Faculty of Tropical Medicine, Mahidol University

DEPARTMENTS AND ACTIVITIES

Department of

Clinical Tropical Medicine

Office of the Department, Telephone: 0 2354 9100 ext. 1423, 1428
Fax: 0 2354 9168

Prof. Punnee Pitisuttithum

M.B., B.S., D.T.M.& H. (Bangkok), Grad. Dip. in Clin. Sc. (Med.), Dip. Thai Board of Internal Medicine.
FIELD OF EXPERTISE: Tropical disease vaccine trials, especially Phase I, II vaccine trials eg. cholera, rotavirus, AIDS vaccines. Clinical studies of tropical diseases eg. cryptococcal meningitis in AIDS; chronic diarrhea in AIDS, drug trials in AIDS and opportunistic infections, especially oral candidiasis
E-MAIL: *tmppt@mahidol.ac.th, headtmmd@mahidol.ac.th*
TELEPHONE: 0 2643 5599, 0 2354-9100-19 ext. 2061

Head

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, Dip. Thai Board in Allergy and Clinical Immunology
FIELD OF EXPERTISE: Internal medicine/Allergy/ Clinical immunology
E-MAIL: *tmwmk@mahidol.ac.th*
TELEPHONE: 0 2354 9100 ext. 2060 press 13

Deputy Head

Prof. Sornchai Looareesuwan

M.D., D.T.M. & H. (Bangkok), Grad. Dip. in Clin. Sc. (General Med.), Dip. Thai Board of General Medicine, F.A.C.T.M. F.R.C.P.
FIELD OF EXPERTISE: Pathophysiology of severe malaria, Chemotherapy of malaria
E-MAIL: *tmslr@mahidol.ac.th*
TELEPHONE: 0 2354 9159

Prof. Sasithon Pukrittayakamee

MB.,B.S., Grad. Dip. in Clin. Sc. (Radiology), D.T.M. & H. (Bangkok), D. Phil (Oxon.)
FIELD OF EXPERTISE: Tropical medicine
E-MAIL: *sasithon@tropmedres.ac*
TELEPHONE: 0 2354 9100 ext. 1435

Prof. Polrat Wilairatana

B.Sc., M.D., Dip. Thai Board of Internal Medicine and Gastroenterology, M.Sc. (Gastroenterology), Ph.D (Trop. Med.), F.A.C.T.M., F.A.C.G.
FIELD OF EXPERTISE: Tropical gastroenterology, Pathophysiology of severe malaria, Clinical management of malaria
E-MAIL: *tmpwl@mahidol.ac.th*
TELEPHONE: 0 2354 9100 ext. 1454

Assoc. Prof. Wichai Supanaranond

B.Sc. (Med. Tech.), M.B.,B.S., D.T.M. & H. (Bangkok), M.Sc. (C.T.M.), Dip. in Dermatology
FIELD OF EXPERTISE: Dermatology/Sexually, Acupuncture transmitted diseases
E-MAIL: *tmwsn@mahidol.ac.th*
TELEPHONE: 0 2354 9100 ext. 1424

Assoc. Prof. Yupaporn Wattanagoon

M.B., B.S., D.T.M. & H. (Bangkok), Dip. Thai Board of Internal Medicine.
FIELD OF EXPERTISE: Internal medicine
E-MAIL: *tmywt@mahidol.ac.th*
TELEPHONE: 0 2354 9168, 0 2354 9100 ext. 1428

Assoc. Prof. Wattana Leowattana

B.Sc., M.D., Dip. Thai Board of Clinical Pathology, M.Sc. (Clinical Science), Dip. Thai Board of Family Medicine, MRCPath (Thai)
FIELD OF EXPERTISE: Clinical chemistry, screening of cancer, laboratory automation
E-MAIL: *leowattana@yahoo.com*
TELEPHONE: 0 2354 9100-19 ext. 2039, 081-4878848

Assoc. Prof. Lakana Leohirun

B.Sc., (Med. Tech), M.Sc. (Clin. Path)
FIELD OF EXPERTISE: Environmental and industrial toxicology, Health risk assessment from toxicants, Biochemistry
E-MAIL: *tmllh@mahidol.ac.th*
TELEPHONE: 0 2354 9100-19 ext.1434,

Assoc. Prof. Benjaluck Phonrat

B.Sc. (Biology), M.Sc. (Trop. Med.).
E-MAIL: *tmbpr@mahidol.ac.th*
TELEPHONE: 0 2354 9100 ext. 2060 press 13

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: *tmwpr@mahidol.ac.th*
TELEPHONE: 0 2354 9168, 0 2354 9100-19 ext.1423

Assist. 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: *tmusl@mahidol.ac.th*
TELEPHONE: 0 2354 9168, 0 23549100-19 ext.1423

Assist. Prof. Valai Bussaratid

M.D., M.Sc. (Dermatology)
FIELD OF EXPERTISE: Dermatology/Internal medicine
E-MAIL: *tmvbs@mahidol.ac.th*
TELEPHONE: 0 2354 9168, 0 23549100-19 ext. 2065

Assist. Prof. Jittima Dhitavat

M.D. (Hon.), M.Sc., Dip. Thai Board of Dermatology, D. Phil.
FIELD OF EXPERTISE: Dermatology, Mycology, Cell biology
E-MAIL: *jittima_pu@yahoo.com*
TELEPHONE: 0 2354 9168, 0 2354 9100-19 ext. 2068

Dr. Supat Chamnachanan

M.D., D.T.M. & H. (Bangkok), Dip Thai Board of Hematology
E-MAIL: *tmscc@mahidol.ac.th*
TELEPHONE: 0 2354 9100 ext. 1691
LECTURER

Dr. Watcharapong Piyaphanee

M.D. (1st Class honor), Grad. Dip. in Clin., Dip. Thai Board of Internal Medicine
FIELD OF EXPERTISE: Travel Medicine
E-MAIL: *tewpe@mahidol.ac.th*
TELEPHONE: 0 2354 9168, 0 2354 9100 ext 1428
LECTURER

Dr. Wichai Ekataksin

M.D., Ph.D.
FIELD OF EXPERTISE: Liver microcirculation, Computer-assisted 3D imaging angioarchitectural morphology
E-MAIL: *scwek@mahidol.ac.th*
TELEPHONE: 0 2354 9100-19 ext.1691
LECTURER

Dr. Wipa Thanachartwet

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: *tmvtn@mahidol.ac.th*
TELEPHONE: 0 2354 9168, 23549100-19 ext.1423
LECTURER

Dr. Wirongrong Chierakul

M.D., Thai Board of Internal Medicine
FIELD OF EXPERTISE: Tropical infectious diseases, esp. melioidosis, leptospirosis, scrub typhus
E-MAIL: *tmwer@mahidol.ac.th*
TELEPHONE: 0 2354 1395, 08 105 8571
LECTURER

Dr. Karnchana Pornpininworakij

M.D., D.T.M. & H. (Bangkok), M.C.T.M.
E-MAIL: *tmkpp@mahidol.ac.th*
TELEPHONE: 0 23549168, 0 23549100 ext. 1429
LECTURER

Dr. Raweerat Sitcharungsi

M.D., D.T.M. & H. (Bangkok)
TELEPHONE: 0 23549168, 08 859 4478
LECTURER

Dr. Theeratus Jongboonyanuparp

M.D., D.T.M. & H. (Bangkok)
E-MAIL: *theeratus@hotmail.com*
TELEPHONE: 02 3549168, 02 3549100 ext.1423,1428, 081 563 5354
LECTURER

Dr. Chatporn Kittitrakul

M.D., D.T.M. & H. (Bangkok)
TELEPHONE: 0 23549168
LECTURER

OVERVIEW

The Department was established in 1960, to pursue research and training in the methods of research work which contribute to the advancement of knowledge and clinical care in tropical medicine. The Department of Clinical Tropical Medicine comprises 13 units; each unit has one chief and unit staff. The units are: Biochemistry Unit, Critical Care Research Unit, Clinical Infectious Disease Research Unit, Clinical Pathophysiology Research Unit, Clinical Pharmacology Unit, Dermatology Unit, Gastroenterology Unit, Liver Research Unit, Nephrology Unit, Tropical Infectious Research Unit, Traditional Chinese Medicine Unit, Tropical Medicine Laboratory Unit, and Travel Medicine Research Unit. The Department has a total of 38 academic staff, with one Head of Department, one Deputy Head, four professors, five associate professors, eight assistant professors, fourteen lecturers, four scientists, one medical science associate and two general officers. The Department of Clinical Tropical Medicine has a long and proud history of contributions to clinical care and research in tropical medicine.

Dr. Sant Muangnoicharoen
M.D. & D.T.M. & H. (Bangkok)
TELEPHONE: 0 23549168
LECTURER

Dr. Virawan Ruvira
M.D., D.T.M. & H. (Bangkok)
TELEPHONE: 02 3549168, 02 3549100 ext.1423,1428, 0 22754041
LECTURER

Assoc. Prof. Varunee Desakorn
B.Sc. (Med. Tech.), M.P.H. (Biostatistics), M.Sc. (Microbiology & Immunology)
FIELD OF EXPERTISE: Immunodiagnosis of tropical diseases, Biostatistics
E-MAIL: *tmvds@mahidol.ac.th*
TELEPHONE: 0 2354 9168, 0 2354 9100-19 ext.2064, 2066
MEDICAL TECHNOLOGIST

Assist. Prof. Apichart Nontprasert
B.Sc., (Biology), M.Sc. (Public Health), Ph.D. (Trop. Med.)
FIELD OF EXPERTISE: Neurotoxicity
E-MAIL: *apichart@tropmedres.ac*
TELEPHONE: 0 2354 9100-19 Ext. 1437

Assist. Prof. Kesinee Chotivanich
B.Sc. (Nursing Science), M.Sc. (Pathobiology), Ph.D. (Pathobiology)
FIELD OF EXPERTISE: Pathophysiology of malaria
E-MAIL: *nok@tropmedres.ac*
TELEPHONE: 0 2354 9100-19 Ext. 1427

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*
TELEPHONE: 0 2354 9100-19 Ext. 1406

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*
TELEPHONE: 0 2354 9100-19 ext. 2025, 1426
LECTURER

Mr. Noppadon Tangpukdee
B.N.S., Dip. Med. Micro., M.Sc. (Toxicology)
FIELD OF EXPERTISE:
Clinical Study in field of Toxicology and Safety
E-MAIL: *tmntp@mahidol.ac.th*
TELEPHONE: 0 2354 9159, 0 2354 9100 ext.1421
LECTURER

Ms. Gedsuda Pattanapen
M.Sc. (Anatomy)
FIELD OF EXPERTISE:
Hepatic Stellate Cells or Arachnocytes in Liver
E-MAIL: *tmgpt@mahidol.ac.th*
TELEPHONE: 0 2354 9168 , 0 2354 9100 ext. 1698
LECTURER

Mr. Trithar Pholcharoen
B.Sc. (Med. Tech.)
TELEPHONE: 0 2354 9100-19 ext.1434, 0 2643 5588
MEDICAL TECHNOLOGIST

Ms. Sompong Mingmongkol
B.Sc. (Med. Tech.)
TELEPHONE: 0 2354 9100-19 ext.1434, 0 2643 5588
MEDICAL TECHNOLOGIST

Ms. Borimas Hanboonkunuparkarn
B.Sc. (First Class Honors)
FIELD OF EXPERTISE: hepatic ischemia-reperfusion injury
TELEPHONE: 0 2354 9100 ext. 1698
SCIENTIST

Mr. Surong Prasartpan
Dip. Med. Sci. Tech.
TELEPHONE: 0 2354 9100-19 ext.1434, 0 2643 5588
MEDICAL SCIENCE ASSOCIATE

Mrs. Chuanpit Preechawuthiwong
B.A. (Political Science)
TELEPHONE: 0 2354 9168, 0 2354 9100-19 ext.1428-1429
GENERAL AFFAIRS OFFICER

HIGHLIGHT

The Department is the base for tropical medicine academic programs and is actively involved in teaching and training postgraduate courses of the Faculty, such as:

1. Master of Science in Tropical Medicine (M. Sc.)
2. Doctor of Philosophy in Tropical Medicine (Ph. D.)
3. Graduate Diploma in Tropical Medicine& Hygiene (D.T.M. & H.).
4. Master in Clinical Tropical Medicine (M.C.T.M.)
5. Doctor of Philosophy in Clinical Tropical Medicine (Ph. D.)

CURRENT RESEARCH ACTIVITIES

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

Malaria research activities have focused on clinical trials, pathophysiology, clinical pharmacology and clinically related laboratory studies. Staff of the Department studied about 2500 admitted malaria cases. Most cases were falciparum and vivax malaria, with a few cases of mixed infections of malariae malaria and ovale malaria. The major focus is on clinical trials of multidrug-resistant falciparum malaria in uncomplicated and complicated cases. Experiments with combinations of various antimalarial drugs were conducted continuously; with 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 methods to predict *Plasmodium falciparum* treatment failure. Pathophysiologic alterations in malaria have been widely investigated. Interesting results were the dynamic alteration in splenic function during acute falciparum malaria, in erythrocyte survival following clearance of malaria parasites, defective production of, and response to, IL-2 in acute falciparum malaria, cytoadherence and ultrastructure of *Plasmodium falciparum*-infected erythrocytes from splenectomized patients, and hepatic blood flow and metabolism in severe falciparum malaria.

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

Parasitic infestations have also been studied, such as drugs trials and investigations for gnathostomiasis and the use of parenteral local drugs strongyloidiasis, opisthorchiasis, paragonimiasis, and teniasis.

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

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

Vaccine Trials The Department's staff is also responsible for various HIV-1 Vaccine trials at the Vaccine Trial Centre, in addition to other vaccine trials, such as cholera, Shigella and Human Papilloma Viruses vaccines.

SERVICES

Services consist of clinical services and laboratory services.

Daily clinical services are in-patient and out patient care at the Hospital for Tropical Diseases. The Hospital for Tropical Diseases is a 250-bed hospital with an Intensive Care Unit and other facilities for the management of endemic tropical diseases.

Special routine laboratory services are provided for patients who are admitted for tropical diseases at other hospitals.

The Clinical Research Unit (CRU) was established under the Clinical Infectious Disease Research Unit in 2005 for providing service training for doctors and nurses in the research methodology, conduction of vaccine or clinical trials and Good Clinical Practices (GCP).

CURRENT DEPARTMENTAL RESEARCH ACTIVITIES:

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 (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 ValN, 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. Effect of drug accumulation in the neurotoxicity of artemether, dosing regimens with variable drug-free intervals in a mouse model
7. Observational probe study of *in vitro* immune response parameters to candidate HIV-1 vaccine antigens among subjects from Thailand
8. Neuropathological toxicity of artemisinin derivatives in a mouse model
9. Development of field methods and investigations of the molecular basis of sulfonamide resistance in *Plasmodium vivax*
10. Novel point mutations in the dihydrofolate reductase gene of *Plasmodium vivax*: evidence for sequential selection by drug pressure
11. Asexual and sexual stage antimalarial activities of artesunate and primaquine in falciparum malaria
12. Research and development for Thai people living on the Thai-Myanmar border to free from tropical diseases
13. Research and development on drugs and diagnostic tools for diagnosis and treatment of tropical diseases in Thailand.
14. Liver megaproject Phase 1: from basic research to education science and applied technology in clinical study
15. A two-stage, phase II study to evaluate the safety and efficacy of CKBM-A01 in treating HIV patients in Thailand
16. Assessing the psychosocial burden in women with an abnormal pap results after screening interventions

INTERNATIONAL LINKAGES

- INTERNATIONAL COLLABORATION

1. Collaboration with GeoSentinel Network

Travel medicine research unit, on behalf of Faculty of Tropical Medicine has joined the GeoSentinel Surveillance Networks since 2006. It is the largest international network of travel/tropical medicine clinics. This network was initiated in 1995 by International Society of Travel Medicine (ISTM) and the Center of Diseases Control (CDC). Its main objective is to create and maintain international collaboration among travel clinics around the world in the surveillance and academic purpose.

2. Collaboration with International Society of Travel Medicine

Dr. Watcharapong, Head of Travel Medicine Research Unit, became the member of the International Society of Travel Medicine since 2006. It is the largest society of Travel Medicine field, with over 2,000 members in 65 countries. ISTM advocates and facilitates education, service and research activities in the field of travel medicine.

3. Visiting Professor

Professor David O. Freedman visited Travel Medicine Research Unit on November 2006. He is the Professor of Medicine in University of Alabama. He is the director of Gorgas course and also the Project Director of GeoSentinel Network. He has extensive experiences in the field of Travel Medicine. He has many researches and publications including the latest study of GeoSentinel Network published in NEJM in January 2006.

- WHO COLLABORATING CENTRE FOR CLINICAL MANAGEMENT OF MALARIA

United to be Center of Excellence in tropical Diseases
and International Health

LIST OF ABSTRACTS

LIST OF ABSTRACTS (Continued)

Department of

Helminthology

Office of the Department Telephone: 0 2354 9100 ext. 1820 1821
Fax: 0 2643 5600

Assoc. Prof. Wichit Rojekittikhun
B.Sc. (Med. Tech.), M.Sc. (Trop. Med.), D.A.P.& E., Ph.D. (Med. Sci.)
FIELD OF EXPERTISE: Med. helminthology (esp. Gnathostoma & immunodiagnosis)
E-MAIL: *tmwrj@mahidol.ac.th*
TELEPHONE: 1820, 1821
Head
(To 30 September 2006)

Assist. Prof. Chalit Komalamisra
B.Sc. (Biol.), M.Sc. (Trop. Med.), D.A.P.& E., Dr. Med. Sci.
FIELD OF EXPERTISE: Medical helminthology
E-MAIL: *tmckm@mahidol.ac.th*
TELEPHONE: 1822, 1820, 1821
Head
(From 1 October 2006)

Assist. Prof. Paron Dekumyoy
B.S. (Biol.), M.Sc. (Trop. Med.), Ph.D. (Trop. Med.)
FIELD OF EXPERTISE: Immunodiagnosis of helminthiases
E-MAIL: *tmpdk@mahidol.ac.th*
TELEPHONE: 1820, 1821

Assoc. Prof. Jitra Waikagul
B.Sc. (Biol.), M.Sc. (Trop. Med.), M.Sc. (Parasit.), Ph.D. (Med. Sci.)
FIELD OF EXPERTISE: Taxonomy/Biology of helminths
E-MAIL: *tmjwk@mahidol.ac.th*
TELEPHONE: 1820, 1821; 1332

Assoc. Prof. Malinee Thairungroj
D.V.M., D.A.P.& E., Ph.D. (Med. Sci.)
FIELD OF EXPERTISE: Medical helminthology/ Immunodiagnosis
E-MAIL: *tmmtr@mahidol.ac.th*
TELEPHONE: 1820, 1821

Assist. Prof. Panyawut Hiranyachattada
B.S. (Biol.), M.Sc. (Trop. Med.)
FIELD OF EXPERTISE: Medical helminthology
E-MAIL: *tmphr@mahidol.ac.th*
TELEPHONE: 1820, 1821

Dr. Dorn Watthanakulpanich
B.Sc. (Med. Tech.), M.Sc. (Trop. Med.), M.D.
FIELD OF EXPERTISE: Medical helminthology
E-MAIL: *tmdwl@mahidol.ac.th*
TELEPHONE: 1820, 1821
Lecturer

Dr. Teera Kusolsuk
M.D., D.A.P.& E., M.Sc. (Community Med.), D.T.M. & H.
FIELD OF EXPERTISE: Medical helminthology
E-MAIL: *tmtku@mahidol.ac.th*
TELEPHONE: 1820, 1821
Lecturer

Assoc. Prof. Wanna Maipanich
B.Sc. (Biol.), M.S.P.H. (Med. Parasit.), D.A.P.& E.
FIELD OF EXPERTISE: Medical helminthology
E-MAIL: *tmwmp @mahidol.ac.th*
TELEPHONE: 1820, 1821
Expert Scientist

Mr. Chatree Muennoo
B.Ed. (Gen. Sci.)
FIELD OF EXPERTISE: Soil-transmitted helminths
TELEPHONE: 1820, 1821
Expert Scientist

Mrs. Supaporn Nuamtanong
B.S. (Biol.), M.Sc. (Trop. Med.)
FIELD OF EXPERTISE: Medical helminthology
E-MAIL: *tmsnt@mahidol.ac.th*
TELEPHONE: 1820, 1821
Senior Scientist

Mr. Surapol Sa-nguankiat
B.Ed. (Gen. Sci.), D.A.P.& E.
FIELD OF EXPERTISE: Soil-transmitted helminths
TELEPHONE: 1820, 1821
Senior Scientist

Mrs. Tippayarat Yoonuan
B.S. (Microbiol.), B.B.A. (General Management)
FIELD OF EXPERTISE: Medical helminthology
E-MAIL: *teesuphanat@yahoo.com*
TELEPHONE: 1820, 1821
Scientist

Mr. Wallop Pakdee
B.Sc. (Biol)
FIELD OF EXPERTISE:
Immunodiagnosis of helminthiases
TELEPHONE: 1820, 1821
Scientist

Ms. Urusa Thaenkham
B.S. (Biol.), M.Sc. (Environ. Biol.)
FIELD OF EXPERTISE: Molecular parasitology
E-MAIL: *urusat@yahoo.com*
TELEPHONE: 1820, 1821
Scientist

Mrs. Somchit Pubampen
Cert. in Med. Tech., B.B.A. (Money & Banking)
FIELD OF EXPERTISE: Medical helminthology
E-MAIL: *tmspb@mahidol.ac.th*
TELEPHONE: 1820, 1821
Senior Medical Science Associate

Mr. Kasidis Visiadsuk
Cert. in Med. Tech.
FIELD OF EXPERTISE:
Laboratory study of trematodes
TELEPHONE: 1820, 1821
Medical Science Associate

Mrs. Supaporn Naowarat
B.A. (General Management)
E-MAIL: *tmsnw@mahidol.ac.th*
TEL: 1820, 1821
General Affairs Officer

CURRENT RESEARCH ACTIVITIES

ANGIOSTRONGYLIASIS

- Angiostrongyliasis: partially purified antigens of *Angiostrongylus cantonensis* adult worms for diagnosis using immunoblot
- Angiostrongyliasis: potential fractionated antigens of *Angiostrongylus cantonensis* adult worms for diagnosis using ELISA
- 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
- mtDNA sequences of *Taenia* spp

ECHINOCOCCOSIS

- Analysis of fluid antigens of *Echinococcus* cyst for diagnosis
- Mitochondrial DNA sequence of protoscoleces of *Echinococcus* cysts from four patients
- Serodiagnosis of suspected echino-coccosis 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

- Effect of ivermectin on *Gnathostoma spinigerum* morphology
- Immunoblot-diagnostic specificity for gnathostomiasis.
- Prevalence of *Gnathostoma spinigerum* in cats and dogs in Buddhist temples in Bangkok

OPISTHORCHIASIS

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

PARAGONIMIASIS

- 32-33 kDa-eluted *Paragonimus heterotremus* antigen for serodiagnosis
- Comparative studies on surface ultrastructure of adult worm of *Paragonimus* sp. in Thailand
- Chromosomes and occurrence of chromosome breakage of lung fluke, *Paragonimus heterotremus*
- Isozyme discrimination between *Paragonimus heterotremus* and *P. miyazakii*
- Molecular systematic of *Paragonimus* lung flukes and intestinal trematodes
- Studies on *Paragonimus* populations: morphology, enzymology, molecular biology and epidemiology

SOIL-TRANSMITTED HELMINTHIASES

- Effect of mebendazole on *Trichuris trichiura* morphology.
- Efficacy of high dose mebendazole against trichuriasis in adult patients
- Epidemiology and treatment of strongyloidiasis with ivermectin
- Herbal medicinal effects on soil-transmitted helminthiasis
- Impact of deworming on anemic status of children and adolescence girls
- Relationship between behavior and soil-transmitted helminthiasis in seaman
- Soil-transmitted helminthiases control through school-based intervention

TOXOCARIASIS

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

TRICHINELLOSIS

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

OTHER PARASITES

- Diagnosis of liver and intestinal flukes by PCR
- Differential serodiagnosis between liver and intestinal trematodes
- Fish-borne trematodes in Thailand
- Research and development of the intergrated project on chemotherapy on control of malaria and parasitic infections

LIST OF ABSTRACTS

Department of

Medical Entomology

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

Assoc. Prof. Chamnarn Apiwathnasorn
B.Sc., M.Sc. (Trop. Med.), M.T.H., Ph.D. (Trop. Med.), Ph.D. (Medical Entomology)
FIELD OF EXPERTISE: Medical entomology/Mosquito taxonomy/Ecology/Field study
E-MAIL: *tmcaw@mahidol.ac.th*
TELEPHONE: 1575
HEAD

Assoc. Prof. Narumon Komalamisra
B.Sc. (Biology), M.Sc. (Trop. Med.), Dr. Med. Sc.
FIELD OF EXPERTISE: Medical entomology/ Isoenzyme of vectors/Vector genetics/Molecular entomology/Vector control
E-MAIL: *tmnkm@mahidol.ac.th*
TELEPHONE: 1843
DEPUTY HEAD

Assoc. Prof. Supatra 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: *tmstr@mahidol.ac.th*
TELEPHONE: 1574

Assoc. Prof. Somjai Leemingsawat
B.Sc., M.Sc. (Trop. Med)., Dr. Med. Sc.
FIELD OF EXPERTISE: Medical entomology/Tick and mite-borne diseases/Filarial parasites and vectors
E-MAIL: *tmslm@mahidol.ac.th*
TELEPHONE: 1574

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*
TELEPHONE: 1530, 1578

Assist. Prof. Achara Asavanich
B.Sc., M.Sc. (Entomology), Ph.D.
FIELD OF EXPERTISE: Malaria vector/ Medical entomology
E-MAIL: *tmaas@mahidol.ac.th*
TELEPHONE: 1576

Ms. Peangpim Burivong
B.Sc. (Medical Technology), M.Sc. (Immunology)
FIELD OF EXPERTISE: Molecular Entomology/ Dengue virus
E-MAIL: *peangpim@hotmail.com*
TELEPHONE: 1577
LECTURER

Dr. Yuwadee Trongtokit
Ph.D. (Trop. Med.)
FIELD OF EXPERTISE: Medical Entomology, Vector control, Plant-based insecticides
E-MAIL: *ytrongtokit@yahoo.com*
TELEPHONE: 1577
LECTURER

Mr. Yudthana Samung
Cert. Medical Science Technology, B.Ed., M.Sc. (Infectious Disease)
FIELD OF EXPERTISE: Medical Entomology, Field study
E-MAIL: *tmysm@mahidol.ac.th*
TELEPHONE: 1578, 2109
RESEARCHER

Ms. Rutcharin Potiwat
B.Sc. (Biology), M.Sc. (Genetic Engineering)
FIELD OF EXPERTISE: Molecular Biology, Protein Purification, Isoenzyme of vector
E-MAIL: *Kae _ rutc@hotmail.com*
TELEPHONE: 1577
RESEARCHER

Mrs. Keawmala Palakul
B.Ed., D.A.P.&E., Traditional Pharmacy, Traditional Medicine
FIELD OF EXPERTISE: Vector control by using medicinal plants
TELEPHONE: 1578, 1844
SCIENTIST

Mrs. Raweewan Srisawat
B.Sc., M.Sc., D.A.P. & E.
FIELD OF EXPERTISE: Insecticide resistance
E-MAIL: *tmrsw@mahidol.ac.th*
TELEPHONE: 1844
SCIENTIST

Mr. Samrerng Prummongkol
Cert. Medical Science Technology, D.A.P. & E. B.Sc. (Health Education)
FIELD OF EXPERTISE: Medical Entomology, Parasitology, Field study
E-MAIL: *tmspl@mahidol.ac.th*
TELEPHONE: 1578, 2109, 2100
MEDICAL SCIENCE ASSOCIATE

Mr. Theerawit Phanphoowong
Cert. Medical Science Technology
E-MAIL: *tmtpp@mahidol.ac.th*
TELEPHONE: 1844
MEDICAL SCIENCE ASSOCIATE

Ms. Nuchthathip Rodphadung
B.A. (General Management)
TELEPHONE: 1573
GENERAL AFFAIRS OFFICER

HIGHLIGHT

Study of insecticidal activity 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*), have been formulated in the forms of cream or gel. The extract of "thong pun chang" (*Rhinacanthus nasutus*), which provided high larvicidal activity, has been prepared as tablet form. A mosquito repellent formulation of mixture volatile oil, *Artemisia annua*, is in the process of patent application.

CURRENT RESEARCH ACTIVITIES

Research conducted by the staff of the Department of Medical Entomology involves both basic and applied knowledge for controlling insect and arthropod vectors of tropical diseases, with an emphasis on mosquito-borne diseases. Biology of vectors and their relationships with pathogens at molecular level are of research interest. Studies of the population dynamics and vector competence of dengue vectors in urban and suburban areas are ongoing, as well as the population genetics of vectors of malaria, dengue fever, and lymphatic filariasis, such as the *Anopheles barbirostris* group, *An. sundaicus*, *Aedes niveus* subgroup, and *Ae. albopictus*.

Another important goal is to resolve entomological problems through research and to make research results available to other scientists, educators and the general public. In the light of a previous study on the tsunami's impact on the occurrence of mosquito vectors in Phang Nga Province, where small-scale control of mosquito larvae inhabiting swamps and ponds contaminated by sea water was successfully achieved using *Bacillus thuringiensis israelensis* (VectoBac® WDG), the application has been extended to cover a larger scale in the most affected area, Ban Nam Khem village. The Department, with the Department of Disease Control, Ministry of Public Health, are conducting a project in collaboration with the European Research Community entitled "Toward successful dengue prevention and control" to determine the field efficacy of commercial impregnated long lasting curtains and IGR in control dengue vector populations in Laem Chabang Commune municipal area, Chon Buri Province.

Furthermore, mosquito repellents extracted from various medicinal plants are being screened and determined for efficacy to develop commercial formulations for public use. Recently, we were granted a petty patent for a natural mosquito repellent cream formula, with more than 3 hours protection against major mosquito vectors.

Our Department also works with local public health officials to help investigate emerging and re-emerging diseases, e.g. investigations of autochthonous leishmaniasis cases in Nan and Phang Nga Province, mite infestations of the external ear canals of shallot farmers in Si Saket Province, outbreaks of contact dermatitis due to infestation of rove beetles around apartments in Phra Nakhon Si Ayutthaya Province, and identification of medically important insects, such as maggots causing myiasis, ticks and mites, for general hospitals.

Laboratory colonies of different strains of mosquito vector species - *Anopheles*, *Aedes*, *Culex*, and *Mansonia* - are 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 establishment of the Mosquito Museum Annex. Academic consultation, especially on mosquito-borne diseases and their control measures, and also services on detection of filarial parasites, identification of mosquitoes and other medically important insects and arthropods, are provided regularly.



LIST OF ABSTRACTS

Department of

Microbiology and Immunology

Office of the Department, Telephone: 0 2354 9100 ext. 1591-7
Fax: 0 2643 5583

Assoc. Prof. Manas Chongsa-nguan

B.Sc., M.P.H., Ph.D.
FIELD OF EXPERTISE: Immunodiagnosis of tropical infections
E-MAIL: tmmcs@mahidol.ac.th
TELEPHONE: 1593
HEAD

Prof. Srisin Khusmith

B.Sc., M.Sc., Doctorat D'Etat es Sciences
FIELD OF EXPERTISE: Immunology/molecular biology/malaria
E-MAIL: *tmskm@mahidol.ac.th*
TELEPHONE: 1594
VICE PRESIDENT FOR RESEARCH

Assoc. Prof. Wipawee Jampangern

B.Sc., M.Sc., Dr. Med. Sc.
FIELD OF EXPERTISE: Immunology and molecular biology of Dengue viruses/Bird Flu
E-MAIL: *tmwus@mahidol.ac.th*
TELEPHONE: 1595, 2098

Assist. Prof. Usanee Suthisarnsuntorn

M.D., Dip. American Board of Paediatrics, D.T.M. & H.
FIELD OF EXPERTISE: Clinical microbiology/bacteriology/ paediatric infectious diseases
E-MAIL: *tmuss@mahidol.ac.th*
TELEPHONE: 1592

Asst. Prof. Yuvadee Mahakunkijcharoen

B.Sc., M.Sc., Ph.D.
FIELD OF EXPERTISE: Immunology / Aeromonas
E-MAIL: *tmymh@mahidol.ac.th*
TELEPHONE: 1596, 2094

Assoc. Prof. Varee Wongchotigul

B.Sc., Ph.D.
FIELD OF EXPERTISE: Immunology, rickettsiology (scrub typhus)
E-MAIL: *tmvwc@mahidol.ac.th*
TELEPHONE: 1595, 2097

Asst. Prof. Thareerat Kalambaheti

B.Sc., M.Sc., Ph.D.
FIELD OF EXPERTISE: Molecular biology/microbiology/ immunology
E-MAIL: *tmtkl@mahidol.ac.th; kalambah@lycas.com.*
TELEPHONE: 1592, 1673

Dr. Jintana Patarapotikul

B.Sc., M.Sc., Ph.D.
FIELD OF EXPERTISE: Immunology/molecular biology of malaria/human genetics
E-MAIL: *tmjpt@mahidol.ac.th*
TELEPHONE: 1666, 1668
LECTURER

Dr. Pornsawan Leaungwutiwong

B.Sc., M.Sc., Ph.D.
FIELD OF EXPERTISE: Medical Virology
E-MAIL: *tmpam@mahidol.ac.th*
TELEPHONE: 1597, 1591
LECTURER

Dr. Nitaya Indrawattana

B.Sc., M.Sc., Ph.D.
FIELD OF EXPERTISE: Regenerative medicine/Biosensor/ Molecular microbiology
E-MAIL: *tmniw@mahidol.ac.th*
TELEPHONE: 1592, 2092
LECTURER

Miss Akanitt Jittmittraphap

B.Sc., M.Sc.
FIELD OF EXPERTISE: Immunology / Molecular biology of dengue viruses
E-MAIL: *tmajm@mahidol.ac.th*
TELEPHONE: 1597
LECTURER

Mrs. Phanita Chanket
B.Sc., M.Sc., D.M.M.
FIELD OF EXPERTISE: Bacteriology, molecular biology
E-MAIL: *tmtck@mahidol.ac.th*
TELEPHONE: 1673, 1671
SCIENTIST

Mrs. Jarinee Tongshoob
B.Sc., M.Sc.
FIELD OF EXPERTISE: Immunology/Malaria
E-MAIL: *tmjpc@mahidol.ac.th*
TELEPHONE: 2096, 1592
RESEARCHER

Mr. Witawat Tunyong
B.Sc., D.M.M.
FIELD OF EXPERTISE: Bacterial identification
E-MAIL: *tmwty@mahidol.ac.th*
TELEPHONE: 1671, 1673
MEDICAL TECHNOLOGIST

Miss Siriporn Chattanadee
Cert. Medical Science Technology
FIELD OF EXPERTISE: Bacterial identification/Leptospira diagnosis (M.A.T.)
E-MAIL: *tmscn@mahidol.ac.th*
TELEPHONE: 1671, 1673
MED. TECH. ASST.

Miss. Natnaree Saiprom
B.Sc.
FIELD OF EXPERTISE:
Flow cytometry/Rickettsiology (cscrub typhus)
E-MAIL: *natnareesatprom@hotmail.com*
TELEPHONE: 2097
SCIENTIST

Miss Siranun Setasubun
B.Sc.
FIELD OF EXPERTISE: Enzyme immunoassay/Biology
E-MAIL: *fonfufufu@hotmail.com*
TELEPHONE: 2094
SCIENTIST

Mrs. Saijai Sawanng-arom
Dip. Business Admin.
E-MAIL: *saijai_2005@hotmail.com*
TELEPHONE: 1591
BUSINESS ASSISTANT

Mrs. Sukanya Buaphun
B.Ed.
E-MAIL: *sukanyabua@hotmail.com*
TELEPHONE: 1591
BUSINESS ASSISTANT

HIGHLIGHT

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

CURRENT RESEARCH ACTIVITIES

1. Studies of cytokine and gene polymorphism related to severity of malaria
2. Natural immunity in vivax malaria individuals
3. Immune regulation of malaria
4. Immunological parameters involved in severity of malaria
5. Immunology and biotechnology for diagnosis of malaria
6. Molecular study of malaria
7. Study of gene and genetic susceptibility to severe or cerebral malaria
8. Clinical and immunological study on difficulty in the treatment of TB
9. Immunodiagnosis of dengue virus infection
10. Dengue virus infection in mosquitoes
11. Biochemical study and epitope mapping of receptor molecules for dengue virus
12. Studies of the molecular biology of dengue virus in Thailand

13. Production of recombinant dengue viral protein for serodiagnosis
14. Study of the molecular mechanisms in the transmission of bird flu virus
15. Determination of the receptor molecules of the H5N1 viruses isolated from Thailand
16. Regulatory T cells in an autoimmune mouse model
17. Studies of *S. typhi* infection in Vietnam
18. Identification of *Legionella* spp. isolated in Thailand
19. Serodiagnosis of scrub typhus
20. Detection of virulence factor from *Aeromonas* spp. in relation to diarrhea
21. Identification of specific antigens of *Aeromonas* spp. by mouse polyclonal antibodies
22. Development of a monoclonal antibody for identification of pathogenic *Aeromonas* spp.
23. Molecular characterization of Leptospira isolates in Thailand
24. Serovar identification of *Leptospira* spp. based on specific gene sequences
25. Production of recombinant leptospiral protein antigen for serodiagnosis
26. Production of monoclonal antibody to tetanus by using phage display technique
27. Development of school-based approach to emerging infectious disease control
28. Proteomics of *Trichinella spiralis*
29. Recombinant tropomyosin of American cockroach
30. Preparation of human monoclonal antibody that neutralizes tetanus toxin using phage display technology

LIST OF ABSTRACTS

Department of

Protozoology

Office of the Department, Telephone: 0 2354 9100 ext. 1833, 1830-32, 1834-5
Fax: 0 2643 5601

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: *Toxoplasma gondii* / Oto-Rhino-Laryngology
E-MAIL: *tmymv@mahidol.ac.th*
TELEPHONE: 02-3549100 ext. 1833
HEAD

Assoc. Prof. Porntip Petmitr
B.Sc. (Med. Tech.), M.Sc. (Trop.Med.), Ph.D. (Biochemistry)
FIELD OF EXPERTISE: Biochemistry of malaria parasites/ Cultivation of *P. falciparum* gametocytes and *T. vaginalis*
E-MAIL: *tmppm@mahidol.ac.th*
TELEPHONE: 02-3549100 ext. 1835

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*
TELEPHONE: 02-3549100 ext. 1834

Ms. Rachatawan Chiabchalard
B.Sc. (Physical Therapy), M.Sc. (Biology)
FIELD OF EXPERTISE: Cultivation of intestinal protozoa
E-MAIL : *tmrcc@mahidol.ac.th*
TELEPHONE: 02-3549100 ext. 1832
LECTURER

Mr. Amorn Lekkla
B.Sc. (Health Education), M.Sc. (Public Health)
E-MAIL: *tmalk@mahidol.ac.th*
TELEPHONE: 02-3549100 ext. 1831
RESEARCHER

Miss Chantira Suthikornchai
B.Sc. (Biology), M.Sc. (Trop. Med.)
E-MAIL: *momotaro162@yahoo.com*
TELEPHONE: 02-3549100 ext. 1831
RESEARCHER

Miss Ruenruetai Udonsom
B.Sc., D.A.P. & E.
E-MAIL: *udonsom@hotmail.com*
TELEPHONE: 02-3549100 ext. 1831
SCIENTIST

Ms. Somsri Kajorndechakiat
Cert. Medical Science Technology
TELEPHONE: 02-3549100 ext. 1831
MEDICAL SCIENCE TECHNICIAN

Ms. Kanthinich Thima
Cert. Medical Science Technology, B.P.H. (Public Health)
E-MAIL: *tmktm@mahidol.ac.th*
TELEPHONE: 02-3549100 ext. 1831
MEDICAL SCIENCE TECHNICIAN

Mr. Nuttpong Getmarchom
Cert. Medical Science Technology
TELEPHONE: 02-3549100 ext. 1832
MEDICAL SCIENCE ASSOCIATE

Mrs. Nontiya Sensiriwattana
M.B.A.
E-MAIL: *tmnsr@mahidol.ac.th*
TELEPHONE: 02-3549100 ext. 1830
GENERAL AFFAIRS OFFICER

HIGHLIGHT

To respond to the Faculty's Mission to be "Asia's Leader in Tropical Medicine", the Department of Protozoology is responsible for the Research-based Diagnostic Unit". We, therefore, provide diagnostic techniques based on up-to-date research from enzyme to community level.

CURRENT RESEARCH ACTIVITIES

1. Ultrastructure of acute and chronic toxoplasmosis after pyrimethamine and artesunate administration *in vivo* study.
2. Viability of *Giardia* in water.
3. Effect of ultraviolet irradiation on the viability of *Cryptosporidium*.
4. Biological contamination-free Thai frozen food.
5. Molecular technique for diagnosis of toxoplasmosis and neosporosis in Thai dairy cows.
6. Molecular and immunohistochemistry studies on stage interconversion of toxoplasmosis in immunocompromised hosts.
7. Protozoa contamination on Thai vegetables.
8. Studies on DNA replication and DNA repair in *Plasmodium falciparum*.
9. Differential diagnosis of *Entamoeba* spp. found in humans by molecular biological method.
10. Development of molecular methods for drug resistance markers in *Plasmodium falciparum*.

LIST OF ABSTRACTS

Department of

Social and Environmental Medicine

Office of the Department, Telephone: 0 2354 9100-19 ext. 1562-4
Fax: 0-2354-9166-7

Assoc. Prof. Wijitr Fungladda
B.Sc. (Med. Sc.), M.D., D.T.M. & H., Dr.P.H.
FIELD OF EXPERTISE: Social epidemiology of tropical diseases (malaria, opisthorchiasis, leptospirosis)
E-MAIL: *tmvfd@mahidol.ac.th*
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*
DEPUTY HEAD

Assoc. Prof. Piyarat Butraporn
D.V.M., M.P.H., D.A.P. & E, Dr.P.H. (Social Epidemiology)
FIELD OF EXPERTISE: Social epidemiology in tropical diseases (malaria, DHF) and health impact assessment of water resource development
E-MAIL: *tmpbt@mahidol.ac.th*

Assoc. Prof. Kamolnetr Okanurak
B.Sc. (Pub. Hlth.), M.A. (Med. Soc. Sci.), Ph.D. (Medical Anthropology)
FIELD OF EXPERTISE: Community participation in disease control/ Treatment-seeking behavior
E-MAIL: *tmkok@mahidol.ac.th*

Assist. Prof. Wanchai Phatihatakorn
D.V.M., M.P.H.
FIELD OF EXPERTISE: Environmental health impact assessment/ GRD monitoring, evaluation and surveillance of parasitic diseases
E-MAIL: *tmwpk@mahidol.ac.th*

Assist. Prof. Voranuch Wangsuphachart
B.Sc., M.Sc. (Trop Med.), M.S. (Med. Epidemiology), Ph.D. (Med. Epidemiology)
FIELD OF EXPERTISE: Environmental epidemiology/ Comparative risk assessment/ Epidemiology and internet/ Health Impact Assessment (HIA)
E-MAIL: *tmvws@mahidol.ac.th*

Assist. Prof. Pongrama Ramasoota
D.V.M., M.P.H., M.Sc. (Microbiology), Ph.D. (Microbiology)
FIELD OF EXPERTISE: Molecular biology/ Phage display technology/ Environmental microbiology
E-MAIL: *tmprt@mahidol.ac.th, pongrama@yahoo.com*

Dr. Prapin Tharnpoophasiam
B.Sc. (Med. Tech), M.Sc. (Toxicology), Ph.D. (Trop Med)
FIELD OF EXPERTISE: Environmental toxicology
E-MAIL: *tmpbw@mahidol.ac.th, tprapin@hotmail.com*
LECTURER

Dr. Suwalee Worakhunpiset
B.N.S., M.Sc. (Technology of Environmental Management), Ph.D. (Trop. Med.)
FIELD OF EXPERTISE: Environmental toxicology
E-MAIL: *tmstw@mahidol.ac.th, minehoney@yahoo.com*
LECTURER

Mr. Rungwit Mas-ngammueng
B.A. (Pol. Sci.), B.A. (Thai Studies) (Hon.), M.A. (Med. & Hlth. Soc. Sci.), Cert. Technician, Cert. Social Sciences Research
FIELD OF EXPERTISE: Eating & drinking behavior, Community participation in health development
E-MAIL: *tmrmn@mahidol.ac.th*
EXPERT RESEARCHER

Mr. Wiwat Wanarangsikul
B.P.H. (Pub. Hlth. Admin.), M.A. (Med. & Hlth. Soc. Sci.), Cert. Junior Health Worker
FIELD OF EXPERTISE: Health social science
E-MAIL: *tmwsl@mahidol.ac.th*
RESEARCHER

Mrs. Pusadee Sri-aroon
B.Sc. (Biology), M.A. (Med. & Hlth. Soc. Sci.), Cert. Special Malacological Subjects and Techniques
FIELD OF EXPERTISE: Brackish and freshwater malacology/ Medical malacology/ Health social science/ Health impact assessment of water resource development
E-MAIL: *tmpsa@mahidol.ac.th*
Senior Scientist

Mrs. Phuntira Pongsaskulchoti
B.Ed. (Biology)
FIELD OF EXPERTISE:
Biology of blood fluke schistosome
Senior Scientist

Mr. Jaremate Limsomboon
Cert. Medical Science Technology, Senior Medical
Science Associate

Mr. Prasasana Charoenjai
Cert. Med. Tech., B.A. (Pol. Sc.)
Medical Science Associate

Mrs. Yupa Chusongsang
Cert. Med. Tech., B.Ed. (Science-Biology), M.Sc. (Public Health)
E-MAIL: *tmycs@mahidol.ac.th*
Medical Science Associate

Mr. Phiraphon Chusongsang
Cert. Med., B.Sc. (Health Education), M.Sc. (Public Health)
E-MAIL: *tmpcs@mahidol.ac.th*
Scientist

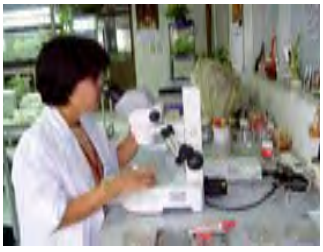
Mrs. Chonlawan Koolapunt
B.Ed. (Library Science)
E-MAIL: *tmckl@mahidol.ac.th*
General Affairs Officer

HIGHLIGHT

In regard to teaching, the Department offers various postgraduate courses leading to the M.Sc. and Ph.D. in Tropical Medicine. With its focus on social medicine, environmental health and environmental toxicology, the Department integrated the concepts of health promotion and disaster management in some of the course syllabi for the first time, in 2006.

The research activities of the Department have expanded to cover both laboratory and field investigations, which have attracted funding, i.e., government budget and research funds from various organizations such as World Health Organization (WHO), Thailand Research Fund (TRF), Universita Degli Studi Di Brescia, etc.

In addition to various laboratory investigations and other academic services, the Department, during the year 2006, offered technical services to the SEAMEO TROPMED Network by taking part in conducting external evaluations of the Mekong Basin Disease Surveillance (MBDS) Project (under the support of the Rockefeller Foundation) and the National Malaria Control Programme of Lao PDR (under the Global Fund to Fight against AIDS, Tuberculosis and Malaria-GFATM). Advice was also given to the Mekong River Commission Secretariat in conducting a transboundary risk assessment along the borders of Thai-Lao PDR and Vietnam-Cambodia. In addition, the Department offered a 3-week training course in "Global Infectious Diseases" to a group of Japanese medical/health personnel.

CURRENT RESEARCH ACTIVITIES

1. Integrated studies of human and animal leptospirosis in endemic areas of Nakhon Ratchasima, Thailand : Disease mapping aspect
2. Collaborative study to evaluate operational programme of insecticide treated bednets for malaria control in Thailand
3. Factors associated with completion and default among DOTS and self-administered therapy (SAT) for treatment of TB
4. Rapid detection of rifampicin-resistant *M. tuberculosis* from indoor air
5. Development of leptospiral serovar specific diagnostic test using phage display technique
6. Early detection of quinolone-resistant *M. tuberculosis* from Thailand
7. Epitope mapping of monoclonal antibody specific to *Burkholderia pseudomallei* using phage technique
8. Determination of surface- and drinking-water quality in a Tsunami-affected area of Phang-nga Province, Thailand
9. Health watch on emerging fresh- and brackish-water snails that transmit human parasitic diseases, after the tsunami in Phang-nga Province, southern Thailand
10. Transboundary risk assessment (human health risk, ecological and environmental risk of the Mekong River – surface water)
11. Avian flu prevention behaviors of poultry farmers in selected areas of Kanchanaburi Province
12. Modifying mosquito age structure to eliminate dengue haemorrhagic fever: community participation in dengue haemorrhagic fever prevention and control
13. Development of a surveillance system for obesity among school children of high risk groups
14. Development of Avian influenza diagnostic test using phage display technique

INTERNATIONAL LINKAGES

The Department of Social and Environmental Medicine plays a major role in WHO Collaborating Center for Environmental for Disease Vector Control in Sustainable Development (WHO CC No. 115). Its terms of reference include technical collaboration covering the entire area of environmental management, information exchange, conference/ training, and research.




LIST OF ABSTRACTS

Department of

Tropical Hygiene

Office of the Department, Telephone: 0 2354 9100-19 ext. 1682-4, 1694-5
Fax: 0 2644 4436

Assist. Prof. Jaranit Kaewkungwal
B.Sc., M.Ed., M.A., Ph.D. (Applied Statistics and Program Evaluation)
FIELD OF EXPERTISE:
Research Methodology/ Data Management/ Statistical Modeling
E-MAIL: *tmjkk@mahidol.ac.th*
TELEPHONE: ext.1682-4
Head

Mr. Pitak Wuthisen
B.Sc. (Biology), M.Sc. (Trop.Med.)
FIELD OF EXPERTISE: Tropical disease field work & Diagnostic parasitology
E-MAIL: *tmpwt@mahidol.ac.th*
TELEPHONE: ext.1682-3
Deputy Head

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: *tmpsh@mahidol.ac.th*
TELEPHONE: ext.1680, 1682-3
Dean

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*
TELEPHONE: ext.1682-4
Deputy Dean for Administration and Finance

Assoc. Prof. Srivicha Krudsood
B.Sc. (Biology), M.D., D.T.M. & H., M.Sc. (C.T.M.), Diplomate, Thai Board of Internal Medicine
FIELD OF EXPERTISE: Clinical Management of Malaria
E-MAIL: *tmsks@mahidol.ac.th*
TELEPHONE: ext. 1682-4
Lecturer

Dr. Natthanej Luplerdlop
M.D., Ph.D. (Anatomy/ Molecular Immunovirology),
FIELD OF EXPERTISE: Molecular immunovirology (Dengue)/Molecular Immunopathophysiology in Malaria
E-MAIL: *tmnll@mahidol.ac.th*
TELEPHONE:. ext.1682-3
Lecturer

Dr. Saranath Lawpoolsri
M.D., D.T.M. & H.
FIELD OF EXPERTISE: General Practitioner
E-MAIL: *tmslw@mahidol.ac.th*
TELEPHONE: ext.1682-3
Lecturer

Ms. Pannamas Maneekan
B.Sc. (Nursing), M.Sc. (Community medicine)
FIELD OF EXPERTISE: Communities study
E-MAIL: *tmpmk@mahidol.ac.th*
TELEPHONE: ext.1682-3
Lecturer

Mr. Irwin F. Chavez
B.Sc. (Public Health), M.Sc. (Epidemiology)
FIELD OF EXPERTISE: Epidemiology/Data analysis
E-MAIL: *fricv@mahidol.ac.th*
TELEPHONE: ext.1695
Lecturer

Mr. Supalarp Puangsa-art
B.Sc. (Agriculture), B.A. (Political Science), M.Sc. (Trop. Med), M.Sc. (Biostatistics)
FIELD OF EXPERTISE: Biostatistics/Data analysis/Field research
E-MAIL: *tmspa@mahidol.ac.th*
TELEPHONE: ext.1694
Scientist

Mr. Surapon Yimsamran
Cert. Medical Science Technology, B.Ed. (Biology), M.Sc. (Epidemiology)
FIELD OF EXPERTISE: Epidemiology, Research methodology, Data management and analysis
E-MAIL: *tmsys@mahidol.ac.th*
TELEPHONE: ext.1695
Researcher

Mr. Nipon Thanyavanich

Cert Medical Science Technology, B.A. (Political Science), B.Sc. (Health Education), M.Sc. (Infectious Disease)
FIELD OF EXPERTISE: Diagnostic parasitology/Field research
E-MAIL: *tmnty@mahidol.ac.th*
TELEPHONE: ext.1682-3
RESEARCHER

Mr. Thanapat Chupraphawan

B.Sc. (Agriculture), M.Sc. (Agriculture System)
FIELD OF EXPERTISE: Geographic information system/ Remote sensing
E-MAIL: *tmscp@mahidol.ac.th*
TELEPHONE: ext.1695
RESEARCHER

Mr. Wanchai Maneeboonyang

Cert. Medical Science Technology, B.Sc. (Education), M.Sc. (Infectious Disease)
FIELD OF EXPERTISE: Diagnostic parasitology/Field research
E-MAIL: *tmwmn@mahidol.ac.th*
TELEPHONE: ext.1694
RESEARCHER

Mr. Prasert Rukmanee

Cert. Medical Science Technology, B.Sc. (Environmental Science), M.Sc. (Trop. Med.)
FIELD OF EXPERTISE: Diagnostic parasitology, General laboratory
E-MAIL: *tmprn@mahidol.ac.th*
TELEPHONE: ext. 1694
MEDICAL SCIENCE ASSOCIATE

Ms. Natefa Rukmanee

Cert. Medical Science Technology, B.Sc. (Health Education), M.Sc. (Trop Med.)
FIELD OF EXPERTISE: General laboratory, Computer data entry
E-MAIL: *tmnut@mahidol.ac.th*
TELEPHONE: 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 systems
E-MAIL: *teswd@mahidol.ac.th*
TELEPHONE: ext.1694
COMPUTER SYSTEM OFFICER

Mr. Sutthiporn Prommongkol

Cert. Medical Science Technology
FIELD OF EXPERTISE: Diagnostic parasitology/Field research
TELEPHONE: ext.1694
MEDICAL SCIENCE ASSOCIATE

Ms. Muntana Nakmuan

FIELD OF EXPERTISE: Computer data entry
TELEPHONE: ext.1682-3
MEDICAL SCIENCE ASSOCIATE

Ms. Chotima Charusabha

B.Sc. (Computer)
FIELD OF EXPERTISE: Data management and analysis
E-MAIL: *tmccs@mahidol.ac.th*
TELEPHONE: ext.1682-3
RESEARCH OFFICER

Mr. Wutthichai Chaimoongkun

B.A. (Business Administration)
FIELD OF EXPERTISE: Malaria laboratory, Computer data entry/Field research
E-MAIL: *tmwcm@mahidol.ac.th*
TELEPHONE: ext.1694
RESEARCH OFFICER

Mr. Samarn Sonklom

FIELD OF EXPERTISE: Malaria laboratory/Field research
TELEPHONE: ext.1694

Ms. Kamornwan Chaipakdee

B.Ed. (Social Study)
FIELD OF EXPERTISE: General administration
E-MAIL: *tmkcp@mahidol.ac.th*
TELEPHONE: ext.1682-3
GENERAL AFFAIRS OFFICER

Ms. Ketsaraporn Thongpakdee

B.A. (Communication)
FIELD OF EXPERTISE: General administration, Educational media
E-MAIL: *ractd@mahidol.ac.th*
TELEPHONE: ext.1682-3
GENERAL AFFAIRS OFFICER

HIGHLIGHT

The Tropical Hygiene Section was formed as one of the original units of the Faculty of Tropical Medicine which was established in 1960. Since then, the section has been responsible for providing lectures and field training as part of the Diploma in Tropical Medicine and Hygiene (D.T.M. & H.) curriculum. Research activities of the section were comprised mainly of epidemiological research related to public health problems among rural populations in Thailand. In 1974 along with the rapid growth of the faculty, the Tropical Hygiene Section was upgraded into the Department of Tropical Hygiene. At present, the department is responsible for providing instruction and training to the masteral and doctoral degree programs in Tropical Medicine in addition to the existing D.T.M. & H. course. And continuing its research tradition, activities being carried out at the moment are mainly in the field of epidemiology with the application of Geographical Information System (GIS) on various tropical diseases. The department is also involved in providing specialized short training courses on epidemiology, data analysis, and GIS. Furthermore, the department has direct responsibility in managing the Rajanagarindra Tropical Disease International Centre (RTIC) located in a malaria-endemic rural community near the Thai-Myanmar border in Suan Phung District, Ratchaburi Province. For many years now the RTIC, through its malaria clinic, takes pride in its continuous delivery of free and quality health services to local residents.

CURRENT RESEARCH 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
2. Application of GIS in monitoring multi-drug resistant malaria in the Greater Mekong Sub-Region of Southeast Asia III
3. Assessment of disability and quality of life in the Tsunami-affected provinces in Thailand
4. Comparative study of dihydroartemisin (DHA) and artesunate safety in healthy volunteers (Phase 1B)
5. Epidemiological study of *Enterobius vermicularis* in preschool children in Tanowsri Subdistrict, Suan Phung, Ratchaburi Province
6. Epidemiological study of asymptomatic malaria parasitemia in endemic area
7. Epidemiology and control of malaria in Ratchaburi Province, Thailand
8. Epidemiology and health education program and treatment evaluation of *Pediculosis capitis* with Leech Lime cream in schoolchildren, Suan Phung District, Ratchaburi Province
9. 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
10. Field-based study of reappearance *Plasmodium vivax* malaria cases in the area near the Thai-Myanmar border, Suanphung, Ratchaburi Province
11. Health behavior and risk factor of soil transmitted helminth and malaria infection in primary school children in Saiyok district, Kanchanaburi Province
12. Integrated studies of human and animal leptospirosis in endemic areas of Nakorn Rajasima, Thailand
13. Monitoring of key health indicators (TRIAMS) at sub-district health facilities level in Tsunami-affected provinces in Thailand
14. Occurrence of heterophyid metacercariae *Haplorchis* in cyprinoid fish of 2 reserviors in Tanowsri subdistrict, Suan Phung, Ratchaburi Province
15. Relationship of intestinal parasitic infections to malnutrition
16. Search for genes susceptible to clinical malaria
17. Seroprevalence of rickettsia infections among Thai troops working along the Thai-Myanmar border, Suan Phung, Ratchaburi Province
18. Serotypic assay of dengue viral infection by real-time PCR
19. Spatio-temporal pattern of human and animal leptospirosis in endemic areas of Nakhon Ratchasima, Thailand

20. Study of health behaviors and factors associated with intestinal parasitc infections in the community and air-force unit in Ubolratchatani Province
21. Study of the ecology of anopheline larvae in malaria endemic area of 7 hamlets in Tanowsri Subdistrict, Suan Phung, Ratchaburi Province
22. The effectiveness of rehabilitation program for sub-acute stroke patients
23. Study of hepatitis B among health care workers at Prasat Neurological Institute
24. Study of tuberculosis and other occupationally acquired infections in health care workers at Prasat Neurological Institute

INTERNATIONAL LINKAGES

1. Dorothée MISSE IRD/CNRS, 911, avenue d Agropolis - BP 64501 - 34394 Montpellier Cedex5
2. Erik (Rik) Thompson, PhD Head, VBCRC Invasion and Metastasis Unit, University of Melbourne Department of Surgery and St. Vincent's Institute of Medical Research Director of Research, Bernard O'Brien Institute for Microsurgery Australia
3. Francisco Veas, Ph.D., Director Viral and Molecular Immunology Lab, France
4. The Rockefeller Foundation



LIST OF ABSTRACTS



LIST OF ABSTRACTS

Department of

Tropical Nutrition & Food Science

Office of the Department, Telephone: 0 2354 9100 ext. 2080-88
Fax: 0 2644 7934

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*
TELEPHONE: ext 2083
HEAD

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*
TELEPHONE: ext. 2082
DEPUTY 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: *tmrtg@mahidol.ac.th*
TELEPHONE: ext. 2081

Assist. Prof. Talabporn Harnroongroj
B.Sc. (Medical Technology), M.Sc. (Tropical Medicine), Dr. oec. troph. (Nutrition and Food Sciences)
FIELD OF EXPERTISE: Community nutrition/Biochemical nutrition
E-MAIL: *tmtbr@mahidol.ac.th*
TELEPHONE: ext. 2088

Dr. Sarunya Kaewprasert
B.Sc. (Biotechnology), M. Agr. (Nutritional Biochetristry), Ph.D. (Nutritional Biochemistry)
E-MAIL: *tmskp@mahidol.ac.th*
TELEPHONE: ext. 2088
LECTURER

Dr. Dumrongkiet Arthan
B.Sc. (Biochemistry), M.Sc. (Biochemistry) Ph.D. (Biochemistry)
E-MAIL: *tedat@mahidol.ac.th*
TELEPHONE: ext. 2086
LECTURER

Dr. Pornrutsami Jintaridhi
B.Sc. (Nursing), M.Sc. (Nutrition), Ph.D. (Biochemistry)
E-MAIL: *tmpjt@mahidol.ac.th*
TELEPHONE: ext. 2082
SCIENTIST

Dr. Anong Kitjaroentham
B.Sc. (Medical Technology), M.Sc. (Tropical Medicine), Ph.D. (Biochemistry)
E-MAIL: *tmakj@mahidol.ac.th*
TELEPHONE: ext. 2088
RESEARCHER

Ms. Apanchanid Thepouyporn
B.Sc. (Agriculture), M.Sc. (Biopharmaceutical Sciences)
E-MAIL: *tmato@mahidol.ac.th*
TELEPHONE: ext. 2082
RESEARCHER

Mrs. Yaovamarn Chantaranipapong
Cert.(Medical Science Laboratory Assistant)
TELEPHONE: ext. 2086
MEDICAL SCIENCE ASSOCIATE

Mr. Somchai Puduang
(Cert. Med. Sc. Tech.)
TELEPHONE: ext. 2085
MEDICAL SCIENCE ASSOCIATE

Ms. Saijai Paisiri
B.A. (General Management)
E-MAIL: *tmspr@mahidol.ac.th*
TELEPHONE: ext. 2088
General Affairs Officer

HIGHLIGHT

The four-day-workshop on "Methods in nutritional assessment and research Department instructor" was organized by all staff of the Department of Tropical Nutrition and Food Science on 25-28 April and 1-4 May 2006, respectively Faculty of Tropical Medicine, Mahidol University. The objective was to provide knowledge on methodologies in nutritional research, such as anthropomettic and biochemical assessment, including a computer program for dietary assessment, to lecturers, researchers and nutritionists.

CURRENT RESEARCH ACTIVITIES

Research activities of the Department of Tropical Nutrition and Food Science are concerned with nutritional problems in Thailand, such as micronutrient deficiencies, lifestyles and dietary patterns of different age groups, the impact of overnutrition, oxidative stress and antioxidants in relation to health, especially dislipidemia, coronary heart disease, cancer, the effect of smoking on work performance in relation to homocysteine concentration, and the molecular biology of obesity. Health and nutritional surveys of Tsunami victims in Southern Thailand have been conducted. Likewise, molecular carcinogenesis of several human cancers, such as breast cancer, cholangiocarcinoma, colorectal cancer, head and neck cancer, and hepatocellular carcinoma, were also investigated.

CURRENT RESEARCH PROJECTS

1. Vitamin B12 status of Thai women with neoplasia of the cervix uteri.
2. Health and nutrition survey of Tsunami victims in Phang-Nga Province, Thailand.
3. Plasma resistin, insulin concentration in non-diabetic and diabetic overweight/obese Thai.
4. Mutagenicity study of weeds and common plants used in traditional medicine and for animal feed.
5. The genetic association between alpha-2-macroglobulin (A2M) gene deletion polymorphism and low serum A2M concentration in overweight/obese Thais.
6. hMSH2 gene alterations associated with recurrence of oral squamous cell carcinoma.
7. Genetic alterations in chromosome 10q24.3 and glutathione S-transferase omega 2 gene polymorphism in ovarian cancer.
8. Polymorphism of glutathione S-transferase omega gene and risk of cancer.
9. HLa-class II (DRB & DQB1) in Thai sudden unexplained death syndrome (Thai SUDS) families (Lai-Tai families).
10. β-glucosidase catalyzing specific hydrolysis of an Iridoid β-glucoside from plumeria obtusa.

