. In contrast, only a few organism were seen in the brain, however, it was only immunohistochemistry that the number and distribution of *Toxoplasma gondii* organisms could be identified.

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¹Department of Protozoology, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; ²Department of Obstetric and Gynecology, Queen Sirikit Children’s Hospital, Bangkok, Thailand

**ABSTRACTS**
OXOPLASMOsis is usually asymptomatic in the normal host, but primary infection during pregnancy can be transmitted to the fetus. Congenital toxoplasmosis, though rare, is nevertheless a health and economic burden. Early correct diagnosis is thus important for intervention and proper management. Laboratory diagnosis for congenital toxoplasmosis relies mainly on demonstrating serum specific antibodies and isolation of T. gondii DNA from amniotic fluid.

Toxoplasma sero-conversion rate was studied in 4,000 pregnant Thai women and IgM antibody was also determined in 8,000 neonates. We found no IgM antibody in any neonate and the sero-conversion rate was found to be 2 per 1,000 pregnancies. With such low prevalence, it is perhaps not cost effective to carry out nationwide perinatal screening of Toxoplasma antibody in pregnant women in Thailand. Care should be confined to individual case detection in both pregnant woman and the newborn who are suspected of acquiring the disease.

(This study was financially supported by Mahidol University Fund)

Oral presentation in: Joint International Tropical Medicine Meeting, 30 November – 2 December 2005, Bangkok, Thailand.

CYCLOSPORA INFECTION IN HEALTHY BOY AT THAI – MYANMAR BORDER
Jaremate Limsomboon1, Wanchai Maneeboonyoung2, Amorn Lekkla1, Surapon Yimsamran1, Yaowalark Sukthana3
1Department of Social and Environment Medicine, Faculty of Tropical Medicine, Mahidol University; 2Department of Tropical Hygiene, Faculty of Tropical Medicine, Mahidol University; 3Department of Protozoology, Faculty of Tropical Medicine, Mahidol University

We report a case of healthy boy, from Thai-Myanmar border, who infected with Cyclospora. Stool concentration and modified Acid-Fast stain were performed. Round organisms size 7–8 µm, pink colour compatible with unpopulated Cyclospora oocysts were found. Cyclospora infection can be found in both competent and immunocompromised hosts, which less sever symptom in former group. Good personal hygiene and sanitation are important for preventing transmission of this infection.

(This study was financially supported by Royal Golden Jubilee-PhD Programme)

Poster presentation in: Joint International Tropical Medicine Meeting, 30 November – 2 December 2005, Bangkok, Thailand.

MULTIPLEX RT-PCR ASSAY FOR THE DETECTION OF STAGE CONVERSION PROCESSES IN TOXOPLASMA GONDII: A PUTATIVE FUTURE TOOL FOR THE DETECTION OF TOXOPLASMIC ENCEPHALITIS
Aongart Mahittikorn1, Hannes Wickert2, Markus Meissner2, Yaowalark Sukthana1
1Department of Protozoology, Faculty of Tropical Medicine, Mahidol University, Bangkok, 10400, Thailand; 2Department of Parasitology, Hygiene Institute, Heidelberg University, 69120 Heidelberg, Germany.

We have developed a multiplex reverse transcription-polymerase chain reaction (RT-PCR) assay that facilitates the analysis of large numbers of samples for differences in sag-1 and sag-4 mRNA abundance, genes which are selectively expressed by either tachyzoites or bradyzoites. In our assay, we further co-amplified alpha-tubulin cDNA as an internal control. The results obtained from our RT-PCR assay show that the multiplex RT-PCR, consisting of the parallel amplification of sag-1, sag-4 and tubulin cDNA offers a simple, rapid and sensitive technique for the detection of T. gondii tachyzoite/bradyzoite stage conversion. In the future, the established RT-PCR technique may serve as a feasible alternative tool to diagnose TE in severely immunocompromised patients.

IN VITRO CULTIVATION OF TOXOPLASMA GONDII FOR DYE TEST IN CAPTIVE WILD FELIDS
Ruangrat Buddhirongawat1,2, Siriporn Tangsudjai1, Krisada Chaichoun1, Rattapan Pattanarangsan1, Roschong Boonyaritichaaikij1, Charoonluck Sangloung2, Nittipan Tantawiwattananon1, Yaowalark Sukthana2
1Faculty of Veterinary Science, Mahidol University, Bangkok, 10400, Thailand; 2Department of Protozoology, Faculty of Tropical Medicine, Mahidol University, Bangkok, 10400, Thailand.

Toxoplasma gondii is an obligate intracellular coccidia parasite that infects virtually all species of warm-blooded animals, including people and causes serious diseases in immunocompromised hosts. Live tachyzoites derived from serial passage in Hela culture was used in the Sabin-Feldman dye test for detection of T. gondii antibody. Serum samples of 21 captive wild felids including one fishing cat (Prionailurus), one leopard (Panthera pardus), two flat-headed cat (Prionailurus planiceps), six tigers (Panthera tigris), two leopard cats...
CULTIVATION OF GIARIDA LAMBLIA IN MONGOLIAN GERBILS

Nitipan Tantawiwattananon1, Charoonluck Sangloung1, Ruangrat Buddhirongawat1,2, Yaowalark Sukthana1

1Department of Protozoology, Faculty of Tropical Medicine, Mahidol University, Bangkok, 10400, Thailand; 2Faculty of Veterinary Science, Mahidol University, Bangkok, 10400, Thailand.

MONGOLIAN gerbils (Meriones unguiculatus) were susceptible to infection with Giardia lamblia trophozoites. The trophozoites were obtained in vitro in Diamond's TYIS-33 culture medium. The animals were infected orally with 0.5 ml culture medium containing 10^6 trophozoites. Cysts were then collected and concentrated by sucrose gradient centrifugation technique. G. lamblia cysts were first observed in feces on day 5 post infection. The characteristic of G. lamblia infection on gerbils was intermittent cyst release.

(This study was financially supported by DAAD through SEAMEO Tropmed).

IN VIVO CULTURE OF CRYPTOSPORIDIUM OOCYSTS FOR LABORATORY USE

Charoonluck Sangloung1, Ruangrat Buddhirongawat1, Nitipan Tantawiwattananon1, Yaowalark Sukthana1

1Department of Protozoology, Faculty of Tropical Medicine, Mahidol University, Bangkok, 10400, Thailand; 2Division of Clinical Microbiology, Mayo Clinic, Rochester Minnesota, United States; 3Department of Protozoology, Faculty of Tropical Medicine, Mahidol University, Bangkok, 10400, Thailand.

Cryptosporidium oocysts are needed for laboratory and research works such as drug trials, viability studies and irradiation methods. Adequately oocysts can be obtained by in vitro and in vivo techniques. We used an in vivo technique in the laboratory. Seven-day-old mice were infected with 100,000-200,000 Cryptosporidium oocysts. At 8 days post infection, the small and large intestine were collected. A simple extraction procedure was used and purification was by Ficoll gradient centrifugation. After purification, the oocysts were preserved in phosphate buffered saline with antibiotic at 4 °C.

TRANSMISSION OF ENTEROCYTOZOOON BIENEUSI GENOTYPE A IN THAI ORPHANAGE

Saowanee Leelayoova1, Ittisak Subungruang1, Ram Rangsin1, Porntip Chavalitshewinkoon-Petmitr2, Jeerapan Worapong3, Taiwa Naaglor1, Mathirut Munghin1

1Department of Parasitology, Department of Military and Community Medicine, Phramongkutklao College of Medicine, Bangkok, Thailand; 2Department of Protozoology, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; 3Center for Biotechnology and Department of Biotechnology, Institute of Science and Technology for Research and Development, Salaya, Nakornprathom, Thailand

A CROSS-SECTIONAL study of Enterocytozoon bieneusi infection in children who lived in an orphanage in Bangkok, Thailand was conducted in April 2003. Two hundred ninety stool specimens were collected and examined under light microscopy after staining with gram-chromotrope. Confirmation of E. bieneusi was done using transmission electron microscopy. Of 290 samples, 12 (4.1%) were positive for E. bieneusi. Genotypic characterization of 10 E. bieneusi showed that all were genotype A, which might indicate the same source of infection. Multivariate analysis showed that orphans who were 12-23 months old, girls and living in one particular house were independently associated with E. bieneusi infection. Our study suggests that E. bieneusi infection in this orphanage might be transmitted person to person.

This study was supported by Thailand-Tropical Disease Research Programme (T-2).

EVALUATION OF A REAL-TIME PCR ASSAY FOR THE DIAGNOSIS OF MALARIA IN PATIENTS FROM THAILAND

Heather Swan1, Lynne Sloan1, Anthony Muyombwe1, Porntip Chavalitshewinkoon-Petmitr2, Sricha Krudsood3, Wattana Leowwattana1, Polrat Wilairatana2, Sorntchai Loowreesuwan1, Jon Rosenblatt1

1Division of Clinical Microbiology, Mayo Clinic, Rochester Minnesota, United States; 2Department of Protozoology and 3Department of Tropical Medicine, Phramongkutklao College of Medicine, Bangkok,Thailand

A real-time PCR assay was evaluated for its diagnostic potential in detecting Plasmodium falciparum and Plasmodium vivax from clinical samples. The assay was highly specific and sensitive, with a detection limit of 10 parasites/mL. The assay was able to detect low levels of parasitaemia and could be used as a rapid diagnostic test for malaria in resource-limited settings.
We compared the diagnosis of malaria in 297 patients from Thailand by a real-time PCR assay using the LightCycler (Roche Applied Science) with conventional microscopy using Giemsa-stained thick and thin blood films. The PCR assay can be completed in an hour and allowed detection and identification of four species of *Plasmodium* in a single reaction by use of melting temperature curve analysis. Blood was collected, stored, and transported on IsoCode STIX (Schleicher & Schuell), which provide a stable matrix for the archiving and rapid simple extraction of DNA. A genus specific primer set corresponding to the 18S rRNA was used to amplify the target sequence. FRET Hybridization probes were designed for *Plasmodium falciparum* over a region containing base pair mismatches for differentiation of the other *Plasmodium* species. The PCR results correlated with the microscopic results in 282 of the total 297 (95%) patient specimens. The majority of these were single species infections caused by *P. vivax* (150) and *P. falciparum* (120) along with 5 *P. malariae*, 2 mixed infections (*P. falciparum/P. vivax*) and 5 negative specimens. No negative microscopy specimens were positive by PCR (100% specificity for detection of any *Plasmodium*). The 15 discrepant results could not be resolved but given the subjective nature of microscopy and the analytical objectivity of PCR, it is possible that the PCR results are correct. The ability of the PCR method to detect mixed infections or to detect *P. ovale* could not be determined by this study. Within the limitations of initial equipment costs, this real-time PCR assay is a rapid, accurate and efficient method for the specific diagnosis of malaria which may have application in clinical laboratories as well as in epidemiologic studies and antimalarial efficacy trials.

In this study, DNA helicase of *Plasmodium falciparum* was isolated and purified from crude extract by 80% ammonium sulfate precipitation and FPLC. The protein was loaded onto Resource Q column and two peaks of DNA helicase activity were found. Peak II enzyme was further purified by using Hitrap heparin, Mono S and ssDNA columns respectively. DNA helicase activity was detected by measuring the unwinding of 32P-labeled partial duplex DNA. The directionality of unwinding reaction was 3’ to 5’ with respect to the single-stranded DNA to which the enzyme was bound. The apparent molecular weight of *P. falciparum* DNA helicase is 90 kDa. It cannot unwind blunt-ended duplex DNA. Unwinding activity requires Mg2+ as a divalent cation. Only ATP or dATP supports the unwinding activity of parasite enzyme. The helicase activity is inhibited by 200 mM KCl or NaCl. Anthracycline antibiotics including aclacinomycin, daunorubicin, doxorubicin, and nogalamycin inhibits unwinding activity of *P. falciparum* 3’-5’ DNA helicase with IC50 values of 9, 2, 8 and 5 µM whereas IC50 values of these drugs against parasite growth are 1.8, 2.5, 1.5 and 0.1 µM, respectively.

This work was supported by the Thailand Research Fund.

**Preparation and Evaluation of Dihydroartemisinin in Nanosuspension**

Jiraporn Chingunpitak1, Satit Puttipipatkachorn2, Pornpit Petmitr2, Yuichi Tozuka1, Kunikazu Moribe1, Keiji Yamamoto1

1Faculty of Pharmacy, Mahidol University, Bangkok 10400, Thailand; 2Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand; 3Graduate School of Pharmaceutical Sciences, Chiba University, Chiba 263-8522, Japan

Dihydroartemisinin (DHA) is an effective antimalarial drug especially against tolerant species *Plasmodium falciparum*. However, poor solubility in water makes it difficult to formulate in an effective dosage form. Particle size reduction to micro- or nanometer range is a promising technology to overcome solubility and bioavailability problems of poorly water soluble drugs by increasing of solution velocity and saturation solubility. Co-grinding technique using hydrophobic drugs with hydrophilic polymer(s) and/or combination with co-polymer(s) was interesting method that can produce fine particles with narrow particle size distribution. This technique is attractive due to organic solvent free and simple step operation. In this research, DHA particles were prepared by co-grinding method, the formation of DHA particles as nanosuspension from ternary ground
mixtures of DHA, polyvinylpyrrolidone and sodium deoxycholate was studied. Physical characterization of the co-ground mixtures and suspension and in vitro antimalarial activity against *P. falciparum* of the obtained suspension was determined. In conclusion, the nanosuspensions with high percentage of DHA nanoparticles were obtained by reconstitution of the coground mixture in distilled water with particle size of 80-200 nm. The nanosuspension was effective antimalarial activity against *P. falciparum* K1 strain. The PXRD patterns indicating that the co-grinding technique decreased crystallinity of DHA in the coground mixtures to amorphous state whereas DHA existed as crystalline solid in physical mixtures.


DNA REPLICATING AND DNA REPAIRING ENZYMES OF PLASMODIUM FALCIPARUM

Porntip Petmitr

Department of Protozoology, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand.

MALARIA caused by *Plasmodium falciparum* remains a major global health problem especially the development of parasite drug resistance. New chemotherapeutic targets are urgently needed to achieve effective malaria treatment and control. The potential targets that should be explored and studied at the biological and molecular level are enzymes in DNA replication and DNA repair. DNA polymerase plays an important and crucial role not only in DNA replication, translation, DNA synthesis, DNA recombination but also in DNA repair of all prokaryotic and eukaryotic cells in order to maintain the integrity of the cell’s genomes. In *P. falciparum*, there are at least three types of DNA polymerases that have been identified and characterized. *P. falciparum* DNA polymerase α and δ were fully cloned and sequenced. The third enzyme, DNA polymerase γ playing an important role in replication of mitochondrial DNA was also isolated from parasite mitochondria and characterized by using various specific inhibitors. Parasite DNA polymerases show some different properties from human enzymes.

Another enzyme with a great potential as a chemotherapeutic target and which is known to act as a repairing enzyme in cells, is the DNA polymerase β. DNA polymerase β is known to be the major enzyme that operates during the repair synthesis of base excision repair in higher organisms. The mechanism apparently involves the short patch repair pathway by the removal and replacement of a single nucleotide and the long patch repair pathway by removal and replacement of a few nucleotides. It is possible that the *P. falciparum* parasite has a greater need for these repair pathways because genome analysis indicates that 80% of the genetic material is adenine and thymine (A+T).

In our recent study, a new type of DNA polymerase from *P. falciparum* is isolated and characterized. Partially purified DNA polymerase was highly resistant to aphidicolin and NEM, as seen in the other eukaryotic enzymes. Interestingly, partially purified DNA polymerase β of *P. falciparum* was strongly resistant to ddTTP whereas the other eukaryotic enzymes are sensitive to ddTTP. The partially purified enzyme was also resistant to the nucleoside analogs. Its low processivity was demonstrated by having 10 nucleotides product. The role of partially purified DNA polymerase β on base excision repair was investigated using UG mismatch of the 28-mer substrate. The results showed a patch size of 3 nucleotides. This is the first evidence demonstrating a role for DNA polymerase β in *P. falciparum* base excision repair.


DETECTION OF PFCRT T76 MUTATION IN FALCIPARUM MALARIA PATIENTS FROM THAILAND BY REAL-TIME PCR ASSAY

Pongruj Rattaprasert1, Souwanit Nakasiri2, Saranya Siribal1, Jon Rosenblatt1, Sornchai Loaareesuwan2, Porntip Chavalitshewinkoon-Petmitr1

1Department of Protozoology, Faculty of Tropical Medicine, Mahidol University Bangkok, Thailand; 2Department of Tropical Medicine, Faculty of Tropical Medicine, Mahidol University Bangkok, Thailand; 3Division of Clinical Microbiology, Mayo Clinic, Rochester Minnesota, United States

CHLOROQUINE resistance of *Plasmodium falciparum* is associated with the mutation in a transporter gene found on food vacuole membrane (chloroquine resistance transporter, CRT). Pfcrt T76 mutation is strongly correlated with in vitro chloroquine resistance. In this study, Pfcrt T76 mutation was investigated from 130 blood samples from falciparum malaria patients admitted at the Hospital for Tropical Diseases, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand by real-time PCR assay using Light Cycler. Parasite DNA of each blood sample was extracted and purified by High Pure PCR Template Preparation Kit (Roche Applied Science). Pfcrt T76 mutation was detected by using Pfcrt specific primers labeled with LCRed 640 and fluorescent-labeled hybridization probes. T76 Pfcrt mutation was detected by melting temperature curve analysis and an assay...
can be completed in an hour. In our study, Pfcrt T76 mutation was found in all specimens. The result shows an existence of the high prevalence of chloroquine resistance in this area. Moreover, a real-time PCR can demonstrate mixed infections of wild-type and mutant \( P. falciparum \) strains. Based on the results, a real-time PCR LightCycler-based technique is rapid, informative and useful for molecular surveillance of chloroquine resistance of \( P. falciparum \).

**Oral Presentation in:** Joint International Tropical Medicine Meeting 2005, 30 November-2 December 2005 at The Grand Hotel, Bangkok, Thailand.

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**HEALTH PROMOTION PROGRAM FOR THE SAFE USE OF PESTICIDES IN THAI FARMERS**

Janhong K, Lohachit C, Butraporn P, Pansuwan P  
Department of Public Health, Boromrajonani College of Nursing, Bangkok 10400, Thailand. Kleebkaewj@hotmail.com

The purpose of this study was to determine the knowledge, attitudes and practices (KAP) concerning the safe use of pesticides of Thai farmers in Don Kha subdistrict, Bang Phae district, Ratcbhuri Province. Thirty-three voluntary Thai farmers of thirty-three farming families, recruited by convenience sampling, participated in a training program for six months. Data were collected by questionnaire interviews, and KAP on the safe use of pesticides were compared by paired t-test. Research findings showed that the mean scores of KAP in the posttest were significantly higher than the pretest. The results of this study provided health professionals with information to develop more effective prevention and intervention programs. To prevent illness, the most important role of health officers should to be focus on education and information for individuals, families, and communities.

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**REDUCTION OF LOW BACK MUSCULAR DISCOMFORT THROUGH AN APPLIED ERGONOMICS INTERVENTION PROGRAM**

Poosanthanasarn N, Sriboorapa S, Fungladda W, Lohachit C  
Division of Environmental Science, Faculty of Science, Ramkhamhaeng University, Ramkhamhaeng Road, Huamark, Bangkapi, Bangkok 10240, Thailand.

An applied ergonomics intervention program (AEIP) was conducted with male employees who work in the pressing and storage sections of a metal auto parts factory in eastern Thailand. The objective of this study was to reduce worker muscular discomfort at the low back. The study design was a participatory research approach, with quasi-experimental pretest-posttest, and with a non-equivalent control group. Thirty-five persons participated in the AEIP (AEIP group) and 17 persons did not (non-AEIP group). The AEIP was composed of three major categories: (1) top management support; (2) equipment designed for workstations and manual material handling; and (3) administrative intervention, training, and health education. Muscle activity was measured by surface electromyography of the left and right erector spinae, and multifidus muscles; and evaluated by multivariate test for dependent samples (paired observation) and for independent samples. After the AEIP, the low back muscular loads of the AEIP group was significantly reduced, while those of the non-AEIP group were not. Comparison of the means of percentage maximum voluntary contractions (% MVC) of low back muscular activity between the AEIP group and non-AEIP group indicated that the AEIP group had significantly reduced low back muscular load, with a 95% confidence level (p-value < 0.05).

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**EPITOPE MAPPING OF MONOCLONAL ANTIBODIES SPECIFIC TO SEROVAR OF LEPTOSPIRA, USING PHAGE DISPLAY TECHNIQUE**

Ramasoota P1, Tungtrakaponoung R1, Pitaksajjakul P1, Ekpo P2, Froman G3, Chaicumpa W4  
1Department of Social and Environmental Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok; 2Faculty of Medicine at Siriraj Hospital, Mahidol University, Bangkok, Thailand; 3Department of Medical Biochemistry, Uppsala University, Biomedical Center, Uppsala, Sweden; 4Faculty of Allied Health Sciences, Thammasart University, Pratum Thani, Thailand

Random heptapeptide library displayed by bacteriophage T7 was used to characterize epitopes of five monoclonal antibodies that were specific to \( L. australis \), \( L. bangkok \), and \( L. bratislava \). Phages selected by biopanning were cloned by plaque isolation, and the binding specificity of individual clones was confirmed by enzyme-linked immunosorbent assay, before being further amplified and checked for phage peptide sequence using PCR and DNA sequencing. Almost all of the peptide epitopes were continuous or linear. Interestingly, in phages reacting with the monoclonal antibody (MAB) clones F11, F20, 2C3D4, and 8C6C4A12, the deduced amino acid sequence of the displayed peptides corresponded to a segment
ABSTRACTS

of hypothetical protein of the Leptospira genome (L. interrogans serovar Lai and Copenhageni). Considering the deduced amino acid sequences of phages reacting with the MAb clones F11, F20, 2C3D4, and 8C6C4A12, the consensus motif -SKSSRC-, -TLINIF-, -SSKSYR- and -CTPKSKGR- appeared respectively. No similarity was observed among phage reacting with the MAb clone F21. The results demonstrate that T7 phage display technique has potential for epitope mapping of leptospiral MAb s, and for rapid analysis of the interactions between phage display peptides with the MAb. The finding of a phage peptide that binds to MAb with protective activity can be further tested as a candidate for leptospirosis vaccine in the future.


EMERGENCE OF OPISTHORCHIS VIVERRINI CERCARIAE FROM NATURALLY INFECTED BITHYNIA (DIGONIOSTOMA) SIAMENSIS GONIOMPHALOS

Phongsasakulchoti P, Sri-aroon P, Kerdpuech Y
Department of Social and Environmental Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand.

Under natural conditions, the emergence of Opisthorchis viverrini cercariae from naturally infected Bithynia (Digoniostoma) siamensis goniomphalos showed diurnal periodicity, peaking between 8:00-10:00 AM. The cercariae did not emerge during darkness, but low-intensity light could induce a release. Cercariae shedded from each field infected B.(D.) s. goniomphalos were recorded daily. The maximum output from one snail was 1,728 cercariae in a day. The total cercarial output from all five infected snails was 56,555 from one snail was 1,728 cercariae in a day. The total cercarial output from all five infected snails was 56,555.


THE ASSOCIATION BETWEEN ENVIRONMENTAL FACTORS AND TUBERCULOSIS INFECTION AMONG HOUSEHOLD CONTACTS

Department of Health Education, Faculty of Physical Education, Srinakharinwirot University, Sukhumvit Road, Bangkok 10110, Thailand. songpoltor@yahoo.com

A CROSS-SECTIONAL study was conducted to determine the association between environmental factors and tuberculosis infection among household contacts aged less than 15 years in Bangkok, Thailand, between May and December 2003. During the study period, 480 household contacts aged under 15 years were identified. The prevalence of tuberculosis infection among household contacts was 47.08% (95% CI = 42.60-51.56). A generalized estimating equation (GEE) indicated that the risk of positive tuberculin skin testing in household contact was found to increase with household crowding. Children living in a crowded household were five times more likely to have tuberculosis infection (OR = 5.19, 95% CI = 2.65-8.69). The association between environmental factors and tuberculosis infection assists community tuberculosis staff in understanding the risks for tuberculosis infection in the community and planning appropriate preventive actions based on this risk.


COMPARATIVE STUDIES ON THE PATHOLOGICAL FINDINGS AND MORTALITY IN SCHISTOSOMA MANSONI INFECTED MICE AFTER TREATMENT WITH ARTESUNATE AND THE CURRENT ANTI-SCHISTOSOMAL DRUGS

Chaiworaporn R1, Maneerat Y2, Rojekittikhun W3, Ramasoota P1, Jancharut T4, Matsuda H5, Kitikoon V1
1Department of Social and Environmental Medicine, Faculty of Tropical Medicine, Mahidol University; 2Department of Tropical Pathology, Faculty of Tropical Medicine, Mahidol University; 3Department of Helmintology, Faculty of Tropical Medicine, Mahidol University; 4Department of Biology, Faculty of Science, Silapakorn University, Nakhon Pathom, Thailand; 5Department of Tropical Medicine and Parasitology, Dokkyo University School of Medicine, Tochigi, Japan

The effect of artesunate (ART) on the pathology and mortality rate of in Schistosoma mansoni infected mice was comparatively studied with the current drugs of choice for the treatment of schistosomiasis mansoni: praziquantel (PZQ) and oxamniquine (OX). S. mansoni experimentally infected mice were treated at 9th week of infection with ART, PZQ or OX at an oral dosage of 300 mg kg(-1), 600 mg kg(-1) and 100 mg kg(-1), respectively. Untreated, infected mice and non-infected mice were added as controls. Samples of mice were sacrificed and examined for the pathological findings at 1 week, 1 month, and 3 months after treatment. At 1 week after treatment, both gross and microscopic lesions were observed. No significant differences were noted among the infected groups. Differences were observed at 1 month after treatment. The lesions decreased more rapidly in groups treated with PZQ and OX. At 3 months after treatment, there were significant differences in the pathological findings among groups. In the groups treated with PZQ and OX, the lesions were markedly reduced and rarely found,
but they were clearly observed in the group treated with ART and in the untreated, infected group. High mortality was also recorded in the group treated with ART and in the untreated, infected group. Therefore, the treatment of S. mansoni infected mice at 9 weeks of infection with ART did not reduce the pathologic findings or the mortality rate compared to treatment with the current recommended schistosomicides, PZQ and OX.