INTERNATIONAL LINKAGES

Department of Tropical Nutrition and Food Science assigned Mr. Kitisak Thawnashom, a Ph.D. student, for training about the determination of trans thyretin and retinol-binding protein in obese and diabetic patients, which is a part of the thesis entitled "Gene Polymorphisms in Homocysteine Pathway in relation to Homocysteine and Vitamin Status in Overweight/Obese Thais". Also, Mr. Somchai Phuduang, a laboratory technician, was assigned to visit laboratory techniques concerning about protein determination and analysis during November 15, 2006 to December 15, 2006 under the supervision of:

Prof. Dr. Florian J. Schweigert
Mathematisch-Naturwissenschaftliche Fakultat
Institut fur Ernahrungswissenschaft
Lehrstuhl fur Physiologie und Pathophysiologie der Ernahrung
Universitat Potsdam, Postfach 601553 m 14415 Potsdam, Germany

Futhermore, the department accepted volunteer students for assistance of research work entitled "Health Behaviors and Nutritional Status of Tsunami Victims" directed by Assist. Prof. Karunee Kwanbunjan as the project head. This research project is funded by Brescia University, Italy. The foreign students includes Ms. Julia Breuninger, Ms. Wibke Toenjes, and Ms. Maria Feuerstein, Justus Liebig University, Ludwigstrasse 23, 35390 Giessen,

LOCAL COOPERATION

1. Provincial section of Public Health, Phang-Nga
2. Head of Takuapa District, Phang-Nga
3. Public Health Center, Takuapa District, Phang-Nga
4. Head of Bannamkem Health Station
5. Head of Bangnaisri Health Station
6. Head of Bangmuang Health Station
7. Mr. Maitree Jongkraijak
8. Director of Takuapa Hospital
9. Director of Bannamkem School
10. Head of Vector-transmitted Disease Control Center, Phang-Nga

LIST OF ABSTRACTS

Department of

Tropical Pathology

Office of the Department, Telephone: 0 2354 9100-19 ext. 1670, 1622
Fax: 0 2644 7938

Assoc. Prof. Emsri Pongponratn
B.Sc., D.V.M, Ph. D. (Trop. Med.)
FIELD OF EXPERTISE: Electronmicroscopy; Pathology of malaria
E-MAIL: *tmepp@mahidol.ac.th*
TELEPHONE: 1621
HEAD

Assist. Prof. Benjanee Punpoowong
B.Sc. (Biol.). M.Sc. (Trop. Med.)
FIELD OF EXPERTISE: Laboratory technics for histopathological and cytological investigations
E-MAIL: *tmbpp@mahidol.ac.th*
TELEPHONE: 1678
DEPUTY HEAD

Assoc. Prof. Parnpen Viriyavejakul
B.S. (Biology-Genetics), M.D., D.T.M. & H., M.C.T.M., Dip. Thai Board of Anatomical Pathology
FIELD OF EXPERTISE: Anatomical pathology/Opportunistic infections in AIDS/Tissue cytokines in AIDS
E-MAIL: *tmpvr@mahidol.ac.th*
TELEPHONE: 1677

Assoc. Prof. Mario Riganti
M.D. Dip. American Board of Pathology
FIELD OF EXPERTISE: General and tropical pathology; Gnathostomiasis
TELEPHONE: 1674
CONSULTANT

Assoc. Prof. Yaowapa Maneerat
D.V.M., Ph.D. (Pathobiology)
FIELD OF EXPERTISE: Pathology of malaria (cytokines and nitric oxide involvement)
E-MAIL: *tmymn@mahidol.ac.th*
TELEPHONE: 1629

Assist. Prof. Urai Chaisri
B.Sc. (Biol.), M.Sc. (Trop. Med.), Ph.D. (TropMed.)
FIELD OF EXPERTISE: Electronmicroscopy, Immunology
E-MAIL: *tmuch@mahidol.ac.th*
TELEPHONE: 1628

Mr. Vasant Khachonsaksumet
B.Sc. (Biol.), M.Sc. (Infectious Diseases)
TELEPHONE: 1676
MEDICAL SCIENCE ASSOCIATE

Ms. Rungrat Nintasen
B.Sc. (Microbiology), M.Sc. Infectious Disease and Epidemiology (Microbiology)
FIELD OF EXPERTISE: Laboratory technics for histopathological, cytological investigations, and Molecular microbiology
TELEPHONE: 1670, 1679

Ms. Supattra Suwanmanee
B.N.S., M.Sc. (Anatomy)
FIELD OF EXPERTISE: Electronmicroscopy
TELEPHONE: 1622

Ms. Wimon Yomana
B.Ed. (Psychology and Guidance)
E-MAIL: *tmwym@mahidol.ac.th*
TELEPHONE: 1670
GENERAL AFFAIRS OFFICER

CURRENT RESEARCH ACTIVITIES

1. A murine model of cerebral malaria, with particular emphasis on histopathology, immunohistochemistry and electron microscopy
2. Pathology, pathogenesis of severe malaria in human organs: ultrastructural studies and cytokine involvement
3. *In vitro* model for studying pathogenesis of atherosclerosis
4. Ig class switching in human B Cell induced by *Plasmodium falciparum*
5. Ig class switching in human B Cell induced by *Gnathostoma spinigerum*
6. Ultrastructural study of malarial parasites and infected red blood cells after drug treatment
7. Cytokine expression in HIV-positive and AIDS patients
8. Cytokines expression in squamous cell carcinoma patients
9. Roles of NOS inhibitors and COX-2 inhibitors in oral squamous cell carcinoma and salivary gland tumor
10. Ultrastructural changes in peritrophic membrane of *Aedes aegypti* infected with Denque virus

AWARDS 2006

No.	Title of Award	Award Recipient	Awarded by	Awarded Date
1.	Poster Presentation Award, First Prize	Assist. Prof. Urai Chaisri *et al*	5th Seminar on Food- and Water-borne Parasitic Zoonoses	28-30 November 2006
2.	Poster Presentation Award, Third Prize	Asoc. Prof. Emsri Pongponratn *et al*	Joint International Tropical Medicine Meeting 2006	29 November - 1 December 2006
3.	Poster Presentation Award, Consolation Prize	Assist. Prof. Benjanee Pungpoowong *et al*	Joint International Tropical Medicine Meeting 2006	29 November - 1 December 2006
4.	Student Oral Presentation Award, Consolation Presentation Award	Ms. Sudarat Nguansangiam	Joint International Tropical Medicine Meeting 2006	29 November - 1 December 2006
5.	Professor Emeritus Khunying Tranakchit for the most outstanding student of the Doctor of Philosophy in Tropical Medicine Class of 2005	Mr. Sumate Aumpawong	Faculty of Tropical Medicine, Mahidol University	22 June 2006
6.	Best Presentation Award in Student Academic Forum 2006	Mr. Kraisorn Sappayatosok	Academic Affairs, Faculty of Tropical Medicine, Mahidol University	18 - 19 November 2006

LIST OF ABSTRACTS

Department of

Tropical Pediatrics

Office of the Department, Telephone: 0 2354 9100, 0 2354 9161 ext. 1462, 1466
Fax: 0 2354 9163

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/Dengue infection
E-MAIL: *tmkps@mahidol.ac.th*
HEAD

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/Dengue infection
E-MAIL: *tmcsw@mahidol.ac.th*

Prof. Emeritus Arunee Sabchareon

M.D., Dip. Amer. Board of Ped., Cert. Neonatology, D.T.M.&H., Cert. Pediatric Infectious Diseases
E-MAIL: *tmasc@mahidol.ac.th*
CONSULTANT

Assoc. Prof. Pornthep Chanthavanich

D.T.C.H., Cert. Pediatric Infectious Diseases
FIELD OF EXPERTISE: Chemotherapy of parasitic diseases, Chemotherapy of malaria in children, Vaccination in children
E-MAIL: *tmpct@mahidol.ac.th*

Assist. Prof. Watcharee Chokejindachai

M.D., Dip. Thai Board of Pediatrics, D.T.M. & H., Ph.D (LSHTM)
FIELD OF EXPERTISE: Chemotherapy of malaria in children, Chemotherapy of parasitic diseases, Vaccine/ General pediatrics, Molecular genetics
E-MAIL: *tmwcj@mahidol.ac.th*

Assist. Prof. Kriengsak Limkittikul

M.D., Dip. Thai Board of Pediatrics, D.T.M.&H., Dip. Virology
FIELD OF EXPERTISE:
General pediatrics/Tropical virology
E-MAIL: *tmklk@mahidol.ac.th*

Assist. Prof. Phanorsri Attanath

B.Sc. (Med. Tech), Dip. Med. Microb., M.Sc. (Trop. Med.)
FIELD OF EXPERTISE: *In vitro* sensitivity test to antimalarials, Pharmacokinetics of antimalarials
E-MAIL: *tmpat@mahidol.ac.th*

Mr. Chanathep Pojjaroen-anant

B.Sc. (Med. Tech.), M.Sc. (Trop. Med.)
FIELD OF EXPERTISE: Cultivation and drug sensitivity test of *P. falciparum*
E-MAIL: *tmcpj@mahidol.ac.th*
SCIENTIST

Mrs. Patraporn Wisetsing

Cert. Med. Tech., B.Ed. (General Science)
SCIENTIST

Ms. Udomluk Thangtaweewaroaj

B.A. (Medical Secretary)
GENERAL AFFAIRS OFFICER

HIGHLIGHT

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

Master of Clinical Tropical Medicine (Tropical Pediatrics) is the major training course of the department. The curriculum consists of the basic knowledge 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. The department involves in Diploma of Tropical Medicine & Hygiene Course (D.T.M.&H.) and also several training courses organized by the faculty.

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

Research topics of the department are emphasized on tropical pediatrics including common pediatric infectious diseases and vaccine trials, eg. dengue, Japanese encephalitis and rabies vaccines

CURRENT RESEARCH ACTIVITIES

Research activities of the department comprise mainly the research related to dengue and rabies infections. Seven research projects are:

1. Safety and immunogenicity of tetravalent dengue vaccine formulations in healthy Thai children: evaluation of a booster dose and five-year antibodies persistence
2. Epidemiological study of dengue infection in children age 3-10 years in Ratchaburi province (RAT0148)
3. FavirabTM post prescription event monitoring
4. Dengue antibodies level and incidence of dengue infection in pre-school-aged children
5. Evaluation of long term immunity against rabies in children vaccinated with different pre-exposure regimens of PCECV (Rabipur®) and the immunity after two IM injections of PCECV (Rabipur®) post-exposure in the children previously vaccinated with PCEC pre-exposure regimens (I49P6 extension)
6. Evaluation of long-term-immunity against Japanese encephalitis in children vaccinated with Japanese encephalitis vaccine (Extension of study M49P2 and I49P6) amendment I
7. Current situation of antimicrobial resistance in Thailand: a review

INTERNATIONAL LINKAGES

1. London School of Tropical Medicine : Staff of the Department is a PhD candidate. (Asst. Prof. Watcharee Chokejindachai)

2. International Vaccine Institute (IVI) 6th International Advanced Course on Vaccinology in Asia - Pacific Regions on May 15-20, 2006 supported by Pediatric Dengue Vaccine Initiatives (PDVI) at Seoul, KOREA. (Assoc. Prof. Chukiat Sirivichayakul)

LIST OF ABSTRACTS

Department of

Tropical Radioisotopes

Office of the Department, Telephone: 0 2354 9100-19 ext. 2040-2046
Fax: 0 2643 5585

Assist.Prof. Channarong Sanghirun
D.V.M., M.P.H.
FIELD OF EXPERTISE: Radioisotopes in medical science and biology, Monoclonal antibody for diagnosis of parasites
E-MAIL: *headtmrd@mahidol.ac.th*
TELEPHONE: ext. 2046
Head

Dr. Voravannee Tolyayon
M.D
FIELD OF EXPERTISE:
Radioisotopes in medical science and biology
E-MAIL: *tmvty@mahidol.ac.th*
TELEPHONE: ext. 2045
Lecturer

Dr. Duangamol Viroonudomphol
Ph.D.
E-MAIL: *tmdkv@mahidol.ac.th*
TELEPHONE: ext. 2046
Lecturer

Ms. Cheeraratana Cheeramakara
B.Ed., M.Sc. (Biology)
FIELD OF EXPERTISE: Radioisotopes in medical science and biology
E-MAIL: *tmcar@mahidol.ac.th*
TELEPHONE: ext. 2044, 2045
Scientist

Mrs. Korbkit Cherdchu
B.Sc., M.Sc. (Pharmacology)
FIELD OF EXPERTISE: Radioisotopes in medical science and biology
E-MAIL: *tmkcr@mahidol.ac.th*
TELEPHONE: ext. 2042, 2044
Scientist

Mrs. Wanyarat Nakosiri
B.sc., M.Sc. (TropMed)
FIELD OF EXPERTISE: Radioisotopes in medical science and biology
E-MAIL: *tmwtn@mahidol.ac.th*
TELEPHONE: ext. 2044, 2045
Scientist

Mrs. Suporn Paksanont
B.Sc., M.Sc. (Zoology)
FIELD OF EXPERTISE: Radioisotopes in medical science and biology
E-MAIL: *tmspn@mahidol.ac.th*
TELEPHONE: ext. 2042, 2044
Scientist

Ms. Kriyaporn Songmuaeng
B.Sc., M.Sc. (Environmental Biology)
FIELD OF EXPERTISE: Radioisotopes in medical science and biology
E-MAIL: *tmskm@mahidol.ac.th*
TELEPHONE: ext. 2043, 2044
Scientist

Mr. Naphachai Suthisai
Cert. Med. Sci. Tech.
TELEPHONE: ext. 2043, 2044
Medical Science Associate

Mrs. Bangon Sukchart
Cert. Med. Sci. Tech.
TELEPHONE: ext. 2043, 2044
Medical Science Associate

Ms. Duangduen Phienpicharn
B.Ed. (English)
E-MAIL: *tmdph@mahidol.ac.th*
TELEPHONE: ext. 2040, 2041
General Affairs Officer

CURRENT RESEARCH ACTIVITIES

1.1 Distribution of C^{14}-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 of 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

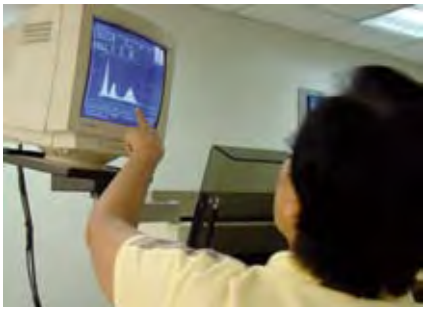
COLLABORATIVE RESEARCH:

2.1 Studies on lethal dose LD50 of 4 Thai medicinal herbs in mice

2.2 Homocysteins and thrombosis in Thai children: a case-control study

2.3 Studies on correlation of serum vitamin B12, serum folic acid, red blood cell folate, plasma homocysteine, micronucleus frequency in human lymphocytes, DNA methylation, and nutritional status in aging and young adults Thai people

2.4 Increase hemoglobin in iron deficiency wistar rat after eating crocodile blood freezed and thawed. Effect of oral oxymetholone on lean body mass and insulin resistance in end-stage renal disease patients undergoing maintenance hemodialysis



LIST OF ABSTRACTS

Mahidol Oxford Tropical Medicine Research Unit (MORU)

Faculty of Tropical Medicine, Mahidol University, Telephone: 0 2354 1395-8
Fax: 0 2354 9169

Prof. Nicholas J. White
Chairman, SEA
E-MAIL: *nickw@tropmedres.ac*

Prof. Nicholas Day
Director
E-MAIL: *nickd@tropmedres.ac*

Dr. Arjen Dondorp
Deputy Director
Head of Malaria
E-MAIL: *amdondorp@yahoo.com*

Prof. François Nosten
Director, SMRU
E-MAIL: *francois@tropmedres.ac*

Dr. Sharon Peacock
Head of Microbiology
E-MAIL: *sharon@tromedres.ac*

Dr. Wirongrong Chierakul
E-MAIL: *kae@tropmedres.ac*
Physician

Dr. Sunee Chueasuwanchai
E-MAIL: *sunee@tropmedres.ac*
Physician

Dr. Prakaykaew Tipmanee
E-MAIL: *jib@tropmedres.ac*
Physician

Dr. Direk Limmathurotsakul
E-MAIL: *direk@tropmedres.ac*
Physician

Dr. Wirichada Pan-ngum
E-MAIL: *pan@tropmedres.ac*
Statistician

Dr. Kesinee Chotivanich
Head of Malaria Laboratory
Lecturer & Scientist
E-MAIL: *nokowellcome97@hotmail.com*

Dr. Kamolrat Silamut
E-MAIL: *oye@tropmedres.ac*
Scientist

Mrs. Vanaporn Wuthiekanun
E-MAIL: *lek@tropmedres.ac*
Scientist

Dr. Stuart Blacksell
E-MAIL: *stuart@tropmedres.ac*
Microbiologist

Mrs. Piengchan Sonthayanon
E-mail: *piengchan@tropmedres.ac*
Microbiologist

Ms. Narisara Anantagool
E-MAIL: *narisara@tropmedres.ac*
Microbiologist

Ms. Sarinna Tumapa
E-MAIL: *sarinna@tropmedres.ac*
Microbiologist

Ms. Janjira Thaipadungpanich
E-MAIL: *janjira@tropmedres.ac*
Microbiologist

Mr. Sayan Langla
E-MAIL: *sayan@tropmedres.ac*
Lab Technician

Ms. Premjit Amornchai
E-MAIL: kung@tropmedres.ac
Lab Technician

Ms. Anchalee Thanwisai
E-MAIL: anchalee@tropmedres.ac
Lab Technician

Ms. Kemajittra Jenjaroen
E-MAIL: kamajittra@tropmedres.ac
Lab Technician

Ms. Nuntipa Akkanit
E-MAIL: nuntipa@tropmedres.ac
Lab Technician

Mr. Weerawat Wong-asa
E-MAIL: jik@tropmedres.ac
Lab Assistant

Mr. Gumphol Wongsuvan
E-MAIL: gumphol@tropmedres.ac
Lab Technician

Ms. Juntima Sritabal
E-MAIL: juntima@tropmedres.ac
Lab Technician

Ms. Forradee Nuchsongsin
E-MAIL: Forradee@tropmedres.ac
Lab Technician

Ms. Pattamon Tharaphan
E-MAIL: pattamon@tropmedres.ac
Lab Technician

Dr. Niklas Lindegardh
E-MAIL: niklas@tropmedres.ac
Head of Pharmacology

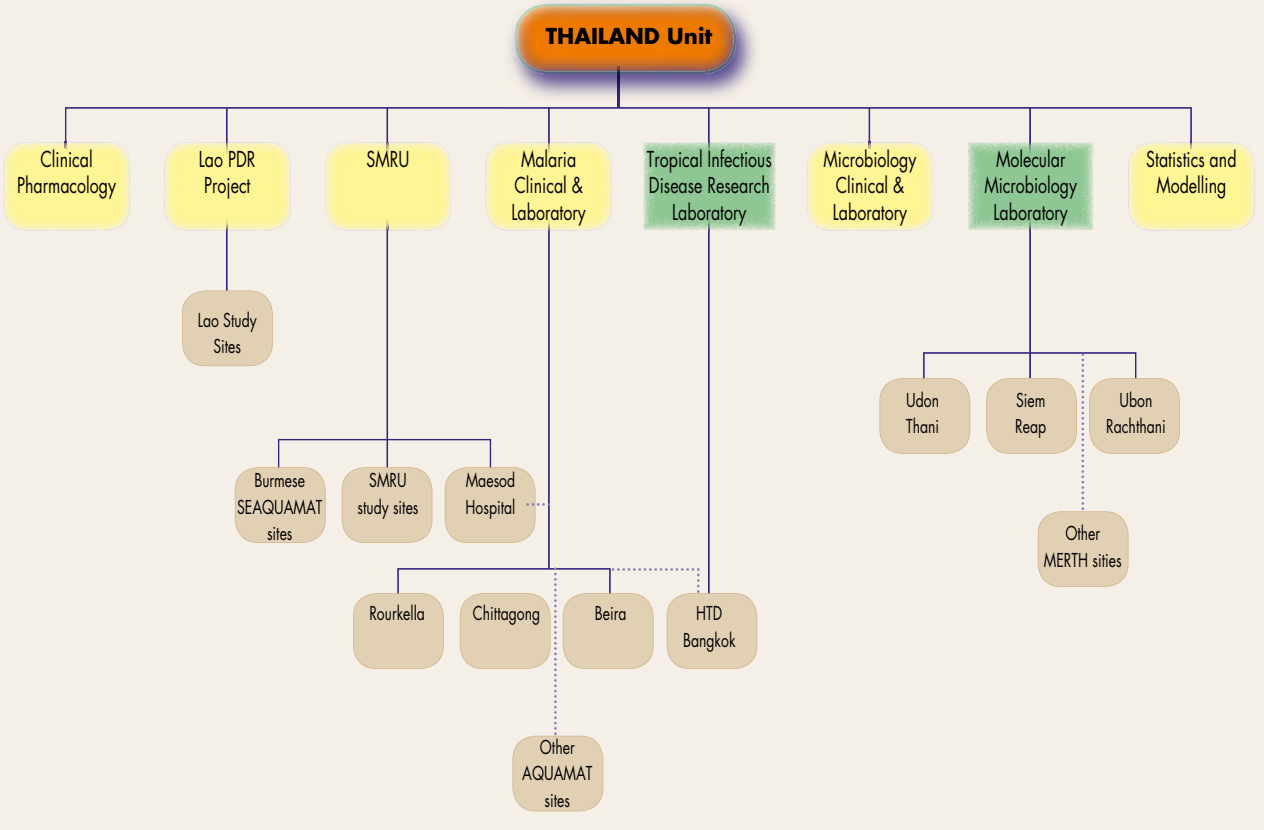
Ms. Anna Annerberg
E-MAIL: anna@tropmedres.ac
Pharmacologist

Dr. Thida Singtoroj
E-MAIL: thida@tropmedres.ac
Pharmacologist

Dr. Warunee Hanpithakpong
E-MAIL: warunee@ tropmedres.ac
Pharmacologist

Ms. Benjamas Kamanikom
E-MAIL: benjamas@tropmedres.ac
Lab Assistant

Mahidol-Oxford Tropical Medicine Research Unit (MORU)



CURRENT RESEARCH ACTIVITIES

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.



LIST OF ABSTRACTS

LIST OF ABSTRACTS (Continued)

Vaccine Trial Centre

Vaccine Trial Centre Floor 10, 11 Chamlong Harinasuta Building, Tel. 66 (0) 2354 9100-19 ext. 1501-4
Data Management Unit Floor 9 Anek Prasong Building, Tel. 66 (0) 2354 9100-19 ext 1890, Fax. 00(0) 2354 9187
AIDS Vaccine Trial Project Floor 9 Anek Prasong Building, Tel. 66 (0) 2354 9100 ext. 1891-4

Assoc. Prof. Pratap Singhasivanon
FIELD OF EXPERTISE: Epidemiology of Tropical Diseases/ Research Methodology
E-MAIL: *tmpsh@mahidol.ac.th*
DIRECTOR

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 operated by the Faculty of Tropical Medicine on their behalf. The major purpose of the centre is testing newly developed vaccines that reach clinical-trial stage. However, the centre is currently expanding its service to the pharmaceutical drug development where evaluation in human participants is needed. The VTC has experience 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 involves in the world largest HIV vaccine community trial with 16,000 healthy informed consenting volunteers.

The VTC renders its service in both clinical management and data management of the trial. The Centre is the first and the only facility of its kind in Thailand, in the region, and perhaps also in developing countries. The VTC's goal, since its establishment, has been 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 the VTC are trusted for the validity of data and the ethical, scientific, and technological quality of the trials.

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

CURRENT RESEARCH:

- 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

Data Management Unit

Assist. Prof. Jaranit Kaewkungwal
B.Sc., M.Ed., M.A., Ph.D. (Applied Statistics and Program Evaluation)
E-MAIL: *tmjkk@mahidol.ac.th*
CHIEF

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, conducting the first large-scale HIV vaccine trial in Thailand. Its establishment and the early years of operation 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 operates under the VTC, Dean's Office, Faculty of Tropical Medicine. The DMU also provides renders database development, consultation and training in data management and analysis for biomedical research services through the Applied and Technological Service Centre of Mahidol University. The major objectives of the DMU comprise: (1) To establish a data management centre of excellence 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 the 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 set such that its mission will provide the data quality for a particular clinical trial or an epidemiological study and, if required, data management in a regulatory compliance environment. Thus, the DMU has organised its teams into three major areas. Besides the chief, administrative and secretarial staff, the data management personnel are divided into the "data quality group", the "information-communication technology (ICT) group" and the "quality assurance group". The personnel assigned to each group depend on the complexity and amount of data and workload of the trial.

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

Currently, the DMU is playing a major rol in the data management of the world's largest HIV vaccine trial, being conducted in Thailand. In this trial, all of the data management processes for over 25,000 volunteers during the 5-year study period are being done within the DMU; and, as this is the first trial in Thailand to maintain primary database subject to be audited 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 has been collaborating with other institutions in conducting research studies as well as consultation and development of a database, for example the database development for quality control and assurance processes for the Department of Medical Science, Ministry of Public Health.

Vaccine Trial Section

Prof. Dr. Punnee Pitisuttithum
M.B.B.S., D.T.M. & H., F.R.C.P.C. (T)
E-MAIL: *tmppt@mahidol.ac.th*
TELEPHONE: 66(0) 2354 9173; 66 (0) 2543 9175
Principal Investigator

CURRENT PROJECTS

1. A Phase III Trial of Aventis Pasteur Live Recombinant ALVAC-HIV (vCP1521) priming with VaxGen gp 120 B/E (AIDSVAX™ B/E) Boosting in HIV-uninfected Thai Adults.
2. Safety, Immunogenicity, and Efficacy of GARDASIL™ (Human Papillomavirus [Types 6, 11, 16, 18] Recombinant Vaccine) in Mid-Adult Women-The FUTURE III (Females United to Unilaterally Reduce Endo/Ecto Cervical Cancer) Study.
3. A Worldwide, Phase I Dose-Escalating study of the tolerability and immunogenicity of a three-dose regimen of the MRKAd5 HIV-1 gag vaccine in healthy adults.
4. Establishment of a *Shigella sonnei* challenge model for evaluation of future vaccine candidates.

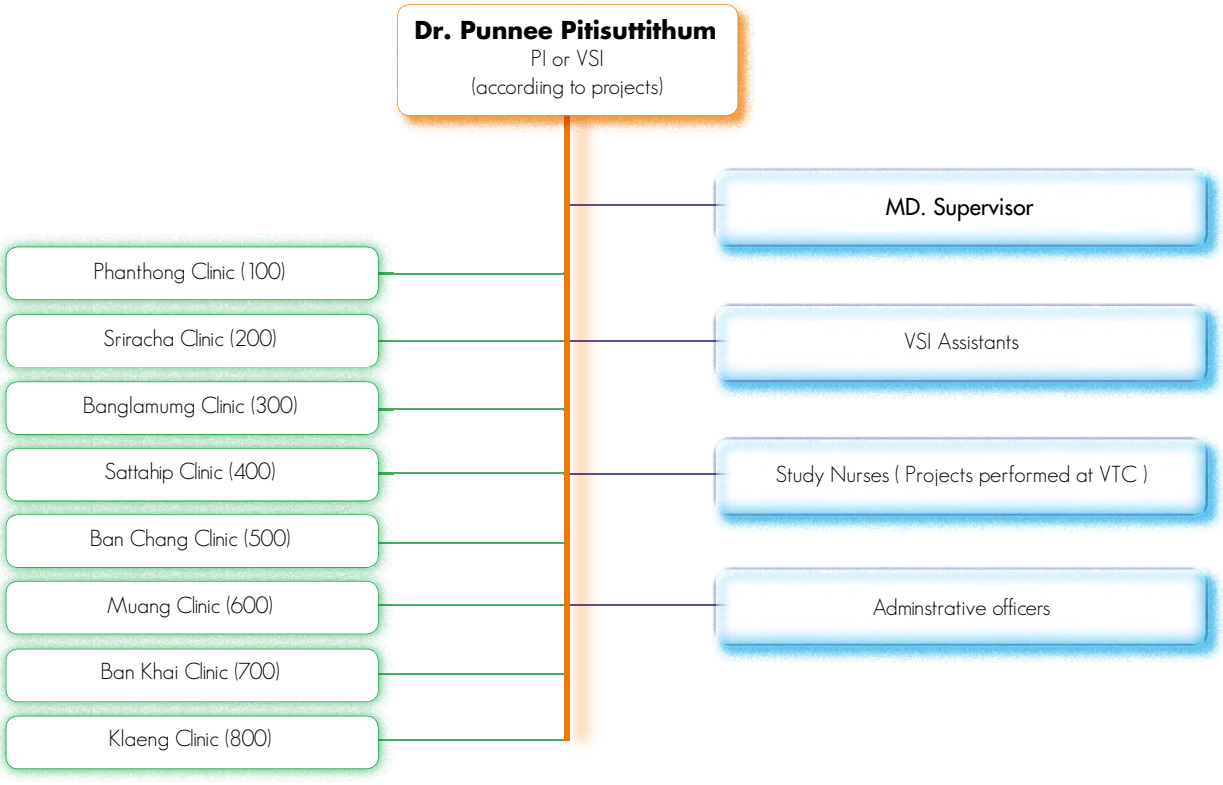
STAFF PROJECTS PERFORMED AT VTC

Name-Surname	Position	Education
PUNNEE PITISUTTITHUM	Principal Investigator	
VALAI BUSSARATID	M.D.	
JITTIMA DHITAVAT	M.D.	
WIRACH MAEK-A-NANTAWAT	M.D.	
SUPAT CHAMNACHANAN	M.D.	
SUPA NAKSRISOOK	Study Nurse	Bachelor of Nursing, Mahidol University
ADJHAWEE CHONWEERAWONG	Study Nurse	Bachelor of Science (Nursing and Midwifery), Mahidol University
NARUMON THANTAMNU	Study Nurse	Bachelor of Nurse, Prince of Songkla University
KAEWTA INTALAPAPORN	Study Nurse	Master of Science (Public Health) major in Infectious diseases and epidemiology, Mahidol University
VATCHARACHAI NGAMDEE	Study Nurse	Bachelor degree of Science, Suan Dusit Rajabhat University
RUNGRAPAT MUANAUM	Study Nurse	Certificate in Practical Nurse, Mahidol University
JARIYA MAHARATCHAMONGKOL	Research Assistant	Bachelor of Business Administration, Siam University
SAWANYA LEKHACHINNABUT	Research Assistant	Bachelor of Arts, Dhurakijpundit University

STAFF SUMMARY

Field Study		Projects performed at VTC	
Vaccine Trial Senior Investigator	1	Primary Investigator	1
MD. Supervisor	6	Medical Doctor	4
Clinicl Research Coordinator	62	Study Nurse	6
Research Assistant	32	Research Assistant	2

ORGANIZATION CHART OF PROJECTS (In house & Field Sites)



TRAINING COURSE , WORKSHOP, MEETING-2006

Date	Activities	Lecturers / Instructors
Friday, 11.00-16.00	Weekly meeting at VTCVSI, MD.	Supervisors, CRC-VTC, Chief CRCs
10-Feb-06, 13.00-15.30 Cholchan Hotel, Chonburi	Conducting a clinical trial	Prof. Punnee Pitisuttithum
18-Feb-06, 10.00-14.00 VTC	Effective communication in the organization	Dr. Somkit Issarawat, Mahidol University
27-28 Feb - 1 Mar 06 08.00-20.00 Botany Beach Resort, Chonburi	Counseling workshop	Dr. Prayuk Serisathien and Team Department of Mental Health, MoPH
18-May-06, 14.00-18.00 (Botany Pattaya)	- Lessons Learned from the PBIII project (all staff) - Examination (all staff)	VSI, MD. supervisors
8-9 September 2005 Botany Beach Resort, Chonburi	GCP refresher course - GCP overview - Informed consent process & workshop - Study procedure - SOP review workshop - Safety reporting & workshop	Prof. Punnee Pitisuttithum & Team
6-Oct-06, 13.00-16.00 Ambassador Hotel	Training on sexually transmitted infection	Dr. Ankana Chareonwattanachokchai MoPH
15-Dec-06, 13.00-16.30 Faculty of Tropical Medicine	Media development	Mr. Somboon Sukhavanich

Counseling Workshop
Botany Beach Resort, Chonburi Province
27-28 Feb - 1 Mar 2006

Counseling Workshop
Botany Beach Resort, Chonburi Province
6-8 Mar 2006

Counseling Workshop

Volunteer Activities at the clinical sites

HSRRB at clinical site 13-12-2006

Booth & Board in the Public Area

Valentine's Day at the clinical sites
14-02-2006

Cleaning the beach, Rayong

Activities on Mother's Day

Weekly site visits by MDs
from VTC

Talking about AIDS, 01 Sep 2006
Rayong

Motorcycle Safety Rally
Rayong Province 26-11-2006

Volunteer Club Activities

World AIDS Day

Volunteer meeting (HPV012&019) 04 November 2006

The Bangkok School Of Tropical Medicine

GRADUATE DIPLOMA IN TROPICAL MEDICINE AND HYGIENE

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.

MASTE R 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 5.5. 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.

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

1. Applicants should have a TOEFL English language proficiency level of 500 or more, or an IELTS score of 5.5 or more.
2. 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.
3. 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. programs, the applicants should be accepted by an appropriate advisor before enrolment.

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:

1. Hold 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.).

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-couse.

For the Ph.D. Plan 2, 3 year-couse.

COMMENCEMENT

Normally the first Monday of June each year. There is another intake in November each year for the Ph.D. programs, 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 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 5.5 and not more than 2 years from the application date.

B. Plan II

Candidates are required to:

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 TITLE

Program	Department	Name	Title of Thesis	Adviser
M.C.T.M.	Clinical Tropical Medicine	Dr. Maie Aramaki	Immune reconstitution inflammatory syndrome druging highly active antiretroviral therapy in advanced HIV-infected patients	Asst. Prof. Udomsak Silachamroon
	Clinical Tropical Medicine	Dr. Darin Areechokchai	Adverse effects of antiretroviral drugs during pregnancy: a five-year review at Chonburi Regional Hospital, Thailand	Asst. Prof. Wirach Maek-a-nantawat
	Clinical Tropical Medicine	Dr. Jirapus Pongprapruet	Clinical manifestation and outcome of nontuberculous mycobacterial infections in HIV/AIDS patients at Bamrasnaradura Institute, in the year 2005	Prof. Punnee Pitisuttithum
M.C.T.P.	Tropical Pediatrics	Dr. Clara Nauluta Seneadza	Early clinical manifestations of HIV infection in Thai children aged younger than 18 months	Asst. Prof. Watcharee Chokejindachai
M. Sc. (Trop. Med.) 2nd year students	Clinical Tropical Medicine	Ms. Premjit Amornchai	Comparison of latex agglutination for the identification of *Burkholderia pseudomallei*	Dr. Wirongrong Chierakul
	Clinical Tropical Medicine	Ms. Supparat Wannasilp	Study of solubility and efficacy of antimalarial drugs on *Plasmodium falciparum*	Asst. Prof. Kesinee Chotivanich
	Helminthology	Dr. Do Trung Dung	Trematode infections in people of Nghia Phu and Nghia Lac Communes, Nghia Hung District, Nam Dinh Province, Vietnam	Assoc. Prof. Jitra Waikagul
	Helminthology	Ms. Megumi Ishida	Discrimination of small liver flukes and intestinal flukes eggs by ribosomal DNA-based PCR	Assoc. Prof. Jitra Waikagul
	Medical Entomology	Mr. Wilfredo E. Aure	Insecticide susceptibility level of *Aedes aegypti* (Linn.) from municipality of Cabuyao and City of Manila, Philippines	Assoc. Prof. Narumon Komalamisra
	Social and Environmental Medicine	Ms. Suporn Thongyuan	Differences of dengue epidemiology in semi-rural and semi-urban community settings	Assoc. Prof. Piyarat Butraporn
M. Sc. (Trop. Med.) 3rd year students	Clinical Tropical Medicine	Ms. Juntima Sritabal	Effects of primaquine and its metabolites on the infectivity of *P. falciparum* gametocyte	Asst. Prof. Kesinee Chotivanich
	Helminthology	Mr. Panupong Sahaisook	Analysis of crude and excretory-secretory antigens of *Dirofilaria immitis* adult worms against antibody of Brugian filariasis by ELISA and immunoblot	Asst. Prof. Paron Dekumyoy
	Medical Entomology	Ms. Intira Pipitgool	Effectiveness of *Bacillus thuringiensis israelensis*, against temephos-resistant *Aedes aegypti* populations from Thailand, under laboratory conditions	Assoc. Prof. Somjai Leemingsawat
	Entomology	Ms. Patcharee Khongtak	Study of the specific IGE response and allergen analysis of mosquitoes species found in Thailand	Assoc. Prof. Somjai Leemingsawat
	Microbiology and Immunology	Maj. Orawan Nunthamongkol	Characterization of recombinant leptospiral lipoprotein	Asst. Prof. Thareerat Kalambaheti

Program	Department	Name	Title of Thesis	Adviser
	Microbiology and Immunology	Ms. Somrudee Attachit	Serodiagnosis of scrub typhus and melioidosis by dual immuno-peroxidase test	Asst. Prof. Varee Wongchotigul
	Microbiology and Immunology	Ms. Ampai Tanganuchitcharnchai	Production of monoclonal antibody to *Orientia tsutsugamushi*	Asst. Prof. Thareerat Kalambaheti
	Microbiology & Immunology	Mr. Kata Gunlabun	Molecular typing of *Leptospira* species based on putative o-antigen polymerase gene sequence	Asst. Prof. Thareerat Kalambaheti
	Microbiology & Immunology	Miss Siriluk Feangvad	A comparative evaluation of four techniques for the serological diagnosis of scrub typhus infection	Asst. Prof. Varee Wongchotigul
	Protozoology	Mr. Nitipan Tantawiwattananon	Viability of *Giardia* cysts in water	Assoc. Prof. Yaowalark Sukthana
	Protozoology	Ms. Charoonluk Sangloung	Effect of ultra violet on viability of *Cryptosporidium* oocysts in water	Assoc. Prof. Yaowalark Sukthana
	Tropical Nutrition & Food Science	Ms. Kulrat Chitcharoenrung	Identification of gene alteration in DNA fingerprinting amplified from AE3 primer in colorectal cancer	Assoc. Prof. Songsak Petmitr
	Tropical Nutrition & Food Science	Ms. Sudaporn Kengkarn	Determination of DNA amplification in DNA fingerprinting amplified from AD15 primer in colorectal cancer by gene cloning and DNA sequencing	Assoc. Prof. Songsak Petmitr
	Tropical Nutrition & Food Science	Ms. Tawiwan Sareebot	Analysis of DNA amplification in colorectal cancer by AP-PCR using AB19 primer, gene cloning and DNA sequencing	Assoc. Prof. Songsak Petmitr
	Tropical Hygiene	Dr. Mohammad Jahirul Karim	Age-period-cohort analysis and spatial pattern of tuberculosis incidence in Bangladesh	Assoc. Prof. Pratap Singhasivanon
	Social and Environmental Medicine	Ms. Nipaporn Tewawong	Mimotope identification from monoclonal antibodies specific to house dust mite, using phage displayed random peptide libraries	Asst Prof. Pongram Ramasoota
	Social and Environmental Medicine	Ms. Issariya Ieamsuwan	Mimotope identification from monoclonal antibody and patient's sera specific to *Gnathostoma spinigerum*, using phage displayed random peptide libraries	Asst Prof. Pongrama Ramasoota
Ph.D. (Trop. Med.) 2nd year students	Social and Environmental Medicine	Ms. Nardlada Khantikul	Vivax malaria patients and their drug adherence in Northern Thailand	Assoc. Prof. Piyarat Butraporn
Ph.D. (Trop. Med.) 3rd year students	Clinical Tropical Medicine	Dr. Srivicha Krudsood	New method for measurement of red blood cell destruction in malaria	Prof. Polrat Wilairatana
	Clinical Tropical Medicine	Ms. Tippawan Sungkapong	Identification of antigenic proteins on the surface of *P. vivax*-infected erythrocytes	Asst. Prof. Kesinee Chotivanich
	Clinical Tropical Medicine	Mrs. Narisara Chantratita	Phenotypic plasticity of clinical *Burkholderia pseudomallei* isolates	Prof. Sasithorn Pukrittayakamee
	Medical Entomology	Ms. Nuananong Jirakanjanakit	Morphometric analysis of wing geometry in the main dengue vector, *Aedes aegypti*	Assoc. Prof. Somjai Leemingsawat
	Medical Entomology	Ms. Parichat Lapcharoen	The use of gene silencing to study the effects of lysozyme on *Plasmodium* in malaria vector *Anopheles dirus*	Assoc. Prof. Narumon Komalamisra

Program	Department	Name	Title of Thesis	Adviser
	Protozoology	Ms. Ruangrat Buddhirongawatr	*Toxoplasma gondii* genotyping in domestic and wild felids in Thailand	Assoc.Prof. Yaowalark Sukthana
	Tropical Hygiene	Dr. Suthat Chottanapund	Survival rate of HIV-infected patients with cryptococcal meningitis	Assoc. Prof. Pratap Singhasivanon
	Social and Environmental Medicine	Ms. Pannamthip Pitaksajjakul	Construction of phage antibody library specific to H5N1 avian influenza virus	Asst. Prof. Pongrama Ramasoota
	Social and Environmental Medicine	Mr. Patthanasak Khammaneechan	Social impact assessment of central healthcare waste incinerator project in Yala Province	Assoc. Prof. Kamolnetr Okanurak
Ph.D. (Trop. Med.) 4th year students	Clinical Tropical Medicine	Mrs. Piengchan Sonthayanon	Molecular diagnosis and multilocus sequence typing of scrub typhus	Prof. Sasithorn Pukrittayakamee
	Medical Entomology	Mrs. Raweewan Srisawat	The effect of gene mutations to the voltage gated sodium channel in resistant pyrethroid *Aedes aegypti*	Assoc. Prof. Narumon Komalamisra
	Medical Entomology	Mr. Apiwat Tawatsin	Novel repellents derived from phytochemicals against mosquito vectors and common cockroaches in Thailand	Assoc. Prof. Narumon Komalamisra
	Microbiology and Immunology	Miss Natharinee Horata	Polymorphism and function of PfEMP1 extracellular domains in Thai *Plasmodium falciparum* isolates causing severe and uncomplicated malaria	Prof. Srisin Khusmith
	Microbiology and Immunology	Mr. Trung Dac Nguyen	Molecular characterization of antibiotic resistance in clinical strains of *Salmonella enterica* serovar *typhi* from Vietnam	Asst. Prof. Usanee Suthisarnsuntorn
	Protozoology	Mr. Aongart Mahittikorn	Molecular and immunohistochemistry studies on tachyzoite and bradyzoite stage conversion in toxoplasmosis	Assoc. Prof. Yaowalark Sukthana
	Tropical Hygiene	Mrs. Tassanee Silawan	The spatiotemporal dynamics of dengue infection in Northeastern Thailand	Assoc. Prof. Pratap Singhasivanon
	Tropical Hygiene	Dr. Le Huu Tho	Alcohol consumption and sexual risk behaviors among adolescents and young adults in Nhathrang city, Vietnam: linear structural equation model.	Assoc. Prof. Pratap Singhasivanon
	Tropical Pathology	Mr. Kraisorn Sappayatosok	Expression of NOS, VEGF, COX-2 and their clinicopathological correlation in oral and para-oral squamous cell carcinoma	Asst. Prof. Urai Chaisri
	Tropical Pathology	Ms. Navakanit Sachanonta	The effects of antimalarial-drug-induced changes on *Plasmodium falciparum* and Pf-infected red blood cell ultrastructure	Assoc. Prof. Emsri Pongponratn
	Tropical Pathology	Ms. Jaiaue Wongtanachai	Effects of antimalarial drugs on *Plasmodium falciparum*: morphology, viability, and multiplication rate	Asst. Prof. Urai Chaisri
	Tropical Nutrition & Food Science	Ms. Ubol Chuensumran	Identification of genetic alterations in intrahepatic cholangiocarcinoma by arbitrarily primed-polymerase chain reaction (AP-PCR) and DNA sequencing	Assoc. Prof. Songsak Petmitr
	Tropical Nutrition & Food Science	Mr. Kittisak Thawnashom	Gene polymorphisms in homocysteine pathway in relation to homocysteine and vitamin status in overweight/obese Thais	Assoc. Prof. Rungsunn Tungtrongchitr
	Social and Environmental Medicine	Mr. Tuc Phong Vu	Impacts of pesticide exposure on sperm quality among male farmers in Thaibinh Province, Vietnam	Asst. Prof. Voranuch Wangsuphachart

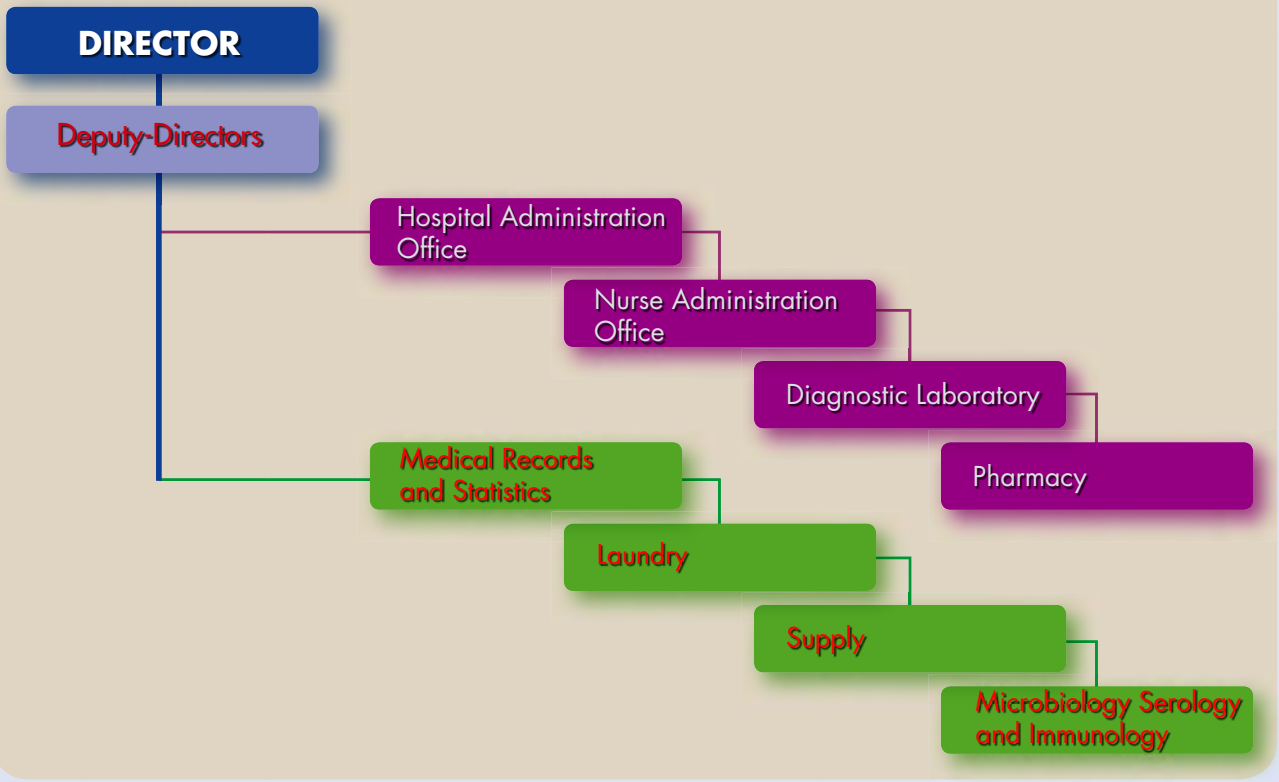
The Hospital For Tropical Diseases

Telephone: (0) 2354 9154, (0) 2354 9100 ext. 1324, 1625

Assoc. Prof. Wattana Leowattana
DIRECTOR
B.Sc., (Med., M.D., M.Sc. (Clinical Science),
Diploma Thai Board of Clinical Pathology,
Diploma Thai Board of Family Medicine, F.R.C.P. (T)
E-MAIL: *leowattana@yahoo.com*

The Hospital for Tropical Diseases (HTD), a specialized research hospital, is one of the three hospital 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 specialist 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 Avia 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.

ORGANIZATION AND ADMINISTRATION OF THE HOSPITAL FOR TROPICAL DISEASES



TRAVEL CLINIC HOSPITAL FOR TROPICAL DISEASES FACULTY OF TROPICAL MEDICINE, MAHIDOL UNIVERSITY

FACILITIES AND SERVICES

- Pre travel counseling and immunization
- Malaria prevention and prophylaxis
- Post travel screening
- Diagnosis and treatment of tropical diseases
- On-site screening and medical service for travelers
- Malaria checking 24 hours/day
- Information center for tropical diseases and emerging diseases
- Health check up and certificate
- Online information and appointment available at www.thaitravelclinic.com

VISITORS IN 2006

- Prof. David O. Freedman University of Alabama, Birmingham
- Thai Red Cross Society staffs
- Many medical doctors and medical students

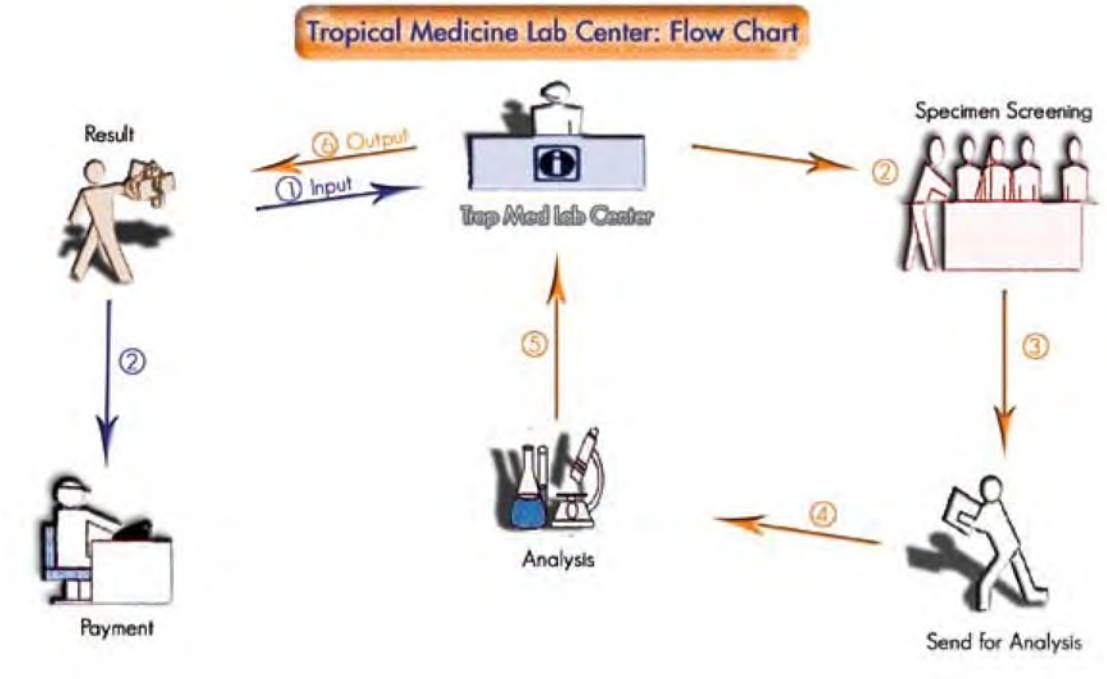
RESEARCH AND PUBLICATIONS

Piyaphanee W, Krudsood S, Silachamroon U, Pornpininworakij K, Danwiwatdecha P, Chamnachanan S, Wilairatana P, Looareesuwan S,2006. Travelers' malaria among foreigners at the Hospital for Tropical Diseases, Bangkok, Thailand - a 6-year review (2000-2005). Korean J Parasitol. Sep; 44(3):229-32.

Abstract: We retrospectively examined the charts of travelers admitted to the Hospital for Tropical Diseases,Bangkok, Thailand, with malaria during the year 2000-2005. Twenty-one cases of malaria were identified, of which 12 (57%) were Plasmodium vivax infections and 9 (43%) were P. falciparum infections. There was one mixed casewith vivax and falciparum infection. Only 1 P. falciparum case had complications. All case were successfully treated with standard antimalarial drugs. Only 3 of the 21 cases were thought to be acquired in Thailand, the rest were regarded to be imported.

MALARIA THOUGHT TO BE ACQUIRED IN NO. (%)

India	5 (23.8)
Cambodia	3 (14.2)
Thailand	3 (14.2)
Myanmar	2 (9.5)
African country,unspecifed	2 (4.7)
Papau New Guinea	1 (4.7)
Malaysia	1 (4.7)
Laos	1 (4.7)
Mozambique	1 (4.7)
Unknown	2 (9.5)



TROP MED LAB CENTER 2006

	Out Patients	In Patients	Total Patients
January - December 2006	5,414	474	5,847

Department of Helminthology	Out Patients	In Patients	Total Patients	Price Per Test (Baht)
- Gnathostomiasis Ab	676	334	1,010	250
- Angiostrongyliasis Ab	59	3	62	250
- Cysticercosis Ab	204	3	207	250
- Strongyloidiasis Ab	53	-	53	250
- Filariasis Ab	48	5	53	250
- Toxocariasis Ab	49	1	50	250
- Echinococcosis Ab	18	-	18	250
- Parasite Identification	23	-	23	100
- Paragonimiasis Ab	15	-	15	250
- Trichinellosis Ab	22	-	22	250
TOTAL	1,167	346	1,513	-

Department of Entomology	Out Patients	In Patients	Total Patients	Price Per Test (Baht)
- Microfilaria (Thick blood film)	24	3	27	100
- Insect Identification	1	-	1	120
TOTAL	25	3	28	-

Department of Microbiology & Immunology	Out Patients	In Patients	Total Patients	Price Per Test (Baht)
- Leptospira titer	297	-	297	200
- CD4,CD8	676	15	691	400
- Scrub Typhus (IFA)	70	-	70	150
- Murine Typhus	18	-	18	150
- Bacteria/Fungus in Herb	1	-	1	2,500
- AFB	-	286	-	-
- Culture (Non Departure by)	-	356	-	-
- Hemo Culture (TROP MED LAB)	-	444	-	-
- GS	-	152	-	-
TOTAL	1,062	15	1,077	-

Department of Social & Environmental Medicine	Out Patients	In Patients	Total Patients	Price Per Test (Baht)
- Schistosomiasis Ab	30	3	33	400
- PCR for TB	-	1	1	400
TOTAL	30	4	34	-

TROP MED LAB CENTER 2006 (Continued)

Department of Protozoology	Out Patients	In Patients	Total Patients	Price Per Test (Baht)
- *Toxoplasma gondii*	55	104	159	300
- Cryptosporidium	11	-	11	200
- *E.histolytica* (stain)	9	-	9	200
- Microsporidium	2	-	2	250
- Isospora	3	-	3	200
- Leishmania	3	-	3	100
TOTAL	83	104	187	-

Department of Tropical Nutrition & Food Science	Out Patients	In Patients	Total Patients	Price Per Test (Baht)
- Vitamin B1	65	1	66	400
- Vitamin B2	23	-	23	400
- Vitamin B6	65	-	65	400
TOTAL	153	1	154	-

Department of Tropical Pathology	Out Patients	In Patients	Total Patients	Price Per Test (Baht)
- Fat in Stool	14	-	14	200
- Sudan Black B	2	-	2	200
- Biopsy	-	1	1	300
TOTAL	16	1	17	-

Department of Tropical Radioisotopes	Out Patients	In Patients	Total Patients	Price Per Test (Baht)
- Vitamin B12	14	-	14	250
- Folate in Serum	285	-	285	200
- Folate in Serum and RBC	286	-	286	400
- Insulin	2	-	2	250
TOTAL	587	-	587	-

Clinical Microscopy/Urine/Stool Unit	Out Patients	In Patients	Total Patients	Price Per Test (Baht)
- CBC	12	-	12	80
- Routine Urine Examination	5	-	5	50
- Routine Stool Concentration	255	-	255	60
TOTAL	272	-	272	-

Hematology Unit	Out Patients	In Patients	Total Patients	Price Per Test (Baht)
- Hb Typing	133	-	133	110
- Blood Group	15	-	15	40
- G6PD	2	-	2	60
- DCIP	2	-	2	40
TOTAL	152	-	152	-

TROP MED LAB CENTER 2006 (Continued)

Clinical Chemistry Unit	Out Patients	In Patients	Total Patients	Price Per Test (Baht)
- Liver Function	68	-	68	360
- Lipid Profile	100	-	100	380
- Creatine Kinase	4	-	4	200
- Glucose	165	-	165	40
- Uric Acid	56	-	56	80
- Cholesterol	179	-	179	60
- Triglyceride	156	-	156	60
- HDL-C	156	-	156	60
- LDL-C	156	-	156	60
- b-HCG	254	-	254	200
- Prolactin	7	-	7	200
- CEA	30	-	30	250
- AFP	41	-	41	250
- PSA	15	-	15	450
- HBs Ag	62	-	62	120
- HBe Ag	4	-	4	350
- Anti HBs	62	-	62	350
- Anti HBc	4	-	4	120
- Anti HBe	3	-	3	350
- Free for Blood Collection	204	-	204	40
TOTAL	1,726	-	1,726	-

Serology Unit	Out Patients	In Patients	Total Patients	Price Per Test (Baht)
- Leptospira Ab	41	-	41	150
- Weil Felix Test	32	-	32	120
- Widal Test	3	-	3	100
- Melioidosis	31	-	31	80
- Scrub Typhus	7	-	7	150
- Murine Typhus	5	-	5	150
- VDRL	6	-	6	60
- Dengue IgG & IgM	12	-	12	250
- *E.histolytica*	2	-	2	150
- Salmonella	1	-	1	100
- Cryptococcus	1	-	1	150
TOTAL	141	-	100	-

RESEARCH IN THE HOSPITAL FOR TROPICAL DISEASES

Item	Project Name	Project Head	Department	Approval Date
1.	Comparison of the Safety and Efficacy of a Unique Intravenous Iron Preparation (VIT-45) versus Oral Iron in the Treatment of Anemia in Non-Dialysis Dependent Chronic Kidney Disease.	Assoc. Prof. Yupaporn Wattanagoon	Clinical Tropical Medicine	MUTM 2006-014 Date of approval 25 April 2006
2.	Open label extension study evaluating the long term safety, tolerability and efficacy of an iron maintenance dosing strategy utilizing intravenous VIT-45 in the treatment of anemia in Non-Dialysis Dependent (NDD) Chronic Kidney Disease (CKD).	Assoc. Prof. Yupaporn Wattanagoon	Clinical Tropical Medicine	MUTM 2006-015 Date of approval 25 April 2006
3.	A Phase II, Double-Blind, Parallel-Group, Randomized, Dose Ranging Study Assessing the Antimalarial Activity and Safety of RBx 11160 Administered for 7 Days in Patients with Acute Uncomplicated *Plasmodium falciparum* Malaria) (Protocol number RBx/MMV05-06; Date 21 March 2006; Version 02).	Prof. Sornchai Looareesuwan	Clinical Tropical Medicine	MUTM 2006-017 Date of approval 8 June 2006
4.	Gene expression profiles of the intra-erythrocytic stage of *P. vivax* and identification of antigenic proteins on the surface of *P. vivax*-infected erythrocytes.	Assist. Prof. Dr. Kesinee Chotivanich	Clinical Tropical Medicine	MUTM 2006-020 Date of approval 8 June 2006
5.	Assessment of the *in vitro* antimalarial activity of new antimalarial compounds against *P. vivax* isolates in Thailand.	Assist. Prof. Dr. Kesinee Chotivanich	Clinical Tropical Medicine	MUTM 2006-021 Date of approval 8 June 2006
6.	Pharmacologic study of Oseltamivir in healthy volunteers.	Assoc. Prof. Yupaporn Wattanagoon	Clinical Tropical Medicine	MUTM 2006-025 Date of approval 30 June 2006
7.	Effects of serum lipid concentration on the efficacy of lumefantrine against falciparum malaria: *in vitro*.	Assist. Prof. Dr. Kesinee Chotivanich	Clinical Tropical Medicine	MUTM 2006-032 Date of approval 8 Aug 2006
8.	Evaluation of fosmidomycin and clindamycin, when administered concurrently to adult subjects with acute uncomplicated *Plasmodium falciparum* malaria.	Prof. Sornchai Looareesuwan	Clinical Tropical Medicine	MUTM 2006-034 Date of approval 15 Aug 2006
9.	A clinical monitoring study of efficacy and safety of artesunate plus mefloquine divided over either two or three days in the treatment of acute uncomplicated *Plasmodium falciparum* malaria together with the correlation of drug sensitivity and clinical responses.	Prof. Sornchai Looareesuwan	Clinical Tropical Medicine	MUTM 2006-037 Date of approval 8 Sep 2006
10.	A clinical monitoring study of efficacy and tolerability of Artesunate 7 days and Artesunate 5 days with standard dose of Mefloquine (25 mg/kg) for the treatment of severe *falciparum* malaria together with the correlation of *in vitro* and *in vivo* responses.	Prof. Sornchai Looareesuwan	Clinical Tropical Medicine	MUTM 2006-038 Date of approval 8 Sep 2006

RESEARCH IN THE HOSPITAL FOR TROPICAL DISEASES (Continued)

Item	Project Name	Project Head	Department	Approval Date
11.	A clinical monitoring study of efficacy and safety of chloroquine follow by either standard dose or high dose of primaquine for treatment of *Plasmodium vivax* malaria together with the correlation of drug sensitivity and clinical responses.	Prof. Sornchai Looareesuwan	Clinical Tropical Medicine	MUTM 2006-039 Date of approval 8 Sep 2006
12.	An open randomized clinical study to assess the safety and efficacy of fixed dose formulation of artemisinin-piperaquine-primaquine (Artequick®) 5 tablets *vs* 6 tablets given once a day for 3 days in the treatment of acute uncomplicated malaria.	Prof. Sornchai Looareesuwan	Clinical Tropical Medicine	MUTM 2006-041 Date of approval 8 Sep 2006
13.	Bioequivalence Study of Generic Glimepiride Tablets to Innovator Amaryl® (Glimepiride 3 mg) in Healthy Thai Volunteers.	Assoc. Prof. Yupaporn Wattanagoon	Clinical Tropical Medicine	MUTM 2006-042 Date of approval 22 Sep 2006
14.	A phase III comparative, open-label, randomized, multi-centre, clinical study to assess the safety and efficacy of fixed dose formulation oral pyronaridine artesunate (180:60 mg tablet) versus mefloquine (250 mg tablet) plus artesunate (100 mg tablet) in children and adult patients with acute uncomplicated *Plasmodium falciparum* malaria.	Prof. Sornchai Looareesuwan	Clinical Tropical Medicine	MUTM 2006-043 Date of approval 22 Sep 2006
15.	A phase III multi-centre, randomized, double blind, double dummy, comparative clinical study to assess the safety and efficacy of fixed-dose formulation of oral pyronaridine artesunate (180:60 mg tablet) versus chloroquine (155 mg tablet), in children and adult patients with acute *Plasmodium vivax* malaria.	Prof. Sornchai Looareesuwan	Clinical Tropical Medicine	MUTM 2006-044 Date of approval 22 Sep 2006
16.	Pathogenesis of severe malaria anemia in Thailand.	Prof. Sornchai Looareesuwan	Clinical Tropical Medicine	MUTM 2006-046 Date of approval 15 Sep 2006
17.	Bioequivalence Study of Generic Filgrastim Injection to an Innovator Neupogen® (Filgrastim 300 mcg/0.5ml syringe) in Healthy Thai Volunteers.	Assoc. Prof. Yupaporn Wattanagoon	Clinical Tropical Medicine	MUTM 2006-047 Date of approval 10 Oct 2006
18.	Characterization of drug and solute transport in *Plasmodium vivax* malaria parasites.	Assist. Prof. Dr. Kesinee Chotivanich	Clinical Tropical Medicine	MUTM 2006-051 Date of approval 7 Nov 2006
19.	Pharmacologic study of Oseltamivir in Healthy Volunteers (Protocol amendment version 2, Date 9 October 2006).	Assoc. Prof. Yupaporn Wattanagoon	Clinical Tropical Medicine	MUTM 2006-052 Date of approval 8 Nov 2006
20.	Pharmacologic study of oseltamivir in healthy volunteers) (Protocol amendment version 2.1, Date 20 December 2006).	Assoc. Prof. Yupaporn Wattanagoon	Clinical Tropical Medicine	MUTM 2006-060 Date of approval 22 Dec 2006
21	Bioequivalence study of generic Sertraline tablets to the innovator Sertraline 50 mg/tablet in healthy Thai volunteers.	Assoc. Prof. Yupaporn Wattanagoon	Clinical Tropical Medicine	MUTM 2006-061 Date of approval 26 Dec 2006

SEAMEO TROPMED Regional Centre for Tropical Medicine

(TROPMED Thailand)

Assoc. Prof. Pratap Singhasivanon
Director
FIELD OF EXPERTISE: Epidemiology of Tropical Diseases/ Research Methodology
E-MAIL: *tmpsh@mahidol.ac.th*

FACULTY OF TROPICAL MEDICINE, MAHIDOL UNIVERSITY BANGKOK, THAILAND

The Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand was appointed by Southeast Asian Ministers of Education Organization (SEAMEO) as the TROPMED National Centre for Tropical Medicine in 1967 and was later promoted to become the SEAMEO TROPMED Regional Centre for Tropical Medicine (TROPMED/Thailand), in 1994. Its objectives are to provide 3 major functions, namely: 1) Teaching and training 2) Research, and 3) Services. The three functions of the Centre'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. TROPMED/Thailand offers five post-graduate regular courses at the international level with a total of 240 students from 23 countries.

1.2 Undergraduate courses.

TROPMED/Thailand also offers 2 undergraduate courses:

1) Elective program in tropical medicine with 23 both medical doctors and medical students from 8 countries.

2) Certificate in Nurse Assistant with 212 students.

In the year FY 2005/2006, TROPMED/Thailand had 475 students from 23 countries; among these, 235 were new enrolled students. 460 of these students were fee-paying attendants.

Table 1 : Details of students attending the 5 regular postgraduate programs.

Programe	Number of Students	No. of Nationalities	No. of Fee paying Students	No. of Graduates
DTM&H 6-month course	29	11 (Australia, Austria, Germany, Myanmar, Nigeria, Singapore, Taiwan, Thailand, UK, USA, Somalia)	29 (100%)	29 (100%)
MCTM 1-year course	13	6 (Austria, Japan, Germany, Myanmar, Taiwan, Thailand)	13 (100%)	13 (100%)
M.Sc. (TM) 1st year	16	5 (Thailand, Bhutan, Vietnam, Japan, Philippines)	54 (77.8%)	11 (16.5%)
2nd year	24	3 (Thailand, Bangladesh, Nepal)		
3rd year (onward)	29	1 (Thailand)		

Programe	Number of Students	No. of Nationalities	No. of Fee paying Students	No. of Graduates
PhD (TM)				
1st year	17	3 (Thailand, Bangladesh, Nepal)	125 (100%)	10 (8%)
2nd year	21	3 (Thailand, Bangladesh, Japan)		
3rd year	19	3 (Thailand, Vietnam, China)		
4th- 9th years	68	4 (Thailand, Switzerland, Korea, Malaysia)		
PhD (Clin. Trop. Med.)				
1st year	-	- (-)	4 (100%)	1 (25%)
2nd year (Onward)	4	3 (Myanmar, Nepal, Thailand)		
Total	240	23	225 (93.6%)	64 (26.6%)

1.3 Training course/Workshop/Meeting. 12 international short training courses were organized with 133 participants from 17 countries, Elective Program in Tropical Medicine for overseas medical students. With 23 participants from 8 countries, and 1 international meeting (Joint International Tropical Medicine Meeting 2005) were convened during FY 2005/2006 with a total of 571 participants.

KRA 2. INCREASED ACCESS TO MARKET

2.1 Active Marketing. 18 TV series were broadcast, 9 news items published in local newspapers, journals and magazines, 20 radio announcements. 5,000 copies of 6 tropical diseases/related fields information leaflets were produced and distributed to the publics 1,250 copies of inhouse journal were produced and 100 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 as a WHO Collaborating Centre for Environmental Management for Disease Vector Control in Sustainable Development, and WHO Collaborating Centre for Clinical Management of Malaria.