MUTATIONS IN THE GYRA AND GYRB GENES OF FLUOROQUINOLONE-RESISTANT MYCOBACTERIUM TUBERCULOSIS FROM TB PATIENTS IN THAILAND

Pitaksajjakul P¹, Wongwit W¹, Punprasit W², Eampokalap B³, Peacock S⁴, Ramasoota P

¹Faculty of Tropical Medicine, Mahidol University, Bangkok; ²Faculty of Public Health, Mahidol University, Bangkok; ³Bamrasnaradura Infectious Disease Institute, Ministry of Public Health, Nonthaburi; ⁴Wellcome Trust-Mahidol University-Oxford Tropical Medicine Research Program, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

Among fluoroquinolone-resistant Mycobacterium tuberculosis (FQ’-MTB) isolates. mutation at positions 90, 91. and 94 in gyrA gene and at positions 495, 516, and 533 in gyrB gene have been frequently reported. In this study. 35 isolates of FQ’-MTB were collected from Siriraj Hospital and Chest Disease Institute. The quinolone resistance-determining regions (QRDR) of gyrA and gyrB genes in all 35 FQ’-ITB isolates and from the H37Rv ITBS strain were amplified using polymerase chain reaction (PCR). DΣ.\(^2\)-sequencing and single-strand conformation polymorphism (SSCP) were further utilized for characterization of the mutations in the QRDR of gyrA and gyrB genes and mutation screening, respectively. From DNA-sequencing, 21 of 35 (60%) exhibited single-point mutations in different positions. at Ala90’al. Ser91’P. and Asp94(Gly/Ala/ His/Asn); and one novel mutation position at Gly88Cys in the gyrA gene and Asp495Asn in the gyrB gene. These positions were previously frequently reported to be responsible for FQ’-ITB. The other 14 FQ’-MTB isolates (40%) had no mutation. This study is the first report of mutation occurring only in the QRDR of the gyrB gene. without prior mutation in the gyrA QRDR among FQ’-MTB isolates. By SSCP analysis for screening of the mutant FQ’-MTB, the SSCP patterns of mutated FQ’-ITB isolates were clearly differentiated from the SSCP patterns ofFQ’-MTB.

BRACKISH-WATER MOLLUSKS OF SURAT THANI PROVINCE, SOUTHERN THAILAND

Sri-arnoon P¹, Lohachit C¹, Harada M²

¹Department of Social and Environmental Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; ²Department of International Medical Zoology, Kagawa Medical University, Kagawa, Japan

Brackish-water mollusks inhabiting the mangrove areas along the Gulf of Thailand of Surat Thani Province were investigated for distribution, abundance and natural infections. Nine families and thirty-two species of brackish-water snails were recovered from 14 sampling stations. Cerithidea (Cerithideopsis) cingulata, C. (C.) djadjaeni, and C. (Cerithidea) charbonnieri, of the family Potamididae, were naturally infected with 2 types of cercariae, and one which was undetermined. C. (C.) cingulata had the highest infection rate (38.5%). Viewing two snail communities, the first community on the mainland and the second on Samui Island in Surat Thani Province, 28 brackish-water mollusk species were present on the mainland, 15 species were evident on Samui Island, and 11 snail species were common to both the mainland and Samui Island. Measurement of community similarity based on species presence revealed an index of similarity of 0.51. Concerning land use by the local people in the station areas investigated, brackish-water snails in Surat Thani Province are facing habitat degradation by human use.

SPECTROPHOTOMETRIC DETERMINATION OF PLASMA AND RED BLOOD CELL CHOLINESTERASE ACTIVITY OF 53 FRUIT FARM WORKERS PRE- AND POST-EXPOSED TO CHLORPYRIFOS FOR ONE FRUIT CROP


Department of Industrial Hygiene and Safety, Faculty of Public Health, Burapha University

We sought to investigate the early biological effects of chlorpyrifos among 53 Thai fruit farm workers by measuring the plasma cholinesterase (PChE) and red blood cell cholinesterase (AChE) activities, a biomarker of organophosphate (OPs) pesticide during one fruit crop. The ChE activity (V(m)/K(m)) was spectrophotometrically analyzed before and after exposing to chlorpyrifos. The V(m)/K(m) values of both non-spraying and spraying seasons are found as normal distribution pattern. The median PChE and AChE activities among farm workers in the...
non-spraying season were $2.3 \times 10^{-3}$ s$^{-1}$ and $7.26 \times 10^{-5}$ s$^{-1}$, respectively. The median $V(m)/K(m)$ values of PChE and $AChE$ activities of the farm workers in the spraying season were $2.02 \times 10^{-3}$ s$^{-1}$ and $5.95 \times 10^{-5}$ s$^{-1}$, respectively. The mean $V(m)/K(m)$ values of PChE shifted left (t-test, $p=0.013$), indicating a decrease in PChE activity in the farm workers exposed to chlorpyrifos. However, the $V(m)/K(m)$ values of AChE in nonspraying season and in the spraying season were not different (t-test, $p=0.246$). We propose that PChE activity can be used as a biomarker for monitoring early toxicity induced by chlorpyrifos insecticide.

**AN ERGONOMICS INTERVENTION PROGRAM TO PREVENT WORKER INJURIES IN A METAL AUTOPARTS FACTORY**

Poosanthanasarn N, Lohachit C, Fungladda W, Srboorapa S, Pulkate C

Division of Environmental Science, Faculty of Science, Ramkhamhaeng University, Ramkhamhaeng Road, Huamark, Bangkapi, Bangkok 10240, Thailand.

An ergonomics intervention program (EIP) was conducted with male employees working in the pressing and storage sections of a metal autoparts factory in Samut Prakan Province, Thailand. The objectives of this study were to assess the causes of injuries in the pressing and storage sections of that factory, and to improve working conditions by reducing worker injuries from accidents and low back muscular discomfort, using an EIR The study design used a participatory research approach which was quasi-experimental with pretest-posttest evaluations, with a non-equivalent control group. A total of 172 male participants working in Building A were the target group for assessing causes of injury. A retrospective study of official accident information, and questionnaires for general information, health and muscular discomfort, injury frequency rate (IFR), injury severity rate (ISR), medical expenses, and EIP design. Two groups of employees volunteered for the study on muscular back discomfort. The first group of 35 persons volunteered to participate in the EIP (EIP group), and the second 17 persons from Building B did not (non-EIP group). The EIP was composed of 4 major categories: (1) engineering improvement, (2) change in personal protective equipment, (3) environmental improvement, (4) administrative intervention, training, and health education. Low back muscular discomfort was measured through questionnaires on subjective feelings of muscular discomfort, and by surface electromyography (sEMG). Muscle activities were measured by sEMG of the left and right erector spinae and multifidus muscles, and evaluated by multivariate test for dependent samples (paired observation), and multivariate test for two independent samples. After EIP, ISR decreased 65.46%, IFR decreased 41.02%, and medical expenses decreased 42.79%. The low back muscular loads of the EIP group were significantly reduced, with a 95% confidence level (p < 0.05) while those of the non-EIP group were not. Subjective feelings of muscular discomfort, determined by Wilcoxon Signed Ranks test, showed that after applying the EIP to the EIP group, the mean scores for general bodily discomfort and low back muscular discomfort in the EIP group had significantly reduced, while those of the non-EIP group increased, (p < 0.05).

**FACTORS ASSOCIATED WITH THE HOUSEHOLD CONTACT SCREENING ADHERENCE OF TUBERCULOSIS PATIENTS**


Department of Social and Environmental Medicine, Faculty of Tropical Medicine, Mahidol University, Thailand. Songpoltor@yahoo.com

A CROSS-SECTIONAL study was conducted to explore factors associated with the adherence of tuberculosis patients in bringing their household contacts to a TB clinic in Bangkok, Thailand. During the study period, May to December 2003, 325 sputum-smear-positive tuberculosis patients were recruited into the study. Of the 325 eligible tuberculosis patients, 169 (52.00%, 95% CI = 47.00-57.00) brought their household contacts to the TB clinic. Psychosocial and cues to action factors were examined as indicators of the household contact screening adherence of tuberculosis patients. The results reveal that the household contact screening adherence of tuberculosis patients was significantly associated with a higher perceived susceptibility (Adjusted OR = 2.90, 95% CI = 1.18-7.16), lower perceived barriers (Adjusted OR = 4.60, 95% CI = 1.99-10.60), a higher intention to bring the contacts to the TB clinic (Adjusted OR = 3.35, 95% CI = 1.44-7.76), and a short distance from home to the TB clinic (Adjusted OR = 11.47, 95% Cl = 4.57-28.79). The results from this study provide information for TB clinic staff for developing an appropriate intervention program. Through effective intervention and active policy enforcement, a higher percentage of household contact screening adherences can be achieved.

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**EFFECT OF ANTISENSE-SGTPS ON THE GLUCOSE UPTAKE OF THE BLOOD FLuke SCHISTOSOMA MANSONI: OBSERVATIONS IN ADULT WORMS AND SCHISTOSOMULA**

Wongwit W, Rivera E, Tao LF
Department of Social and Environmental Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand.

As-ODNs, complementary to Schistosoma mansoni glucose transporter proteins (SGTP1 and SGTP4), were chosen as potential therapeutic agents for schistosomiasis. AS-SGTP1 oligos lowered the glucose uptake of adult worms both in vitro and ex vivo. The most effective AS-ODN was that of 21 nucleotides complementary to the SGTP1 nucleotide sequence, including the initiation region of mRNA translation. This oligo was found to decrease glucose uptake in vitro by as much as 50% and at a concentration of 4.0 mg/ml, it killed all adult worms within 24 hours. A significant decrease, up to 34%, in glucose uptake was also noted when 100 mg/kg x2 (with a 2 hours interval) of AS-ODN was administered ex vivo. Two out of six anti-SGTP4 oligos also decreased the glucose uptake of adult worms in vitro by 25-44%. Added to the culture of schistosomula, two AS-SGTP4 oligos were found to decrease glucose uptake by 20-43%.

**DEVELOPMENT OF MULTIPLEX PCR FOR THE DETECTION OF TOTAL COLIFORM BACTERIA FOR ESCHERICHIA COLI AND CLOSTRIDIUM PERFRINGENS IN DRINKING WATER**

Tantawiwat S, Tansuphasiri U, Wongwit W, Wongchotigul V, Kitayaporn D
Department of Social and Environmental Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand.

Multiplex PCR amplification of lacZ, uidA and plc genes was developed for the simultaneous detection of total coliform bacteria for *Escherichia coli* and *Clostridium perfringens* in drinking water. Detection by agarose gel electrophoresis yielded a band of 876 bp for the lacZ gene of all coliform bacteria; a band of 147 bp for the uidA gene and a band of 876 bp for the lacZ gene of all strains of *E. coli*; a band of 280 bp for the plc gene for all strains of *C. perfringens*; and a negative result for all three genes when tested with other bacteria. The detection limit was 100 pg for *E. coli* and *C. perfringens*, and 1 ng for coliform bacteria when measured with purified DNA. This assay was applied to the detection of these bacteria in spiked water samples. Spiked water samples with 0-1,000 CFU/ml of coliform bacteria and/or *E. coli* and/or *C. perfringens* were detected by this multiplex PCR after a pre-enrichment step to increase the sensitivity and to ensure that the detection was based on the presence of cultivable bacteria. The result of bacterial detection from the multiplex PCR was comparable with that of a standard plate count on selective medium (p=0.62). When using standard plate counts as a gold standard, the sensitivity for this test was 99.1% (95% CI 95.33, 99.98) and the specificity was 90.9% (95% CI 75.67, 98.08). Multiplex PCR amplification with a pre-enrichment step was shown to be an effective, sensitive and rapid method for the simultaneous detection of these three microbiological parameters in drinking water.

**FRESHWATER MOLLUSKS OF MEDICAL IMPORTANCE IN KALASIN PROVINCE, NORTHEAST THAILAND**

Department of Social and Environmental Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand. mtpss@mahidol.ac.th

A SNAIL survey was performed in six districts around irrigation areas of Lampao Dam, in Kalasin Province. The survey caught a total of 5,479 live snails and classed them into five families, 12 genera and 15 species, of which 7 species are suspected of transmitting human parasitic diseases. The seven species were *Pila polita*, *Pomacea canaliculata*, *Filopaludina (S.) m. martensi*, *Bithynia (Digonostoma) siamensis goniomphalos*, *Melanoideas tuberculata*, *Radix rubiginosa*, and *Indoplanorbis exustus*. Of these, *B. (D.) s. goniomphalos* and *I. exustus* were found to harbor emergent cercariae. Only *B. (D.) s. goniomphalos* hosted several types of cercariae—*Opisthorchis viverrini*, unidentified species of intestinal flukes, echinostomes, xyphidiids and furcocercous cercariae. *Indoplanorbis exustus* shed only echinostome cercariae. *B. (D.) s. goniomphalos* showed a rather high natural infection rate with *O. viverrini*, 1.3% in Yang Talat district, and 0.61% in Kamalasai district, in Kalasin Province.


WILLINGNESS TO BE VACCINATED AGAINST SHIGELLA AND OTHER FORMS OF DYSENTERY: A COMPARISON OF THREE REGIONS IN ASIA

Pack R1, Wang Y2, Singh A1, Seidlein LV1, Pach A1, Kaljee L1, Butraporn P3, Youlong G2, Blum L1, Bhutta Z2, Santosou SS2, Trach DD1, Waluyo P1, Nyamete A1, Clemens J1, Stanton B2

1Department of Community Medicine, West Virginia University School of Medicine, P.O. Box 9190, Morgantown, WV 26506_9190, USA; 2Department of Social and Environmental Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

We conducted a cross sectional survey of 3163 women and men in six Asian countries to examine willingness for children and adults to be vaccinated against shigellosis and other forms of dysentery. The six sites were clustered into three regions for ease of comparison. The regions are: Northeast Asia (China), Southeast Asia (Thailand, Vietnam, and Indonesia) and South Asia (Bangladesh and Pakistan). We used multiple logistic regression to identify region-specific models for willingness of vaccination for both adults and children. A vaccine to protect against dysentery, if available would be very much in demand throughout the three Asian regions for children. For adults, the responses indicate that vaccine uptake by adults will vary. A large proportion of respondents in all regions, specifically in China, do not perceive themselves at risk yet still consider a shigellosis vaccine desirable.

THE HEALTH OF WORKERS IN A METAL AUTOPARTS FACTORY IN EASTERN THAILAND

Poosanthanasarn N, Lohachit C

One hundred and seventy-two male employees working in the pressing and store sections of a metal autoparts factory in eastern Thailand participated in the study. The aim of this study was to survey the health and well-being condition of Thai workers prior to corporation initiatives in applied ergonomics with the workers of the company. A retrospective study of official accident information, and questionnaires regarding general information, health, muscular discomfort, accidents, posture disorders, and subjective feelings of fatigue or discomfort were filled out for the survey. The results of the study provided 48 categories of important information on the health and wellness of the employees in their workplace. Regression analysis revealed that, based on the working history of the employees, the small and large pressing sections of the workplace had a greater impact on the muscular discomfort of the employees (0.322) (p = 0.001). Based on the health information, the independent factors influencing the employee's muscular discomfort were frequency of muscular discomfort (0.240) (p = 0.004), no disease of muscle and bone (0.165) (p = 0.025), and finally, regularly taking medicine for muscular pain (0.163) (p = 0.024). The factors influencing accidents in the employees were working where they could be cut by sharp material or metal (0.257) (p = 0.008), muscular discomfort (0.169) (p = 0.059), and not using protective equipment (0.146) (p = 0.076). Thus the applied ergonomics intervention program for preventing worker injuries in the sections studied should be implemented, in order to promote the health and well-being of the employees.

THERAPEUTIC EFFECT OF SUBCURATIVE DOSE PRAZIQUANTEL ON SCHISTOSOMA MANSONI INFECTED MICE AND RESISTANCE TO CHALLENGE INFECTION AFTER TREATMENT

Chaiworaporn R1, Maneerat Y2, Rojekittikhun W3, Ramasoota P4, Janecharut T4, Matsuda H5, Kitikoon V1

1Department of Social and Environmental Medicine, Faculty of Tropical Medicine, Mahidol University; 2Department of Tropical Pathology, Faculty of Tropical Medicine, Mahidol University; 3Department of Helminthology, Faculty of Tropical Medicine, Mahidol University; 4Department of Biology, Faculty of Science, Silapakorn University, Nakhon Pathom, Thailand; 5Department of Tropical Medicine and Parasitology, Dokkyo University School of Medicine, Tochigi, Japan

The therapeutic effect of a subcurative dosage of praziquantel (PZQ) on Schistosoma mansoni infected mice and resistance to challenged worm infection after treatment were assessed and compared with conventional treatment using a curative dosage of PZQ. S. mansoni infected mice were treated with PZQ at a curative dosage (600 mg kg−1) or a subcurative dosage (300 mg kg−1) at 9 weeks after infection. Untreated mice and non-infected mice were added as controls. The therapeutic affect of the drug was evaluated in terms of the mortality of mice after treatment, and the parasitological and pathological finding in mice sacrificed at 1 week, 1 month, or 3 months after treatment. Another sample of mice was not killed but challenged with S. mansoni cercariae at 1 week, 1 month, or 3 months after treatment. Resistance to re-infection was evaluated by the extent of challenged worm reduction. In conclusion, there was no significant difference in mortality, or parasitological and pathological findings between mice treated with PZQ at the two dosages. However, resistance to challenged worm infection was more sustained in the group treated with subcurative dose PZQ, especially at 3 months after treatment.
COMMUNITY-BASED APPROACH FOR PREVENTION AND CONTROL OF DENGUE HEMORRHAGIC FEVER IN KANCHANABURI PROVINCE, THAILAND

Manirat Therawiwat¹, Wijitr Fungladda², Jaranit Kaewkungwal², Nirat Imamee¹ and Allan Steckler¹

¹Department of Health Education and Behavioral Sciences, Faculty of Public Health, Mahidol University, Bangkok; ²Department of Social and Environmental Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; ³Department of Health Behavior and Health Education, School of Public Health, University of North Carolina, North Carolina, USA

An action research design was conducted in two villages of Mueang District, Kanchanaburi Province to assess the effectiveness of a community-based approach program. Knowledge, perceived susceptibility, self-efficacy, and regular larval survey behavior were measured for program outputs. Container Index (CI), House Index (HI), and Breteau Index (BI) were used to confirm program outcomes. Key community stakeholders in the experimental village were identified and empowered through active learning in the village. Monthly meetings with the key stakeholders were used to share experiences learned, to reflect on the program outputs and outcomes as well as to plan for the next cycle of program activities. The program was quite successful. Knowledge, perception, self-efficacy, and larval survey practices in the experimental group were significantly higher than before the experiment, and higher than the comparison group. CI, HI, and BI were decreased sharply to better than the national target. Community status as community leaders was the best predictor for larval survey behavior at the first survey. Participating in the study program activities was the best predictor at the end of the program. The results from this study suggest that the dengue hemorrhagic fever (DHF) prevention and control program at the sub-district health level should be more proactive and emphasized at the village level. Monitoring the disease control program outputs and outcomes should be performed regularly during monthly meetings. Finally, local health officers need to be empowered for these matters.


CAUSAL RELATIONSHIP BETWEEN HEALTH PROMOTING BEHAVIOR AND QUALITY OF LIFE IN CERVICAL CANCER PATIENTS UNDERGOING RADIOTHERAPY

Taechaboonsermsak P, Kaewkungwal J, Singhasivanon P, Fungladda W, Wilailak S

The purpose of this cross-sectional study was to examine the causal relationships among age, education, family income, and stage of carcinoma, perceived benefits, perceived barriers, perceived self-efficacy, health promoting behavior and quality of life in patients with cervical cancer. Pender’s Health Promotion Model (1996) provided a guide for the conceptual framework of this study. Purposive sampling was employed to recruit 488 cervical cancer patients who were undergoing radiotherapy at seven public hospitals in five areas of Thailand. The instruments used in this study included a Personal Data Form, Cognitive perception Form, Health promoting behavior scale, the social support questionnaire and The Functional Assessment of Cancer Therapy General (FACT-G) form. The proposed model was tested and modified by the LISREL Program. The modified model adequately fitted with the data. The results demonstrate that health promoting behavior had a significant direct positive effect on quality of life (beta = 0.71, p < 0.01). Cognitive perceptual factors had a significant direct effect on health promoting behaviors (P = 0.69, p < 0.01). Social support had a significant direct effect on the cognitive perceptual factors (P = 0.64, p < 0.01), health promoting behavior (beta = 0.70, p < 0.01), and the quality of life (beta = 0.48, p < 0.01). Age and education did not have a significant total effect on the quality of life. Family income had a significant direct effect on cognitive perceptual factors (beta = 0.10, p < 0.05). The stage of cancer had a significant direct negative effect on cognitive perceptual factors (beta = -0.11, p < 0.05) and the quality of life (beta = -0.12, p < 0.01). The direct effect of the predictors on the quality of life indicated that cervical cancer patients with higher practice of health promoting behavior tended to have a higher quality of life. The findings indicate that Pender’s Health Promotion Model is a useful guide for explaining and predicting the health promoting behavior and the quality of life of Thai cervical cancer patients who were undergoing radiotherapy. The significance of cognitive perceptual factors and social support confirm health promoting behavior as a goal directed towards the level of well being. This has implications for health care systems in planning interventions to promote health promoting behavior in a health promotion setting in cervical cancer patients for a better quality of life and healthy. A longitudinal study and experimental study are recommended for further study.


EPITOPE MAPPING OF MONOCLONAL ANTIBODIES SPECIFIC TO SEROVARS OF LEPTOSPIRA, USING PHAGE DISPLAY TECHNIQUE

Pongrama Ramasoota1, Rogdej Tungtrakarnpoung1, Pannamthip Pitaksajakul1, Patama Eksop1, Wanpen Chaicumpa1

1Department of International Medical Zoology, Kagawa University, 2Department of Medicine, Siriraj Hospital, Mahidol University, 3Faculty of Alliences Health Sciences, Thammasart University

Random heptapeptide library displayed by bacteriophage T7 was used to characterized epitopes of the monoclonal antibodies (mAb) clone F11, F20, F21, 2C3D4, and 8C6C4A12, which specific to serovar L. australis, L. bratislava, and L. bangkok, respectively. Phage selected by biopanning was cloned by plaque isolation, and the binding specificity of individual clones was confirmed by enzyme-linked immunosorbent assay, before further amplified and checked for phage peptide sequence using PCR and DNA sequencing. Interestingly, in phage reacting with the mAb clone F11, F20, 2C3D4, and 8C6C4A12, the deduced amino acid sequence of the displayed peptides was corresponded to a segment of hypothetical protein of Leptospira genome (L. interrogans serovar Lai and Copenhageni). Considering the deduced amino acid sequences of phage reacting with the mAb clone F11, F20, 2C3D4, and 8C6C4A12, the consensus motif -SKSSRC-, -TLINIF-, -SSKSYR- and -CTPKKSGRC- appeared respectively. No similarity was observed among phage reacting with the mAb clone F21. The results demonstrate that T7 phage display technique has potential for display of peptides and for rapid analysis of the interactions between these peptides with the mAb antibodies.


ECOLOGICAL SURVEY OF BRACKISH-WATER SNAILS AND THEIR PARASITIC TREMATODES IN TIDAL FLATS IN JAPAN AND THAILAND

Harada M1, Sri-aroon P2, Lohachit C2, Suguri S1

1Department of International Medical Zoology, Kagawa University Medical School, Kagawa, Japan; 2Department of Social and Environmental Medicine, Faculty of Tropical Medicine, Mahidol University,Bangkok, Thailand

Many kinds of snails inhabit tidal flats in the temperate and tropical zones. In Japan, however, tidal flats were decreased during this half century, moreover polluted by various wastes. So the decrease of abundance and number of species of snails leads to serious damage to their parasitic trematodes. In Thailand shrimp farms have been developed immensely during the past decades. These developments have had adverse impacts on water resources and mangrove forests, and hence some species in them have also been disturbed and may be extinct, including brackish-water snails. In order to clarify the situations of snails and trematodes in west Pacific Ocean we have conducted this survey in Japan and Thailand. Forty-one tidal flats were surveyed in western Japan and 13 types of cercaria of parasitic trematodes were found from 12 species of snails. The diversity of snails in tidal flat was highest on Iriomote Island (south end of Japan) and that of cercaria was also highest on the same island. The sites of high infection rates of snails to cercariae were scattered in Japan, i.e., the Urauchi River on Iriomote is. (76.9% in Cerithidea cingulata), the Doki River (69.1 % in Cerithidea rhizophorarum) and Bishamon (45 % in Batillaria cumingii). In Thailand snails were collected at 21 places in tidal flats and mangrove forests along the eastern coast. Twenty-two snail species were examined and 7 types of cercariae were found from only 7 snail species. The sites with high infection rates of snails were Ban Klong Klaeng (TH 17) (100 % in Cerithidea cingulata), Ban Tanon Sung (TH 20) (90.5 % in Cerithidea djadjariensis), and Khuk Khi Kai (TH 22) (57.5 % in Cerithidea djadjariensis). The common snails in Japan and Thailand were only two, however, 4 types of cercaria out of 13 in Japan and 7 in Thailand were common. We also present some ecologically interesting results such as host selection of trematodes.

From these results the habitats with the high diversity both in snails and trematodes were extremely restricted in Japan and Thailand. Although the environmental conditions of the tidal flats are growing worse in Japan, they are thought to be deteriorating more than expected in Thailand. The improvement of environmental conditions in the tidal flats and mangrove forests are required in order to protect the snail-parasite community in west Pacific Ocean.