3.2 Visitors: 66 visitors from 10 countries visited TROPMED / Thailand during FY2005/2006, consisting of lecturers, academic staff, 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

Sources	Amount in million Baht	Percentage Increase / Decrease
1. Government budget	159.4	+ 3.4 %
2. Revenue from services and other activities	125.0	+ 3.1 %
3. Research funds from other organizations	113.7	- 5.4 %

KRA 5. ENHANCED QUALITY OF CENTRE MANAGEMENT

TROPMED/Thailand has a total of 747 staff comprising 95 academic staff, 197 academic assistants and research staff, 298 administrative personnel and employees, 157 university employees. The qualifications and academic posts for these 292 academic staff in the year under review are shown in Table 3.

Table 3: Qualifications of 292 academic and academic assistant staff

Qualification	No	Percentage (%)
1. PhD	70	23.9%
2. Master	71	24.3%
3. Bachelor	151	51.7%
Total	292	100 %

The academic posts of 95 academic staff compared to those of Mahidol University are shown in Table 4.

Table 4: Academic posts of 95 staff of TROPMED/Thailand

Academic Posts	Academic Posts Held by FTM Staff No. (%)	Academic Posts Held by Mahidol Staff No. (%)
Professors	5 (5.2%)	145 (6.7%)
Associate Professors	30 (31.6%)	755 (34.8%)
Assistant Professors	28 (29.4%)	769 (35.4%)
Lecturers	32 (33.7%)	501 (23.1%)
Total	95 (100.0%)	2.168 (100.0%)

5.1 Number of staff promoted or obtaining higher qualifications

Table 5: Number of staff promoted

Academic rank	Professors	= -
	Associate Professors	= 2
	Assistant Professors	= -
	Lecturers	= -
Career rank	Higher rank	= 24
Higher qualification	Higher degree	= 5
Total		= 31

5.2 Number of research projects and publications. TROPMED/Thailand staff undertook 134 research projects with total research grants of 113.7 million Baht and 131 published research papers.

Table 7: Number of research projects and publications

	New Project	On-going	Accomplished
Number of research projects	42 (31.3%)	69 (51.8%)	23 (16.9%)
Number of published papers	131		

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

7 (0.93%) staff took study leave for higher education. 660 staff (98.34%) attended training, meetings, seminars, and workshops in country and abroad. One staff member may have attended more than one training/meeting/seminar/workshop.

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

Category of staff development	In-country	Abroad	Total
Study leave	3 (0.8%)	4 (2.2%)	7 (1.7%)
Attending training courses Seminars, meetings workshops	567 (99.2%)	93 (97.8%)	660 (98.3%)
Number of staff	570 (100.0%)	97 (100.0%)	667 (100.0%)

5.4 Special talks / lectures

To develop and/or improve the knowledge of staff, 16 lunch talks/lectures on various topics for 715 attendces, 4 CME lectures (Continuing Medical Education) including 2 information technology training courses were organized for 82 attendances. 64 academic staff were invited to give lectures in 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, 78 nurses and 67 nurse assistants. Total out-patients treated number 69,775, with 2,054 admissions. 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 a field research on tropical diseases, and is located in Suan Phung District, Rachaburi Province.

2. The Tropical Diseases Research Centre, Kanchanaburi is one of the Faculty's centres for conducting tropical diseases research and is a field training center for students; it is located at the Kanchanaburi Campus of Mahidol University.

3. 17 computers were installed in the computer center for training and study, and for the administration of the Faculty of Tropical Medicine.

4. During the FY 2005/2006, renovations of the Faculty were conducted, including the Hospital for Tropical Diseases and Bangkok School of Tropical Medicine.

5. Since the International Guest House, with 66 rooms, opened, 1,114 students/guests/visitors from 26 countries were served in the FY 2005/2006.

WHO Collaborating Centre for Clinical Management of Malaria

Professor Polrat Wilairatana
Director of the Centre
E-MAIL : tmpwl@mahidol.ac.th

The activities performed under this report is 1 January - 31 December 2006

- The centre conducted 3 short training courses :
  1. Training course on management of malatia to Ache doctors from Indonesia in May 2006.
  2. The 4th international training course on management of malaria in September 2006.
  3. Training course on management of malaria in Sudan in November 2006.
- The centre sent experts to conduct the training courses on management of malaria in Timor Leste in April, 2006 and in Nepal in June 2006.
- The centre revised the final versions (edition 2006) of Regional guidelines for the management to of severe malaria in small and large hospitals in collaboration with WHO SEARO.
- Publications and other outcomes
  1. Regional guidelines for the management of severe malaria in small hospital (edition 2006). ISBN 92 9022 280.8
  2. Regional guidelines for the management of severe malaria in large hospital (edition 2006). ISBN 92 9022 281.6
- Collaborations with other organization/institutions
  1. with Ministry of Public Health, Thailand to revise doctor's guidelines in the management of malaria in Thailand.
  2. with WHO Collaborating Centre for Nursing and Midwfery Development, Faculty of Nursing, Siriraj Hospital and the Nursing Department, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Thailand
  3. with WHO Mekong Malaria Programme to conduct training course on management of malaria in Thailand.
- Support from WHO
  1. WHO/WHO SEARO staff visited the centre.
  2. The centre staff visited WHO offices in Timor Leste, Nepal and Sudan
  3. WHO SEARO supported fellows from SEARO countries to Participate in the training course on management of malaria in Thailand.

WHO Collaborating Centre for Environmental Management for Disease Vector Control in Sustainable Development

Assoc. Prof. Pratap Singhasivanon
Director of the Centre
(19 May 2005 - 25 December 2006)
E-MAIL: tmpsh@mahidol.ac.th

DURATION OF REPORT

1 January - 31 December 2006

WORK PERFORMED/ACTIVITIES IN RELATION TO THE TERM OF REFERENCE (TOR)

The Faculty of Tropical Medicine (FTM), which is the host institute for the WHO CC, has three main functions, (1) teaching and training, (2) research and (3) medical and academic services, with an emphasis on tropical diseases. FTM's activities are listed under two headings: (1) activities in direct/or indirect collaboration with WHO and (2) activities within the thematic areas defined in the ToR of this WHO CC.

TECHNICAL COLLABORATION

The Centre has collaborated with national and international institutes on research and training activities, namely:

- Ministry of Foreign Affairs, Thailand
- Ministry of Public Health, Thailand
- Bureau of Policy and Plans for National Resources and Environment, Thailand
- SEAMEO TROPMED Network
- Universita degli Studi di Brescia, Italy
- Japan International Corporation Agency (JICA), Japan
- Japan International Corporation of Welfare and Services (JICWELS), Japan
- Rockefeller Foundation
- Global Fund
- WHO Centre for Health Development, Kobe, Japan

ACADEMIC SERVICES/INFORMATION EXCHANGE

In 2006, the Centre provided scientific information and technical support in relation to disease-vector control to various institutes, both national and international. Such services included:

- Identification of mosquitoes, flies, Phebotomine sandflies, and other medically important insects
- Determination of insecticide efficacy, persistence and resistance for private and government sectors based on WHO standard protocols
- Providing scientific information, technical support and advice on vector-borne diseases, vector biology, field surveys and vector-control techniques to the Ministry of Public Health, Thailand, for example:
  - Determination of malaria vector status, *Anopheles sundaicus* in tsunami-affected areas in Phang Nga Province
  - Investigation of indigenous leishmaniasis in Nan and Phang Nga provinces
  - Identification of bulb mites infesting the ears of shallot handlers in Sri Saket Province.
  - Incrimination of *Aedes albopictus* as an additional vector of rural Bancroftian filariasis in Tak Province.
  - External Evaluation and Monitoring Process of the Mekong Basin Disease Surveillance (MBDS) Project supported by Rockefeller Foundation, June - August 2006
- External evaluation of the prevention and control of malaria project in the Lao People's Democratic Republic (Lao PDR) under the Global Fund to Fight AIDS, Tuberculosis and Malaria

(GFATM) covering the periods of Round I (May 2003-April 2006) and Round IV (July 2005-June 2006), 12 July – 4 August 2006

- Integration of disaster management and health promotion for environmental health and disease prevention in M.Sc. (Trop. Med.) and Ph.D. (Trop. Med.) curricula
- Establishment of Dengue Diagnostic Centre

CONFERENCE AND TRAINING

The Centre co-organized two international conferences:

(1) The 5th Seminar on Food- and Water-borne Parasitic Zoonoses (5th FBPZ) 28-30 November 2006, which was attended by 222 participants from 20 countries.

(2) Joint International Tropical Medicine Meeting 2006 and 6th Asia-Pacific Travel Health Conference (JITMM 2006- 6th APTHC) 29 November-1 December 2006, which was attended by 512 participants from 36 countries.

Short training courses related to the ToR of the Centre were conducted for various groups of health personnel from both local and international agencies. These courses were offered in partnership with national, regional, and international organizations and academic institutions. In 2006, the following short training courses were organized:

- Microscopic diagnosis for malaria and parasitic infections for 6 participants from Lao PDR, 1-3 March 2006
- Entomology and susceptibility testing for 10 participants from Lao PDR, 20 April-2 June 2006
- Tsunami recovery impact assessment and monitoring system (TRIAMS) workshop for 80 participants from India, Indonesia, Maldives, Myanmar, Sri Lanka, and Thailand, 3-5 May 2006
- Training course on partnership building capacity for healthy borders, 7 August-1 September 2006.
- GIS Disease Surveillance System in Mekong Region, Phase II: Regional training course on basic GIS for 12 participants from Cambodia, China, Lao PDR, Thailand, and Vietnam, 21 August-1 September 2006.
- GIS Disease Surveillance System in Mekong Region, Phase II: Advanced course on GIS for 12 participants from Cambodia, China, Lao PDR, Thailand ,and Vietnam, 24 October-3 November 2006.
- Training on global infectious disease control for Japanese doctors and health personnel, 2-20 October 2006.
- Training course on malaria prevention and control for participants from Mozambique, DPR Korea, and Vietnam, in collaboration with Bureau of Vector-borne Diseases, Department of Disease Control, Ministry of Public Health.
- Molecular and radioisotope-based techniques applied to malaria epidemiology for participants from Myanmar, 3 October-30 December 2006.

RESEARCH AND PUBLICATIONS

Ongoing research activities conducted by the Centre in relation to vector and environmental management of tropical diseases, including epidemiology and control methods under the year in review were:

- Efficacy of VectoBac®WDG, VectoLex®WDG and mixture of VectoBac®WDG and VectoLex®WDG in killing mosquito larvae inhabiting slum areas of Bangkok, 2005-2006
- Field application of *Bacillus thuringiensis israelensis* (B.t.i) (VectoBac®WDG) for the control of mosquito larvae in salt-marsh habitats in tsunami-affected areas, Phang Nga Province, Thailand: monitoring the reduction of adult density, 2006
- DENCO: towards successful dengue prevention and control, 2006-2008
- Geographical distribution of *Aedes albopictus* in Bangkok Metropolitan Area
- Emerging and re-emerging viral infectious diseases: prevention, diagnosis, treatment, and prognosis, 2006
- Efficacy of insecticide-impregnated products against dengue vector, *Aedes aegypti* in selected endmic areas of Thailand, 2006
- Epidemiological study of dengue infection in children in Ratchaburi Province, 2006
- Collaborative study to evaluate the operational programme of insecticide treated-bed nets for malaria control in Thailand, 2004-2006
- Monitoring of medical important brackish water snails in Thailand, 2004-2006
- Post-tsunami water quality survey in Phang Nga Province, Southern Thailand, 2006
- Application of GIS to the epidemiology of leptospirosis in endemic areas of Nakhon Ratchasima, Thailand, 2006
- Helminthic infection in tsunami-affected area: soil contamination and infection rates in the population
- Paragonimus population: morphology, molecular biology, enzymology, and epidemiological aspects
- Epidemiological study of Opisthorchis in Sa Kaew and Nan Provinces
- Discrimination of small liver and intestinal fluke eggs by ribosomal DNA-based PCR

RESEARCH PUBLICATIONS RELATED TO THE TOR OF THE CENTRE IN THE YEAR UNDER:

Apiwathnasorn C, Asavanich A, Komalamisra N, Samung Y, Prummongkol S, Kanjanopas K. The relationship between the abundance of Mansonia mosquitoes inhabiting a peat swamp forest and remotely sensed data. Southeast Asian J Trop Med Public Health 2006;37(3):463-7.

Apiwathnasorn C, Samung Y, Prummongkol S, Asavanich A, Komalamisra N. Surveys for natural host plants of Mansonia mosquitoes inhabiting Toh Daeng peat swamp forest, Narathiwat Province, Thailand. Southeast Asian J Trop Med Public Health 2006;37(2):279-82.

Apiwathnasorn C, Samung Y, Prummongkol S, Asavanich A, Komalamisra N, Mccall P. Bionomics studies of Mansonia mosquitoes inhabiting the peat swamp forest. Southeast Asian J Trop Med Public Health 2006;37(2):272-8.

Chanthavanich P, Luxemburger C, Sirivichayakul C, Lapphra K, Pengsaa K, Yoksan S, et al. Short report: immune response and occurrence of dengue infection in Thai children three to eight years after vaccination with live attenuated tetravalent dengue vaccine. Am J Trop Med Hyg 2006;75(1):26-8.

Develoux M, Dekumyoy P, Baygon E, Aractingi S. Imported gnathostomiasis acquired in Myanmar. Med Mal Infect 2006;36(6):340-2.

Jadsri S, Singhasivanon P, Kaewkungwal J, Sithiprasasna R, Siriruttanapruk S, Konchom S. Spatio-temporal effects of estimated pollutants released from an industrial estate on the occurrence of respiratory disease in Maptaphut Municipality, Thailand. Int J Health Geogr 2006;5:48.

Kwanbunjan K, Mas-Ngammueng R, Chusongsang P, Chusongsang Y, Maneekan P, Chantaranipapong Y, et al. Health and nutrition survey of tsunami victims in Phang-Nga Province, Thailand. Southeast Asian J Trop Med Public Health 2006;37(2):382-7.

Limmathurotsakul D, Chaowagul W, Chierakul W, Stepniewska K, Maharjan B, Wuthiekanun V, et al. Risk factors for recurrent melioidosis in northeast Thailand. Clin Infect Dis 2006;43(8):979-86.

Okabayashi H, Thongthien P, Singhasvanon P, Waikagul J, Looareesuwan S, Jimba M et al. Keys to success for a school-based malaria control program in primary schools in Thailand. Parasitol Int 2006;55(2): 121-6.

Piyaphanee W, Krudsood S, Silachamroon U, Pornpininworakij K, Danwiwatdecha P, Chamnachanan S, et al. Travelers' malaria among foreigners at the Hospital for Tropical Diseases, Bangkok, Thailand - a 6-year review (2000-2005). Korean J Parasitol 2006;44(3):229-32.

Sri-aroon P, Lohachit C, Harada M, Chusongsang P, Chusongsang Y. Malacological survey in Phang-Nga Province, southern Thailand, pre- and post-Indian Ocean tsunami. Southeast Asian J Trop Med Public Health 2006; 37(Suppl. 3): 104-9.

Stuetz W, McGready R, Cho T, Prapamontol T, Biesalski HK, Stepniewska K, et al. Relation of DDT residues to plasma retinol, alpha-tocopherol, and beta-carotene during pregnancy and malaria infection: a case-control study in Karen women in northern Thailand. Sci Total Environ 2006;363(1-3):78-86.

Sukthana Y. Toxoplasmosis: Beyond animals to humans. Trends Parasitol 2006;22(3): 137-42.

Tawatsin A, Asavadachanukorn P, Thavara U, Wongsinkongman P, Bansidhi J, Boonruad T, et al. Repellency of essential oils extracted from plants in Thailand against four mosquito vectors (Diptera: Culicidae) and oviposition deterrent effects against *Aedes aegypti* (Diptera: Culicidae). Southeast Asian J Trop Med Public Health 2006;37(5):915-31.

Vesaratchavest M, Tumapa S, Day NPJ, Wuthiekanun V, Chierakul W, Holden MTG, et al. Nonrandom distribution of *Burkholderia pseudomallei* clones in relation to geographical location and virulence. J Clin Microbiol 2006;44(7):2553-7.

Waikagul J, Dekumyoy P, Anantaphruti MT. Taeniasis, cysticercosis and echinococcosis in Thailand. Parasitol Int 2006;55(Suppl):S175-80.

Waikagul J, Dekumyoy P, Yoonuan T, Praevanit R. Conjunctiva philophthalmosis: a case report in Thailand. Am J Trop Med Hyg 2006;74(5):848-9.

Wuthiekanun V, Chierakul W, Langa S, Chaowagul W, Panpitpat C, Saipan P, et al. Development of antibodies to *Burkholderia pseudomallei* during childhood in melioidosis-endemic northeast Thailand. Am J Trop Med Hyg 2006;74(6): 1074-5.

Wuthiekanun V, Chierakul W, Rattanalertnavee J, Langa S, Sirodom D, Wattanawaitunechai C, et al. Serological evidence for increased human exposure to *Burkholderia pseudomallei* following the tsunami in Southern Thailand. J Clin Microbiol 2006;44(1):239-40.

SUCCESSFUL RESEARCH HAS BEEN STANDARDIZED AND TRANSFERRED TO THE COMMUNITY AND COMMERCIAL LEVELS:

- Petty patent for natural mosquito repellent cream formula
- Laboratory for insecticide susceptibility testing and evaluation of insecticides and repellents" was established in 2006 as a service centre for insecticide testing for public health use based on the guidelines provided by the WHO Pesticide Evaluation Scheme (WHOPES)

Office Of The Dean

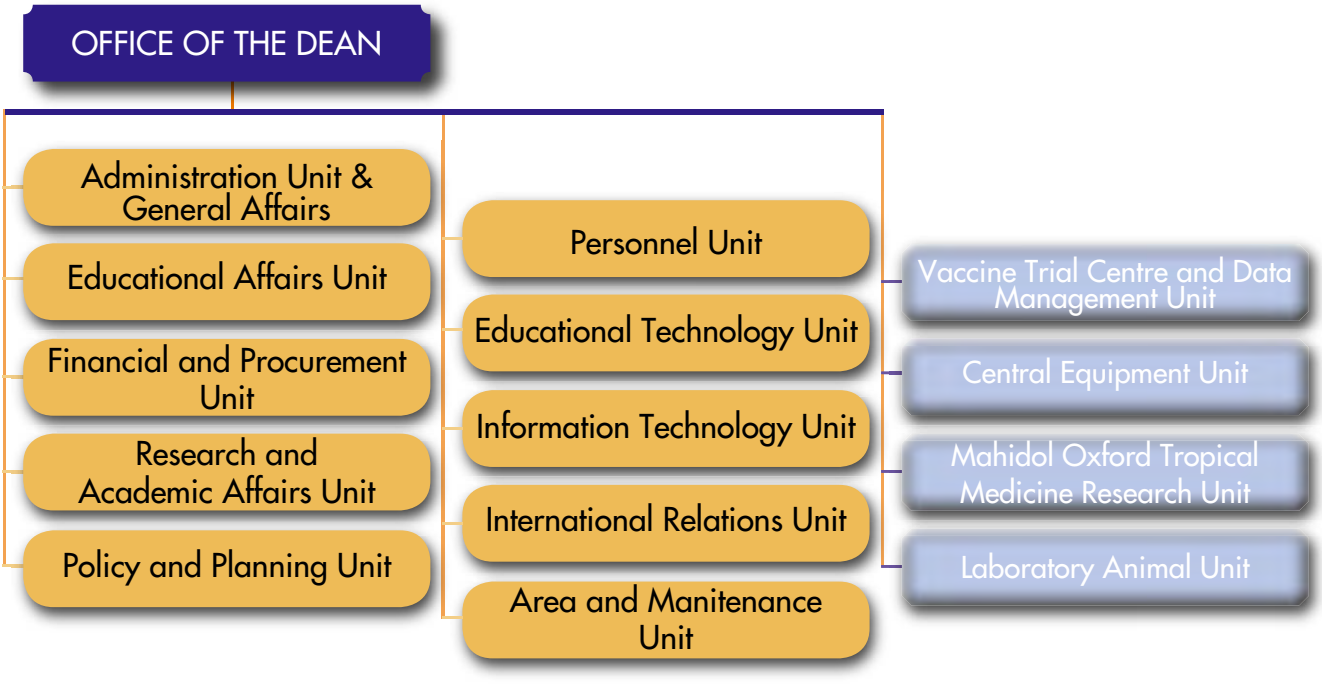
Telephone: 0 2354 9100-19 ext. 1326, 1328,
Fax: 0 2354 9139

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

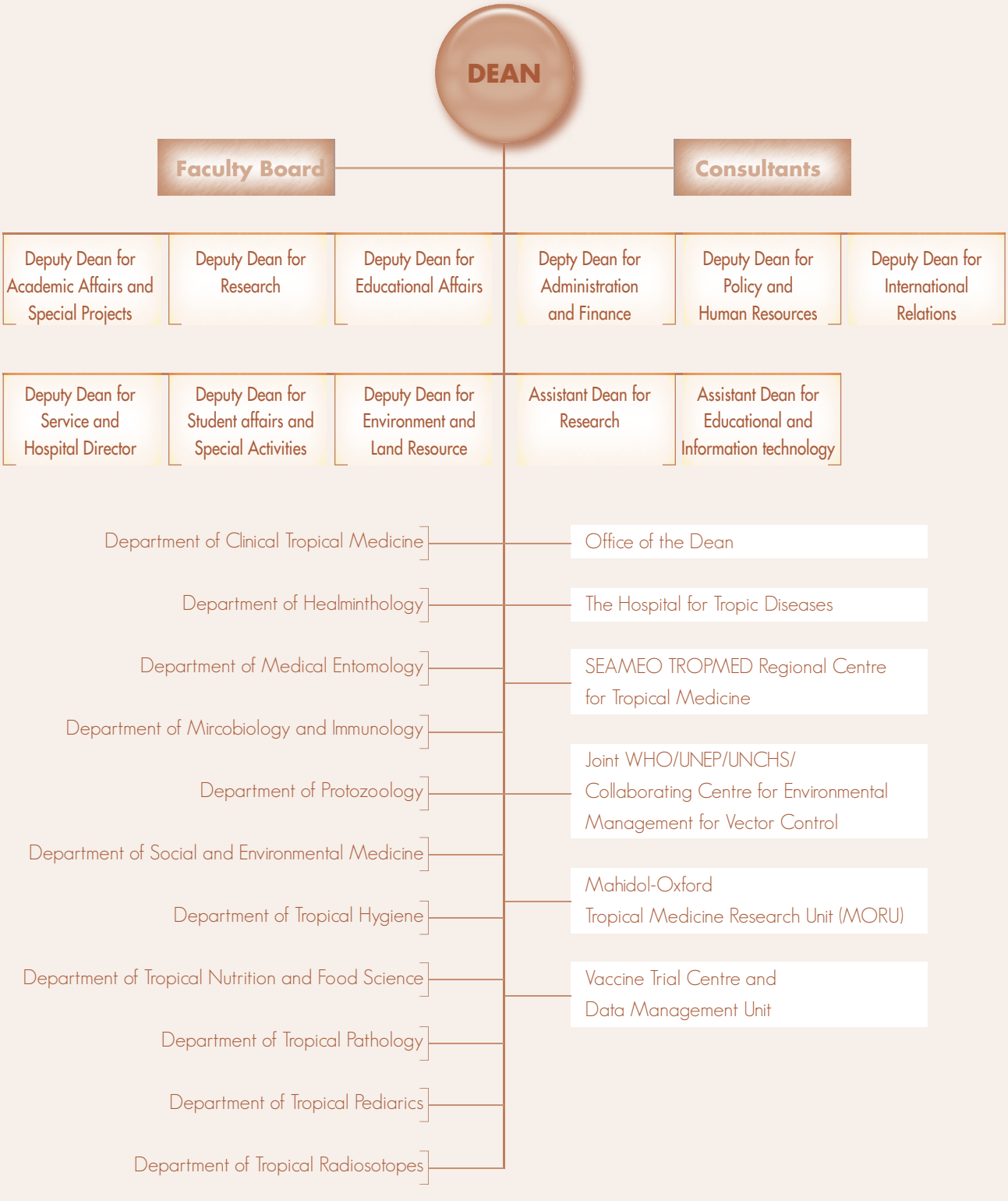
The Office of the Dean is a support unit facilitating the major tasks of the Faculty, such as teaching, research, academic services, and hospital services, to meet the goals of the Faculty. The Office of the Dean functions under the authority and supervision of the Secretary of the Faculty and Deputy Deans with related duties. It consists of 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.

"PLEASED TO BE OF SERVICE"

ORGANIZATION CHART



Organization Chart



Consultants

1. Prof. Emeritus Chamlong Harinasuta
2. Prof. Emeritus Danai Bunnag
3. Prof. Emeritus Tan Chongsuphajaisiddhi
4. Prof. Emeritus Chaisin Viravan
5. Prof. Emeritus Prayong Radomyos
6. Assoc. Prof. Mario Riganti
7. Prof. Emeritus Mukda Trishnananda
8. Prof. Emeritus Santasiri Sornmani
9. Prof. Emeritus Sirivan Vanijjanonta
10. Prof. Emeritus Wanpen Chaicumpa
11. Assoc. Prof. Supranee Changbumrung
12. Dr. Lalive Jitkarun
13. Assoc. Prof. Yupa Rongsriyam
14. Assoc. Prof. Suvanee Supavej
15. Dr. Porn Pongnitanond
16. Dr. Vute Winothai
17. Dr. Pornlerd Jitpratoom
18. Dr. Manoch Aoo-wutthipong
19. Dr. Supat Panyanukul
20. Dr. Tienchai Kijsanayothin
21. Dr. Nithipat Siripan
22. Dr. Preecha Pinyopornpanich
23. Dr. Arun Sattayapisal
24. Dr. Suporn Kullapat
25. Dr. Thiti Sricharoenchai
26. Ms. Jirawan Akaranuchart
27. Mrs. Piengraw Itthisawatphan
28. Mrs. Kiriya Kartudom
29. Amporn Kongthaweelerd

Visiting Professors FY 2006

	Name	Institute	Country
1.	Prof. Andrew Thompson	Murdoch University	Australia
2.	Dr. Hannes Wickert	University of Heidelberg	Germany
3.	Dr. E.B. Dobernstyn	WHO Regional Office for the Western Pacific, Manila, Philippines	Philippines
4.	Prof. David Ferguson	Oxford University	United Kingdom
5.	Dr. Gareth D.H. Turner	Wexwam Pare Hospital	United Kingdom
6.	Assist. Prof. Chris Beyrer	John Hopkins Bloomberg School of Public Health	USA
7.	Dr. Donald Pinkston Francis	Global Solution for Infectious Diseases	USA
8.	Dr. Jose Esparza	Bill and Melinda Gates Foundation	USA

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. Porntip Petmitr	Vice-Chair
3.	Assoc. Prof. Punnee Pitisuttithum	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 Chiabchalard	Representative, Department of Protozoology
10.	Assist. Prof. Talabporn Harnroongroj	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 Nontprasert	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/AssistantSecretary

No.	Date	Courses	Country/No. Participants
1.)	6 February - 31 May 2006	Pre-course Training for DTM&H and DAP&E	Lao PDR / 2
2.)	2 February - 31 March 2006	Training Course on Clinical Epidemiology and Management of HIV/AIDS	Japan / 5, Lao PDR / 3, Vietnam / 2, Cambodia / 2, Myanmar / 1, Thailand / 2
3.)	1-23 March 2006	Training course on Microscopic Diagnosis for Malaria and Parasites	Lao PDR / 6
4.)	20 - 24 March 2006	Orientation Workshop for Trainers on Service Availability Mapping (SAM)	India / 7, Bangladesh / 3, USA / 1, Bhutan / 1, Sri Lanka / 3, Myanmar / 2, Maldives / 1, Indonesia / 3, Nepal / 3, Timor-Leste / 2, Switzerland / 1, Thailand / 2
5.)	3 April - 31 May 2006	Pre-course Training for MSc.	Lao PDR / 1
6.)	7 -17 May 2006	Asian Clinical Tropical Medicine	USA / 14, Germany / 2, Canada / 1, UK / 2, Austria / 1, Japan / 1, Korea / 1, Lao PDR / 1, Cambodia / 1
7.)	20 April - 2 June 2006	Training Course on Entomology and Susceptibility Testing	Lao PDR / 10
8.)	20 - 23 June 2006	Dengue Training Course for Hong Kong Hospital Authority	Hong Kong / 8
9.)	26 June - 7 July 2006	Training Course Management of Severe Malaria for Banda Ache	Indonesia / 3
10.)	3 - 9 August 2006	Overseas Program for Master of Tropical Medicine 2006 (Nagasaki University, Japan)	Japan / 12
11.)	21 August – 1 September 2006	Basic course on Application of GIS in Disease Surveillance	Vietnam / 2, Cambodia / 2, Lao PDR / 2, China / 3, Thailand / 3
12.)	25 - 29 September 2006	International Training Course on Management of Malaria	Bhutan / 11, Switzerland / 1, Lao PDR / 3, Myanmar / 2, Japan / 4, Philippines / 1, Cambodia / 3, Burundi / 1, Solomon Island / 1
13.)	4 - 29 September 2006	Training Course on Clinical Emerging and Re-emerging Infectious Diseases Control	Japan / 6
14.)	2 - 20 October 2006	Training Course on Infectious Diseases Control	Japan / 3

MOUs/Agreements between Faculty of Tropical Medicine and Overseas Institutes

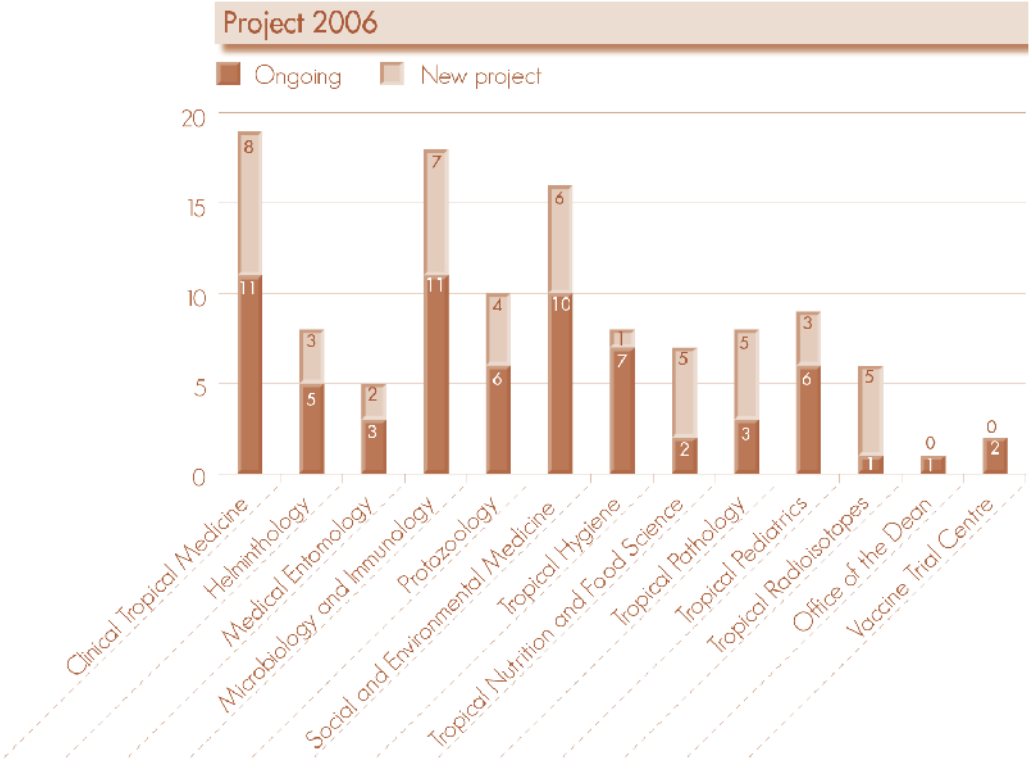
FY 2006 (Revised)

No.	Institute	Duration	Start	Finish	Remarks
1.	Chiangrai Regional Hospital, MoPH	5 yrs	15 June 2004	14 June 2009	MOU
2.	Department of Medical Sciences, MoPH	5 yrs	28 May 2004	27 May 2009	MOU
3.	Canadian Food Inspection Agency, Government of Canada,Saskatoon,Canada		3 Sep. 1998	Not specified	MOU
4.	University of Leicester, United Kingdom		1 April 2002	present	MOU
5.	Freie Universitat at Berlin		30 May 1985	present	Agreement
6.	The Swiss Tropical Institute, Basel, Switzerland		3 June 1998	present	MOU
7.	University of Innsbruck, Austria		12 May 1992	present	Agreement
8.	Nagasaki University, Japan	5 yrs	1 Nov. 1999	Automatic extended every 5 yrs	Agreement
9.	University of Shizuoka School of Pharmaceutical Science	5 yrs	2005	3000	MOU
10.	Ubon Rajathanee University	5 yrs	Sep 2004	2008	MOU
11.	The Wellcome Trust-Mahidol University, Oxford Tropical Medicine Research Programme	5 yrs	Sep. 2004	Sep. 2010	MOU
12.	Japan International Corporation of Welfare Services	1 month	Feb.2005	March 2005	MOU
13.	Southeast Asian Ministers of Education Organization (SEAMEO) and the Government of Thailand		18 May 1971		MOU
14.	The University of Texas Health Science Center at Houston	3 yrs	15 Nov. 2005	2009	Agreement
15.	University of Sumatera Utara	5 yrs	15 May 2006	2011	MOU
16.	University of Brescia	5 yrs	6 Nov. 2006	2011	Agreement

No.	Institutions	Countries
1.	Department of Microbiology Faculty of Medicine, Nursing and Health Sciences, Monash University	Australia
2.	Department of Parasitology, School of Veterinary Science, Murdoch University of South Street, Murdoch, Western Australia	Australia
3.	Department of Pathology, Faculty of Medicine, University of Sydney	Australia
4.	Instiute Pasteur Unit of Molecular Immunology Parasites	France
5.	Department of Parasitology and Tropical hygiene, Heidelberg University, Germany	Germany
6.	Department of Respiratory Diseases, Research Institute, International Medical Center of Japan, Tokyo	Japan
7.	Department of Biomedical Sciences, College of Life and Health Sciences, Chubu University	Japan
8.	Institute of Tropical Medicine, Nagasaki University	Japan
9.	Department of Human Genetics School of International Health Graduate School of Medicine, The University of Tokyo	Japan
10.	Division of Tropical Diseases and Parasitology, Department of Infectious Diseases, Kyorin University School of Medicine, Tokyo	Japan
11.	Division of Cellular and Molecular Immunology, Center of Molecular Biosciences, University of the Ryukus, Okinawa	Japan
12.	Department of International Biomedical Sciences, Division of International Health, Graduate School of Medicine, University of Tokyo, Tokyo	Japan
13.	Department of Appropriate Technology Development and Transfer, Research Institute, International Medical Center of Japan	Japan
14.	Biomaterials Center, National Institute for Materials Science	Japan
15.	Research Institute for Cell Engineering, National Institute of Advanced Industrial Science and Technology	Japan
16.	Department of Medical Zoology, Kagawa Medical University	Japan
17.	Department of Appropriated Technology Development and Transfer, Research Institute, International Medical Center of Japan	Japan
18.	Department of Immunology, University of Stockholm	Sweden
19.	Department of Immunology, The Wenner Gren Institute, Stockholm University	Sweden
20.	Department of Pharmacology and Therapeutics, Liverpool School of Tropical Medicine	United Kingdom
21.	Nuffield Department of Pathology, University of Oxford, John Radcliffe Hospital, UK	United Kingdom
22.	Division of Electron Microscopy, Department of Cellular Pathology, The John Radcliff Hospital, Oxford University	United Kingdom
23.	The University of Texas Health Science Center at Houston	U.S.A.
24.	Pathology and Laboratory Medicine Graduate Program in Immunology & Microbial Pathogenesis Weill Medical College of Cornell University	U.S.A.
25.	Division of Enteric Infections, National Institute of Hygiene and Epidemiology, Ha noi, Viet Nam	Viet Nam

Visitors FY 2006

	Name	Country	Date
1.	Dr. Fernanda Nevas	Republic of Mozambique	16-29 January 2006
2.	Dr. Ivete Dimande	Republic of Mozambique	16-29 January 2006
3.	Dr. Maria Helena Da Costa	Republic of Mozambique	16-29 January 2006
4.	Dr. Antonio Almenjane	Republic of Mozambique	16-29 January 2006
5.	Dr. Catarina Mbule	Republic of Mozambique	16-29 January 2006
6.	Dr. Ines Tomo	Republic of Mozambique	16-29 January 2006
7.	Dr. Azelia Ernesto Novela	Republic of Mozambique	16-29 January 2006
8.	Dr. Armindo Tonela	Republic of Mozambique	16-29 January 2006
9.	Dr. Impasso Impasso	Republic of Mozambique	16-29 January 2006
10.	Dr. Remmi Forrat	France	21 June 2006
11.	Dr. Anh Wartel Tram	France	21 June 2006
12.	Ms. Nadia Souag	France	21 June 2006
13.	Mr. Vincent	France	21 June 2006
14.	Dr. Birger Torllfors	Sweden	10 October 2006
15.	Dr. Bo Claesson	Sweden	10 October 2006
16.	Dr. Hans Carlberg	Sweden	10 October 2006
17.	Major Dr. Elmar Elsner	Germany	18 Sep. - 15 Oct. 2006
18.	Prof. David O. Freedman	UK	2 November 2006
19.	Mr. Deepak Thapa	India	13 - 14 Nov. 2006
20.	Dr. Madhu Ghimire	India	13 - 14 Nov. 2006
21.	Prof. Huw Smith	UK	27 November 2006
22.	Dr. Ugen Dophu	Bhutan	28 December 2006
23.	Mr. Naichu	Bhutan	28 December 2006
24.	Dr. Gup Kanjur	Bhutan	28 December 2006
24.	Ms. Jambay Zangmo	Bhutan	28 December 2006
26.	Dr. Duptho Sonam	Bhutan	28 December 2006
27.	Ms. Sangay Lham	Bhutan	28 December 2006
28.	Mr. Passing	Bhutan	28 December 2006
29.	Ms. Yangchen Pelden	Bhutan	28 December 2006
30.	Dr. Lungen Z. wangchuk	Bhutan	28 December 2006
31.	Mr. Tashi Tobgay	Bhutan	28 December 2006


Project 2006
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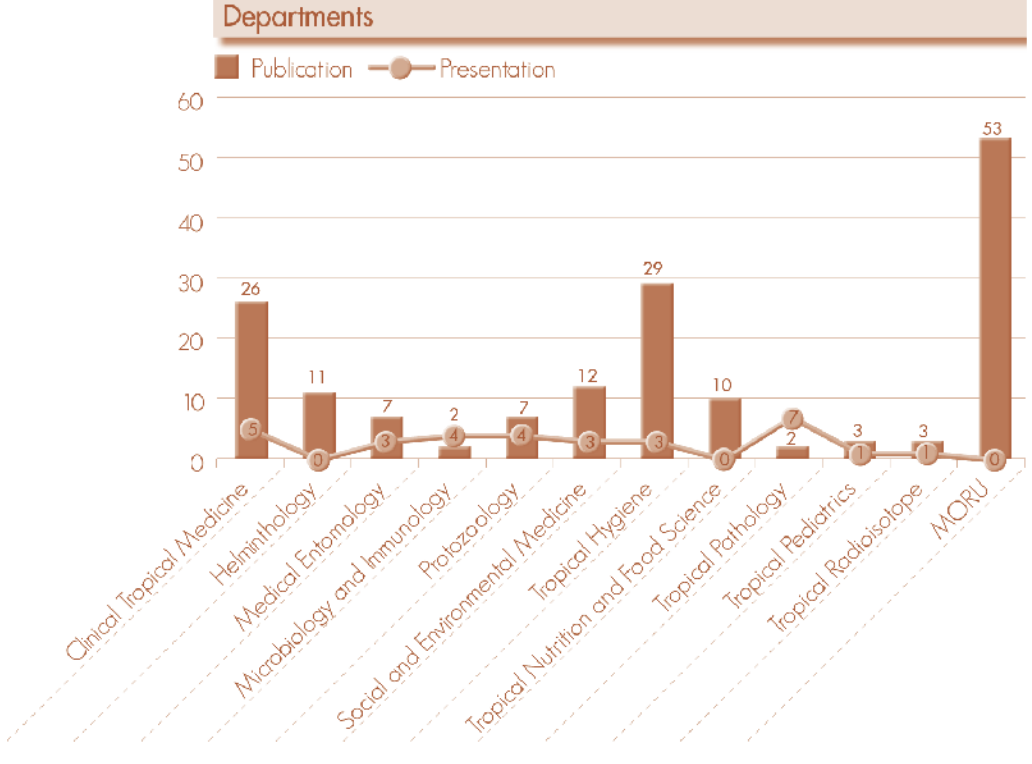
Clinical Tropical Medicine
Helminthology
Medical Entomology
Microbiology and Immunology
Protozoology
Social and Environmental Medicine
Tropical Hygiene
Tropical Nutrition and Food Science
Tropical Pathology
Tropical Pediatrics
Tropical Radioisotopes
Office of the Dean
Vaccine Trial Centre


Departments
Publication
Presentation
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Clinical Tropical Medicine
Helminthology
Medical Entomology
Microbiology and Immunology
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Social and Environmental Medicine
Tropical Hygiene
Tropical Nutrition and Food Science
Tropical Pathology
Tropical Pediatrics
Tropical Radioisotope
MORU

Ongoing Research Projects of the Faculty of Tropical Medicine in 2006

No.	Research Title	Grant	Principal Investigator
Department of Clinical Tropical Medicine			
1	A multicenter, randomized, double-blind, phase II study to evaluate the safety, tolerance and efficacy of multiple doses of SCH 56592 versus fluconazole in the treatment of oropharyngeal candidiasis (OPC) in HIV-positive patients	Schering Plough Research Institute	Prof. Punnee Pitisuttithum
2	Open-label, treatment protocol for the safety and efficacy of SCH 56592 (Oral Suspension) in the treatment of invasive fungal infections	Schering Plough Research Institute	Prof. Punnee Pitisuttithum
3	Observational probe study of *in vitro* immune response parameters to candidate HIV-1 vaccine antigens among subject from Thailand	MERCK and Co., Inc	Prof. Punnee Pitisuttithum
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)	MERCK and Co., Inc	Prof. Punnee Pitisuttithum
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	The Henry M. Jackson Foundation for The Advancement of Military Medicine, Inc. and The Government of Thailand Ministry of Public Health	Prof. Punnee Pitisuttithum
*6.	A cross-sectional study to screen for and generate broadly neutralizing monoclonal antibodies from HIV infected individuals	International AIDS Vaccine Initiative (IAVI)	Prof. Punnee Pitisuttithum
*7	A randomized, International, double-blinded (with in-house blinding), controlled with GARDASIL™, tolerability, immunogenicity, and efficacy study of a second generation human papillomavirus (HPV) L1 virus-like particle (VLP) vaccine administered to 16-to-26-year-old women		Prof. Punnee Pitisuttithum
8	Research and development on drugs and diagnostic tools for diagnosis and treatment of tropical diseases in Thailand	Government Budget	Prof. Sornchai Looareesuwan
9	Liver megaproject Phase I: from basic research to education science and applied technology in clinical study	National Science and Technology Development Agency	Dr.Wichai Ekataksin
10	Genotyping of *Plasmodium vivax*; development of field methods	Wellcome Trust of Great Britain	Assist. Prof. Mallika Imwong
11	Development of field methods and investigators of the molecular basis of Sulfonamide resistance in *Plasmodium vivax*	Wellcome Trust of Great Britain	Assist. Prof. Mallika Imwong

* New project

No.	Research Title	Grant	Principal Investigator
Department of Clinical Tropical Medicine (Continued)			
12	Novel point mutations in the dihydrofolate reductase gene of *Plasmodium vivax*: evidence for sequential selection by drug pressure	Wellcome Trust of Great Britain	Assist. Prof. Mallika Imwong
* 13	Development of molecular technique for evaluation of Mefloquine resistance in *Plasmodium falciparum* in Asia	Commission on Higher Education & The Thailand Research Fund	Assist. Prof. Mallika Imwong
14	Cell derived microparticles in malaria infection	Wellcome Trust of Great Britain	Assist. Prof.Kesinee Chotivanich
* 15	Effect of serum lipid concentration on the efficacy of lumefantrine against falciparum malaria: *in vitro*	Faculty of Tropical Medicine, Mahidol University	Assist. Prof. Kesinee Chotivanich
* 16	A phase III, randomized, non-inferiority trial, to assess the efficacy and safety of dihydroartemisinin + piperaquine (DHA+PPQ, Artekin) in comparison with Artesunate+Mefloquine (AS+MQ) in patients affected by acute, uncomplicated *Plasmodium falciparum* malaria	MMV (Medicine for Malaria Venture) and Sigma Tao	Prof. Sasithon Phukrittayakamee
*17	Gnathostomiasis and correlation of skin test with *Gnathostoma spinigerum* specific antigen and IgE	Faculty of Tropical Medicine, Mahidol University	Assist. Prof. Wirach Maek-a- nantawat
* 18	Comparison of the safety and efficacy of a unique intravenous iron preparation (VIT-45) versus oral iron in the treatment of Anemia in non-dialysis dependent chronic kidney diseases	Luitpold Pharmaceutical, Inc, USA	Assoc. Prof. Yupaporn Wattanagoon
* 19	Bioequivalence study of generic filgrastim injection to an innovator Newpogen (Filgrastim 300mcg/0.5 ml syringe) in healthy Thai volunteers	International Bio Service, Co., Ltd.	Assoc. Prof. Yupaporn Wattanagoon
Department of Helminthology			
20	Helminthic infection in a tsunami-affected area: soil contamination and infection rates in the population	Brescia University, Italy	Assoc. Prof. Wanna Maipanich
21	Research and development of the intergrated project on chemotherapy and control of malaria and parasitic infections	Government Budget	Assoc. Prof. Jitra Waikagul
22	Research and development of an application to purify *Bithynia* snail antigen in serodiagnosis of opisthorchiasis	Government Budget	Assoc. Prof. Jitra Waikagul
23	Study on *Paragonimus* population: morphology, molecular biology, enzymology and epidemiology aspects	Ministry of Foreign Affairs	Assoc. Prof. Jitra Waikagul
24	Control of soil-transmitted helminth through primary health care activities	Tropical Disease Trust	Assoc. Prof. Jitra Waikagul

* New project

No.	Research Title	Grant	Principal Investigator
Department of Helminthology (Continued)			
* 25	Development of a school-based approach on emerging infectious disease control with emphasis on avian influenza in Thailand	International Medicine Center of Japan, Ministry of Health, Labor and Welfare, Japan	Assoc. Prof. Jitra Waikagul
* 26	Trematodes infection in human of Nghia Phu and Nghia Lac Commune, Nghia Hung, Nam Dinh Province, Vietnam	DANIDA	Assoc. Prof. Jitra Waikagul
* 27	Discrimination of small liver and intestinal flukes eggs by ribosomal DNA-based PCR	JICA	Assoc. Prof. Jitra Waikagul
Department of Medical Entomology			
28	DNA bank of mosquito vectors of Thailand	Government Budget	Assoc. Prof. Chamnarn Apiwathnasorn
29	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	Brescia University, Italy	Dr. Yuwadee Trongtokit
30	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	Faculty of Tropical Medicine	Dr. Yuwadee Trongtokit
* 31	Survey and study on geographical distribution of *Aedes albopictus* in Bangkok Metropolitan	Faculty of Tropical Medicine, Mahidol University	Mr. Yudthana Samung
* 32	Genetic structure of natural population of *Aedes albopictus*; urban, rural and sylvatic strain	Faculty of Tropical Medicine, Mahidol University	Ms. Rutcharin Potiwat
Department of Microbiology and Immunology			
33	Analysis of sequence polymorphism of T-cell epitope regions, Th2R and Th3R on *Plasmodium falciparum* circumsporozoite proteins in Thai isolates	The Thailand Research Fund	Prof. Srisin Khusmith
34	Cytokine gene polymorphism in severe malaria	The Thailand Research Fund	Prof. Srisin Khusmith
35	Relationship between cytokine gene polymorphism and severity of falciparum malaria	The Thailand Research Fund	Prof. Srisin Khusmith
36	Polymophism of Pf EMP1 extracellulae domain in Thai isolates causes severe malaria uncomplicated *P. falciparum* malaria	The Thailand Research Fund	Prof. Srisin Khusmith
37	Chemokine gene polymorphism and their susceptibility to tuberculoses	The Thailand Research Fund and Commission on Higher Education	Prof. Srisin Khusmith
38	Dengue infection rates in *Aedes* related to environmental factors	Ministry of Public Health	Assoc. Prof. Wipawee Champangern

* New project

No.	Research Title	Grant	Principal Investigator
Department of Microbiology and Immunology (Continued)			
39	Development of strategies for serovar identification of *Leptospira* sp. based on specific gene sequences within rfb locus	Thailand-Tropical Diseases Research Programmes	Assist. Prof. Thareerat Kalambaheti
40	Study the immunoreactive membrane protein of Leptospirosis	Vejdusit Foundation	Assist. Prof. Thareerat Kalambaheti
* 41	Production of recombinant Leptospiral protein antigen for serodiagnosis	Faculty of Tropical Medicine, Mahidol University	Assist. Prof. Thareerat Kalambaheti
* 42	Epidemiology of travelers' diarrhea in Thailand	University of Texas, USA	Assist. Prof. Thareerat Kalambaheti
43	Development of dipstick assay technology during *Plasmodium falciparum* as model	Mahidol University	Miss Jarinee Panitchakorn
44	Identification of genus- and species- specific antigens of *Aeromonas* spp. by Western blotting with mouse polyclonal antibodies	Faculty of Tropical Medicine	Assist. Prof. Yuwadee Mahakunkijcharoen
* 45	Development of a monoclonal antibody test for identification of pathogenic *Aeromonas* spp	Government Budget	Assist. Prof. Yuwadee Mahakunkijcharoen
46	Determination of the receptor binding specificity of the H5N1 viruses isolated from Thailand	Faculty of Tropical Medicine	Dr. Pornsawan Leaungwutiwong
* 47	Influence factors program the development of CD4+ Regulatory T cells in autoimmune mouse model and The Thailand	Commission on Higher Education Research Fund	Dr. Pornsawan Leaungwutiwong
* 48	Serodiagnosis of scrub typhus and meliodosis by dual immunoperoxidase test	Faculty of Tropical Medicine, Mahidol University	Assoc. Prof. Varee Wongchotigul
* 49	Detection of specific antibodies to recombinant dengue virus DEIII/NS1 dengue viral protein using indirect enzyme immunoassay	Faculty of Tropical Medicine, Mahidol University	Dr. Akanitt Jittmittraphap
* 50	Preparation of human monoclonal antibody that Neutralizes tetanus toxin using phage display technology	Commission on Higher Education and The Thailand Research Fund	Dr. Nitaya Intrawattana
Department of Protozoology			
51	Purification and characterization of DNA polymerase B of *Plasmodium falciparum* and its role in base excision repair	Thailand-Tropical Diseases Research Programmes	Assoc. Prof. Porntip Petmitr
52	Ultrastructure effects on *Toxoplasma gondii* tachyzoites after pyrimethamine and artemisinin derivative administration in animal model	The Thailand Research Fund	Assoc. Prof. Yaowalark Sukthana
53	Viability study of *Giardia* cysts in water used in Thai frozen food industry	DAAD	Assoc. Prof. Yaowalark Sukthana
54	Biological contamination-free Thai frozen food	National Research Council of Thailand	Assoc. Prof. Yaowalark Sukthana
* 55	Research and development of biological contamination-free frozen food to world kitchen	National Research Council of Thailand	Assoc. Prof. Yaowalark Sukthana
* 56	*Toxoplasma gondii* genotyping in domestic and wild felids in Thailand	Commission on Higher Education	Assoc. Prof. Yaowalark Sukthana

* New project

No.	Research Title	Grant	Principal Investigator
Department of Protozoology (Continued)			
* 57	Molecular characterization of *Plasmodium falciparum* polynucleotide kinase	TRF (RGJ Program)	Assoc. Prof. Porntip Petmitr
*58	Development of differential diagnosis of *Entamoeba histolytica*, *Entamoeba dispar* and *Entamoeba moshkovskii* and study on virulent genes of *Entamoeba histolytica* based on arbitrarily primed PCR and Real-time PCR	Government Budget	Assoc. Prof. Porntip Petmitr
59	PCR assays for detection of *Toxoplasma gondii* in Thai commercial meat products	Mahidol University	Ms. Rachatawan Chiabchalard
60	Detection of protozoal viability contamination of water used in Thai frozen food industry by cell culture PCR technique	Faculty of Tropical Medicine	Ms. Chantira Sutthikornchai
Department of Social and Environmental Medicine			
61	Intergrated studies of human and animal leptospirosis in endemic areas of Nakhon Ratchasima, Thailand	Government Budget	Assoc. Prof. Wijitr Fungladda
62	Collaborative study to evaluated operational programme of insecticide treated bednets for malaria control in Thailand	WHO	Assoc. Prof. Piyarat Butraporn
63	Modifying mosquito population age structure to eliminate dengue transmission	Gates Foundation	Assoc. Prof. Piyarat Butraporn
64	Factors associating with completion and default among DOTS and self-administered therapy (SAT) for treatment of TB	WHO	Assoc. Prof. Kamolnetr Okanurak
65	Construction of monoclonal antibody phage library for developing avian influenza virus' diagnostic test	Commission on Higher Education and The Thailand Research Fund	Assist. Prof. Pongrama Ramasoota
66	Mimotope identification from monoclonal antibody Leptospiral serovar specific using phage display technique	Commission on Higher Education and The Thailand Research Fund	Assist. Prof. Pongrama Ramasoota
67	Rapid detection of quinolone resistant *Mycobacterium tuberculosis* using molecular techniques	Thailand-Tropical Diseases Research Programmes	Assist. Prof. Pongrama Ramasoota
68	Rapid detection of multidrug resistant *Mycobacterium tuberculosis* (MDR-TB) from indoor air using molecular techniques	Thailand-Tropical Diseases Research Programmes	Assist. Prof. Pongrama Ramasoota
69	Rapid detection of *Legionella pneumophilla* from indoor air using molecular techniques	Faculty of Graduate Studies, MU	Assist. Prof. Pongrama Ramasoota
* 70	Development of a suveillance system for obesity among school children of high risk groups	WHO	Assist. Prof. Voranuch Wangsuphachart
* 71	Trans-boundary risk assessment (human health risk, ecological and environmental risk of the Mekong River-surface water)	Mekong River Commission Secretariat: MRCS	Assist. Prof. Voranuch Wangsuphachart
72	Integrated research network on Tachin-Maeklong Basin	Mahidol University	Assist. Prof. Wanchai Phatihattakorn
* 73	Monitoring and treatment of surface and ground water in tsunami affected area, Ban Nam Khem, Phang-Nga Province, Thailand	Brescia University, Italy	Dr. Prapin Tharnpoophasiam

* New project

No.	Research Title	Grant	Principal Investigator
Department of Social and Environmental Medicine (Continued)			
* 74	Health watch on an emerging of fresh- and brackish-water snails that transmit human parasitic diseases, after tsunami in Phang-Nga Province, Southern Thailand	Brescia University, Italy	Mrs. Pusadee Sri-aroon
* 75	Preventive behaviors associated with avian influenza in poultry farmers	Government Budget	Mr. Wiwat Wanarangsikul
* 76	Modifying mosquitoes age structure to eliminate dengue haemorrhagic fever: community participation in dengue haemorrhagic fever prevention & control		Assoc. Prof. Piyarat Butraporn
Department of Tropical Hygiene			
77	Application of GIS in monitoring multi-drug resistant malaria in Greater Mekong Subregion of Southeast Asia(III)	EC RBM-WHO	Assoc. Prof. Pratap Singhasivanon
78	Integrated GIS disease surveillance (Ids) System in Mekong Region	Rockefeller Foundation	Assoc. Prof. Pratap Singhasivanon
79	A phase III trial of Aventis Pasteur live recombinant ALVAC-HIV (vCP 1521) priming with VaxGen gp120 B/E (AIDSVAX™ B/E) boosting in HIV-uninfected the advancement of Thai-adults (Data Management)	The Henry M. Jackson Foundation for Military Medicine, Inc.	Assist. Prof. Joranit Kaewkungwal
80	A phase III trial of Aventis Pasteur live recombinant Thai adults	Walter Reed Army Institute of Research	Assist. Prof. Jaranit Kaewkungwal
81	Field based study of reappearance *Plasmodium vivax* malaria cases in the area near Thai-Myanmar border Suanphung Ratchaburi Province	Faculty of Tropical Medicine	Mr. Wanchai Maneeboonyoung
82	Health behavior and risk factor of soil transmitted helminth and malaria infection in primary schoolchildren in Saiyok District, Kanchanaburi Province	Faculty of Tropical Medicine	Ms. Pannamas Maneekarn
83	Epidemiology and health education program and treatment evaluation of *Pediculosis capitis* with Leech Lime cream in school children, Suan Phung District, Ratchaburi Province	Faculty of Tropical Medicine	Mr. Nipon Thanyavanich
* 84	Molecular rapid serotypic identification of dengue viruses based on Real-Time PCR by using SYBR Green I and hybridization probes	Faculty of Tropical Medicine	Dr. Natthanej Luplerdlop
Department of Tropical Nutrition and Food Science			
85	Identification of gene alterations in breast cancer	BIOTEC	Assoc. Prof. Songsak Petmitr
*86	Determination of gene alterations in colon cancer using arbitrarily primed polymerase chain reaction and gene cloning	Government Budget	Assoc. Prof. Songsak Petmitr
*87	Detection of proteins and obesity genes mutation in Thai over weight and obese children	Government Budget	Assoc. Prof. Rungsunn Tungtrongchitr
*88	Development of health behaviors and nutritional status of the tsunami victims in Phang-nga Province	Brescia University, Italy	Assist. Prof. Karunee Kwanbunjan

* New project

No.	Research Title	Grant	Principal Investigator
Department of Nutrition and Food Sciences (Continued)			
89	Purification and characterization of β-glucosidose specifically hydrolyzing iridoid glucoside from Thai plants	Commission on Higher Education	Dr. Dumrongkiet Arthan
* 90	Studies on correlation of serum vitamin B12, serum folic acid, red blood cell folate, plasma homocysteine, micronucleus frequency in human lymphocytes, DNA methylation, and nutritional status in aging and young adults Thai people	Faculty of Tropical Medicine	Dr. Pornrutsami Jintaridhi
* 91	Polymorphism of ATP binding cassette transporter A1 (ABCA1) in relation to lipid profiles of overweight/obese Thais	Mahidol University	Dr. Anong Kitjaroentham
Department of Tropical Pathology			
92	Pathology and immunohistochemistry of liver in AIDS: a necropsy study	Mahidol University	Assoc. Prof. Parnpen Viriyavejakul
93	Causes of diarrhea in HIV/AIDS patients	Mahidol University	Assoc. Prof. Parnpen Viriyavejakul
94	*Plasmodium falciparum* induce IgE class switching	Swedish International Development Corporation A. (SIDA)	Assoc. Prof. Yaowapa Maneerat
* 95	A murine model of cerebral malaria, histopathology, immunohistochemistry and electron microscopy	Thailand Center for Excellent of life Science (TCELS)	Assoc. Prof. Emsri Pongponratn
* 96	The effects of antimalarial drugs induced changes on *Plasmodium falciparum* and Pf-infected red blood cells Ultrastructure	The Thailand Research Fund (RGJ)	Assoc. Prof. Emsri Pongponratn
* 97	Immunohistopathological studies of cytokine profiles in liver tissue of AIDS with opportunistic infections and HIV – infected patients: a necropsy study	The Thailand Research Fund (RGJ)	Assoc. Prof. Emsri Pongponratn
* 98	Pathogenesis of acute renal failure in severe malaria: ultrasturctural and immunoapathological	The Thailand Research Fund (RGJ)	Assoc. Prof. Emsri Pongponratn
* 99	Time consuming and penetration efficacy of dengue virus type 2 (D2-16681) pass through the peritrophic membrane to midgut epithelial cell in *Aedes aegypti* mosquitoes	Faculty of Tropical Medicine	Ms. Supattra Suwanmanee
Department of Tropical Pediatrics			
100	A phase II, pilot, randomized, open-label, single-center study to evaluate immunogenicity and safety after PCECV rabies vaccine (Rabipur®) administered concomitantly with Japanese encephalitis vaccine as a pre-exposure regimen in 12 to 18 month old toddlers in Thailand	Chiron Vaccines, Co., Ltd.	Prof. Arunee Sabchareon
101	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)	Department of Tropical Pediatrics	Assoc. Prof. Pornthep Chanthavanich

* New project

No.	Research Title	Grant	Principal Investigator
Department of Tropical Pediatrics (Continued)			
102	Evaluation of long-term immunity against Japanese encephalitis in children vaccinated with Japanese encephalitis vaccine (Extension of study M49P2)	Department of Tropical Pediatrics	Assoc. Prof. Pornthep Chanthavanich
103	Accuracy assessment of using WHO criteria in diagnosis of dengue infection	Department of Tropical Pediatrics	Assoc. Prof. Pornthep Chanthavanich
104	Epidemiological study of dengue infection in children age 3-10 years in Ratchaburi Province	Ministry of Public Health	Assoc. Prof. Pornthep Chanthavanich
105	Development of surveillance system for under five mortality in Samut Sakhon Province, Thailand	WHO	Assoc. Prof. Chukiat Sirivichayakul
* 106	Dengue antibodies level and incidence of dengue Infection in preschool-aged children		Assoc. Prof. Krissana Pengsaa
* 107	Favirab™ post prescription event monitoring	Sanofi Pasteur Co., Ltd.	Assoc. Prof. Pornthep Chanthavanich
* 108	Evaluation of long term immunity against rabies in children vaccinated with different pre-esposure regimens of PCEC (Rabipur®) and the immunity after two IM infections of PCEC (Rabipur®) post exposure in the children previously vaccinated with PCEC pre-exposure regimens (I49P6)		Assist. Prof. Kriengsak Limkittikul
Department of Tropical Radioisotopes			
109	Studies on radiation effect on mouse macrophage cell line (RAW 264.7) and radioprotective effect by various Thai medicinal plants	Faculty of Tropical Medicine	Ms. Cheeraratana Cheeramakara
* 110	Studies on heme oxygenase-1 activation in malaria Infected mice after artemisinin derivatives treatment	Department of Radioisotopes	Ms. Cheeraratana Cheeramakara
* 111	Studies on vitamin B12 and folic acid contents in foods	Department of Radioisotopes	Assist. Prof. Channarong Sanghirun
* 112	Studies on folic acid contents in fruit juice	Department of Radioisotopes	Mrs. Wanyarat Thanomsak
* 113	Studies on vitamin B12 and folic acid contents in Thai monks	Department of Radioisotopes	Mrs. Korbkit Cherdchu
* 114	Comparison of folic acid in human with assay method and radio assay method	Department of Radioisotopes	Assist. Prof. Channarong Sanghirun
Office of the Dean			
15	Research management innovation in the Faculty of Tropical Medicine, Mahidol University	The Thailand Research Fund	Prof. Sasithon Phukrittayakamee

* New project

No.	Research Title	Grant	Principal Investigator
Vaccine Trial Centre			
116	A phase III trial to determine the efficacy of AIDSVAX™ B/E vaccine in intravenous drug users in Bangkok, Thailand	AIDSVAX	Bangkok AIDS Vaccine Evaluation Group (Prof. Punnee Pitisuttithum)
117	A phase III trial of Aventis Pasteur live recombinant ALVAC-HIV (VCP1521) priming with Vaxgen gp 120 B/E (AIDSVAX B/E) boosting in HIV-uninfected Thai adults	Walter Reed Army Institute of Research	Dr. Supachai Rueknggam (Assoc. Prof. Punnee Pitisuttithum)

* New project

Faculty of Tropical Medicine International Publications 2006 in ISI Web of Science Database

Impact Factor from JCR : Science Edition 2005 - ISI Database
Time Cited on 12 April 2007 - ISI Database

No.	List of Publication	Impact Factor	Time Cited
1	Anuntagool N, Wuthiekanun V, White NJ, Currie BJ, Sermswan RW, Wongratanacheewin S, Taweechaisupapong S, Chaiyaroj SC, Sirisinha S. Lipopolysaccharide heterogeneity among *Burkholderia pseudomallei* from different geofraphic and clinical origins. *Am J Trop Med Hyg* 2006;74:348-52.	2.482	1
2	Ashley EA, Lwin KM, McGready R, Simon WH, Phaiphun L, Proux S, Wangseang N, Taylor W, Stepniewska K, Nawamaneerat W, Thwai KL, Barends M, Leowattana W, Olliaro P, Singhasivanon P, White NJ, Nosten F. An open label randomized comparison of mefloquine-artesunate as separate tablets vs. a new co-formulated combination for the treatment of uncomplicated multidrug-resistant falciparum malaria in Thailand. *Trop Med Int Health* 2006; 11(11):1653-60.	2.021	0
3	Ashley EA, McGready R, Singhasivanon P, Nosten F, Carrara V, Price R. *In vivo* sensitivity monitoring of mefloquine monotherapy and artesunate-mefloquine combinations for the treatment of uncomplicated falciparum malaria in Thailand in 2003. *Trop Med Int Health* 2006; 11(12):1898-9.	2.021	0
4	Ashley EA, Stepniewska K, Lindegardh N, McGready R, Hutagalung R, Hae R, Singhasivanon P, White NJ, Nosten F. Population pharmacokinetic assessment of a new regimen of mefloquine used in combination treatment of uncomplicated falciparum malaria. *Antimicrob Agents Chemother* 2006; 50(7):2281-5.	4.379	2
5	Biagini GA, Viriyavejakul P, O'neill PM, Bray PG, Ward SA. Functional characterization and target validation of alternative complex 1 of *Plasmodium falciparum* mitochondria. *Antimicrob Agents Chemother* 2006; 50(5): 1841 - 51.	4.379	0
6	Blacksell SD, Doust JA, Newton PN, Peacock SJ, Dat NP, Dondorp AM. A systematic review and meta-analysis of the diagnostic accuracy of rapid immunoochromatographic assays for the detection of dengue virus IgM antibodies during acute infection. *Trans R Soc Trop Med Hyg* 2006; 100:775-84.	1.665	0
7	Blacksell SD, Khounsy S, Phetsouvanh R, Newton PN. A simple and inexpensive container for the transport of biological specimens in limited resource situations. *Trans R Soc Trop Med Hyg* 2006; 100: 1084-6.	1.665	0
8	Blacksell SD, Newton PN, Bell D, Kelley J, Mammen MP, Jr., Vaughn DW, Wuthiekanun V, Sungkakum A, Nisalak A, Day NP. The comparative accuracy of 8 commercial rapid immunochromatographic assays for the diagnosis of acute dengue virus infection. *Clin Infect Dis* 2006;42: 1127-34.	6.510	3
9	Blacksell SD, Smythe L, Phetsouvanh R, Dohnt M, Hartskeerl R, Symonds M, Slack A, Vongsouvath M, Davong V, Lattana O, Phongmany S, Keolouangkot V, White NJ, Day NP, Newton PN. Limited diagnostic capacities of two commercial assays for the detection of *Leptospira* immunoglobulin M antibodies in Laos. *Clin Vaccine Immunol* 2006; 13: 1166-9.	NA	0
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International Publications 2006 (non ISI)

No.	List of Publication
1	Apiwathnasorn C, Asavanich A, Komalamisra N, Samung Y, Prummongkol S, Kanjanopas K. The relationship between the abundance of *Mansonia* mosquitoes inhabiting a peat swamp forest and remotely sensed data. *Southeast Asian J Trop Med Public Health* 2006;37(3):463-7.