MUTATIONS IN THE RPOB GENE OF THE RIFAMPICIN-RESISTANT MYCOBACTERIA STRAINS FROM THAILAND

Pongrama Ramasoota1, Pannamthip Pitaksajakul1, Oranuch Kongpetsatit1, Wanchai Phathhattakorn1, Vijittra Pransujarit1, Jirakan Boonyasopun2

1Department of Social and Environmental Medicine, Faculty of Tropical Medicine, Mahidol University, 4206 Rajivithi Road, Bangkok 10400, Thailand; 2Central Chest Institute, Nonthaburi, Thailand.
IFAMPICIN (RIF) is the main drug for the treatment of tuberculosis and leprosy, and the Rifampicin derivative namely Rifabutin, is the main drug for the treatment of M. avium Complex (MAC). Here we reported forms of mutation never before described in the rpoB gene for samples of 70 rifampicin-resistant (RIF) M. tuberculosis (MTB), 20 (MAC) and 9 M. leprae strains from Thailand. Sequence analysis of these strains revealed mutations in a 435 bp region of the rpoB gene (MTB), 542 bp (M. avium) and 289 bp (M. leprae). Among 70 MTB, twenty-eight strains (40.0%) had single mutations, and 26 of those strains had mutations at positions never before reported. Of those 26, just one had a substitution at Val-432 (Asp), and the remaining 25, a silent mutation at Gln-517. All other strains had multiple mutations. Twenty-four (34.3%) had mutations at two positions; nine (12.8%), at three positions; two (2.8%), at five positions; and one (1.4%), at six positions. Five strains (7.1%), reported to have the RIF phenotype, contained no mutation in the examined region of the rpoB gene. Surprisingly, one RIF strain had silent mutations at twenty-nine positions. By far the dominant mutation was the silent mutations at Gln-517 (85.7% of strains). Among 20 MAC, 1 strain (5%) has missense mutation at Lys-626 (Thr), 5 strains (25%) had silent mutations at only one position, 7 (35%) at two, 7 (35%) at three, and 1 (5%) at seven positions. The dominant mutation was silent mutations at Ala-630 (15, 75% of strains), followed by Val-581 in 8 strains (40%), Tyr-578 and Thr-600 in 4 strains (20%), and Gly-597 in 3 strains (15%). Among 9 M. leprae, two of the nine had mutations at 2 positions (codons); three, at 3 positions; one, at 6 positions; one, at 7 positions; one, at 8 positions, and one, at 9 positions. point mutations at the Glu-546 (Lys) and His-554 (Asn) positions predominated. Mutations at both of these positions occurred 3 times (8.3%). For two other positions, Val-550 (Met) and Gly-556 (Arg), mutations occurred two times (5.5%); and for the remaining codon positions, only once. This investigation demonstrates that mutation in the rpoB gene of Mycobacteria strains from Thailand are more varied than previously reported for RIF of Mycobacteria strains. Screening by means of PCR-SSCP clearly separated RIF strains from rifampicin-susceptible (RIF) strains.

#Corresponding author: Pongrama Ramasoota, Department of Social and Environmental Medicine, Faculty of Tropical Medicine, Mahidol University, 420/6 Rajjithii Road, Bangkok 10400, Thailand. E-mail tmsr@mahidol.ac.th

where were pomona, ranarum, sarmin, sejroe, shermani, and tarassovi. *Leptospira interrogans* was found in 10/1,126 (0.9%) rodent samples. The predominant serogroup isolated from rodents was Autumnalis, and only one isolated sample was Pyrogenes.

**Conclusions:** The results revealed that in this endemic area, transmission of subclinical leptospirosis in the general population occurred throughout the year. The main serovar found in humans was Bratislava, which was also found in dogs and pigs in the same community. Urine cultures, for isolating serovars from dogs, pigs and other animals, are being processed to identify and confirm the maintenance hosts of leptospires in this endemic community. These results will be useful for preventing and controlling leptospirosis.


### MIMOTOE IDENTIFICATION FROM MONOCLONAL ANTIBODIES SPECIFIC TO SEROVAR OF *LEPTOSPIRA*, USING PHAGE-DISPLAYED RANDOM PEPTIDE LIBRARY


1Faculty of Tropical Medicine, Mahidol University, Bangkok; 2Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok; 3Department of Medical Biochemistry, Uppsala University, Uppsala, Sweden; 4Faculty of Allied Health Sciences, Thammasart University, Pratumtani, Thailand

**METHODS:** Random heptapeptide library displayed by bacteriophage T7 was used to identify mimotopes from phages bound to fifteen monoclonal antibodies (mAbs) that specific to different serovar of *Leptospira spp.*, and four leptospirosis patient sera respectively. Phage selected by biopanning was cloned by plaque isolation, and the binding specificity of individual clones was confirmed by enzyme-linked immunosorbent assay, before further amplified and checked for phage peptide sequence using PCR and DNA sequencing. The obtained sequences were compared with the protein sequences database of Gene Bank using BLASTP software.

**Results:** Considering the peptide sequences of phages bound to fifteen mAbs and four leptospirosis patient sera, the consensus motif -LTPCD was determined by the ELISA method and immunoblotting identification and the MW of the specific antigen were revealed sequence homology in the central region. FlaB was included in a group of protein antigens that were targeted to humoral immune response during natural infection. Substantial production of anti-FlaB antibodies was observed among the positive cases of MAT test. In this study, leptospiral FlaB specific MAb has been produced and characterized. The MAb will be further investigated for its role in protective immunity against leptospirosis infection.


### PRODUCTION AND CHARACTERIZATION OF MONOCLONAL ANTIBODY SPECIFIC TO *LEPTOSPIRAL FLAGELLIN*

Artonturasook S., Pengpanich U., Junsong N., Ramasoota P., Ekpo P.

1Department of Immunology Faculty of Medicine Siriraj Hospital; 2Department of Social and Environmental Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok 10700, Thailand

**BACKGROUND:** Leptosporal flagellin (FlaB) has been reported as a highly conserved protein among pathogenic *Leptospira spp.* Sequence alignment revealed sequence homology in the central region. FlaB was included in a group of protein antigens that were targeted to humoral immune response during natural infection. Substantial production of anti-FlaB antibodies was observed among the positive cases of MAT test. In this study, leptospiral FlaB specific MAb has been produced and characterized. The MAb will be further investigated for its role in protective immunity against leptospirosis infection.

**Methods:** FlaB specific MAb was produced from immunizing BALB/c mice with the whole cell antigen prepared from *L. interrogans* serovar Cynopteri. The specificity of the MAb was tested by and indirect enzyme link immunosorbent assay (ELISA) and microscope agglutination test (MAT) using panel of antigens prepared from 20 pathogenic, a saprophytic leptospires and 9 other bacterial genera. The isotype identification and the MW of the specific antigen were determined by the ELISA method and immunoblotting respectively. The biochemical nature of the specific antigen was analyzed by immunoblotting using the antigen prepared from serovar Cynopteri which had been

**Results:** Leptospiral FlaB specific monoclonal antibody, 7A5F12; IgG2b, was produced. Indirect ELISA...
and MAT using the panel antigens showed that MAb 7ASF12 reacted with 15 serovars of pathogenic *L. interrogans* which were Bangkok, Bratislava, Louisiana, Ballum, Bataviae, Canicola, Cddidoni, Cynopteri, Djasiman, Grippotyphosa, Hebdomadis, Sarmin, Javanica, Sejroe, and Tarassovi, but reacted with neither nonpathogenic *Leptospira* nor other bacterial genera. Western blot staining of whole cell antigens prepared from serovar Cynopteri or the partial purified recombinant-leptospiral FlaB revealed recognition of MAb to the antigen at MW 37 kDa. The hand of specific reactivity was disappeared when using the same antigen treated with proteinase K but still remained for the same antigen treated with sodium meraperidolate. Identification of the specific epitope of MAb and the corresponding region on the FlaB sequence will be further discussed. The MAb specific to leptospiral FlaB was produced. This MAb showed cross-reactivity with 15 serovars of *L. interrogans* but not nonpathogenic *Leptospira* or other bacterial genera. Specific reactivity with recombinant leptospiral FlaB confirmed the identity of the specific target antigen of this MAb. According to its broad specificity across FlaB of many leptospiral serovars, this MAb may have a broadly protective role against leptospiral infection, and this suspected capability will be further investigated.

**Conclusion:** The MAb specific to leptospiral FlaB detection aerosols *Legionella* from the exhausted air of positive result cooling tower water using the culture as the gold standard method.

**Result:** The detection limit of quantification detection of aerosol *Legionella* using the combination of air sampling and real time PCR was at least 10 fg of *Legionella* DNA which corresponding to 10 *Legionella* cells (1 *Legionella* genome = 4.3 fg). The developed method was enabled detection of aerosols *Legionella* in less than 4 hours compare with 4-7 days using culture base method.

**Conclusion:** The developed method was quantitative, sensitive, specific and rapid for the detection of an aerosol *Legionella* spp. within 4 hours, in contrast to the traditional culture method, which required a minimum of 5 days. This approach could be further apply to study the expulsion of infectious particle and may permit assessment studies of airborne environmental control.

**Oral Presentation in:** *Joint International Tropical Medicine Meeting 2005. 30 Nov – 2 Dec 2005.*

### MUTATIONS IN THE *RPOB* GENE OF THE RIFAMPICIN-RESISTANT MYCOBACTERIA STRAINS FROM THAILAND

Pongrama Ramasoota1, Pannamthip Pitaksajjakul1, Oranuch Kongpetsatit1, Wanchai Phathithakkorn1, Vijittra Pransujarit2, Jirakan Boonyasopun2

1Department of Social and Environmental Medicine, Faculty of Tropical Medicine, Mahidol University, 4206 Rajvithii Road, Bangkok 10400, Thailand; 2Central Chest Institute, Nonthaburii, Thailand.

**RFAMPICIN (RIF) is the main drug for the treatment of tuberculosis and leprosy, and the Rifampicin derivative namely Rifabutin, is the main drug for the treatment of *M. avium* Complex (MAC). Here we reported forms of mutation never before described in the *rpoB* gene for samples of 70 rifampicin-resistant (RIF) *M. tuberculosis* (MTB), 20 (MAC) and 9 *M. leprae* strains from Thailand. Sequence analysis of these strains revealed mutations in a 435 bp region of the *rpoB* gene (MTB), 542 bp (*M. avium*) and 289 bp (*M. leprae*). Among 70 MTB, twenty-eight strains (40.0%) had single mutations, and 26 of those strains had mutations at positions never before reported. Of those 26, just one had a substitution at Val-432 (Asp), and the remaining 25, a silent mutation at Gln-517. All other strains had multiple mutations. Twenty-four (34.3%) had mutations at two positions; nine (12.8%), at three positions; two (2.8%), at five positions; and one (1.4%), at six positions. Five strains (7.1%), reported to have the RIF phenotype, contained no mutation in the examined region of the *rpoB* gene. Surprisingly, one RIF strain had silent mutations at twenty-nine positions. By far the dominant mutation was the silent...**

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**OBJECTIVES:** To develop and optimize the combined method of air sampling and real time polymerase chain reaction (Real-time PCR) for quantification detection of an aerosol *Legionella* spp.

**Methods:** Based on the 5S rRNA gene primers, and TaqMan hydrolysis probe were constructed for a real time PCR assay using the detection system (Rotor Gene 2000 detector) and dual labeled fluorogenic probe. The specific of primers and probe were evaluated by nine non *Legionella* airborne bacteria to avoid the false positive results. The impinger air sampler plus T-100 sampling pump (rotary vane) was used to collect air sample with f10w rate 25 liters per min for 20 min. The developed method will be validated and applied for...
mutations at Gln-517 (85.7% of strains). Among 20
MAC, 1 strain (5%) has missense mutation at Lys-626
(Thr), 5 strains (25%) had silent mutations at only one
position, 7 (35%) at two, 7 (35%) at three, and 1 (5%)
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554 (Asn) positions predominated. Mutations at both of
these positions occurred 3 times (8.3%). For two other
positions, Val-550 (Met) and Gly-556 (Arg), mutations
occurred two times (5.5%); and for the remaining codon
positions, only once. This investigation demonstrates
that mutation position at Trp308Pro in katG gene and
Thymine → Cytosine at position –8 of inhA gene is firstly
reported here.

Oral Presentation in: Joint International Tropical Medicine

THAILAND TSUNAMI HEALTH IMPACT STUDY
Piyarat Buttraporn, Sasithon Pukrittayakamee,
Pratap Singhasivanon, Pornpimol Adams
Faculty of Tropical Medicine, Mahidol University

THE main mechanism of drug resistant
Mycobacterium tuberculosis that falling in to
mutations in specific genes, altering in drug
target enzyme, have been frequently reported. By this
mechanism, several molecular techniques have been
used to verify these mutations. For the rapidity and
simplest of molecular techniques, in present study, the
mutations in gyrA, gyrB, (drug target of FQr-MTB) katG,
and inhA genes (drug target for INHr-MTB) of MDR-TB
isolates have been studied by PCR-DNA sequencing.
For FQr, 92 isolates of FQr-MTB were studied and the
result shown that 70 of 92 (76.08%) exhibited single-
point mutations in different positions, at Asp94 (Gly/
Ala/His/Asn) (42.39%), Ala90Val (20.65%), Ser91Pro
(9.78%), Gly88 (Cys/Ala) (2.17%), in gyrA QRDR and
one isolates (1.09%) with Asp495Asn mutation in the
gyrB QRDR. The other 22 FQr-MTB isolates (23.91%)
had no mutation. For INHr, 29 isolates of INHr-MTB
were studied. Single point mutations at one or two
positions of katG gene were found (both Ser315Thr
and Arg463Leu, 58.6%, only Arg463Leu, 34.5%, only
Ser315Thr, 3.4%, Thr308Pro, 3.4%). Accordingly, 9 of 29
isolates were identified as mutants in inhA promoter
and inhA-ORF, of which 5 isolates found Cytosine →
Thymine mutation at position –15 (17.2%), 1 isolate
found Thymine → Cytosine mutation at upstream
position –8 (3.4%), 1 isolate found Cytosine → Thymine
mutation at position -15 plus mutation at ile21Thr
(3.4%), 1 isolate found Cytosine → Thymine mutation
at position -15 plus Ser94Ala (3.4%), and 1 isolate with
ile21Val (3.4%), whereas 20 isolates (69%) had no
mutation at any position. Furthermore, it was found
that mutation position at Trp308Pro in katG gene and
Thymine → Cytosine at position –8 of inhA gene is firstly
reported here.

Oral Presentation in: Joint International Tropical Medicine

ABSTRACTS
vector-borne disease, water quality, health behavior and nutrition, dengue mosquito, helminthology, and snail intermediate host. Tsunami has highlighted the vulnerability of groups such as women, children and elderly, much more attention should be given to protecting and improving sanitation, maternal care, vector-borne disease transmission, health education, and food intakes.


**PRELIMINARY WATER QUALITY SURVEY AFTER TSUNAMI IN PHANG-NGA, THAILAND**

Prapin Tharnpoophasa1, Usanee Suthisarnsuntorn2, Suwalee Tantawiwat1, Prasasana Charoenjai1, Witawat Tanyong1, Suwannee Promin1, Siriporn Jetanadee2

1Department of Social and Environmental Medicine, Faculty of Tropical Medicine, Mahidol University; 2Department of Microbiology and Immunology, Faculty of Tropical Medicine, Mahidol University

This preliminary water quality survey was performed at the eight weeks after the tsunami attack in Phang-nga province on December 26, 2004. Water samples collected from the affected area where 10 km parallel along the seaside were compared with water samples from the control area where approximately four km from the seaside which tsunami waves could not reach. These samples included 18 surface water samples, 37 well water samples and 8 drinking water samples that were examined for microbiology and physical-chemical properties. Microbiological examination was focused on enteric bacteria which were isolated from culture method, while physical-chemical properties were on-site testing for pH, salinity, dissolved oxygen (DO), conductivity and total dissolved solids (TDS) by a portable electrochemical meter (Sens lon 156). Results from microbiological examination showed that water samples in the affected area were contaminated with enteric bacteria more than that in the control area: 45.45% of surface water samples in the affected area and 40.00% in the control area, 19.05% of well water samples in the affected area and 7.69% in the control area. All eight drinking water samples were clear from enteric bacteria. Tests of physical-chemical properties showed that salinity, pH, conductivity, and TDS of surface water samples from the affected area were significantly higher than the control area. Salinity, conductivity, and TDS of well water samples from the affected area were also significantly greater than those from the control area. Surface water and well water in the Tsunami affected area have been greatly changed and need to be improved.


**MALACOLOGICAL SURVEY IN PHANG-NGA PROVINCE, SOUTHERN THAILAND, PRE- AND POST INDIAN OCEAN TSUNAMI**

Pusadee Siri-aroon1, Chantima Lohachit1, Masakazu Harada2, Phiraphol Chusongsang3, Yupa Chusongsang1

1Applied Malacology Centre, Department of Social and Environmental Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; 2Department of International Medical Zoology, Kagawa University Medical School, Kagawa, Japan

Three malacological surveys were conducted in the Takua Pa District of Phang-nga Province, southern Thailand, before and after the Indian Ocean tsunami disaster. Twenty nine species of freshwater and brackish-water snails were found, in which 10 species of freshwater snails were present, including live Pila polita; 8 species were of medical importance. Two brackish-water snails, Nerita anieulata and Littorinopsis sea bra, were absent after the tsunami disaster, while brackish-water Cerithidea eingulata and C. djadjariensis harbored 9 types of trematode cercariae.


**HEALTH BEHAVIOR OF TSUNAMI VICTIMS IN PHANG-NGA PROVINCE, THAILAND**

Mas-ngammueang R1, Kwanbunjan K2, Chusongsang P1, Chusongsang Y1, Chantaranipapong Y2, Pooudong S2, Maneekan P3, Butraporn P1

1Department of Social and Environmental Medicine, Faculty of Tropical Medicine, Mahidol University; 2Department of Tropical Nutrition and Food Science, Faculty of Tropical Medicine, Mahidol University; 3Department of Tropical Hygiene, Faculty of Tropical Medicine, Mahidol University

The health behaviors of 250 tsunami victims in Phang-nga Province were surveyed three months after the disaster struck. Questionnaires and non-participant observation were used to study the effects of the disaster on their lifestyles and health behaviors, and the effects of environmental change, which included sanitation, personal hygiene, illness and prophylaxis, and local health care and promotion while residing in temporary shelters provided by government and private donors. Our findings indicated good management of drinking water in the temporary shelters. Toilet construction and water supply were sufficient, but wastewater and sewage systems were poorly managed. Most of the study group complained of back pain, stress, and sleep disturbance. A local hospital and health stations provided medical care. Health
ABSTRACTS


EPIDEMIOLOGICAL SURVEILLANCE OF NON-FATAL-UNINTENTIONAL INJURY AMONG CHILDREN UNDER FIVE YEARS OLD IN TAMBON AMPANG, AMPHOR BAN PAEW, SAMUT SAKHON PROVINCE, THAILAND

Wangsuphachart V, Leamsuwan I, Tewawong N
Department of Social and Environmental Medicine, Faculty of Tropical Medicine, Mahidol University

By the year 2015, all UN Member States including Thailand have pledged to meet the Millennium Development Goals in reducing by two thirds the mortality rate among children under five and ensuring safe environment for children. We want to assess if morbidity of childhood injury in a pilot province would reflect a cause of death in another parallel study. Epidemiological monthly surveillance of non-fatal unintentional injury among 248 children under five was conducted in seven villages of Ampang District, Samut Sakhon Province using questionnaires with face-to-face interview. Key informants were either parents or relatives or teachers who took care of the children. Data collection was conducted through a parent-teacher network of a local day care center and the village health volunteers. Preliminary study of injury during the six months follow up among the target population showed that 52% of the study samples were boys. Major causes of injury accounted for was falls, mild to moderate degrees, during walking and running (74.7%) followed by injury relating to toys (0.5%), poisoning (9%) and others (6%: burn, traffic, drowning). Location of injury occurred mostly in the indoor setting (68%). Time at which injury happened the most was during noon-afternoon (62.8%) followed by in the evening (22.6%), at night (27%). At the time of injury, most children were under the care of their grand parents (43.3%), followed by parents (09%) and relatives.

Preliminary data collected from this study on types, major causes, location and time of injury among children under five in Samut Sakhon province can be used as baseline information for planning towards prevention and control policy in reducing childhood injury rates and promoting a safer environment for children. It can also be used to validate if such injuries among children under five would be leading causes of death in this locality. Cause-specific cumulative incidence rates by age and sex in major types of injury and effect association analysis on key risk factors are undertaken.


CYCLOSPORA INFECTION IN HEALTHY BOY AT THAI-MYANMAR BORDER

Jaremate Limsomboon1, Wanchai Maneeboonyoung2, Amorn Lekklai3, Surapat Yimsamran1, Yaowalak Sukhana3
1Department of Social and Environmental Medicine, Faculty of Tropical Medicine, Mahidol University; 2Department of Tropical Hygiene, Faculty of Tropical Medicine, Mahidol University; 3Department of Pratozoology, Faculty of Tropical Medicine, Mahidol University

We report a case of a healthy boy, from the Thai-Myanmar border, infected with Cyclospora. Stool concentration and modified acid-fast stain were performed. Round organisms, size 7-8 µm, pink color, compatible with unpopulated Cyclospora oocysts, were found. Cyclospora infection can be found in both competent and immunocompromised hosts, with less severe symptoms in the former group. Good personal hygiene and sanitation are important for preventing transmission of this infection.


CAUSAL RELATIONSHIP BETWEEN HEALTH PROMOTING BEHAVIOR AND QUALITY OF LIFE IN CERVICAL CANCER PATIENTS UNDERGOING RADIOTHERAPY

Pimsurang Taechabooneersak1, Jaranit Kaewkungwae, Pratap Singhasivanon2, Wijitr Fungladda1, Sarigapan Wilailak4
1Department of Family Health, Faculty of Public Health; 2Department of Tropical Hygiene, Faculty of Tropical Medicine, Mahidol University; 3Department of Social and Environmental Medicine, Faculty of Tropical Medicine, Mahidol University; 4Department of Obstetrics and Gynecology, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

The purpose of this cross-sectional study was to examine the causal relationships among age, education, family income, and stage of carcinoma, perceived benefits, perceived barriers, perceived self-efficacy, health promoting behavior and quality of life in patients with cervical cancer. Pender’s Health Promotion Model (996) provided a guide for the conceptual framework of this study. Purposive sampling was employed to recruit 488 cervical cancer patients who were undergoing radiotherapy at seven public hospitals in five areas of Thailand. The instruments used in this study included personal data form, cognitive perception form, health promoting behavior scale, the social support questionnaire and the Functional Assessment of Cancer Therapy General (FACT-G) form. The proposed model was tested and modified by the LISREL Program. The modified model adequately fitted with the data and accounted for 63%. The results demonstrate that health promoting...
behavior had a significant direct positive effect on quality of life ($\beta$ =0.71, p<0.01). Cognitive perceptual factors had a significant direct effect on health promoting behaviors ($\beta$=0.69, p<0.01). Social support had a significant direct effect on the cognitive perceptual factors ($\beta$ =0.64 p<0.01), health promoting behavior ($\beta$ =0.70, p<0.01), and the quality of life ($\beta$ =0.48 p<0.01). Age and education did not have a significant total effect on the quality of life. Family income had a significant direct effect on cognitive perceptual factors ($\beta$ =0.10, p<0.05). The stage of cancer had significant direct negative effect on cognitive perceptual factors ($\beta$ = -0.11, p<0.05) and the quality of life ($\beta$ = -0.12, p<0.01). The direct effect of the predictors on the quality of life indicated that cervical cancer patients with higher practice of health promoting behavior tended to have a higher quality of life.

The findings indicate that Pender’s Health Promotion Model is a usual guide for explaining and predicting the health promoting behavior and the quality of life of Thai cervical cancer patients who were undergoing radiotherapy. The significance of cognitive perceptual factors and social support confirm health promoting behavior as a goal directs toward the level of well being. That have implications for health care systems in planning interventions to promote health promoting behavior, in a health promotion setting in cervical cancer patients for a better quality of life and healthy. A longitudinal study and experimental study are recommended for further study.

Correspondence: Pimsurang Taechaboonsermsak, Department of Family Health, Faculty of Public Health, Mahidol University, 420/1 Ratchawithi Road, Bangkok 10400. Thailand.


A RANDOMIZED TRIAL OF ARTEMETHER-LUMEFANTRINE VERSUS MEfloquine-ArtESUNATE FOR THE TREATMENT OF UNCOMPROMIZED MULTI-DRUG RESISTANT PLASMODIUM FALCIPARUM ON THE WESTERN BORDER OF THAILAND


Shoklo Malaria Research Unit, Mae Sod, Tak Province, Thailand. robert@shoklo-unit.com

BACKGROUND: The use of antimalarial drug combinations with artemisinin derivatives is recommended to overcome drug resistance in Plasmodium falciparum. The fixed combination of oral artemether-lumefantrine, an artemisinin combination therapy (ACT) is highly effective and well tolerated. It is the only registered fixed combination containing an artemisinin. The trial presented here was conducted to monitor the efficacy of the six-dose regimen of artemether-lumefantrine (ALN) in an area of multi-drug resistance, along the Thai-Myanmar border.

Methods: The trial was an open-label, two-arm, randomized study comparing artemether-lumefantrine and mefloquine-artesunate for the treatment of uncomplicated falciparum malaria with 42 days of follow up. Parasite genotyping by polymerase chain reaction (PCR) was used to distinguish recrudescent from newly acquired P. falciparum infections. The PCR adjusted cure rates were evaluated by survival analysis.

Results: In 2001-2002 a total of 490 patients with slide confirmed uncomplicated P. falciparum malaria were randomly assigned to receive artemether-lumefantrine (n=245) or artesunate and mefloquine (n=245) and were followed for 42 days. All patients had rapid initial clinical and parasitological responses. In both groups, the PCR adjusted cure rates by day 42 were high: 98.8% (95% CI 96.4, 99.6%) for artemether-lumefantrine and 96.3% (95% CI 93.1, 98.0%) for artesunate-mefloquine. Both regimens were very well tolerated with no serious adverse events observed attributable to either combination.

Conclusion: Overall, this study confirms that these two artemisinin-based combinations remain highly effective and result in equivalent therapeutic responses in the treatment of highly drug-resistant falciparum malaria.

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BEYOND DEWORMING

Jimba M, Waikugul, Kojima S, Takeuchi T, Singhasivanon P

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CHRONICLE OF MALARIA EPIDEMICS IN THAILAND, 1980-2000


Bureau of Vector Borne Disease, Department of Disease Control, Ministry of Public Health, Nonthaburi 11000, Thailand. supwadee@health.moph.go.th

THE occurrence of malaria epidemics in Thailand was reviewed from the malaria surveillance report of the National Malaria Control Program. The literature review revealed that the four epidemic periods recorded during 1980-2000 almost always occurred in the provinces and districts located along international borders. Malaria epidemics are caused by
various factors such as: extensive population movement, multi-drug resistance development, low immune status of the population, lack of knowledge and appropriate personal protection against mosquito biting, and the re-emergence of malaria transmission in low malarious areas. Such factors can lead to changes in the parasite ratio and appearance of malaria epidemics throughout the country. Evidence related to the burden of malaria epidemics was also reviewed to identify causal factors that will be helpful in future research.


**FACTORS ASSOCIATED WITH OBESITY AMONG WORKERS IN A METROPOLITAN WATERWORKS AUTHORITY**

Kantachuvessiri A, Sirivichayakul C, KaewKungwal J, Tungtrongchitr R, Lotrakul M

Department of Social and Environmental Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand. akanta@medscape.com

To examine the relationship of socio-demographic characteristics, psychological factors, knowledge, attitude and behavior towards obesity among Metropolitan Waterworks Authority (MWWA) officers, a cross-sectional study was conducted between July and September, 2004. Two hundred and eighty-eight obese [body mass index (BMI) \( \geq 25 \) kg/m\(^2\)] and 106 non-obese persons, aged 20-60 years, were recruited as study subjects. Data were collected by a self-administered questionnaire, comprised of three parts: socio-demographic; psychological factors (depression and stress); and knowledge, attitude, behavior related to obesity. Univariate analyses and Logistic regression models were used to study the association between obesity and possible risk factors. The results demonstrate significant associations between older age and obesity. Volunteers in the age groups of 40-49 and 50-59 years had a significantly higher risk of being obese than the age group of less than 40 years (adjusted OR = 3.4, 95% CI = 1.1-11.1 and adjusted OR = 10.4, 95% CI = 3.3-32.7, respectively). Volunteers with unhealthy behaviors were at significantly higher risk than those with healthy behaviors (adjusted OR = 10.3, 95% CI = 2.0-52.4) while persons with moderately healthy behaviors also had increased risk, but to a lesser extent (adjusted OR = 4.5, 95% CI = 1.7-11.4). There were no associations between psychological factors and obesity in this group of volunteers. When we focused on whether they consumed more food when they were stressed, it was found that the obese consumed significantly more food during stress (p-value = 0.003). Watching television, videos, or playing computer continuously for more than 3 hours, were significantly associated with obesity. We conclude that although the obese have a good knowledge and attitude towards obesity, they still practise unhealthy behavior, have a sedentary lifestyle, and over eat when they are stressed. Future research regarding behavioral modification should be implemented at both community and country levels.


**IKONOS-DERIVED MALARIA TRANSMISSION RISK IN NORTHWESTERN THAILAND**

Sithiprasasna R, Ugsang DM, Honda K, Jones JW, Singhasivanon P

Department of Entomology, US Army Medical Component, Armed Forces Research Institute of Medical Sciences, Bangkok

We mapped overall malaria cases and located each field observed major malaria vector breeding habitat using Global Positioning System (GPS) instruments from September 2000 to October 2003 around the three malaria-endemic villages of Ban Khun Huay, Ban Pa Da, and Ban Tham Seau, Mae Sod district, Tak Province, Thailand. The land-use/land-cover classifications of the three villages and surrounding areas were performed on IKONOS satellite images acquired on 12 November 2001 with a spatial resolution of 1 x 1 m. Stream network was delineated and displayed. Proximity analysis was performed on the locations of the houses with and without malaria cases within a 1.5 km buffer from *An. minimus* immature mosquito breeding habitats, mainly stream margins. The 1.5 km used in our proximity analysis was arbitrarily estimated based on the *An. minimus* flight range. A statistical t-test at 5% significance level was performed to evaluate whether houses with malaria cases have higher proximities to streams than houses without malaria cases. The result shows no significant difference between proximity to streams between houses with malaria cases and houses without malaria cases. We suspect that the actual flight range of *An. minimus* may be greater than 1.5 km. The *An. minimus* larval habitat deserves more detailed investigation. Further studies on human behavior contrary to that required for adequate malaria control among these three villages are also recommended.

WATER QUALITY AND BREEDING HABITATS OF ANOPHELINE MOSQUITO IN NORTHWESTERN THAILAND

Kengluecha A, Singhasivanon P, Tien suwan M, Jones JW, Sithiprasasna R

Department of Entomology, US Army Medical Component, Armed Forces Research Institute of Medical Sciences, Bangkok.

MALARIA transmission is dependent upon many hydrology-driven ecological factors that directly affect the vectorial competence, including the presence of suitable habitats for the development of anophele ne larvae. Larval habitats were identified and characterized at three malaria endemic villages (Ban Khun Huay, Ban Pa Dae, and Ban Tham Seau) in Mae Sot district, Tak Province, in northwestern Thailand between July 2002 and June 2003. The Global Positioning System (GPS) was used to provide precise locational data for the spatial distribution of anophele ne mosquito larvae and their habitats. Ten habitat categories were identified. Eighteen adult Anopheles species were identified from larvae in all the surveyed habitats. An. minimus was the most common species throughout the year. The relationship between eight abiotic variables (temperature, hardness, carbon dioxide, dissolved oxygen, nitrate, phosphate, silica and pH) and the abundance of four major species of malaria vectors (An. (Cel.) dirus, An. (Cel.) minimus, An. (Cel.) maculatus, and An. (Cel.) sawadwongporni), and six species of non-vectors (An. (Cel.) kochi, An. (Cel.) jamesii, An. (Ano.) peditaeniatus, An. (Ano.) barbirostris, An. (Ano.) campestris, and An. (Cel.) vagus) larvae was investigated. The results from the multiple regression models suggest that hardness, water temperature and carbon dioxide are the best predictor variables associated with the abundance of An. minimus larvae (p < 0.001); water pH for An. dirus larvae (p < 0.001); temperature and pH for An. kochi larvae (p < 0.01); temperature and silica concentration for An. jamesii larvae (p < 0.001); dissolved oxygen and silica concentration for An. campestris larvae (p < 0.001); and pH and silica concentration for An. vagus larvae (p < 0.001). We could not identify key environmental variables for An. maculatus, An. sawadwongporni, An. peditaeniatus, and An. barbirostris.


EPIDEMIOLOGY OF INTESTINAL PARASITIC INFECTIONS AMONG KAREN SCHOOL CHILDREN ON THE WESTERN BORDER OF THAILAND

Wanchai Maneebonyang¹, Jareemet Lim somboon², Irwin F Chavez³, Nipon Thanyavanich⁴, Suthiporn Prommongkol⁵, Supalarp Puangsa-art⁶, Pitak Wuthisen⁷

¹Department of Tropical Hygiene, ²Department of Social Medicine and Environment, Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand

We studied the stool samples of 701 school children from three primary schools near the Thai-Myanmar border, in Suanphung District, Ratchaburi, Thailand, to determine the prevalence and intensity of intestinal parasitic infections in August and September, 2005. The samples, 49.4% male and 50.6% female were examined using the Kato-Katz technique to detect helmint h ova, and simple smear method to detect protozoa. The intensity of infection was categorized as light, moderate or heavy according to the thresholds set by the World Health Organization. The results revealed a helmint h infection rate of 40.8%, while protozoa infections accounted for 26.4%, mixed infections were common, resulting in a total prevalence of both parasites of 55.1%. The most common infection was hookworm (24.5%) followed by trichuriasis (22.4%) and ascariasis (7.9%). The protozoal infections were Entamoeba coli (14.1%), Giardia intestinalis (8.4%), Endolimax nana (4.9%), Entamoeba histolytica (2.6%) and Cyclospora cayetanensis (0.1%). The prevalence rates of trichuriasis and ascariasis infection were significantly different among the three schools. Males were more frequently infected with hookworm (30.4%) than females (18.9%), but no significant difference in prevalence rates for both sexes were observed for whipworm and roundworm infections. The prevalence rates of hookworm tended to increase among the age group of 12-16 years (41.4%). Roundworm infections were more common among those aged <12 years, with the highest prevalence rate among children in the age group of 8-11 years (10.0%). Hookworm and trichuriasis infections among Karen children were significantly higher than Thai, and children from other ethnic groups (p < 0.05). More than 80% of individuals with hookworm and trichuriasis had light infections. Among those with ascariasis, 10.9 and 49.1%, had moderate and heavy infections, respectively. Heavy infections with ascariasis were frequently observed in children aged 4-7 years.

AZITHROMYCIN COMBINATION THERAPY WITH ARTESUNATE OR QUININE FOR THE TREATMENT OF UNCOMPPLICATED FALCIPARUM MALARIA IN ADULTS. PROMISING RESULTS: FROM A RANDOMIZED PHASE 2 CLINICAL TRIAL IN THAILAND

Noedl H1, Krudsood S2, Chalermratana K2, Silachamroon U3, Looareesuwan S2, Miller RS3, Jongsakul K3, Fukuda M3, Ohrt C4, Rowan J5, Knirsch C6

1Usamc-afrims, Bangkok; 2Hospital for Tropical Diseases, Mahidol University, Bangkok; 3Usamc-afrims, Bangkok; 4Wrair, Silver Spring, Md, USA; 5Anti-Infectives, Pfizer Inc, New York, NY, USA; 6Anti-Infectives, Pfizer Inc, New York, NY, USA

AZITHROMYCIN may have an important role as an antimalarial due to its safety in children and experience with use in pregnancy. The study was designed as a phase II open label, randomized 28-day inpatient study of acute, uncomplicated falciparum malaria, comparing the safety and efficacy of 2 azithromycin (AZ)–artesunate (AS) combinations with 2 AZ – quinine (QN) regimens in 100 adult patients: 1. Three days of AZ 750 mg BID + AS 100 mg BID 2. Three d of AZ 1000 mg QD + AS 200 mg QD 3. Three d of AZ 750 mg BID + QN 10 mg/kg BID 4. Three d of AZ 500 mg TID daily + QN 10 mg/kg TID. After completion of the first 50 subjects failure rates, PCT, and FCT were compared in a preliminary efficacy analysis. The presentation at the IFTM meeting will be based on the final study results. The 28-day cure rates for the 4 groups were 100 (95%CI: 71.5-100), 100 (73.5-100), 72.7 (39.0-94.0), and 91.7% (61.5-99.8), respectively. No failures were seen in either of the artesunate arms, two RIIIs and one RI failure in the BID quinine arm, and one RI in the TID quinine arm. With a mean PCT and FCT of 34±12 and 26±18 hours the artesunate combinations led to a significantly (P<0.001) faster clinical and parasitological improvement than the quinine arms (80±34 and 60±39 hours). Clinical treatment response was closely correlated with in vitro drug sensitivity data. No drug-related SAEs were seen and the drug combinations were well tolerated and safe. In conclusion, these data suggest that azithromycin-artesunate, even when given only once daily for 3 days, as well as azithromycin-quinine TID may be safe and highly efficacious combination treatments for uncomplicated falciparum malaria.


MALARIA REATMENT 2005: 1. TREATMENT OF SEVERE MALARIA

Srivicha Krudsood1, Polrat Wilairatana2, Chaiporn Rojanawatsirivej1, Sornchai Looareesuwan2

1Department of Tropical Hygiene, Faculty of Tropical Medicine, Mahidol University, Bangkok Thailand; 2Department of Clinical Tropical Medicine, Mahidol University, Bangkok Thailand; 3Malaria Division, Department of Communicable Disease Control, Tiwanond Road, Nonthaburi 11000, Thailand, Ministry of Public Health

T HE treatment for uncomplicated malaria is aimed at producing a radical cure using the combination of (1) artesunate (4 mg/kg/day) plus mefloquine (8 mg/kg/day) for 3 dyas (2) a fixed dose of artemether and lumefatrine (20/120 mg tablet) named Coartem (4 tablets twice a day for three days for adults weighing more than 35 kg) (3) quinine 10 mg/kg 8-hourly plus tetracycline 250 mg 6-hourly for 7 dyad (or doxycycline 200 mg once a day for 7 days as an alternative to tetracycline) in patients aged 8 years and over (4) a combination of atovaquone and proquani called “Malarone” (in adult, 4 tablets given daily x 3 days). In treating severe malaria, early diagnosis and early treatment with a potent antimalarial drug is recommended to save the patient’s life. The antimalarial drugs of choice are (1) intravenous quinine loading dose 20 mg/kg i.v. drip in 2-4 hours followed by maintainances dose 10 mg/kg i.v. drip in 2 hour every 8 hours or (2) a parenteral form of an artemisinin derivative (2.1) (artesunate i.v. 24 mg/ kg at 0, 12, 24 hours then daily with the total dose of 12, 15 mg/kg or (2.2) artesunate suppository (5 mg/kg) given rectally 12 hourly for 3 days). Oral artemisinin derivatives (artesunate, artemether, dihydroartemisinin with the dose 4 mg/kg/day should replace parenteral forms when patients can tolerate oral medication to complete the total dose (12-15 mg/kg). Oral mefloquant (25 mg/kg divided into two doses 8 hrs apart) should be given at the end of the artemisinin treatment course to reduce recrudescence if the course of treatment is shorten than 7 days. Treatment of vivax malaria is chloroquine (30 mg/kg given in 3 days) followedby primaquine (0.3-0.5 mg/kg/day) for 14 days.

ARTEMIFONE, A NEW ANTI-MALARIAL ARTEMISININ DERIVATIVE: OPEN PILOT TRIAL TO INVESTIGATE THE ANTIPARASITIC ACTIVITY OF BAY 44-9585 IN PATIENTS WITH UNCOMPLICATED P. FALCIPARUM MALARIA

Krudosod S1, Wilairatana P1, Chalermrut K1, Leowattana W1, Voith B2, Hampel B2, Looaeresuwan S1

1Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; 2Bayer HealthCare, Wtal, Germany

During 28 days of treatment, serum DHEAS and Hb levels were analyzed on day 0, day 7, day 14, day 21 and day 28 for monitoring the association. We found that, DHEAS levels were significantly associated with decreased parasite density, and also significantly associated with increased hemoglobin levels through 4 weeks of follow up, even after adjustment for other determinants of hemoglobin level. These findings support the hypothesis that DHEAS, an adrenal androgen which is low in childhood and rises with the development of secondary sexual characteristics, is necessary for resistance to malarial infection. Moreover, the physiological hormone DHEAS is a potent inhibitor of G6PD activity, and G6PD deficiency is known to exert antimalarial protection via enhanced opsonization and phagocytosis of rings, the early forms of the parasite. This study suggests that DHEAS should be analyzed in malaria patients and also be used as adjuvant therapy to stimulate red blood cell production in severe falciparum malaria patients.


EPIDEMIOLOGY OF HIV INFECTIONS AMONG SCREENED VOLUNTEERS PARTICIPATED IN AN HIV VACCINE PHASE III TRIAL, THAILAND

Premsri Nakorn1, Namwat Chawetsan1, Woratanarat Thira1, Rerks-Ngarm Suphachai1, Chunsuttiwat S1, Nitayaphan S2, Eamsila C2, Kitayaporn D1, Keawkungwal J1, Kim J1

1Prime-Boost HIV Vaccine Phase III Trial, Dept. of Disease Control, MOPH Thailand, 2Armed Forces Research Institute of Medical Services (AFRIMS), Thai and US components, Thailand, 3Faculty of Tropical Medicine, Mahidol University, Thailand

BACKGROUND: The trend of HIV infection has shown striking transmission among adolescents and young adults. The Prime-Boost HIV Vaccine phase III trial has thus selected screen healthy Thai adults aged 20-30 years in Chon Buri and Rayong since September 2003. We describe preliminary epidemiological data among those screened volunteers.

Methods: As of November 2004, we have screened 12,094 volunteers using the standard EIA and confirmation tests. Demographic data of volunteers were obtained using standardized interviewed questionnaires.

Results: We found 207 infected screened volunteers (1.7%). There was no difference of prevalence between gender (p=0.23) or among birthplaces (p=0.07). The married and ex-married volunteers were found higher of HIV infection prevalence than the single

INTERNATIONAL COLLABORATION IN DATA MANAGEMENT FOR A LARGE SCALE PHASE III VACCINE TRIAL, THAILAND

Kaewkungwal J1, Kitayaporn D1, Khamsiriwatchara A1, Wongwit W1, Pitsutthithum P1, Nitayapan S1, Garner R1, Kim J1, Rerks-Ngarm S1, Nitayapan S1, MoPH TAVEG For5

1Data Management Unit, Faculty of Tropical Medicine, Mahidol University, Thailand, 2Clinical Research Unit, Faculty of Tropical Medicine, 3Armed Forces Research Institute of Medical Sciences, Thailand, 4Walter Reed Institute of Army Research, US, 5Ministry of Public Health, Thailand

ISSUES: Data management and quality assurance play important roles in efficacy trial conclusions. The collaboration between different teams involving in data processing is essential. Can this process be performed and accepted in international standards in a developing country?

Project: A Prime-Boost HIV Vaccine Phase III Trial is currently conducted in Thailand. This trial will screen 25,000 and enroll 16,000 volunteers. There will be approximately 500,000 forms capturing trial data during 3-years follow-up period.

Results: The current community-based trial requires several data management teams. Thai teams include 323 clinic-data staff members (48 sites), 9 laboratory data staff, 10 QA coordinators and 16 DMU personnel. Data flow also involves US teams including 7 members in data analysis coordinating team, 2 independent statisticians and 2 adverse event coding staff. The DMU gained experiences in managing secondary database for VaxGen gp120 trial. As this is the first trial in Thailand to maintain primary database subject to be audited by the US FDA, technology transfer including infrastructure installation, system validation and training according to international standards are fully supported.

Lessons learned: This collaboration is an ideal example for cooperation between sponsor and host countries. Data management with industry standard compliance can be done in developing countries.

NOVEL DNA AMPLIFICATION ON CHROMOSOMES 2P25.3 AND 7Q11.23 IN CHOLANGIO-CARCINOMA IDENTIFIED BY ARBITRARILY PRIMED POLYMERASE CHAIN REACTION

S Charyalertsak1, T Khuhaprema2, V Bhudsawadsi3, B Sripa4, S Wongkham5 S Petmitr6  
1Department of Tropical Nutrition and Food Science, Faculty of Tropical Medicine, Mahidol University, 4206 Rajvithi Road, Bangkok; 2National Cancer Institute, Bangkok; 3Liver Fluke and Cholangiocarcinoma Research Center, Faculty of Medicine Khon Kaen University, Khon Kaen, Thailand

PURPOSE: To detect and characterize amplified DNA sequences in cholangiocarcinoma (CCA). Patients and methods: We extracted DNA from tumor and corresponding normal tissues of 30 patients with CCA and amplified with 30 random ten-mer arbitrary primers by the arbitrary primers polymerase chain reaction (AP-PCR) technique. Results: Our results showed gains of genomic sequences at high frequency. Using the AX-11 arbitrary primer, we determined an amplified DNA fragment occurred frequently in the tumors analyzed. The DNA fragment was isolated and identified as two sequences mapped to chromosomes 2p25.3 and 7q11.23. Specific primers were designed employing these sequences and used for detecting amplification by realtime quantitative PCR. The amplification of the DNA sequences on chromosomes 2p25.3 and 7q11.23 was detected in 10 (33%) and 6(20%) cases, respectively. Thirteen (43%) cases showed amplification on both or one of the chromosomes. In addition, amplification of the DNA on chromosome 2p25.3 was predominantly observed in poorly differentiated tumors. Conclusions: Our findings suggest that the novel amplified DNA on chromosomal regions at 2p25.3 and 7q11.23 might be the reason that obese people frequently develop type 2 diabetes mellitus. Further research into the pathophysiology of adiponectin and obesity is needed to elucidate this relationship.


ADIPONECTIN/ACP30, A COLLAGEN-LIKE PLASMA PROTEIN, IN RELATION TO ANTHROPOMETRIC MEASUREMENT IN THAI OVER-WEIGHT AND OBESE SUBJECTS

Rungsunn Tungtrongchitr1, Piyawan Sricharoen2, Praneet Pongpaew3, Benjaluck Phonrat2, Dumrongkiet Arthan1, Niyomsri Vudhivai1, Anchalee Tungtrongchitr1, Suporn Paksanont4, Somchai Pououdong1, Frank Peter Schelp5  
1Department of Tropical Nutrition and Food Science, Faculty of Tropical Medicine, Mahidol University, 4206 Ratchawithi Road, Ratchathewi, Bangkok; 2Department of Tropical Medical, Faculty of Tropical Medicine, Mahidol University, Bangkok; 3Department of Parasitology, Faculty of Medicine Siriraj Hospital, Mahidol University; 4Department of Tropical Radioisotopes, Faculty of Tropical Medicine, Mahidol University, Thailand; 5Center for Humanity and Health Sciences, Free University, Berlin and Humboldt University, Berlin, Germany

A DIPONECTIN, anthropometric parameters including weight, height, BMI, arm circumference, triceps skinfold, subscapular skinfold, waist, hip circumferences and waist/hip ratio in 48 male and 166 female overweight and obese Thai volunteers (BMI ≥ 25.00 kg/m²), and 26 male and 81 female normal subjects (BMI = 18.5-24.9 kg/m²), were recorded. Thai volunteers were investigated. Statistically significantly lower adiponectin concentrations in overweight and obese subjects were found when compared to control subjects of both sexes. Anthropometric parameters, including weight, height, BMI, arm circumference, triceps skinfold, subscapular skinfold, waist, hip circumferences and waist/hip ratio, except arm span, were statistically significantly higher in overweight and obese subjects than in control subjects. The overweight and obese subjects had higher glucose concentrations than the control subjects. BMI and glucose concentrations were found to be significantly related, under these conditions, to adiponectin. The decrease in adiponectin concentration in the overweight and obese subjects, which was related to high glucose concentration, might be the reason that obese people frequently develop type 2 diabetes mellitus. Further research into the pathophysiology of adiponectin and obesity is needed to elucidate this relationship.


HOMOCYSTEINE AND VITAMIN IN HEALTHY THAI SMOKERS

Kanjana Suriyaprom1, Rungsunn Tungtrongchitr1, Praneet Pongpaew1, Benjaluck Phonrat1, Talaporn Harroonrojg1, Niyomsri Vudhivai1, Anchalee Tungtrongchitr1, Suporn Paksanont4, Somchai Pououdong1, Frank Peter Schelp5  
1Department of Tropical Nutrition and Food Science, Faculty of Tropical Medicine, Mahidol University, Bangkok; 2Department of Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok; 3Department of Parasitology, Faculty of Medicine Siriraj Hospital, Mahidol University; 4Department of Tropical Radioisotopes, Faculty of Tropical Medicine, Mahidol University, Thailand; 5Center for Humanity and Health Sciences, Free University, Berlin and Humboldt University, Berlin, Germany

B ACKGROUND: Cigarette smoking is considered to increase morbidity and the mortality risk of cardiovascular diseases. B vitamins regulate the metabolism of homocysteine via remethylation and transsulfuration pathways.

Objective: The purpose of this study was to investigate homocysteine concentrations, vitamin status, anthropometric and haematological measurements of healthy smokers compared with healthy nonsmoking subjects.

Design: This cross-sectional study was carried...
out among smokers and nonsmokers from suburban and urban residential areas in Bangkok, Thailand.

**Subjects:** 174 smokers and 97 nonsmokers (aged 19-62), who participated voluntarily in the study, were investigated. Total homocysteine, folate, vitamin B₂, B₁₂, and C concentrations were measured.

**Results:** Total homocysteine concentrations in plasma were significantly higher in smokers than nonsmokers. Vitamin B₂, folate, B₁₂, and C concentrations were significantly lower among smokers than nonsmokers but vitamin B₁ was not significantly different between these groups. Total homocysteine concentration was significantly positive correlation with waist/hip ratio and smoking characteristics such as the number of cigarettes per day and pack-years but significantly negative association with folate and vitamin B₁₂. There were significant positive associations among the number of cigarettes smoked per day WBC count and waist/hip ratio. Furthermore, the prevalence of hyper-homocysteinemia in smokers (62%) was more common than in nonsmokers (33%).

**Conclusion:** These findings suggest that increased plasma total homocysteine Concentrations in Healthy Thai smokers may be explained by low B vitamin status that are involved in homocysteine metabolism such as vitamin B₂, folate, and B₁₂. The elevation of the number of cigarettes smoked per day and pack-years, WBC count, and high percentage of hyperhomocysteinemia among smokers may contribute to increased risk of atherosclerosis or cardiovascular disease development.

**ABSTRACTS**

**METHYLENETETRAHYDROFOLATE REDUCTASE (MTHFR) POLYMORPHISM (C677T) IN RELATION TO HOMOCYSTEINE CONCENTRATION IN OVERWEIGHT AND OBESE THAI**

Kittisak Thawnashom¹, Rungsun Tungtrongchitr⁴, Songsak Petmitr¹, Praneet Pongpaew¹, Benjaluck Phonrat², Anchalee Tungtrongchitr³, Frank Peter Schelp⁵

¹Department of Tropical Nutrition and Food Science, Faculty of Tropical Medicine, Mahidol University, Bangkok; ²Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok; ³Department of Parasitology, Faculty of Medicine Siriraj Hospital, Mahidol University, Prannok Road, Bangkok, Thailand; ⁴Department of Epidemiology, Institute of Social Medicine, Free University, Berlin, Germany

Methylenetetrahydrofolate reductase (MTHFR) is one of the main enzymes of homocysteine metabolism. Several studies have examined the association of a common mutation C677T with plasma homocysteine and vitamin status involved in the metabolic pathway and related to many diseases. We analyzed the association between MTHFR (C677T) gene polymorphism with serum concentration of homocysteine, folate and vitamin B₁₂ in 37 male and 112 female overweight/obese Thai volunteers (BMI ≥25.00 kg/m²) compared with 23 male and 90 female control subjects (BMI = 18.5-24.99 kg/m²). Statistically significantly higher levels of serum homocysteine concentration were found in the overweight/obese than the control subjects (p<0.05). Serum folic acid levels in the overweight/obese subjects were statistically significantly lower than the control subjects (p< 0.05). When the data were grouped according to homocysteine concentration and MTHFR gene polymorphism, there were statistically significantly higher homocysteine concentrations in the overweight/obese than the control subjects only in wide type gene polymorphism (CC) in the hyperhomocysteine group (homocysteine >10.0 μmol/L) (p<0.05), while in all genotype polymorphism (CC, CT, TT) there were lower folic acid and vitamin B₁₂ concentrations in the overweight/obese than in the control subjects. In hyperhomocysteine groups, there was no statistically significant difference in frequencies of MTHFR (C677T) gene polymorphism between the overweight/obese and control subjects. Folic acid and gene polymorphism were found to be significantly related to overweight/obese and control groups in logistic regression analysis (p<0.05). The results supported the supposition that folic acid is more important than vitamin B₁₂. It can be concluded that gene polymorphism C677T, which is also significant difference in frequencies of MTHFR (C677T) gene polymorphism between the overweight/obese and control subjects.