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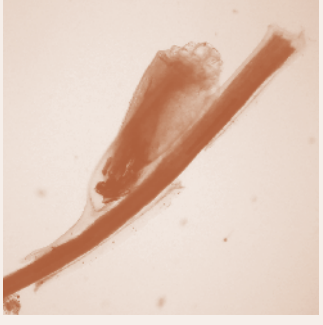
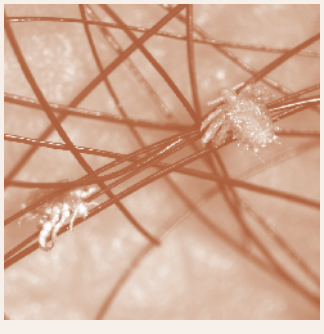
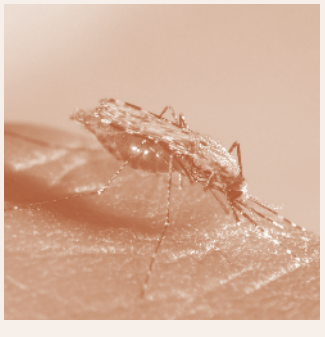
Research Abstracts

Faculty of Tropical Medicine, Mahidol University

2006







LABORATORY DIAGNOSIS OF MALARIA INFECTION – A SHORT REVIEW OF METHODS

Kesinee Chotivanich[1], Kamolrat Silamut[2] and Nicholas PJ Day[2,3]

[1] *Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand;*
[2] *Wellcome Trust-Mahidol University-Oxford Tropical Medicine Programme, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand;*
[3] *Center for Clinical Vaccinology and Tropical Medicine, Nuffield Department of Clinical Medicine, Churchill Hospital, University of Oxford, Oxford, United Kingdom*

Malaria is one of the most important tropical infectious diseases. The incidence of malaria worldwide is estimated to be 300-500 million clinical cases each year with a mortality of between one and three million people worldwide annually. The accurate and timely diagnosis of malaria infection is essential if severe complications and mortality are to be reduced by early specific antimalarial treatment. This review details the methods for the laboratory diagnosis of malaria infection.

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AZITHROMYCIN COMBINATION THERAPY WITH ARTESUNATE OR QUININE FOR THE TREATMENT OF UNCOMPLICATED *PLASMODIUM FALCIPARUM* MALARIA IN ADULTS: A RANDOMIZED, PHASE 2 CLINICAL TRIAL IN THAILAND

Harald Noedl[1,3], Srivicha Krudsood[2], Kobsiri Chalermratana[2], Udomsak Silachamroon[2], Wattana Leowattana[2], Noppadon Tangpukdee[2], Sornchai Looareesuwan[2], Robert Scott Miller[1], Mark Fukuda[1], Krisada Jongsakul[1], Sabaithip Sriwichai[1], Jacqueline Rowan[4], Helen Bhattacharyya[4], Colin Ohrt[5], Charles Knirsch[4]

[1] *Department of Immunology and Medicine, USAMC-AFRIMS.*
[2] *Hospital for Tropical Diseases, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand.*
[3] *Department of Specific Prophylaxis and Tropical Medicine, Medical University of Vienna, Austria.*
[4] *Clinical Research and Development, Pfizer, New York, New York.*
[5] *Division of Experimental Therapeutics, WRAIR, Silver Spring, Maryland.*

Background: Because antimalarial drug resistance is spreading, there is an urgent need for new combination treatments for malaria, which kills >1 million people every year. Azithromycin is a macrolide antibiotic that is particularly attractive as an antimalarial because of its safety in children and the extensive experience with its use during pregnancy. METHODS: We undertook a randomized, controlled, 28-day inpatient trial involving patients with acute, uncomplicated Plasmodium falciparum malaria. We compared the safety and efficacy of 2 azithromycin-artesunate combinations and 2 azithromycin-quinine regimens in adults with malaria. Treatments were as follows: cohort 1 received 3 days of azithromycin (750 mg twice daily) plus artesunate (100 mg twice daily), cohort 2 received 3 days of azithromycin (1000 mg once daily) plus artesunate (200 mg once daily), cohort 3 received 3 days of azithromycin (750 mg twice daily) plus quinine (10 mg/kg twice daily), and cohort 4 received 3 days of azithromycin (500 mg 3 times daily) plus quinine (10 mg/kg 3 times daily). The enrollment target was 25 evaluable subjects per group.

RESULTS: The 28-day cure rates were similarly high in the artesunate and the standard-dose quinine cohorts: 92.0% (95% confidence interval [CI], 74.0%-99.0%), 88.9% (95% CI, 70.8%-97.6%), and 92.0% (95% CI, 74.0%-99.0%), for cohorts 1, 2, and 4, respectively. Late R1 treatment failures were seen in each of the artesunate and the standard-dose quinine cohorts. The cure rate for cohort 3 was 73.3% (95% CI, 44.9%-92.2%). In this cohort, 3 early treatment failures led to the termination of enrollment after 16 subjects had been enrolled. With mean parasite and fever clearance times (+/-SD) of 34+/-13 h and 20+/-20 h, the artesunate combinations were found to have led to a significantly (P<.001) faster clinical and parasitological improvement than occurred in the quinine cohorts (74+/-32 h and 43+/-37 h, respectively). Treatment-related adverse events were significantly more common in the quinine cohorts (P<.001). No deaths or drug-related serious adverse events were observed. In vitro results suggest that the treatment failures--particularly in the low-dose quinine cohort--were associated with decreased susceptibility to quinine, as well as with mefloquine cross-resistance.

CONCLUSIONS: These data suggest that azithromycin-artesunate, even when given only once daily for 3 days, and azithromycin-quinine, given 3 times daily, are safe and efficacious combination treatments for uncomplicated falciparum malaria, and they deserve additional study in special patient populations. ∅

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EMERGENCE AND CLEARANCE OF GAMETOCYTES IN UNCOMPLICATED *PLASMODIUM FALCIPARUM* MALARIA

Watcharapong Piyaphanee[1,2], Srivicha Krudsood[2,3], Noppadon Tangpukdee[1], Wipa Thanachartwet[1,2], Ucomsak Silachamroon[1,2], Nantaporn Phophak[2], Chatnapra Duangdee[2], Orathai Haoharn[2], Suparat Faithong[2], Polrat Wilairatana[1,2], Wattana Leowattana[1,2] & Sornchai Looareesuwan[1,2]

[1] *Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand;*
[2] *Hospital for Tropical Diseases, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand;*
[3] *Department of Tropical Hygiene, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand*

We reviewed the records of 1,175 patients with uncomplicated Pladmodium falciparum malaria to determine the prevalence of gametocytemia. All patients were admitted and received artemisinin combination therapy. Blood films were checked daily until discharge. Circulating gametocytes were observed in 240 (20.2%) of patients, and in most case (222 of 240, 92.5%) gametocytemia was detected during the first 24 hours after admission. Gametocytes were first seen in 174 cases on admission, in 24 cases at 12 hours, and in 24 cases at 24 hours. The longest interval between admission and first appearance of gametocytes was 192 hours. The median gametocyte clearance time was 163 hours (range = 12-806) in the 219 patients in whom gametocytemia resolved. However, 21 patients (9.8%) still had gametocytemia on discharge. Gametocytemia generally is present within the first 24 hours after admission, and emerges in only 1.9% of patients later on during treatment with artemisinin. ∅

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SENSITIVE AND INEXPENSIVE MOLECULAR TEST FOR FALCIPARUM MALARIA: DETECTING *PLASMODIUM FALCIPARUM* DNA DIRECTLY FROM HEAT-TREATED BLOOD BY LOOP-MEDIATED ISOTHERMAL AMPLIFICATION

Leo LM Poon[1], Bonnie WY Wong[1], Edmund HT Ma[1], Kwok H Chan[1], Larry MC Chow[2], Wimal Abeyewickreme[3], Noppadon Tangpukdee[4], Kwok Y Yuen[1], Yi Guan[1], Sornchai Looareesuwan[4] and JS Malik Peiris[1]

[1] *Department of Microbiology, The University of Hong Kong, Hong Kong SAR;*
[2] *Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University, Hong Kong SAR;*
[3] *Department of Parasitology and Molecular Medicine Unit, Faculty of Medicine, University of Kelaniya, Sri Lanka;*
[4] *Department of Clinical Tropical medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand;*

Background: Malaria is one of the most important parasitic infections in humans. A sensitive diagnostic test for malaria that could be applied at the community level could be useful in programs to control the disease. The aim of the present work was to develop a simple, inexpensive molecular test for *Plasmodium falciparum*.

Methods: Blood was collected from controls (n = 100) and from patients diagnosed with falciparum malaria infection (n = 102), who were recruited to the study. Heat-treated blood samples were tested by a loop-mediated isothermal amplification (LAMP) assay for *P. falciparum*. Results were interpreted by a turbidity meter in real time or visually at the end of the assay. To evaluate the assay, DNA from these samples was purified and tested by PCR. Results from the LAMP and PCR assays were compared.

Results: The LAMP assay detected *P. falciparum* directly from heat-treated blood. The quantitative data from the assay correlated to the parasite counts obtained by blood-film microscopic analyses. When we used the PCR assay as the comparison

method, the sensitivity and specificity of the LAMP assay were 95% and 99%, respectively.

Conclusions: Unlike PCR, the LAMP assay does not require purified DNA for efficient DNA amplification, thereby reducing the cost and turnaround time for *P. falciparum* diagnosis. The assay requires only basic instruments, and assay positivity can be verified by visual inspection. ∅

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POSSIBLE ACUTE COINFECTIONS IN THAI MALARIA PATIENTS

Tasawan Singhsilarak[1], Sawatdirak Phongtananant[1], Mongkol Jenjittikul[2], George Watt[1,3], Noppadon Tangpakdee[1], Nantaporn Popak[4], Kobsiri Chalermrut[4], Sornchai Looareesuwan[1]

[1] *Department of Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand;*
[2] *Department of Medical Sciences, Ministry of Public Health, Nonthaburi, Thailand;*
[3] *Department of Medicine, Hawaii AIDS Clinical Research Program, University of Hawaii, Manoa, Honolulu, Hawaii, USA;*
[4] *Hospital for Tropical Diseases, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand*

Patients who acquire malaria in Thailand's mountainous border regions are at increased risk for other infections. However, systematic searches for duel infections in malaria-infected individuals have not been previously performed. We therefore conducted serodiagnostic testing for dengue virus infection, murine typhus, scrub typhus and leptospirosis in *Plasmodium falciparum*-infected individuals in Thailand. Sera from 194 malaria patients with a median age of 24 years were tested. No antibody titers diagnostic of dengue virus infection were demonstrated, but 29 (15%) of patients had serological evidence of scrub typhus, 45 (23.2 %) patients had evidence of murine typhus, and 15 (7.7%) sera tested positive for leptospirosis. Our serological results suggest that duel infections are not uncommon in malaria acquired in Thailand. However, our results must be confirmed by prospective studies aimed at demonstrating the causative organisms. Mixed infections would have multiple implications for clinicians, including unexpected clinical findings and apparent poor responses to antimalarial treatment in patients thought only to have malaria. ∅

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DOWN-REGULATION OF TIGHT JUNCTION mRNAS IN HUMAN ENDOTHELIAL CELLS CO-CULTURED WITH *PLASMODIUM FALCIPARUM*-INFECTED ERYTHROCYTES

Pannapa Susomboon[1,2], Yaowapa Maneerat[2], Paron Dekumyoy[3], Thareerat Kalambaheti[4], Moritoshi Iwagami[5], Kanako Komaki-Yasuda[5], Shin-ichiro Kawazu[5], Noppadon Tangpukdee[1], Sornchai Looareesuwan[1], Shigeyuki Kano[5]

[1] *Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, 420/6 Ratchavithi Road, Bangkok 10400, Thailand;*
[2] *Department of Tropical Pathology, Faculty of Tropical Medicine, Mahidol University, 420/6 Ratchavithi Road, Bangkok 10400, Thailand;*
[3] *Department of Helminthology, Faculty of Tropical Medicine, Mahidol University, 420/6 Ratchavithi Road, Bangkok 10400, Thailand;*
[4] *Department of Microbiology and Immunology, Faculty of Tropical Medicine, Mahidol University, 420/6 Ratchavithi Road, Bangkok 10400, Thailand;*
[5] *Department 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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MINOR LIVER PROFILE DYSFUNCTIONS IN *PLASMODIUM VIVAX, P. MALARIAE* AND *P. OVALE* PATIENTS AND NORMALIZATION AFTER TREATMENT

Noppadon Tangpukdee[1], Vipa Thanachartwet[1], Srivicha KRudsood[1], Nutthanej Luplertlop[1], Karnchana Pornpininworakij[1], Kobsiri Chalermrut[1], Sasikarn Phokham[1], Shigeyuki Kano[2], Sornchai Looareesuwan[1] Polrat Wilairatana1

[1] *Faculty of Tropical Medicine, Mahidol University, Bangkok, 10400, Thailand;*
[2] *Department of Appropriate Technology Development and Transfer, Research Institute, International Medical Center of Japan, Tokyo, Japan*

Liver function tests were performed in 61 vivax, 54 malariae and 15 ovale malaria patients who wereadmitted to Bangkok Hospital for Tropical Diseases between 2001 and 2004. The objective of the study was to evalu-ate changes in hepatic biochemical indices before and after treatment with artemisinin derivatives. On admission andprior to treatment, hepatic dysfunction was found among the 3 groups. Serum liver function tests and physical exami-nations were performed weekly during the 28-day follow-up period. Initially elevated serum bilirubin and diminishedalbumin returned to normal within 2 weeks of treatment. Serum alkaline phosphatase and aminotransferases returnedto within normal limits within 3 weeks. We conclude that patients with Plasmodium vivax, P. malariaeand P. ovaleinfections had slightly elevated serum bilirubin, aminotransferase and alkaline phosphatase levels, and hypoalbu-minemia. These minor abnormalities returned to normal within a few weeks after treatment with therapies based onartemisinin derivatives. Key words:Plasmodium vivax, Plasmodium malariae, Plasmodium ovale, malaria, liver profile dysfunction,artemisinin derivatives. ∅

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CROSS-CLADE REACTIVITY OF HIV-1-SPECIFIC T-CELL RESPONSES IN HIV-1-INFECTED INDIVIDUALS FROM BOTSWANA AND CAMEROON

Gupta SB, Mast CT, Wolfe ND, Novitsky V, Dubey SA, Kallas EG, Schechter M, Mbewe B, Vardas E, Pitisuttithum P, Burke D, Freed D, Mogg R, Coplan PM, Condra JH, Long RS, Anderson K, Casimiro DR, Shiver JW, Starus WL

An effective HIV type 1 (HIV-1) vaccine will likely require elicitation of broadly reactive cell-mediated immune (CMI) responses against divergent HIV-1 clades. We compared anti-HIV-1 T-cell immune responses among 363 unvaccinated adults infected with diverse HIV-1 clades. Response rates to clade B Gag and/or clade B Nef in Botswana (95%) and Cameroon (98%) were similar when compared with those in countries previously studied, including Brazil (92%), Thailand (96%), South Africa (96%), Malawi (100%), and the United States (100%). Substantial cross-clade cell-mediated immune responses in Botswana and Cameroon confirm previous findings in a larger, more genetically diverse collection of HIV-1 samples. ∅

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COMPARISON OF ONE WEEK WITH TWO WEEK REGIMENS OF AMPHOTERICIN B BOTH FOLLOWED BY FLUCONAZOLE IN THE TREATMENT OF CRYPTOCOCCAL MENINGITIS AMONG AIDS PATIENTS

Somsit Tansuphaswadikul[1], Wirach Maek-a-Nantawat[2] , Benjaluck Phonrat[2], Lamom Boonpok[1], Aneley Getahun[2] and Punnee Pitisuttithum[2]

[1] *Bamrasnaradura Infectious Disease Institute, Department of Disease Control, Nonthaburi, Thailand;*
[2] *Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand*

Background: Amphotericin B treatment in cryptococcosis requires daily hospital visits or admission. Its toxicities and hospital costs have been concerned. Short course amphotericin B regimen warrants to be evaluated.

Objectives: To compare the safety and efficacy of one-week (AmB1) with two-week (AmB2) amphotericin B both followed by fluconazole.

Methods: 57 AIDS with cryptococcal meningitis were randomly assigned to either AmB1 or AmB2. Microbiological and clinical clearances were the outcomes of the study.

Results: The treatment success at 6 weeks was 63.3% in AmB1 and 70.4 % in AmB2 (p= 0.574). Clinical assessment at week 10 and renal toxicities were not significantly different between both regimens. Mortality rate was 14% however, 75% of deaths were in AmB2.

Conclusions: AmB1 was comparably effective and safe as the standard AmB2 regimen in treatment of AIDS related cryptococcal meningitis. It can be an alternative regimen to lower hospital based care and cost effective for source limiting health care centers.

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CROSS SECTIONAL VOLUNTEERS' SATISFACTION SURVEY IN PHASE III PRIME-BOOST HIV PREVENTIVE VACCINE TRIAL IN THAILAND

T Woratanarat[1], PA Morgan[1], RM Paris[1], N Sirijongdee[1], M Benenson[1], P Singharaj[1], P Pitisutthitham[2], S Rerks-Ngarm[3] and JH Kim[1]

[1] *Department of Retrovirology, US Army Medical Component, Armed Forces Research Institute of Medical Sciences, Bangkok, Thailand;*
[2] *Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand;*
[3] *Department of Disease Control, Ministry of Public Health, Bangkok, Thailand*

Background: A vaccine for the prevention of HIV infection remains an urgent need as part of the efforts to control the HIV pandemic. This Phase III trial using 'prime-boost' vaccine strategy with ALVAC-HIV (vCP 1521) and AIDSVAX gp 120 B/E has enrolled and vaccinated 16,000 HIV uninfected volunteers in Thailand. Volunteers' satisfaction is believed to be one of key factors for achieving good retention of volunteers. Here, we conducted a site survey of study volunteer satisfaction.

Objectives: To assess volunteers' satisfaction with participating clinical sites in terms of service, staff, facilities, and volunteers' attitude to the trial. Factors influencing volunteers' satisfaction were explored.

Methods: A cross-sectional survey was conducted at 4 of 8 clinical sites using an anonymous voluntary sample and a standardized questionnaire during October-December 2005. Data collected from each volunteer included gender, visit number, a 5-point satisfaction scale scored for 4 aspects from 10 questions, along with comments. Descriptive statistics, parametric and/or non-parametric tests were used as appropriate, as well as multiple logistic regression analysis to explore potential factors.

Results: There were 532 participants from 4 sites located in both study provinces. 54.8% were men, and 85% were in the immunization phase of the study. All sites were evaluated with average scores more than 80% (range 81.5-89.3), but there were significant differences in total score among sites (P<0.05) and between provinces (P<0.01), consistent across most of sub-categorical scores. Regression analysis showed potential model to predict sum of score in each aspect varying from 68-85%(R2) including site, gender,and several potential interactions between variables. No difference in total score and subgroups between those in the vaccination or follow-up phases was detected. Interestingly, significant differences in scores were strongly, associated with gender

throughout the analysis (P=0.03). Males were tented to give higher scores than females in the study, Which may suggest gender related differences in either treatment of volunteers or perception of treatment of the volunteers.

Conclusion: In conducting large-scale HIV vaccine clinical trials, investigators should periodically evaluate factors that may impact volunteers' satisfaction and indirectly affect trial retention. Well-planned time series satisfaction survey should be beneficial. ∅

Presented at: AID Vaccine o6 , 29 August - 1 September 2006, Amsterdam, the Netherlands.

EFFICACY AND SAFETY OF GENERIC FIXED-DOSE COMBINATION OF STAVUDINE, LAMIVUDINE AND NEVIRAPINE (GPO-VIR®) IN ADVANCED HIV INFECTION

Aneley Getahun[1] , Somsit Tansuphasawadikul[2], Varunee Desakorn[1], Jittima Dhitavat[1], Punnee Pitisuttithum[1]

[1] *Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand;*
[2] *Bamrasnaradura Infectious Disease Institute, Department of Disease Control, Nonthaburi, Thailand*

Objectives: To assess the efficacy and safety of generic fixed-dose combination of stavudine, lamivudine and nevirapine; GPO-vir® in advanced HIV infection.

Methods: Open-label combined prospective and retrospective study involving 102 HIV infected patients with baseline CD4cell count <100 cells/mm^3. All patients received GPO-vir® for 48 weeks. The CD4 cell count and plasma viral load (pVL) was measured at 48 weeks.

Results: The median baseline CD4 cell count and pVL were 13 cells/mm^3 and 363,500 copies/ml, respectively. At 48 weeks, the median CD4 cell count increased to191 cells/mm^3 and 63.7% in intention-to treat and 82.3% in on-treatment analysis had pVL <50 copies/ml. There was no significant difference in pVL between patients with baseline pVL >100,000 or ≤100,000 copies/ml (p = 0.312). The incidence of hepatotoxicity, rash and peripheral neuropathy was 4.9%, 14.7% and 6.9%, respectively.

Conclusions: GPO-vir® is well-tolerated and effective in increasing CD4 cell count and suppressing plasma viremia in advanced HIV infection during the 48 weeks follow-up period. ∅

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SAFETY OF LONG-TERM ORAL POSACONAZOLE USE IN THE TREATMENT OF REFRACTORY INVASIVE FUNGAL INFECTIONS

Raad II, Graybill JR, Bustamante AB, Cornely OA, Gaona-Flores V, Afif C, Graham DR, Greenberg RN, Hadley S, Langston A, Negroni R, Perfect JR, Pitisuttithum P, Restrepo A, Schiller G, Pedicone L, Ullmann AJ

The University of Texas MD Anderson Cancer Center, Houston, TX 77030, USA

Background: Invasive fungal infections are found most frequently in immunosuppressed and critically ill hospitalized patients. Antifungal therapy is often required for long periods. Safety data from the clinical development program of the triazole antifungal agent, posaconazole, were analyzed.

METHODS: A total of 428 patients with refractory invasive fungal infections (n = 362) or febrile neutropenia (n = 66) received posaconazole in 2 phase II/III open-label clinical trials. Also, 109 of these patients received posaconazole therapy for > or = 6 months. Incidences of treatment-emergent, treatment-related, and serious adverse events and abnormal laboratory parameters were recorded during these studies.

RESULTS: Treatment-emergent, treatment-related adverse events were reported in 38% of the overall patient population. The most common treatment-related adverse events were nausea (8%) and vomiting (6%). Treatment-related serious adverse events occurred in 8% of patients. Low rates of treatment-related corrected QT interval and/or QT interval prolongation (1%) and elevation of hepatic enzymes (2%) were reported as adverse events. Treatment-emergent, treatment-related adverse events occurred at similar rates in patients who received posaconazole therapy for < 6 months and > or = 6 months.

CONCLUSIONS: Prolonged posaconazole treatment was associated with a generally favorable safety profile in seriously ill patients with refractory invasive fungal infections. Long-term therapy did not increase the risk of any individual adverse event, and no unique adverse event was observed with longer exposure to posaconazole. ∅

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RAPID DIAGNOSIS OF SCRUB TYPHUS IN RURAL THAILAND USING THE POLYMERASE CHAIN REACTION

Piengchan Sonthayanon[1,2], Wirongrong Chierakul[1,2], Vanaporn Wuthiekanun[2], Stuart Blacksell[2,3], Kriangsak Pimda, Yupin Suputtamongkol, Sasithon Pukrittayakamee, Nicholas J White, Nicholas P Day and Sharon Peacock[2,3]

[1] *Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand;*
[2] *Wellcome Unit, Faculty of Tropical Medicine, Mahidol University, Bangkok Thailand;*
[3] *Center for Clinical Vaccinology and Tropical Medicine, Nuffield Department of Clinical Medicine, University of Oxford, UK;*
[4] *Medical Department, Udon Thani Hospital, Udon Thani, Thailand;*
[5] *Department of Medicine, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand*

The aim of this study was to evaluate the utility of PCR amplification of the O. tsutsugamushi 16S rRNA gene for the diagnosis of scrub typhus in rural Thailand. A prospective study of acute febrile illness in Udon Thani, northeast Thailand identified 183 patients as having scrub typhus on the basis of immunofluorescent antibody testing (IFA) of paired sera. A further 366 febrile patients admitted concurrently with a range of other diagnoses acted as negative controls. Diagnostic sensitivity and specificity of 16S rRNA PCR was 44.8% and 99.7%, respectively compared with IFA. PCR positivity was related to duration of symptoms and presence of eschar ($p < 0.001$, both cases). PCR using primers to amplify a fragment of the 56-kDa gene had a sensitivity and specificity of 29.0% and 99.2%, respectively. PCR has a high specificity but low sensitivity for the rapid diagnosis of scrub typhus in this endemic setting. ∅

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EFFICACY OF IVERMECTIN TREATMENT OF CUTANEOUS GNATHOSTOMIASIS EVALUATED BY PLACEBO-CONTROLLED TRIAL

Valai Bussaratid[1], Varunee Desakorn[1], Srivicha Krudsood[2], Udomsak Silachamroon[1] & Sornchai Looareesuwan[1]

[1] *Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand;*
[2] *Department of Tropical Hygiene, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand*

Previous studies have revealed that ivermectin treatment for gnathostomiasis can reduce parasitic loads in animals and make recurrent subcutaneous swelling subside in 76% of patients. Our study aimed to evaluate the efficacy of ivermectin for cutaneous gnathostomiasis treatment in a placebo-controlled trial. This study was a prospective randomized placebo-controlled study performed at The Bangkok Hospital for Tropical Diseases, Mahidol University, Thailand. Thirty patients with a serologically confirmed diagnosis of cutaneous gnathostomiasis were enrolled. Seventeen patients in the ivermectin treated group received a single dose of 12 mg ivermectin (200 l.Jg/kg bodyweight), while 13 patients in the control group received a single dose of 40 mg of vitamin B1. The follow-up period was 1 year. Of the 17 patients, 7 (41.2%) responded to ivermectin, while no patient responded to placebo. The mean (95% CI) time to the first recurrence of subcutaneous swelling with ivermectin and in the placebo groups were 257 (184-331) and 146 (42-250) days, respectively, (p=0.102). Although this study revealed no significant difference in the mean time to first recurrence of swelling between the ivermectin and placebo groups, there was a trend towards ivermectin efficacy against gnathostomiasis in previous animal and human studies. Further studies with different doses of ivermectin and larger sample sizes, and close monitoring for ivermectin tolerability and treatment response are necessary to confirm an efficacy of ivermectin. ∅

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EARLY TREATMENT FAILURE IN SEVERE MALARIA RESULTING FROM ABNORMALLY LOW PLASMA QUININE CONCENTRATIONS

Paul N Newton[1,2], Steven Ward[3], Brain J Angusa[2], Wirongrong Chierakul[1], Arjen Dondorp[1,2], Ronnatrai Ruangveerayuth[4], Kamolrat Silamut[1], Pramote Teerapong[5], Yupin Suputtamongkol[6], Sornchai Looareesuwan[1], Nicholas J White[1,2]

[1] *Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand;*
[2] *Centre for Clinical Vaccinology and Tropical Medicine, Nuffield Department of Clinical Medicine, Churchill Hospital, Oxford OX3 7LJ, UK;*
[3] *Liverpool School of Tropical Medicine, Liverpool, UK;*
[4] *Mae Sot Hospital, Mae Sot, Tak, Thailand;*
[5] *Department of Pharmacology, Mahidol University, Bangkok, Thailand;*
[6] *Department of Medicine, Siriraj Hospital, Bangkok, Thailand*

A patient admitted with severe *Plasmodium falciparum* malaria in western Thailand had an early treatment failure with quinine, despite full dosing. Plasma quinine concentrations were subtherapeutic. Abnormal quinine pharmacokinetics may explain sporadic reports of quinine treatment failures in severe malaria.

Although there is increasing evidence that parenteral artemisinin derivatives may reduce mortality from severe malaria, this is not yet convincing, and parenteral quinine remains the standard therapy. Quinine resistance has been reported for nearly 100 years, but there is a paucity of well- documented cases of high-level resistance. In Southeast Asia, there has been evidence of a minor decline in quinine efficacy in the treatment of *Plasmodium falciparum* malaria over the past 25 years (Pukrittayakamee *et al*, 1994), although recent in-vitro surveys in Thailand suggest that parasites still remain susceptible (Brockman *et al*, I 2000; Lopes *et al*, 2002). There have been occasional case reports of apparent high-grade *P. falciparum* quinine resistance from Thailand, Cambodia and Viet Nam (Clyde and Miller, 1970; Giboda and Denis, 1988; Jaroovesma *et al*, 1974; Pinswadi and Chaereonkwan, 1965), but without measurements of plasma quinine concentrations from patients with in-vivo failures, differentiation of parasite drug resistance from abnormal pharmacokinetics resulting in unusually low, subtherapeutic plasma quinine concentrations is not possible. The therapeutic range of quinine in severe malaria is not known precisely; plasma total quinine concentrations in the range 8 to 15 mg/l (Krishna and White, 1996; Looareesuwan *et al*, 1990; White, 1995) are associated with maximum effects in severe malaria and, for optimum cure rates, need to be maintained for the duration of the 7 -day treatment course (Pukrittayakamee *et al*, 2003). Two patients with Rill responses to quinine, despite plasma qui- nine concentrations >10mg/l, have recently been described from French Guiana (Demar and Carmel, 2004). The possibility that pharmacokinetic factors could explain treatment failure was raised 15 years ago; a Thai patient who died from severe malaria with apparent Rill resistance to quinine had, despite full dosing, abnormally low plasma quinine levels (Looareesuwan *et al*, 1990). Measurement of plasma quinine in patients with in-vivo failures is essential, therefore, if parasite drug resistance is to be distinguished from abnormal pharmacokinetics.

In a recent randomized comparison of artesunate and quinine in the treatment of adults with severe falciparum malaria in western Thailand, a patient with apparent RII resistance to quinine was described (Newton *et al*, 2003). We report the results of plasma quinine concentration assays. ∅

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KEYS TO SUCCESS FOR A SCHOOL-BASED MALARIA CONTROL PROGRAM IN PRIMARY SCHOOLS IN THAILAND

Hironori Okabayashi[1,2], Pimpimon Thongthien[3], Pratap Singhasvanon[1], Jitra Waikagul[1], Sornchai Looareesuwan[1], Masamine Jimba[4], Shigeyuki Kano[5], Somei Kojima[1,6], Tsutomu Takeuchi[7], Jun Kobayashi[1,2], Seiki Tateno[2]

[1] *The Asian Centre of International Parasite Control, Faculty of Tropical Medicine, Mahidol University, Thailand;*
[2] *Expert Service Division, Bureau of International Cooperation, International Medical Center of Japan, Ministry of Health, Labour and Welfare, Japan;*
[3] *Office of Basic Education Commission, Ministry of Education, Thailand;*
[4] *Department of International Community Health, Graduate School of Medicine, The University of Tokyo, Japan;*
[5] *Research Institute, International Medical Center of Japan, Ministry of Health, Labour and Welfare, Japan;*
[6] *Center for Medical Science, International University of Health and Welfare, Japan;*
[7] *Department of Tropical Medicine and Parasitology, Keio University School of Medicine, Japan*

School-based malaria control has been recognized as a new approach for the control of this disease in the Greater Mekong Subregion since 2000. We evaluated a school-based malaria control program near the western border of Thailand using a before-after intervention study. The major intervention activities included teacher training with specialized malaria teaching materials and participatory learning methods. The target population was 17 school principals, 111 teachers and 852 schoolchildren of grade 3, 4, and 5 in 17 schools. After the intervention, the teachers taught about malaria more actively than before. The teachers who could design a lesson plan on malaria increased from 30.7% to 47.7% (p=0.015) and the teachers who had taught about malaria increased from 71.9% to 84.3% (p=0.035). As a result of the program, the schoolchildren changed their behavior positively towards malaria prevention with significant difference in 6 of 7 questions. For example, the schoolchildren 'who always took care of mosquito bites' increased from 42.7% to 62.1% (p<0.001) and the schoolchildren 'who always reported their parents or teachers when they had fever' increased from 36.0% to 56.0% (p<0.001). In conclusion, the keys to a successful intervention lie in good teaching materials and a participatory approach utilizing the well-established Thailand's school health system. Beyond Thailand, school-based malaria control could be applied to other Greater Mekong Subregion countries with careful analysis of school health context in each country. ∅

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TRAVELERS' MALARIA AMONG FOREIGNERS AT THE HOSPITAL FOR TROPICAL DISEASES, BANGKOK, THAILAND – A 6-YEAR REVIEW (2000-2005)

Watcharapong Piyaphanee[1], Srivicha Krudsood[2], Udomsak Silachamroon[1], Karnchana Pornpininworakij[3], Phatcharee Danwiwatdecha[4], Supat Chamnachanan[1], Polrat Wilairatana[1] & Sornchai Looareesuwan[1]

[1] *Department of Clinical Tropical Medicine, Mahidol University, Bangkok 10400, Thailand;*
[2] *Department of Tropical Hygiene, Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand;*
[3] *Department of Medical Entomology, Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand;*
[4] *Hospital for Tropical Diseases, Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand*

We retrospectively examined the charts of travelers admitted to the Hospital for Tropical Diseases, Bangkok, Thailand, with malaria during the years 2000-2005. Twenty-one cases of malaria were identified, of which 12 (57%) were *Plasmodium vivax* infections and 9 (430%) were *P. falciparum* infections. There was one mixed case with vivax and falciparum infection. Only 1 *P. falciparum* case had complications. All cases were successfully treated with standard antimalarial drugs. Only 3 of the 21 cases were thought to be acquired in Thailand, the rest were regarded to be imported. ∅

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PERIPHERAL GANGRENE IN PATIENTS WITH SEVERE FALCIPARUM MALARIA: REPORT OF 3 CASES

Vipa Thanachartwet[1], Srivicha Krudsood[2], Polrat Wilairatana[1], Weerapong Phumratanaprapin[1], Udomsak Silachamroon[1], Sornchai Looareesuwan[1]

[1] *Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand;*
[2] *Department of Epidemiology, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand*

Peripheral gangrene, characterized by distal ischemia of the extremities, is a rare complication in patients with falciparum malaria. Patients with this complication have generally undergone early amputation of the affected areas. In this report, we describe 3 adult Thai patients presented at the Hospital for Tropical Diseases, Bangkok, with high grade of fever ranged 6-9 days, jaundice, acute renal failure, respiratory failure, alteration of consciousness and shock. Two patients had gangrene developed at the lower extremities on day 1 of hospitalization and 1 patient had gangrene developed on day 3. Blood smears

revealed hyperparasitemia with *Plasmodium falciparum*. These patients were diagnosed as having severe malaria with peripheral gangrene. The resolution of gangrene was successfully achieved by treatment with artesunate and conservative treatment in 2 of 3 cases. ∅

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NATURAL HUMAN HUMORAL RESPONSE TO SALIVARY GLAND PROTEINS OF *ANOPHELES* MOSQUITOES IN THAILAND

Amornrat Waitayakul[1,2], Sangdao Somsri[2], Jetsumon Sattabongkot[3], Sornchai Looareesuwan[4], Liwang Cui[5], Rachanee Udomsangpetch[1,2]

[1] *Department of Parasitology, Faculty of Medical Technology, Mahidol University, Salaya, Nakhonpathom, Thailand;*
[2] *Department of Pathobiology, Faculty of Science, Mahidol University, Rama VI Road, Bangkok 10400, Thailand;*
[3] *Entomology Department, Armed Forces Research Institute of Medical Sciences, 315/6 Rajavithi Road, Bangkok 10400, Thailand;*
[4] *Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Rama VI Road, Bangkok 10400, Thailand;*
[5] *Department of Entomology, The Pennsylvania State University, 501 ASI, University Park, PA 16802, USA*

During blood feeding, arthropod vectors inject saliva into vertebrate hosts. The saliva is biochemically complex and pharmacologically active, and may play an important role in pathogen transmission. To examine whether mosquito saliva could elicit humoral immune response in humans under natural conditions, we have collected sera from malaria patients, healthy villagers, and people from a non-malarious region in Thailand. Here we have demonstrated that anti-*Anopheles* salivary protein antibodies occurred predominantly in patients with acute *Plasmodium falciparum* or *P. vivax* malaria, whereas people from a non-malarious area had no such antibodies. Besides, antibody levels against mosquito salivary proteins in malaria patients were highly variable, which may be related to the levels of mosquito exposure. Despite variability, patients' sera with high IgG titers consistently detected several proteins in *Anopheles dirus* salivary gland protein extracts. Immunohistochemical staining of *Anopheles* salivary glands with human sera showed that the salivary gland-specific IgGs reacted strongly with the median lobe. Comparison using *Anopheles* and *Aedes* salivary proteins suggests that the anti-salivary protein antibodies detected in malaria patients were *Anopheles*-specific, consistent with the major malaria vector status of *An. dirus* in this area. ∅

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POPULATION PHARMACOKINETICS OF ARTESUNATE AND DIHYDROARTEMISININ FOLLOWING INTRA-RECTAL DOSING OF ARTESUNATE IN MALARIA PATIENTS

Simpson JA[1], Agbenyega T[1], Barnes KI[1], Di Perri G[1], Folb P[1], Melba Gomes[1], Krishna S[1], Srivicha Krudsood[2], Sornchai Looareesuwan[2], Mansor S[1], McIlleron H[1], Robert Scott Miller[1], Molyneux M[1], Mwenechanya J[1], Navaratnam V[1], Nosten F[1], Olliaro P[1], Pang L[1], Ribeiro I[1], Tembo M[1], van Vugt [1]M, Ward S[1], Weerasuriya K[1], Win K[1], Nicholas J White[1]

[1] *Centre for Molecular, Environmental, Genetic and Analytic Epidemiology, The University of Melbourne, Melbourne, Australia;*
[2] *Faculty of Tropical Medicine, Mahidol University, 420/6 Rajvithi Road, Bangkok 10400, Thailand*

Background: Intra-rectal artesunate has been developed as a potentially life-saving treatment of severe malaria in rural village settings where administration of parenteral antimalarial drugs is not possible. We studied the population pharmacokinetics of intra-rectal artesunate and the relationship with parasitological responses in patients with moderately severe falciparum malaria.

METHODS AND FINDINGS: Adults and children in Africa and Southeast Asia with moderately severe malaria were recruited in two Phase II studies (12 adults from Southeast Asia and 11 children from Africa) with intensive sampling protocols, and three Phase III studies (44 children from Southeast Asia, and 86 children and 26 adults from Africa) with sparse sampling. All patients

received 10 mg/kg artesunate as a single intra-rectal dose of suppositories. Venous blood samples were taken during a period of 24 h following dosing. Plasma artesunate and dihydroartemisinin (DHA, the main biologically active metabolite) concentrations were measured by high-performance liquid chromatography with electrochemical detection. The pharmacokinetic properties of DHA were determined using nonlinear mixed-effects modelling. Artesunate is rapidly hydrolysed in vivo to DHA, and this contributes the majority of antimalarial activity. For DHA, a one-compartment model assuming complete conversion from artesunate and first-order appearance and elimination kinetics gave the best fit to the data. The mean population estimate of apparent clearance (CL/F) was 2.64 (l/kg/h) with 66% inter-individual variability. The apparent volume of distribution (V/F) was 2.75 (l/kg) with 96% inter-individual variability. The estimated DHA population mean elimination half-life was 43 min. Gender was associated with increased mean CL/F by 1.14 (95% CI: 0.36-1.92) (l/kg/h) for a male compared with a female, and weight was positively associated with V/F. Larger V/Fs were observed for the patients requiring early rescue treatment compared with the remainder, independent of any confounders. No associations between the parasitological responses and the posterior individual estimates of V/F, CL/F, and AUC0-6h were observed.

CONCLUSIONS: The pharmacokinetic properties of DHA were affected only by gender and body weight. Patients with the lowest area under the DHA concentration curve did not have slower parasite clearance, suggesting that rectal artesunate is well absorbed in most patients with moderately severe malaria. However, a number of modelling assumptions were required due to the large intra- and inter-individual variability of the DHA concentrations. ∅

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MONOCYTE CHEMOATTRACTANT PROTEIN 1 (MCP-1) GENE POLYMORPHISM IS NOT ASSOCIATED WITH SEVERE AND CEREBRAL MALARIA IN THAILAND

Dechkum N[1], Hatairat Hananantachai[1], Jintana Patarapotikul[1], Ohashi J[4], Srivicha Krudsood [3], Sornchai Looareesuwan[2], Katsushi Tokunaga[4]

[1] *Department of Microbiology and Immunology, Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand;*
[2] *Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand;*
[3] *Department of Tropical Hygiene, Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand;*
[4] *Department of Human Genetics, School of International Health, Graduate School of Medicine, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113, Japan*

The pathogenesis of cerebral malaria from Plasmodium falciparum infection is thought to involve inflammation of the central nervous system. Since monocyte chemoattractant protein 1 (MCP-1) is a chemokine strongly involved in the inflammatory process, we here study MCP-1 gene polymorphisms in association with severe or cerebral malaria in Thailand. Malaria patients in the northwest of Thailand were grouped into mild (n=206), severe (165), and cerebral (110) malaria case groups. Five single nucleotide polymorphisms (SNPs) in the promoter (-2518A/G, -2348G/C, -2158C/T, -2076A/T, and -2072T/C), and 1 SNP in intron 1 (764C/G) were analyzed by PCR-RFLP, PCR-SSP, or direct sequencing. The SNP -2158 was a novel polymorphism found in this study. For all SNPs, genotype and allele frequencies were not significantly different between mild and severe or mild and cerebral malaria. Strong linkage disequilibrium was found among 4 SNPs (-2518A/G, -2348G/C, -2076A/T, and 764C/G), resulting in 4 major estimated haplotypes. The most common haplotype was GGAC. The results indicated that MCP-1 gene polymorphisms were not associated with malaria severity, implying that MCP-1 was not a cause of malaria severity in this Thai population. ∅

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TRANSMISSION-BLOCKING ACTIVITIES OF QUININE, PRIMAQUINE, AND ARTESUNATE

Kesinee Chotivanich[1], Jetsumon Sattabongkot[4], Rachanee Udomsangpetch[2], Sornchai Looareesuwan[1], Day NP[3], Coleman RE[3], Nicholas J White[3]

[1] Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand;
[2] Department of Pathobiology, Faculty of Science, Mahidol University, Bangkok, Thailand;
[3] Mae Sot, Tak and Faculty of Tropical Medicine, Mahidol University, 420/6 Rajvithi Rd., Bangkok 10400, Thailand;
[4] Entomology Department, Armed Forces Research Institute of Medical Sciences, 315/6 Rajavithi Road, Bangkok 10400, Thailand

The infectivity of Plasmodium falciparum gametocytes after exposure in vitro to quinine, artesunate, and primaquine was assessed in Anopheles dirus, a major vector of malaria in Southeast Asia. Mature gametocytes (stage 5) of a Thai isolate of P. falciparum were exposed to the drugs for 24 h in vitro before membrane feeding to A. dirus. After 10 days, the mosquito midguts were dissected and the oocysts were counted. In this system, artesunate showed the most potent transmission-blocking activity; the mean (standard deviation [SD]) 50% and 90% effective concentrations (EC(50), and EC(90), respectively, in nanograms per milliliter) were 0.1 (0.02) and 0.4 (0.15), respectively. Transmission-blocking activity of quinine and primaquine was observed at relatively high concentrations (SDs): EC(50) of quinine, 642 (111) ng/ml; EC(50) of primaquine, 181 (23) ng/ml; EC(90) of quinine, 816 (96) ng/ml; EC(90) of primaquine, 543 (43) ng/ml. Artesunate both prevents the maturation of immature P. falciparum gametocytes and reduces the transmission potential of mature gametocytes. Both of these effects may contribute to reducing malaria transmission. ∅

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DEPLOYMENT OF EARLY DIAGNOSIS AND MEFLOQUINE-ARTESUNATE TREATMENT OF FALCIPARUM MALARIA IN THAILAND: THE TAK MALARIA INITIATIVE

Carrara VI[1], Sirilak S[1], Thonglairuam J[1], Rojanawatsirivet C[1], Proux S[1], Gilbos V[1], Brockman A[1], Ashley EA[1], McGready R[1], Srivicha Krudsood[3], Somjai Leemingsawat[3], Sornchai Looareesuwan[2], Pratap Singhasivanon[3], Nicholas J White[1], Nosten F[1]

[1] Shoklo Malaria Research Unit, Tak, Thailand;
[2] Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand;
[3] Department of Tropical Hygiene, Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand

Background: Early diagnosis and treatment with artesunate-mefloquine combination therapy (MAS) have reduced the transmission of falciparum malaria dramatically and halted the progression of mefloquine resistance in camps for displaced persons along the Thai-Burmese border, an area of low and seasonal transmission of multidrug-resistant Plasmodium falciparum. We extended the same combination drug strategy to all other communities (estimated population 450,000) living in five border districts of Tak province in northwestern Thailand.

METHODS AND FINDINGS: Existing health structures were reinforced. Village volunteers were trained to use rapid diagnostic tests and to treat positive cases with MAS. Cases of malaria, hospitalizations, and malaria-related deaths were recorded in the 6 y before, during, and after the Tak Malaria Initiative (TMI) intervention. Cross-sectional surveys were conducted before and during the TMI period. P. falciparum malaria cases fell by 34% (95% confidence interval [CI], 33.5-34.4) and hospitalisations for falciparum malaria fell by 39% (95% CI, 37.0-39.9) during the TMI period, while hospitalisations for P. vivax malaria remained constant. There were 32 deaths attributed to malaria during, and 22 after the TMI, a 51.5% (95% CI, 39.0-63.9) reduction compared to the average of the previous 3 y. Cross-sectional surveys indicated that P. vivax had become the predominant species in Thai villages, but not in populations living on the Myanmar side of the border. In the displaced persons population, where the original deployment took place 7 y before the TMI, the transmission of P. falciparum continued to be suppressed, the incidence of falciparum malaria remained low, and the in vivo efficacy of the 3-d MAS remained high.

CONCLUSIONS: In the remote malarious north western border area of Thailand, the early detection of malaria by trained village volunteers, using rapid diagnostic tests and treatment with mefloquine-artesunate was feasible and reduced the morbidity and mortality of multidrug-resistant *P. falciparum*. ∅

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PHARMACOKINETICS OF DIHYDROARTEMISININ FOLLOWING ORAL ARTESUNATE TREATMENT OF PREGNANT WOMEN WITH ACUTE UNCOMPLICATED FALCIPARUM MALARIA.

McGready R[1], Stepniewska K[1], Ward SA[1], Cho T[1], Gilveray G[1], Sornchai Looareesuwan[2], Nicholas J White[1], Nosten F[1]

[1] *Shoklo Malaria Research Unit, P.O. Box 46, Mae Sot, Thailand;*
[2] *Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand*

Objective: To determine the pharmacokinetic properties of dihydroartemisinin (DHA) following oral artesunate treatment in women with recrudescent multi-drug resistant falciparum malaria, in the second and third trimesters of pregnancy.

METHODS: Serial plasma concentrations of artesunate and DHA were measured in 24 women after the final dose of a 3 day treatment with artesunate (4 mg kg(-1) day(-1)) and atovaquone (20 mg kg(-1) day(-1)) plus proguanil (8 mg kg(-1) day(-1)), daily. Conventional non-compartmental modelling and a population one-compartment pharmacokinetic model were applied to the data.

RESULTS: Artesunate was very rapidly eliminated. For DHA the median [90% range] estimate of oral clearance (Cl/F) was 4.0 [0.8-20.7] l hour(-1) kg(-1), total apparent volume of distribution (Vd/f) was 3.4 [0.9-60.7] l/kg, and terminal elimination half-life was 1.0 [0.6-2.4] h.

CONCLUSION: The kinetics of DHA are modified by pregnancy. The plasma levels of the active antimalarial metabolite DHA are lower than reported previously in non-pregnant adults. Dose-optimisation studies in pregnant women are needed.

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MEMORY T CELLS PROTECT AGAINST *PLASMODIUM VIVAX* INFECTION

Jangpatarapongsa K[1], Sirichaisinthop J[1], Jetsumon Sattabongkot[3], Cui L[3], Montgomery SM[3], Sornchai Looareesuwan[2], Troye-Blomberg M[3], Rachanee Udomsangpetch[1]

[1] *Department of Pathobiology, Faculty of Science, Mahidol University, Bangkok 10400, Thailand;*
[2] *Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand;*
[3] *Entomology Department, Armed Forces Research Institute of Medical Sciences, 315/6 Rajavithi Road, Bangkok 10400, Thailand*

Immunity induced by *Plasmodium vivax* infection leads to memory T cell recruitment activated during "relapse" or "re-infection". This study aims to characterise memory T cells in patients with acute or convalescent *P. vivax* infection. Lymphocytes were collected from patients infected by *P. vivax*, immune controls and naive controls. The proportion of immature memory T cells, expressing CD45RO(+)CD27(+), and mature cells lacking CD27 was assessed. A statistically significant increase in the median percentage of memory T cell subsets expressing CD4(+) was observed in material from patients with an acute infection compared with that from either naive or immune controls. The high percentage of memory T cells in infected patients was maintained until 60 days post treatment. The immune controls living in a malaria endemic area had a somewhat increased proportion of memory T cell subsets expressing CD8(+). An approximately three-fold increase of these cell types was shown in patients with an acute infection and the level persisted until 60 days post treatment. Phenotypic characterisation of the peripheral lymphocytes during acute infection revealed that a large fraction of the lymphocytes carried the gammadelta phenotypes suggesting a role for these cells in the early response against *P. vivax*. Very low levels of *P. vivax* specific antibody were found. This might suggest that cell-mediated immunity may play a greater role in the development of naturally acquired protection against *P. vivax* infection than humoral immunity. Our results provide further insight into the mechanism of cell-mediated immunity to *P. vivax* infection that could be important for the future development of a successful vaccine and anti-malarial drug designation. ∅

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RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED EFFICACY TRIAL OF A BIVALENT RECOMBINANT GLYCOPROTEIN 120 HIV-1 VACCINE AMONG INJECTION DRUG USERS IN BANGKOK, THAILAND

Pitisuttithum P[1], Gilbert P[4], Gurwith M[5], Heyward W[5], Martin M[3], van Griensven F[3], Hu D[6], Tappero JW[3], Choopanya K[2]; Bangkok Vaccine Evaluation Group

[1] *Department of Clinical Tropical Medicine, Mahidol University;*
[2] *Bangkok Metropolitan Administration, Bangkok;*
[3] *Thailand Ministry of Public Health-US Centers for Disease Control and prevention Collaboration, Nonthaburi, Thailand;*
[4] *Statistical Center for HIV/AIDS Research and Prevention, Fred Hutchinson Cancer Research Center, Seattle, Washington;*
[5] *VaxGen, Inc., Brisbane, California;*
[6] *US Centers for Disease control and Prevention, Alanta, Georgia*

Background: In Thailand, phase 1/2 trials of monovalent subtype B and bivalent subtype B/E (CRF01_AE) recombinant glycoprotein 120 human immunodeficiency virus type 1 (HIV-1) vaccines were successfully conducted from 1995 to 1998, prompting the first HIV-1 vaccine efficacy trial in Asia.

METHODS: This randomized, double-blind, placebo-controlled efficacy trial of AIDSVAX B/E (VaxGen), which included 36-months of follow-up, was conducted among injection drug users (IDUs) in Bangkok, Thailand. The primary end point was HIV-1 infection; secondary end points included plasma HIV-1 load, CD4 cell count, onset of acquired immunodeficiency syndrome-defining conditions, and initiation of antiretroviral therapy.

RESULTS: A total of 2546 IDUs were enrolled between March 1999 and August 2000; the median age was 26 years, and 93.4% were men. The overall HIV-1 incidence was 3.4 infections/100 person-years (95% confidence interval [CI], 3.0-3.9 infections/100 person-years), and the cumulative incidence was 8.4%. There were no differences between the vaccine and placebo arms. HIV-1 subtype E (83 vaccine and 81 placebo recipients) accounted for 77% of infections. Vaccine efficacy was estimated at 0.1% (95% CI, -30.8% to 23.8%; P=.99, log-rank test). No statistically significant effects of the vaccine on secondary end points were observed.

CONCLUSION: Despite the successful completion of this efficacy trial, the vaccine did not prevent HIV-1 infection or delay HIV-1 disease progression. Ø

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SAFETY AND TOLERABILITY OF ELUBAQUINE (BULAQUINE, CDRI 80/53) FOR TREATMENT OF *PLASMODIUM VIVAX* MALARIA IN THAILAND

Srivicha Krudsood[1], Polrat Wilairatana[1], Noppadon Tangpukdee[1], Kobsiri Chalermrut[1], Siripun Srivilairit[1], Vipa Thanachartwet[1], Sant Muangnoicharoen[1], Natthanej Luplertlop[1], Gary M Brittenham[2] & Sornchai Looareesuwan[1]

[1] *Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand.*
[2] *Department of Pediatrics and Medicine, Columbia University, College of Physicians and Surgeons, New York City, USA.*

We conducted a study to compare the safety and tolerability of anti-relapse drugs elubaquine and primaquine against *Plasmodium vivax* malaria. After standard therapy with chloroquine, 30 mg/kg given over 3 days, 141 patients with *P. vivax* infection were randomized to receive primaquine or elubaquine. The 2 treatment regimens were primaquine 30 mg once daily for 7 days (group A, n = 71), and elubaquine 25 mg once daily for 7 days (group B, n = 70). All patients cleared parasitemia within 7 days after chloroquine treatment. Among patients treated with primaquine, one patient relapsed on day 26; no relapse occurred with elubaquine treatment. Both drugs were well tolerated. Adverse effects occurred only in patients with G6PD deficiency who were treated with primaquine (group A, n = 4), whose mean hematocrit fell significantly on days 7, 8 and 9 (*P* = 0.015, 0.027, and 0.048, respectively). No significant change in hematocrit was observed in patients with G6PD deficiency who were treated with elubaquine (group B, n = 3) or in patients with normal G6PD. In conclusion, elubaquine, as anti-relapse therapy for *P. vivax* malaria, was as safe and well tolerated as primaquine and did not cause clinically significant hemolysis. Ø

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QUANTITATIVE PCR OF *ORIENTIA TSUTSUGAMUSHI* IN SCRUB TYPHUS PATIENTS

Piengchan Sonthayanon[1,2], Wirongrong Chierakul[1,2], Vanaporn Wuthiekanun[2], Stuart Blacksell[2,3], Sharon Peacock[2,3], and Nicholas P Day [2,3]

[1] *Department of Clinical Tropical Medicine,*
[2] *Wellcome Unit, Faculty of Tropical Medicine, Mahidol University, Bangkok Thailand;*
[3] *Center for Clinical Vaccinology and Tropical Medicine, Nuffield Department of Clinical Medicine, University of Oxford, UK*

Orientia tsutsugamushi, which causes the rickettsial infection scrub typhus, is a major pathogen in the Asia-Pacific region. However, the understanding of how bacterial determinants affect the pathogenesis of the disease is very limited. We have performed quantitative real-time PCR based on the 16S ribosomal RNA gene of *O. tsutsugamushi* in order to quantify the number of bacteria in the blood of scrub typhus patients. Absolute quantitative PCR was achieved by using the plasmid harboring the specific sequence of 16S rRNA as DNA standard. The specific TaqMan® probe could detect the standard DNA down to a limit of at least 0.4 copy per µl. DNA was extracted form 5 ml whole blood from scrub typhus patients and 5 µl DNA was used in the quantitative PCR. The results showed that the copy number of the target gene in patient blood varied from 1 to 89,400 copies per 5 ml blood. The geometric mean (95% CI) was 119 (77.8-181) copies per 5 ml blood. The data was further analyzed to determine the relationship between the number of bacteria in blood and clinical features, diseases severity, drug treatment and outcome. ∅

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ALVAC HIV/AIDSVAX B/E PRIME BOOST, THE COMMUNITY PHASE III HIV-1 PREVENTIVE VACCINE TRIAL: AN UPDATE – 2006

S Rerks-Ngarm[1], P Pitisuttithum[2], S Nitayaphan[3], J Kaewkungwan[2], J Kim[3], M Benenson[3], S Gurunathan[4], M Gurwith[5], AE Brown[6], N Michael[6], C Khamboonroeng[1], P Thongcharoen[1] and P Kunasol[1]

[1] *Department of Disease Control, Ministry of Public Health, Thailand;*
[2] *Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand;*
[3] *Armed Forces Research Institute of Medical Sciences, Bangkok, Thailand;*
[4] *Sanofi Pasteur, Swiftwater, Pennsylvania, USA;*
[5] *VaxGen Inc., Brisbane, CA, USA;*
[6] *Walter Reed Army Institute of Research, Rockville, MD, USA*

Background: In 2003 the Ministry of Public Health launched a Phase III HIV vaccine trial with the ultimate goal of having an HIV vaccine for Thailand.

Objectives: To determine if this prime-boost vaccine strategy prevents HIV infection among young adults and if it can alter disease course after breakthrough infection.

Methods: Recruitment teams from communities were trained, community leaders were informed, friend referred friend and various local media were used. Screened volunteers were randomized to receive ALVAC HIV canarypox vaccine (or placebo) prime at 0, 4, 12, 24 weeks, with an AIDSVAX B/E gp120 (or placebo) boost at 12, 24 weeks. Follow up for safety, HIV status, counseling and social impact events will be performed at 6 month intervals for 3 years.

Results: 26,675 potential volunteers were screened, and 16,402 were enrolled in the vaccine trial. The major reasons of not enrolled were having preexisting medical illnesses, failure of the test of understanding, inconvenience to comply with vaccine protocol, and being HIV positive. The average number of enrollees was 481 per month in the first year, which gradually increased to 656 per month for the second year due to expanding the eligible pool of participants to nearby health centers. 60% of volunteers were male and about half came from other provinces. Half were married and had education ≥ than junior secondary school. 56% reported that other participants were their referral source to the project. 36%, 22% and 27% reported that the project staff, other participants and information from screening video respectively were the source of a decision to participate. A total 57,857 injections have been administered without notable safety or reactogenicity concerns. A total of 953 serious adverse events have

been reported thru 1 April 2006. The majority of were due to motor cycle accidents and were not related to vaccination. So far, 382 participation impact events have been reported. The majority (83%) were due to personal relationship types. 94% of the participation impact events have been resolved satisfactorily.

Conclusion: Full enrollment of 16,402 volunteers was achieved. The vaccine appears to be safe and follow-up for three years is planned. ∅

Presented at: AID Vaccine o6 , 29 August - 1 September 2006, Amsterdam, the Netherlands.

PHASE III TRIAL OF HIV PRIME-BOOST VACCINE COMBINATION IN THAILAND: COMPLETION OF THE SCREENING PHASE

S Rerks-Ngarm[1], P Pitisutthithum[2], S Nitayaphan[3], J Kim[3], J Kaewkungwal[2], S Gurunathan[4], M Gurwith[5], AE Brown[6], J Khamboonrueng[1], P Thongcharoen[1], P Kunasol[1]

[1] *Prime-Boost HIV Vaccine Trial Phase III, Dept of Disease Control, Muang, Thailand,*
[2] *Mahidol University, Faculty of Tropical Medicine, Bangkok, Thailand,*
[3] *Armed Forces Research Institute of Medical Sciences, Bangkok, Thailand,*
[4] *Aventis Pasteur, Pennsylvania, United States,*
[5] *VaxGen Inc, CA, United States,*
[6] *Walter Reed Army Institute of Research, MD, United States*

Background: A Phase III prime boost HIV vaccine trial was initiated in 2003. The objectives were to determine if this prime-boost vaccine strategy 1) prevents infection, 2) alters disease course in vaccinees who become infected, and 3) is safe.

Methods: Vaccines were designed specifically for the predominant circulating HIV serotypes in Thailand (subtypes E and B). The prime vaccine is a recombinant canarypox ALVAC-HIV (vCP 1521) with a subtype B gag/pro and gp41, and subtype E gp120 (R5) gene insertions (sanofi Pasteur). The boost was AIDSVAX®gp120 B/E, monomers of gp 120B (X4) + gp120E (R5) with alum (VaxGen). The study is designed as a randomized, placebo-controlled, double-blind phase III trial. Immunization will be intramuscular over 6 months with a 3-year follow up period.

Results: After two years of recruitment and screening activities, the community-based, phase III efficacy trial of a prime-boost HIV vaccine combination in Thailand completed enrolment of 16,402 volunteers.

Conclusions: The world's first efficacy trial of a prime-boost HIV vaccine combination started in September 2003. By December 2005, 16,402 Thai-adults (ages 18-30), were recruited through the health care system of the Ministry of Public Health. With the large number of volunteers and a long duration of follow-up, volunteer compliance to the scheduled trial appointments will be a real challenge. ∅

Presented at: XVI International AIDS Conference. Toronto Canada. August 13-18, 2006.

ADOLESCENTS PARTICIPATION IN THE PHASE III EFFICACY TRIAL OF ALVAC HIV-1 VACCINE PRIMING, AIDSVAX VACCINE BOOSTING IN THAILAND

P Pitisuttithum[1], S Rerk-Ngam[2], J Kaewkungwal[1], W Wiriyakitja[4], S Watana[3], K Palasudhi[4], C Pobsuk[3], M Benenson[5], and J Kim[5]

[1] *Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand;*
[2] *Department Of Disease Control, Ministry of Public Health, Bangkok, Thailand;*
[3] *Chon Buri Provincial Health Office, Chon Buri, Thailand;*
[4] *Rayong Provincial Health Office, Rayong, Thailand; and*
[5] *Armed Forces Research Institute of Medical Sciences.*

Background: The phase III HIV vaccine community trial started in 2003 with the initial enrollment of participants aged 20-30 years. Since there is an increasing trend of the incidence of HIV infection among persons between 15-20 years of age, the protocol was amended and approved to include volunteers between 18 and 20 years of age who are

considered not legally independent .

Study Design: It is a randomized, double-blind, placebo controlled trial. Participants aged below 20 years old were enrolled as part of the modified protocol. General demographic characteristics, reasons for participation, and social impact events were analyzed and compared between those volunteers under 20 years of age with those over 20 years of age.

Results: 4,201 participants aged 18-20 years were screened, 2,540 were enrolled which accounts for 15% of all enrollees (16402). Twenty-two percent, 26% and 20% reported their occupation as factory workers, students or laborers respectively. 75% had a secondary school or higher educational level. 74% reported reasons for participating in the trial as wanting to help society or wanting to do something good. 44% reported wanting to know HIV information. The major sources of decision to participate in the trial were project staff, friends, and information from the screening video. There were no statistically significant differences in the above parameters between those under 20 and those over 20 years of age. 68/ 2,540 (2.7%) reported a social impact event of which 43% had minimal impact to normal daily living, 84% resolved satisfactorily. 17 of these volunteers withdrew consent, eleven of which were students., The reason for withdrawal was the disagreement with a family member. About 7 % of the participants under the age 20 were lost to follow up.

Conclusion: Participation of volunteers between the ages of 18 and 20 in the vaccine trial is feasible. A comprehensive educational campaign for parents and the community is an important tool to avoid conflict or harm among them. Ø

Presented at: AIDS Vaccine 2006. Amsterdam, Netherlands. August 29 - September 1, 2006.

CLINICAL EFFICACY OF CHLOROQUINE AND ARTEMETHER-LUMEFANTRINE FOR *PLASMODIUM VIVAX* TREATMENT IN THAILAND

Srivicha Krudsood[1], Noppadon Tangpukdee[2], Sant Muangnoicharoen[2], Vipa Thanachartwet[2], Nutthanej Luplertlop[1], Siripan Srivilairit[1], Polrat Wilairatana[1], Shigeyuki Kano[3], Pascal Ringwald[4], Sornchai Looareesuwan[2]

[1] *Department of Tropical Hygiene, Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand;*
[2] *Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok, 10400, Thailand;*
[3] *Department of Appropriate Technology Development and Transfer,Research Institute, International Medical Center of Japan, Japan;*
[4] *Roll Back Malaria Department, World Health Organization, Switzerland*

Chloroquine remains the drug of choice for the treatment of vivax malaria in Thailand. Mixed infection of falciparum and vivax malaria is very common in South-East Asia. Laboratory confirmation of malaria species is not generally available. The study is aimed to find alternative regimens for treating both malaria species by using falciparum antimalarial drugs. From June 2004 to May 2005, 98 patients infected with *Plasmodium vivax* were randomly treated with either artemether-lumefantrine (n = 47) or chloroquine (n = 51). Both treatments were followed by primaquine over 14 days. Adverse events and clinical and parasitological outcome were recorded and revealed similar in both groups. The cure rate was 97.4% for the artemether-lumefantrine treated group and 100% for the chloroquine treated group. We concluded that the combination of artemether-lumefantrine and primaquine was well tolerated, as effective as chloroquine and primaquine and can be an alternative regimen for treatment of vivax malaria especially in the event of chloroquine resistant vivax malaria or mixed infection of falciparum and vivax malaria could not be ruled out. Ø

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KINETIC OBSERVATION OF AN INFECTION WITH *PLASMODIUM VIVAX* MALARIA AND IMPLICATIONS FOR CROSS-IMMUNITY AGAINST *PLASMODIUM FALCIPARUM*

Yoshiro Nagao[1], Brian de Souza[4], Masako Kimura[2], Porntip Chavalitshewinkoon Petmitr[1], Supatra Thongrungkiat[1], Srivicha Krudsood[1], Polrat Wilairatana[1], Peerapan Tan-aria[3], Takafumi Ishida[2], Sornchai Looareesuwan[1]

[1] Faculty of Tropical Medicine, Mahidol University 420/6 Rajvithi Road, Bangkok, 10400, Thailand;
[2] Department of Physical Anthropology, Faculty of Science, University of Tokyo, Hongo 3, Bunkyo, Tokyo, Japan;
[3] Faculty of Science, Mahidol University;
[4] London School of Hygiene and Tropical Medicine Succinct title: Kinetic study of vivax malaria

Background: It has often been reported that *Plasmodium vivax* suppressed *Plasmodium falciparum* in patients infected with both these species. We hypothesised that host immunological responses stimulated by *P. vivax* might playa role in suppressing co-infecting *P. falciparum*.