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

Supaluk Poprak¹, Rungsun Tungtrongchitr¹, Praneet Pongpaew¹, Benjaluck Phonrat ², Anchalee Tungtrongchitr³, Siriwan Vudhivai antennae, Frank Peter Schelp⁵

¹Department of Tropical Nutrition and Food Science, Faculty of Tropical Medicine, Mahidol University, Bangkok; ²Department of Tropical Medicine, Faculty of Tropical Medicine, Mahidol University; ³Department of Parasitology, Faculty of Medicine Siriraj Hospital, Mahidol University; ⁴Department of Radiology, Faculty of Medicine Siriraj Hospital, Mahidol University; ⁵Department of Tropical Medicine, Mahidol University; ⁶Department of Epidemiology, Institute of Social Medicine, Free University, Berlin, Germany

The median and 95% confidence interval (CI) for median of age, anthropometric variables, soluble leptin receptor, serum leptin and lipid profile levels of 48 overweight ( BMI = 25.00-29.99 kg/m²) and obese (BMI ≥ 30.00 kg/m²) subjects were calculated.
Thai males and 166 overweight and obese Thai females, compared with 26 males and 81 females in a control group (BMI = 18.50-24.99 kg/m²), were determined. The study subjects were persons who turned up regularly for physical check-ups at the Out-patient Department, General Practice Section, Ratchawithi Hospital, Bangkok, aged between 18-60 years. Serum leptin, triglyceride and low density lipoprotein cholesterol/high density lipoprotein cholesterol ratios (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 the 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 between weight, BMI, waist, hip and HDL-C, with leptin. Serum soluble leptin receptor levels were significantly negatively correlated with leptin and BMI. The results can elucidate the causes and consequences of obesity, and are negatively correlated with leptin and BMI. The results can aid the provision of care for overweight and obese people.


LOW FOLATE STATUS AS A RISK FACTOR FOR CERVICAL DYSPLASIA IN THAI WOMEN

Kwanbunjun K¹, Saengka P¹, Cheeramakara C², Thanomsak W², Benjachai W³, Laisupasin P¹, Buchachart K¹, Songmuang K², Boontaveeyut N³

¹Department of Tropical Nutrition and Food Science, Mahidol University, Bangkok; ²Department of Tropical Radioisotopes, Mahidol University, Bangkok; ³National Cancer Institute, Bangkok; ²Chonburi Cancer Center, Chonburi; ¹Department of Nutrition, Faculty of Public Health, Mahidol University, Bangkok 10400, Thailand

Serum folate was markedly lower in both low-grade and high-grade cervical neoplasia cases compared with the control women. Using logistic regression, the odds ratio for low-grade cervical neoplasia with low serum folate level (19.82 nmol/L) was 6.13, whereas that of the high-grade group with the same folate level was 5.57. The findings support the contention that folate deficiency of women in this study had an increased risk of cervical change.


ANALYSIS OF SEQUENCE VARIATION IN GNATHOSTOMA SPINIGERUM MITOCHONDRIAL DNA BY SINGLE-STRAND CONFORMATION POLYMERASE MIMICRY ANALYSIS AND DNA SEQUENCE

Charinthorn Ngarmamonpirat¹, Jitra Waikagul¹*, Songsak Petmitr², Paron Dekumyoy³, Wichit Rojekittikhun¹, Malinee T Anantapruti¹

¹Department of Helminthology, Faculty of Tropical Medicine, Mahidol University, Bangkok; ²Department of Tropical Nutrition and Food Science, Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand

MORPHOLOGICAL variations were observed in the advance third stage larvae of Gnathostoma spinigerum collected from swamp eel (Fluca alba), the second intermediate host. Larvae with typical and three atypical types were chosen for partial cytochrome c oxidase subunit I (COI) gene sequence analysis. A 450 bp polymerase chain reaction product of the COI gene was amplified from mitochondrial DNA. The variations were analyzed by single-strand conformation polymorphism and DNA sequencing. The nucleotide variations of the COI gene in the four types of larvae indicated the presence of an intra-specific variation of mitochondrial DNA in the G. spinigerum population.


POLYMORPHISM OF GLUTATHIONE-S-TRANSFERASE OMEGA GENE AND RISK OF CANCER AMONG THAI PATIENTS

Sujan Babu Marahatta¹, Phaibul Punyarit¹, Wanida Pongstaporn¹, Vajarabhaongsa Bhudisawasdi², Banchob Sripa³, Sopit Wongkhiam³, Songsak Petmitr¹

¹Department of Tropical Nutrition and Food Science, Faculty of Tropical Medicine, Mahidol University, Bangkok; ²Department of Pathology, Phramongkutklao College of Medicine, Bangkok; ³Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand

POLYMORPHIC glutathione-S-transferase (GST) genes causing variations in enzyme activity may influence individual susceptibility to cancer. The
omega class glutathione-S-transferases (GSTO) has been reported to exhibit novel glutathione dependent thiol transferase, dehydroascorbate reductase, monomethylarsonate reductase activities and modulate Ca²⁺ release by ryanodine receptors as well as induce IL-1β post translational processing of cytokine releasing inhibitory drugs. Though polymor-phisms have been reported in GSTO1 and GSTO2, their predisposition to cancer risk has not yet been explored. In this case control study, 58 liver cancer cases (28 cases of hepatocellular carcinoma and 30 cases of cholangiocarcinoma), 31 cases of colorectal cancer, 30 cases of breast cancer and 68 controls were compared for frequencies of GSTO1 and GSTO2 genotypes determined by polymerase chain reaction (PCR) restriction fragment length polymorphism (RFLP) based method. The statistical analysis provided the support for the difference in genotypic distribution between hepatocellular carcinoma and control for GSTO1 polymorphisms (GSTO1* A140D: chi squared 2 d.f. = 19.79, P<0.05) as well as in cholangiocarcinoma (GSTO1* A140D: chi squared 2 d.f = 9.02, P<0.05). However, statistically no significant difference was found in genotype distribution for GSTO1 polymorphism (GSTO1* A140D) in colorectal cancer (GSTO1* A140D: chi squared 2 d.f = 1.52, P>0.05), breast cancer (GSTO1* A140D: chi squared 2 d.f = 3.957, P<0.05) and control. Additionally, statistically no significant difference in genotypic distribution for GSTO2 polymorphism (GSTO2* N 140D) was found in all types of cancer cases. An exploratory data analysis also identified statistically significantly increased odds ratio for the combination of GSTO1* A 140/D140 and D140/D140 for hepatocellular carcinoma (P<0.05, OR=8.8, CI 95%: 2.82-28.88), cholangiocarcinoma (P<0.05, OR=3.14, CI 95%: 1.88-8.84) and breast cancer (P<0.05, OR=3.71, CI 95%: 1.09-13.02) but not for colorectal cancer. However, odds ratio for the combination of GSTO2* N142/D142 and D142/D142 in neither of the cancer cases reached a level of significance. The study suggests that GSTO1* A140D polymorphism could play an important role as a risk factor for the development of hepatocellular carcinoma cholangiocarcinoma and breast cancer.


**ABSTRACTS**

**GENETIC POLYMORPHISM OF GLUTATHIONE-S-TRANSFERASE GENE CLASS OMEGA 2 IN ACUTE LYMPHOBLASTIC LEUKEMIA**

Pongstaporn W1, Pakakassama S2, Petmitr S3, Snguansin S4, Thongmee A1, Kanjanpum P4 and Pakeetoot T1

1Rangsit University, Prathamthanaee, Thailand; 2Ramathibodi Hospital, Bangkok, Thailand; 3Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; 4Faculty of Dentistry, Mahidol University, Bangkok, Thailand

**BACKGROUND:** Acute Lymphoblastic Leukemia (ALL) is the most common leukemia in childhood. Glutathione-S-transferases (GST) are a family of enzymes that play an important role in detoxification by conjugation of electrophilic free radicals to glutathione. Glutathione-S-transferase class Omega 2 (GSTO2) is the novel class of GST. Though polymorphism has been reported at codon 142 in GSTO2 gene, the predisposition to cancer risk is still controversial. This is the first study of genetic polymorphism of GSTO2 in acute lymphoblastic leukemia.

**Method:** In this case-control study, 90 cases of ALL and 84 healthy controls were compared for frequencies of GSTO2 genotypes determined by PCR-RFLP based method.

**Results:** The odds ratio for the combination of GSTO2* N142/D142 and GSTO2* D142/D142 polymorphism in neither of the cancer cases reached the level of statistical significance. (odds ratio = 1.071, 95% CI = 0.587 - 1.954). However, there is polymorphism in almost every cases of high risk group and in the cases of abnormal chromosomal study.

**Conclusion:** GSTO2* N142/D142 and GSTO2* D142/D142 genotype is not susceptible to ALL but may be a marker for prediction of the clinical outcome or chemotherapeutic response.

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**IDENTIFICATION OF GENETIC ALTERATION IN CERVICAL CANCER BY ARBITRARILY PRIMED POLYMERASE CHAIN REACTION (AP-PCR) IN THAI PATIENTS**

Rujinee Paditaporn1, Suda Reangrojpitak1, Seangduan Chindavijak2, Anan Korarak2, Phaibul Punyarit3, Songsak Petmitr4

1Department of Pathobiology, Faculty of Science, Mahidol University, Bangkok; 2National Cancer Institute, Bangkok; 3Department of Pathology, Phamongkutkla College of Medicine, Bangkok; 4Department of Tropical Nutrition and Food Science, Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand
CERVICAL cancer is the second most common malignancy in women worldwide, and it remains a leading cause of cancer-related death for women in developing countries. In Thailand, it is the most common gynecologic malignancy. The infection with human papillomavirus and cellular genetic alteration appear to be necessary etiological factors for cervical carcinoma. This study was designed to investigate the genetic instability in cervical carcinoma tissues and provide evidence for discovering new genes and screening diagnostic molecular marker of cervical carcinoma. Genetic alterations in 57 Thai cervical cancer patients were analyzed by Arbitrarily-primed, polymerase chain reaction (AP-PCR) using 57 arbitrary primers. One of the primers, exhibited high frequency of band intensity, 40 out of 57 cases (70.1%). However, other three primers resulted change of banding patterns with frequency 68.4%, 64.9%, and 52.6%, respectively. The results of the current study strongly suggested that AP-PCR is a useful technique for the detection of genetic alterations in cervical cancer.

GENETIC AMPLIFICATION AT CHROMOSOME 4P 15.2 AND 6Q 23-24 IN BREAST CANCER

Wichai Purisa1, Sunanta Chariyalertsak1, Tanett Pakeetoot2, Anant Karalak1, Songsak Petmitr1

1National Cancer Institute, Bangkok 10400, Faculty of Tropical Medicine, Mahidol University, Bangkok; 2Department of Tropical Nutrition and Food Science, Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand

GENE amplification is clearly demonstrated as a promising aspect of tumor growth and development and has prognostic importance in certain cancers. From our previous study, genetic alterations in Thai patients with breast cancer were analyzed by random amplified polymorphic DNA with sixty arbitrary primers, showing that primer D15 can be detected gene gains at the highest frequency (80%). The amplified DNA fragment was then isolated and identified as approximately 600 bp sequences mapped to chromosomes 4p15.2 and 6q23-24, respectively. The specific primers on chromosome 4p15.2 and 6q23-24 were further designed and used to detect gene amplification in paraffin-embedded tissues of patients with breast cancer by real time PCR. Our results found that the gene amplification were detected in 23 out of 34 cases (67.6%) at chromosome 4p15.2 and 14 out of 34 cases (41.1%) at chromosome 6q23-24. The gene amplification at both chromosomes was significantly correlated with advanced stage of cancer (p=0.007 and 0.004 respectively). Moreover, gene amplification at chromosome 4p 15.2 was associated with lymph node metastasis (p=0.009). Our present findings suggest that amplification of the genes located on chromosomes 4p15.2 and 6q 23-24 may be involved in the tumorigenesis of breast cancer in Thai patients.

MICROSATELLITE INSTABILITY AND hMSH2 ALTERATIONS IN THAI SPORADIC COLORECTAL CANCER

Panee Chaksangchaichot1, Phaibul Punyarit2, Songsak Petmitr1

1Department of Tropical Nutrition and Food Science, Faculty of Tropical Medicine, Mahidol University, Bangkok; 2Department of Pathology, Pramongkutklao College of Medicine, Bangkok, Thailand

COLORECTAL cancer can be divided into two types: hereditary and sporadic. Several gene mutations in DNA mismatch repair system (MMR) including hMSH2, hMSH3, hMSH6, hMLH1, hPMS1 and hPMS2 have been widely observed in hereditary and sporadic cancer. The MSH2 gene is a component of the MMR system that is predominantly mutated in tumors showing a mutator phenotype manifested as microsatellite instability thus, an important role in maintaining the stability of microsatellites has been associated to this gene. In this study, we designed to investigate the microsatellite instability by using microsatellite markers (BAT-26 and BAT-40), and genetic alteration (hMSH2) determined by means of PCR-SSCP and nucleotide sequencing technique in sporadic colorectal cancer. Six cases (20%) and five cases (16.6%) of sporadic colorectal cancer manifested microsatellite instability in BAT-26 and BAT-40. With PCR-SSCP, eight cases showed shifted band and were confirmed by DNA sequencing. Seven cases (23%) showed number of poly A alteration in intron 5, only one case revealed mutation in exon 5 of hMSH2. Still, increase knowledge of the properties of MMR system and its connection to other biologic pathway is essential to better understand colorectal cancer development and to identify target for prevention and therapeutics.
MUTAGENICITY STUDY OF WEEDS AND COMMON PLANTS USED IN TRADITIONAL MEDICINE AND FOR ANIMAL FEED

Thepouyporn A1, Kwanbunjan K1, Pooudong S1
1Department of Tropical Nutrition and Food Science, Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand

MUTAGENICITY and antimutagenicity potentials were tested using Ames’ test in crude distilled water and absolute ethanol extracts from the stems and leaves of Peperomia pellucida (Linn.) Kunth, Eichhornia crassipes Solms, Colocasia esculenta Schott and Brachiaria mutica (Forssk.) Stapf, and the stems of Musa sapientum Linn. No mutagenic effect was found in any of the 10 mg/plate crude extracts of these plants for either TA98 or TA100 of Salmonella typhimurium, in a direct test and a mutagenic induced test by S-9 mix. Both distilled water and absolute ethanol extract of 0.5–10 mg/plate B. mutica showed strong antimutagenicity to AFB1, B(a)P and 4NQO in two tester strains. Ethanol extract of 0.1–0.5 mg/plate C. esculenta also showed antimutagenicity to AFB1, B(a)P and 4NQO in two tester strains, but the 0.5–10 mg/plate water extract had an antimutagenic effect for 4NQO in TA98. The ethanol extracts of 5 mg/plate B. mutica and 0.5 mg/plate C. esculenta are cytotoxic, as indicated by their partial killing effect.

Presentation at: Joint International Tropical Medicine Meeting, 30 Nov-2 Dec 2005, Bangkok, Thailand.

VITAMIN B12 STATUS OF THAI WOMEN WITH NEOPLASIA OF THE CERVIX UTERI

Kwanbunjan K1, Saengkar P1, Cheeramakara C2, Tangjitgamol S3, Chitcharoenrung K4
1Department of Tropical Nutrition and Food Science, Mahidol University, Bangkok; 2Department of Tropical Radioisotopes, Mahidol University, Bangkok; 3Bangkok Metropolitan Administration Medical College Vajira Hospital, Bangkok; 4National Cancer Institute, Bangkok, Thailand

The vitamin B12 statuses of Thai women with high- and low-grade cervical dysplasia were studied and compared with women with normal cytological smears. Serum vitamin B12 and vitamin B12 intakes were assessed, as well as demographic characteristics, sexual behavior, reproductive and menstrual history, exogenous hormone used, personal and familial medical history, smoking habit, and other risk factors. The presence or absence of genital HPV DNA was determined by polymerase chain reaction (PCR). Serum vitamin B12 levels and vitamin B12 intakes in women with normal cytological smears were significantly higher than those with both high- and low-grade cervical dysplasia (p<0.001). Increased vitamin B12 serum levels were statistically significantly associated with increased low-grade (OR = 4.08; 95% CI = 1.41-11.79; p<0.05) and increased high-grade cervical dysplasia risk (OR = 3.53; 95% CI = 1.24-10.04; p<0.05) for the highest vs. lowest quartiles of serum vitamin B12. This study indicated a relationship between increased vitamin B12 status and the risk of cervical cancer.

Poster presentation in: Joint International Tropical Medicine Meeting, 30 Nov – 2 Dec 2005, Bangkok, Thailand.

HEALTH BEHAVIOR OF TSUNAMI VICTIMS IN PHANG-NGA PROVINCE, THAILAND

Mas-ngammueng R1, Kwanbunjan K2, Chusongsang P1, Chusongsang Y1, Chantaraniapamong Y2, Pooudong S2, Maneekan P3, Butraporn P1
1Department of Social and Environmental medicine; 2Department of Tropical Nutrition and Food Science; 3Department of Tropical Hygiene, Mahidol University, Bangkok 10400, Thailand

The health behaviors of 250 tsunami victims in Phang-nga Province were surveyed three months after the disaster struck. Questionnaires and non-participant observation were used to study the effects of the disaster on their lifestyles and health behaviors, and the effects of environmental change, which included sanitation, personal hygiene, illness and prophylaxis, and local health care and promotion while residing in temporary shelters provided by government and private donors. Our findings indicated good management of drinking water in the temporary shelters. Toilet construction and water supply were sufficient, but wastewater and sewage systems were poorly managed. Most of the study group complained of back pain, stress, and sleep disturbance. A local hospital and health stations provided medical care. Health awareness according to their perception included food safety, sleeping in mosquito nets, taking medication, and exercise. Most of them regularly slept in mosquito nets and defecated in toilets. They obtained food from donors and occasional purchases. Safe drinking water was free of charge. Some of them smoked tobacco and drank alcohol.

Presentation at: Joint International Tropical Medicine Meeting, 30 Nov-2 Dec 2005, Bangkok, Thailand.
IDENTIFICATION OF DNA AMPLIFICATION ON CHROMOSOME 1P22 IN CERVICAL CANCER

Rujinee Paditaporn1, Suda Reangrojpitak1, Phaibul Punyarit1, Saengduan Chindavijak1, Anant Karalak1, Songsak Petmitr4

1Department of Pathobiology, Faculty of Science, Mahidol University, Bangkok; 2Department of Pathology, Phramongkutklao College of Medicine, Bangkok; 3National Cancer Institute, Bangkok; 4Department of Tropical Nutrition and Food Science, Faculty of Tropical Medicine, Mahidol University, 4206 Rajvithi Road, Bangkok 10400, Thailand

BACKGROUND: In Thailand, cervical cancer is the most common gynecologic malignancy. The infection with human papillomavirus and cellular genetic alteration appear to be necessary etiological factors for cervical carcinoma. This study was designed to investigate the genetic instability in cervical carcinoma tissue and provide evidence for discovering new genes and screening diagnostic molecular marker of cervical carcinoma.

Methods: Genetic alterations in 57 Thai cervical cancer patients were analyzed by Arbitrarily-primed polymerase chain reaction (AP-PCR) with 54 arbitrary primers. The nucleotide sequence of the amplified fragment was performed by DNA sequencing and identified by comparison with the known gene in genome database using Blastn programme.

Results: One of the primers exhibited the highest frequency of a band intensity in 40 of 57 cervical cancer cases (70.1%). The nucleotide sequence of this amplified fragment was homology with the DNA fragment located on chromosome 1p22. Results indicated that the DNA amplification on chromosome 1p22 may be associated with cervical cancer development.

Conclusions: This findings demonstrated that gene amplification in chromosome 1p22 may be associated to cervical cancer and it may be used as a genetic marker of cervical carcinoma.

POLYMORPHISM OF GLUTATHIONE S-TRANSFERASE OMEGA GENE AND RISK OF CANCER

Sujan Babu Marahatta1, Phaibul Punyarit2, Vajarabongs Bhudsawasdi3, Anucha Paupairoj3, Sopit Wongkham3, Songsak Petmitr1,4

1Department of Tropical Nutrition and Food Science, Faculty of Tropical Medicine, Mahidol University, Bangkok; 2Department of Pathology, Phramongkutklao College of Medicine, Bangkok; 3Liver Fluke and Cholangiocarcinoma Research Center, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand

Though polymorphisms have been reported in GSTO1 and GSTO2, their predisposition to cancer risk has not yet been explored. In this case control study, 28 cases of hepatocellular carcinoma, 30 cases of cholangiocarcinoma, 31 cases of colorectal cancer, 30 cases of breast cancer and 98 controls were compared for frequencies of GSTO1 and GSTO2 genotypes. The statistical analysis provided the support for the difference in genotypic distribution for GSTO1*A140D versus hepatocellular carcinoma (OR 23.83, CI 95%: 5.07-127), cholangiocarcinoma (OR 8.5, CI 95%: 2.07-37.85), breast cancer (OR 3.71, CI 95%: 1.09-13.02) and control. With regards to GSTO2*N140D polymorphism, there was no difference in genotypic distribution between all the types of cancer and control. The study suggests that GSTO1*A140D polymorphism could play an important role as a risk factor for the development of hepatocellular carcinoma, cholangiocarcinoma and breast cancer.

Presented in: Empowering Cancer Control For Healthy Thailand, The 8th National Cancer Conference, Bangkok, September 7-9, 2005.

RIBOFLAVIN-DEFICIENT AND TRICHINELLA SPIRALIS-INDUCED STRESSES ON PLASMA CORTICOSTERONE ASSOCIATED WITH SPERMATOGENESIS IN MALE WISTAR RAT

Panas Tumkiratswong1, Hataitip Sukkachart1, Tippawan Buapuan1, Rungsunn Tungtrongchitr2, Anchalee Tungtrongchitr3

1Department of Zoology, Faculty of Science, Kasetsart University, Bangkok, 10900; 2Department of Tropical Nutrition and Food Science, Faculty of Tropical Medicine, Mahidol University, Bangkok; 3Liver Fluke and Cholangiocarcinoma Research Center, Faculty of Medicine, Siriraj Hospital, Prannok road, Bangkok 10700, Thailand

The objective of this study is to investigate effects of riboflavin-deficient and Trichinella spiralis-induced stresses on corticosterone associated with spermatogenesis in male Wistar rats. Rats were allocated into 4 groups: Group 1: control; group 2: riboflavin-deficient diet; group 3: T. spiralis infection; group 4: riboflavin deficiency diet with T. spiralis infection. This experiment lasted for 12 weeks. Plasma corticosterone was significantly enhanced when exposed to acute stress of riboflavin deficiency and/or T. spiralis infection. When rats was chronically subjected to such stresses, T. spiralis per se had prolonged effect on a marked increase of corticosterone. T. spiralis per se tended to be impacted on such sperm characteristics as sperm motility, sperm count and daily sperm production even the defected seminiferous tubules. It was proposed that the Trichinella spiralis-induced stress probably had adverse effect on the level of adrenocortical-testicular axis whenever their habitats on muscle fibers were evident. However the riboflavin-deficient-induced stress was not much implicated on adrenocortical-testicular axis.

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ASSESSMENT OF DIETARY PATTERNS OF THAIS IN GERMANY AND THAILAND

Kwanbunjan K¹, Chaikate S³, Songmuaeng K²

¹Department of Tropical Nutrition and Food Science, Faculty of Tropical Medicine Mahidol University, Bangkok; ²Department of Tropical Radioisotopes, Faculty of Tropical Medicine Mahidol University, Bangkok 10400; ³Department of Home Economics, Faculty of Science, Srinakharinwirot University, Bangkok, Thailand.

This study was conducted to investigate the dietary patterns of Thais living in a different culture. Ninety-eight healthy Thai men and women aged 18-55 years were recruited from many regions of Germany, and compared with 100 healthy Thai men and women aged 17-56 years living in Thailand. A food frequency questionnaire (FFQ) with 85 food items and 24-h recall were used to assess amount and frequent of energy and nutrients intake especially fat, and body weight and height were measured to find out weight change for Thais in Germany. Socio-economic and health status information were gathered by interview. “Nutrisurvey” dietary analysis software was used to analyze the nutrient intakes of the studied group. Statistical analysis was done using Strata version 5.0. The results showed higher intakes of energy, protein and fat in the participants in Germany than those in Thailand. Rice was the staple food of the studied group in Germany. Average age-adjusted BMI for both study groups was above normal. A high consumption of fat is associated with weight increase. Thus, the dietary changes in these Thais may provide a possible explanation associated with the risk of obesity, which is a major health problem and the main risk factor for many fatal diseases.

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SERUM LEPTIN CONCENTRATIONS IN CHRONIC HEPATITIS

Rungsunn Tuntragrichitr¹, Sombat Treeprasertsuk², Nyein Nyein Ei¹, Apanchanid Thepouyporn¹, Benjaluck Phonrat¹, Arun Huntrup¹

¹Department of Tropical Nutrition and Food Science, Faculty of Tropical Medicine, Mahidol University, Bangkok; ²Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok; ³Hospital for Tropical Diseases, Faculty of Tropical Medicine, Mahidol University, 4206 Ratchathevi Road, Ratchatheev, Bangkok 10400, Thailand

The objectives of this research were to investigate leptin levels among Thai chronic hepatitis B virus (HBV), chronic hepatitis C virus (HCV) and non-alcoholic steatosis hepatitis (NASH) diseases of Thai patients compared with controls. Twenty of each HBV, HCV, and NASH patients compared with sixty people as the control group from the Outpatient Department at the Hospital for Tropical Diseases, Bangkok, Thailand were investigated. Fasting blood samples were collected for investigation of leptin concentration of liver patients was significantly higher than that of control subjects. It might be due to the accumulations of fat cells in liver disease patients. However, there is no relationship between leptin level and other parameters such as BMI, ALT, AST, ALP and hematological variables. Liver enzyme functions levels are much higher in patients groups. White blood cells counts, platelets and hematocrit values are slightly lower in liver disease patients. Therefore, it is concluded that physiological regulation of leptin maintain in relation to body fat, even chronic viral liver diseases. This finding and the apparent stage depending suggest the possibility that in the course of chronic viral diseases, serum leptin levels may reflect the extent of liver dysfunction.


FATAL PLASMODIUM FALCI PAR MALARIA CAUSES SPECIFIC PATTERNS OF SPLENIC ARCHITECTURAL DISORGANIZATION

Britta C Urban¹, Tran T Hien², Nicholas P Day¹,³ Nguyen H Phu², Rachel Roberts⁴, Emsri Pongponrat³, Margret Jones⁴, Nguyen TH Mai², Delia Bethell¹, Gareth DH Turner⁴, David Ferguson⁴, Nicholas J White¹,³, David J Roberts⁴,⁵

¹Nuffield Department of Clinical Medicine and Nuffield Department of Clinical Laboratory Sciences, University of Oxford, and National Blood Service, ²John Radcliffe Hospital, Oxford, United Kingdom; Centre for Tropical Diseases, Cho Quan Hospital, Ho Chi Minh City, Vietnam and ³Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand⁴E-mail: tmepp@mahidol.ac.th

The spleen is critical for host defense against pathogens, including Plasmodium falciparum. It has a dual role, not only removing aged or antigenically altered erythrocytes from the blood but also as the major lymphoid organ for blood-borne or systemic infections. The human malaria parasite P. falciparum replicates within erythrocytes during asexual blood stages and causes repeated infections that can be associated with severe disease. In spite of the crucial role of the spleen in the innate and acquired immune response to malaria, there is little information on the pathology of the spleen in human malaria. We performed a histological and quantitative immunohistochemical study of spleen sections from Vietnamese adults dying from severe falciparum malaria and compared the findings with the findings for spleen sections from control patients and patients dying from systemic bacterial sepsis. Here we report that the white pulp in the spleens of patients dying from malaria showed a marked architectural disorganization. We
observed a marked dissolution of the marginal zones with relative loss of B cells. Furthermore, we found strong HLA-DR expression on sinusoidal lining cells but downregulation on cordal macrophages. *P. falciparum* infection results in alterations in splenic leukocytes, many of which are not seen in sepsis.


**A QUANTITATIVE ULTRASTRUCTURAL STUDY OF THE LIVER AND THE SPLEEN IN FATAL FALCIPARUM MALARIA**

Oranan Prommano¹, Urai Chaisri¹, Parnpen Viriyavejakul¹, Polrat Wilairatana², Emsri Pongponratn¹

¹Department of Tropical Pathology, Faculty of Tropical Medicine, Mahidol University, Bangkok; ²Hospital for Tropical Diseases, Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand. E-mail: tmepp@mahidol.ac.th

We performed a retrospective study of 25 patients who died of severe falciparum malaria in Thailand and Vietnam using electron microscopy. The aims of the present study were: to determine if there was any significant association between parasitized red blood cell (PRBC) sequestered in liver or spleen and particular pre-mortem clinical complications and to compare the degree of parasite load between the liver and spleen within the same patients. PRBC sequestration in the spleen was higher than the liver (S.I. median = 3.13, 0.87, respectively) (p<0.05.) The results of quantitative ultrastructural study of the present study showed a significantly higher parasite load in the liver of patients with jaundice, hepatomegaly and liver enzyme elevation (p<0.05). We found a significant correlation between PRBC sequestration in the liver and the level of serum bilirubin, the level of aspartate aminotransferase (AST) and the size of palpable liver (Spearman’s correlation coefficient = 0.688, 0.572, 0.736, respectively).

Furthermore, more parasite load was found in the liver of patients with acute renal failure (ARF) compared to patients without ARF (p<0.05). These findings suggest that PRBC sequestration in the liver is quantitatively associated with pre-mortem hepatic dysfunction and renal impairment.

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ULTRASTRUCTURAL CHANGES OF PANCREATIC ISLETS MICRO CIRCULATION IN NONOBESE DIABETIC (NOD) MICE

Navakanit Sachanonta1,2, Emsrisppongponratn1, Rayawadee Butraporn1, Urai Chaisri1, Benjama Saelim1, Birat Sumeteeewatanakul1, Ticomporn Yamsaad2, Nut Sawadrat1

1Department of Tropical Pathology, Faculty of Tropical Medicine, Mahidol University, Bangkok; 2Laboratory Animal Center, National Institute of Health, Ministry of Public Health, Thailand. E-mail: tmepp@mahidol.ac.th

ULTRASTRUCTURAL INVESTIGATION OF RED CELL DEFORMATION IN SEVERE MALARIA

Emri Pongponratn1, Gareth Turner2, Arjen Dondorp3, Mario Riganti1, Gareth DH Turner3, Sudarar Nguansangiam1, Yaowapa Maneerat1, Urai Chaisri1, Arjen Dondorp2, Mario Riganti1, Gareth DH Turner3, David Ferguson1

1Department of Tropical Pathology, Faculty of Tropical Medicine, Mahidol University Bangkok, Thailand; 2The Wellcome Mahidol Oxford Tropical Medicine Research Unit; 3Nuffield Department of Pathology, The John Radcliffe Hospital, University of Oxford, U.K. E-mail:tmepp@mahidol.ac.th

THE objective of this study was to investigate the ultrastructural changes of vascular pancreatic islets using a transmission electron microscopic technique. The major ultrastructural changes of microvessels in NOD mice are indicated by the swelling and vacuolization of the endothelial cell. Swollen cells are the first noticeable lesion of the cell response in reversible degeneration that is caused by the failure of homeostatic control. Loss in endothelial cell homeostasis is primarily a marker of endothelial dysfunction that plays a key role in the pathogenesis of diabetic vascular disease by losing the control of vascular tone. Diabetes also associates with an increased generation of oxygen-derived free radicals that may impair vasodilatation through the inactivation of vasodilators. In conclusion, consistent with a hypothesis that loss of the modulatory role of the endothelium may be a critical and initiating factor in the development of diabetic vascular disease, the ultrastructural changes in this study may indicate the first sign of endothelial dysfunction. This dysfunction correlates to the relationship between diabetes and reversible lesions of vessels in NOD mice, making for a better understanding of the pathophysiology of diabetic vascular disease to set the stage for further investigation to restore endothelial dysfunction in diabetes.


PATHOGENESIS OF ACUTE RENAL FAILURE IN SEVERE MALARIA: ULTRASTRUCTURAL AND IMMUNOPATHOLOGICAL STUDIES

Sudarat Nguansangiam1, Yaowapa Maneerat1, Urai Chaisri1, Arjen Dondorp2, Mario Riganti1, Gareth DH Turner3, David Ferguson1

1Department of Tropical Pathology, Faculty of Tropical Medicine, Mahidol University Bangkok, Thailand; 2The Wellcome Mahidol Oxford Tropical Medicine Research Unit; 3Nuffield Department of Pathology, The John Radcliffe Hospital, University of Oxford, U.K. E-mail:tmepp@mahidol.ac.th

THE pathogenesis of severe malaria involves the sequestration of malaria-infected red blood cells in the deep vessels of vital organs such as the brain, kidney and lung. Whilst there has been extensive research into the role of receptor mediated adhesion between parasitized red blood cells (PRBC) to host endothelial cells, the role of non-receptor mediated adhesion of both PRBC and uninfected red blood cells (uRBC) is less well understood. These events may play a key role in retarding, but not completely obstructing, blood flow in tissues during severe malaria. Evidence from in vitro and in vivo experiments supports the theory that there are changes to the red cell membrane structure in both PRBC and also uRBC during malaria infection, and that these profoundly effect the rheological characteristics of red cell flow and deformability during severe malaria. We will present pathological data gained from light and electron microscopic examination of fatal malaria cases in 60 adult South East Asian patients, which examined the pathological features of severe malaria in multiple organs including the brain and kidney. Ultrastructural and quantitative histological data will be presented which demonstrates that uRBC are increased in the brain during cerebral malaria, as well as sequestration of PRBC. In addition changes in red cell structure and membrane fluidity occur, which may contribute to vascular sequestration, reduced blood flow and transient hypoxia. We will discuss these findings in the light of the pathological changes in the brain and kidney in severe malaria, where changes in red cell membrane deformability contribute to pathology.

adhered to the glomerular capillary endothelium. Large mononuclear cells were also present within the capillaries, filling most of their lumens. There were only few cases showing mesangial cell proliferation, mesangial matrix expansion and electron dense deposits along the mesangial basement membrane. Statistically results showed that the number of Knob negative (K-) PRBC were significantly higher in the kidney of the ARF compared to NARF cases. The positive immunoreactivity for TNF-α and IL-10 was found in inflammatory cells, renal tubules and endothelial cells of vasculatures. Knob negative (K-)PRBC in the kidney is associated with acute renal failure. The correlation between severity of histopathologic changes in renal tissue and intensity of inflammatory for INFα and IL-10 will be discussed in detail.


TRANSCRIPTION ANALYSIS OF IgE AND IgG IN PERIPHERAL BLOOD MONONUCLEAR CELLS INDUCED BY PLASMODIUM FALCIPARUM ANTIGEN

Potup P1, Maneerat Y1, Kalambaheti T1, Mahakunjkijcharoen Y1, Hirunpetcharat C2, Troye-Blomberg M3, Looraesuwan S1

1Faculty of Tropical Medicine, Mahidol University, Bangkok; 2Faculty of Public Health, Mahidol University, Bangkok, Thailand; 3Wenner-Gren Institute, Stockholm University, Stockholm, Sweden. E-mail: tmymn@mahidol.ac.th

T o investigate whether the crude antigen of *P. falciparum* could induce the transcription of IgE and IgG from the normal peripheral blood mononuclear cells (PBMC). 6x10^6 human PBMC isolated from normal healthy donor were co-cultured with 10 µg or 20 µg of crude *P. falciparum* antigen obtained from parasite clone TM 267. PBMC stimulated with IL-4 was used as positive control. The influence of antigen dosage and their expression during the time interval were determined. RNA was extracted from the stimulated PBMC pellet and RT-PCR was conducted using the specific primers designed from the constant heavy chain region of IgE and IgG. IgE expression was detected later on day 1, 3, 7, and 9, while IgG was detected later on day 5, 7 and 9. IL-4 stimulated PBMC could exhibit both IgE and IgG expression, of which IgE was detected as early as day 1, while IgG was detected later on day 5 whereas unstimulated PBMC shown no expression at all of both IgE and IgG transcripts. This study indicated that the *P. falciparum* antigen at the concentration of 10 µg or 20 µg per 6x10^6 PBMC could induce both IgE and IgG transcription, in the same manner as IL-4.


HISTOPATHOLOGICAL STUDIES OF LIVER TISSUE OF HIV ANTIBODY-POSITIVE PATIENTS: A NECROPSY STUDY

Thanida Tangwanicharoen1, Parnpen Viriyavejakul1, Thamrong Chirachariyavel1, Phaihul Punyarit1, Benjanee Punpoowong1, Jaranit Kaewkungwal1, Urai Chaisri1

1Department of Tropical Pathology, Faculty of Tropical Medicine, Mahidol University, Bangkok; 2Department of Pathology, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok; 3Department of Pathology, Pramongkuklao College of Medicine, Bangkok; 4Department of Social and Environmental Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand E-mail: tmuch@mahidol.ac.th

LIVER necropsy specimens of 117 HIV antibody-positive patients, and 20 liver tissue of healthy person who die by an accident were collected from Ramathibodi Hospital, Pramongkutkla Hospital and Hospital for Tropical Diseases, Mahidol University, Bangkok during 1997-2004. The informed consent for tissue necropsy having been given on explanation of the objectives of the study and its procedures. Tissue necropsy was performed using either a disposable liver biopsy set according to Menghini (biopsy needle size 15 G/1.8 mm, needle length 88 mm, distance sleeve 18 mm or a mini-laparotomy technique). The tissue were immediately fixed with 4% paraformaldehyde, dehydrated with ethanol and embedded in paraffin. The paraffin sections (4-5 µm thick) of individual tissue were placed on slides. Pathological change of liver tissues section which stained by Hematoxylin and Eosin stain (H&E) were examined under a light microscope. Various special stained, i.e. acid fast stain, modified acid fast stain (Kinyoun), Gomori methenamine silver (GMS) stain were used for diagnosis the pathogenic agents.

Among 117 samples, 55 cases (47%) revealed opportunistic infections, while 62 cases (53%) were no pathogenic agents in liver tissue. The result of H&E and special stained revealed 25 cases 45.45% with cryptococcosis, 19 cases (34.55%) with tuberculosis, 6 cases (10.91%) with cytomegalovirus, 4 cases (7.27%) with penicillosis and 1 cases (1.82%) with small fungus infection. Pathological changes in liver tissue were fatty changes, portal inflammation, and reactive hepatitis, chronic active and chronic passive hepatitis and hepatocellular carcinoma. Predominant pathological changes include granuloma and spotty necrosis, which were attributed to tuberculous hepatitis. Infection with cryptococcus did not give any specific associated pathological changes.

The pathological changes associated with HIV-infection in liver tissue were cryptococcosis, tuberculosis, penicillosis and small fungus infection. Abnormalities in liver tissues of HIV-infected patients were presence mainly of opportunistic infection, usually part of a disseminated multi-organ process arising in the setting profound of immune suppression. Additionally
CONSEQUENCES OF MALARIA PARASITE-ENDOTHELIAL CELL BINDING

Parnpen Viriyavejakul1,2, Giancarlo Biagini2, Patrick G Bray2, Steve A Ward2

1Department of Tropical Pathology, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; 2Molecular and Biochemical Parasitology, Liverpool School of Tropical Medicine, University of Liverpool

YTOADHERENCE of Plasmodium falciparum-infected erythrocytes to the microvasculature of endothelial cells is thought to play a crucial role in malaria pathogenesis. Our hypothesis is that the binding process is vital in causing aggravation of host cell signaling processes leading to a loss of cellular function. We have used both a physiological and a proteomic approach to investigate the interaction between cytoadherence of endothelial cells and malaria parasites.

Human umbilical vein endothelial cells (HUVEC) were incubated with Plasmodium falciparum-infected erythrocytes and studied with the aid of Confocal Laser Scanning Microscopy (CLSM). We identified apoptotic cells using morphological features, annexin V and propidium iodide stains. We were able to document apoptotic changes with time in the HUVEC incubated with malaria parasite with the aid of Calcein-AM. We found that HUVEC with adhered Plasmodium falciparum-infected erythrocytes demonstrated significant apoptotic features at 3, 6 and 24 hours post incubation as compared to HUVEC incubated with red blood cells alone. These included cellular shrinkage, fragmentation, blebbing of plasma membrane and contracted organelles. Not all morphologically apoptotic cells were annexin positive. We are working on caspase inhibitors for apoptosis.

For a global approach, we have studied the proteome of endothelial cells after malaria parasite binding to understand the pathways involved in parasite-host cell communication. Isolated HUVEC protein samples were separated by two-dimensional polyacrylamide gel electrophoresis (2D-PAGE), visualized by silver staining or by an image processing program (Phoretix 2D Evolution software). Proteins of interest were extracted by in-gel digestion with trypsin and quantified by matrix-assisted laser desorption-ionization-time-of-flight mass spectrometry (MALDI-TOF-MS). The resulting mass fingerprint was searched against the National Center for Biotechnology Information protein-sequence database using Mascot search engine. More than 1000 protein spots were detected by 2D electrophoresis using a non-linear pH range of 3-10. A number of protein spots which are differentially expressed upon malaria parasite binding have been observed. Definitive protein identification of these spots is ongoing.

THE DIVERSE PATHOLOGIES OF INFECTED LIVER WITH OPISTHORCHIS VIVERINI

Mario Riganti1, Vasant Khachonsaksumet1, Wichai Ekataksin2

1Department of Tropical Pathology, Faculty of Tropical Medicine, 2Liver Research Unit, Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Thailand

O. viverini (Liver fluke) is one of the causative agent of food-borne parasitic zoonoses, which infects animals or humans that found mainly in the North and the Northeast Thailand, Laos and Kampuchea. Transmission to humans probably occurs often from eating raw fish, raw crayfish, etc., containing viable metacercariae. We performed a retrospective studied of the twenty-nine autopsy cases of patients aged from 7 to 68 years who lived in the Northeastern part of Thailand and were infected with these adult worms. By gross examination of the liver appeared enlargement of the liver (28 cases), dilation of the bile ducts (16 cases at intrahepatic, 13 cases at subcapsular), fibrosis (7 cases at portal area, 4 cases at peripheral area of bile ducts), intrahepatic tumors (10 cases) and congestion of the liver (5 cases). The adult worms were found in the bile ducts of all cases. The liver was processed for microscopic examination. The diverse pathologies were pericholangitis (28 cases), fibrous tissue infiltration at the wall of the bile ducts (27 cases), adenomatous formation (25 cases), dilatation of the bile ducts (24 cases), hyperplasia of epithelium (21 cases), desquamation of epithelium (20 cases), proliferation of epithelium (19 cases), dense fibrous tissue at portal areas (16 cases), cholestasis (12 cases), adenocarcinoma of the bile ducts (8 cases), hepatocellular carcinoma (2 cases), ruptured dilated bile duct with peritonitis (1 case) and perioval granuloma (1 case).

The data presented in this study indicated that O. viverini is one of the causative agent of liver disease of human. Enlargement of the liver was a common finding. The pathology was confined to the large and medium sized bile ducts where the worms inhabited.
THE DIVERSE PATHOLOGIES OF INFECTED LUNG WITH PARAGONIMUS HETEROTREMUS

Vasant Khachonsakum1, Mario Riganti1, Ruchareka Asavisanu2, Gedsuda Pattanapen3, Borimas Hanboonkunupakarn3, Parkpoom Piyaman3, Narumon Chunwimalveang3 Wichai Ekataksin3

1Department of Tropical Pathology, Faculty of Tropical Medicine, 2Library and Information Center, 3Liver Research Unit, Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Thailand

P. HETEROTREMUS (Lung Fluke) is one of the food-borne parasitic zoonoses; which infects animals and humans. We studied the pathology of the cat lung which was infected with this parasite caused morbidity and pathology. By gross examination of the lung appeared small hemorrhagic spots. Some of the worms were seen in the pleural cavity together with turbid pleural serosanguinous effusion miliary lung abscesses, cystic lesions with dense fibrous connective tissue around the cysts. The visceral pleura covering the cyst was thickened and inflamed. By microscopic examination, revealed a worm located in the subpleural alveolar parenchyma, cross sections of the worm in the dilated bronchus which has already undergone squamous metaplasia, Adjacent and surrounding the worm is a large granulomatous tissue contusing, around the cystic lesion were compressed and was surrounded by an acute hemorrhagic area. The adjacent lung tissue showed marked congestion, atelectasis and pneumonia.


DETECTION OF LEGIONELLA PNEUMOPHILA IN WATER SAMPLES BY USING NESTED POLYMERASE CHAIN REACTION

Rungrat Nintsan1, Orasa Suthienkul2, Kanokrat Siripanicchgon2, Fuangfa Utrarachkij2

1Department of Tropical Pathology, Faculty of Tropical Medicine; 2Department of Microbiology, Faculty of Public Health, Mahidol University, Bangkok 10400, Thailand. E-mail: phost@mahidol.ac.th

L. PNEUMOPHILA, the causative agent of legionnaires’ disease and pontiac fever, can colonize in water distribution systems as well as in natural aquatic waters. In this study, nested polymerase chain reaction (PCR) was applied to detect the macrophage infectivity potentiator (mip) gene of L. pneumophila in water samples, and to determine sensitivity, specificity of primers and compare with conventional culture method. One hundred and thirty-five water samples were collected from cooling towers, water reservoir, condenser drain water, pool, river, and canal. Thirty-four swab samples were collected from showerheads and condenser drains.

The nested PCR assay amplified a specific product size of 471 bp. The sensitivity of nested PCR for detecting L. pneumophila DMS 6283 was 10 fg of genomic DNA or 10 colony forming unit (cfu)/ml, which was seeded in phosphate buffer (PB). The primers used in nested PCR were specific for L. pneumophila, without cross-reaction to other tested gram negative and gram positive bacteria. Results showed that the sensitivity of detection of seeded L. pneumophila DMS 6283 in majority of water samples was equal to that of seeding in PB. It was found that water samples from river and canal contained amplification inhibitors, which could be removed by using spin column (Qiagen). The nested PCR was applied to detect L. pneumophila directly in water samples from various sources. The detection rate of L. pneumophila by nested PCR was 30.8% higher than that of the conventional culture method at 2.4%. L. pneumophila were found in 35 out of 63 cooling tower water samples, 1 out of 5 samples from water reservoirs, 1 out of 4 water samples from fountain, 2 out of 11 samples from hot water faucet, 3 out of 8 samples from condenser drain water, and 10 out of 27 samples from swab of condenser drains. All PCR products of 52 positive samples were confirmed by restriction analysis with the digestion of EcoR I and Kpn I. Restriction fragments of the PCR products were the same expected sizes as those of the positive control.

The nested PCR had improved sensitivity and specificity for the detection of L. pneumophila in non-culturable state in water samples from various sources. It could be applied for rapid screening in detection of L. pneumophila from water and swab samples in the environmental laboratory.


EARLY ANTIBODY RESPONSE TO MULTIPLE IM DOSES OF PURIFIED VERO CELL RABIES VACCINE

Pornthep Chanthavanich1, Kriengsak Limkittikul1, Keswadee Laphra1, Chukiat Sirivichayakul1, Krisana Pengsaa1, Pakamas Kavpolod2, Achara Jakstud1, Yongyuth Wangroongsarb4, Henry Wilde2, Arunee Sabchareon1

1Department of Tropical Pediatrics, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; 2Queen Saovabha Memorial Institute, Thai Red Cross Society; 3Army Institute of Pathology; 4Sanofi Pasteur Ltd.

We studied early antibody response to multiple IM-dose regimens of purified Vero cell rabies vaccine in 120 healthy adults with no history of previous rabies immunization, who were randomly given one of 3 PVRV IM post-exposure regimens: Gr A 22111 (2 doses each on days 0, 3), Gr B 31111 (3 doses on day0), and...
Gr C 11111 one dose each on days 0, 3, 7, 14, 28 (reference standard Essen schedule). RFFIT were performed for rabies NAbs (RNAb). Age, weight, height and sex ratio were similar between the 3 groups. Nine subjects were excluded from immunity analysis because they had RNAb titers on D0 <0.07 IU/ml. The antibody response patterns of the subjects in Gr. A and B were similar. At D5, early antibody response (titers >0.07 IU/ml) was observed in 5.4 and 2.6% in Gr. A and B, respectively, with none in Gr. C. At D7, 67.6% of the subjects in Gr. A, and 60.5% in Gr. B, had RNAb titers >0.07 IU/ml, about 1.7-1.6 times greater, respectively, than Gr. C (38.9%). In addition, 5% of subjects in Gr. A and B also had RNAb titers >0.5 IU/ml (WHO protective level), compared to none in Gr. C. On days 14 and 28, all subjects in the 3 groups had RNAb titers >0.5 IU/ml. By one year, the proportions of subjects with RNAb titers >0.5 IU/ml in Gr. A, B and C were 65, 92 and 75%, respectively. The RNAb GMTs for days 7, 14, 28, and 365 of the 3 groups were similar. The side effects of the 3 regimens were transient and in the acceptable range (<5%).

In conclusion, at day 7, early antibody responses (>0.07 IU/ml) were observed in 60-67% of the subjects who received the two multiple-dose IM PVRV regimens; the proportion was 1.6-1.7 times higher than the reference schedule. However, the titers reached the protective level of >0.5 IU/ml in only 5% of subjects, and no subject in the reference group. Therefore, where rabies immunoglobulin is not available, a rabies vaccine schedule that produces the earliest and highest RNAb responses would be the best option.


KINETICS OF MATERNALLY TRANSFERRED NEUTRALIZING DENGUE ANTIBODIES AND WILD TYPE DENGUE INFECTIONS IN THE FIRST TWO YEARS OF THAI INFANTS

Krista Pengsaa1, Christine Luxemburger2, Kiengsak Limkittikul1, Sutee Yoksan3, Laurent Chambonneau2, Udom Chaowarind4, Keswadee Lapphra1, Pornthep Chanthavanich1, Jean Lang1, Arunee Sabchareon1

1Department of Tropical Pediatrics, Faculty of Tropical Medicine, Mahidol University; 2Sanofi Pasteur, Lyon, France; 3Faculty of Allied Health Sciences, Thammasat University, Pathum Thani, Thailand; 1Rajavithi Hospital, Ministry of Public Health, Bangkok, Thailand

BACKGROUND: It is important to determine the minimum age that is appropriate to administer the available dengue vaccine which based upon the immunogenicity and safety of dengue vaccine and also the duration of persistent maternal antibody.

Methods: A prospective study of maternally transferred dengue neutralizing antibodies and dengue infections in the first two years of life were assessed in the endemic area of dengue infection.

Results: Ninety-seven percent of the 219 pregnant women in Bangkok had neutralizing antibody to at least one dengue serotype at delivery. Placental transmission of dengue neutralizing antibodies from almost all the mothers to their infants was demonstrated in the cord sera. Maternal transferred neutralizing antibodies to dengue tended to decline six months after birth. At least one dengue serotype antibody persisted in the infants at age 3, 6, and 9 months in 94.7, 73.1%, and 20.2%, respectively. At 12 months of age, 5.5% (6/110) of them had low maternal dengue antibody titers against DEN-1 or DEN-2. No dengue antibody was detected in 102 infants at age 18 months. In-apparent dengue infections were observed in 12 infants during the 2-year follow up period. The infected dengue serotypes were DEN-2 nine cases and one each for DEN-1, DEN-3, and DEN-4. The 6-month incidence rates of acute dengue infection were 28.8 and 41.7 per 1,000 infants at the age between 13-18 and 19-24 months, respectively with the cumulative incidence rate of 11%.

Conclusions: Most infants have maternally transferred antibodies and no maternal dengue antibody was detected in infants at age 18 months. Eleven percent of the studied infants acquired dengue infection during the 2-year period. In dengue endemic area, the optimal period to immunize infants with live attenuated tetravalent dengue vaccine between 12 and 18 months of age would be considered.