METHODS: To give insight to this question, sera were taken sequentially from a volunteer (YN of the authors) infected with *P. vivax*, and were added to in vitro cultures of *P. falciparum*. We measured several species of cytokines, nitrite (NO2-), complement activity, acute phase proteins (APPs) and antibody titers against Merozoyte Surface Protein (MSP) 19 of *P. falciparum* and of *P. vivax* in the sera.

RESULTS: A strong growth inhibitory effect upon *P. falciparum* cultures (>65% inhibition) was observed in the sera collected during the acute phase. Temporal correlations of this growth inhibition to antibody titres against *P. vivax*/*P. falciparum*-MSP19 and to APPs suggest synergetic involvement of cross-reactive antibodies and APPs. Among all the cytokines measured, Interleukin (IL)- 12 showed the highest correlation with *P. vivax* parasitemia in the volunteer, suggesting that IL- 12 represents the most direct response to schizont rupture. IFN- "I appeared only in the first few paroxysms; IL-6 in the hepatic phase and in paroxysms; IL-I {3 level progressively increased toward the self-limitation of infection. Nitrite was elevated most notably in hepatic phases, but showed no correlation with growth inhibition upon *P. falciparum*.

IMPLICATIONS: IL- 12 is the best indicator of bioactivity of "malaria toxin" (i.e. inducer of acute fever), released from rupturing schizonts. ∅

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ANALYSES OF CYTOCHROME B MUTATIONS IN *PLASMODIUM FALCIPARUM* ISOLATES IN THAI-MYANMAR BORDER

Yasuko Naoshima-Ishibashi[1,2], Moritoshi Iwagami[1], Shin-ichiro Kawazu[1], Sornchai Looareesuwan[3], Shigeyuki Kano[1,2]

[1] Research Institute, International Medical Center of Japan, 1-21-1 Yoyama, Shinjuku, Tokyo 162-8655, Japan;
[2] Graduate School of Comprehensive Human Sciences, University of Tsukuba, 1-1-1 Tennodai, Tsukuba, Ibaraki 305-8577, Japan;
[3] Faculty of Tropical Medicine, Mahidol University, 420/6 Ratchawithi Rd, Bangkok 10400, Thailand

Background: The combination of atovaquone and proguanil (Malarone™) has been established as a drug of choice to prevent and treat multi-drug resistant *Plasmodium* (*P.*) *falciparum* malaria in travelers. However, several cases of resistance against Malarone™ have been reported in some parts of Africa, and many of the cases are believed to be associated with mutations at the codon 268 of cytochrome *b* gene in mitochondria of *P. falciparum*. The aim of the study was to estimated the effectiveness of Malarone™ in treatment and prophylaxis for the travelers to Thai-Myanmar border where multi-drug resistant malaria is highly endemic.

Method: Seventy *P. falciparum* samples obtained from patients from Thai-Myanmar border were sequenced to detect mutations around the codon 268. The same samples were also sequenced to detect *P. falciparum* Chloroquine resisstance transporter mutation (PfCRT K76T).

Results: All the 70 samples showed no mutations at the codon 268 of cytochrome *b* gene. Whereas, 50 samples, whose *pfcrt* genes were sequenced successfully, had an identical genotype for K76T mutation.

Conclusion: In Asian countries, even in the multi-drug resistant areas in the great Mekong region, no case of Malarone™ resistance has been reported clinically or genetically thus far. In this study, all the *P. falciparum* parasites tested successfully were shown to be Chloroquine resistant but atovaquone susceptible genetically. The more the usefulness of Malarone™ increases for both treatment and prophylaxis, the wider the drug-resistance against Malarone™ may spread in the region. Although the total number of samples examined is not large, it is concluded from these findings that Malarone™ should be recommended for prophylaxis of malaria for travelers to the Mekong region.

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IN VITRO BLOOD BRAIN BARRIER STUDY IN CEREBRAL MALARIA INFECTION

Lertyot Treeratanapiboon[1,2], Katherina Psathaki[3], Joachim Wegener[3], Sornchai Looareesuwan[4], Hans-Joachim Galla[3] & Rachanee Udomsangpetch[1,2]

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

The contribution of blood-brain barrier breakdown in the complex pathogenesis of cerebral malaria is incompletely understood and difficult to study. In this study an *in vitro* model for brain capillary permeability was prepared from primary cultures of porcine brain endothelial cells (PBCEC). Membrane associated malaria antigens obtained from lysed *P. falciparum* schizont- infected erythrocytes stimulated peripheral blood mononuclear cells (PBMC) to secrete tumor necrosis factor alpha (TNF-a). In co-cultivation with the brain endothelial cell model, the malaria- activated PBMC stimulated expression of E-selectin and ICAM-I on the PBCEC was shown. Using a biophysical measurement called electric cell-substrate impedance sensing (ECIS), we detected a significant decrease of endothelial barrier function within 4 hours of incubation with the malaria- activated PBMC. LPS-activated PBMC were used for comparison. Immunocytochemical studies showed the disruption of tight junctional complexes by a more diffuse ZO-I and claudin-5 localization, which confirmed dysfunction of the endothelial barrier. This study shows that activation of PBMC by malaria antigens disrupts brain capillary integrity and this might contribute to the pathogenesis of cerebral malaria. Combination of biochemical and biophysical techniques in the described model provides a promising tool to study changes in blood brain barrier function associated with cerebral malaria. ∅

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IDENTIFICATION OF DENGUE SEROTYPES ALONG THE THAI-LAOS BORDER USING THE NASBA TECHNIQUE

Wipawee Usawattanagul[1], Sangchai Yingsakmongkon[1], Mammen P Mammen, JR[2], Akanitt Jittmittraphap[1], Sombat Treeprasertsuk[1], Kriengsak Limkittikul[1], Thareerat Kalambaheti[1], Saravudh Suvannadabba[3], Sornchai Looareesuwan[1], Prat Bonyawongvirot[3], Vallop Phaineua[3]

[1] *Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand;*
[2] *Armed Forces Research Institute of Medical Sciences, Bangkok, Thailand;*
[3] *Ministry of Public Health, Nonthaburi, Thailand*

In this study, the detection of dengue serotypes was determined by NASBA technique. The samples were 336 suspected DF/DHF patients and 171 students, aged 2-15 years and living in Nhong Kai, Nakhorn Phanom, and Mukdahan provinces. Data were collected from June to September 2002. The samples were tested by enzyme-linked immunosorbent assay (ELISA), polymerase chain reaction (PCR) and nucleic acid sequence-based amplification (NASBA). Statistical analyses used were descriptive statistics, Cochran's Q test, McNemar test, and Kappa. Four serotypes of dengue virus were found in all provincial hospitals, except in Mukdahan Provincial Hospital, Mainly, dengue virus infections were due to dengue 2, by PCR and NASBA. There was excellent correlation in determination of dengue serotypes between PCR and NASBA (P = 0.065), When compared to the PCR method, the sensitivities of NASBA by dengue 1-4 were 100, 100, 88.89, and 100%, respectively, while the specificities of NASBA by dengue 1-4 were 100, 99.32, 100, and 100%, respectively. For serotyping, NASBA showed similar specificity and sensitivity to PCR (κ= 0.96), was also rapid and used only a heating block and water bath. Therefore, the NASBA technique was more suitable in the field than PCR. ∅

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

Polrat Wilairatana[1], Victor R Gourdeuk[2], Christine E McLaren[3], Srivicha Krudsood[4], Sombat Treeprasertsuk[1], Udomsakdi Silajumroon[1], Wannipa Chingchairit[1], Sornchai Looareesuwan[1], Gary M Brittenham[5]

[1] *Department of Clinical Tropical Medicine and Hospital for Tropical Diseases, Faculty of Tropical Medicine, Mahidol University;*
[2] *The George Washington University Medicine Center, Suite 3-428, 2150 Pennsylvania Avenue N.W, Washington, D.C., USA;*
[3] *Division of Epidemiology, Department of Medicine, 224 Irvine Hall, University of California, Irvine, California 92697, U.S.A;*
[4] *Department of Tropical Hygiene, Faculty of Tropical Medicine, Mahidol University;*
[5] *Department of Pediatrics and Medicine, Columbia University, College of Physicians and Surgeons, Harkness Pavillion, Room HP 568, 630 West 168th Street, New York, New York 10032-3795, U.S.A.*

Improved means of treating severe malaria are urgently needed because this progressive multisystem disease remains a frequently lethal illness, despite the best available antimalarial therapy and medical management. Therapy with both artesunate and deferoxamine B might be of particular benefit to patients with severe malaria by combining (i) the rapid effect of derivatives of *qinghaosu* on clearing parasitemia with (ii) the dual actions of iron chelation therapy on enhancing parasite clearance while protecting against cellular damage by inhibiting iron-induced peroxidant damage. Despite these potential benefits, the combination of artesunate and deferoxamine B has not yet been examined in patients with severe malaria, in part because earlier studies *in vitro* suggested that these agents may be antagonists (11). Since no evidence for antagonism was found *in vivo* in a trial in patients with uncomplicated malaria (12), we examined the possibility of combining these chemotherapeutic agents by carrying out a study in patients with severe and complicated malaria. We excluded patients with either renal failure or cerebral malaria. Patients with renal failure were excluded because the principal route of excretion of deferoxamine is through the kidneys. Those with cerebral malaria were excluded because of the difficulty in detecting adverse events in these gravely ill, comatose patients.

Because any decrease in the antimalarial activity of artesunate by deferoxamine would produce a prolongation of parasitemia, our primary hypothesis was that, as compared to single agent intravenous artesunate therapy, the combination of intravenous deferoxamine B and intravenous artesunate would not increase the parasite clearance time in adults with severe and complicated malaria. Our subsidiary hypotheses were that therapy with intravenous deferoxamine B in addition to artesunate would decrease the incidence and duration of medical complications as determined by clinical examination and laboratory studies. To test these hypotheses, we conducted a prospective, randomized, double-blind trial comparing the combination of intravenous deferoxamine B and intravenous artesunate to artesunate alone in adults with severe malaria but with neither renal failure not cerebral malaria. Ø

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PPARγ AGONISTS CONFER PROTECTION TO EXPERIMENTAL CEREBRAL MALARIA AND IMPROVE OUTCOME TO *PLASMODIUM FALCIPARUM* MALARIA IN A RANDOMIZED PLACEBO-CONTROLLED TRIAL

Lena Serghides[1], Samir N Patel[1], Andrea K[1], Boggild[1], Kodjo Ayi[1], Srivicha Krudsood[2], Nopaddon Tangpukdee[2], W Conrad Liles[1], Sornchai Looareesuwan[2], Kevin C Kain[1,2]

[1] *Tropical Disease Unit, Division of Infectious Diseases, Department of Medicine, UHN-Toronto General Hospital, Toronto, Ontario, Canada M5G 2C4;*
[2] *Faculty of Medicine, University of Toronto, Toronto, Canada M5S 1A5;*
[3] *McLaughlin-Rotman Centre, McLaughlin Centre for Molecular Medicine, UHN and University of Toronto.*

Despite the development of more potent anti-malarial drugs there has been little progress in identifying interventions that improve the outcome of severe malaria syndromes such as cerebral malaria[1,2]. Here we show that PPARγ agonists, developed and FDA-approved for unrelated conditions[3], modulate host innate responses to malaria by enhancing phagocytic clearance of malaria-infected erythrocytes and by decreasing excessive and deleterious inflammatory responses to infection via

inhibition of malaria toxin (*pf*GPI)-induced MAPK and NF-κB activation. We demonstrate that one PPARγ agonist currently approved for human use (rosiglitazone) modulated innate responses to infection and conferred protection in a fatal experimental model of cerebral malaria. The efficacy of rosiglitazone was then examined in a randomized double blind placebo-controlled treatment trial of multi-drug resistant malaria on the Thai-Burmese border. Rosiglitazone-treated patients experienced significantly faster parasite clearance, faster fever clearance, lower parasite burdens, and had significantly reduced levels of malaria-induced inflammatory biomarkers, including IL-6 and MCP-1, high levels of which are associated with adverse clinical outcomes[4, 5]. In summary, we demonstrate that PPARγ agonists represent a novel class of immunomodulatory drugs that may have applications to the management of severe inflammatory states such as falciparum malaria. ∅

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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

The lung flukes, Thai *Paragonimus heterotremus* and Japanese *P. miyazakii* were assayed usingpolyacrylamide 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 *P. 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 specie-specific marker between the two different populations. ∅

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CHROMOSOMES AND CHROMOSOME BREAKAGE IN THE LUNG FLUKE, *PARAGONIMUS HETEROTREMUS*

Chalit Komalamisra

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

The chromosomes of the lung fluke, *Paragonimus heterotremus*, were studied by air-drying technique. The results showed the chromosome numbers were 2n = 22 and n = 11, which consisted of one pair of large metacentric, four pairs of medium subtelocentric, three small metacentric or submetacentric, and three small submetacentric or subtelocentric, whereas the relative lengths of the chromosomes were 20.5 ± 0.4, 12.6 ± 0.2, 11.2 ± 0.2, 9.3 ± 0.2, 8.9 ± 0.2, 7.8 ± 0.2, 7.4 ± 0.1, 6.0 ± 0.1, 6.0 ± 0.1, 6.0 ± 0.1 and 4.2 ± 0.0%, respectively. The results also revealed chromosome breakage on the small chromosome (No. 8). ∅

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PAST AND PRESENT STATUS OF SOIL-TRANSMITTED HELMINTHIASES IN THAILAND

Muennoo C, Rojekittikhun W, Maipanich W

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

Control measures for soil-transmitted helminthiases (STH) in Thailand commenced in 1917. With the assistance of the Rockefeller Foundation, hookworm infection control began in Chiang Mai Province, where 80.1% (25,540/31,893) of the population had hookworm eggs in their feces. In 1957, Vajrasthira and Harinasuta reported the prevalence of intestinal helminthic infections in Thailand to be 62.9%. In 1980-81, Pruksaraj *et al* found nationwide STH prevalence to be 87.0%, and in 1990 Dulyapiree found a similar rate of 87.4% in seven provinces in far southern Thailand. Jongsuksuntigul *et al*, in 1991, reported the STH prevalence in Thailand for hookworm, *Ascaris*, *Trichuris*, and *Strongyloides* as 27.7, 1.5, 4.3, and 0.2%, respectively. In 1998-2000, Muennoo *et al* found the STH infection rates in southern Thailand were higher in villages with clustered housing than with dispersed housing, and that the rates were highest in fishermen, followed by farmers, gardeners, and townspeople, respectively. Jongsuksuntigul *et al* assessed the effectiveness of helminthiasis control in 2001, the final year of the 8th Health Development Plan (1997-2001), and reported an overall hookworm prevalence of 11.4% for Thailand; areas with higher prevalence were regions 3, 4, 7, 8, 9, 11, and 12 with averages of 12.9, 11.0, 11.6, 10.3, 11.6, 19.7, and 21.1%, respectively, with mostly low-moderate infection intensities. Muennoo and Rojekittikhun, in 2003, noted overall STH prevalence and intensity in primary schoolchildren and villagers in Nakhon Si Thammarat Province, 1991-2001, and found prevalence rates of 87.0% (1991), 81.4% (1993), 81.0%(1994), 55.4%(1995), 76.1 and 91.6% (1998), 46.8%(1999), 58.3%(2000), and 48.3%(2001). These included *A. lumbricoides* (3.7-18.5%), *T. trichiura* (28.5-66.9%), hookworm (18.0-80.0%), *E. vermicularis* (0.7%), and *S. stercoralis* (0.3-1.8%). In 2004, Muennoo *et al* reported the prevalence of fintestinal helminth infections in Prachuap Khiri Khan, Chumphon, and Khon Kaen provinces to be 8.0, 9.9, and 10.5%, repectively; and Maipanich *et al* reported those in Nan, Kanchanaburi, and Sakaeo provinces to be 55.8, 49.4, and 49.5%, respectively. Ø

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CONJUNCTIVA PHILOPHTHALMOSIS: A CASE REPORT IN THAILAND

Jitra Waikagul*, Paron Dekumyoy, Tippayarat Yoonuan and Rungson Praevanit

Department of Helminthology; Bangkok School of Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Thailand

A 31-year-old Thai woman, a resident of Mapthaphut, Rayong Province, eastern Thailand, attended Rayong Provincial Hospital after suffering from consistent irritation of the eye for 5 days. Examination conducted by an ophthalmologist revealed a small worm moving on the conjunctiva of the right eye. The worm was removed and sent for identification. It was 2.9 mm in length, elongated oval, pharynx very large, ceca end close to the excretory pore, genital pore opens in front of the ventral sucker at the cecal bifurcation; it was identified as *Philophthalmus* sp., a trematode that parasitizes the eyes of birds. This is the first human case of *Philophthalmus* infection in Thailand. Ø

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TAENIASIS, CYSTICERCOSIS AND ECHINOCOCCOSIS IN THAILAND

Waikagul J, DekumyoyP, Anantaphruti MT

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

Taeniasis is one of the major food-borne parasitic zoonoses in Thailand. During the years 1957-1997, the prevalence was low in most parts of the country. Recent (2000-2005) country prevalence was lower than 1%. A high prevalence (5.9%) was found among 1450 villagers from 30 villages in the North, and among 1233 stool samples from 19 provinces in the

Northeast (2.8%). Taenia saginata was the dominant species. Cysticercosis in Thailand is somewhat under-reported/recorded. During the period 1965-2005, diagnosis was based on techniques other than serodiagnosis, giving a total of cysticercosis cases of less than 500. However, an immunoblot technique using delipidized cyst antigen showed 314 positive cases out of 754 samples tested in 2000-2005. Reports of neurocysticercosis appeared more often than cutaneous cysticercosis. A total of 24 cases of echinococcosis, mostly hydatid cysts (only 2 cases of alveolar cysts), were recorded during 1936-2005. These records included 3 cases of foreigners seeking surgery in hospitals in Bangkok. Most Thai patients were migrant workers from the Middle East, and only a few cases were indigenous. The prevalence of cysticercosis and echinococcosis is increasing resulting from sensitive modern diagnostic tests. Taeniasis will persist in Thailand as the consumption of raw/half-cooked meat dishes is still a normal practice for Thai people. Ø

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SEQUENCE ANALYSIS OF ITS2 AND CO1 GENES OF *PARAGONIMUS HARINASUTAI*

QIAN Bao-zhen[1], H sugiyama[2], J Waikagul[3], ZHU Shi-hang[4]

[1] *Institute of Bio-engineering, Zhejiang Academy of Medical Sciences, Hangzhou 310013, china;*
[2] *Department of Parasitology, National Institute of Infectious Diseases, Japan;*
[3] *Department of Tropical Medicine, Mahidol University, Thailand;*
[4] *Nighai CDC, Ninghai 315600, China*

To identify *Paragonimus harinasutai* from Ninghai, Zhejiang Province, China. Methods Metacercariae wee collected from the crabs *Sinopotamon chekiangenes* in Xixi village of Ninghai country for ITS2 sequence analysis, CO1 sequence analysis and endonuclease *Bsa*HI and StuI analysis by PCR-RFLP. Results The fingerprintings of PCR-RFLP were virtually same to the isolate from Thailand (Nakorn-nayok). The Its2 sequence with 366 bp and CO1 sequence with 390 bp of the metacercariae collected from Thailand (Nakorn-nayok). The ITS2 sequence with 366 bp and CO1 sequence with 390 bp of the metacercariae collected from Ninghai revealed a nucleotide identity 95.6% and 89.5% respectively to the Thai isolate. Conclusion The study confirmed that *Paragonimus harinasutai* is present in Ninghai, China, with certain variation on molecular biology in comparison to the Thai isolate. Ø

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IMPORTED GNATHOSTOMIASIS ACQUIRED IN MYANMAR

M Develoux[1]*, P Dekumyoy[2], E Baygon[3], S Aractingi[3]

[1] *Serice de parasiologie, hôspital Tenon, 4, rue de la Chine, 75020 Paris, France;*
[2] *Department of Helminthology, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand;*
[3] *Service de dermatologie, hospital Tenon, 4, rue de la Chine, 75020 Paris, France*

We report a case of cutaneous gnathostomiasis acquired in Myanmar where this parasitic zoonosis was considered as non-endemic until a recent outbreak. Myanmar must be added to the list of countries where the infection can be acquired in Southeast Asia. Despite a treatment with ivermectin the patient relapsed after an apparent cure. A double-dose of ivermectin is now recommended for the treatment of gnathostomiasis. Ø

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MULTI-IMMUNODOT FOR RAPID DIFFERENTIAL DIAGNOSIS OF EOSINOPHILIC MENINGITIS DUE TO PARASITIC INFECTIONS

Eamsobhana P[1], Ongrotchanakun J[1], Yoolek A[1], Punthuprapasa P[1], Monkong N[1], Dekumyoy P[2]

[1] *Department of Parasitology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand;*
[2] *Department of Helminthology, Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand*

A multi-dot enzyme-linked immunosorbent assay (ELISA) was developed for the rapid and simple differential diagnosis of eosinophilic meningitis due to helminth infections. Ultrafiltered, purified antigens of *Parastrongylus* (=*Angiostrongylus*) *cantonensis*, *Gnathostoma spinigerum* and *Taenia solium* metacestodes, the most common parasites that invade the central nervous system and cause eosinophilic pleocytosis, were dotted onto a single nitrocellulose membrane strip. Antigen-coated strips, when blocked with 5% skimmed milk and dried, were stable for at least 6 months at 4°C. With peroxidase conjugated anti-human immunoglobulins and 4-chloro-1-naphthol as a substrate, antibodies in the corresponding patients' sera were clearly detected on the membrane strip as well-defined blue dots. Although cross-reactions between *P. cantonensis* and *G. spinigerum* antigens were observed with the use of partially purified antigens, the darkest dot correlated well with the infecting parasites in all cases. This fast, easy and economical multiple dot-blot ELISA method is useful for the differential diagnosis of eosinophilic meningitis caused by parasitic helminths, as semi-purified antigens can be easily obtained by ultrafiltration and used. Further improvements using highly specific parasite antigens may make this multi-immunodot test more suitable for wide-scale use in field studies and diagnostic laboratories. ∅

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SOIL-TRANSMITTED HELMINTHIASES AND POSSIBLE SOURCES OF ASCARIASIS AND TRICHURIASIS INFECTIONS IN PRIMARY SCHOOL CHILDREN, NAKHON SI THAMMARAT PROVINCE

Sa-nguankiat S, Maipanich W, Pubampen S, Muennoo C

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

In southern Thailand, the prevalence rate of soil-transmitted helminthiases (STH) among Thai muslims was quite high, especially among seaside communities, Their households were built in cluster. Poor environmental sanitation in the village and optimal conditions for the development of egg provoked high infection rates in the population. Infected persons spread the disease to the whole community and the major of infection rate was found among school-aged children.

Prevalence rates and intensity of infection were studied among 502 primary school children by stool examination (Katz's modified thick smear technique). Helminth eggs were detected from soil (sugar flotation method) and nail dirt. The results showed that the school children had trichuriasis (46.6%), ascariasis (17.9%), and hookworm infection (7.0%). Whipworm and roundworm infection were commonly found among the aged <12 years. The highest prevalence rate of trichuriasis (49.7%) and ascariasis (19.5%) were in the age group 8-11 years while hookworm infection rate was high among the age group of 4-7 years (10.2%). Heavy STH infections were mostly persisted in children aged 4-7 years, being 51.7%, 23.0%, and 18.8% for Ascaris, Trichuris, and hookworm infection, respectively.

Whipworm and pinworm eggs were found in the nail dirt (3.3%) of the school children. Whipworm eggs were also detected in soil samples. The findings indicated the sources of helminth infection in the community, and the transmission cycle in the endemic area. Mixed infections of two kinds of worm were found in 28.1%, and 5.9% had triple infections. ∅

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CONTROL OF SOIL-TRANSMITTED HELMINTHS THROUGH PRIMARY HEALTH CARE ACTIVITIES

Wanna Maipanich[1], Wichit Rojekittikhun[1], Chatree Muennoo[1], Surapol Sa-nguankiat[1], Somchit Pubampen[1], Thongchai Sarakul[2]

[1] *Department of Helminthology, Faculty of Tropical Medicine, Mahidol University, 420/6 Ratchawithi Road, Bangkok 10400, Thailand*
[2] *Primary Health Care Development Center, Nakhon Si Thammarat Province, Phatthanakan Khukhuang Road, Nakhon Si Thammarat 80000, Thailand*

The Helminthiasis Control Program in Thailand, run by the Ministry of Public Health, reduced the high prevalence of liver fluke infection to 9.6%, and hookworm infection to 11.4%, within 25 years. However, *Opisthorchis* infections in endemic areas were high (47.6%), and in the south, where soil-transmitted helminthes are abundant, the prevalence in schoolchildren was 27.7%. In rural areas, many problems were easily solved when people realized the hazardous effects on the community. The Primary Health Care Development Center in the region is responsible for promoting health activities in the village, to provide better lifestyles and good health for the people with the help of health volunteers.

Our study aimed to control helminth infections in the community with the aid of village health volunteers. The passing of roundworms by infected children showed that helminth infections persisted in the community, and greatly affected the growth and development of the youth. If they want their children to be free from infection, all infected persons must be treated. We offered them diagnosis by stool examination and treatment of infected cases. Village health volunteers were responsible for the distribution and collection of stool containers among the population. The results showed that in Phangsing Village, the number of stool samples collected was quite low. Many people refused to submit samples for examination. The prevalence of helminth infection had not decreased. Environmental sanitation in the village was poor and no improvement was noted during the study. In another village, Ban Nai Thung, more people submitted stool samples. After treatment, many people collected stool samples for examination to confirm that they were free from infection. In this area, prevalence decreased from 67.1% to 40.8% within 18 months. In this particular area, the village health volunteers also refused to work for us after a few days, but we offered some incentives to them so that the project could be conducted.

Collecting stool samples was hard work for the village health volunteers. They spent many days collecting stool containers and sometimes, very few people returned them. This showed that village health volunteers were probably useful for several health activities, but not so for collecting stool samples in the community. ∅

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PROCAMALLANUS (*SPIROCAMALLANUS*) *ANGUILLAE* SP. N. (CAMALLANIDAE) AND SOME OTHER NEMATODES FROM THE INDONESIAN SHORTFIN EEL *ANGUILLA BICOLOR* IN THAILAND

F Moravec[1], H Taraschewski[2], M Thairungroj Anantaphruti[3], W Maipanich[3], T Laoprasert[4]

[1] *Institute of Parasitology, Academy of Sciences of the Czech Republic, Branišovská 31, 370 05 Ceské Budešjovice, Czech Republic;*
[2] *Abteilung Okologie und Parasitologie, Zoologisches Institut der Universitat Karlsruhe(TH), Kaiserstrasse 12, 76128 Karlsruhe, Germany;*
[3] *Department of Helminthology, Faculty of Tropical Medicine, Mahidol University, 420/6 Ratchawith Road, Ratchathewee, Bangkok 10400, Thailand;*
[4] *Department of Fisheries, Aquatic Animal Health Research Institute, Paholyothid Road, Chatuchak, Bangkok 10900, Thailand*

A new species of parasitic nematode, *Procamallanus* (*Spirocamallanus*) *anguillae* sp. n. (family Camallanidae), is described based on specimens recovered from the intestine of the Indonesian eel *Anguilla bicolor* McClelland (type host) from southern Thailand (type locality Phuket Island). It is characterized mainly by the presence of 10-13 spiral ridges in the buccal capsule, length of spicules (366-372 µm and 198-216 µm), presence of a gubernaculum, arrangement of caudal papillae, and by the broad female tail with a digit-like projection bearing two cuticular spikes. In addition, two species of larval nematodes, Physalopteridae gen. sp. and *Anisakis* cf. *simplex* (Rudolphi 1809), were recorded from *A. bicolor*. All species are briefly described and illustrated. ∅

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TRICHINELLOSIS PAPUAE IN BAN-RAI DISTRICT, UTHAITHANI PROVINCE, THAILAND

Teera Kusolsuk[1], Chowalit Khumjui[2], Paron Dekumyoy[1], Urusa Thaenkhum[1], Surapol Sa-nguankiat[1], Wanna Maipanich[1], Supaporn Nuamtanong[1], Somchit Pubampen[1], Tippayarat Yoonuan[1], Malinee Thairungroj[1], Amara Thonghong[2], Jitra Waikagul[1]

[1] *Department of Helminthology, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand.;*
[2] *Bureau of Epidemiology, Department of Disease Control, Ministry of Public Health, Nonthaburi Province, Thailand*

Trichinellosis has been described as an emerging and/or re-emerging disease in Europe and the world. In Thailand since 1962, outbreaks of *Trichinella spiralis* infection have occurred in the north almost every year, and *T. pseudospiralis* was reported once in Chumphon Province, in the south. In one outbreak, 19 patients were admitted on July, 2006 in Ban-Rai and Uthaithani hospitals, with chief complaints of muscle hypertrophy on their faces, arms, and legs, with periorbital swelling, mild pain, and weakness. They had consumed undercooked wild-pig meat prior to the onset of clinical signs and symptoms. One muscle biopsy sample of a patient and the sera of patients (19) and villagers (64) were sent to the Department of Helminthology, Faculty of Tropical Medicine, Mahidol University. Non-encapsulated larvae of *Trichinella* sp. were found, and a partial sequence of a COI gene (320 base pair) showed it was *T. papuae*. Serodiagnoses of 18/19 patients and 14/64 villagers by immunoblot using *T. spiralis* L3 antigen were positive.

Follow-up with 19 of the treated patients found minimal symptoms of weakness, no fever, no muscle hypertrophy or swelling, and muscle tone and muscle power were normal. In addition, a reservoir-host survey was conducted and no larvae were found in the muscle biopsy samples of rats, domestic pig, palm civet, or one patient's cat. A total of 128 stool samples (villagers 63; school children 65) gave a prevalence of helminthic infection at 27.34% (35/128). Hookworm was the most common infection at 25.0% (32/128); other infections were *Enterobius vermicularis* at 1.56% (2/128) and Taenia sp. at 0.78% (1/128). Interviews of villagers about their food consumption and hygiene behaviors using a constructed questionnaire indicated that 80.0% (76/95) had a history of eating uncooked or undercooked meat, such as wild pig. This is the first finding of *T. papuae* in Thailand. Immunoblot using *T. spiralis* L3 antigen can detect serum antibody of trichinellosis papuae. Villagers are at risk of re-infection due to their habit of consuming raw meat. ∅

INSECTICIDE SUSCEPTIBILITY OF MOSQUITOES INVADING TSUNAMI-AFFECTED AREAS OF THAILAND

Narumon Komalamisra, Yuwadee Trongtokit, Kaewmala Palakul, Samrerng Prummongkol, Yudthana Samung, Chamnarn Apiwathnasorn, Theerawit Phanpoowong, Achara Asavanich and Somjai Leemingsawat

Department of Medical Entomology, Faculty of Tropical Medicine, Mahidol University. E-mail: tmnkm@mahidol.ac.th

In order to control the mosquitos invading tsunami-affected areas of Thailand, the insecticide susceptibility status of field larvae and mosquitoes (*Anopheles sundaicus* and *Culex sitiens*) was tested under laboratory conditions. Larval bioassay tests were conducted using the WHO standard method. Three larvicides: temephos, malathion, and plant extract (ethanolic extract of the Southeast Asian long pepper, *Piper retrofractum* Vahl), were used in the experiments. The results revealed that *Cx. sitiens* was more susceptible to temephos than malathion and the plant extract, with LC_{50} ranges of 0.0008 - 0.0014 mg/l, 0.0046 - 0.0078 mg/l, and 5.3180 - 10.1030 mg/l, respecetively. *Cx. quinquefasciatus* showed greater tolerance to every tested larvicide than *Cx. sitiens*. Adult bioassay tests using a WHO test kit and diagnostic doses of 5% malathion, 0.75% permethrin, 0.05% deltamethrin, and 4% DDT were also conducted. The results revealed that *Cx. sitiens* and *An. sundaicus* were susceptible to all tested insecticides. The LC_{50} of 5% malathion ranged between 25.7 - 26.0 minutes for *Cx. sitiens*, and 44.7 minutes for *An. sundaicus*. In addition, *Cx. quinquefasciatus* showed susceptibility to malathion, with LT_{50} of 19.7 minutes. However, it showed resistance to both pyrethroid insecticides, with LT_{50}

of 33.1 minutes for 0.75% permethrin, and 19.6 minutes for 0.05% deltamethrin; it showed low percentage mortality at 24 hour post-exposure, of 48 and 32%, respectively. In conclusion, every tested larvicide could be used for controlling *Cx. sitiens* larvae, even in beackish water, pyrethroid insecticides for adult *Cx. sitiens* and *An. sundaicus*, and malathion for all three species. ∅

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REPELLENCY OF ESSENTIAL OILS EXTRACTED FROM PLANTS IN THAILAND AGAINST FOUR MOSQUITO VECTORS (DIPTERA: CULICIDAE) AND OVIPOSITION DETERRENT EFFECTS AGAINST *AEDES AEGYPTI* (DIPTERA: CULICIDAE)

Apiwat Tawatsin[1,5], Preecha Asavadachanukorn[2], Usavadee Thavara[1], Prapai Wongsinkongman[3], Jaree Bansidhi[3], Thidarat Boonruad[3], Pranee Chavalitumrong[3], Noppamas Soonthornchareonnon[4], Narumon Komalamisra[5] and Mir S Mulla[6]

[1] *National Institute of Health, Department of Medical Sciences, Ministry of Public Health;*
[2] *Department of Statistics, Faculty of Commerce and Accountancy, Chulalongkorn University;*
[3] *Medicinal Plant Research Intitute, Department of Medical Sciences, Ministry of Public Health;*
[4] *Department of Pharamacognosy, Faculty of Pharmacy, Mahidol University;*
[5] *Department of Medical Entomology, Faculty of Tropical Medicine, Mahidol University, E-mail: tmnkm@mahidol.ac.th Bangkok, Thailand;*
[6] *Department of Entomology, University of California, Riverside, California, USA.*

In this study we evaluated and reported repellent effects of essential oils from Thai plants against 4 mosquito vectors: *Aedes aegypti, Ae. albopictus, Anopheles dirus* and *Culex quinquefasciatus* under laboratory conditions using human volunteers. The essential oils were extracted from 18 plant species, belonging to 11 families, and the oils were then prepared as 10% solution in absolute ethanol with additives. Two chemical repellents, deet and IR3535, were also prepared in the same formulation as the essential oil repellents and tested for repellency as controls. The essential oils were also evaluated for oviposition deterrent effects against *Ae. aegypti* under laboratory conditions. The results show night-biting mosquitoes (*An. dirus* and *Cx. quinquefasciatus*) and *Ae. albopictus* were more sensitive to all the essential oils (repellency 4.5 - 8 hours) than was *Ae. aegypti* (repellency 0.3 - 2.8 hours), whereas deet and IR3535 provided excellent repellency against all four mosquito species (repellency 6.7 - 8 hours). All essential oils exhibited oviposition deterrent activity against *Ae. aegyti* with various degree of repellency ranging from 16.6 to 94.7%, whereas deet and IR3535 had no repellency. The present study demonstrates the potential for using essential oils as mosquito repellents and oviposition deterrents. These findings may lead to new and more effective strategies for protection from and control of mosquitoes. ∅

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SUSCEPTIBILITY OF TWO KARYOTYPIC FROMS OF *ANOPHELES ACONITUS* (DIPTERA: CULICIDAE) TO *PLASMODIUM FALCIPARUM* AND *P. VIVAX*

Anuluck Junkum[1], Atchariya Jitpakdi[1], Narissara Jariyapan[1], Narumon Komalamisra[2], Pradya Somboon[1], Wannapa Suwonkerd[3], Aungkana Saejeng[3], Paul A Bates[4] and Wej Choochote[1]

[1] *Department of Parasitology, Faculty of Medicine; Chiang Mai University,*
[2] *Department of Medical Entomology, Faculty of Tropical Medicine, Mahidol University;*
[3] *Office for Vector Borne Diseases Control 2; Department of Communicable Diseases Control, Ministry of Public Health, Bangkok, Thailand;*
[4] *Molecular and Biochemical Parasitology Group, Liverpool School of Tropical Medicine, University of Liverpool, Liverpool, United Kingdom. tmnkm@mahidol.ac.th*

Four laboratory-raised colonies of two karyotypic forms of *Anopheles aconitus*, i.e., Form B (Chiang Mai and Phet Buri strains) and C (Chiang Mai and Mae Hong Son strains), were experimentally infected with *Plasmodium falciparum* and *P. vivax* using an artificial membrane feeding technique and dissected eight and 12 days after feeding for oocyst and sporozoite rates, respectively. The results revealed that *An. aconitus* Form B and C were susceptible to *P. falciparum* and *P. vivax*, i.e., Form B (Chiang

Mai and Phet Buri strains/*P. falciparum* and *P. vivax*) and Form C (Chiang Mai and Mae Hong Son strains/*P. vivax*). Comparative statistical analyses of the oocyst rates, average number of oocysts per infected midgut and sporozoite rates among all strains of *An. aconitus* Form B and C to the ingroup control vectors. *An. minimus* A and C, exhibited mostly no significant differences, confirming the high potential vector of the two *Plasmodium* species. The sporozoite-like crystals found in the median lobe of the salivary glands, which could be a misleading factor in the identification of true sporozoites in salivary glands were found in both *An. aconitus* Form B and C. Ø

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SURVEYS FOR NATURAL HOST PLANTS OF MANSONIA *MOSQUITOES INHABITING* TOH DAENG PEAT SWAMP FOREST, NARATHIWAT PROVINCE, THAILAND

Chamnarn Apiwathnasorn, Yudthana Samung, Samrerng Prummongkol, Achara Asavanich and Narumon Komalamisra

Department of Medical Entomology, Faculty of Tropical Medicine, Mahidol University, tmcaw@mahidol.ac.th

Surveys were carried out monthly from April-October 2002 to examine 68 sampling sites aroud "Toh Daeng" peat swamp forest in Narathiwat Province, Thailand, of which 38 were know *Mansonia*-positive habitats and 30 were *Mansonia*-negative sites. The present larval surveys were qualitative owing to features of the host plants (location, distribution, and abundance), difficulties in locating and selecting the host plants in the swamp forest, and time constraints. Twenty attempts were made for each species for larvae. The presence of *Mansonia* larvae on each plant species was confirmed 6 times for each plant and location. Larvae of *Ma. bonneae* and *Ma. uniformis* were obtained feom 18 plant species (10 famillies): *Metroxylon sagu, Melaleuca cajuputi, Pandanus militaris, Pandanus immerses, Hanguana malayana, Typha angustifolia, Hymenachne acutigluma, Scirpodendron ghaeri, Scleria sumatrensis, Rhynchospora corymnosa, Sacclolepis indica, Cyperus babakan, Cyperus corymbosus, Lepironia articulata, Leersia hexandra, Eichhornia crassipes, Pistia stratriotes and ferns. The emergent grasses, S. ghaeri, S. sumatrensis, H. acutigluma, R. corymnosa, S. indica, C. babakan, C. corymbosus* and *L. articulata*, were the preferred host plants. Samples from larger trees, *M. sagu* and *M. cajuputi*, yielded low numbers of 1-7 larvae per scraping. *Ma. uniformis* was recovered from most of the host plants, while *Ma. bonneae* preferred submerged plants and was not found on the floating aquatic plants. *E. crassipes* and *P. stratriotes*. The description of modified dipper and dipping techniques are given and discussed. Ø

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THE RELATIONSHIP BETWEEN THE ABUNDANCE OF *MANSONIA* MOSQUITOES INHABITING A PEAT SWAMP FOREST AND REMOTELY SENSED DATA

Chamnarn Apiwathnasorn[1], Achara Asavanich[1], Narumon Komalamisra[1], Yudthana Samung[1], Samrereng Prummongkol1 and Kobkan Kanjanopas[2]

[1] *Department of Medical Entomology, Faculty of Tropical Medicine, Mahidol University;*
[2] *Department of Disease Control, Ministry of Public Health. tmcaw@mahidol.ac.th*

The present study aimed to demonstrate the relationship of some environment factors, vegetation greenness index (NDVI) and land surface temperature (LST), with the seasonal variations of *Mansonia bonneae* and *Ma. uniformis* in Khosit Subdistrict, Narathiwat Province. It was found that the *Mansonia* population lagged one month behind but correlated positively to NDVI, LST and rainfall. A rise in the number of mosquitoes was directly related to a rise in vegetation, temperature and rainfall. Ø

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LABORATORY COLONIZATION OF *MANSONIA* MOSQUITOES WITH AN EMPHASIS ON *MA. ANNULATA* AND *MA. BONNEAE*

Yudthana Samung, Kaewmala Palakul, Chamnarn Apiwathnasorn, Samereng Prummongkol, Achara Asavanich and Somjai Leemingsawat

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

The present study records the first successful colonization of *Mansonia annulata* and describes colony maintenance with modification of rearing medium and host plants. Three species of *Mansonia* mosquitoes (*Ma. uniformis, Ma. indiana* and *Ma. annulifera*) were successfully reared in ambient environments with adult emergence reates >50%, while *Ma. bonneae* and *Ma. dives* yielded emergence rates >30%. Colonization of *Ma. annulata* was modified and improved so that they were successfully raised to adult with emergence rates of 23%. Tube sedge, Lepironia articulata, was utillized as a host plant and peat swamp water was used as a rearing medium. Yeast and small lizard droppings were added daily to the larval medium to maintain microorganisms and pH in the infusion. However, identifying suitable culture medium remains an obstacle to establishing colonies of *Ma. annulata*, as the culture medium is difficult to mimic in the laboratory. Further study, focusing particularly on larval attachment substrates and rearing medium, is needed to develop a standardized and practical rearing technique for *Mansonia* mosquitoes. ∅

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BIONOMICS STUDIES OF *MANSONIA* MOSQUITOES INHABITING THE PEAT SWAMP FOREST

Chamnarn Apiwathnasorn[1], Yudthana Samung[1], Samrerng Prummongkol[1], Achara Asavanich[1], Narumon Komalamisra[1] and Phillip Mccall[2]

[1] *Department of Medical Entomology, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand tmcaw@mahidol.ac.th;*
[2] *Liverpool School of Tropical Medicine, University of Liverpool, United Kingdom*

The present study was conducted in the years 2000-2002 to determine the bionomics of *Mansonia* mosquitoes, vectors of nocturnally subperiodic *Brugia malayi*, inhabiting the peat swamp forest, "Phru Toh Daeng", Narathiwat Province, Thailand. Fifty-four species of mosquitoes belonging to 12 genera were added, for the first time, to the list of animal fauna in the peat swamp forest. *Mansonia* mosquitoes were the most abundant (60-70%) by all collection methods and occurred throughout the year with a high biting density (10.5-57.8 bites per person-hour). *Ma. bonneae* was most prevalent (47.5%) and fed on a variety of animal hosts, including domestic cats, cows, monkeys, and man with a maximum biting density of 24.3 bites per person-hour in October. The infective bites were found for the first time in *Ma. annulata* collected at Ban Toh Daeng (13.00-14.00 hours) and also *Ma. bonneae* at forest shade (16.00-17.00 hours) and in village (20.00-21.00 hours) with rates of 0.6, 1.1 and 1.0%, respectively. The biting activities of these two spcies occurred in both the day and night time, with two lower peaks at 10.00 hours (18.5 bites per person hours) and 13.00-15.00 (8.5 - 10.0 bites per person-hours) hours, but the highest peak was 19.00-21.00 hours (31.5-33.0 bites per persone-hour). The biting activity patterns corresponded with the periodicity found in man and domestic cats and may play an important role in either transmission or maintenance of the filarial parasites in the peat swamp forest. The relative role of *Ma. bonneae* and *Ma. uniformis* in different environmental settings (primary swamp forest and open swamp) on the transmission of nocturnally subperiodic *B. malayi* merits further study. ∅

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FORMULATION OF TABLETS FROM THE CRUDE EXTRACT OF *RHINACANTHUS NASUTUS* (THAI LOCAL PLANT) AGAINST *AEDES AEGYPTI* AND *CULEX QUINQUEFASCIATUS* LARVAE: A PRELIMINARY STUDY

Yupha Rongsriyam[1], Yuwadee Trongtokit[1], Narumon Komalamisra[1], Nuttanan Sinchaipanich[2], Chamnarn Apiwathnasorn[1] and Aumpol Mitrejet[2]

[1] *Department of Medical Entomology, Faculty of Tropical Medicine, Mahidol University;*
[2] *Department of Industrial Pharmacy, Faculty of Pharmacy, Mahidol University.*

Dried root powder of *Rhinacanthus nasutus*, Thong Phan Chang (Thai name) were extracted with methanol (MeOH) in a Soxhlet apparatus and made into 2 formulations of tablet containing the extract at 5% and 10% concentration. Due to the viscous and poor flow properties of the crude MeOH extract obtained, a wet granulation method was conducted in developing the tablets. Lactose was used as a filler. Polyvinyl pyrrolidone (PVP) K30 (15% w/w solution in alcohol) was used as the binding agent, while stearic acid (2% w/w) was used as a lubricant. Both formulas of prepared tablets had a smooth shiny surface with a round shape. Other physical properties of the tablets, such as weight variation, friability and disintegration time, met the requirements of the USP XX standard. The mosquito larvicidal activity of prepared tablets containing 5% and 10% *R. nasutus* extract against *Aedes aegypti* were not significantly different from each other ($p>0.05$), with 48-hour LC_{50} values of 13.6 and 14.2 mg/l for the 5% and 10% tablets, respectively, while their activities against *Culex quinquefasciatus* were similar ($p>0.05$) with LC_{50} values of 18.7 and 17.3 respectively. The larvicidal activity levels against *Ae. aegypti* and *Cx. quinquefasciatus* were also not significantly different from each other ($p>0.05$). No larval mortality was observed in the two control groups: lactose solution and dechlorinated water. Toxicity to female and male fish (*Poecilia reticulata*) was tested with the prepared tablets. The toxicity of tablets containing 5% and 10% extracts were not significantly different from each other for the *P. reticulata* females with 48-hour LC_{50} values of 105.2 and 110.8 mg/l, respectively, and for *P. reticulata* males with LC_{50} values of 99.1 and 103.4 mg/l, respectively. Female and male *P. reticulata* were sensitive to the same dose of the extract. No fish died in the two control groups, with lactose solution and dechlorinated water. Acute-toxicity bioassay with fish showed that with an exposure of 48 hours the LC_{50} values of the tablets containing 5% and 10% were 5- to 10-fold higher than the LC_{50} of *R. nasutaus* against mosquito larvae. These prepared tablets could possibly used to control mosquito vectors and be introduced into the mosquito control program. ∅

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INSECTICIDE SUSCEPTIBILITY STATUS OF DENGUE VECTOR, *AEDES AEGYPTI*, IN BANGKOK METROPOLITAN

Narumon Komalamisrd[1], Chamnarn Apiwatanasorn[1], Sompis Oatwaree[2] and Pornpimol Kijnitinan[2]

[1] *Department of Medical Entomology, Faculty of Tropical Medicine, Mahidol University. tmnkm@mahidol.ac.th*
[2] *Vector control Subdivision, Disease control Division, Health Department, Bangkok Metropolitan Administation*

DF/DHF/DSS is one of the top ten importance diseases under surveillance in Bangkok Metropolitan. There were 4,379 of the dengue cases and 11 death in the year 2005. During September-December 2005 the study of density, vector species and key container of breeding sites were conducted by the staff of Vector control Subdivision, Health Department, BMA. Mosquito larvae were collected from the dengue patient 's house just before the control measure by space spray were conducted and sent to Department of Medical Entomology, Faculty of Tropical Medicine, Mahidol University for insecticide susceptibility test. The specimens were collected from 25 out of 50 districts in Bangkok Metropolitan. Larvae were tested with temephos by WHO bioassay technique. Adult mosquitoes were tested for susceptible/resistance to permethrin, deltamethrin,

cyfluthrin, malathion, and DDT by using diagnostic doses and WHO test kit. The result revealed that most of the tested larvae were susceptible to temephos. The adults were susceptible to deltamethrin, cyfluthrin and malathion. Most colonies showed resistance to permethrin and all tested colonies resist to DDT. ∅

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LEARNING EXPERIENCE FROM TSUNAMI: ENTOMOLOGICAL PERSPECTIVE

Chamnarn Apiwathnasorn, Narumon Komalamisra, Yuwadee Trongtokit, Yudthana Samung, Samrerng Prummongkol, Teerawit Phanphoowong, Somjai Leemingsawat

Department of Medical Entomology, Faculty of Tropical Medicine, Mahidol University. tmcaw@mahidol.ac.th

December 26, 2004, the largest earthquake southwest of Sumatra in 40 years (registering 9 on the Richter scale) caused Tsunami in the Indian Ocean. The tsunami wave sent unprecedented amounts of seawater swept through villages and resorts right along the southern coastal region of Thailand, affecting Ranong, Phangnga, Krabi, Phuket, Trang and Satun Province. As many as 5,388 people were killed, 3,120 people were reported missing, and 8,457 people were wounded. Tsunami not only destroyed human settlements but also made agricultural land and wells unusable due to salination and sanding. In the most affected province, Phang Nga, seawater volume of about 2,500,000-5,000,000 m^3 invaded inland for 2.5 km and flooded along the coastline for more than 40 km. Rural water systems were badly contaminated with debris, salt water and bacteria risk people to drinking water contaminations and outbreak of infectious diseases. A large number of breeding places of *Culex sitiens* and *Anopheles sundaicus*, a coastal species of malaria vector, obviously increased as a consequence of seawater intrusion and contamination into such large collections of water as abandoned tin-mines, aquaculture ponds, swamps and ground pools. Although there have been few annual reported malaria cases previously, there have been little studies for assessing the potential risk of malaria outbreaks due to *An. sundaicus*. The emergent study, therefore, was performed during February to June 2004 to provide in-depth information on *An. sundaicus* and determine whether the ecological and entomological factors could influence malaria transmission in Phang Nga Province or not. The entomological data available from this study included larval abundance, distribution and composition, characteristics of breeding places, life-cycle, biting habits and insecticide susceptibility as well as Bacillus thuringiensis israelensis-based formulations. The results concluded that *An. sundaicus* was a potential vector of malaria in tsunami-affected areas whenever source of infection was available. The presence of green algae and grass debris mats on surface of the water contaminated by seawater would be a good indication of proliferation of *An. sundaicus* and time for larval control (1-2 months after tsunami hit). The information would contribute to improving future tsunami preparedness for monitoring and assessing the risk of malaria outbreaks and implementation of appropriate vector control measures. Entomological workers would be important members of tsunami-response teams to collect data relating potential vectors, map and treat all breeding sources as well as designing appropriate control strategies wherever need. ∅

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FIRST REPORT OF STORAGE MITES IN EXTERNAL EAR CANAL OF THAI AGRICULTURAL WORKER

Yudthana Samung, Chamnarn Apiwathnasorn, Sutee Wonglakorn and Anon Phayakkaphon

Department of Medical Entomology, Faculty of Tropical Medicine, Mahidol University; Department of Otolaryngology, Si Sa Ket Hospital, Si Sa Ket, Thailand

A 57-year-old woman in Si Sa Ket Province was infested with more than 20 mites in external auditory canal and complained of severe itching and feeling insects crawling in right ear with apparently during shallot (*Allium ascalonicum*) harvest season. Mite specimens were collected from patients's ear and preserved in 90% alcohol. The rest were then removed by suction. The specimens were mounted with Hoyer's medium and identified as stored product mite, *Suidasia potifica*. An attempt was carried out to seek for source of infestation by inspecting and collecting mites on dried chilies, shallots and garlic bulbs as well as house dust and other materials related to their cultivations such as straws from the patient house. *S. pontifica* was recovered from house dust, shallots and garlic bulbs. Handing materials infested with these arthropod hosts were thought to be overrun by these mites into ear. This is first report of storage mites implicated occupational health in Thailand. Several species of mites have been reported to infest stored products, therefore, more species of the mites injurious to agricultural workers are expected to be found. Proper collection of the mites to allow proper identification and bionomics study is needed. Ø

Poster presentations in: Joint International Tropical Medicine Meeting 2006, The Miracle Grand Convention Hotel, Bangkok Thailand, 29 November - 1 December 2006

THIOSIALOSIDE POLYMER AS A NEW CLASS OF INFLUENZA NEURAMINIDASE INHIBITORS

Koji Matsuoka[1,*], Chiharu Takita[1], Tetsuo Koyama[1], Daisei Miyamoto[2,3], Sangchai Yingsakmongkon[4], Kazuya IPJ Hidari[2,3], Wipawee Jampangern[5], Takashi Suzuki[2,3], Yasuo Suzuki[3,6], Ken Hatano[1], and Daiyo Terunuma[1]

[1] *Division of Materials Science, Graduate School of Science and Engineering, Saitama University, Sakura, Saitama 338-8570, Japan*
[2] *Department of Biochemistry, University of Shizuoka, School of Pharmaceutical Sciences, and COE program in the 21st century, Suruga, Shizuoka 422-8526, Japan*
[3] *Core Research for Evolutional Science and Technology (CREST), Japan Science and Technology Agency, Kawaguchi, Saitama 332-0012, Japan*
[4] *Department of Microbiological Immunology, Faculty of Veterinary Medicine, Kasetsart University, Bangkok 10900, Thailand*
[5] *Department of Microbiology and Immunology, Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand*
[6] *Department of Biomedical Sciences, College of Life and Health Sciences, Chubu University, Kasugai, Aichi 487-8501, Japan*

A conventional synthesis of -thioglycoside of sialic acid as a glycomonomer was accomplished. Radical copolymerization of the glycomonomer with vinyl acetate proceeded smoothly to afford a glycopolymer having thiosialoside residues, in which all protection was removed by a combination of transesterification and saponification to provide a water-soluble thiosialoside cluster. The results of a preliminary study on biological responses against influenza virus neuraminidases using the thiosialoside polymer as a candidate for a neuraminidase inhibitor showed that the glycopolymer has potent inhibitory activity against the neuraminidases. Ø

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THIOSIALOSIDE CLUSTERS USING CARBOSILANE DENDRIMER CORE SCAFFOLDS AS A NEW CLASS OF INFLUENZA NEURAMINIDASE INHIBITORS†

Jun-Ichi Sakamoto[Þ], Tetsuo Koyama[Þ], Daisei Miyamoto[2,3], Sangchai Yingsakmongkon[4], Kazuya IPJ Hidari[2,3], Wipawee Jampangern[5], Takashi Suzuki[2,3], Yasuo Suzuki[3,6], Yasuaki Esumi[7], Ken Hatano[1], Daiyo Terunuma[1], and Koji Matsuoka[1,*]

[1] *Division of Materials Science, Graduate School of Science and Engineering, Saitama University, Sakura, Saitama 338-8570, Japan*
[2] *Department of Biochemistry, University of Shizuoka, School of Pharmaceutical Sciences, and COE program in the 21st century, Suruga, Shizuoka 422-8526, Japan*
[3] *Core Research for Evolutional Science and Technology (CREST), Japan Science and Technology Agency, Kawaguchi, Saitama 332-0012, Japan*
[4] *Department of Microbiology and Immunology, Faculty of Veterinary Medicine, Kasetsart University, Bangkok 10900, Thailand*
[5] *Department of Microbiology and Immunology, Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand*
[6] *Department of Biomedical Sciences, College of Life and Health Sciences, Chubu University, Kasugai, Aichi 487-8501, Japan*
[7] *The Institute of Physical and Chemical Research (RIKEN), Wako, Saitama 351-0198, Japan*

An efficient synthesis of a series of carbosilane dendrimers uniformly functionalized with α-thioglycoside of sialic acid was accomplished. The results of a preliminary study on biological responses against influenza virus sialidases using thiosialoside clusters showed that some of the glycodendrimers have inhibitory potencies against the sialidases. ∅

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

Akanitt Jittmittraphap[1], Suwich Thammapalo[2], Nitipon Ratanasetyuth[1], Narong Wongba[2], Mammen P Mammen[3], Wipawee Jampangern[1*]

[1] *Department of Microbiology and Immunology, Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand.*
[2] *Department of Disease Control, Ministry of Public Health, Nonthaburi 11000, Thailand.*
[3] *Department of Virology, Armed Forces Research Institute of Medical Sciences (AFRIMS), Bangkok 10400, Thailand.*

RNA amplification by nucleic acid sequence-based amplification (NASBA) was used to detect serotype specific dengue viruses in artificially-infected female *Aedes* mosquitoes, in comparison with RT-PCR technique. NASBA could detect dengue virus serotype 2 and 4 below 0.1 PFU, which was more sensitive than RT-PCR, but this technique was as sensitive as RT-PCR when detecting dengue virus serotype 1 and 3. Dengue viruses could be detected at the thorax of mosquitoes at 0, 7, and 14 days after inoculation with dengue virus serotype 2. This method should be useful for virological surveillance of dengue infected *Aedes* mosquitoes, as an early warning system to predict outbreaks of dengue viruses. ∅

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TRAFFIC OF ANTIBODY-SECRETING CELLS AFTER IMMUNIZATION WITH A LIPOSOME-ASSOCIATED, CPG-ODN-ADJUVANTED ORAL CHOLERA VACCINE

Srinuan Somroop[1], Pongsri Tongtawe[1], Urai Chaisri[2], Pramuan Tapchaisri[1], Manas Chongsa-nguan[2], Potjanee Srimanote[1*] and Wanpen Chaicumpa[1]

[1] *Faculty of Allied Health Sciences, Thammasat University, Rangsit Center, Pathumthani 12121, Thailand;*
[2] *Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand*

An oral cholera vaccine made up of heat-treated recombinant cholera toxin (rCT), *V. cholerae* lipopolysaccharide (LPS), and recombinant toxin-co-regulated pili subunit A (rTcpA), entrapped in liposomes in the presence of unmethylated bacterial CpG-DNA (ODN# 1826) was used to orally immunize a group of eight week old rats. A booster dose was given 14 days later. Control rats received placebo (vaccine diluent). The kinetics of the immune response were investigated by enumerating the antigen specific-antibody secreting cells (ASC) in the blood circulation and intestinal lamina propria using the ELISPOT assay and a histo-immunofluorescence assay (IFA), respectively. ASC of all antigenic specificities were detected in the blood of the vaccinated rats as early as two days after the booster dose. The numbers of LPS-ASC and TcpA-ASC in the blood were at their peak at day 3 post booster while the number of CT-ASC was highest at day 4 after the booster immunization. At day 13 post immunization, no ASC were detected in the blood. A several fold increase in the number of ASC of all antigenic specificities in the lamina propria above the background numbers of the control animals were found in all vaccinated rats at days 6 and 13 post booster (earlier and later time points were not studied). Vibriocidal antibody and specific antibodies to CT, LPS and TcpA were detected in 57.1% and 52.4%, 14.3% and 19.0% of the orally vaccinated rats, respectively. The data indicated that rats orally primed with the vaccine could produce a rapid anamnestic response after re-exposure to the *V. cholerae* antigens. Thus, a single dose of the vaccine is expected to elicit

a similar anamnestic immune response in people from cholera endemic areas who have been naturally primed to *V. cholerae* antigens, while two doses at a 14 day interval should be adequate for a traveler to a disease endemic area. ∅

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THE ENHANCING ANTIBODIES OF DENGUE VIRUS INFECTION IN THAI PATIENTS' SERA

Huan-Yao Lei[1], Natthakorn Khuendee[2], Akanitt Jittmittraphap[2], Robert V Gibbons[3], Kriengsak Limkittikul[2], Prasong Witayathawornwong[4], Pathom Sawanpanyalert[4] and *Wipawee Jampangern[2]

[1] *Medical College, National Cheng-Kung University, Taiwan*
[2] *Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand*
[3] *Armed Force Research Institute of Medical Science (AFRIMS)*
[4] *Ministry of Public Health, Bangkok, Thailand*
* *Correspondence : Wipawee Jampangern*

Dengue virus (DENV) can cause a wide spectrum of diseases, from undifferentiated febrile illness to dengue fever, dengue hemorrhagic fever (DHF), and dengue shock syndrome (DSS). Children with secondary infection with a different dengue virus serotype may have more severe DHF/DSS, which can be fatal. Antibody-dependent enhancement of infection (ADE) is widely accepted as central to the development of these clinical entities. Non-neutralizing anti-dengue antibody bound to the dengue virion enhanced the virus' entrance into the target cells via the Fc receptor. To detect the enhancing antibodies of dengue virus infection, we used sensitive flow cytometry to detect dengue virus-infected K562 cells; a serial 3 to 9 – fold of patient serum was diluted and mixed with dengue virus, incubated with K562 cells, and then the percentage infected cells was determined by cytoplasmic staining with anti-NS1 antibody. The titer of enhancement was determined as the reciprocal of the serum dilution that ceased to provide enhancing activity.

The study found that Thai dengue patients' sera contained high titers of enhancing antibodies. The enhancing antibodies increased gradually post-dengue virus infection; The convalescent phase had higher titers of enhancing antibodies than the acute phase. Furthermore, The Thai dengue patients' sera contained high titers of enhancing antibodies against their own dengue virus isolate, and the titers were similar to other serotypes of dengue virus. It was concluded that anti-dengue antibody would enhance dengue virus infection in a concentration-dependent, but serotype-independent manner. ∅

Presented at: Asia-Pacific congress of Medical Virology 2006, November 13-15. India Habitat Centre, New Delhi India.

RECEPTOR BINDING SPECIFICITY OF THE HIGHLY PATHOGENIC H5N1 AVIAN INFLUENZA VIRUSES-MUTATION FOR THE BINDING TO HUMAN-TYPE RECEPTORS

Y Suzuki[1], S Yamada[2], Y Kawaoka[2], C-T Guo[3,4], H Hiramatsu[1], W Narongwanichgarn[5], P Leaungwutiwong[6], A Jittmittraphap[6], S Yingsakmongkon[7], P Akkapaiboon[8], P Auewarakul[9], T Songserm[7], S Damrongwatanapokin[5], P Sawanpanyalert[8], P Indrakamhang[5], P Warachit[8], W Jampangern[6], T Takahashi[4], Y Sakano[4], KIPJ Hidari[4], D Miyamoto[4], T Suzuki[4]

[1] *Coll. Life & Health Sci. Chubu Univ, CREST, JST, Japan,*
[2] *Inst. Med. Sci. Univ. Tokyo. CREST JST, Japan,*
[3] *Zhejiang Acad. Med. Sci., China,*
[4] *Univ. Shizuoka Sch. Pharm. Sci., CREST, JST; COE Program, 21th Century, Japan,*
[5] *National Inst. Animal Health, Thailand,*
[6] *Dept. Trop. Med. Mahidol Univ, Thailand,*
[7] *Faculty of Vet. Sci., Kasetsart Univ, Thailand,*
[8] *National Inst. Thailand,*
[9] *Dept. Microbiol., Faculty of Med., Siriraj Hospital, Mahidol Univ, Thailand*

Human influenza A viruses bind predominantly N-acetylneuraminic aciad (Neu5Ac) α2-6 Galactose (Gal) linkages (2-6), whereas bird viruses bind Neu5Ac2-3 Gal (2-3) predominantly [1]. We found that H5N1 isolated from a boy visiting Fujian province in China bound to both 2-3 and 2-6 [2], suggesting the adaptation of the avian H5N1 isolated from humans. We also detected similar mutations in the avian H5N1 isolated from humans in Hanoi, Vietnam [3]. Thus, the initial mutation of the highly pathogenic bird influenza viruses (H5N1) into the viruses which easily transmit among humans will primarily be an adaptation of receptor binding specificity of the H5N1 virus from 2-3 (bird type) to 2-6 (human type). We found that mutations of single amino acid at positions in the HAs of H5N1 independently converted the virus known to recognize the avian receptor to ones that recognize the human receptor [4]. These mutations introduce the molecular signs of the next influenza pandemic in the human world. We developed a new assay system for the receptor binding surveillance to detect the change of receptor binding specificity of the highly pathogenic avian influenza virus (H5N1) into human type. This method is simple, sensitive and useful to detect the mutation of the host range of the highly pathogenic avian influenza virus (H5N1) into humans. Receptor binding surveillance should be started globally in addition to gene and antigenic analyses of influenza viruses. ∅

Presented at : The Joint International Tropical Medicine Meeting (JITMM) 2006, 29 Novermber-1 December 2006, Miracle Grand Hotel, Bangkok, Thailand.

DETECTION OF *ORIENTIA TSUTSUGAMUSHI* IN FIELD RODENTS FROM FIVE PROVINCES, THAILAND, BY NESTED POLYMERASE CHAIN REACTION

W Saisongkorh[1], A Imvithaya[1], D Paengjai[1], C Klaiyaithong[1], V Wongchotigul[2]

[1] *National Institute of Health, Department of Medical Sciences, Ministry of Public Health, Nonthaburi 11000, Thailand;*
[2] *Department of Microbiology and Immunology, Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand*

A total of 312 field rodents representing 10 species in 4 genera were collected from 5 provinces, Thailand. Among them except *Suncus murinus*, 88 field rodents were seropositive (≥1:50) for *Orientia tsutsugamushi* by the indirect immunofluorescent assay. In this study, *Rattus berdmorei* had the highest seropositive rate of 69.6% while none of the cases of *Mus cervicolor* gave antibody titers ≤1:25. When testing the blood samples for the presence of *O. tsutsugamushi* DNA by the nested polymerase chain reaction, 16 of *R. surifer* and 1 of *R. rattus* were positive against the gene encoding for the 56 kDa protein of *O. tsutsugamushi*. However, only 3 of 88 seropositive rodents show the evidence of acute infection. These results suggest that rates of rickettsial infections in rodents could not be determined by the antibody detection alone. ∅

Presented at: Joint International Tropical Medicine Meeting 2006, 29 Novermber-1 December 2006, Bangkok, Thailand.