LIFE-SAVING RECTAL ARTESUNATE FOR COMPLICATED MALARIA IN CHILDREN

Krisana Pengsaa1, Chukiat Sirivichayakul1, Kesara Na-Bangchang2, Ithiphon Thairaporn3, Anong Chaivisuth4, Amnaj Wongsuwan5, Phanorsri Attanath1, Chanathep Pojaroenanant1, Pataraporn Wisetsing1, Pornthep Chanthavanich1, and Arunee Sabchareon1

1Department of Tropical Pediatrics, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; 2Faculty of Allied Health Sciences, Thammasat University, Pathum Thani, Thailand; 3Thong Pha Phum Hospital, Kanchanaburi Province; 4Paholpolpayausahaan Hospital, Kanchanaburi Province; 5Mae Sot Hospital, Tak Province, Thailand

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W E report the effectiveness of two regimens of rectal artesunate formulation in the treating 13 Thai children with cerebral/complicated falciparum malaria. The drug was given at an initial dose of 40 mg/kg bodyweight once daily for three consecutive days. Mefloquine at the dose of 15 mg/kg bodyweight was given orally at 72 hr after
the initial dose of artesunate, followed by 10 mg/kg bodyweight 6 hours later. Three cases with cerebral malaria gained consciousness within 20 hours of artesunate administration. The median time required for the reduction of parasitemia by 90% of the initial value ($P_c$) in 13 children was 11.2 hr. No recrudescence was observed in any of the patients during the 28-day follow-up period. Plasma concentrations of artesunate and dihydroartemisinin (active plasma metabolite of artesunate) measured in two patients who received the high initial dose regimen (20 mg/kg bodyweight) suggested rapid absorption and adequate plasma concentrations of both compounds following the administration of artesunate via the rectal route. Further studies for the optimized regimen of rectal artesunate in the treatment of cerebral/complicated childhood falciparum malaria in the area of multidrug resistance are warranted.

**A COMPARISON OF PAIN SCALES IN THAI CHILDREN**

Christopher John Newman¹, Rangsima Lolekha², Kriengsak Limkittikul⁴, Khornsavan Luangxay⁴, Taiwee Chotpitayasunondh², Pornthep Chanthavanich¹

¹Department of Paediatrics, Centre Hospitalier Universitaire Vaudois (CHUV), Lausanne, Switzerland; ²Queen Sirikit National Institute of Child Health, Bangkok, Thailand; ³Department of Tropical Pediatrics, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

**PRE-EXPOSURE IM AND ID REGIMENS OF RABIES VACCINE ADMINISTERED CONCOMITANTLY WITH JAPANESE ENCEPHALITIS VACCINE IN TODDLERS**

Krisana Pengsaa¹, Kriengsak Limkittikul², Pornthep Chanthavanich³, Cherdchoo Cheeramakara¹, Cheeraratana Cheeramakara¹, Wanyarat Thanomsak¹, Nopachai Suthisai¹, Suvit Areekul¹

¹Department of Tropical Pediatrics, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; ²Department of Tropical Pediatrics, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; ³Chiron Vaccines, Marburg, Germany.

**OBJECTIVE:** To compare the immunogenicity and safety of Purified Chick Embryo Cell rabies vaccine (PCECV) for primary pre-exposure prophylaxis after intramuscular (IM) and intradermal (ID) injections given concomitantly with Japanese encephalitis vaccine (JEV) in toddlers with booster dose at one year.

**Methods:** Two-hundred healthy toddlers aged 12 to 18 months were randomly allocated into one of four pre-exposure PCECV regimens administered within 28 days: 1 ml IM x 3, 0.5 ml IM x 3, 0.1 ml ID x 3, 0.1 ml ID x 2. These four groups also received JEV x 2. The control group received JEV x 2 only. Toddlers in studies group received one booster dose of PCECV at one year later according to the previous allotted regimens. JEV was also given to all toddlers at one year follow-up as well. Safety was evaluated after each injection. Pre- and post-vaccination blood samples were analyzed for neutralizing antibodies (NA) to rabies and Japanese encephalitis virus (JE).

**Results:** At day 49 after the first injection, all PCECV recipients achieved adequate titers against rabies (RFIT antibody titers $> 0.5$ IU/ml) and JE (JE antibody titers $> 10$ serum dilution). After receiving a booster dose one year after the primary vaccination, a rapid increase in rabies NA was detected, demonstrating an excellent anamnestic immune response. Both vaccines were well tolerated.

**Conclusions:** PCECV and JEV administration concomitantly in toddlers is safe and induces protective antibodies against both rabies and JE. Long term follow-up to evaluate the persistence of immunogenicity in terms of rabies virus NA titers is on going.

**ELEVATION OF SERUM TRANSCOBALAMIN II IN PATIENTS WITH SCRUB TYPHUS**

Cheeraratana Cheeramakara¹, Wanyarat Thanomsak¹, Kriyaporn Songmeang², Apichart Nontprasert², Charinnarong Sanghirun¹, Nopachai Suthisai¹, Suvit Areekul¹

¹Department of Tropical Radioisotopes, Faculty of Tropical Medicine, Mahidol University; ²Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Thailand

**SERUM transcobalamin II level were measured in scrub typhus patients. Eighteen out of fifty-two patients admitted to Maharat Nakhon Ratchasima Hospital were diagnosed as scrub typhus infection. The serum unsaturated vitaminB$_{12}$ binding protein (UBBC) and total vitamin B$_{12}$ binding protein (TBBC) levels in these patients were significantly higher than in normal subjects ($P < 0.001$). The mean serum transcobalamin II level in the typhus patients was also significantly higher than...**
in the normal subject (P =0.004). There was a significant correlation between serum TCII levels and typhus IgG titer (P < 0.05), but not to total IgM levels. These finding indicated that patients with scrub typhus had stimulation of recticuloendothelial system as a result of a considerable increase of transcobalamin II levels.

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**TRANSIENT REPORTER RNA ASSAY; QUANTIFICATION OF REPORTER GENE MRNA DURING IMMEDIATE EARLY RESPONSE IN MAMMALIAN CELLS BASED ON REAL-TIME REVERSE TRANSCRIPTION POLYMERASE CHAIN REACTION**

Hiroshi Ishihara1, Izumi Tanaka1, Fumiko Ishihara1, Keiko Suzuki1, Chieko Yoshino1, Cheeraratana Cheeramakara2, Hong Wan1, Shingo Akashi1

1Radiation Safety Research Center, National Institute of Radiological Sciences, Japan; 2Department of Tropical Radioisotopes, Faculty of Tropical Medicine, Mahidol University, Thailand  

**We developed a method for the exact quantification of a reporter gene RNA based on the use of real-time RT-PCR following the transient introduction of the gene into cultured cells. Using a reporter gene controlled by an upstream region of the murine junB gene and responsive to phorbol ester, the immediate early and temporal activation and subsequent decrease in transcription were determined. The results showed that relative reporter gene RNA levels decreased to 11- and 7-fold at 4 and 6 h after induction, respectively. The attenuation of promoter activity subsequent to the immediate-early induction observed by the reporter RNA assay was similar to the profile of endogenous junB mRNA. These results indicate that the reporter gene RNA level determined with this method precisely reflects the transcriptional activity of the reporter gene.**

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**ARE TRANSPORTER GENES OTHER THAN THE CHLOROQUINE RESISTANCE LOCUS (PFCRT) AND MULTIDRUG RESISTANCE GENE (PFMDR) ASSOCIATED WITH ANTIMALARIAL DRUG RESISTANCE?**

Timothy JC Anderson1*, Shalini Nair1, Huang Qin1, Sittaporn Singlam2, Lucy Paiphun2, François Nosten2,3,4

1Southwest Foundation for Biomedical Research, P.O. Box 760549, San Antonio, Texas 78245; 2Shoklo Malaria Research Unit, Mae Sai, Tak, Thailand; Faculty of Tropical Medicine, 3 Mahidol University, Bangkok, Thailand; and 4Nuffield Department of Clinical Medicine, John Radcliffe Hospital, Oxford, United Kingdom

**We first examined associations between genotype and drug response in 108 unique single-clone parasite isolates. We found strong associations between single nucleotide polymorphisms in pfmdr-1042 and mefloquine (MFQ), artesunate (AS), and lumefantrine (LUM) response. We also observed associations between an ABC transporter (G7) and response to AS and between another ABC transporter (G49) and response to dihydro-artemisinin (DHA). We reexamined significant associations in an independent sample of 199 unique single-clone infections from the same location. The significant associations with pfmdr-1042 detected in the first survey remained. However, with the exception of the G7-artesunate association, all other associations observed with the nine new candidate transporters disappeared. We also examined linkage disequilibrium (LD) between markers and phenotypic correlations between drug responses. We found minimal LD between genes. Furthermore, we found no correlation between chloroquine and quinine responses, although we did find expected strong correlations between MFQ, QN, AS, DHA, and LUM. To conclude, we found no evidence for an association between 8/9 candidate genes and response to eight different antimalarial drugs. However, the consistent association observed between a 3-bp indel in G7 and AS response merits further investigation.**


**HIGH THROUGHPUT ASSAY FOR THE DETERMINATION OF LUMEFANTRINE IN PLASMA**

Annerberg Anna1, Singtoroj Thida1, Tipmanee Prakaykaew1, White Nicholas1,2, Day Nicholas1,2, Lindegardh Niklas1,2

**Wellcome Trust-Mahidol University-Oxford Tropical Medicine Research Programme funded by the Wellcome Trust of Great Britain.**
A high throughput bioanalytical assay for the determination of lumefantrine in plasma has been developed and validated extensively. The within-day precisions for lumefantrine were 5.2, 3.5 and 2.5% at 200, 2000 and 15000 ng/mL, respectively. The between-day precisions were 4.0–2.8 and 3.1% at 200, 2000 and 15000 ng/mL, respectively. The lower limits of quantification (LLOQ) and the limits of detection (LOD) were 25 and 10 ng/mL, respectively using 0.250 mL plasma. The average recovery of lumefantrine was 85% and independent upon concentration. The use of 96-well plate format and short chromatographic run has increased the daily sample throughput four times. The assay is particularly suitable for large therapeutic drug monitoring studies using day 7 sampling.

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


**A RANDOMIZED, CONTROLLED STUDY OF A SIMPLE, ONCE-DAILY REGIMEN OF DIHYDROARTESMININ-PIPERAQUINE FOR THE TREATMENT OF UNCOMPROMICATED, MULTIDRUG-RESISTANT FALCIPARUM MALARIA**

Ashley Elizabeth1,2,3, McGready Rose1,2,3, Hutagalung Robert1, Phaiphun Lucy1, Slight Thra1, Proux Stephane1, Thwai Kyaw Lay1, Barneds Marion1, Looareesuwan Sornchai2, White Nicholas1,2, Nosten Francois1,2,3.

1Shoklo Malaria Research Unit, Mae Sot, Thailand; 2Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; and 3Centre for Clinical Vaccinology and Tropical Medicine, Churchill Hospital, Oxford, UK.

**BACKGROUND:** Dihydroartemisinin-piperaquine (DP) is a fixed-combination antimalarial drug increasingly deployed in Southeast Asia. The current regimen involves 4 doses given over 3 days. Simplification of the dose regimen should facilitate treatment adherence and thereby increase effectiveness.

**Methods:** In a randomized, controlled, 3-arm trial conducted along the northwestern border of Thailand, the standard 4-dose course of DP (DP4) was compared to an equivalent dose given as a once-daily regimen (DP3) and to the standard treatment of mefloquine-artesunate (MAS3).

**Results:** A total of 499 patients were included in the study. Times to fever and parasite clearance were similar in all groups. The PCR genotyping-adjusted cure rates at day 63 after treatment initiation were 95.7% (95% confidence interval [95% CI], 92.2%-98.9%) for MAS3, 100% for DP4, and 99.4% (95% CI, 98.1%-100%) for DP3. The DP4 and DP3 cure rates were significantly higher than that for MAS3 (P = .008 and P = .03, respectively). All regimens were well tolerated. There were 3 deaths (1 in the MAS3 group and 2 in the DP3 group), all of which were considered to be unrelated to treatment. Rates of other adverse events were comparable between the groups, except for diarrhea, which was more common in the DP4 group (P = .05 vs. the MAS3 group).

**Conclusions:** A once-daily, 3-dose regimen of DP is a highly efficacious treatment for multidrug-resistant falciparum malaria. This simple, safe, and relatively inexpensive fixed combination could become the treatment of choice for falciparum malaria.

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**POPULATION BIOLOGY AND ANTIMALARIAL RESISTANCE: THE TRANSMISSION OF ANTIMALARIAL DRUG RESISTANCE IN PLASMODIUM FALCIPARUM**

Barnes Karen1, White Nicholas2,3.

1Division of Clinical Pharmacology, Department of Medicine; University of Cape Town, Cape Town 7925, South Africa; 2Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; and 3Centre for Vaccinology and Tropical Medicine, Churchill Hospital, Oxford, UK.

**MALARIA** morbidity and mortality continue to increase across sub-Saharan Africa. This is largely as a result of the continued use of chloroquine and sulfadoxine-pyrimethamine, despite widespread resistance. Although eliminating the asexual stages of *Plasmodium falciparum* is the focus of treatment of individual symptomatic patients, at a population level, reducing the carriage of gametocytes – the sexual stage responsible for infection of the mosquito vector – is necessary to limit the transmission of malaria parasites and the spread of antimalarial resistance. The probability of a mosquito being infected depends on the prevalence, duration and density of viable gametocyte carriage in the human host, although additional humoral and leukocyte factors also affect transmissibility. There is a log–sigmoid relationship between gametocyte density in the patients’ blood and infectivity to the mosquito. The infectivity and thus transmission potential associated with a particular
antimalarial treatment can be characterised as a function of blood gametocyte density and time, summing these over the acute and all subsequent recrudescences of that infection. Gametocyte carriage and infectivity to mosquitoes is consistently higher in patients infected with drug resistant compared with drug sensitive malaria parasites. It is the ratio of transmission potential in drug resistant versus sensitive infections that drives the spread of resistance.

Early access to highly effective antimalarial treatment reduces the risk of disease progression and limits gametocyte carriage. The remarkable spread of sulfadoxine-pyrimethamine (SP) resistance across vast regions results from the very high post-treatment prevalence and density of gametocyte carriage following SP treatment. In areas of low intensity malaria transmission, the gametocyte-reducing effect of widespread use of artemisinin-based combination therapy has resulted in a sustained decrease in malaria transmission and a decrease in the spread of resistance. Malaria treatment policy should be based primarily on therapeutic efficacy against asexual stages, but should also consider transmission reduction potential. Artemisinin-based combination therapies are the only antimalarials currently available which rapidly reduce both asexual and gametocyte stages of the *P. falciparum* lifecycle.

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**BASELINE CORRELATAION AND COMPARATIVE KINETICS OF CEREBROSPINAL FLUID COLONY-FORMING UNIT COUNTS AND ANTIGEN TITERS IN CRYPTOCOCCAL MENINGITIS**

Brouwer Annemarie1,2,3, Teparrukkul Paprit2, Pinpraphaporn Supraphada2, Larsen Robert1, Chierakul Wirongrong1, Peacock Sharon1,4, Day Nicholas1,4, White Nicholas1,4, Harrison Thomas3

1Faculty of Tropical Medicine, Mahidol University, Bangkok; 2Department of Medicine, Sappasitprasong Hospital, Ubon Ratchathani, Thailand; 3Department of Infectious Diseases, St. George’s Hospital Medical School, London; 4Centre for Tropical Medicine, Nuffield Department of Clinical Medicine, University of Oxford, John Radcliffe Hospital, Oxford, United Kingdom; 5Division of Infectious Diseases, Department of Medicine, University of Southern California, Los Angeles; and 6Department of Internal Medicine and Infectious Diseases, University Medical Centre, Nijmegen, The Netherlands

CEREBROSPINAL fluid (CSF) cryptococcal colony-forming unit counts and CSF cryptococcal antigen titers serve as alternative measures of organism load in cryptococcal meningitis. For these measures, we correlated baseline values and rates of decline during the first 2 weeks of therapy in 68 human immunodeficiency virus-seropositive patients with cryptococcal meningitis. At baseline, there was a strong correlation between CSF cryptococcal colony-forming unit counts and CSF cryptococcal antigen titers. During the first 2 weeks of therapy, CSF cryptococcal colony-forming unit counts decreased by >5 logs, and CSF cryptococcal antigen titers decreased by 1.5 dilutions. In individual patients, there was no correlation between the rate of decline in CSF cryptococcal colony-forming unit counts and that in CSF cryptococcal antigen titers.

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**BURKHOLDERIA PSEUDOMALLEI STRAIN TYPE, BASED ON PULSED-FIELD GEL ELECTROPHORESIS, DOES NOT DETERMINE DISEASE PRESENTATION IN MELIOIDOSIS**

Cheng Allen1,2, Day Nicholas,3 Mayo Mark,1 Gal Daniel,1 Currie Bart1,2

1Tropical and Emerging Infectious Diseases Division, Menzies School of Health Research, Charles Darwin University, Darwin, Australia; 2Northern Territory Clinical School, Flinders University, Darwin, Australia; and 3Wellcome Trust–Oxford University–Mahidol University Tropical Medicine Research Programme, Bangkok, Thailand

MELIOIDOSIS, the infection due to *Burkholderia pseudomallei*, may present with a spectrum of severity and may affect any site in the body. Differential strain virulence and tropism suggested by previous studies would have implications for virulence and vaccine work. We explored clinical correlations using pulsed-field gel electrophoresis (PFGE) typing in a well-characterised clinical collection. Two methods of analysis were used based on band-based similarity values: first, a conventional cluster analysis formed by the unweighted paired group mean analysis, and second, an analysis of the distribution of the “within-group” and “between-group” Dice coefficient. Clinical isolates from 114 cases of melioidosis occurring in the Northern Territory, Australia were studied; 71 strain types were defined with a Simpson’s index of 0.91. No correlation was found between strain type and disease severity or site of melioidosis on presentation, with no differences in similarity values found when comparing within and between-groups. In particular, isolates from patients with neurological melioidosis were not clustered. There was evidence of geographical localisation. This study suggests that the variation in strain type may not be as important as host and environmental factors in determining the pattern of disease.
THE GLOBAL THREAT OF COUNTERFEIT DRUGS: WHY INDUSTRY AND GOVERNMENT MUST COMMUNICATE THE DANGERS

Cockburn Robert1, Newton Paul2, Agyarko Kyeremateng3, Akunyili Dora4, White Nicholas2 5

1The Times, London, United Kingdom; 2Centre for Clinical Vaccinology and Tropical Medicine, Churchill Hospital, University of Oxford, United Kingdom; 3Food and Drug Board, Accra, Ghana; 4National Agency for Food and Drug Administration and Control, Lagos, Nigeria; and 5Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

The production of substandard and fake drugs is a vast and underreported problem, particularly affecting poorer countries. It is an important cause of unnecessary morbidity, mortality, and loss of public confidence in medicines and health structures. The prevalence of counterfeit drugs appears to be rising (see “The Scale of the Problem”) and has not been opposed by close cooperation between drug companies, governments, or international organizations concerned with trade, health, customs and excise, and counterfeiting.

In this article we suggest that many pharmaceutical companies and governments are reluctant to publicize the problem to health staff and the public, apparently motivated by the belief that the publicity will harm the sales of brand-name products in a fiercely competitive business. Publicly, at least, several industry sources say the justification for secrecy is to avoid any alarm that could prevent patients taking their genuine medicines. We argue that this secrecy, and the subsequent lack of public health warnings, is harming patients and that it is also not in the long-term interests of the legitimate pharmaceutical industry. We urge a change to mandatory reporting to governmental authorities, which should also have a legal duty to investigate, issue appropriate public warnings, and share information across borders. This is not a role for the pharmaceutical industry, which has a serious conflict of interest.

While some drug companies have given public warnings to protect patients, others have been criticized for withholding information and, in a recent development in the United States, taken to court for failing to act. The industry is addressing the problem. In 2003, US pharmaceutical companies made an agreement with the US Food and Drug Administration (FDA) that they would report suspected counterfeit drugs to the FDA within five days of discovery (see “Companies That Have Warned”), although this remains a voluntary arrangement. In many poorer countries, where the problem is at its worst, there are no similar governmental and industry initiatives.

ACTIVATION OF CYTOTOXIC LYMPHOCYTES IN PATIENTS WITH SCRUB TYPHUS

De Fost Maaike, Chierakul Wirongrong, Pinda Kriangsak, Dondorp Arjan, White Nicholas, van Der Poll Tom

Laboratory of Experimental Internal Medicine and Department of Infectious Diseases, Tropical Medicine and AIDS, Academic Medical Center, University of Amsterdam, Amsterdam, the Netherlands; Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; Department of Medicine, Udon Thani General Hospital, Udon Thani, Thailand; Centre for Tropical Medicine, Nuffield Department of Clinical Medicine, John Radcliffe Hospital, University of Oxford, Oxford, United Kingdom

Thai patients with scrub typhus caused by the intracellular pathogen Orientia tsutsugamushi displayed elevated plasma concentrations of granzymes A and B, interferon-γ (IFN-γ)-inducible protein 10, and monokine induced by IFN-γ. These data suggest that activation of cytotoxic lymphocytes is part of the early host response to scrub typhus.

STAGE-DEPENDENT PRODUCTION AND RELEASE OF HISTIDINE-RICH PROTEIN 2 BY PLASMODIUM FALCIPARUM

Desakorn Varunee1, Dondorp Arjen1 2, Silamut Kamolrat1, Pongtavornpinyo Wirichada1, Sahassananda Duangjai1, Chotivanich Kesinee1, Pitisuttithum Punnnee1, Smithyman AM1, Day Nicholas1 2, White Nicholas1 2

1Faculty of Tropical Medicine, Mahidol University, 420/6 Rajvithi Road, Bangkok, 10400, Thailand; 2Centre for Tropical Medicine, Nuffield Department of Clinical Medicine, John Radcliffe Hospital, University of Oxford, Oxford, UK; and 3Cellabs Pty Ltd, P.O. Box 421, Brookvale, NSW 2100, Australia

Because of their sequestration in the microcirculation, the pathogenic late stages of Plasmodium falciparum are under-represented in peripheral blood samples from patients with falciparum malaria. Excreted products of the parasite might help to estimate this sequestered biomass. We quantified the stage-dependent production and release per parasite of P. falciparum histidine-rich protein 2 (PfHRP2) with the objective of measuring the sequestered biomass.


A simple method to relate parasite stage to parasite age was developed to facilitate this. In four isolates of \textit{P. falciparum}, the median (range) PFHR2 content was 2.0 fg (0.5-4.3 fg) for a young ring stage infected erythrocyte, and 5.4 fg (2.1-10.2 fg) for the schizont stage. The amount of PFHR2 in the parasitized erythrocyte increased most during development to the mature trophozoite stage. The median (range) amount of PFHR2 secreted per parasite per entire erythrocytic cycle was 5.2 fg (1.1-13.0 fg). A median of 89% of the total PFHR2 was excreted at the moment of schizont rupture. This assessment of the stage-dependent release of PFHR2 is an essential prerequisite for future studies aimed at estimating the total patient parasite mass from the peripheral blood PFHR2 concentration.

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\section*{PRACTICAL PCR GENOTYPING PROTOCOLS FOR \textit{PLASMODIUM VIVAX} USING PVCS ANF PVMS1}

M. Mallika, 1 P. Sathitham, 1 G. Anne, 2 L. Frank, 3 L. Sornchai, 1 W. Nicholas, 4, 5 S. Georges 6, 7

1Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; 2Département d’Immunologie, INSERM U767, CNRS UMRB104, Institut Cochin, Université René Descartes, Paris 75014, France; 3Laboratoire Commun de Séquençage, Institut Cochin, Université René Descartes, Paris 75014, France; 4Wellcome Unit, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; 5Centre for Vaccine and Tropical Medicine, Churchill Hospital, Oxford, UK; 6Unité de Parasitologie Bio-Médicale, CNRS UMR8251, Institut Pasteur, Paris, France; 7Parasitologie Comparée et Modèles Expérimentaux USM307, CNRS IFR101, Muséum National d’Histoire Naturelle, CPS2, 61 Rue Buffon, 75231 Paris Cedex 05, Paris, France

\textbf{ABSTRACTS}

A simple method to relate parasite stage to parasite age was developed to facilitate this. In four isolates of \textit{P. falciparum}, the median (range) PFHR2 content was 2.0 fg (0.5-4.3 fg) for a young ring stage infected erythrocyte, and 5.4 fg (2.1-10.2 fg) for the schizont stage. The amount of PFHR2 in the parasitized erythrocyte increased most during development to the mature trophozoite stage. The median (range) amount of PFHR2 secreted per parasite per entire erythrocytic cycle was 5.2 fg (1.1-13.0 fg). A median of 89% of the total PFHR2 was excreted at the moment of schizont rupture. This assessment of the stage-dependent release of PFHR2 is an essential prerequisite for future studies aimed at estimating the total patient parasite mass from the peripheral blood PFHR2 concentration.