MOLECULAR TYPING OF *LEPTOSPIRA* SPP. BASED ON PUTATIVE O-ANTIGEN POLYMERASE GENE (*ORF14*) WITHIN THE *RFB* LOCUS

P Wangroongsarb[1], T Chanket[1], K Gunlabun[1], Do Hoang Long[1], P Sateinmethakul[1], S Jetanadee[1], U Wongthongsri[1], Y Mahakunkijjaroen[1], W Jumpangern[1], J Thaipadungpanit[2], V Wuthienkanun[2], S J Peacock[2], SD Blacksell[2], P Srimanote[3], L Smythe[4] and T Kalambaheti[1]

[1] *Department of Microbiology and Immunology, Faculty of Tropical Medicine, Mahidol University , Bangkok, Thailand;*
[2] *The Wellcome Trust unit, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand;*
[3] *Faculty of Allied Health Sciences, Thammasat University, Bangkok, Thailand;*
[4] *WHO/FAO/OIE Collaborating Centre for Reference & Research on Leptospirosis, Australia*

Molecular classification of *Leptospira* spp. strains based on variation within putative O-antigen polymerase gene (*orf14*) was determined for reference and patient strains. Using the PCR primers designed from flanking gene of *orf14* derived from *L. interrogans* serovar Copenhagenii, all *L. interrogans* serovars could be amplified as well as human and rodent

- leptospiral isolates from Thailand. The limitation of these primer pairs was the inability to amplify some remote species in this study including *L. biflex, L. borgpetersenii* serovar Tarassovi, *L. kirscherneri* of serovar Bim, Bulgarica, Butembo. When *orf14* sequence data were subjected to phylogenetic tree construction using the posterior probabability of the Bayesian, the reliability value is acceptable. The genotyping based on *orf14* sequence was then categorized Leptospiral serovars into 7 genetically related group, e.g. Hardjobovis, Bataviae, Pomona, Australis, Autumnalis, Pyrogenes and Icterohaemorrhagiae. The Hardjobovis group was quite distinct from other group and shared approximately 50% similarity to other groups. The Thai leptospiral isolates could be classified along the subgroup clade. This molecular typing system was able to catagorize unknown Leptospiral isolates into group, of which its differentiation power was better that the conserved 16S rRNA genotyping. ∅

Presented at: The Joint International Tropical Medicine Meeting 2006, 29 Novermber-1 December 2006, Bangkok, Thailand.

IN VIVO CULTURE OF *CRYPTOSPORIDIUM* OOCYSTS FOR LABORATORY USE

Sangloung C, Buddhirongawatr R, Tantawiwattananon N, Sukthana Y

In the present study, we describe *in vivo* cultivation to produce oocysts. Seven-day-old mice were orally infected with 100,00120,000 *Cryptosporidium* oocysts. On day 8 post-infection, the mice were killed by ether, and the small and large intestines collected. A simple extraction procedure was used and purified using Ficoll gradient centrifugation. After purification, the oocysts were preserved in phosphate buffered saline with antibiotic at 4°C before use. ∅

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CULTIVATION OF *GIARDIA DUOENALIS* IN MONGOLIAN GERBILS

Tantawiwattananon N, Sangloung C, Buddhirongawatr R, Sukthana Y

The Mongolian gerbil (*Meriones unguiculatus*) is susceptible to infection with *Giardia duodenalis* trophozoites. Each animal was orally infected with 0.5 ml Diamond's TYIS-33 culture medium containing 10^6 trophozoites. Cysts were then collected and concentrated by sucrose gradient centrifugation. *G. duodenalis* cysts were first observed in feces on day 5 post-infection. The characteristic of *G. duodenalis* infection in gerbils was intermittent cyst release. The range in the number of cysts released per gerbils for a 4-hour collection period was 0-1.5 x 10^3. ∅

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DETECTION OF *TOXOPLASMA GONDII* IN CAPTIVE WILD FELIDS

Buddhirongawatr R, Tantawiwattananon N, Sangloung C, Sukthana Y

Toxoplasma gondii can infect all species of warm-blooded animals, including humans, and causes serious diseases in immunocompromized hosts. Live tachyzoites derived from serial passage in HeLa culture were used in the Sabin-Feldman dye test for detection of *Toxoplasma gondii* antibody in serum samples of 21 captive wild felids including one fishing cat (*Prion nailurus viverrina*), one leopard (*Panthera pardus*), two flat-headed cats (*Prion nailurus planiceps*), 6 tigers (*Panthera tigris*), two leopard cats (*Felis bengalensis*), two clouded leopards (*Felis nebulosa*), 3 pumas (*Puma concolor*), and 4 jungle cats (*Felis chaus*). Antibodies to *Toxoplasma gondii* were founded in 9 of 21 felids (42.8%). This study revealed that cell culture-derived tachyzoites can be used successfully as a source of live organism in a gold standard Sabin-Feldman dye test, which is simpler, cheaper and less ethically sensitive than *in vivo* inoculation. ∅

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TOXOPLASMOSIS: BEYOND ANIMALS TO HUMANS

Sukthana Y

The parasitic zoonosis toxoplasmosis, which was poorly understood before the advent of the HIV epidemic, has become a major clinical problem worldwide. Humans acquire toxoplasmosis from cats, from consuming raw or undercooked meat and from vertical transmission to the foetus through the placenta during pregnancy. Studies of the unique environmental factors in various communities indicate the important roles that eating habits and culture have on the transmission of this infection. The socioepidemiological aspects of toxoplasmosis are thought to be important contributing factors for the spread of this disease. Preventative measures should consider the cultures and beliefs of people in various communities more than solving poverty and giving orthodox health education. ∅

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PURIFICATION AND CHARACTERIZATION OF A NOVEL 3'-5' DNA HELICASE FROM *PLASMODIUM FALCIPARUM* AND ITS SENSITIVITY TO ANTHRACYCLINE ANTIBIOTICS

Pattra Suntornthiticharoen[1], Songsak Petmitr[2], and Porntip Chavalitshewinkoon-Petmitr[1]

[1] *Department of Protozoology, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand,*
[2] *Department of Tropical Nutrition and Food Science, Faculty of Tropical Medicine, Mahidol University, Bangkok,Thailand, Parasitology 2006; 133:389-398*

Plasmodium falciparum has developed resistance to most antimalarials; therefore, an investigation of potential targets should be performed. DNA helicases are enzymes that catalyze the unwinding of double stranded DNA to provide single stranded templates for DNA replication, repair and recombination. In this study, a DNA helicase (PfDH A) was purified from a crude extract of *Plasmodium falciparum*. DNA helicase activity was measured by assaying unwinding activity. The apparent molecular weight of PfDH A by SDS-PAGE was 90 kDa. PfDH A moved unidirectionally in the 3' -to- 5' direction along the bound strand and preferred a fork-like substrate structure and could not unwind blunt-ended duplex DNA. Unwinding activity required Mg^{2+} and could be inhibited by 200 mM NaCl or KCl and was dependent on hydrolysis of ATP or dATP. Anthracyclines, including daunorubicin, nogalamycin, doxorubicin, and aclarubicin, inhibited PfDH A activity with IC_{50} values of 2, 5, 8 and 9 M, respectively. Based on the results, PfDH A differs from all known human DNA helicases. However, its function and roles in parasite DNA replication need to be elucidated in the future. ∅

This study was supported by the Thailand Research Fund.

DIFFERENTIAL DETECTION OF *ENTAMOEBA HISTOLYTICA*, ENTAMOEBA DISPAR AND ENTAMOEBA MOSHKOVSKII BY A SINGLE-ROUND PCR ASSAY

Zulhainan Hamzah[1], Songsak Petmitr[2], Mathirut Mungthin[3], Saovanee Leelayoova[3] and Porntip Chavalitshewinkoon-Petmitr[1]

[1] *Department of Protozoology, Faculty of Tropical Medicine, Mahidol University;*
[2] *Department of Tropical Nutrition and Food Science, Faculty of Tropical Medicine, Mahidol University;*
[3] *Department of Parasitology, Phramongkutklao College of Medicine, Bangkok., Journal of Clinical Microbiology 2006; 44: 3196-3200.*

A single-round polymerase chain reaction (PCR) assay was developed for detection and differential diagnosis of the three *Entamoeba* species found in humans that are morphologically identical as both cysts and trophozoites; *E. moshkovskii*, *E. histolytica* and *E. dispar*. A conserved forward primer was derived from the middle of the small-subunit rRNA gene and reverse

primers were designed from signature sequences specific to each of these three *Entamoeba* species. PCR generates a 166-bp product with *E. histolytica* DNA, a 752-bp product with *E. dispar* DNA and a 580-bp product with *E. moshkovskii* DNA. Thirty clinical specimens were examined and the species present were successfully detected and differentiated using this assay. It was possible to detect as little as 10 pg of *E. moshkovskii* and *E. histolytica* DNA while for *E. dispar* the sensitivity was about 20 pg of DNA. Testing with DNA from different pathogens, including bacteria and other protozoa, confirmed the high specificity of the assay. We propose the use of this PCR assay as an accurate, rapid and effective diagnostic method for the detection and discrimination of these three morphological indistinguishable *Entamoeba* species, in both routine diagnosis of amoebiasis and epidemiological surveys. ∅

This study was supported by Mahidol University.

IDENTIFICATION OF GENOTYPES OF *ENTEROCYTOZOON BIENEUSI* FROM STOOL SAMPLES FROM HUMAN IMMUNODEFICIENCY VIRUS-INFECTED PATIENTS IN THAILAND

Saovanee Leelayoova S[1], Ittisak Subrungruang[2], Yupin Suputtamongkol[3], Jeerapun Worapong[4], Porntip Chavalitshewinkoon-Petmitr[2], and Mathirut Mungthin[1]

[1] *Department of Parasitology, Phramongkutklao College of Medicine, Bangkok,Thailand;*
[2] *Department of Protozoology, Faculty of Tropical Medicine, Mahidol University, Bangkok,Thailand;*
[3] *Department of Medicine, Faculty of Medicine, Siriraj Hospital, Mahidol University,*
[4] *Center for Biotechnology and Department of Biotechnology, Institute of Science and Technology for Research and Development, Salaya, Nakornpratom, Thailand., Journal of Clinical Microbiology 2006; 44: 3001-3004.*

We identified genotypes of *Enterozytozoon bieneusi* from 33 stool samples of Thai human immunodeficiency virus(HIV)-infected patients. Genotype D was identified at the highest frequency (36.4%), while genotype E was the second most common (15.1%). Genotype O and *Pig* EBITS 7, previously found only in pigs, were observed in Thai HIV-infected patients. Phylogenetic analysis supported a zoonotic nature for *E. bieneusi*. ∅

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

DETECTION OF VIABLE *GIARDIA* CYSTS BY REVERSE TRANSCRIPTION-PCR ASSAY

Nitipan Tantawiwattananon, Yaowalark Sukthana

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

Giardia is a flagellate protozoan which infects humans and other animals and is currently considered as one of the most common causes of gastroenteritis in the world. We developed a reverse transcription-PCR for detecting viable *Giardia* spp. cysts from clinical samples. We also designed new primers for giardin beta subunit which used to detect viable *Giardia* spp. We were able to detect as few as 10 organisms. Cysts inactivated by freezing and heating were not detected by RT-PCR assay. The RT-PCR technique is interested as a diagnostic method for detecting viable Giardia spp. not only clinical but also environmental water samples. ∅

MICROSPORA : TWO STAIN METHODS FOR DIAGNOSIS

Lekkla A[1], Lertlaituan P[2], Sutthikornchai C[1], Sukthana Y[1]

[1] *Department of Protozoology, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand;*
[2] *Department of Parasitology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand*

Microspora spp. are opportunistic protozoa infected in HIV/AIDS patients. Diagnosis of *Microspora* depend on the detection of typical spores. Grame-chromotope staining is a famous laboratory diagnosis method. By this

method oocyst appeared purple to pink, oval to round in shape, with the characteristic belt like strip. Trichrome-methylene blue staining is another new method with can be used. The spores stained pink-red and clear vacuole-like zone seen in *Microsporidia*. The blue background ensured a good contrast and the spores could be identified even in high magnification. Two stain method for diagnosis microsporidia spores were not statistic significant p>0.05 by 26 researchers commitment for a new way to routine screening for much number of patients. ∅

SEROPREVALENCE OF *TOXOPLASMA GONDII* ANTIBODY IN VIETNAMESE VILLAGERS

Ruenruetai Udonsom[1], Phan Thi Thu Chung[2], Phung Dac Cam[2], Yaowalark Sukthana[1]

[1] *Department of Protozoology, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand;*
[2] *Division of Enteric Infections, National Institute of Hygiene and Epidemiology, Vietnam*

Toxoplasmosis caused by protozoa namely *Toxoplasma gondii*, which is world-wide infections. Toxoplasmosis causes non-specific symptom in normal person, but in pregnant woman and in immunocompomised persons, diseases will be more severe. Many serological studies have been done in many parts of the world, but not in Vietnam. Seroprevalence study of *T. gondii* antibody in Vietnamese villagers (n = 650) is therefore performed by using Sabin-Feldman dye test. It was found that the average of 4.19% (95% CI =1.78-4.62) of *T. gondii* seroprevalence, including 6.36% (95% CI = 3.22-11.09), 4.73% (95% CI = 1.92-9.50) and 1.09 % (95% CI = 0.23-3.15) from Nghe An, Lao Cai and Tien Giang provinces, respectively. This study indicates that *T. gondii* antibody also present in Vietnam, but low prevalence similarly occurs in this area. More extensive studies are needed in order to know a real situation in Vietnam. ∅

NOVEL DRUG COMPOUNDS AGAINST *NEOSPORA CANINUM* AND *TOXOPLASMA GONDII* IN VITRO

Jitbanjong Wiengcharoen[1,3], Ryan O'Hanley[2], Tanya Armstrong[2] , Wayne Best, Yaowalark Sukthana[1] and RC Andrew Thompson[2]

[1] *Department of Protozoology, Faculty of Tropical Medicine, Mahidol University, Thailand;*
[2] *Division of Veterinary and Biomedical Sciences, Murdoch University, WA;*
[3] *Epichem Pty Ltd, Murdoch University, WA 6150., 4 Faculty of Veterinary Medicine, Mahanakorn University of Technology, Thailand*

Neospora *caninum* has recently been identified as an important cause of abortion in cattle world wide. This parasite is closely related to *Toxoplasma gondii*. To identify the drug compounds for potential use against both parasites in vitro, nine novel drug compounds were incubated with either parasite on microtiter plate. The number of extracellular tachyzoites and the quantities of vero cells left in the wells after incubating with those nine drugs were compared to the conventional drug control, a combination of sulfadiazine 25μg/ml and pyrimethamine 0.1μg/ml. The most effective drugs against both *N. caninum* and *T. gondii* in this study were trifluralin analogues. ∅

MALACOLOGICAL SURVEY IN PHANG-NGA PROVINCE, SOUTHERN THAILAND, PRE- AND POST-INDIAN OCEAN TSUNAMI

Pusadee Sri-aroon[1], Chantima Lohachit[1], Masakazu Harada[2], Phiraphol Chusongsang[1] and Yupa Chusongsang[1]

[1] *Applied Malacology Center, Department of Social and Environmental Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok Thailand;*
[2] *Department of International Medical Zoology, Kagawa Medical University, 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 fresh- 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 artieulata* and *Lit/orinopsis scabra*, were absent after the tsunami disaster, while brackish-water *Cerithidea eingulata* and *C. djadjariensis* harborcd 9 types of trematode cercariae. ∅

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PRELIMINARY POST-TSUNAMI WATER QUALITY SURVEY IN PHANG-NGA PROVINCE, SOUTHERN THAILAND

Prapin Tharnpoophasiam[1], Usanee Suthisarnsuntorn[2], Suwalee Worakhunpiset[1], Prasasana Charoenjai[1], Witawat Tunyong[2], Suvannee Phrom-in[2] and Siriporn Chattanadee[2]

[1] *Department of Social and Environmental Medicine,*
[2] *Department of Microbiology and Immunology, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand*

This preliminary water quality survey was perfonned eight weeks after the tsunami hit Phang-Nga Province on 26 December 2004. Water samples collected from the affected area, 10 km parallel to the seaside, were compared with water samples from the control area approximately 4 km from the seaside, which the tsunami waves could not reach. These samples included 18 surface-water samples, 37 well-water samples, and 8 drinking water samples, which were examined for microbiology and physical-chemical properties. The microbiological examinations focused on enteric bacteria, which were isolated by culture method, while physical-chemical properties comprised on-site testing for pH, salinity, dissolved oxygen (DO), conductivity and total dissolved solids (TDS) by portable electrochemicalmeter (Sens Ion 156). The results of the microbiological examinations showed that water samples in the affected areas were more contaminated with enteric bacteria than the control area: 45.4% of surface-water samples in the affected area, and 40.0% in the control; 19.0% of well-water samples in the affected area, and 7.7% in the control. All eight drinking-water samples were clear of enteric bacteria. Tests for physical-chemical properties showed that the salinity, pH, conductivity, and TDS of surface-water samples from the affected area were significantly higher than the control. The salinity, conductivity, and TDS of the wellwater samples from the affected areas were also significantly greater than those from the control area. The surface and well water in the tsunami-affected area have been changed greatly and need improvement. ∅

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MUTATION IN THE *rpoB* GENE OF THE RIFAMPICIN RESIST ANT *M. AVIUM* COMPLEX STRAINS FROM THAILAND

Oranuch Kongpetchsatit[1], Wanchai Phatihattakorn[1], Yuvadee Mahakunkijcharoen[1], Boonchuay Eampokalarp[2], Jirakan Boonyasopun[3] and Pongrama Ramasoota[1]

[1] *Faculty of Tropical Medicine, Mahidol University, Bangkok;*
[2] *Bamrasnaradura Institute, Ministry of Public Health, Nonthaburi;*
[3] *Chest Disease Institute, Ministry of Public Health, Nonthaburi, Thailand*

Forms of mutation never before described in the *rpoB* gene are reported for a sample of 20 rifampicinresistant *Mycobacterium avium* Complex (MAC) strains isolated from AIDS patients in Thailand. All strains were analyzed by polymerase

chain reaction-single strand conformation polymorphism (PCR-SSCP) and polymerase chain reaction-DNA sequencing (PCR-DNA sequencing). Sequence analysis of these strains revealed that only one strain (5%) has missense mutation at Lys-626 (Thr) and the rest of the strains had 15 different silent mutations within a 542 bp region of the *rpoB* gene. Five strains (25%) had a silent mutation at only one position, 7 (35%) at 2 positions, 7 (35%) at 3 positions, and 1 (5%) at 7 positions. The silent mutation at the Ala630 codon occurred in the largest proportion of the strains (\5 strains, 75%), followed by the Val-581 in 8 strains (40%), Tyr-578 and Thr-600 in 4 strains (20%), and Gly-597 in 3 strains (\5%). This investigation demonstrates that mutation in the *rpoB* gene of MAC strains from Thailand are more varied than previously reported for RIP ' MAC strains. PCR-SSCP screening clearly separated RIP' strains from rifampicin-susceptible (RIP ') strains. Ø

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DEVELOPMENT OF A COMBINED AIR SAMPLING AND QUANTITATIVE REAL-TIME PCR METHOD FOR DETECTION OF *LEGIONELLA* SPP

Sirigul C[1], Wongwit W[1], Phanprasit W[2], Paveenkittiporn W[3], Blacksell DS[4], Ramasoota P[1]

[1] *Department of Social and Environmental Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok;*
[2] *Department of Occupational and Health Safety, Faculty of Public Health, Mahidol University, Bangkok;*
[3] *NationalInstitute of Health, Ministry of Public Health, N.onthaburi;*
[4] *Wellcome Trust-Mahidol University-Oxford Tropical Medicine Research Programme, Mahidol University, Bangkok, Thailand*

The objective of this study was to develop and optimize the combined methods of air sampling and real time polymerase chain reaction (real-time PCR) for quantifying aerosol *Legionella* spp. Primers and TaqMan hydrolysis probe based on 5S *rRNA* gene specific for *Legionella* spp were used to amplify a specific DNA product of 84 bp. The impinger air sampler plus T-1 00 sampling pump was used to collect aerosol *Legionella* and as low as 10 fg of *Legionella* DNA per reaction could detected. Preliminary studies demonstrated that the developed method could detect aerosol *Legionella* spp 1.5-185 organisms /500 l of air within 5 hours, in contrast to culture method, that required a minimum of 7 -10 days. Ø

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PREPARATION OF *IN VIVO* COW CONTROL BLOOD SAMPLES FOR CADMIUM ANALYSIS

Foihirun K[1], Wongwit W[2], Kaewkungwal J[2], Ramasoota P[2], Sangdee P[3]

[1] *Regional Medical Sciences Cent er Chon Buri, Department of Medical Sciences, Ministry of Public Health, Chon Buri;*
[2] *Department of Social and Environmental Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok;*
[3] *Department of Medical Sciences, Ministry of Public Health, Nonthaburi, Thailand*

Quality control is essential for any analysis in the laboratory. The objective of this study was to prepare *in vivo* cow control blood samples. The experiment was performed by feeding cows with a single dose of cadmium in the form of cadmium chloride, withdrawing the blood at an appropriate time to get the highest level of cadmium and detecting the level of cadmium in the blood. It was found that feeding the cow a single dose of 0.06 mg cadmium per kg body weight resulted in the highest cadmium level of 3.622 µg/l 30-60 minutes after feeding. The samples were homogeneous because feeding the cows with single dose of cadmium let the cadmium be absorbed and distributed naturally. In addition, the samples were stable during transport. Therefore, they may be used as quality control samples to detect cadmium levels without using a lyophilized process. They could be used for proficiency testing and to evaluate whole blood analysis in the laboratory. Ø

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FACTORS RELATED TO VOLUNTEER COMPREHENSION OF INFORMED CONSENT FOR A CLINICAL TRIAL

Nantawan Kaewpoonsri[1], Kamolnetr Okanurak[1], Dwip Kitayaporn[2], Jaranit Kaewkungwal[3], Saowanit Vijaykadga[4] and Sopit Thamaree[5]

[1] *Department of Social and Environmental Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok;*
[2] *Bumrungrad Clinical Research Center, Bumrungrad International Hospital, Bangkok;*
[3] *Department of Tropical Hygiene, Faculty of Tropical Medicine, Mahidol University, Bangkok;*
[4] *Bureau of Vector Borne Disease, Department of Disease Control, Ministry of Public Health, Nonthaburi;*
[5] *Department of Pharmacology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand*

The informed consent process has become a universal requirement for research involving human subjects. Its goal is to inform volunteers regarding research In order to make decision to participate or not. This study aimed to measure volunteers' comprehension levels concerning the clinical trial and to find out factors associated with that comprehension levels. Eighty-one volunteers who enrolled in a malaria clinical trial were recruited into the study. A semi-structured questionnaire was used to collect the information. Non-participant observation was used to observe the process of informed consent. Volunteers were interviewed three days after being recruited into the trial. The results show the volunteers' comprehension was low. Only 44% of volunteers had an acceptable level of comprehension. It also revealed that 20 volunteers were not aware of being volunteers. Most volunteers knew about the benefits of participating in the trial and realized that they had the right to Withdraw from the study, but not many knew about the risks of the trial. The results Indicated the method of informing about the trial affected the volunteers' comprehension level. No relationship was found between comprehension level and volunteers' socio-demographic characteristics and their attitude toward the consent process. The findings from this study demonstrate volunteers who participated in the clinical trial were not truly informed. Further studies regarding enhancing volunteers' understanding of the trial are needed. ∅

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HEALTH AND NUTRITION SURVEY OF TSUNAMI VICTIMS IN PHANG-NGA PROVINCE, THAILAND

Karunee Kwanbunjan[1], Rungwit Mas-ngammueng[2], Phirapol Chusongsang[2], Yupa Chusongsang[2], Pannamas Maneekan[3], Yaowamarn Chantaranipapong[1], Somchai Pooudong[1] and Piyarat Butraporn[2]

[1] *Department of Tropical Nutrition and Food Science,*
[2] *Department of Social and Environmental Medicine,*
[3] *Department of Tropical Hygiene, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand*

The post-tsunami health and nutritional statuses of suivivors were surveyed three months after the disaster struck. Non-participant observations and questionnaires were used to study the effects of the disaster on their lifestyles and health while residing in temporary shelters provided by the government and private donors. Anthropometries were measured and dietary surveys conducted to elicit nutritional status. Our findings indicated good management of drinking water in the temporary shelters. Toilet construction and water supply were adequate, but wastewater and sewage systems were poorly managed. The study group still suffered from injuries after the disaster, and complained of back pain, stress, and sleep disorders. Most in the study group had unsatisfactory health behaviors, and obesity was an increasing problem among female participants. ∅

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MODIFIED INFORMANT QUESTIONNAIRE ON COGNITIVE DECLINE IN THE ELDERLY (IQCODE) AS A SCREENING TEST FOR DEMENTIA FOR THAI ELDERLY

Sukhontha Siri[1], Kamolnetr Okanurak[1], Sirintorn Chansirikanjana[2], Dwip Kitiyaporn[3] and Anthony F Jorm[4]

[1] *Department of Social and Environmental Medicine, Faculty of Tropical Medicine, Mahidol University;*
[2] *Department of Medicine, Faculty of Medicine at Ramathibodi Hospital, Mahidol University, Bangkok;*
[3] *The Bumrungrad International Clinical Research Center , Bumrungrad International Hospital, Bangkok Thailand;*
[4] *Department of Psychiatry, University of Melbourne, Australia*

A potential test for early detection of dementia in the elderly is the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE), which is based on information from the informant for the elderly about the changes of the elderly in everyday cognitive functioning associated with dementia, The present study aimed to modify and assess the reliability and validity of the modified IQCODE consisting of 32 items, The study consisted of two methods of assessing dementia: DSMIV diagnosis carried out by clinicians, and informants responding to the IQCODE. The subjects were 200 pairs of elderly subjects and their informants who visited the Geriatric Clinic, Ramathibodi Hospital, The optimal cutoff score on the modified IQCODE was 3,42, with 90% sensitivity and 95% specificity, The positive predictive values, negative predictive values, and accuracy were 0,94,0,90, and 0,92, respectively. The IQCODE items had high internal consistency. The IQCODE associated with the elderly person's age, but not with their gender and educational level; nor were they associated with the demographic characteristics of the informant. Therefore, the IQCODE could be used as an alternative screening test for dementia in Thailand with acceptable sensitivity and specificity, This tool may be useful for dementia screening in the community and the geriatric clinic for early detection of disease. Ø

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PERIPLANETA AMERICANA ARGININE KINASE AS A MAJOR COCKROACH ALLERGEN AMONG THAI PATIENTS WITH MAJOR COCKROACH ALLERGIES

Sookrung N, Chaicumpa W, Tungtrongchitr A, Vichyanond P, Bunnag C, Ramasoota P, Tongtawe P, Sakolvaree Y, Tapchaisri P

Periplaneta americana is the predominant cockroach (CR) species and a major source of indoor allergens in Thailand. Nevertheless, data on the nature and molecular characteristics of its allergenic components are rare. We conducted this study to identify and characterize the P. americana allergenic protein. A random heptapeptide phage display library and monoclonal antibody (MAb) specific to a the P. americana component previously shown to be an allergenic molecule were used to identify the MAb-bound mimotope and its phylogenic distribution. Two-dimensional gel electrophoresis, liquid chromatography, mass spectrometry, peptide mass fingerprinting, and BLAST search were used to identify the P. americana protein containing the MAb-specific epitope. We studied the allergenicity of the native protein using sera of CR-allergic Thai patients in immunoassays. The mimotope peptide that bound to the MAb specific to P. americana was LTPCRNK. The peptide has an 83-100% identity with proteins of Anopheles gambiae, notch homolog scalloped wings of Lucilia cuprina, delta protein of Apis mellifera; neu5Ac synthase and tyrosine phosphatase of Drosophila melanogaster, and a putative protein of Drosophila pseudoobscura. This finding implies that the mimotope-containing molecule of P. americana is a pan-insect protein. The MAb-bound protein of P. americana was shown to be arginine kinase that reacted to IgE in the sera of all of the CR-allergic Thai patients by immunoblotting, implying its high allergenicity. In conclusion, our results revealed that P. americana arginine kinase is a pan-insect protein and a major CR allergen for CR-allergic Thai patients. Ø

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MIMOTOPE OF LEPTOSPIRA FROM PHAGE-DISPLAYED RANDOM PEPTIDE LIBRARY IS REACTIVE WITH BOTH MONOCLONAL ANTIBODIES AND PATIENTS' SERA

Tungtrakanpoung R, Pitaksajjakul P, Na-Ngarm N, Chaicumpa W, Ekpo P, Saengjaruk P, Froman G, Ramasoota P

The study aim was to use random heptapeptide library displayed by bacteriophage T7 for identifying mimotopes from 15 monoclonal antibodies (MAbs) specific to Leptospira spp., and from four leptospirosis patient sera, respectively. The bound phages, selected from fourth round of bio-panning with each antibody, were cloned by plaque isolation and the binding specificity of individual clones were confirmed by enzyme-linked immunosorbent assay, before being further amplified and checked for phage peptide sequence using PCR and DNA sequencing. All together 150 phages were selected, mimotope from 86 phages (56.6%) were found to match with protein sequences of Leptospira from GenBank database. The predominant mimotopes were mimotope with sequence LTPCD that found in 27.3%, followed by TPCSK (16%), KSKKSS (4%), KTKRXAS (4%), SSKSYR (3.3%), DPNXNSF (3.3%), KSGRC (2.6%), TLINIF (2%), TPCI (2%), 1.33% each with mimotopes PKKS, PCNTKXTA, and CTKKK, and one phage each (0.66%) with mimotopes PTFGS, TNSKRK, SKSSRC, RSKRIR, VTNNTP, and CSNXSKR. Interestingly, mimotopes LTPCD, TPCSK, and TPCI were found to react with both MAb and patient's sera. The matched proteins from GenBank namely, leptospiral putative outer membrane protein (matched with mimotope PTFGS), thermolysin precursor protein (matched with mimotope TPCIXXGSAS), and hypothetical protein LIC12228 (matched with mimotope CSNXSKR), were found to locate at outer membrane of Leptospira. These phage mimotopes and matched proteins may have potential for further use as diagnostic reagent and immunogen against leptospirosis in the future. The results demonstrate that phage display technique has potential for rapidly identifying phage mimotopes that interact with leptospiral MAbs and patient's sera.

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MUTATIONS IN THE rpoB GENE OF RIFAMPICIN-RESISTANT MYCOBACTERIUM TUBERCULOSIS STRAINS FROM THAILAND AND ITS EVOLUTIONARY IMPLICATION

Ramasoota P, Pitaksajjakul P, Phatihattakorn W, Pransujarit V, Boonyasopun J.

Novel mutations in the rpoB gene are reported for 70 rifampicin-resistant (RIFr) M. tuberculosis strains from Thailand. Sequence analysis of these strains revealed mutations in a 435 base-pair region of the rpoB gene. Twenty-eight strains (40%) had single mutations, and 26 of those strains had mutations at positions never before reported, of which, 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, of which 24 (34%) had mutations at two positions; 9(13%), at three positions; 2(3%), at five positions; and 1(1%) at six positions. Five strains (7%), reported to have the RIFr phenotype, contained no mutation in the examined region of the rpoB gene. Surprisingly, one RIFr strain had silent mutations at 29 positions. By far the dominant mutation was the silent mutations at Gln-517 (86%). This investigation demonstrates that mutations in the rpoB gene of M. tuberculosis strains from Thailand are more varied than previously reported for RIFr M. tuberculosis strains. Screening by means of PCR-SSCP clearly separated RIFr strains from rifampicin-susceptible (RIFs) strains. There was no correlation between RIFr mutations and random amplified polymorphic DNA (RAPD) types.

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WILLINGNESS TO BE VACCINATED AGAINST SHIGELLA AND OTHER FORMS OF DYSENTERY: A COMPARISON OF THREE REGIONS IN ASIA

Pack R, Wang Y, Singh A, von Seidlein L, Pach A, Kaljee L, Butraporn P, Youlong G, Blum L, Bhutta Z, Santoso SS, Trach DD, Waluyo I, Nyamete A, Clemens J, Stanton B

Department of Community Medicine, West Virginia University School of Medicine, P.O. Box 9190, Morgantown, WV 26506-9190, USA. rpack@hsc.wvu.edu

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 vaccination willingness 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.

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DEVELOPMENT OF A SURVEILLANCE SYSTEM FOR OBESITY AMONG SCHOOL CHILDREN OF HIGH RISK GROUPS IN BANGKOK

Voranuch Wangsuphachart[1], Nipaporn Tewawong[1], Chukiat Sirivichayakul[2], Supalarp Pungsa-ard[3]

[1] *Department of Social and Environmental Medicine,*
[2] *Department of Tropical Pediatrics,*
[3] *Department of Tropical hygiene, Faculty of Tropical Medicine, Mahidol University Corresponding author: Voranuch Wangsuphachart, E-mail:<tmvws@mahidol.ac.th>*

This project assessed current status of data on prevalence of overweight and obesity in school children of high risk groups in Bangkok and identified if obesity surveillance system existed, including key coupling systems-programs and their current status. Quality, validity and reliability of these data, and the sustainability of such activity and system were explored. Two private schools in the affluent urban were selected to participate in the study based upon the overall readiness of the school and the parent-teacher network. These schools had suitable infra-structure and capacity which ensure the success of a long term obesity monitoring and weight reduction intervention strategy programs being implemented. Prevalence surveys of overweight and obese children were completed in both schools. For the girl school of 1010 students, grade 1-7, yielded the BMI prevalence of 15.34% at risk to overweight and 7.53% overweight (classify BMI-for-age at or above the 95th percentile as overweight and between the 85th and 95th percentile as at risk of overweight; U.S.CDC Growth Charts, 2000). For the boy school, the prevalence surveys were conducted for both semesters in the year 2005 with total sample size of 5,818 students. In semester 1/2005, the prevalence survey of 2,919 students yielded the BMI prevalence of 54.29% underweight and 9.42 % overweight. In semester 2/2005, the prevalence survey of 2,899 students yielded the BMI prevalence of 54.78% underweight and 8.79% overweight. None of the children was obese. Both schools continue to monitor weight, height and BMI of the students on a regular basis. The girl school is about to establish an electronic database for proper child growth. The boy school has just had an electronic database and recently developed a program to assess student's body efficiency test on an individual basis. The executive team of both schools showed a strong interest to continue, maintain and update the obesity surveillance system. The P.I. and the research team have recommended the schools to form a school based program to promote healthy eating and physical activity towards a pro-active lifestyle which is designed to prevent obesity in childhood, with social supports from the School Parent-Teacher Association. The P.I. and the PTA would propose a program to establish models for building preventions and interventions which encompass multiple strategies (social marketing, policy and environmental change, management of current overweight and obesity, networking, forum-awareness seminar) in multiple settings and sectors. Empowering partnerships, inspiring leadership and sponsorship, monitoring and research, training and capacity building would also be purported for carrying on the task of childhood obesity surveillance system towards sustainable child development for a healthy built environment. ∅

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BIO-PATHOGENS CONTAMINATION OF THE MEKONG RIVER IN CHIANG RAI PROVINCE, THAILAND

Voranuch Wangsuphachart[1] and Narong Surinkul[2]

[1] Department of Social and Environmental Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok
[2] Department of Environmental Engineering and Management, School of Environment, Resources and Development, Asian Institute of Technology, Pathumthani
Corresponding author: Voranuch Wangsuphachart, E-mail:<tmvws@mahidol.ac.th>

Waterborne diseases caused by bio-pathogens are serious public health concerns regarding water quality and water resource management of the Mekong River. Microbial and bio-pathogens indicators of water pollution have been in use for decades. They were originally developed as measures of faecal pollution of source waters and subsequently the same organisms were applied to measure efficiency of treatment and post-treatment contamination and deterioration. This study identified potential hot spots along the Mekong River in Chiang Saen and Chiang Khong, Chaing Rai Province which posed possible human health risk. There is no study or spatial data available for the existence of the bio-pathogens in the Mekong River through seasonal changes. Water samples were collected from eight high risk areas along the Mekong River in August, 2006 at Sob Som, Sob Ing, water intake for Chiang Khong and Chiang Sean water supply, Chiang Sean discharge canals or drainage lines from domestic waste and runoff directly into the Mekong River, Sob Kham, Sob Kok, and Sob Ruok near the Golden Triangle. Grab sampling technique was used to collect water samples from each location. Sampling procedure was according to the Standard Method for Examination of Water and Wastewater. Sterilized glass bottles were used for microbiological examination with secured cold chain system. Every water sample from the Mekong River appeared in natural color with reddish brown sediment. Total coliforms (2.1 x 10^3-2.4 x 10^6), total faecal coliforms (2 x1 0-1.1 x 10^4) or *E. coli*, an indicator of fecal pollution, were detected in every water sample, including raw water intake for water supply. Enteric bacteria like *Aeromonas hydrophila* and/or *A. sorbia* were also detected in every sample. No *Giardia lambia* was detected. Detection of enteric viruses was not conducted. Total faecal coliforms and the total coliforms detected were considerably high given the large volume of water level in the Mekong River during the rainy season. It can be therefore, speculated that during the dry season, the amount of these two bio-pathogens indicating the water quality of the Mekong River could be much higher than those detected in the rainy season. These results may suggest that bio-pathogens in the Mekong River and lack of sanitation system can pose possible risk to human health. ∅

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HUMAN HEALTH RISK ASSESSMENT USING RAW WATER FROM THE MEKONG RIVER FOR DRINKING BY BAYESIAN NETWORK MODELING

Chawalit Ratanathamskul[1], Voranuch Wangsuphachart[2], Pornsak Jevasuwan[3] and Bouakeo Suvanthong Suvanthong[4]

[1] Department of Environmental Engineering, Faculty of Engineering, Chulalongkorn University, Bangkok;
[2] Department of Social and Environmental Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok;
[3] Department of Water Resources, Ministry of Natural Resources and Environment, Bangkok;
[4] National Center for Environmental Health and Water Supply, Laos PDR
Corresponding author: Voranuch Wangsuphachart, E-mail:<tmvws@mahidol.ac.th>

This study assessed if there was a serious risk to human health from using raw water from the Mekong River for drinking and cooking, and if so, what was the magnitude of the problem by Bayesian Network Modeling (BN). Spatial data covered the Mekong River from the confluence of the Ruak River (border with Myanmar) to 10km south of Chiang Khong, the catchment of the Kok River in Thailand and Bokeo Province in Lao PDR. The major threats relevant to this study were bio-pathogens (faecal coliform bacteria and water related bacteria bacteria, *Giardia lambia*), chemical agents-toxicants (organic toxicants: organophosphate pesticides (OPs), organochlorine (OCs), carbamate, paraquat), key aromatic hydrocarbon from vessel fuel (BTEX) and inorganic toxicants (arsenic, nitrate). Cause-effect conceptual model was established with four major sources of pollution, namely domestic

waste water, storm water, agricultural runoff to and pollution from China. In the conceptual model, the health risks were divided into two parts, one due to bio-pathogens and the other due to chemical agents, in order to more easily calculate the risks from each parameter in drinking water. Flow regime node was directed to raw water node as dilution factor in the Mekong River for both health risks. Treatment node was also included, no treatment option as alternative, when no treatment was done for the river water quality. An initial sensitivity analysis was performed with the results of the top twelve ranking of health risks, of which the top five were health-effect from using raw water, drinking-cooking, health-effects (diarrhoea) and water treatment (yes/no). Contamination of bio-pathogens in the water was ranked at the 7th. At this stage the BN network was based entirely upon expert opinion. The main parameters affecting health risks from bio-pathogens were drinking water quality, water treatment, raw water quality, flow regime of the Mekong River and concentration of bio-pathogens in the water. The rest variables were of less effect such as aldrin, dieldrin, lindane, carbamate and paraquat. On the other hand, the results showed that arsenic, nitrate and BTEX. have no significant effect. ∅

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Presented at: MRC Environmental Risk Assessment Workshop, November 5-10, 2006, Luang Prabang, Laso PDR.

A CASE-CONTROL AUDITORY EVALUATION OF PATIENTS TREATED WITH ARTEMETHER-LUMEFANTRINE

Hutagalung R, Htoo H, Nwee P, Arunkamomkiri J, Zwang J, Carrara VI, Ashley E, Singhasivanon P, White NJ, Nosten F

Artemether-lumefantrine is the first registered, fixed, artemisinin-based combination treatment. Artemisinin derivatives are highly effective antimalarials with a favorable safety profile. Concerns remain over their potential neurotoxicity, although there has been no clinical evidence of this in humans. In animals (rats, dogs, and monkeys) artemether, a derivative of artemisinin is associated with an unusual toxicity pattern in specific brain nuclei involving the auditory and vestibular pathways. A recent report from Mozambique described a small but significant and irreversible hearing loss in patients exposed to artemether-lumefantrine. To explore this issue, we conducted a case-control study using tympanometry, audiometry and auditory brain-stem responses. We assessed 68 subjects who had been treated with artemether-lumefantrine within the previous five years and 68 age- and sex-matched controls living in the malarious region along the Thailand-Myanmar border. There were no differences in the test results between cases and controls. There was no neurophysiologic evidence of auditory brainstem toxicity that could be attributed to artemether-lumefantrine in this study population. ∅

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A SIMPLE AND RAPID LIQUID CHROMATOGRAPHIC ASSAY FOR EVALUATION OF POTENTIALLY COUNTERFEIT TAMIFLU

Lindegardh N, Hien TT, Farrar J, Singhasivanon P, White NJ, Day NP

A simple and rapid liquid chromatographic assay for the evaluation of potentially counterfeit oseltamivir (Tamiflu has been developed and assessed. The assay uses approximately 1mg Tamiflu powder when used for authentication and content estimate. The procedure was validated using 50 replicates analysed during five independent series with a total R.S.D. of 11.2%. The assay can also be used to monitor the exact content of oseltamivir in Tamiflu capsules. One Tamiflu capsule was transferred to a 250 mL volumetric flask and 150 mL water was added. The flask was placed in an ultrasonic bath at 40 degrees C for 20 min to dissolve the capsule. The solution was allowed to cool to room temperature before the flask was filled up to the mark (250 mL). A small aliquot was centrifuged and then directly injected into the LC-system for quantification. Oseltamivir was analysed by liquid chromatography with UV detection on a Hypersil Gold column (150 mm x 4.6 mm) using a mobile phase containing methanol-phosphate buffer (pH 2.5; 0.1 M) (50:50, v/v) at a flow rate of 1.0 mL/min. The assay was implemented for the analysis of Tamiflu

purchased over the Internet and at local pharmacies in Thailand and Vietnam. ∅

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AN OPEN LABEL RANDOMIZED COMPARISON OF MEFLOQUINE-ARTESUNATE AS SEPARATE TABLETS VS. A NEW CO-FORMULATED COMBINATION FOR THE TREATMENT OF UNCOMPLICATED MULTIDRUG-RESISTANT FALCIPARUM MALARIA IN THAILAND

Ashley EA, Lwin KM, McGready R, Simon WH, Phaiphun L, Proux S, Wangseang N, Taylor W, Stepniewska K, Nawamaneerat W, Thwai KL, Barends M, Leowattana W, Olliaro P, Singhasivanon P, White NJ, Nosten F

Background: Delivering drugs in a fixed combination is essential to the success of the strategy of artemisinin-based combination therapy. This prevents one drug being taken without the protection of the other, reducing the chance of emergence and spread of drug resistant strains of *Plasmodium falciparum*. A lower tablet burden should also facilitate adherence to treatment. A new fixed combination of mefloquine plus artesunate has been developed. This was compared with the conventional regimen of separate tablets for the treatment of uncomplicated multidrug-resistant falciparum malaria.

Methods: On the north-western border of Thailand 500 adults and children with uncomplicated falciparum malaria were randomized to receive either the new fixed combination or separate tablets. They were followed up weekly for 63 days.

Results: The day 63 polymerase chain reaction-adjusted cure rates were 91.9% (95% CI 88.2-95.6) in the fixed combination group and 89.2% (85.0-93.4) in the loose tablets group (P=0.3). There was a lower incidence of early vomiting in the group receiving the fixed combination.

Conclusion: This new fixed combination of mefloquine and artesunate was efficacious, well tolerated and convenient to administer. ∅

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C-REACTIVE PROTEIN, INTERLEUKIN-6, AND TUMOR NECROSIS FACTOR-ALPHA LEVELS IN OVERWEIGHT AND HEALTHY ADULTS

Chaikate S, Harnroongroj T, Chantaranipapong Y, Puduang S, Mahaisiriyodom A, Viroonudomphol D, Singhasivanon P, Schelp FP, Tornee S, Tribunyatkul S, Changbumrung S

Department of Tropical Nutrition and Food Science, Clinical Chemistry Unit, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

This study aimed to 1) compare levels of high sensitivity c-reactive protein (hs-CRP), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-alpha) between overweight Thais and apparently healthy controls, and 2) investigate the association between serum hs-CRP, IL-6, and TNF-alpha levels and other biochemical parameters. A total of 180 health-conscious adults aged 25-60 years, who resided in Bangkok, participated in this study. No significant difference was found in age and sex between the overweight subjects and controls. Serum levels of hs-CRP, IL-6, TNF-alpha, glucose, lipid profile, body mass index (BMI), waist circumference (WC), hip circumference (HC) and waist hip ratio (WHR) were determined in these volunteers. The mean levels of white blood cells (WBC), uric acid, total cholesterol (TC), triglyceride (TG), and hs-CRP were significantly higher in the overweight subjects than those in the controls, whereas high density lipoprotein-cholesterol (HDL-C) values were significantly higher in the controls than the overweight subjects ($p < 0.05$). Hs-CRP levels were significantly positively correlated with levels of TG, BMI, WC, HC and WHR. HDL-C levels were significantly negative correlated with hs-CRP levels. In conclusion, the prevalence of elevated serum hs-CRP levels was higher in overweight subjects than controls. However, more data in larger and other population groups are needed to confirm this study. ∅

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DENGUE-VIRUS-INFECTED DENDRITIC CELLS TRIGGER VASCULAR LEAKAGE THROUGH METALLOPROTEINASE OVERPRODUCTION

Luplerdlop N, Misse D, Bray D, Deleuze V, Gonzalez JP, Leardkamolkarn V, Yssel H, Veas F

Institut de Recherche pour le Developpement, IRD, Immunologie Virale et Moleculaire, UR178 IFR122, 34094 Montpellier, France

Dengue virus (DV) is an important re-emerging arthropod-borne virus of global significance. The defining characteristic of DV infection-associated pathology is haemorrhagic fever, which often leads to a fatal shock-like syndrome (DHF/DSS) owing to an increase in vascular endothelial permeability. Here, we show, in a viral dose-dependent manner, that DV-infected immature dendritic cells overproduce soluble gelatinolytic matrix metalloproteinase (MMP)-9-and to a lesser extent MMP-2-which enhances endothelial permeability, but which are reduced by specific inhibitors and a neutralizing anti-MMP-9 antibody. This permeability was associated with a loss of expression of the platelet endothelial adhesion molecule 1 (PECAM-1) and vascular endothelium (VE)-cadherin cell adhesion molecules and redistribution of F-actin fibres. These in vitro observations were confirmed in an in vivo vascular-leakage mouse model. These results provide a molecular basis for DHF/DSS that could be a basis for a general model of haemorrhagic fever-inducing viruses, and identify a new therapeutic approach for the treatment of viral-induced vascular leakage by specifically targeting gelatinolytic metalloproteases. ∅

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ESTIMATION OF NON-FATAL ROAD TRAFFIC INJURIES IN THAI NGUYEN, VIETNAM USING CAPTURE-RECAPTURE METHOD

Van HT, Singhasivanon P, Kaewkungwal J, Suriyawongpaisal P, Khai LH

Department of Tropical Hygiene, Faculty of Tropical Medicine, Mahidol University, 420/6 Ratchawithi Road, Bangkok 10400, Thailand. hungtrinhvan@yahoo.com

Road traffic injuries (RTIs) are increasing in developing countries where accurate routine data are usually not available. Although a capture-recapture technique has increasingly been employed in studies of human populations to provide reliable estimates of the magnitude of problems, it has rarely been used in road traffic injury research. We applied two sample capture-recapture methods using hospital and traffic police records to estimate non-fatal road traffic injuries in Thai Nguyen City during the years 2000-2004. We generated a conservative adjusted estimate of non-fatal RTIs using data from the two sources matched by name, surname, sex of victims and at least one of the other matching variables, of age, address of victim and date of injuries. We then compared the estimated rates with those reported based on police and hospital data. The results show that during years 2000-2004, the police reported 1,373 non-fatal RTIs, while hospital records revealed 6,069 non-fatal RTIs. Most reported victims on both hospital and police reports were males (67.3 % and 74.4%, respectively). More than half the victims on both hospital and police reports were drivers (77.5% and 66.1%, respectively) or pedestrians (10.6% and 7.1%, respectively). Youth and young adults (ages 15-34) constituted the majority of the victims on the hospital and police reports (52.8% and 63.7%, respectively). The capture-recapture analysis estimated that 11,140 (95% CI: 10,626-11,654) subjects were involved in RTIs during the study period. In comparison to the estimated figure, official sources accounted for only 21.9 to 60.1% of total non-fatal RTIs. Estimated rates of non-fatal RTIs were 105.5 injuries/10,000 population per year and 393 injuries/10,000 vehicles. Given the fact that under reporting of RTIs has been a major limitation of routine official data sets in developing countries, we suggested the capture-recapture method be used as a tool to provide affordable and reliable estimates of RTIs in resource-poor countries. ∅

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MISSED APPOINTMENTS AT A TUBERCULOSIS CLINIC INCREASED THE RISK OF CLINICAL TREATMENT FAILURE

Srisaenpang S, Pinitsoontorn S, Singhasivanon P, Kitayaporn D, Kaewkungwal J, Tatsanavivat P, Patjanasoontorn B, Reechaipichitkul W, Thiratakulpisan J, Srinakarin J, Srisaenpang P, Thinkamrop B, Apinyanurak C, Chindawong BO

Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand. sompong@kku.ac.th

We investigated the charts of 381 new smear-positive tuberculosis patients at Khon Kaen Medical School during 1997-2001 using World Health Organization definitions to evaluate associations among treatment success or failure (defaulted, failed, died, or not evaluated) and tuberculosis clinic contact, demographics and clinical characteristics of the patients. Multinomial logistic regression was used for three-category outcome analysis: treatment success, transferred-out and clinical treatment failure. The treatment success and clinical treatment failure rates were 34.1% and 34.4%, respectively. About 46.5% and 85.8% of patients missed appointments at the tuberculosis clinic in the treatment success and treatment failure groups, respectively. The results show that patients who were absent from the tuberculosis clinic were 5.95 times more likely to have clinical treatment failure than treatment success, having adjusted for the effect of transfering-out and the effect of the treatment regimen and the sputum conversion status (adjusted odds ratio = 5.95; 95% CI: 2.99 to 11.84). The review showed that absence from the tuberculosis clinic was an independent risk factor for clinical treatment failure. We recommended that all new smear-positive tuberculosis patients should be followed closely at a tuberculosis clinic. ∅

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MOLECULAR AND PHARMACOLOGICAL DETERMINANTS OF THE THERAPEUTIC RESPONSE TO ARTEMETHER-LUMEFANTRINE IN MULTIDRUG-RESISTANT *PLASMODIUM FALCIPARUM* MALARIA

Price RN, Uhlemann AC, van Vugt M, Brockman A, Hutagalung R, Nair S, Nash D, Singhasivanon P, Anderson TJ, Krishna S, White NJ, Nosten F

Centre for Vaccinology and Tropical Medicine, Nuffield Department of Clinical Medicine, John Radcliffe Hospital, Headington, Oxford, United Kingdom. ricprice@doctors.org.uk

Background: Our study examined the relative contributions of host, pharmacokinetic, and parasitological factors in determining the therapeutic response to artemether-lumefantrine (AL).

Methods: On the northwest border of Thailand, patients with uncomplicated *Plasmodium falciparum* malaria were enrolled in prospective studies of AL treatment (4- or 6-dose regimens) and followed up for 42 days. Plasma lumefantrine concentrations were measured by high performance liquid chromatography; malaria parasite pfmdr1 copy number was quantified using a real-time polymerase chain reaction assay (PCR), and in vitro drug susceptibility was tested.

Results: All treatments resulted in a rapid clinical response and were well tolerated. PCR-corrected failure rates at day 42 were 13% (95% confidence interval [CI], 9.6%-17%) for the 4-dose regimen and 3.2% (95% CI, 1.8%-4.6%) for the 6-dose regimen. Increased pfmdr1 copy number was associated with a 2-fold (95% CI, 1.8-2.4-fold) increase in lumefantrine inhibitory concentration (50) (P=.001) and an adjusted hazard ratio for risk of treatment failure following completion of a 4-dose regimen, but not a 6-dose regimen, of 4.0 (95% CI, 1.4-11; P=.008). Patients who had lumefantrine levels below 175 ng/mL on day 7 were more likely to experience recrudescence by day 42 (adjusted hazard ratio, 17; 95% CI, 5.5-53), allowing prediction of treatment failure with 75% sensitivity and 84% specificity. The 6-dose regimen ensured that therapeutic levels were achieved in 91% of treated patients.

Conclusions: The lumefantrine plasma concentration profile is the main determinant of efficacy of artemether-lumefantrine. Amplification in pfmdr1 determines lumefantrine susceptibility and, therefore, treatment responses when plasma lumefantrine levels are subtherapeutic. ∅

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POPULATION PHARMACOKINETIC ASSESSMENT OF A NEW REGIMEN OF MEFLOQUINE USED IN COMBINATION TREATMENT OF UNCOMPLICATED FALCIPARUM MALARIA

Ashley EA, Stepniewska K, Lindegardh N, McGready R, Hutagalung R, Hae R, Singhasivanon P, White NJ, Nosten F

Shoklo Malaria Research Unit, P.O. Box 46, Mae Sot, Tak 63110, Thailand. SMRU@tropmedres.ac

A fixed artesunate-mefloquine combination, comprising three daily doses of 8 mg of mefloquine/kg of body weight and 4 mg of artesunate/kg, has been developed recently. This study was designed to construct a population pharmacokinetic model describing this new dosage regimen of mefloquine given as loose tablets together with artesunate. In two randomized trials in Thailand which evaluated the efficacy, safety, and tolerability of this new regimen, the members of a subgroup of 50 patients were randomized to have capillary blood sampling before treatment and at five randomly assigned time points during the 63-day follow-up period. Mefloquine levels in capillary whole blood were assayed by liquid chromatography with UV detection. A pharmacokinetic model for mefloquine was constructed using mixed-effects modeling. A one-compartment model with first-order absorption and elimination was selected to describe the kinetic properties of mefloquine. For capillary whole-blood mefloquine, the area under the concentration curve (AUC) was 40% higher than previous estimates for patients given the equivalent conventional-dose regimen (mefloquine given as 15 mg/kg and then 10 mg/kg on the second and third days of treatment). The half-life (t1/2) of the carboxylic acid metabolite was estimated as 26 days, and the metabolite was eliminated more slowly than the parent drug (population t1/2 estimate, 10.5 days). Splitting the 25 mg/kg dose of mefloquine into three doses of 8 mg/kg each resulted in improved oral bioavailability compared to the conventional split-dose regimen results. This new regimen is well tolerated and results in an equivalent therapeutic response. ∅

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RAPID DEGRADATION OF OSELTAMIVIR PHOSPHATE IN CLINICAL SAMPLES BY PLASMA ESTERASES

Lindegardh N, Davies GR, Tran TH, Farrar J, Singhasivanon P, Day NP, White NJ

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

The anti-influenza drug oseltamivir is an ester prodrug activated by hepatic carboxylesterases. Plasma esterases also convert up to 31.8% of the parent compound to the active metabolite after 4 h ex vivo, with wide interindividual variation. This source of error is removed by adding the esterase inhibitor dichlorvos to blood collection tubes. ∅

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SEROPREVALENCE AND RISK FACOTRS OF HEPATITIS B VIRUS INFECTION IN HEALTH CARE WORKERS AT PRASAT NEUROLOGICAL INSTITUTE, THAILAND

Chiarakul S[1], Eunmjitkul K[1], Vuttiopas S[1], Kaewkungwal J[2], Poovorawan Y[3]

[1] *Prasat Neurological Institute, Bangkok, Thailand;*
[2] *Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand;*
[3] *Chulalongkorn University and Hospital, Bnagkok, Thailand*

Background: The prevalence of hepatits B carriers in Thailand is about 6-10%. Hepatitis B vaccination was includes in the Extended Program of Immunization (EPI) and has been introduced to all Thai newborns since 1992, but did not include retroactive vaccination of health care workers (HCWs). The purpose of this study was to define the seroepidemiology

of Hepatitis B virus (HBV) infection among HCWs in Presat Neurological Institute (PNI), and to evaluate the risk factors of HBV markers.

Methods: Blood samples were taken from HCWs in PNI for HBV profiling (HBsAg, antiHBs and antiHBc) by Microparticle Enzyme Immunoassay (MEIA) methods. Questionnaires include demographics, type and duration of work, history of blood exposure, HBV vaccination and non occupation risks of hepatitis were interviewed.

Results: Among 548 enrolled HCWs, 79(14.4%) were male and 463 (85.6 %) were female, aged ranges between 20 to 61 years old, working year between 1 to 41 years. Among 548 HCWs 29 (5.29%) were HBsAg positive, 135 (24.6 %) had immunity from past HBV infection, 40 (7.3 %) were Isolated antiHBc, 105 (19.2 %) had protective level antiHBs, 7 (1.3 %) had low antiHBc level and 232 (42.3 %) had full negative profiles. Comparing between HBsAg positive and negative gropups, no statistically significant different levels of occupational exposure, frequency of blood contact and working years. However, there were statistically differences in sex (male: 11.39 % vs. non-vaccinated: 7.42 %, p=0.0014), family history of hepatoma (12.77 %) vs. 4.04 %, p=0.002), history of jaundice (17.39 %vs. 4.4 %, p=0.008) and history of viral hepatitis (29.63 vs. 3.66 %, p=0.000).

Conclusions: Not different from Thai populations, prevalence of HBV carriers among HCWs at PNI was 5.29 %. Based on the significant risk factors of HBsAg positive, current HBV vaccination program should also include HCWs who were born Thailanc EPI program. ∅

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SPATIO-TEMPORAL EFFECTS OF ESTIMATED POLLUTANTS RELEASED FROM AN INDUSTRIAL ESTATE ON THE OCCURRENCE OF RESPIRATORY DISEASE IN MAPTAPHUT MUNICIPALITY, THAILAND

Jadsri S, Singhasivanon P, Kaewkungwal J, Sithiprasasna R, Siriruttanapruk S, Konchom S

Department of Tropical Hygiene, Faculty of Tropical Medicine, Mahidol University, Rajvithi Road, Bangkok, Thailand. baiyok@yahoo.com

Background: Maptaphut Industrial Estate (MIE) was established with a single factory in 1988, increasing to 50 by 1998. This development has resulted in undesirable impacts on the environment and the health of the people in the surrounding areas, evidenced by frequent complaints of bad odours making the people living there ill. In 1999, the Bureau of Environmental Health, Department of Health, Ministry of Public Health, conducted a study of the health status of people in Rayong Province and found a marked increase in respiratory diseases over the period 1993-1996, higher than the overall prevalence of such diseases in Thailand. However, the relationship between the pollutants and the respiratory diseases of the people in the surrounding area has still not been quantified. Therefore, this study aimed to determine the spatial distribution of respiratory disease, to estimate pollutants released from the industrial estates, and to quantify the relationship between estimated pollutants and respiratory disease in the Maptaphut Municipality.

Results: Disease mapping showed a much higher risk of respiratory disease in communities adjacent to the Maptaphut Industrial Estate. Disease occurrence formed significant clusters centred on communities near the estate, relative to the weighted mean centre of chimney stacks. Analysis of the rates of respiratory disease in the communities, categorized by different concentrations of estimated pollutants, found a dose-response effect. Spatial regression analysis found that the distance between community and health providers decreased the rate of respiratory disease ($p < 0.05$). However, after taking into account distance, total pollutant ($p < 0.05$), SO2 ($p < 0.05$) and NOx ($p < 0.05$) played a role in adverse health effects during the summer. Total pollutant ($p < 0.05$) and NOx ($p < 0.05$) played a role in adverse health effects during the rainy season after taking into account distance, but during winter there was no observed relationship between pollutants and rates of respiratory disease after taking into account distance. A 12-month time-series analysis of six communities selected from the disease clusters and the areas impacted most by pollutant dispersion, found significant effects for SO2 ($p < 0.05$), NOx ($p < 0.05$), and TSP ($p < 0.05$) after taking into account rainfall.

Conclusion: This study employed disease mapping to present the spatial distribution of disease. Excessive risk of respiratory disease, and disease clusters, were found among communities near Maptaphut Industrial Estate. Study of the relationship between

estimated pollutants and the occurrence of respiratory disease found significant relationships between estimated SO2, NOx, and TSP, and the rate of respiratory disease. ∅

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THE PHARMACOKINETICS OF ARTEMETHER AND LUMEFANTRINE IN PREGNANT WOMEN WITH UNCOMPLICATED FALCIPARUM MALARIA

McGready R, Stepniewska K, Lindegardh N, Ashley EA, La Y, Singhasivanon P, White NJ, Nosten F.

Shoklo Malaria Research Unit, P.O. Box 46, Mae Sot, Tak, Thailand

Objective: To determine the pharmacokinetic properties of artemether and lumefantrine (AL) in pregnant women with recrudescent uncomplicated multi-drug resistant falciparum malaria.

Methods: Pregnant women who had recurrence of parasitaemia following 7 days supervised quinine treatment were treated with AL. Serial blood samples were taken over a 7-day period, and pharmacokinetic parameters were estimated. For lumefantrine, these data were compared in a population pharmacokinetic model with data from non-pregnant, mainly male adults with acute malaria.

Results: The pregnant women (five in the second trimester and eight in the third trimester) had lower concentrations of artemether, dihydroartemisinin and lumefantrine, and the elimination of lumefantrine in pregnant women was more rapid than reported previously in non-pregnant adults.

Conclusion: Pregnancy is associated with reduced plasma concentrations of both artemether and lumefantrine. This is likely to be of therapeutic significance as plasma concentrations of lumefantrine, after elimination of artemether, are an important determinant of cure. Further studies are needed to determine the optimum dose regimen of artemether-lumefantrine in pregnancy. ∅

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BASELINE EPIDEMIOLOGICAL STUDY OF MALARIA AND SOIL-TRANSMITTED HELMINTHIASIS IN THAI RURAL COMMUNITIES NEAR THE MYANMAR BORDER

Wanchai Maneeboonyang[1], Surapon Yimsamran[1], Nipon Thanyavanich[1], Supalarp Puangsa-art[1], Pitak Wuthisen[1], Sutthiporn Prommongkol[1], Chotima Charusabha[1], Jareemet Limsomboon[2]

[1] *Department of Tropical Hygiene,*
[2] *Department of Social and Environmental Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand*

An analytic cross-sectional epidemiological study was conducted in January – March 2001 to measure the prevalence of malaria and helminthic infections, and to identify associated socio-behavioral risk factors in rural communities near the Thai-Myanmar border, in Suanphung, Ratchaburi Province, Thailand. A total of 2,898 individuals (85.6% of the total population) in two villages participated in the study. Of 2,280 individuals examined, 243 (10.7%) were positive for malaria. Among the positive cases, 129 (53.1%) were infected with *Plasmodium falciparum*, 109 (44.8%) with *P. vivax* and 5 (2.1%) with mixed infections. Males had significantly higher malaria prevalence (14.0%) than females (7.3%). Almost 56% of malaria cases occurred among those aged <16 years; and the highest prevalence was in the 4-15 year group. About 89% and 71% of the individuals in villages 4 and 6, respectively, stated that they always slept under mosquito nets; however, only 49% in village 6 possessed nets that were in good condition. The prevalence of malaria among those with damaged nets was 1.7 times higher than among those with nets in good condition.

A total of 2,095 stool samples were collected and examined; more than half of the individuals (52.4%) were infected with at least one type of intestinal worm. The most common infection was Hookworm (43.2%), followed by Trichuriasis (15.9%), and

ascariasis (13.2%). The prevalence of hookworm infection was significantly higher in village 6 (44.6%) than village 4 (39.1%); however, the prevalence of Trichuriasis and ascariasis in village 4 was significantly greater than village 6. Males were more frequently infected with hookworm (47.0%) compared to females (39.1%), but no significant difference in prevalence between the sexes was observed for Whipworm or roundworm. Ninety percent of individuals with hookworm and Trichuriasis had light infections. Among those with Ascariasis 40.1% and 12.7% had moderate and heavy infections, respectively. Heavy infections with Ascariasis were frequently observed in children aged < 7 years. About 13% and 31% of the households in villages 4 and 6 did not have latrines. In village 4, about 77% used latrines with septic tanks, with only 50% in village 6. Approximately one-third of individuals in village 6 defecated on the ground and 49% used paper/leaves or sticks to clean themselves after defecation. ∅

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INFECTION OF DENDRITIC CELLS BY DENGUE VIRUS INDUCES THE PRODUCTION OF MATRIX METALLOPROTEINASES CAUSING LOSSENING OF ENDOTHELIAL INTEGRITY

Natthanej Luplerdlop,[1,2] Dorothée Missé,[1] Hans Yssel[3] and Francisco Veas[1]

[1] *Laboratoire d'Immunologie Rétrovirale et Moléculaire, Institut de Recherche pour le Développement, UR 178, 34094 Montpellier, France.*
[2] *Department of Tropical Hygiene, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand.*
[3] *Institut National de la Santé et de la Recherche Médicale, U 454, 34295 Montpellier, France*

Dengue virus (DV) is a major, re-emerging, mosquito-borne Flavivirus of global significance. The hallmark of the pathology associated with DV infection is a hemorrhagic fever, often leading to a fatal shock-like syndrome, which is caused by an increase in the permeability of vascular endothelium. However, the molecular mechanisms underlying the changes in endothelial cell function remain unclear. Here, we show that *in vitro* generated immature dendritic cells produce high levels of the matrix metalloproteinase (MMP)-9, and to a lesser extent, MMP-2 following infection with DV. Culture supernatants, derived from these virally infected cells, enhanced endothelial permeability in an MMP-dependent manner, as demonstrated by the use of SB-3TC, a specific inhibitor of MMP-mediated gelatinolytic activity. Moreover, MMP-mediated disruption of cell-cell interactions, associated with a loss of expression of the junctional adhesion molecules PECAM-1 and VE-cadherin, as well as F-actin stress fibers, measured on confluent layers of primary human umbilical vein endothelial cells, was also prevented by SB-3TC. Taken together, our results provide molecular bases for a common pathogenic feature caused by Dengue viruses that could be extended to the other hemorrhagic fever-inducing viruses and provide a novel therapeutic approach against vascular leakage that are caused by infection with this family of pathogens by specifically targeting MMP. ∅

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REAPPEARANCE PATTERN OF *PLASMODIUM VIVAX* MALARIA IN A COMMUNITY NEAR THAI-MYANMAR BORDER, RATCHABURI PROVINCE

Rukmanee N[1], Singhasivanon P[1], Krudsood S[1], Buchachart K[1], Konchom S[2], Yimsamran S[1], Chupraphawan S[1], Chavez IF[1], Kaewkungwal J[1], Wuthisen P[1], Thanyavanich N[1], Puangsa-art S[1], Maneeboonyoung W[1], Prommongkol S[1], Maneekan P[1], Charusabha C[1], Rukmanee P[1]

[1] *Department of Tropical Hygiene, Faculty of Tropical Medicine, Mahidol University;*
[2] *Malaria Cluster, Bureau of Vector Borne Disease, Department of Diseases Control, Ministry of Public Health, Nonthaburi, Thailand*

Malaria is one of the most severe public health problems worldwide; it is responsible for over 300-500 million cases and is serious in developing countries. Many malaria infections do not show the classic pattern of recurrent fever at all. According to the dormant stage of the hypnozoite form, relapses occur in *Plasmodium vivax* infections and it is difficult to predict when they will occur.

The study was conducted at Rajanagarindra Tropical Disease International Center (RTIC) under the supervision of personnel from the Faculty of Tropical Medicine, Mahidol University. This study found reappearance patterns, to identify the times and associated factors for the reappearance of *P. vivax* cases on the Thai-Myanmar border.

In a six-year retrospective cohort from 1998-2003, the assumed risk-free period in rates within 60 and 90 days were 0.34 and 0.35 episodes per person-year respectively.

The cohort of 647 slide-positive *P. vivax* cases was separated into 2 groups. The reappearance cases for criteria-positive slides "60 days was 87 persons, while the other group "90 days" was 130 persons. The maximum for reappearance in the 60-day group was 5 times, and in the 90-day group 6 times. The median days for the reappearance in the 60-day group was 42 days and for the 90-day group 55 days. The reappearance pattern showed fluctuation but these peaks were at days 43, 60 and 65, 68 for the 60- and 90-day groups, respectively. Reappearance at 60 days was highest in July and lowest in January; reappearance at 90 days was highest in July, August and October, and lowest in January and February. Risk of reappearance for the 60- and 90-day groups was 13.4 % and 20.1 %, respectively. The rate of reappearance per 100 episodes in 60- and 90-day groups was 9.7 and 15.7 episodes, respectively.

In conclusion, the follow-up time was 60 days, because the median of reappearance was not greater than 60 days. The factor associated with reappearance was age, suggesting drug compliance was related to age ≤ 8 years. ∅

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PREVENTIVE AND CONTROLLABLE FACTORS ASSOCIATED WITH EPIDEMIOLOGICALLY IMPOT\RTANT INTESTINAL PARASITES AMONG HOUSEHOLDS AT THAI-MYANMAR BORDER OF RATCHABURI PROVINCE

Rukmanee P, Wuthisen P, Thanyavanich N, Puangsa-art S, Yimsamran S, Maneekan P, Rukmanee N, Kawkungwal J

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

Intestinal parasitic infection is still widely distributed in tropical and subtropical regions and related health, growth and physical fitness. The analytical cross-sectional study at Thai-Myanmar border in 2001, focused on the preventive and controllable factors of intestinal parasitosis that is dependence due to their common household environment. Therefore, the generalized estimation equation was performed among the correlated infection within household. The formalin-ether concentration technique was used to 2,173 stool examinations.

The determination of which factors associated with infection among household members after controlling for confounder was as follows. Age was found to be significantly associated with the presence of all epidemiologically important intestinal parasites. This finding might imply to immunologic and/ or nutritional status. Male was found significantly associated with hookworm infection. For education level, kindergarten seemed to have lower understanding of protection than higher education. The living places were probably indicated the geographical difference of contaminated source. Different kind of latrine yielded conflicting risk levels which may be according to the study design. The improper personal hygiene, dirty nail and no water treatment had a risk of infection. The material of house was indirect of economic status that related the infection.

The results of this study revealed several hygienic and public health issues. Factors in the model could be applied for disease prevention and control. ∅

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VITAMIN B_{12} STATUS OF THAI WOMEN WITH NEOPLASIA OF THE CERVIX UTERI

Karunee Kwanbunjan[1], Phimonsri Saengkar[1], Cheeraratana Cheeramakara[2], Siriwan Tangjitgamol[3] and Kulrat Chitcharoenrung[4]

[1] *Department of Tropical Nutrition and Food Science,*
[2] *Department of Tropical Radioisotopes, Faculty of Tropical Medicine, Mahidol University, Bangkok;*
[3] *Bangkok Metropolitan Administration Medical College and Vajira Hospital, Bangkok;*
[4] *National Cancer Institute, Bangkok, Thailand*

The vitamin B_{12} statuses of Thai women with high-and low-grade cervical dysplasia were studied and compared with women with normal cytological smears. Serum vitamin B_{12} and vitamin B_{12} intakes were assessed, as well as demographic characteristics, sexual behavior, reproductive and menstrual history, exogenous hormone use, 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 B_{12} levels in women with normal cytological smears were significantly higher than those with both high-and low-grade cervical dysplasia ($p<0.001$). Low vitamin B12 serum levels were significantly statistically 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 B_{12}. This study indicated a relationship between low vitamin B12 status and increased risk of cervical cancer. ∅

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PLASMA RESISTIN, INSULIN CONCENTRATION IN NON-DIABETIC AND DIABETIC OVERWEIGHT/OBESE THAI

Siriporn Chanchay[1], Rungsunn Tungtrongchitr[1], Talabporn Harnroongroj[1], Benjaluck Phonrat[2], Orapin Rungseesakorn[3], Suporn Paksanont[4], Somchai Pooudong[1], Sastri Saowakontha[5], Chusak Varongchayakul[6]

[1] *Department of Tropical Nutrition and Food Science, Faculty of Tropical Medicine, Mahidol University, 420/6 Rajavithi Road, Rajthevee, Bangkok 10400, Thailand;*
[2] *Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Thailand'*
[3] *Department of Public Health Foundation, Faculty of Public Health, Burapha University, Muang District, Chonburi 20131, Thailand'*
[4] *Department of Tropical Radioisotopes, Faculty of Tropical Medicine, Mahidol University, Thailand'*
[5] *Faculty of Public Health, Burapha University, Thailand'*
[6] *Bang-Yai Hospital, Bang-Yai District, Nontaburi, Thailand*

This study investigated levels of fasting plasma glucose (FBS), homeostasis model of the assessment of the insulin resistance (HOMA), lipid profile, insulin, and resistin hormones in 202 individuals, divided into four groups. Two groups had type II diabetes mellitus (DM): one group had been overnourished (DM/OB) (body mass index: BMI equal or above 25) and the other had not (DM/nOB). Two additional groups not suffering from diabetes were either overnourished (nDM/OB) or of normal nutritional status (nDM/nOB). Only the DM/OB group had insulin levels elevated above the other three groups. Resistin levels had been lowest in the nDM/nOB group. When participants of the two nOB groups were pooled into one group and the subjects of the two OB groups were combined into another group, the median plasma resistin levels of the OB groups were significantly higher compared with the nOB groups. Likewise the DM groups had higher resistin levels than the nDM groups. A significant correlation of plasma resistin with BMI, waist circumference, waist-to-hip ratio, FBS, and HOMA score had been observed. The result suggests that plasma resistin has a role in linking central obesity and obesity-related insulin resistance to type II diabetes mellitus. ∅

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MUTAGENICITY STUDY OF WEEDS AND COMMON PLANTS USED IN TRADITIONAL MEDICINE AND FOR ANIMAL FEED

Apanchanid Thepouyporn, Karunee Kwanbunjan, Somchai Pooudong and Supranee Changbumrung

Department of Tropical Nutrition and Food Science, Faculty of Tropical Medicine, Mahidol University, Bangkok, 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 only for B(a)P 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. ∅

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THE GENETIC ASSOCIATION BETWEEN ALPHA-2-MACROGLOBULIN (A2M) GENE DELETION POLYMORPHISM AND LOW SERUM A2M CONCERNTRATION IN OVERWEIGHT/OBESE THAIS

Wilaiwan Rugsarash[1], Rungsunn Tungtrongchitr[1], Songsak Petmitr[1], Benjaluck Phonrat[2], Praneet Pongpaew[1], Talabporn Harnroongroj[1] & Anchalee Tungtrongchitr[3]

[1] *Department of Tropical Nutrition and Food Science, Faculty of Tropical Medicine, Mahidol University, 420/6 Ratchawithi Road, Ratchathewi, Bangkok 10400, Thailand*
[2] *Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, 420/6 Ratchawithi Road, Ratchathewi, Bangkok 10400, Thailand*
[3] *Department of Parasitology, Faculty of Medicine Siriraj Hospital, Mahidol University, 2 Pranok Road, Bangkoknoi, Bangkok 10700, Thailand*

The study subjects were 192 overweight and obese Thais (BMI > 25.00 kg/m2), and 103 Thai controls (BMI = 18.50-24.99 kg/m2), whose ages ranged from 18-60 years. All subjects were evaluated for serum Alpha-2-macroglobulin (A2M), globulin, albumin concentration, and polymorphic variation in the A2M gene. Serum A2M and albumin were significantly lower in the overweight/obese group (P<0.05). For the overweight/obese and control group, the median ages were 38 and 37 years, serum A2M 200.2; 252.0 (mg/L), albumin 4.4; 4.5 (g/dL), and globulin 3.0; 2.95 (g/dL), respectively. A2M deletion polymorphism genotyping showed no association between A2M deletion polymorphism and the two groupings. At serum A2M concentration < 250 mg/L, there was no relationship between A2M delation polymorphism and age. Serum A2M had a significant negative correlation with age in all subjects (R2 = 0.09, P< 0.05). The results did not support the hypothesis that A2M had a significant negative correlation with age; serum A2M can possibly be used to indicate the aging of cells in vivo, including the brain. Further studies are needed to investigate other A2M genes located on chromosome 12 to prove A2M polymorphism's association with low serum A2M and aging. ∅

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hMSH2 GENE ALTERATIONS ASSOCIATED WITH RECURRENCE OF ORAL SQUAMOUS CELL CARCINOMA

S Sanguansin[1], S Petmitr[2], P Punyarit[3], V Vorasubin[4], W Weerapradist[5], R Surarit[1]

[1] Department of Physiology and Biochemistry, Faculty of Dentistry, Mahidol University,
[2] Department of Tropical Nutrition and Food Science, Faculty of Tropical Medicine, Mahidol University,
[3] Department of Pathology, Phramongkutklao Medical College;
[4] Department of Otolaryngology, Rajavithi Hospital, Bangkok, Thailand;
[5] Department of Pathology, Faculty of Dentistry, Mahidol University

Oral cancer, one of the ten most widespread cancers in Thailand, is a major public health problem. The aim of the study was to assess *hMSH2* and *hMLH1* gene mutations, microsatellite DNA alterations, and investigate the association between these alterations and clinicopathological features of oral squamous cell carcinomas (SCC) in a sample of Thai patients. Microsatellite alterations at D2S391, D3S647, D17S513, and D17S520 were detected at a frequency of 40.6%. Among these alterations, 12.5 exhibited loss of heterozygosity (LOH) at D3S647 and D17S513, while 34.4% exhibited microsatellite instability (MI) at D2S391, D17S513, and D17S520. Polymorphic change in the intronic region of *hMSH2* at IVS 1 nt 211+9, c→g was observed in 50% of cases. Significant correlation was observed between IVS 1 nt 211+9 polymorphism and the recurrence status of the patients (p=0.030, OR=10.67). This study demonstrated that the polymorphism of *hMSH2* at IVS 1 nt 211+9, (c→g) was associated with oral cancer recurrence status and could be used as a biomarker for prognosis and follow-up treatment of oral cancer. ∅

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GENETIC ALTERATIONS IN CHROMOSOME 10Q24.3 AND GLUTATHIONE S-TRANSFERASE OMEGA 2 GENE POLYMORPHISM IN OVARIAN CANCER

W Pongstaporn[1], M Rochanawutanon[2], S Wilailak[3], V Linasamita[3], S Weerakiat[3], and S Petmitr[4]

[1] Department of Tropical Nutrition and Food Science, Faculty of Tropical Medicine;
[2] Department of Pathology,
[3] Department of Obstetrics and Gynecology, Faculty of Medicine; Ramathibodi Hospital, Bangkok Thailand

The molecular basis of ovarian cancer development has not been fully elucidated. In this study, genetic alterations in ovarian cancer were identified by arbitrarily primed polymerase chain reaction (AP-PCR). A gene in DNA fingerprinting, amplified from primer AE11, was cloned, sequenced, and identified by comparison with known genes in the genome database. Gene amplification in chromosome 10q24.3 was identified and measured by real-time PCR. Three out of 20 cases harbored this gene amplification. This amplified region was identified as IVS-4 of the gluthathione-S-transferase Omega 2 (*GSTO2*) gene. Therefore, the mutations in all 6 exons of the *GSTO2* gene were determined. The A to G transition at codon 142 in exon 4 (AAT GAT, N142D) was observed. The frequency of *GSTO2* gene polymorphism was analyzed in 20 ovarian cancers, compared with 41 normal individuals. The gene frequencies of D142 and N142 allele in ovarian cancer cases were 0.3 and 0.7, whereas in normal females, they were 0.2 and 0.8, respectively. The odds ratio of D142 allele in ovarian cancer was 1.73 (95% CI=0.51-5.89), indicating that this *GSTO2* gene polymorphism may be associated with the risk of ovarian cancer. ∅

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POLYMORPHISM OF GLUTATHIONE S-TRANSFERASE OMEGA GENE AND RISK OF CANCER

Sujan Babu Marahatta[1], Phaibul Punyarit[2], Vajarabhongsa Bhudisawasdi[3], Anucha Paupairoj[3], Sopit Wongkham[3], Songsak Petmitr[1],*

[1] Department of Tropical Nutrition and Food Science, Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand;
[2] Department of Pathology, Phramongkutklao College of Medicine, Bangkok, Thailand;
[3] Liver Fluke and Cholangiocarcinoma Research Center, Faculty 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. 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 cholangiocarcinom, 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* between 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*N142D* polymorphism, there was no difference in genotypic distribution between all the types of cancer 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. ∅

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HLA-CLASS II (DRB & DQB1) IN THAI SUDDEN UNEXPLAINED DEATH SYNDROME (THAI SUDS) FAMILIES (LAI-TAI FAMILIES)

Himmunngan P, Sangwatanaroj S, Petmitr S*, Viroonudomphol D, Siriyong P, Patmasiriwat P

Institute of Pathology, Department of Medical Services, Bangkok, Thailand.
** Department of Tropical Nutrition and Food Science, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand*

Thai Sudden Unexplained Death Syndrome (Thai SUDS), or Lai-Tai, is a major health problem among rural residents of northeastern Thailand. The cause has been identified as a genetic disease. SUDS, a disorder found in Southeast Asia, is characterized by an abnormal electrocardiogram with ST-segment elevation in leads V1-V3, identical to that seen in Brugada Syndrome (Brugada Sign, BS) and sudden death due to ventricular fibrillation and cardiac arrest (represents an arrhythmogenic marker that identifies high-risk for SUDS). SUDS victims have a sleeping disorder (narcolepsy). The HLA-DR locus is tightly associated with narcoleptic Japanese patients and HLA-DR2, DQ haplotypes were also found in Oriental narcoleptic patients. These circumstances prompted us to study the association between the disease and HLA Class II by HLA DNA typing using a PCR-SSO method, with five Thai SUDS families (18 BS-positive subjects as the cases, and 27 BS-negatives as the controls). We found that the HLA-DRB1 *12021 allele was significantly increased in BS-positive subjects (p = 0.02; OR = 4.5), the same as the HLA-DRB1*12021-DQB1 *0301/09 haplotype (p = 0.01; OR = 7.95). Our data suggests that the HLA-DRB1* 12021 allele associated with BS and the HLA-DRB1*12021-DQB1 *0301/09 is a haplotype susceptible to arrhythmogenic markers that can identify a high risk for SUDS. ∅

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β-GLUCOSIDASE CATALYZING SPECIFIC HYDROLYSIS OF AN IRIDOID β-GLUCOSIDE FROM *PLUMERIA OBTUSA*

Doungkamol Boonclarm[1,3], Thakorn Sornwatana[1,3], Dumrongkiet Arthan[4], Palangpon Kongsaeree [2,3], and Jisnuson Svasti[1,3]*

[1] *Department of Biochemistry*
[2] *Department of Chemistry*
[3] *Center for Excellence in Protein Structure and Function, Faculty of Science, Mahidol University, Bangkok 10400, Thailand*
[4] *Department of Tropical Nutrition and Food Science, Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand*

An iridoid β-glucoside, namely plumieride coumarate glucoside, was isolated from the *Plumeria obtusa* (white frangipani) flower. A β-glucosidase, purified to homogeneity from *P. obtusa*, could hydrolyze plumieride coumarate glucoside to its corresponding 13-O-coumarylplumieride. *Plumeria* β-glucosidase is a monomeric glycoprotein with a molecular weight of 60.6 kDa and an isoelectric point of 4.90. The purified β-glucosidase had an optimum pH of 5.5 for p-nitrophenol (pNP)- β-D-glucoside and for its natural substrate. The K_m values for pNP- β-*D*-glucoside and *Plumeria* β-glucoside were 5.04 ± 0.36 mM and 1.02 ± 0.06 mM, respectively. The enzyme had higher hydrolytic activity towards pNP- β-*D*-fucoside than pNP- β-*D*-glucoside. No activity was found for other pNP-glycosides. Interestingly, the ezyme showed a high specificity for the glucosyl group attached to the C-7" position of the coumaryl moiety of

plumieride coumarate glucoside. The enzyme showed poor hydrolysis of 4-methylumbelliferyl- β-glucoside and esculin, and did not hydrolyze alkyl- β-glucosides, glucobioses, cyanogenic- β-glucosides, steroid β-glucosides, nor other iridoid β-glucosides. In conclusion, the *Plumeria* β-glucosidase shows high specificity for its natural substrate, plumieride coumarate glucoside. ∅

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FUNCTIONAL CHARACTERIZATION AND TARGET VALIDATION OF ALTERNATIVE COMPLEX I OF PLASMODIUM FALCIPARUM MITOCHONDRIA

Giancarlo A Biagini[1], Parnpen Viriyavejakul[1,2], O'neill PM[1], Patrick G Bray[1], Steve A Ward[1]

[1] *Molecular and Biochemical Parasitology, Liverpool School of Tropical Medicine, University of Liverpool, United Kingdom;*
[2] *Department of Tropical Pathology, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand*

This study reports on the first characterization of the alternative NADH:dehydrogenase (also known as alternative complex I or type II NADH:dehydrogenase) of the human malaria parasite *Plasmodium falciparum*, known as PfNDH2. PfNDH2 was shown to actively oxidize NADH in the presence of quinone electron acceptors CoQ(1) and decylubiquinone with an apparent K(m) for NADH of approximately 17 and 5 MU, respectively. The inhibitory profile of PfNDH2 revealed that the enzyme activity was insensitive to rotenone, consistent with recent genomic data indicating the absence of the canonical NADH:dehydrogenase enzyme. PfNDH2 activity was sensitive to diphenylene iodonium chloride and diphenyliodonium chloride, known inhibitors of alternative NADH:dehydrogenases. Spatiotemporal confocal imaging of parasite mitochondria revealed that loss of PfNDH2 function provoked a collapse of mitochondrial transmembrane potential (Psi(m)), leading to parasite death. As with other alternative NADH: dehydrogenases, PfNDH2 lacks transmembrane domains in its protein structure, and therefore, it is proposed that this enzyme is not directly involved in mitochondrial transmembrane proton pumping. Rather, the enzyme provides reducing equivalents for downstream proton-pumping enzyme complexes. As inhibition of PfNDH2 leads to a depolarization of mitochondrial Psi(m), this enzyme is likely to be a critical component of the electron transport chain (ETC). This notion is further supported by proof-of-concept experiments revealing that targeting the ETC's Q-cycle by inhibition of both PfNDH2 and the bc(1) complex is highly synergistic. The potential of targeting PfNDH2 as a chemotherapeutic strategy for drug development is discussed.

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RENAL PATHOLOGY IN FALCIPARUM MALARIA

Sudarat Nguansangiam[1,2], Gareth Turner [3,4] , Yaowapa Maneerat[1], Urai Chaisri[1], Margaret Jones[4], Arjen Dondorp[3], Mario Riganti[1], Nick White[3], David Ferguson[4], Nick Day[3], Emsri Pongponratn[1]

[1] *Department of Tropical Pathology, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand;*
[2] *Department of Anatomical Pathology, Bangkok Metropolitan Administration Medical College and Vajira Hospital, Bangkok, Thailand;*
[3] *The Wellcome Mahidol Oxford Tropical Medicine Research Unit, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand;*
[4] *Nuffield Department of Clinical Laboratory Sciences, John Radcliffe Hospital, University of Oxford, UK*

Objectives: 1. To examine the pathological features of renal disease in fatal *P. falciparum* malaria, using histopathology, ultrastructural morphology and immunohistochemistry.

2. To examine the relationship between parasitized red blood cell (PRBC) sequestration in the kidney with the clinical syndrome of acute renal failure in severe falciparum malaria.

3. To evaluate the role of leukocyte responses, cytokine release and hypoxia in *P. falciparum* malaria associated renal failure.

Methods: Samples of post mortem renal tissue were collected from 80 patients who died from severe falciparum malaria

in Thailand and Vietnam. To examine histopathological changes, tissue was processed for i) light microscopy (H&E, PAS and Silver staining), ii) ultrastructural examination with electron microscopy and iii) immunoperoxidase staining for immune complex deposition. Leukocyte responses were examined using immunohistochemistry to identify specific cell subsets, including macrophages (CD68), B cells (CD20), T cells (CD8) and plasma cells (VS38c), compared to controls. Markers of hypoxic gene expression were also examined including hypoxia inducible factor (HIF) and CA-9. Double immunofluorescence labeling was performed to detect cytokine release by leukocytes and other cell types, for TNF-a, IFN-γ, IL-10, and IL-6.

Results : Clinical analysis: Renal dysfunction in this group of patients was common (>60% of cases), and more severe than in paediatric African cases. Renal failure and acidosis contribute to systemic disease in severe malaria and are poor prognostic signs. Acute renal failure is characterized by a combination of pre-renal and renal patterns, and presents clinically as acute tubular necrosis. This is potentially reversible using treatment such as ambulatory peritoneal dialysis.

Histopathological changes: No membranous glomerulonephritis was found, in contrast to previous studies, although there was mesangial expansion and variable hypercellularity in some cases. We found evidence for PRBC sequestration in glomerular and peritubular vessels. Large numbers of mononuclear leukocytes were present within microvessels, many of which possessed cytopalsmic vacuoles containing malarial pigment.

Electron Microscopy: No evidence of glomerular basement membrane immune complex deposition was seen to indicate an acute membranous glomerulonephritis. Immunoperoxidase staining for immunoglobulins and complement was also negative. Glomerular and peritubular capillary interstitial vessels contained uninfected red cells, numerous mononuclear leukocytes and PRBC, including significantly higher numbers of Knob negative (K-) compared to Knob positive (K+). No quantitative association was found between the degree of PRBC sequestration in the kidney and the incidence of renal failure, unlike the association between cerebral sequestration and coma.

Immunohistochemistry: We found no evidence for increased expression or secretion of cytokines or HIF/CA-9 in glomerular or tubular epithelial cells, endothelium or leukocytes.

Conclusion: The clinical syndrome of acute renal failure in malaria was accompanied by a variable pathological picture of renal disease including acute tubular necrosis, and a 'post-infectious' hypercellular glomerulonephritis, with a significant increase in the number of CD68+ monocytes. Potential mechanisms for acute tubular necrosis in this setting do not appear to include an acute hypoxic injury.

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AN ULTRASTRUCTURAL STUDY OF THE KIDNEY IN *P. FALCIPARUM* MALARIA

Sudarat Nguansangiam[1], Nicholas Day[2,5], Tran Tinh Hien[3], Nguyen Hoan Thi Mai[3], Urai Chaisri[1], Mario Riganti[1], Arjen Dondorp[2,5], Nguyen Hoan Phu[3], Gareth Turner[2,4], Nicholas White[2,5], David Ferguson[4], Emsri Pongponratn[1]

[1] *Department of Tropical Pathology, and*
[2] *The Wellcome Mahidol Oxford Tropical Medicine Research Unit, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand;*
[3] *Centre for Tropical Diseases, Cho Quan Hospital, Ho Chi Minh City, Viet Nam; Nuffield Departments of*
[4] *Clinical Laboratory Sciences and 5Medicine, The John Radcliffe Hospital, Oxford University, Oxford, United Kingdom.*

Falciparum malaria is the most important parasitic infection of humans and is one of the most serious health problems facing the inhabitants of developing countries, contributing greatly to the high mortality rates in the developing world. Acute renal failure is a serious complication of severe malaria due to *P. falciparum* infection. The incidence and clinical course of malaria-associated renal failure (MARF) is variable between different populations. The histopathological findings and pathophysiology of MARF are not well characterised, and there is doubt as to whether renal failure results from an acute glomerulonephritis or acute tubular injury. We have performed an ultrastructural pathological correlation of renal disease in Southeast Asian adults (n=63) who died from severe malaria. Electron microscopy on post mortem renal tissues was used to examine the major pathological features of severe malaria disease in this group, and quantitate the degree of parasitized red blood cell (PRBC) sequestration. These features were correlated with the pre-mortem clinical picture, and peripheral parasite counts. There was a high incidence of MARF in this

population (>40%) and a correlation between the incidence of MARF. The pathological features included PRBC sequestration in glomerular and tubulo-interstitial vessels, acute tubular damage and mild glomerular hypercellularity due to host monocytes within glomerular capillaries. Large numbers of mononuclear leukocytes were present within microvessels, many of which containing malarial pigment. There was a correlation between PRBC sequestration in the kidney and pre-mortem renal failure, although overall levels of sequestration were low. Knob positive PRBCs and sequestration index in renal tissues of fatal falciparum malaria were significantly higher in MARF compare to non acute renal failure group ($P<0.05$). No evidence for an immune complex mediated glomerulonephritis was found. In conclusion, this study demonstrates that MARF is a common and serious complication of severe *P. falciparum* malaria in this population, associated with acute tubular injury rather than glomerulonephritis, and, in contrast with the coma of cerebral malaria in the same population, is linked to localisation of host monocytes in the kidney as well as sequestration of parasitized red blood cells.

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MICROCIRCULATORY OBSTRUCTION IN SEVERE MALARIA: ULTRASTRUCTURAL STUDY

Emsri Pongponratn[1], Gareth Turner[2], Urai Chaisri[1], Arjen Dondorp[3], Nick Day[3,4], Nick White[3,4], David Ferguson[2]

[1] *Department of Tropical Pathology, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand;*
[2] *Nuffield Department of Pathology, The John Radcliffe Hospital, Oxford, U.K.;*
[3] *The Wellcome Mahidol Oxford Tropical Medicine Research Unit; 4Nuffield Department of Medicine, The John Radcliffe Hospital, Oxford, U.K.*

The pathophysiology and pathogenesis of severe falciparum malaria is complex, but one well-established feature is the concept of microcirculatory obstruction. In an extensive electron microscopic study in 60 autopsy severe falciparum malaria cases we demonstrate variable obstruction of the microcirculation of human organs. The results provide an ultrastructural explanation for the development of circulatory disturbances caused by the malaria parasite.

Mostly, capillaries and post capillary venules were congested with red blood cell (RBC) and parasitized red blood cell (PRBC) of different parasite stages. Blockage of the cerebral microvasculature by PRBC is the principal pathological finding in human cerebral malaria. Knobs, which appear on the membrane of the PRBC adhere to the endothelium, causing obstruction of cerebral microvessels. However, the distribution of parasites was not uniform, with vessels packed by parasites in one segment, but only scarce parasites in an adjacent segment.

Additional causes of microcirculatory obstruction include a reduction in RBC deformability, auto-agglutination and aggregation, which could all be observed in our series. Phagocytes containing malarial pigment were abundant in every organ, but especially in the spleen and liver. Endothelial cell swelling containing phagocytosed malarial pigment were occasionally seen.

Fibrin deposition within blood vessels was sporadically found. Occasionally RBC and PRBC were seen clumped together by fibrin and fibrillary material. In some cases microvessels appeared to be blocked by a mass of necrotic material or sometimes clearly visible residual malarial pigment within a mass of fibrin and degenerating material. Neither fibrin deposited as fibrillary protein within the vessel lumen, nor the presence of fibrin platelet thrombus formation was a frequent feature of this series. However, in patients with cerebral malaria it was found more frequently than in the other cases. .

In some cases the kidney showed abundant cellular debris within the capillary lumen, mainly composed of lysed RBC and other unidentified materials. An interesting finding in one kidney was the presence of fibrin admixed with RBC, PRBC, mononuclear cells and platelets in the lumen of capillaries and venules.

The ultrastructural findings can offer a better understanding of pathophysiology and pathogenesis of severe falciparum malaria, for the development of better therapies for this severe disease, which remains to have an unacceptable high death toll.

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IMMUNOTHERAPY OF LEPTOSPIROSIS USING HUMANIZED-MURINE MONOCLONAL ANTIBODY

Santi Maneewatchararangsri[1], Pramuan Tapchaisri[1], Yuwaporn Sakolvaree[1], Patcharin Saengjaruk[2], Surasakdi Wongratanachewin[3], Pongsri Tongtawe[1], Uari Chaisri[4], Wanpen Chaicumpa[1]

[1] *Graduate Studies, Faculty of Allied Health Sciences, Thammasat University, Rangsit Center, Pathumthani, 12121;*
[2] *Faculty of Medicine, Srinakarinwiroj University, Bangkok;*
[3] *Faculty of Medicine, Khon Kaen University, Khon Kaen;*
[4] *Department of Tropical Pathology, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand*

Leptospirosis is a worldwide zoonosis caused by pathogenic *Leptospira* spp. Drugs of choice of leptospirosis are penicillin and the derivatives. Nevertheless, massive lysis of the bacteria as a result of the remedy may give rise to undesirable outcome, i.e., hypersensitivity, Jarisch Herxheimer reaction (JHR) which often aggravates the disease. Antibody therapeutics has been used for treatment of various infectious and non-infectious diseases. However, most of antibodies are derived from non-human sources. Anti-globulin response leads to various forms of hypersensitivity in the hosts.

The objective of this research is to construct humanized-murine monoclonal antibody specific to pathogenic *Leptospira* spp. For used as immunotherapeutic agent against human leptospirosis.

Murine hybridomas clone LD5 secreting MAb specific to an epitope shared by several proteins of pathogenic *Leptospira* spp. were produced previously. Protective capability of the MAb against pathogenic *Leptospira* was determined both *in vitro* and *in vivo*. VH-and VL-immunoglobulin genes were amplified from hybridoma cDNA and subsequently linked *via* a linker as muscFv using an overlapping extension PCR. MuscFv antibody phage clones were constructed. They were screened by bio-panning method. Amino acid of the selected clones were aligned with human VH-and VL-immunoglobulin sequences in the databank and the highest homology human antilody canonical sequences to the muscFv amino acid were selected. Complementarity determining regions (CDRs) of the muscFV were concurrently identified and grafted onto the selected human antibody frameworks to produce humanized-murine scFV (huscFV) by genetic engineering technique. Three dimensional structure of scFvs were predicted. Soluble scFvs proteins were purified and tested their protective efficacy against leptospirosis both *in vitro* and in animal model. Pathology of dead and survived hamster was studied.

It was found that a hybridoma clone LD5 were protective against experimental leptospirosis *in vivo* and could neutralize *Leptospira*-mediated hemolysis *in vitro*. Murine scFv phage clones were successfully constructed. CDRs of the murine MAb were successfully grafted onto the most matched human canonical framework. Soluble muscFv and huscFv retained antigenic specificity to original antibody. Three dimensional structures of muscFv and huscFv show the integrity of their predicted protein. Purified muscFv and huscFv can inhibit 57.07 and 58.75 % of 3HD50 of hemolysis caused from pathogenic leptospires, respectively. At lethal dose of high virulent leptospires (1,000LD50) with single dose of huscFv (100 µg), the efficacy was 40% and survivor didn't show tissue pathology when compared to positive leptospirosis hamsters.

Humanized-murine single chain antibodies against pathogenic *Leptospira* spp. were successfully produced. The huscFv neutralizes Leptospira mediated hemolysis *in vitro* and protected hamsters from lethal leptospirosis *in vivo*. The therapeutic trials of huscFv should merits further investigation. ∅

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APOPTOSIS AND CALCIUM INVOLVEMENT IN HUVEC-MALARIA PARASITE BINDING

Parnpen Viriyavejakul[1,2], Giancarlo Biagini[1], Patrick G Bray[1], Steve A Ward[1]

[1] *Molecular and Biochemical Parasitology, Liverpool School of Tropical Medicine, University of Liverpool, United Kingdom;*
[2] *Department of Tropical Pathology, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand*

Cerebral malaria (CM) is one of the most life-threatening complications of severe malaria. It is known that adhesion of malaria-infected erythrocytes to host endothelial cells is critical for the pathogenesis of CM, however the pathophysiology of the processes involved are poorly understood. Using a single cell imaging approach, we have examined the down-stream events following the binding of malaria parasite-infected erythrocytes to human umbilical vein endothelial cells (HUVEC). Apoptosis of HUVEC was determined morphologtically by the appearance of membrane blebbing and/or externalization of plasma membrane phosphatidylserine with Annexin V. Apoptosis of HUVEC was highly correlated with attachment to infected erythrocytes. Experiments carried out on un-stimulated (i.e. without addition of TNF α) cells revealed apoptosis in 89.59% ± 3.29 (SE) of all parasite-bound HUVEC after 3 hours of co-culture. Malaria parasite-induced apoptosis was reduced with the addition of the general caspase inhibitor (Z-VAD-FMK). Occurrence of apoptosis was further confirmed with elevation in luminescence of caspases 8 and 9 activities, indicating involvement of both receptor-mediated and mitochondrial-mediated apoptotic pathways. Pre-treatment with intracellular calcium chelator, BAPTA-AM reduced HUVEC apoptosis significantly, implicating calcium involvement in this apoptotic process. These findings are discussed in context with recent clinical findings of increased levels of apoptotic bodies from patients with severe malaria complicated with coma. ∅

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LIFE CYCLE OF PATHOGENIC FREE-LIVING AMOEBAE

Chutatip Siripanth[1], Benjanee Punpoowong[2], Urai Chaisri[2]

[1] *Department of Protozoology and*
[2] *Tropical Pathology, Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand*

Naegleria spp. and Acanthamoeba spp. are two pathogenic free-living amoebae which caused fatal diseases to human. Negleria caused Primary Amoebic Meningoencephalitis or PAM, *Acantbamoeba* caused Granulomatous Amoebic Encephalitis or GAE. PAM, occurs in healthy persons whereas GAE occurs in imunocompromised hosts. The diagnosis of both free-living amoeba infections are reliable on the detection of those pathogens in the specimens. This is the presentation of both pathogenic free-living amoeba life cycles. The specimens were collected from symptomatic patient and all images were taken from fresh observation, staing and transmission electronmicroscopy. Therefore, the basic knowledge of their life cycles are quite important for the detection and differentiation of these protozoa from specimens. ∅

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CRAFTING PONORAMIC HIGH-RESOLUTION LARGE-MAGNIFICATION PHOTOGRAPHY OF THE TWO STAGES OF RECOVERED *GNATHOSTOMA SPINIGERUMS* FROM THAI PATIENTS FOR COMPARATIVE SURFACE TOPOGRAPHY

Vasant Khachonsaksumet[1], Mario Riganti[1], Gedsuda Pattanapen[2], Borimas Hanboonkunupakarn[2], Wichai Ekataksin[2]

[1] *Department of Tropical Pathology;*
[2] *Liver Research Unit, Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Thailand*

More than 20 species of the genus gnathostoma have been identified so far. *Gnathostoma spinigerum* is one of the causative agents of food-borne parasitic zoonoses that found mainly in the Far East. During the years 1985 to now, many cases of human gnathostomiasis were seen at the Hospital for Tropical Diseases, Bangkok, Thailand. They were treated and some of the worms were recovered from some organs of the patients. The morphology of one (It was identified as an adult) of these

worms is different from the others (They were identified as third stage larvae). We performed a crafting photographic technique to photograph the two stages of the worms for comparative surface topography of external bodies. The adult and third stage larva were fixed in 95% alcohol. The adult was photographed by a 4.0 mega-pigxel digital camera under a Nicon light microscope. The third stage larva was processed for scanning electron microscope photography (SEMP). Depth and serial photographic techniques were applied. Nineteen serial monochrome pictures of the third stage larva (negative films of the third stage larva under SEMP were scanned at 1200 dpi.) and 100 digital color photographs of the adult were used as the template. Depth and montage reconstruction were applied by using an Adobe Photoshop program. The files were finished as TIFF, on an Macintosh computer about 500-1,000 MB and output from an HP DesignJet 5,500 inkjet printer, 60 inches, 6 colors at 600 dpi.

There are apparent distinguished features of the surface topography as seen in the adult and the third stage larva; the larva has only 4 lows of which about 40 hook-lets per row while the adult has 9 rows of which about 50 hook-lets per low of the cepalics; the third stage larva is covered with minute cuticular spines all over the body while the cuticular spines of the adult vary in size and shape according to their locations on the body. So it is quite convenient, therefore, for the experience observer to judge if the specimen is adult or larva by mere observation of the size and the surface topography. ∅

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AN ULTRASTRUCTURAL STUDY OF THE KIDNEY IN *P. FALCIPARUM* MALARIA

Sudarat Nguansangiam[1], Nicholas Day[2,5], Tran Tinh Hien[3], Nguyen Hoan Thi Mai[3], Urai Chaisri[1], Mario Riganti[1], Arjen Dondorp[2,5] , Nguyen Hoan Phu[3], Gareth Turner[2,4], Nicholas White[2,5], David Ferguson[4], Emsri Pongponratn[1]

[1] *Department of Tropical Pathology, and*
[2] *The Wellcome Mahidol Oxford Tropical Medicine Research Unit, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand;*
[3] *Centre for Tropical Diseases, Cho Quan Hospital, Ho Chi Minh City, Viet Nam; Nuffield Departments of*
[4] *Clinical Laboratory Sciences and* [5]*Medicine, The John Radcliffe Hospital, Oxford University, Oxford, United Kingdom.*

Falciparum malaria is the most important parasitic infection of humans and is one of the most serious health problems facing the inhabitants of developing countries, contributing greatly to the high mortality rates in the developing world. Acute renal failure is a serious complication of severe malaria due to *P. falciparum* infection. The incidence and clinical course of malaria-associated renal failure (MARF) is variable between different populations. The histopathological findings and pathophysiology of MARF are not well characterised, and there is doubt as to whether renal failure results from an acute glomerulonephritis or acute tubular injury. We have performed an ultrastructural pathological correlation of renal disease in Southeast Asian adults (n=63) who died from severe malaria. Electron microscopy on post mortem renal tissues was used to examine the major pathological features of severe malaria disease in this group, and quantitate the degree of parasitized red blood cell (PRBC) sequestration. These features were correlated with the pre-mortem clinical picture, and peripheral parasite counts. There was a high incidence of MARF in this population (>40%) and a correlation between the incidence of MARF. The pathological features included PRBC sequestration in glomerular and tubulo-interstitial vessels, acute tubular damage and mild glomerular hypercellularity due to host monocytes within glomerular capillaries. Large numbers of mononuclear leukocytes were present within microvessels, many of which containing malarial pigment. There was a correlation between PRBC sequestration in the kidney and pre-mortem renal failure, although overall levels of sequestration were low. Knob positive PRBCs and sequestration index in renal tissues of fatal falciparum malaria were significantly higher in MARF compare to non acute renal failure group ($P<0.05$). No evidence for an immune complex mediated glomerulonephritis was found. In conclusion, this study demonstrates that MARF is a common and serious complication of severe *P. falciparum* malaria in this population, associated with acute tubular injury rather than glomerulonephritis, and, in contrast with the coma of cerebral malaria in the same population, is linked to localisation of host monocytes in the kidney as well as sequestration of parasitized red blood cells. ∅

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DENGUE VIRUS INFECTIONS IN THE FIRST 2 YEARS OF LIFE AND THE KINETICS OF TRANSPLACENTALLY TRANSFERRED DENGUE NEUTRALIZING ANTIBODIES IN THAI CHILDREN

Krisana Pengsaa[1], Christine Luxemburger[4], Arunee Sabchareon[1], Kriengsak Limkittikul[1], Sutee Yoksan[3], Laurent Chambonneau[4], Udom Chaovarind[2], Chukiat Sirivichayakul[1], Keswadee Lapphra[1], Ponthep Chanthavanich[1], and Jean Lang[4]

[1] *Department of Tropical Pediatrics, Faculty of Tropical Medicine, Mahidol University;*
[2] *Rajavithi Hospital, Ministry of Public Health, Bangkok;*
[3] *Center for Vaccine Development, Institute of Sciences and Technology for Research Development, Mahidol University, Salaya Campus, Nakorn Prathom, Thailand;*
[4] *Sanofi Pasteur, Lyon, France*

Background. Understanding dengue virus infection in children and the kinetics of maternal dengue neutralizing antibodies is essential for effective dengue immunization of children in endemic areas.

Methods. Serum samples from 219 mother-child pairs and 140 children at 3, 6, 9, 12, 18, and 24 months of age from Bangkok, Thailand, were tested for serotype-specific dengue antibodies. Febrile episodes in the children were recorded.

Results. Antibodies were found in 97% of cord serum samples and disappeared in 27%, 80%, and 95% of the children by the age of 6, 9, and 12 months, respectively. Geometric mean titers (GMTs) of the antibodies to 4 dengue serotypes decreased to 5.4-15.5 in 6-month-old infants. Eleven of 12 children acquired dengue virus infection at 6 months of age and beyond; 1 had the infection at 3 months of age. Two exhibited undifferentiated febrile illnesses, and 10 had subclinical infections.

Conclusion. Evidence of dengue virus infection and very low GMTs against all dengue serotypes in children at 6 months of age and beyond was demonstrated. There was no evidence that maternal antibodies were harmful to infants. Dengue virus infection rates increase from 12 months of age onward. These data provide information for supporting the optimal age at vaccination.

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SHORT REPORT: IMMUNE RESPONSE AND OCCURRENCE OF DENGUE INFECTION IN THAI CHILDREN THREE TO EIGHT YEARS AFTER VACCINATION WITH LIVE ATTENUATED TETRAVALENT DENGUE VACCINE

Ponthep Chanthavanich[1], Christine Luxemburger[2], Chukiat Sirivichayakul[1], Keswadee Lapphra[1], Krisana Pengsaa[1], Sutee Yoksan[3], Arunee Sabchareon[1], and Jean Lang[2]

[1] *Department of Tropical Pediatrics, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand;*
[2] *Sanofi Pasteur, Lyon, France; 3Centre for Vaccine Development, Institute of Sciences and Technology for Research and Development, Mahidol University at Salaya, Nakhonpathom, Thailand*

From 1992 to 1997, 140 Thai children 4-15 years of age received an investigational live attenuated tetravalent dengue vaccine (LATDV). These children were contacted 3-8 years later in 2001 to assess humoral immunity and investigate whether they were subsequently at higher risk of developing severe dengue. One hundred thirteen were successfully contacted and participated in this retrospective cohort study with two age- and address-matched controls per vaccinee. The number of vaccinated subjects with neutralizing antibodies increased compared with 3-8 years earlier, which was probably due to subsequent wild-type dengue infections. There were no excess hospitalizations for clinically suspected dengue fever (DF) or dengue hemorrhagic fever (DHF) in vaccinees (one with DF and three with DHF) compared with controls (14 with DHF). Results suggest that preexisting dengue antibodies induced by LATDV do not enhance dengue illness, and the use of the vaccine in a dengue-endemic area is safe. Ø

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CONTRASTING SIGNATURES OF SELECTION ON THE *PLASMODIUM FALCIPARUM* ERYTHROCYTE BINDING ANTIGEN GENE FAMILY

Federica Verra[1], Watcharee Chokejindachai[1,2], Gareth D Weedall[1], Spencer D Polley[1], Tabitha W Mwangi[3], Kevin Marsh[3], and David J Conway[1,4]

[1] *Department of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, United Kingdom;*
[2] *Faculty of Tropical Medicine, Mahidol University, Rajthewe, Bangkok 10400, Thailand;*
[3] *Kenya Medical Research Institute/Wellcome Trust Programme, Centre for Geographic Medicine Research, Coast, Kilifi District Hospital, Kilifi, Kenya;*
[4] *Medical Research Council Laboratories, Fajara, P.O. Box 273, Banjul, Gambia*

Erythrocyte binding antigens of *Plasmodium falciparum* are involved in erythrocyte invasion, and may be targets of acquired immunity. Of the five *eba* genes, protein products have been detected for *eba-175*, *eba-181* and *eba-140*, but not for Ψ*eba-165* or *eba-1*, providing opportunity for comparative analysis of genetic variation to identify selection. Region II of each of these genes was sequenced from a cross-sectional sample of parasites in an endemic Kenyan population, and the frequency distributions of polymorphisms analysed. A positive value of Tajima's *D* was observed for *eba-175* (*D* = 1.13) indicating an excess of intermediate frequency polymorphisms, while all other genes had negative values, the most negative being *ebl-1* (*D* = -2.35) followed by Ψ*eba-165* (*D* = -1.79). The *eba-175* and *ebl-1* genes were then studied in a sample of parasites from Thailand, for which a positive Tajima's *D* value was again observed for *eba-175* (*D* = 1.79), and a negative value for *ebl-1* (*D* = -1.85). This indicates that *eba-175* is under balancing selection in each population, in strong contrast to the other members of the gene family, particularly *ebl-1* and Ψ*eba-165* that may have been under recent directional selection. Population expansion simulations were performed under a neutral model, further supporting the departures from neutrality of these genes. ∅

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PRE-EXPOSURE IM AND ID REGIMENS OF RABIES VACCINE ADMINISTERED CONCOMITANTLY WITH JAPANESE ENCEPHALITIS VACCINE IN TODDLERS

Pengsaa K[1], Limkittikul K[1], Chanthavanich P[1], Ariyasriwatana C[2], Lapphra K[1], Sirivichayakul C[1], Attanath P[1], Malerczyk C[3], Sabchareon A[1]

[1] *Department of Tropical Pediatrics, Faculty of Tropical Medicine, Mahidol University;*
[2] *Queen Sirikit National Institute of Child Health, MoPH, Bangkok, Thailand;*
[3] *Novartis Vaccines, Marburg, Germany*

Background: A 3-dose IM or ID pre-exposure rabies vaccine immunization is recommended by WHO for rabies endemic countries. Advantages of pre-exposure vaccination include eliminating the need for rabies immune globulin and 5 doses of rabies vaccine. It might protect persons with delayed post-exposure treatment and also provide protection to persons at risk for inapparent exposures to rabies.

Objective: To study 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. 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 measured for neutralizing antibodies to rabies using Rapid Fluorescent Focus Inhibition Test (RFFIT) and Japanese encephalitis virus.

This study was conducted in accordance with the latest revision of Declaration of Helsinki, GCP & local regulatory requirement. The protocol is approved by Ethical Committee of Ministry of Public Health Thailand.

Results: At day 49 after the first injection, all PCECV recipients achieved adequate titers against rabies (RFFIT antibody titers ≥ 0.5 IU/mL) and JE (JE antibody titers ≥ 1/10 serum dilution). All of them had adequate immune responses by day 7 following a single booster dose administered 1 year. Immune responses to rabies virus were greater with intramuscular schedules. There was no evidence that any of the schedules of rabies vaccination interfered with the immune response to the JEV. Both vaccines were well tolerated.

Conclusions: PCECV and JEV administration concomitantly in toddlers is safe and induces protective antibodies against both rabies and JE viruses. Long term follow-up to evaluate the persistence of immunogenicity in terms of rabies virus NA titers is on going. Ø

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TRANSMISSION OF DENGUE IN THAI CHILDREN: AGE--SPECIFIC SEROPREVALENCE OF ANTIBODIES AGAINST THE FOUR DENGUE SEROTYPES

Krisana Pengsaa[1], Kriengsak Limkittikul[1], Christine LuxembUrger[2], Sutee Yoksan[3], Laurent Chambonneau[2], Churdchoo Ariyasriwatana[4], Keswadee Lapphra[1], Pornthep Chanthavanich[1], Jean Lang[2], and Arunee Sabchareon[1]

[1] *Department of Tropical Pediatrics, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand;*
[2] *Sanofi Pasteur, Lyon, France;*
[3] *Center for Vaccine Development, Institution of Sciences and Technology for Research and Development, Mahidol University, Salaya Campus, Nakhon Pathom, Thailand;*
[4] *Queen Sirikit National Institute of Child Health, Ministry of Public Health, Bangkok, Thailand*

Age- and serotype--specific seroprevalence of dengue antibodies were determined in a cross--sectional survey of 447 healthy children in Bangkok, Thailand in 2000-2001 using hemagglutination inhibition, enzyme-linked immunosorbent assay, and plaque reduction neutralization test. At 9, 12 and 18 months of age 23%, 9% 17% of children had neutralizing antibodies against ≥1 dengue serotype. DEN1 was the most prevalent, followed by DEN3, DEN2 and DEN4. Twelve children had serological evidence of recent dengue infection: five at 9 months of age, one at 12, and six at 18 months. This study confirmed that dengue transmission was very high in this area and that the nadir of dengue antibodies was at 12 months of age. In highly endemic areas, vaccination with a tetravalent dengue vaccine could be needed at an early age and warrants further study. Ø

IMMUNOGENICITY, SAFETY AND BOOSTER RESPONSE OF INTRAMUSCULAR OR INTRADERMAL PRE-EXPOSURE REGIMEN OF PURIFIED CHICK EMBRYO CELL RABIES VACCINE ADMINISTERED CONCOMITANTLY WITH JAPANESE ENCEPHALITIS VACCINE IN 12 TO 18 MONTHS OLD TODDLERS IN THAILAND

Arunee Sabchareon[1], Krisana Pengsaa[1], Kriengsak Limkittikul[1], Chudchoo Ariyasriwatana[2], Pornthep Chanthavanich[1], Phanorsi Attanath[1], and Claudius Malerczyk[3]

[1] *Department of Tropical Pediatrics, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand;*
[2] *Queen Sirikit National Institute of Child Health, MOPH, Bangkok, Thailand; 3Chiron Vaccines, Marburg, Germany*

Background. A 3-dose intradermal (ID) and intramuscular (IM) pre-exposure immunizations (PEI) of rabies vaccine has been recommended by WHO for rabies endemic countries such as Thailand where approximately 1/3 of Thai children are bitten by dogs by the peak age of 2-4 years. One strategic plan of primary prevention is including PEI in EPI program therefore, the immunogenicity, safety and immunologic memory of rabies vaccine given concomitantly with Japanese encephalitis vaccine (JEV) in toddlers are needed for this high risk population.

Methods. Two hundred healthy toddlers aged 12-18 months were randomized in a 2:2:2:2:1 to receive one of the four PEI of purified chick embryo cell rabies vaccine (PCECV): Full-IM, Half-IM, 3-ID, 2-ID. These four groups also received 2 doses JEV with the same as the 5th group. A booster with PCECV according to their study groups was performed concomitantly with a booster of JEV one year after primary vaccination. Safety was evaluated after each injection. Pre-and day 49 post primary vaccination as well as pre-and day 7, day 28 post booster vaccination blood samples were determined for neutralizing antibodies to rabies and JE.

Results. Adequate immune response in all toddlers on day 49 after primary vaccination as well as day 7 after booster dose are demonstrated regardless which immunization schedule was used. However, immune responses were greater with IM schedules with no differences related to dose (Full-IM vs Half IM). No evidence that PCECV interfered with JEV. The reactogenicity profiles were similar regardless of the route of vaccine administration or dose.

Conclusions. Persistence of immunologic memory, good safety and convenience of administration of PCECV together with JEV in toddlers would provide an important new input into the child vaccination in rabies endemic areas. This approach in the routine immunization in rabies endemic areas is warrant further study. ∅

CONGENITAL MALARIA IN THAILAND

Krisana Pengsaa

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

Congenital malaria has long been documented as relatively rare; however, it is now not uncommon, with varying prevalence rates. Fifteen cases of congenital malaria admitted from various parts of Thailand are reviewed. Most came from Thai border areas. ∅

CHRONIC DIARRHEA AND ABNORMAL SERUM IMMUNOGLOBULIN: A CASE REPORT

Krisana Pengsaa[1], Chukiat Sirivichayakul[1], Niyada Vithayasai[2], Sansnee Senawong[3], and Voravich Luangwedchakarn[3]

[1] *Department of Tropical Pediatrics, Faculty of Tropical Medicine, Mahidol University, Thailand;*
[2] *Queen Sirikit National Institute of Child Health, Ministry of Public Health, Thailand;*
[3] *Department of Immunology, Faculty of Medicine Siriraj Hospital, Mahidol University, Thailand*

A 15-year-old Thai boy with multiple episodes of chronic diarrhea caused by giardiasis with hypogammaglobulin M and IgG4 subclass deficiency (but normal antibody response to rabies vaccine) is reported. Immune status follow-up is necessary for a definite diagnosis and proper management. ∅

COMPARATIVE STUDY OF EFFECTIVENESS AND PHARMACOKINETICS OF TWO RECTAL ARTESUNATE/ ORAL MEFLOQUINE COMBINATION REGIMENS FOR THE TREATMENT OF UNCOMPLICATED CHILDHOOD FALCIPARUM MALARIA

Chukiat Sirivichayakul[1], Arunee Sabchareon[1], Krisana Pengsaa[1], Itthipon Thaiarporn[2], Anong Chaivisuth[3], Kesara Na-Bangchang[4], Pataraporn Wisetsing[1], Pornthep Chanthavanich[1], and Chanathep Pojjaroen-anant[1]

[1] *Department of Tropical Pediatrics, Faculty of Tropical Medicine, Mahidol University, Thailand;*
[2] *Thongpaphum Hospital, Thai Ministry of Public Health, Thailand;*
[3] *Paholpholpayuhasena Hospital, Thai Ministry of Public Health, Thailand;*
[4] *Faculty of Allied Health Science, Thammasat University, Thailand*

Background: Rectal artesunate has been shown to be effective for the treatment of falciparum malaria and would be useful in patients who cannot take medicine orally and parenteral medication is inconvenient. A combination with mefloquine can decrease the duration of treatment, increase the compliance and delay development of resistance. There are

no clear data whether higher dosage of rectal artesunate results in better clinical response.

Aim: This study aimed to assess two rectal artesunate/ oral mefloquine regimens for the treatment of uncomplicated multidrug-resistant childhood falciparum malaria.

Methods:A total of 70 children aged 1-14 years with uncomplicated falciparum malaria were randomly assigned to either 10 (range 8-12) or 20 (range 16-24) mg/kg/day of rectal artesunate for 3 days followed by 25 mg/kg of oral mefloquine. The study endpoints were the fever clearance time, parasite clearance time and proportion of the patients who had recrudescence. Serum levels of artesunate and dihydroartemisinin after the first dose of rectal artesunate in 16 subjects were measured for pharmacokinetic study.

Results: Both regimens were safe and effective. The cure rate was 100% in 53 patients who completed a 28-day follow-up. All of the study endpoints were comparable between both treatment groups.

Conclusion: A regimen of rectal artesunate 10 mg/kg/day for 3 days followed by mefloquine 25 mg/kg is optimal for the treatment of uncomplicated falciparum malaria in children. There was no definite benefit from increasing the dosage of rectal artesunate from 10 to 20 mg/kg/day. ∅

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PLASMA RESISTIN, INSULIN CONCENTRATION IN NON-DIABETIC AND DIABETIC, OVERWEIGHT/OBESE THAI

Siriporn Chanchay[1], Rungsunn Tungtrongchitr[1], Talabporn Harnroongroj[1], Benjaluck Phonrat[2], Orapin Rungseesakorn[3], Suporn Paksanont[4], Somchai Pooudong[1], Satri Saowakontha[5], Chusak Varongchayakul[6]

[1] *Department of Tropical Nutrition and food Science, Faculty of Tropical Medicine, Mahidol University, 420/6 Rajavithi Road, Rajthevee, Bangkok 10400, Thailand*
[2] *Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Thailand*
[3] *Department of Public Health Foundation, Faculty of Public Health, Buraph University, Muang District, Chonburi 20131, Thailand*
[4] *Department of Tropical Radioisotopes, Faculty of Tropical Medicine, Mahidol University, Thailand*
[5] *Faculty of Public Health, Burapha University, Thailand*
[6] *Bang-Yai Hospital, Bang-Yai District, Nontaburi, Thailand*

This study investigated levels of fasting plasma glucose (FBS), homeostasis model of the assessment of the insulin resistance (HOMA), lipid profile, insulin, and resistin hormones in 202 individuals, divided into four groups. Two groups had type II diabetes mellitus (DM): one group had been overnourished (DM/OB) (body mass index: BMI eual or above 25) and the other had not (DM/nOB). Two additional groups not suffering from diabetes were either overnourished (nDM/OB) or of normal nutritional status (nDM/nOB). Only the DM/OB group had insulin levels elevated above the other three groups. Resistin levels had been lowest in the nDM/nOB group. When participants of the two nOB groups were pooled into one group and the subjects of the two OB groups were combined into another group, the median plasma resistin levels of the OB groups were significantly higher compared with the nOB groups. Likewise the DM goups had higher resistin levels than the nDM groups. A significant correlation of plasma resistin with BMI, waist circumference, waist-to-hip ratio, FBS, and HOMA score had been observed. The result suggests that plasma resistin has a role in linking central obesity and obesity-related insulin resistance to type II diabetes mellitus. ∅

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STUDY ON SERUM TRANSCOBALAMIN II IN PATIENTS WITH URINE TYPHUS

Cheeraratana Cheeramakara[1], Kriyaporn Songmeang[1], Wanyarat Nakosiri[1], Nopachai Suthisai[1], Apichart Nontprasert[2], and Suvit Areekul[1]

[1] *Department of Tropical Radioisotopes,*
[2] *Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol Unviersity, Bangkok, Thailand*

We measured the serum transcobalamin II in murine typhus-infected patients (n = 16). admitted to the Hospital for Tropical Diseases in 1996-1997, comparted with healthy controls (n = 60). The results showed that the transcobalmin II (TCII) and total serum unsaturated vitamin B12 binding capacity (UBBC) in patients with murine typhus (2,126.5 pg/ml, range 1,262-4,568 and 3,771.5 pg/ml, range 1,576-6,763 pg/ml) were statistically significantly higher than normal subjects (987.5 pg/ml, range 678-2,000 pg/ml and 1,402 pg/ml, range 932-2,470 ml) (p<0.001). Serum TCII levels in patients (63%) were elevated during the febrile period and returned to normal post-treatment. These findings suggest that patients with murine typhus had stimulation of reticulo-endothelial system, spleen, mesenteric lymph nodes, liver and skin and then released TCII into the blood circulation. The elevation in TCII may be used for confirming a diagnosis of murine typhus. Ø

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RADIATION EFFECT OF ULTRAVIOLET AND X-RAY ON MOUSE MACROPHAGE CELL LINE (RAW264.7) AND RADIOPROTECTION BY THAI MEDICINAL PLANTS

Cheeraratana Cheeramakara[1], Kriyaporn Songmuaeng[1], Wanyarat Nakosir[1], Nophachai Suthisai[1], Montri Chairoj[2], Charnnarong Sanghirun[1], Apichart Nontprasert[3]

[1] *Department of Tropical Radioisotopes, Faculty of Tropical Medicine, Mahidol University;*
[2] *X-ray Unit, Bangkok Hospital for Tropical Diseases, Faculty of Tropical Medicine, Mahidol University;*
[3] *Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University*

To investigate the effect of radiation on growth-arrested rate (GA) and micronucleus production rate (MN) and radioprotection of Thai medicinal plants in mouse macrophage cell line (RAW264.7) *in vitro*. The results showed that both GA and MN rates in UV exposure were dose-dependent. The 50% affected dose of UV exposure on GA rate was 159 microwatt/cm^2 for 3 seconds. Longer time of UV exposure caused cell injury and death. No any effects were observed in cells after X-ray exposure even given at 80 KV for 20 times. The Thai medicinal plants (*Kamin-chun capsules, Curcuma longa Linn.; Hed lingeu, Ganoderma lucidum; Ya Pakking capsule, Murdannia loriformis*) could not protect cells damage from radiation. These findings indicated that UV radiation caused more cell death than chromosomal damage. X-ray at therapeutic dose was relatively safe. There were no evidences of cell protection from radiation found in these Thai medicinal plants. Ø

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LIPOPOLYSACCHARIDE HETEROGENEITY AMONG *BURKHOLDERIA PSEUDOMALLEI* FROM DIFFERENT GEOGRAPHIC AND CLINICAL ORIGINS

Narisara Anuntagool ,*Vanaporn Wuthiekanun, Nicholas J White, Bart J Currie, Rasana W Sermswan, Surasakdi Wongratanacheewin, Suwimol Taweechaisupapong, Sansanee C Chaiyaroj, And Stitaya Sirisinha

Faculty of Tropical Medicine, and Department of Microbiology, Faculty of Science, Mahidol University, Bangkok, Thailand; University of Oxford, Oxford, United Kingdom; Tropical and Emerging Infectious Diseases Division, Menzies School of Health Research, Charles Darwin University, Darwin, Northern Territory, Australia; Northern Territory Clinical School, Flinders University, Darwin, Northern Territory, Australia; Melioidosis Research Center, Departments of Biochemistry and Microbiology, Faculty of Medicine, and Department of Oral Diagnosis, Faculty of Dentistry, Khon Kaen University, Khon Kaen, Thailand

Heterogeneous patterns were obtained for lipopolysaccharide (LPS) from 1,327 *Burkholderia pseudomallei* isolates by sodium dodecyl sulfate-polyacrylamide gel electrophoresis, silver staining, and immunoblot analysis. Two LPS serotypes (A and B) possessing different ladder profiles and a rough LPS without ladder appearances were identified. All three LPS types were antigenically distinct by immunoblotting. The predominant type A (97%) produced the lowest amount of biofilm. The two less common types (smooth type B and rough type) were found more in clinical than environmental isolates and more in Australian isolates than Thai isolates. These isolates were more often associated with relapse than with primary infection. Ø

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MALARIA

Elizabeth Ashley[1,2,3], Rose McGready[1,2,3], Stephane Proux1 and Françius Bisten[1,2,3]

[1] Shoklo Malaria Research Unit, 68/30 Ban Toong Road, Mae Sot, Tak, 63110 Thailand;
[2] Faculty of Tropical Medicine, Mahidol University, 420/6 Rajvithi Road, Bangkok, 10400, Thailand;
[3] Centre for Clinical Vaccinology and Tropical Medicine Churchill Hospital, Old Road, Headington, Oxford, UK

Malaria is increasing worldwide due to the emergence and spread of drug resistant strains. This poses major health and economic problems for the population living in endemic areas and increases the risk of infections in travelers. The diagnosis of malaria relies on a biological proof of infection by microscopy or with a rapid test. The treatment must be initiated without delay preferably with an artemisinin containing regimen. Uncomplicated malaria can be treated with oral drugs while severe infections will be hospitalized and treated with injectables. Special attention will be given to the most susceptible groups: children and pregnant women. Ø

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LIMITED DIAGNOSTIC CAPACITIES OF TWO COMMERCIAL ASSAYS FOR THE DETECTION OF LEPTOSPIRA IMMUNOGLOBULIN M ANTIBODIES IN LAOS

Stuart D. Blacksell,[1,2,3]* Lee Smythe,[4] Rattanaphone Phetsouvanh,[1] Michael Dohnt,[4] Rudy Hartskeerl,[5] Meegan Symonds,[4] Andrew Slack,[4] Manivanh Vongsouvath,[1] Viengmone Davong,[1] Olay Lattana,[1] Simmaly Phongmany,[1] Valy Keolouangkot,[1] Nicholas J White,[1,2,3] Nicholas P J Day,[1,2,3] and Paul N. Newton[1,2]*

[1] Wellcome Trust-Mahosot Hospital-Oxford Tropical Medicine Research Collaboration, Microbiology Laboratory, Mahosot Hospital, Vientiane, Lao People's Democratic Republic,
[2] Centre for Clinical Vaccinology and Tropical Medicine, University of Oxford, Churchill Hospital, Oxford OX3 7LJ, United Kingdom,
[3] Faculty of Tropical Medicine, Mahidol University, 420/6 Rajvithi Rd., Bangkok 10400, Thailand,
[4] WHO/FAO/OIE Collaborating Centre for Reference and Research on Leptospirosis, Coopers Plains, Queensland, 4108, Australia,
[5] WHO/FAO/OIE Collaborating Centre for Reference and Research on Leptospirosis, KIT Biomedical Research, Meibergdreef 39, 1105 AZ Amsterdam, The Netherlands

The diagnostic utility of immunochromatographic (Leptotek) and enzyme-linked immunosorbent assay (ELISA; Panbio) tests for the detection of *Leptospira* immunoglobulin M antibodies was assessed in febrile adults admitted in Vientiane, Laos. Both tests demonstrated poor diagnostic accuracy using admission serum (Leptotek sensitivity of 47.3% and specificity of 75.5%: ELISA sensitivity of 60.9% and specificity of 65.6%) compared to the *Leptospira* "gold standard" microscopic agglutination test. Ø

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THE COMPARATIVE ACCURACY OF 8 COMMERCIAL RAPID IMMUNOCHROMATOGRAPHIC ASSAYS FOR THE DIAGNOSIS OF ACUTE DENGUE VIRUS INFECTION

Stuart D Blacksell,[1,2,4] Paul N Newton,[1,4] David Bell,[5] James Kelley,[5] Mammen P Mammen, Jr,[3] David W Vaughn,[3,6] Vanaporn Wuthiekanun,[2] Amornwadee Sungkakum,[2] Ananda Nisalak,[3] and Nicholas PJ Day[1,2,4]

[1] Centre for Clinical Vaccinology and Tropical Medicine, Nuffield Department of Clinical Medicine, Churchill Hospital, University of Oxford, Oxford, United Kingdom;
[2] Faculty of Tropical Medicine, Mahidol University, and
[3] Armed Forces Research Institute of Medical Sciences, Bangkok, Thailand;
[4] Wellcome Trust-Mahosot Hospital-Oxford Tropical Medicine Research Collaboration, Microbiology Laboratory, Mahosot Hospital, Vientiane, Lao People's Democratic Republic;
[5] World Health Organization Regional Office for the Western Pacific, Manila, Philippines; and
[6] Military Infectious Diseases Research Program, US Army Medical Research and Material Command, Fort Detrick, Maryland

Background: The serological diagnosis of acute dengue virus infection relies on the detection of dengue-specific immunoglobulin M (IgM) antibodies. Immunochromatographic tests are rapid diagnostic tests (RDTs) that can be performed at the bedside, but they have not been fully validated for diagnosis of dengue infection.