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\section*{ROLE AND SIGNIFICANCE OF QUANTITATIVE URINE CULTURES IN DIAGNOSIS OF MELIOIDOSIS}

L. Boonjaruwatudaksakon, 1 W. Wangkeerakorn, 1 C. Wirongrong, 1 C. Allen, 1, 2 M. Bina, 1 C. Wipada, 2 W. Nicholas, 1, 4 D. Nicholas, 1, 4 P. Sharon 1, 4

1Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; 2Menzies School of Health Research, Charles Darwin University and Northern Territory Clinical School, Flinders University, Darwin, Australia; 3Medical Department, Sappasitiprasong Hospital, Ubon Ratchathani, Thailand; and 4Centre for Clinical Vaccinology and Tropical Medicine, Nuffield Department of Clinical Medicine, University of Oxford, Churchill Hospital, Oxford OX3 7LJ, United Kingdom

\textbf{MELIOIDOSIS is associated with significant mortality in countries in which it is endemic. Previous studies have demonstrated that quantitative \textit{Burkholderia pseudomallei} counts in blood are predictive of mortality. Here we examine the relationship between outcomes and quantitative \textit{B. pseudomallei} counts in urine.}

A total of 755 patients presenting to Sappasitiprasong Hospital, Ubon Ratchathani, northeast Thailand (in the northeast part of the country), with melioidosis between July 1993 and October 2003 had quantitative urine cultures performed within 72 h of admission. Urine culture results were divided into the following groups: (i) no growth of \textit{B. pseudomallei} from a neat sample or pellet, (ii) positive result from a centrifuged pellet only (<10^5 CFU/ml), (iii) detection of between 10^5 CFU/ml and 10^6 CFU/ml from a neat sample, or (iv) detection of 10^6 CFU/ml from a neat sample. The overall in-hospital mortality rate was 45%. Patients with negative urine cultures had the lowest
DEVELOPMENT AND VALIDATION OF A SOLID-PHASE EXTRACTION-LIQUID CHROMATOGRAPHIC METHOD FOR DETERMINATION OF AMOXICILLIN IN PLASMA

Lindegardh N,1,2 Singtoroj T,1 Annerberg A,1 White NJ,1,2 Day NP1,2
1Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand; and 2Nuffield Department of Clinical Medicine, Centre for Tropical Medicine, University of Oxford, Oxford, UK

A BIOANALYTICAL method for the determination of amoxicillin in plasma by hydrophilic interaction solid-phase extraction and liquid chromatography has been developed and validated. Plasma was precipitated with acetonitrile before samples were loaded onto a zwitterionic hydrophilic interaction liquid chromatography (ZIC-HILIC) solid-phase extraction column. Amoxicillin was analyzed by liquid chromatography on an Aquasil (150 x 4.6 mm) LC column with mobile-phase acetonitrile: phosphate buffer (pH 2.5; 0.1 mol/L; 7:93, v/v) and UV detection at 230 nm. A regression model using 1/concentration weighting was found the most appropriate for quantification. The intraassay precision for plasma was 3.3% at 15.0 μg/mL and 10.9% at 0.200 μg/mL. The interassay precision for plasma was 1.8% at 15.0 μg/mL and 7.5% at 0.200 μg/mL. The total-assay precision for plasma over 4 days using a total of 20 replicates was 13.2%, 5.5%, and 3.8% at 0.200 μg/mL, 3.00 μg/mL, and 15.0 μg/mL, respectively. The lower limit of quantification and the limit of detection were 0.050 μg/mL and 0.025 μg/mL, respectively, for 100 μL plasma. Long-term storage stability studies of amoxicillin in plasma indicate that a temperature of -80 degrees C is necessary to prevent degradation of amoxicillin.

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DEVELOPMENT AND VALIDATION OF A BIOANALYTICAL METHOD USING AUTOMATED SOLID-PHASE EXTRACTION AND LC-UV FOR THE SIMULTANEOUS DETERMINATION OF LUMEFANTRINE AND ITS DESBUTYL METABOLITE IN PLASMA

Lindegardh N,1,2 Annerberg A,1 Blesborn D,1 Bergqvist Y,3 Day N,1,2 White NJ1,2
1Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand; 2Nuffield Department of Clinical Medicine, Centre for Tropical Medicine, University of Oxford, Oxford, UK; and 3Dalarna University College, S-781 88 Borlänge, Sweden

A BIOANALYTICAL method for the determination of lumefantrine (LF) and its metabolite desbutyl-lumefantrine (DLF) in plasma by solid-phase extraction (SPE) and liquid chromatography has been developed. Plasma proteins were precipitated with acetonitrile:acetic acid (99:1, v/v) containing a DLF analogue internal standard before being loaded onto an octysilica (3 M Empore) SPE column. Two different DLF analogues were evaluated as internal standards. The compounds were analysed by liquid chromatography UV detection on a SB-CN (250 mm x 4.6 mm) column with a mobile phase containing acetonitrile-sodium phosphate buffer pH (2.0: 0.1 M) (55:45, v/v) and sodium perchlorate 0.05 M. Different SPE columns were evaluated during method development to optimise reproducibility and recovery for LF, DLF and the two different DLF analogues. The within-day precisions for LF were 6.6 and 2.1% at 0.042 and 8.02 microg/mL, respectively, and for DLF 4.5 and 1.5% at 0.039 and 0.777 microg/mL, respectively. The between-day precisions for LF were 12.0 and 2.9% at 0.042 and 8.02 microg/mL, respectively, while for DLF 0.7 and 1.2% at 0.039 and 0.777 microg/mL, respectively. The limit of quantification was 0.024 and 0.021 microg/mL for LF and DLF, respectively. Different amounts of lipids in plasma did not affect the absolute recovery of LF or DLF.

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death rate (39%). Mortality rates rose with increasing B. pseudomallei counts in urine, from 58% for those with positive spun pellets only to 61% for those with between 10^4 CFU/ml and 10^5 CFU/ml and 71% for those with 10^6 CFU/ml. This was independent of age, presence of bacteremia, known risk factors for melioidosis such as diabetes, and the prior administration of antibiotics. The presence of B. pseudomallei in urine during systemic infection is associated with a poor prognosis.

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ABSTRACTS

HIGH THROUGHPUT ASSAY FOR THE DETERMINATION OF PIPERAQUINE IN PLASMA

Lindegaardh N, Blessborn D, Bergqvist Y
Dalarna University College, 781 88 Borlange, Sweden

A BIOANALYTICAL method is described for the simultaneous quantitative analysis of the highly lipophilic atovaquone and the strong basic proguanil with metabolites in plasma. The drugs are extracted from protein precipitated plasma samples on a novel mixed-mode solid-phase extraction (SPE) column containing carboxypropyl and octyl silica as functional groups. The analytes are further separated and quantitated using a steep-gradient liquid chromatographic method on a Zorbax SB-CN column with UV detection at 245 nm. Two different internal standards (IS) are used in the method to compensate for both types of analytes. A structurally similar IS to atovaquone is added with acetonitrile to precipitate proteins from plasma. A structurally similar IS to proguanil and its metabolites is added with phosphate buffer before samples are loaded onto the SPE columns. A single elution step is sufficient to elute all analytes. The method is validated according to published guidelines and shows excellent performance. The within-day precisions, expressed as relative standard deviation, are lower than 5% for all analytes at three tested concentrations within the calibration range. The between-day precisions are lower than 13% for all analytes at the same tested concentrations. The limit of quantitation is 25 nM for the basic substances and 50 nM for atovaquone. Several considerations regarding development and optimization of a method for determination of analytes with such a difference in physiochemical properties are discussed.

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HIGH THROUGHPUT ASSAY FOR THE DETERMINATION OF PIPERAQUINE IN PLASMA

Lindegaardh Niklas1,2, White Nicholas1,2, Day Nicholas1,2
Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand; Nuffield Department of Clinical Medicine, Centre for Clinical Vaccinology and Tropical Medicine, Churchill Hospital, Old Road, Oxford OX3 7LJ, UK; 2Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

A HIGH throughput assay for the determination of the antimalarial piperaquine in plasma has been developed and validated. The assay utilises 96-wellplate formats throughout the whole procedure, and easily enables a throughput of 192 samples a day using a single LC system. Buffer (pH 2.0; 0.05M) containing internal standard was added to 0.25mL plasma in a 96-wellplate (2ml wells). The samples were extracted on a MPC solid phase extraction deep well 96-wellplate (3M Empore). Piperaquine and internal standard were analysed by liquid chromatography with UV detection on a Chromolith Performance (100mmx4.6mm) column with a mobile phase containing acetonitrile-phosphate buffer (pH 2.5; 0.1M) (8:92, v/v) at a flow rate of 3.0mL/min. The within-day precisions for piperaquine were 3.3 and 2.3% at 40 and 1250ng/mL, respectively. The between-day precisions for piperaquine were 5.8 and 1.3% at 40 and 1250ng/mL, respectively. The total assay precisions using 29 replicates over 5 days were 6.7, 4.5 and 2.7% at 40, 200 and 1250ng/mL, respectively. The lower limit of quantification (LLOQ) and the limit of detection (LOD) were 10 and 5ng/mL, respectively using 0.25mL plasma. Using 1mL of plasma, it was possible to decrease LLOQ and LOD to 2.5 and 1.25ng/mL, respectively.

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CEREBROSPINAL FLUID LEVELS OF MARKERS OF BRAIN PARENCHYMAL DAMAGE IN VIETNAMESE ADULTS WITH SEVERE MALARIA

Medana Isabelle,1 Lindert Ralf-Bjorn,2 Wurster Ulrich,2 Hien Tran Tinh,3 Day Nicholas, Phu Nguyen Hoan,3 Mai Nguyen Thi,4 Chuong Ly Van,4 Chau Tran Th,4 Turner Gareth,4 Farrar Jeremy,4,5 White Nicholas1,6
1Nuffield Department of Clinical Laboratory Sciences, University of Oxford, Oxford, Academic block, Level 4, John Radcliffe Hospital Headington, Oxford OX3 9DU, UK; 2Neurologische Klinik, Medizinische Hochschule Hannover, Carl-Neuberg-Strasse 1, 30623 Hannover, Germany; 3Hospital for Tropical Diseases, Ho Chi Minh City, Viet Nam; 4Oxford University Clinical Research Unit, Ho Chi Minh City, Viet Nam; 5Centre for Clinical Vaccinology and Tropical Medicine, Churchill Hospital, Old Road, Oxford OX3 7LJ, UK; 6Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

A RETROSPECTIVE study of cerebrospinal fluid (CSF) markers of brain parenchymal damage was conducted in Vietnamese adults with severe malaria. Three markers were analysed by immunoassays: the microtubule-associated protein tau, for degenerated axons; neuron-specific enolase (NSE), for neurons; and S100B for astrocytes. The mean concentration of tau proteins in the CSF was significantly raised in patients with severe malaria compared with controls.
Selection strength and hitchhiking around two anti-malaria resistance genes

Nash D,1,2 Nair S,1 Mayxay M,3,4 Newton PN,4 Guthmann JP,3 Nosten F,5,7,8 Anderson TJ1

1 South west Foundation for Biomedical Research (SFBR), PO Box 760549, San Antonio, TX 78245, USA; 2 Our Lady of the Lake University, San Antonio, TX 78207, USA; 3 Faculty of Medicine, National University of Laos, Vientiane, Lao PDR; 4 Wellcome Trust-Mahosot-Oxford Tropical Medicine Research Collaboration, Mahosot Hospital, Vientiane, Lao PDR; 5 Epicentre ( Médecins Sans Frontières-France), 8 rue Saint Sabin, 75011 Paris, France; 6 Shoklo Malaria Research Unit (SMRU), Mae Sot, Tak, Thailand; 7 Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; and 8 Centre for Clinical Vaccinology and Tropical Medicine, Churchill Hospital, Oxford OX3 7LJ, UK


Pharmacokinetics of oral doxycycline during combination treatment of severe falciparum malaria

Newton Paul,1,2 Chaulet Jean-Francois,3 Brockman Alan,1,4 Chierakul Wirongrong,1 Dondorp Arjen,1,2 Ruangveerayuth Ronatrai,1 Loaareesuwan Sornchai,1 Mounier Cyril,3 White Nicholas1,2,4

1 Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; 2 Centre for Clinical Vaccinology and Tropical Medicine, Churchill Hospital, Oxford, United Kingdom; 3 Laboratoire de biochimie, toxicologie et pharmacologie, Hopital d’Instruction des Armées Desgenettes, Lyon, France; 4 Shoklo Malaria Research Unit; and 5 Mae Sot Hospital, Mae Sot, Tak

ABSTRACTS

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DESTABILISATION AND SUBSEQUENT LYSIS OF HUMAN ERYTHROCYTES INDUCED BY PLASMODIUM FALCIPARUM HEAM PRODUCTS

Omodeo-Sale Fausta1, Motti Anna1, Dondorp Arjen2, White Nicholas1, Taramelli Donatella4

1Institute of General Physiology and Biochemistry G. Esposito, University of Milan, Milan, Italy; 2Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; 3Centre for Clinical Vaccinology and Tropical Medicine, Churchill Hospital, Oxford, UK; 4Institute of Microbiology, University of Milan, Milan, Italy.

I n falciparum malaria, both infected and uninfected red cells have structural and functional alterations. To investigate the mechanisms of these modifications, we studied the effects of two Plasmodium falciparum haem products (haematin and malaria pigment in the synthetic form beta-haematin) on isolated human red blood cells (RBCs) and purified RBC ghosts. A dose-and time-dependent incorporation of haematin into RBC ghosts and intact cells was observed, which was in proportion to the extent of haematin-induced haemolysis. RBCs pre-incubated with haematin were more sensitive to haemolysis induced by hypotonic shock, low pH, H2O2 or haematin itself. Haemolysis was not related to membrane lipid peroxidation and only partially to oxidation of protein sulphydryl groups and it could not be prevented by scavengers of lipid peroxidation or hydroperoxide groups. N-acetylcysteine partly protected the oxidation of SH groups and significantly reduced haemolysis. In contrast, beta-haematin was neither haemolytic nor oxidative towards protein sulphydryl groups. Beta-haematin did destabilise the RBC membrane, but to a lesser extent than haematin, inducing increased susceptibility to lysis caused by hypotonic medium, H2O2 or haematin. This study suggests that the destabilising effect of haematin and, to a much less extent, beta-haematin on the RBC membrane does not result from oxidative damage of membrane lipids but from direct binding or incorporation which may affect the reciprocal interactions between the membrane and cytoskeleton proteins. These changes could contribute to the reduced red cell deformability associated with severe malaria.

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A RANDOMIZED COMPARISON OF ORAL CHLORAMPHENICOL VERSUS OFLOXACIN IN THE TREATMENT OF UNCOMPLICATED TYPHOID FEVER IN LAOS

Phongmany Simmaly1,2, Phetsouvnah Rattanaphone1,2, Sisouphone Sliho1,2, Darasavath Chirapha1,2, Vongphachane Pankham1,2,3, Rattanavong Oudayvone1,2, Mayxay Mayfong1,2, Ramsay Andres1,2,3, Blacksell Stuart1,2,3, Thammavong Chanpheng1,2, Sylavong Bounkong1,2, White Nicholas3,4,5, Newton Paul2,5

1Mahosot Hospital, Vientiane, Laos; 2Wellcome Trust-Mahosot Hospital, Oxford Tropical Medicine Research Collaboration, Vientiane, Laos; 3Faculty of Medicine, National University of Laos, Vientiane, Laos; 4Faculty of Tropical Medicine, Mahidol University, 4206 Rajvithi Road, Bangkok 10400, Thailand; 5Centre for Clinical Vaccinology and Tropical Medicine, Churchill Hospital, Oxford OX3 7LJ, UK.

W e conducted a randomized open trial of oral chloramphenicol (50 mg/kg/day in four divided doses for 14 days) versus ofloxacin (15 mg/kg/day in two divided doses for 3 days) in 50 adults with culture-confirmed uncomplicated typhoid fever in Vientiane, Laos. Patients had been ill for a median (range) of 8 (2–30) days. All Salmonella enterica serotype typhi isolates were nalidixic acid-sensitive, four (8%) were chloramphenicol-resistant and three (6%) were multidrug-resistant. Median (range) fever clearance times were 90 (24–224) hours in the chloramphenicol group and 54 (6–93) hours in the ofloxacin group (P < 0.001). One patient in the chloramphenicol group developed an ileal perforation. Three days ofloxacin was more effective than 14 days chloramphenicol for the in-patient treatment of typhoid fever, irrespective of antibiotic susceptibility, and was of similar cost.

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IFN-γ AT THE SITE OF INFECTION DETERMINES OF CLEARANCE OF INFECTION IN CRYTOCOCCAL MENINGITIS

Siddiqui Asna1, Brouwer Annemarie1,2,3, Wuthiekanun Vanaporn2, Jaffar Shabbar1, Shattock Robin1, Irving Diane1, Sheldon Joanna1, Chierakul Wirongrong1, Peacock Sharon1,2, Day Nicholas3,4, White Nicholas1,4, Harrison Thomas1

1Department of Infectious Diseases and Immunology, St. George's Hospital Medical School, London, United Kingdom; 2Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; 3Department of Internal Medicine and Infectious Disease, University Medical Centre, Nijmegen, The Netherlands; 4London School of Hygiene and Tropical Medicine, London, UK; 5Centre for Tropical Medicine, Nuffield Department of Clinical Medicine, University of Oxford, John Radcliffe, Oxford UK.
In animal models, immunity to cryptococcal infection, as in many chronic fungal and bacterial infections, is associated with a granulomatous inflammatory response, intact cell-mediated immunity, and a Th1 pattern of cytokine release. To examine the correlates of human immunity to cryptococcal infection in vivo, we analyzed immune parameters at the site of infection over time and assessed the rate of clearance of infection by serial quantitative cerebrospinal fluid (CSF) fungal cultures in 62 patients in a trial of antifungal therapy for HIV-associated cryptococcal meningitis. CSF IL-6, IFN-gamma, TNF-alpha, and IL-8 were significantly higher in survivors compared with nonsurvivors. There were negative correlations between log TNF-alpha, IFN-gamma, and IL-6 levels and baseline cryptococcal CFU. Log IFN-gamma, G-CSF, TNF-alpha, and IL-6 were correlated positively with the rate of fall in log CFU/ml CSF/day. In a linear regression model including antifungal treatment group, baseline CFU, and these cytokines, only treatment group and log IFN-gamma remained independently associated with rate of clearance of infection. The results provide direct in vivo evidence for the importance of quantitative differences in IFN-gamma secretion in human immune control of granulomatous infections, and increase the rationale for adjunctive IFN-gamma in the treatment of refractory HIV-associated cryptococcosis.

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FATAL PLASMODIUM FALCIPARUM MALARIA CAUSES SPECIFIC PATTERNS OF PLENIC ARCHITECTURAL DISORGANIZATION

Urban Britta,1 Hien Tram,2 Day Nicholas,1,3 Phu Nguyen,2 Roberts Rachel,4 Ponponrat Emstri,3 Jones Margret,4 Mai Nguyen,3 Bethell Delia,3 Turner Gareth,4 Ferguson David,4 White Nicholas,1,3 Roberts David4,5

1Nuffield Department of Clinical Medicine, 2Centre for Tropical Diseases, Cho Quan Hospital, Ho Chi Minh City, Vietnam; 3Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; 4Nuffield Department of Clinical Laboratory Sciences, University of Oxford; 5National Blood Service, John Radcliffe Hospital, Oxford, United Kingdom.

The spleen is critical for host defense against pathogens, including Plasmodium falciparum. It has a dual role, not only removing aged or antigenically altered erythrocytes from the blood but also as the major lymphoid organ for blood-borne or systemic infections. The human malaria parasite P. falciparum replicates within erythrocytes during asexual blood stages and causes repeated infections that can be associated with severe disease. In spite of the crucial role of the spleen in the innate and acquired immune response to malaria, there is little information on the pathology of the spleen in human malaria. We performed a histological and quantitative immunohistochemical study of spleen sections from Vietnamese adults dying from severe falciparum malaria and compared the findings with the findings for spleen sections from control patients and patients dying from systemic bacterial sepsis. Here we report that the white pulp in the spleens of patients dying from malaria showed a marked architectural disorganization. We observed a marked dissolution of the marginal zones with relative loss of B cells. Furthermore, we found strong HLA-DR expression on sinusoidal lining cells but downregulation on cordal macrophages. P. falciparum infection results in alterations in splenic leukocytes, many of which are not seen in sepsis.

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INTERMITTENT PRESUMPTIVE TREATMENT FOR MALARIA

White Nicholas
Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand, and the Centre for Clinical Vaccinology, Tropical Medicine, Churchill Hospital, Oxford, United Kingdom

Intermittent presumptive treatment (IPT) in pregnancy involves giving a curative treatment dose of an effective antimalarial drug at predefined intervals during pregnancy. IPT in pregnancy was first introduced in areas of high malaria transmission as a measure to reduce the adverse impact of Plasmodium falciparum malaria in pregnancy. Later, based on trials showing that IPT could reduce anaemia in young children and also malaria episodes in infants, it was extended as a measure to reduce morbidity and mortality in the first year of life.

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ABSTRACTS

DYNAMIC DETERMINANTS OF THE CYTOADHEREANCE OF PLASMODIUM FALCIPARUM-INFECTED ERYTHROCYTES

White Nicholas
Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand, and the Centre for Clinical Vaccinology and Tropical Medicine, Churchill Hospital, Oxford, United Kingdom

Since Marchiafava and Bignami noted in their pathologic studies of falciparum malaria that “malignancy coincides with an exceptionally abundant quantity of parasitic forms, a quantity much more abundant—where the cases terminate fatally—in the blood of the visera than in the blood of the finger,” sequestration has been considered central to the pathology of this potentially lethal infection. The Roman pathologists also observed that the process was not uniform among the vital organs, noting particularly the “accumulation in the cerebral vessels of red blood corpuscles loaded with amoebeae.” The result of this pathologic process was described as “mechanical alterations in the circulation”; or, in other words, a traffic jam. With the development of methods for ex vivo culture of Plasmodium falciparum, malarialogists have studied this process of cytoadherence of parasitized erythrocytes to endothelial cells (or the purified immobilized cell surface “receptors”) in the laboratory and have progressively tried to recreate the same conditions that occur in vivo. This is not easy, as blood is a thick and complex soup of deformable cells suspended in a variable consommé of plasma proteins, electrolytes, and a variety of small organic molecules. Its effective viscosity changes nonlinearly under the different shear rates encountered in the circulation (non-Newtonian behavior). Malaria is associated with fever, progressive anemia, thrombocytopenia, an increase in acute phase proteins, reduction in serum albumin, and, in severe infections, reduced uninfected red cell deformability.

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RAPID IMMUNOFLUORESCENCE MICROSCOPY FOR DIAGNOSIS OF MELIOIDOSIS

Wuthiekanun Vanaporn,1 Desakorn Varunee,2 Wongsuvan Gumphol,1 Amornchai Premjit,1 Cheng Allen,1,3 Maharjan Bina,1 Limmathurotsakul Direk,1 Chierakul Wirongrong,1,2 White Nicholas,1,4 Day Nicholas,1,4 Peacock Sharon1,4
1Faculty of Tropical Medicine, Wellcome Trust-Oxford University-Mahidol University Tropical Medicine Research Program; 2 Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; 3Menzies School of Health Research, Charles Darwin University, and Northern Territory Clinical School, Flinders University, Darwin, Australia; 4Centre for Clinical Vaccinology and Tropical Medicine, Nuffield Department of Clinical Medicine, University of Oxford, Churchill Hospital, Oxford, United Kingdom

A n immunofluorescent (IF) method that detects Burkholderia pseudomallei in clinical specimens within 10 min was devised. The results of this rapid method and those of an existing IF method were prospectively compared with the culture results for 776 specimens from patients with suspected melioidosis. The sensitivities of both IF tests were 66%, and the specificities were 99.5 and 99.4%, respectively.

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DETECTION OF BURKHOLDERIA PSEUDOMALLEI IN SOIL WITHIN THE LAO PEOPLE’S DEMOCRATIC REPUBLIC

Wuthiekanun Vanaporn,1 Mayxay Mayfong,2 Chierakul Wirongrong,1 Phetsouvanh Rattanaphone,2 Cheng Allen,1,3 White Nicholas,1,4 Day Nicholas,1,4 Peacock Sharon1,4
1Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; 2Mahosot Hospital, Vientiane, Lao People’s Democratic Republic; 3Menzies School of Health Research, Charles Darwin University and Northern Territory Clinical School, Flinders University, Northern Territory, Australia; 4Nuffield Department of Clinical Medicine, John Radcliffe Hospital, University of Oxford, Oxford, United Kingdom

Clinical cases of melioidosis caused by the saprophyte Burkholderia pseudomallei were first noted in the Lao People’s Democratic Republic (PDR) in 1999. In this study, 36% of 110 soil samples in northern Lao PDR were positive for B. pseudomallei, providing further evidence for the presence of melioidosis in this country.

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TRIMETHOPRIME SULFAMETHOXAZOLE RESISTANCE IN CLINICAL ISOLATES OF BURKHOLDERIA PSEUDOMALLEI

Wuthiekanun Vanaporn1, Cheng Allen2, Chierakul Wirongrong1, Amornchai Premjit1, Limmathurotsakul Direk1, Chaowagul Wipada3, Simpson Andrew4, Short Jennifer4, Wongsavan Gumphol1, Maharan Bina1, White Nicholas1,4, Peacock Sharon1,4

1Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; 2Tropical and Emerging Infectious Diseases Division, Menzies School of Health Research, Charles Darwin University, Darwin, Australia; 3Department of Medicine, Sappasitthiprasong Hospital, Ubon Ratchathani, Thailand; 4Nuffield Department of Clinical Medicine, John Radcliffe Hospital, University of Oxford, Oxford, United Kingdom.

OBJECTIVES: Trimethoprim/sulfamethoxazole is commonly used to treat melioidosis. Antimicrobial susceptibility testing using the disc diffusion method is commonly used in melioidosis-endemic areas, but may overestimate resistance to trimethoprim/sulfamethoxazole.

PATIENTS AND METHODS: We performed disc diffusion and Etest on isolates from the first positive culture for all patients presenting to Sappasithiprasong Hospital, Ubon Ratchathani, Thailand, with culture-confirmed melioidosis between 1992 and 2003.

RESULTS: The estimated resistance rate for 1976 clinical Burkholderia pseudomallei isolates was 13% by Etest and 71% by disc diffusion. All isolates classed as either susceptible (n=358) or as having intermediate resistance (n=218) on disc diffusion were susceptible by Etest. Only 258 of the 1400 (18%) isolates classed as resistant on disc diffusion were resistant by Etest.

CONCLUSIONS: Disc diffusion testing of B. pseudomallei may be useful as a limited screening tool in resource poor settings. Isolates assigned as ‘susceptible’ or ‘intermediate’ by disc diffusion may be viewed as ‘susceptible’; those assigned as ‘resistant’ require further evaluation by MIC methodology.


HOW DO PATIENTS USE ANTIMALARIAL DRUGS? A REVIEW OF THE EVIDENCE

Yeung Shunmay,1,2,3 White Nicholas1,2

1Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; 2Centre for Vaccinology and Tropical Medicine, Churchill Hospital, Oxford, UK; 3London School of Hygiene and Tropical Medicine, London, UK

PATIENT adherence is a major determinant of the therapeutic response to antimalarial drugs, as most treatments are taken at home without medical supervision. With the introduction of new, effective, but more expensive antimalarials, there is concern that the high levels of efficacy observed in clinical trials may not be translated into effectiveness in the normal context of use. We reviewed available published evidence on adherence to antimalarial drugs and community drug usage; 24 studies were identified of which nine were ‘intervention’ studies, seven were classified as ‘outcome studies’, and the remainder were purely descriptive studies of antimalarial adherence. Definitions, methods, and results varied widely. Adherence was generally better when treatments were effective, and was improved by interventions focusing on provider knowledge and behaviour, packaging, and provision of correct dosages. There is insufficient information on this important subject, and current data certainly do not justify extrapolation from results with ineffective drugs to new effective treatments. Research in this area would benefit from standardization of methodologies and the application of pharmacokinetic modelling.

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