Methods: More than 20 RDTs for diagnosis of acute dengue infection are commercially available. Of these, 8 were selected for evaluation of performance by use of characterized dengue and nondengue serum specimens, and results were compared with those of a previously published dengue IgM/IgG enzyme-linked immunosorbent assay in conjunction with dengue virus serotyping by reverse-transcriptase polymerase chain reaction.

Results: Assay sensitivities were low, ranging from 6.4% (95% confidence interval [CI], 4.0%–9.7%) to 65.3% (95% CI, 59.9%–70.5%), and specificities ranged from 69.1% (95% CI, 61.4%–76.0%) to 100% (95% CI, 97.8%–100%). Of the 8 tests, only 2 had sensitivities of >50%, the level considered to be clinically useful, and, of these, 1 had relatively low specificity (69.1%). Samples collected early in the infection were less likely to test positive than those collected later. A thermal stability study demonstrated a loss in performance of some RDTs when they were stored at a high ambient temperature for 3 months.

Conclusions: Users of RDTs for dengue should be aware that many of these tests have a diagnostic accuracy that falls well below the manufacturers' claims. If an acute specimen yields a negative result, a convalescent serum sample should be tested to confirm the result. No RDT adequately differentiated primary and secondary dengue infections, and the tests should not be used for this purpose. ∅

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A SYSTEMATIC REVIEW AND META-ANALYSIS OF THE DIAGNOSTIC ACCURACY OF RAPID IMMUNOCHROMATOGRAPHIC ASSAYS FOR THE DETECTION OF DENGUE VIRUS IgM ANTIBODIES DURING ACUTE INFECTION

Stuart D Blacksell[1,2,3], Jenny A Doust[4], Paul N Newton[1,3], Sharon J Peacock[1,4], Nicholas PJ Day[1,2,3], and Arjen M Dondorp[1,2]

[1] *Centre for Clinical Vaccinology and Tropical Medicine, Nuffield Department of Clinical Medicine, Churchill Hospital, University of Oxford, Oxford, UK*
[2] *Wellcome Trust-Mahosot University-Oxford Tropical Medicine Programme, Faculty of Tropical Medicine, Mahidol University, 420/6 Rajvithi Road, Bangkok 10400, Thailand*
[3] *Wellcome Trust-Mahosot Hospital-Oxford Tropical Medicine Research Collaboration, Microbiology Laboratory, Mahosot Hospital, Vientiane, Lao PDR*
[4] *Centre for General Practice, School of Medicine, University of Queensland, Herston, Queensland, Australia*

A meta-analysis of rapid (≤60 min) dengue diagnostic assays was conducted to determine accuracy and identify causes of between-study heterogeneity. A systematic review identified 302 potentially suitable studies, of which 11 were selected for meta-analysis. All selected studies evaluated the immunochromatographic test (ICT) manufactured by Panbio Pty Ltd. Individual study results for sensitivity ranged from 0.45 to 1.0, specificity 0.57–1.0, diagnostic odds ratio 4.5–1287, and positive:negative likelihood ratios 2.3–59 and 0.01–0.56, respectively. Results indicated that the ICT evaluated in the selected studies can both rule in and rule out disease but is more accurate when samples are collected later in the acute phase of infection. Limitations of this meta-analysis were significant between-study heterogeneity caused by inconsistencies in evaluation methodologies, and the evaluation of only the Panbio ICT. It is recommended that additional, standardized evaluations are required for other dengue ICTs. ∅

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A SIMPLE AND INEXPENSIVE CONTAINER FOR THE TRANSPORT OF BIOLOGICAL SPECIMENS IN LIMITED RESOURCE SITUATIONS

Stuart D Blacksell[1,2,3], Syseng Khounsy[4], Rattanaphone Phetsouvanh[1] and Paul N Newton[1,3]

[1] *Wellcome Trust-Mahosot Hospital-Oxford University Tropical Medicine Research Collaboration, Microbiology Laboratory, Mahosot Hospital, Vientiane, Lao PDR*

[2] Wellcome Trust-Mahidol University-Oxford Tropical Medicine Research Programme, Faculty of Tropical Medicine, Mahidol University, 420/6 Rajvithi Road, Bangkok 10400, Thailand,
[3] Centre for Clinical Vaccinology and Tropical Medicine, Nuffield Department of Clinical Medicine, Churchill Hospital, University of Oxford, Oxford, UK
[4] Department of Livestock and Fisheries, Ministry of Agriculture and Forestry, Lao PDR

We describe a diagnostic specimen transport container that is appropriate for limited resource or emergency settings. The transport container is constructed from polyvinyl chloride (PVC) plumbing pipe, which is readily available and inexpensive (US$1-2, depending on size) and has wide flexibility of size due to the range of PVC pipe dimensions available. The PVC transporters are durable, water-resistant and may be easily decontaminated. They have been adapted for the transport of blood culture bottles from provincial hospitals in Laos, where, during a 2-year period, 380 PVC tubes containing blood culture bottles were transported without any leakage or breakage. We have found the PVC transporter to be a useful and cost-efficient durable alternative that meets IATA Packing Instruction 650 biological transport container requirements. Ø

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A NEW APPROACH TO EVALUATE STABILITY OF AMODIAQUINE AND ITS METABOLITE IN BLOOD AND PLASMA

D Blessborn HYPERLINK[1], G Neamin[1], Y Bergqvist[1] and N Lindegårdh[2,3]

[1] Dalarna University College, S-781 88 Borlänge, Sweden;
[2] Faculty of Tropical Medicine, Mahidol University, 420/6 Rajvithi Road, Bangkok 10400, Thailand;
[3] Nuffield Department of Clinical Medicine, Centre for Tropical Medicine, University of Oxford, Oxford, UK

A stability study for amodiaquine (AQ) and desethylamodiaquine (AQm) in whole blood and plasma is reported. AQ, AQm and chloroquine (CQ) were simultaneously analysed and the ratios AQ/CQ and AQm/CQ were used to ensure correct interpretation of the stability results. CQ was stable in whole blood and plasma at all tested temperatures enabling it to be a stability marker in stability studies. Simultaneous analysis of compounds, of which at least one is already known to be stable, permits a within sample ratio to be used as a stability indicator. The new approach significantly reduced bias when compared to the traditional approach. AQ and AQm were stable in plasma at -86 °C and -20 °C for 35 days, at 4 °C for 14 days and at 22 °C for 1 day. AQ and AQm were stable in blood at -86 °C and 4 °C for 35 days, at -20 °C and 22 °C for 7 days and at 37 °C for 1 day. Ø

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PULSED-FIELD GEL ELECTROPHORESIS AS A DISCRIMINATORY TYPING TECHNIQUE FOR THE BIOTHREAT AGENT BURKHOLDERIA MALLEI

Narisara Chantratita, Mongkol Vesaratchavest, Vanaporn Wuthiekanun, Rachaneeporn Tiyawisutsri, Tsedev Ulziitogtokh, Erhan Akcay, Nicholas PJ Day, and Sharon J Peacock

Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; Biocombinat, State-Owned Biological Enterprise, Ulaanbaatar, Mongolia; Tuberculosis Laboratory, Central Veterinary Control and Research Institute, Ankara, Turkey; Center for Clinical Vaccinology and Tropical Medicine, Nuffield Department of Clinical; Medicine, University of Oxford, Churchill Hospital, Oxford, United Kingdom

Pulsed-field gel electrophoresis (PFGE) and multilocus sequence typing (MLST) was used to type 21 laboratory strains of *Burkholderia mallei*. We demonstrated good resolution by PFGE together with clustering of some geographically related isolates, and confirmed previous observations that *B. mallei* is clonal as defined by MLST. Ø

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PROSPECTIVE EVALUATION OF A RAPID IMMUNOCHROMGENIC CASSETTE TEST FOR THE DIAGNOSIS OF MELIOIDOSIS IN NORTHEASR THAILAND

Allen C Cheng[1,2,3], Sharon J Peacock[1,4], Direk Limmathurotsakul[1], Gumphol Wongsuvan[1], Wirongrong Chierakul[1], Premjit Amornchai[1], Nongluk Getchalarat [1], Wipada Chaowagul[1], Nicholas J White1,4, Nicholas PJ Day[1,4] and Vanaporn Wuthiekanun[1]

[1] *Faculty of Tropical Medicine, Mahidol University, 420/6 Rajvithi Road, Bangkok, 10400, Thailand;*
[2] *Menzies School of Health Research, Charles Darwin University and Northern Territory Clinical School, Flinders University, Darwin, Australia;*
[3] *Medical Department, Sappasithiprasong Hospital, Ubon Ratchathani, Thailand;*
[4] *Centre for Clinical Vaccinology and Tropical Medicine, Nuffield Department of Clinical Medicine, University of Oxford, Churchill Hospital, Oxford OX3 7LJ, UK*

A prospective study was performed to compare a rapid immunochromogenic cassette test (ICT) with the indirect haemagglutination assay (IHA) and clinical rules for the diagnosis of melioidosis in an endemic area. The sensitivity and specificity of the IgG ICT was 86% and 47%, and the IgM ICT was 82% and 47%, respectively. These were similar to the results for IHA (sensitivity 73%, specificity 64%) and clinical rules (73% and 37%). ICT lacks clinical utility as a result of high background rates of positive *Burkholderia pseudomallei* serology in this population. Low sensitivity and specificity of clinical rules is consistent with the protean manifestations of melioidosis and clinical difficulty in identifying patients with melioidosis. ∅

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PHARMACOKINETIC AND PHARMACODYNAMIC ASSESSMENT OF CO-AMOXICLAV IN THE TREATMENT OF MELIOIDOSIS

Wirongrong Chierakul[1], Jinda Wangboonskul[2], Thida Singtoroj[3], Wirichada Pongtavornpinyo[3], Jennifer M Short[3,4], Bina Maharjan[3], Vanaporn Wuthiekanun[3], David AB Dance[5], Prapit Teparrukkul[6], Niklas Lindegardh[3,4], Sharon J Peacock[3,4], Nicholas P Day[3,4], Wipada Chaowagul[6] and Nicholas J White[3,4]

[1] *Department of Clinical Tropical Medicine, Faculty of Tropical Medicine Mahidol University, Bangkok, Thailand;*
[2] *Department of Pharmaceutical Chemistry, Faculty of Pharmaceutical Sciences Khon Kaen University, Khon Kaen, Thailand;*
[3] *Faculty of Tropical Medicine, Mahidol University Bangkok, Thailand;*
[4] *Centre for Clinical Vaccinology and Tropical Medicine, Nuffield Department of Clinical Medicine University of Oxford, Churchill Hospital, Oxford OX3 7LJ, UK;*
[5] *Health Protection Agency (South West) Tamar Science Park, 1 Davy Road, Plymouth, Devon PL6 8BX, UK;*
[6] *Medical Department, Sappasithiprasong Hospital Ubon Ratchathani, Thailand*

Objectives: We conducted a prospective pharmacokinetic study of oral co-amoxiclav in patients with melioidosis to determine the optimal dosage and dosing interval in this potentially fatal infection.

Patients and methods: Serial plasma concentrations were measured after administration of two 1 g tablets of Augmentin® (1750 mg of amoxicillin and 250 mg of clavulanate) to 14 adult patients with melioidosis. Monte Carlo simulation was used to predict the concentration of each drug following multiple doses of co-amoxiclav at different dosages and dose intervals. The proportion of the dose-interval above MIC ($T > MIC$) was calculated from 10 000 simulated subject plasma concentration profiles together with chequerboard MIC data from 46 clinical isolates and four reference strains of *Burkholderia pseudomallei*.

Results: The median (range) observed maximum plasma concentrations of amoxicillin and clavulanate were 11.5 (3.3–40.2) mg/L and 5.1 (0.8–12.1) mg/L, respectively. The median (range) elimination half-lives were 94 (73–215) and 89 (57–140) min, respectively. Simulation indicated that co-amoxiclav 1750/250 mg given at 4, 6, 8 or 12 hourly dosing intervals would be associated with a $T > MIC$ of ≤50% in 0.7%, 2.8%, 8.6% and 33.2% of patients, respectively. Corresponding proportions for $T > MIC$ of ≥90% were 95.8%, 78.6%, 50.2% and 10.8%, respectively.

Conclusions: The dosing interval for co-amoxiclav (750/250 mg) in melioidosis should not be greater than 6 h. ∅

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IDENTIFICATION OF IN VIVO-EXPRESSED ANTIGENS OF *STAPHYLOCOCCUS AUREUS* AND THEIR USE IN VACCINATIONS FOR PROTECTION AGAINST NASAL CARRIAGE

Simon R Clarke,[1] Kirsten J Brummell,[1] Malcolm J Horsburgh,[1] Philip W McDowell,[1] Sharifah A Syed Mohamad,[1] Melanie R Stapleton,[1] Jorge Acevedo,[3] Robert C Read,[2] Nicholas PJ Day,[4] Sharon J Peacock,[4] James J Mond,[3] John F Kokai-Kun,[3] and Simon J Foster[1]

[1] *Department of Molecular Biology and Biotechnology and*
[2] *Division of Genomic Medicine, University of Sheffield, Sheffield, United Kingdom;*
[3] *Biosynexus, Gaithersburg, Maryland;*
[4] *Wellcome Trust-Mahidol University Oxford Tropical Medicine Research Programme, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand*

A spectrum of in vivo-expressed Staphylococcus aureus antigens was identified by probing bacteriophage expression libraries of S. aureus with serum samples from infected and uninfected individuals. Eleven recombinant antigenic proteins were produced, and specific antibody titers in a large collection of human serum samples were determined. Significantly increased concentrations of reactive immunoglobulin G (IgG) to 7 antigens were found in serum samples from ill individuals, compared with those in healthy individuals. Significantly higher concentrations of reactive IgG to 4 antigens, including iron. ∅

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EFFICACY OF ARTEMETHER-; UMEFANTRINE FOR THE TREATMENT OF UNCOMPLICATED FALCIPARUM MALARIA IN NORTHWEST CAMBODIA

Mey Bouth Denis[1,2], Reiko Tsuyuoka[2], Pharath Lim[3], Niklas Lindegardh[4,5], Poravuth Yi[1], Sophoan Narann Top[1], Duong Socheat[1], Thierry Fandeur[3], Anna Annerberg[4], Eva Maria Christophe[6] and Pascal Ringwald[7]

[1] *National Center for Parasitology, Entomology and Malaria Control, Phnom Penh, Cambodia;*
[2] *World Health Organization, Phnom Penh, Cambodia;*
[3] *Institut Pasteur du Cambodge, Phnom Penh, Cambodia;*
[4] *Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand;*
[5] *Centre for Clinical Vaccinology and Tropical Medicine, Churchill Hospital, Oxford, UK;*
[6] *World Health Organization, Regional Office for the Western Pacific, Manila, Phillippines;*
[7] *World Health Organization, Geneva, Switzerland*

Objective: To determine the efficacy of artemether-lumefantrine malaria treatment, as an alternative to artesunate + mefloquine, which is becoming ineffective in some areas of the Thai-Cambodian border.

Methods: Two studies were conducted to monitor the efficacy of artemether-lumefantrine in Sampov Lun referral hospital, Battambang Province, in 2002 and 2003, and one study was conducted to assess the efficacy of mefloquine + artesunate in 2003 for comparison. The studies were performed according to the WHO standardized protocol with a follow-up of 28 days. The therapeutic efficacy tests were complemented with *in vitro* tests and in 2003, with the measurement of lumefantrine plasma concentration at day 7 for the patients treated with artemether-lumefantrine.

Results: A total of 190 patients were included: 55 were treated with artemether-lumefantrine in 2002 (AL2002), 80 with artemether-lumefantrine and food supplementation in 2003 (AL2003) and 55 with artesunate + mefloquine in 2003 (AM2003). With the per-protocol analysis, the cure rate was 71.1% in study AL2002, 86.5% in study AL2003 and 92.4% in study AM2003. All the data were PCR corrected. The artemether-lumefantrine cure rate was unexpectedly low in 2002, but it increased with food supplementation in 2003. There was a significant difference ($P = 0.02$) in lumefantrine plasma concentrations between adequate clinical and parasitological responses and treatment failure cases. In vitro susceptibility to lumefantrine was reduced for isolates sampled from patients presenting with treatment failure, but the difference was not statistically different from isolates sampled from patients who were successfully treated.

Conclusion: Treatment failure cases of artemether-lumefantrine are most probably because of low levels of lumefantrine blood concentration. Further investigations are necessary to determine whether resistance of *Plasmodium falciparum* isolates to lumefantrine is present in the region. ∅

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USE OF REFRACTOMETRY AND COLORIMETRY AS FIELD METHODS TO RAPIDLY ASSESS ANTIMALARIAL DRUG QUALITY

Michael D Green[1], Henry Nettey[1], Ofelia Villalva Rojas[2], Chansapha Pamanivong[3], Lamphet Khounsaknalath[3], Miguel Grande Ortiz[2], Paul N Newton[4,5], Facundo M Fernández[6], Latsamy Vongsack[3] and Ot Manolin[3]

[1] *Division of Parasitic Diseases, US Centers for Disease Control and Prevention, Atlanta, GA, United States;*
[2] *Centro Nacional de Control de Calidad, Instituto Nacional de Salud, Lima, Peru*
[3] *Food and Drug Quality Control Center, Ministry of Health, Vientiane, Lao People's Democratic Republic*
[4] *Wellcome Trust-Mahosot Hospital-Oxford Tropical Medicine Research Collaboration, Mahosot Hospital, Vientiane, Lao People's Democratic Republic*
[5] *Centre for Clinical Vaccinology and Tropical Medicine, Churchill Hospital, University of Oxford, UK*
[6] *School of Chemistry and Biochemistry, Georgia Institute of Technology, GA 30332, Atlanta, United States*

The proliferation of counterfeit and poor-quality drugs is a major public health problem; especially in developing countries lacking adequate resources to effectively monitor their prevalence. Simple and affordable field methods provide a practical means of rapidly monitoring drug quality in circumstances where more advanced techniques are not available. Therefore, we have evaluated refractometry, colorimetry and a technique combining both processes as simple and accurate field assays to rapidly test the quality of the commonly available antimalarial drugs; artesunate, chloroquine, quinine, and sulfadoxine. Method bias, sensitivity, specificity and accuracy relative to high-performance liquid chromatographic (HPLC) analysis of drugs collected in the Lao PDR were assessed for each technique. The HPLC method for each drug was evaluated in terms of assay variability and accuracy. The accuracy of the combined method ranged from 0.96 to 1.00 for artesunate tablets, chloroquine injectables, quinine capsules, and sulfadoxine tablets while the accuracy was 0.78 for enterically coated chloroquine tablets. These techniques provide a generally accurate, yet simple and affordable means to assess drug quality in resource-poor settings.

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CHARACTERIZATION OF COUNTERFEIT ARTESUNATE ANTIMALARIAL TABLETS FROM SOUTHEAST ASIA

Krystyn Alter Hall[1], Paul N Newton[2,3], Michael D Green[4], Marleen De Veij[5], Peter Vandenabeele [5], David Pizzanelli[6], Mayfong Mayxay[2], Arjen Dondorp[3,4], and Facundo M Fernandez[1]

[1] *School of Chemistry and Biochemistry, Georgia Institute of Technology, Atlanta, Georgia;*
[2] *Wellcome Trust-Mahosot Hospital-Oxford Tropical Medicine Research Collaboration, Microbiology Laboratory, Mahosot Hospital, Vientiane, Lao People's Democratic Republic;*
[3] *Centre for Clinical Vaccinology and Tropical Medicine, Churchill Hospital, Oxford University, Oxford, United Kingdom;*
[4] *Division of Parasitic Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia;*
[5] *Laboratory of Analytical Chemistry, Ghent University, Ghent, Belgium; 6Light Impressions International, Leatherhead, Surrey, United Kingdom;*
[6] *Wellcome Trust-Mahidol University-Oxford Tropical Medicine Research Programme, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand*

In southeast Asia, the widespread high prevalence of counterfeits tablets of the vital antimalarial artesunate is of great public health concern. To assess the seriousness of this problem, we quantified the amount of active ingredient present in artesunate tablets by liquid chromatography coupled to mass spectrometry. This method, in conjunction with analysis of the packaging, classified tablets as genuine, substandard, or fake and validated results of the colorimetric Fast Red TR test. Eight (35%) of 23 fake artesunate samples contained the wrong active ingredients, which were identified as different erythromycins and paracetamol. Raman spectroscopy identified calcium carbonate as an excipient in 9 (39%) of 23 fake samples. Multivariate unsupervised pattern

recognition results indicated two major clusters of artesunate counterfeits, those with counterfeit foil stickers and containing calcium carbonate, erythromycin, and paracetamol, and those with counterfeit holograms and containing starch but without evidence of erythromycin or paracetamol. ∅

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PLASMODIUM VIVAX: ISOTOPIC, PICOGREEN, AND MICROSCOPIC ASSAYS FOR MEASURING CHLOROQUINE SENSITIVITY IN FRESH AND CRYOPRESERVED ISOLATED

Varakorn Kosaisavee[1], Rossarin Suwanarusk[2], François Nosten[1,3], Dennis E Kyle[4], Marion Barrends[1,3] James Jones[5], Ric Price[2], Bruce Russell[2,5] and Usa Lek-Uthai[1]

[1] *Faculty of Public Health, Mahidol University, Bangkok, Thailand;*
[2] *International Health Program, Infectious Diseases Division, Menzies School of Health Research and Charles Darwin University, Darwin, Australia;*
[3] *Shoklo Malaria Research Unit, Mae Sod, Thailand;*
[4] *Division of Experimental Therapeutics, Walter Reed Institute of Army Research, Silver Spring, MD, USA;*
[5] *Department of Entomology, USAMC, Armed Forces Research Institute of Medical Sciences, Bangkok, Thailand*

In vitro susceptibility tests provide information on the intrinsic response of *Plasmodium vivax* to antimalarials, free from confounding factors such as host immunity or relapse. This study examined the utility of radioisotope and PicoGreen assays as alternatives to the traditional microscopic examination for assessing response of *P. vivax* to antimalarial drugs. There was no significant difference in the mean chloroquine IC_{50} of *P. vivax* (n = 40) as determined by the microscopic (33.4 ng/ml), isotopic (33.6 ng/ml), and PicoGreen (39.1 ng/ml) assays, respectively (F = 0.239, df = 2, 51, and p = 0.788). However measurement of IC_{50}s by the microscopic method was slightly more successful in producing valid assays (57%), compared to the isotopic (32.5%) and PicoGreen (45.5%) methods. In a paired comparison of 20 fresh and cryopreserved isolates as examined by the microscopic method, there were no significant differences between the mean IC_{50} responses (T = 1.58, df = 15, and p = 0.34). Detailed methodologies for the short time culture of field and cryopreserved *P. vivax* are described. Although the microscopic in vitro assay provides a useful method for characterizing the drug susceptibility phenotype of *P. vivax* isolates, its utility is limited by a laborious methodology and need for highly skilled microscopists. Future efforts should focus on further development of high throughput assays such as the PicoGreen assay as described in this study. ∅

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DECREASED PROTEIN C, PROTEINS, AND ANTITHROMBIN LEVELS ARE PREDICTIVE OF POOR OUTCOME IN GRAM-NEGATIVE SEPSIS CAUSE BY *BURKHOLDERIA PSEUDOMALLEI*

Steven P LaRosa[1], Steven M Opal[2], Barbara Utterback[3], Sau Chi Betty Yan[3], Jeffrey Helterbrand[4], Andrew JH Simpson[5], Wipada Chaowagul[6], Nicholas J White[7], and Charles J Fisher Jr[8]

[1] *Division of Infectious Disease, Rhode Island Hospital, Gerry House 113, 593 Eddy Street, Providence, Rhode Island 02903, USA;*
[2] *Infectious Diseases and Microbiologic Divisions of Brown University School of Medicine, Providence, Rhode Island, USA;*
[3] *Lilly Research Laboratories, Indianapolis, Indiana, USA;*
[4] *Genentech, Inc., South San Francisco, California, USA;*
[5] *Microbiology, Dstl Porton Down, Salisbury, Wiltshire, UK;*
[6] *Department of Medicine, Sappasitprasong Hospital, Ubon Ratchathani, Thailand;*
[7] *Nuffield Department of Clinical Medicine, John Radcliffe Hospital, University of Oxford, Oxford, UK;*
[8] *Cardiome Pharma Corp., Vancouver, British Columbia, Canada*

Background: Acute septicemic melioidosis is associated with systemic release of endotoxin and the proinflammatory cytokines tumor necrosis factor (TNF)-alpha, interleukin-1, and interleukin-6. Excessive release of these cytokines may lead to endothelial injury, depletion of naturally occurring endothelial modulators, microvascular thrombosis, organ failure, and death.

Method: Plasma samples drawn at baseline and after initial antimicrobial therapy in 30 patients with suspected acute severe melioidosis were assayed for D-dimer levels, protein C and protein S antigen levels, and antithrombin functional activities.

Results: Both baseline and continued deficiencies of protein C, protein S, and antithrombin were statistically associated with a poor outcome by logistic regression. Baseline D-dimer levels were significantly higher in fatal cases than survivors and correlated inversely with protein C and antithrombin, suggesting both increased fibrin deposition and fibrinolysis.

Conclusion: The inflammatory response to systemic *Burkholderia pseudomallei* infection leads to depletion of the natural endothelial modulators protein C, protein S, and antithrombin. Both baseline and continued deficiency of these endothelial modulators is predictive of poor outcome in melioidosis. ∅

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RISK FACTORS FOR RECURRENT MELIOIDOSIS IN NORTHEWAST THAILAND

Direk Limmathurotsakul,[1] Wipada Chaowagu[1,2] Wirongrong Chierakul,[1] Kasia Stepniewska,[1] Bina Maharjan,[1] Vanaporn Wuthiekanun,[1] Nicholas J White,[1,3] Nicholas PJ Day,[1,3] and Sharon J Peacock[1,3]

[1] *Faculty of Tropical Medicine, Mahidol University, Bangkok, and*
[2] *Medical Department, Sappasithiprasong Hospital, Ubon Ratchathani, Thailand; and*
[3] *Center for Clinical Vaccinology and Tropical Medicine, Nuffield Department of Clinical Medicine, University of Oxford, Churchill Hospital, Oxford, United Kingdom*

Background: Recurrent melioidosis occurs in ~6% of patients in the first year following the initial presentation. A recent study revealed that 25% of patients with recurrence had reinfection rather than a relapse resulting from a failure to cure. The aim of this study was to reevaluate these 2 patient groups to define their individual risk factors.

Methods: All adult patients who presented to Sappasithiprasong Hospital (Ubon Ratchathani, in northeast Thailand) with culture-confirmed melioidosis during the period 1986-2004 and who survived to receive oral antimicrobial therapy were observed until July 2005. Clinical factors and antimicrobial treatment of patients with recurrent disease due to relapse or reinfection, as confirmed by bacterial genotyping, were compared using a time-varying Cox proportional hazard model.

Results: Of 889 patients who survived and underwent follow-up, 86 patients (9.7%) presented with relapse, and 30 patients (3.4%) became reinfected. There was no difference in acute outcome between the relapse and reinfection groups. No risk factors for reinfection were identified. Multivariate analyses identified choice and duration of oral antimicrobial therapy as the most important determinants of relapse, followed by positive blood culture result (hazard ratio [HR], 1.86; 95% confidence interval [CI], 1.18-2.92) and multifocal distribution (HR, 1.95; 95% CI, 1.03-3.67). Patients treated with an appropriate oral antibiotic regimen for 12-16 weeks had a 90% decreased risk of relapse (HR, 0.10; 95% CI, 0.02-0.44), compared with patients who were treated for ≤8 weeks. Trimethoprim-sulfamethoxazole plus doxycycline was an effective oral therapy.

Conclusions: This study highlights clinical factors associated with an increased likelihood of relapse and provides evidence for optimal oral antimicrobial therapy. ∅

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IDENTIFICATION OF AN ISOMER IMPURITY IN PIPERAQUINE DRUG SUBSTANCE

N Lindegårdh[1,2], F Giorgi[3], B Galletti[3], M Di Mattia[3], M Quaglia[3], D Carnevale[3], NJ White[1,2], A Mazzanti[4] and NPJ Day[1,2]

[1] Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand
[2] Nuffield Department of Clinical Medicine, Centre for Tropical Medicine, University of Oxford, Oxford, UK
[3] Sigma-Tau, S.p.A. Analytical Chemistry Dept. R&D, Pomezia, Rome, Italy
[4] Department of Organic Chemistry "A Mangini", University of Bologna, Viale Risorgimento 4, 40136 Bologna, Italy

A significant contaminant of the antimalarial drug piperaquine (1,3-bis-[4-(7-chloroquinolyl-4)-piperazinyl-1]propane) has been identified using liquid chromatography–mass spectrometry (LC–MS) and 2D NMR spectroscopy (^{1}H-^{1}H COSY, ^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC). The impurity was identified as the positional isomer 1-[(5-chloroquinolin-4)-piperazinyl]-3-[(7-chloroquinolin-4)-piperazinyl]propane. The impurity is formed because of contamination of batches of 4,7-dichloroquinoline (a precursor in the synthesis of piperaquine) with 4,5-dichloroquinoline. The amount of impurity (peak area impurity/peak area piperaquine using LC-UV at 347 nm) in old batches of piperaquine and in Artekin (the combination of dihydroartemisinin–piperaquine) ranged from 1.5 to 5%. ∅

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RAPID DEGRADATION OF OSLETAMIVIR PHOSPHATE IN CLINICAL SAMPLES BY PLASMA ESTERATES

Niklas Lindegardh,[1,2]* Geraint R Davies,[1,3] Tran Tinh Hien,[4] Jeremy Farrar,[2,4] Pratap Singhasivanon,[1] Nicholas P J Day,[1,2] and Nicholas J White[1,2]

[1] Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand,
[2] Nuffield Department of Clinical Medicine, Centre for Tropical Medicine, University of Oxford, Oxford, United Kingdom,
[3] Wellcome Trust Centre for Clinical Tropical Medicine, University of Liverpool, Liverpool, United Kingdom,
[4] Hospital for Tropical Diseases, Ho Chi Minh City, Vietnam

The anti-influenza drug oseltamivir is an ester prodrug activated by hepatic carboxylesterases. Plasma esterases also convert up to 31.8% of the parent compound to the active metabolite after 4 h ex vivo, with wide interindividual variation. This source of error is removed by adding the esterase inhibitor dichlorvos to blood collection tubes. ∅

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MICROARRAYS REVEAL THAT EACH OF THE TEN DOMINANT LINEAGES OF *STAPHYLOCOCCUS AUREUS* HAS A UNIQUE COMBINATION OF SURFACE-ASSOCIATED AND REGULATORY GENES

Jodi A Lindsay,[1] Catrin E Moore,[2] Nicholas P Day,[3] Sharon J Peacock,[3] Adam A Witney,[4] Richard A Stabler,[4] Sarah E Husain,[4] Philip D Butcher,[4] and Jason Hinds[4]

[1] Centre for Infection, Division of Cellular and Molecular Medicine, St George's, University of London, Cranmer Terrace, London SW17 0RE, United Kingdom;
[2] Department of Paediatrics, University of Oxford, The John Radcliffe Hospital, Oxford, OX3 9DU, United Kingdom;
3 Faculty of Tropical Medicine, Mahidol University, 420/6 Rajvithi Road, Bangkok 10400, Thailand;
[4] Bacterial Microarray Group, Division of Cellular and Molecular Medicine, St George's, University of London, Cranmer Terrace, London SW17 0RE, United Kingdom

Staphylococcus aureus is the most common cause of hospital-acquired infection. In healthy hosts outside of the health care setting, *S. aureus* is a frequent colonizer of the human nose but rarely causes severe invasive infection such as bacteremia, endocarditis, or osteomyelitis. To identify genes associated with community-acquired invasive isolates, regions of genomic variability, and the *S. aureus* population structure, we compared 61 community-acquired invasive isolates of *S. aureus* and 100 nasal carriage isolates from healthy donors using a microarray spotted with PCR products representing every gene from the seven *S. aureus* sequencing projects. The core genes common to all strains were identified, and 10 dominant lineages of *S. aureus* were clearly discriminated. Each lineage carried a unique combination of hundreds of "core variable" (CV) genes scattered throughout the chromosome, suggesting a common ancestor but early evolutionary divergence. Many CV genes are regulators of virulence genes or known or predicted to be expressed on the bacterial surface and to interact with the host during nasal

colonization and infection. Within each lineage, isolates showed substantial variation in the carriage of mobile genetic elements and their associated virulence and resistance genes, indicating frequent horizontal transfer. However, we were unable to identify any association between lineage or gene and invasive isolates. We suggest that the *S. aureus* gene combinations necessary for invasive disease may also be necessary for nasal colonization and that community-acquired invasive disease is strongly dependent on host factors. ∅

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AN OPEN, RANDOMIZED COMPARISON OF ARTESUNATE PLUS MEFLOQUINE VS. DIHYDROARTEMISININ-PIPERAQUINE FOR THE TREATMENT OF UNCOMPLICATED *PLASMODIUM FALCIPARUM* MALARIA IN THE LAO PEOPLE'S DEMOCRATIC REPUBLIC (LAOS)

M Mayxay[1,2], V Thongpraseuth[3], M Khanthavong[3], N Lindegårdh[4,5], M Barends[5,6], S Keola[7], T Pongvongsa[8], S Phompida[3], R Phetsouvanh[3], K Stepniewska[4,5], NJ White[1,4,5,6] and PN Newton[1,4]

[1] *Wellcome Trust - Mahosot Hospital - Oxford Tropical Medicine Research Collaboration, Mahosot Hospital, Vientiane, Lao PDR;*
[2] *Division of Postgraduate Studies and Research, Faculty of Medical Science, National University of Laos, Vientiane, Lao PDR;*
[3] *Centre of Malariology, Parasitology and Entomology, Vientiane, Lao PDR;*
[4] *Centre for Clinical Vaccinology and Tropical Medicine, Churchill Hospital, Oxford, UK;*
[5] *Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand;*
[6] *Shoklo Malaria Research Unit, Mae Sot, Tak Province, Thailand;*
[7] *Phalanxay District Clinic, Savannakhet Province, Lao PDR;*
[8] *Savannakhet Provincial Malaria Station, Savannakhet Province, Lao PDR*

Objective: To determine the efficacy and safety of oral dihydroartemisinin-piperaquine (DP, Artekin™) in the treatment of uncomplicated *Plasmodium falciparum* malaria in southern Laos.

Methods: An open, randomized clinical trial of oral artesunate-mefloquine (AM) vs. DP in 220 patients with acute uncomplicated falciparum malaria in Savannakhet Province, Laos.

Results: The 42-day cure rates (95% CI), as determined by survival analysis and adjusted for reinfection, were excellent and similar for the two groups [99 (94-100)% and 100 (100-100)% for AM and DP, respectively]. The median (range) fever and parasite clearance times for the AM and DP groups were also similar [20 (4-63) h and 2 (1-4) days vs. 20 (7-57) and 2 (1-4) days, logrank *P* = 0.4 and 0.17, respectively]. There were more patients with at least one potential side effect following treatment in the AM group when compared with the DP group [64/110 (58%) vs. 48/110 (44%), respectively, P = 0.031].

Conclusion: Dihydroartemisinin-piperaquine did not have superior efficacy to AM for the treatment of uncomplicated *falciparum* malaria in Laos but was associated with fewer adverse effects ∅

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MANSLAUGHTER BY FAKE ARTESUNATE IN ASIA—WILL AFRICA BE NEXT?

Paul N Newton[1,2], Rose McGready[1,3,4], Facundo Fernandez[5], Michael D Green[6], Manuela Sunjio[7], Carinne Bruneton[8], Souly Phanouvong[9], Pascal Millet[7], Christopher JM Whitty[10], Ambrose O Talisuna[11], Stephane Proux[1,3,4] Eva Maria Christophel[12], Grace Malenga[13], Pratap Singhasivanon[4], Kalifa Bojang[14], Harparkash Kaur[10], Kevin Palmer[12], Nicholas PJ Day[1,2,4], Brian M Greenwood[10], François Nosten[1,3,4], Nicholas J White[1,2,4]

[1] *Centre for Clinical Vaccinology and Tropical Medicine, University of Oxford, Churchill Hospital, Oxford, United Kingdom;*
[2] *Wellcome Trust-Mahosot Hospital-Oxford Tropical Medicine Research Collaboration, MahosotHospital, Vientiane, Lao PDR;*
[3] *Shoklo Malaria Research Unit, Mae Sot, Tak Province, Thailand;*

[4] Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand;
[5] School of Chemistry and Biochemistry, Georgia Institute of Technology, Atlanta, Georgia, United States of America;
[6] Division of Parasitic Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta,Georgia, United States of America;
[7] EA3677 Bases Thérapeutiques des Inflammations et des Infections, Université Victor Segalen,Bordeaux, France;
[8] Réseau Médicaments et Développement, Paris, France;
[9] Drug Quality and Information Program, Global Assistance Initiatives, United States Pharmacopeia,Rockville, Maryland, United States of America;
[10] Department of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, University of London, London, United Kingdom;
[11] East African Network for Monitoring Antimalarial Treatment, and Ministry of Health, Uganda;
[12] Western Pacific Regional Office of the World Health Organization, Manila, Philippines;
[13] Malaria Alert Centre, Bantyre, Malawi;
[14] MRC Laboratories, Fajara, Banjul, The Gambia

Falciparum malaria kills, and it particularly kills the rural poor. Artemisinin derivatives, such as artesunate, are a vital component of *Plasmodium falciparum* malaria treatment and control in the face of globally increasing antimalarial drug resistance. Since 1998 a worsening epidemic of sophisticated counterfeit "artesunate" tablets (containing no artesunate) has plagued mainland Southeast Asia (see *Figure S1*). In some countries, most of the available artesunate is fake.

Artemisinin derivatives are remarkably rapid in their antimalarial effects, and they are very well tolerated. So where these medicines are available, they are sought after. But as they are relatively expensive, a demand is created for cheaper versions amongst the poorest and most vulnerable people, upon whom the counterfeiters have preyed–with fatal results. ∅

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COUNTERFEIT ANTI-INFECTIVE DRUGS

Paul N Newton[1,2], Michael D Green[3], Facundo M Fernández[4], Nicholas PJ Day[1,2,3] and Nicholas J White[1,2,3]

[1] Wellcome Trust-Mahosot Hospital-Oxford Tropical Medicine ResearchCollaboration, MahosotHospital, Vientiane, Lao PDR
[2] Centre for Clinical Vaccinology and Tropical Medicine, Churchill Hospital, University of Oxford, UK
[3] Division of Parasitic Diseases, CDC, Atlanta, GA, USA
[4] School of Chemistry and Biochemistry. Georgia Institute of Technology, Atlanta
[5] Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

The production of counterfeit or substandard anti-infective drugs is a widespread and under-recognised problem that contributes to morbidity, mortality, and drug resistance, and leads to spurious reporting of resistance and toxicity and loss of confidence in health-care systems. Counterfeit drugs particularly affect the most disadvantaged people in poor countries. Although advances in forensic chemical analysis and simple field tests will enhance drug quality monitoring, improved access to inexpensive genuine medicines, support of drug regulatory authorities, more open reporting, vigorous law enforcement, and more international cooperation with determined political leadership will be essential to counter this threat. ∅

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THE PHARMACOKINETICS OF INTRAVENOUS ARTESUNATE IN ADULTS WITH SEVERE FALCIPARUM MALARIA

Paul N Newton[1,2], Karen I Barnes[3], Peter J Smith[3], Alicia C Evans[3], Wirongrong Chierakul[1], Ronatrai Ruangveerayuth[4] and Nicholas J White[1,2]

[1] Faculty of Tropical Medicine, Mahidol University, 420/6 Rajvithi Rd., Bangkok, 10400, Thailand;
[2] Centre for Clinical Vaccinology and Tropical Medicine, University of Oxford, Churchill Hospital, Oxford, UK;
[3] Division of Clinical Pharmacology, University of Cape Town, Cape Town, South Africa;
[4] Mae Sot Hospital, Mae Sot, Tak, Thailand

Objective: Intravenous artesunate is commonly used in the emergency treatment of patients with severe falciparum malaria in Asia. The choice of doses used has been empirical. To inform dosage recommendations we assessed the pharmacokinetics of intravenous artesunate after the first dose.

Methods: As part of a clinical trial of artesunate in adults with severe falciparum malaria in western Thailand, we assayed plasma concentrations of artesunate and the principal biologically active metabolite dihydroartemisinin (DHA) in 17 patients given an initial dose of 2.4 mg/kg body weight of intravenous artesunate. Drug levels were measured using high performance liquid chromatography with mass spectroscopy-electrospray ionisation detection.

Results: Median (range) observed DHA Cmax was 2128 (513-5789) nmol/L, elimination half-life was 0.34 (0.14-0.87) h, and the time to the last detectable DHA was 2 h.

Conclusion: The large inter-individual variability (10 fold) in DHA Cmax and AUC in patients with potentially lethal, severe malaria, suggests that 2.4 mg/kg should be the minimum daily dose in severe malaria.

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CAUSES OF COMMUNITY-ACQUIRED BACTEREMIA AND PATTERNS OF ANTIMICROBIAL RESISTANCE IN VIENTIANE, LAOS

Rattanaphone Phetsouvanh, Simmaly Phongmany, Douangdao Soukaloun, Bouachanh Rasachak, Vimone Soukhaseum, Seun Soukhaseum, Kamthavi Frichithavong, Sengmanivong Khounnorath, Bounthom Pengdee, Khampong Phiasakha, Vang Chu, Khonesavanh Luangxay, Sayadeth Rattanavong, Konkam Sisouk, Valy Keolouangkot, Mayfong Mayxay, Andrew Ramsay, Stuart D. Blacksell, Jim Cambell, Bertrand Martinez-Aussel, Mayboun Heuanvongsy, Bounthapaany Bounxouei, Chanpheng Thammavong, Bounkong Syhavong, Michel Strobel, Sharon J. Peacock, Nicholas J White, and Paul N Newton*

Wellcome Trust- Mahosot Hospital-Oxford Tropical Medicine Research Collaboration, Mahosot Hospital, Vientiane, Lao PDR; Francophone Institute of Tropical Medicine, Vientiane, Lao PDR; Faculty of Medicine, National University of Laos, Vientiane, Lao PDR; Centre for Clinical Vaccinology and Tropical Medicine, University of Oxford, Churchill Hospital, Oxford, United Kingdom; Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; Oxford University Research Unit, Hospital for Tropical Diseases, Ho Chi Minh City, Viet Nam

There is no published information on the causes of bacteremia in the Lao PDR (Laos). Between 2000 and 2004, 4512 blood culture pairs were taken from patients admitted to Mahosot Hospital, Vientiane, Laos, with suspected community-acquired bacteremia; 483 (10.7%) cultures grew a clinically significant community-acquired organism, most commonly *Salmonella enterica* serovar typhi (50.9%), *Staphylococcus aureus* (19.0%), and *Escherichia coli* (12.4%). *S. aureus* bacteremia was common among infants (69.2%), while children 1-5 years had a high frequency of typhoid (44%). Multi-drug-resistant *S. Typhi* was rare (6%). On multiple logistic regression analysis, typhoid was associated with younger age, longer illness, diarrhea, higher admission temperature, and lower peripheral white blood cell count than non-typhoidal bacteremia. Empirical parenteral ampicillin and gentamicin would have some activity against ~ 88% of clinically significant isolates at a cost of US $1.4/day, an important exception being *B. pseudomallei*. Bacteremic infants in this setting require an anti-staphylococcal antibiotic. ∅

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A TRICHINELLOSIS OUTBREAK IN BORIKHAMXAY PROVINCE, LAO PDR

Somphou Sayasone[1], Peter Odermatt[1], Phengta Vongphrachanh[1,2], Valy Keoluangkot[1,3], Jean Dupouy-Camet[4], Paul N Newton[5,6] and Michel Strobel[1]

[1] *Institut de la Francophonie pour la Médecine Tropicale, Vientiane, Lao PDR;*
[2] *National Center for Epidemiology and Laboratory, Ministry of Health, Vientiane, Lao PDR;*
[3] *Mahosot Hospital, Vientiane, Lao PDR;*
[4] *Laboratoire de Parasitologie-Mycologie, Centre National de Référence des Trichinella, Hôpital Cochin, Paris, France;*
[5] *Wellcome Trust-Mahosot Hospital-Oxford Tropical Medicine Research Collaboration, Microbiology Laboratory, Mahosot Hospital, Vientiane, Lao PDR;*
[6] *Centre for Clinical Vaccinology and Tropical Medicine, Churchill Hospital, University of Oxford, Oxford, UK*

Trichinellosis is documented in Southeast Asia, particularly in Thailand and China. Data from Lao PDR are lacking. An outbreak investigation was conducted in Borikhamxay Province after three patients with suspected trichinellosis consulted the Mahosot Hospital, Vientiane. In total, 22 trichinellosis cases were identified; 21 cases could be confirmed by Western blot. High fever (100%), muscle pain (91%), upper eyelid oedema (86%) and diarrhoea (59%) were observed. Among the 22 patients, 86% had consumed pork meat from the same source. This is the first report of an outbreak investigation in Lao PDR since 1975. It shows that the incidence of trichinellosis is much higher than currently thought. Ø

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A HOSPITAL BASED STUDY OF BLOODSTREAM INFECTIONS IN FEBRILE PATIENTS IN DHULIKHEL HOSPITAL KATHMANDU UNIVERSITY TEACHING HOSPITAL, NEPAL

Sharma NP, Peacock SJ, Phumratanaprapin W, Day N, White N, Pukrittayakamee S

Department of Medicine, Dhulikhel Hospital Kathmandu University Teaching Hospital, Kathmandu, Nepal

The etiology of bloodstream infections in febrile patients remain poorly characterized in Nepal. A retrospective study of febrile patients presenting to Dhulikhel Hospital Kathmandu University Teaching Hospital from July 2002 to June 2004 was performed to evaluate the etiology of bloodstream infections and the drug sensitivity patterns of cultured organisms. The medical and laboratory records of all febrile patients with an axillary temperature > or = 38 degrees C who had a blood culture taken (n = 1,774) were retrieved and analyzed. Of these, 122 (6.9%) patients had positive blood cultures, of which 40.1% were age 11 to 20 years. The male to female ratio was 1.7:1. Antibiotics had been taken prior to hospital presentation by 39 (32%) patients. Salmonella enterica serovar Typhi and serovar Paratyphi A were isolated in 50 (41.0%) and 13 (10.7%) cases, respectively. All S. Typhi and S. Paratyphi isolates were susceptible to ceftriaxone, while susceptibility to ciprofloxacin and chloramphenicol was recorded in 94.8% and 94.5% of cases, respectively. Cephalexin and amoxicillin had the lowest rates of susceptibility (64.2% and 54.1%, respectively). Salmonella spp were usually sensitive to chloramphenicol. These findings provide clinicians in this region of Nepal with a better understanding of the spectrum of pathogens causing bloodstream infections and will help guide empiric antibiotic choice. Ø

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A NEW APPROACH TO EVALUATE REGRESSION MODELS DURING VALIDATION OF BIOANALYTIC ASSAYS

T Singtoroj[1], J Tarning[2], A Annerberg[1], M Ashton[2], Y Bergqvist[3], NJ White[1,4], N Lindegardh[1,4] and NPJ Day[1,4]

[1] *Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand*
[2] *Department of Pharmacology, Sahlgrenska Academy at Göteborg University, Sweden*
[3] *Dalarna University College, Borlänge, Sweden*
[4] *Nuffield Department of Clinical Medicine, Centre for Tropical Medicine, University of Oxford, Oxford, UK*

The quality of bioanalytical data is highly dependent on using an appropriate regression model for calibration curves. Non-weighted linear regression has traditionally been used but is not necessarily the optimal model. Bioanalytical assays generally benefit from using either data transformation and/or weighting since variance normally increases with concentration. A data set with calibrators ranging from 9 to 10,000 ng/mL was used to compare a new approach with the traditional approach for selecting an optimal regression model. The new approach used a combination of relative residuals at each calibration level together with precision and accuracy of independent quality control samples over 4 days to select and justify the best regression model. The results showed that log-log transformation without weighting was the simplest model to fit the calibration data and ensure good predictability for this data set. Ø

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EFFECACY AND EFFECTIVENESS OF DIHYDROARTEMINISININ-PIPERAQUINE VERSUS ARTESUNATE-MEFLOQUINE IN FALCIPARUM MALARIA: AN OPEN-LABEL RANDOMISED COMPARISON

Frank Smithuis[1], Moe Kyaw Kyaw[1], Ohn Phe[1], Khin Zarli Aye[1], Lhin Htet[1], Marion Barends[2,3], Niklas Lindegardh[2,4], Thida Singtoroj[3], Elizabeth Ashley[2,3,4], Saw Lwin[5], Kasia Stepniewska[2,3] and Nicholas J White[3,4]

[1] *Médecins Sans Frontières (Holland), Yangon, Myanmar;*
[2] *Shoklo Malaria Research Unit, Mae Sot, Thailand;*
[3] *Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand;*
[4] *Centre for Clinical Vaccinology and Tropical Medicine, Churchill Hospital, Oxford, UK;*
[5] *Vector Borne Disease Control, Department of Health, Myanmar*

Background: Artemisinin-based combinations are judged the best treatments for multidrug-resistant *Plasmodium falciparum* malaria. Artesunate-mefloquine is widely recommended in southeast Asia, but its high cost and tolerability profile remain obstacles to widespread deployment. To assess whether dihydroartemisinin-piperaquine is a suitable alternative to artesunate-mefloquine, we compared the safety, tolerability, efficacy, and effectiveness of the two regimens for the treatment of uncomplicated falciparum in western Myanmar (Burma).

Methods: We did an open randomised comparison of 3-day regimens of artesunate-mefloquine (12/25 mg/kg) versus dihydroartemisinin-piperaquine (6·3/50 mg/kg) for the treatment of children aged 1 year or older and in adults with uncomplicated falciparum malaria in Rakhine State, western Myanmar. Within each group, patients were randomly assigned supervised or non-supervised treatment. The primary endpoint was the PCR-confirmed parasitological failure rate by day 42. Failure rates at day 42 were estimated by Kaplan-Meier survival analysis. This study is registered as an International Standard Randomised Controlled Trial, number ISRCTN27914471.

Findings: Of 652 patients enrolled, 327 were assigned dihydroartemisinin-piperaquine (156 supervised and 171 not supervised), and 325 artesunate-mefloquine (162 and 163, respectively). 16 patients were lost to follow-up, and one patient died 22 days after receiving dihydroartemisinin-piperaquine. Recrudescent parasitaemias were confirmed in only two patients; the day 42 failure rate was 0·6% (95% CI 0·2–2·5) for dihydroartemisinin-piperaquine and 0 (0–1·2) for artesunate-mefloquine. Whole-blood piperaquine concentrations at day 7 were similar for patients with observed and non-observed dihydroartemisinin-piperaquine treatment. Gametocytaemia developed more frequently in patients who had received dihydroartemisinin-piperaquine than in those on artesunate-mefloquine: day 7, 18 (10%) of 188 versus five (2%) of 218; relative risk 4·2 (1·6–11·0) p=0·011.

Interpretation: Dihydroartemisinin-piperaquine is a highly efficacious and inexpensive treatment of multidrug-resistant falciparum malaria and is well tolerated by all age groups. The effectiveness of the unsupervised treatment, as in the usual context of use, equalled its supervised efficacy, indicating good adherence without supervision. Dihydroartemisinin-piperaquine is a good alternative to artesunate-mefloquine. ∅

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SOME CONSIDERATIONS IN THE DESIGN AND INTERPRETATION OF ANTIMALARIAL DRUG TRIALS IN UNCOMPLICATED FALCIPARUM MALARIA

Kasia Stepniewska[1,2] and Nicholas J White[1,2]

[1] *Mahidol-Oxford Tropical Medicine Research Unit, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand;*
[2] *Center for Clinical Vaccinology and Tropical Medicine, Nuffield Department of Clinical Medicine, University of Oxford, Oxford, United Kingdom*

Background: Treatments for uncomplicated falciparum malaria should have high cure rates. The World Health Organization has recently set a target cure rate of 95% assessed at 28 days. The use of more effective drugs, with longer periods of patient follow-up, and parasite genotyping to distinguish recrudescence from reinfection raise issues related to the design

and interpretation of antimalarial treatment trials in uncomplicated falciparum malaria which are discussed here.

Methods: The importance of adequate follow-up is presented and the advantages and disadvantages of non-inferiority trials are discussed. The different methods of interpreting trial results are described, and the difficulties created by loss to follow-up and missing or indeterminate genotyping results are reviewed.

Conclusions: To characterize cure rates adequately assessment of antimalarial drug efficacy in uncomplicated malaria requires a minimum of 28 days and as much as 63 days follow-up after starting treatment. The longer the duration of follow-up in community-based assessments, the greater is the risk that this will be incomplete, and in endemic areas, the greater is the probability of reinfection. Recrudescence can be distinguished from reinfection using PCR genotyping but there are commonly missing or indeterminate results. There is no consensus on how these data should be analysed, and so a variety of approaches have been employed. It is argued that the correct approach to analysing antimalarial drug efficacy assessments is survival analysis, and patients with missing or indeterminate PCR results should either be censored from the analysis, or if there are sufficient data, results should be adjusted based on the identified ratio of new infections to recrudescences at the time of recurrent parasitaemia. Where the estimated cure rates with currently recommended treatments exceed 95%, individual comparisons with new regimens should generally be designed as non-inferiority trials with sample sizes sufficient to determine adequate precision of cure rate estimates (such that the lower 95% confidence interval bound exceeds 90%). Ø

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RELATION OF DDT RESIDUES TO PLASMA RETINOL, ALPHA-TOCOPHEROL, AND BETA-CAROTENE DURING PREGNANCY AND MALARIA INFECTION: A CASE-CONTROL STUDY IN KAREN WOMEN IN NORTHERN THAILAND

W Stuetz[1,3], R McGready[2,4,5], Thein Cho[2], T Prapamontol[3], HK Biesalski[1], K Stepniewska[4], and F Nosten[2,5]

[1] *Institute of Biological Chemistry and Nutrition, University of Hohenheim, 70599 Stuttgart, Germany*
[2] *Shoklo Malaria Research Unit, PO Box 46, 63110 Mae Sot, Thailand*
[3] *Research Institute for Health Sciences, Chiang Mai University, 50200 Chiang Mai, Thailand*
[4] *Faculty of Tropical Medicine, Mahidol University, 10400 Bangkok, Thailand*
[5] *Centre for Vaccinology and Tropical Medicine, Nuffield Department of Clinical Medicine, John Radcliffe Hospital, Headington, Oxford, United Kingdom*

Populations living in endemic malaria areas maybe exposed simultaneously to DDT and malaria infection. DDT may impair status of vitamins, which are implicated in the immunity and pathophysiology of malaria. To explore possible interactions, DDT residues, retinol, α-tocopherol, β-carotene and cholesterol were measured in plasma samples of malaria-infected pregnant women (cases, *n* = 50) and age matched malaria-free controls (*n* = 58). DDT residues were found in all samples: mean (sd) total DDT levels of 29.7 and 32.7 ng/ml in cases and controls, respectively. Mean (sd) p,p′-DDT was higher in the controls than the cases (13.5 *vs.* 9.5 ng/ml, $p = 0.006$). Malaria infection was associated with lower mean (sd) plasma retinol (0.69 *vs.* 1.23 μmol/L) and cholesterol (2.62 vs. 3.48 mmol/L) compared to controls ($p < 0.001$). Mean (sd) plasma α-tocopherol (7.65 *vs.* 15.58 μmol/L) and α-tocopherol / cholesterol ratio (2.3 *vs.* 6.7 μmol/L/mmol/L) were significantly lower among the controls ($p < 0.001$). Mean (sd) plasma β-carotene was low (< 0.3 μmol/L) in both groups, but higher among malaria cases (0.19 *vs.* 0.15 μmol/L). Plasma retinol among the controls showed highly significant positive correlations with individual DDT compounds, particularly with p,p′-DDT ($r = 0.51$, $p < 0.001$). Plasma α-tocopherol and β-carotene seemed not to be affected by DDT residues. Ø

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CHARACTERIZATION OF HUMAN URINARY METABOLITES OF THE ANIIMALARIAL PIPERAQUINE

J Tarning, Y Bergqvist, NP Day, J Bergquist, B Arvidsson, NJ White, M Ashton, and N Lindegårdh

Department of Pharmacology, Sahlgrenska Academy at Göteborg University, Göteborg, Sweden (J.T., M.A.); Dalarna University College, Borlänge, Sweden (Y.B.); Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand (N.P.D., N.J.W., N.L.); Nuffield Department of Clinical Medicine, Centre for Tropical Medicine, University of Oxford, Oxford, United Kingdom (N.P.D., N.J.W., N.L.); and Department of Physical and Analytical Chemistry, Uppsala University, Uppsala, Sweden (J.B., B.A.)

Five metabolites of the antimalarial piperaquine (PQ) (1,3-bis-[4-(7-chloroquinolyl-4)-piperazinyl- 1]-propane) have been identified and their molecular structures characterized. After a p.o. dose of dihydroartemisinin-piperaquine, urine collected over 16 h from two healthy subjects was analyzed using liquid chromatography (LC)/UV, LC/tandem mass spectrometry (MS/MS), Fourier transform ion cyclotron resonance (FTICR)/MS, and H NMR. Five different peaks were recognized as possible metabolites [M1, 320 m/z; M2, M3, and M4, 551 m/z (PQ + 16 m/z); and M5, 567 m/z (PQ + 32 m/z)] using LC/MS/MS with gradient elution. The proposed carboxylic M1 has a theoretical monoisotopic molecular mass of 320.1166 m/z, which is in accordance with the FTICR/MS (320.1168 m/z) findings. The LC/MS/MS results also showed a 551 m/z metabolite (M2) with a distinct difference both in polarity and fragmentation pattern compared with PQ, 7-hydroxypiperaquine, and the other 551 m/z metabolites. We suggest that this is caused by N-oxidation of PQ. The results showed two metabolites (M3 and M4) with a molecular ion at 551 m/z and similar fragmentation pattern as both PQ and 7-hydroxypiperaquine; therefore, they are likely to be hydroxylated PQ metabolites. The molecular structures of M1 and M2 were also confirmed using H NMR. Urinary excretion rate in one subject suggested a terminal elimination half-life of about 53 days for M1. Assuming formation rate-limiting kinetics, this would support recent findings that the terminal elimination half-life of PQ has been underestimated previously. ∅

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DEVELOPMENT AND VALIDATION OF AN AUTOMATED SOLID PHASE AND LIQUID CHROMATOGRAPHIC METHOD FOR THE DETERMINATION OF PIPERAQUINE ON URINE

J Tarning[1], T Singtoroj[2], A Annerberg[2], M Ashton[1], Y Bergqvist[3], NJ White[2,4], NPJ Day[2,4] and N Lindegardh[2,4]

[1] *Department of Pharmacology, Sahlgrenska Academy, Göteborg, Sweden;*
[2] *Faculty of Tropical Medicine, Mahidol University, 420/6 Rajvithi Road, Bangkok 10400, Thailand;*
[3] *Dalarna University College, Borlänge, Sweden;*
[4] *Nuffield Department of Clinical Medicine, Centre for Tropical Medicine, University of Oxford, Oxford, UK*

A sensitive and specific bioanalytical method for determination of piperaquine in urine by automated solid-phase extraction (SPE) and liquid chromatography (LC) has been developed and validated. Buffered urine samples (containing internal standard) were loaded onto mixed phase (cation-exchange and octylsilica) SPE columns using an ASPEC XL SPE robot. Chromatographic separation was achieved on a Chromolith Performance RP-18e (100 mm x 4.6 mm I.D.) LC column with phosphate buffer (pH 2.5; 0.1 mol/L)-acetonitrile (92:8, v/v). Piperaquine was analysed at a flow rate of 3 mL/min with UV detection at 347 nm. A linear regression model on log-log transformed data was used for quantification. Within-day precision for piperaquine was 1.3% at 5000 ng/mL and 6.6% at 50 ng/mL. Between-day precision for piperaquine was 3.7% at 5000 ng/mL and 7.2% at 50 ng/mL. Total-assay precision for piperaquine over 4 days using five replicates each day (n = 20) was 4.0%, 5.2% and 9.8% at 5000, 500 and 50 ng/mL, respectively. The lower limit of quantification (LLOQ) was set to 3 ng/mL using 1 mL of urine, which could be lowered to 0.33 ng/mL when using 9 mL of urine and an increased injection volume. ∅

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PULMONARY MANIFESTATIONS OF MALARIA: RECOGNITION AND MANAGEMENT

Taylor WR, Canon V, White NJ

Travel and Migration Medicine Unit, Department of Community Medicine, Geneva University Hospital, Geneva, Switzerland

Lung involvement in malaria has been recognized for more than 200 hundred years, yet our knowledge of its pathogenesis and management is limited. Pulmonary edema is the most severe form of lung involvement. Increased alveolar capillary permeability leading to intravascular fluid loss into the lungs is the main pathophysiologic mechanism. This defines malaria as another cause of acute lung injury (ALI) and acute respiratory distress syndrome (ARDS).Pulmonary edema has been described most often in non-immune individuals with Plasmodium falciparum infections as part of a severe systemic illness or as the main feature of acute malaria. P.vivax and P.ovale have also rarely caused pulmonary edema.Clinically, patients usually present with acute breathlessness that can rapidly progress to respiratory failure either at disease presentation or, interestingly, after treatment when clinical improvement is taking place and the parasitemia is falling. Pregnant women are particularly prone to developing pulmonary edema. Optimal management of malaria-induced ALI/ARDS includes early recognition and diagnosis. Malaria must always be suspected in a returning traveler or a visitor from a malaria-endemic country with an acute febrile illness. Slide microscopy and/or the use of rapid antigen tests are standard diagnostic tools. Malaria must be treated with effective drugs, but current choices are few: e.g. parenteral artemisinins, intravenous quinine or quinidine (in the US only). A recent trial in adults has shown that intravenous artesunate reduces severe malaria mortality by a third compared with adults treated with intravenous quinine. Respiratory compromise should be managed on its merits and may require mechanical ventilation. Patients should be managed in an intensive care unit and particular attention should be paid to the energetic management of other severe malaria complications, notably coma and acute renal failure. ALI/ARDS may also be related to a coincidental bacterial sepsis that may not be clinically obvious. Clinicians should employ a low threshold for starting broad spectrum antibacterials in such patients, after taking pertinent microbiologic specimens. Despite optimal management, the prognosis of severe malaria with ARDS is poor.ALI/ARDS in pediatric malaria appears to be rare. However, falciparum malaria with severe metabolic acidosis or acute pulmonary edema may present with a clinical picture of pneumonia, i.e. with tachypnea, intercostal recession, wheeze or inspiratory crepitations. This results in diagnostic confusion and suboptimal treatment. Whilst this is increasingly being recognized in malaria-endemic countries, clinicians in temperate zones should be aware that malaria may be a possible cause of 'pneumonia' in a visiting or returning child. ∅

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NONRANDOM DISTRIBUTION OF *BURKHOLDERIA PSEUDOMALLEI* CLONES IN RELATION TO GEOGRAPHICAL LOCATION AND VIRULENCE

Mongkol Vesaratchavest,[1] Sarinna Tumapa,[1] Nicholas PJ Day,[1,2] Vanaporn Wuthiekanun,[1] Wirongrong Chierakul,[1] Matthew TG Holden,[3] Nicholas J White,[1,2] Bart J Currie,[4] Brian G Spratt,[5] Edward J Feil[6] and Sharon J Peacock[1,2]*

[1] *Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand;*
[2] *Center for Clinical Vaccinology and Tropical Medicine, Nuffield Department of Clinical Medicine, University of Oxford, Churchill Hospital, Oxford, United Kingdom;*
[3] *The Wellcome Trust Sanger Institute, Hinxton, Cambridge, United Kingdom;*
[4] *Menzies School of Health Research, Charles Darwin University, Darwin, Australia;*
[5] *Department of Infectious Disease Epidemiology, Imperial College, London, United Kingdom;*
[6] *Department of Biology and Biochemistry, University of Bath, Bath, United Kingdom*

Burkholderia pseudomallei is a soil-dwelling saprophyte and the causative agent of melioidosis, a life-threatening human infection. Most cases are reported from northeast Thailand and northern Australia. Using multilocus sequence typing (MLST), we have compared (i) soil and invasive isolates from northeast Thailand and (ii) invasive isolates

from Thailand and Australia. A total of 266 Thai *B. pseudomallei* isolates were characterized (83 soil and 183 invasive). These corresponded to 123 sequence types (STs), the most abundant being ST70 (*n* = 21), ST167 (*n* = 15), ST54 (*n* = 12), and ST58 (*n* = 11). Two clusters of related STs (clonal complexes) were identified; the larger clonal complex (CC48) did not conform to a simple pattern of radial expansion from an assumed ancestor, while a second (CC70) corresponded to a simple radial expansion from ST70. Despite the large number of STs, overall nucleotide diversity was low. Of the Thai isolates, those isolated from patients with melioidosis were overrepresented in the 10 largest clones ($P < 0.0001$). There was a significant difference in the classification index between environmental and disease isolates ($P < 0.001$), confirming that genotypes were not distributed randomly between the two samples. MLST profiles for 158 isolates from Australia (mainly disease associated) contained a number of STs (96) similar to that seen with the Thai invasive isolates, but no ST was found in both populations. There were also differences in diversity and allele frequency distribution between the two populations. This analysis reveals strong genetic differentiation on the basis of geographical isolation and a significant differentiation on the basis of virulence potential. ∅

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MODELLING MALARIA CONTROL

Nicholas J White

Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand, and the Centre for Clinical Vaccinology and Tropical Medicine, Churchill Hospital, Oxford, United Kingdom.

In the past ten years, the rich world has begun to get serious about tackling the diseases that predominantly affect poor people, diseases that impose an enormous humanitarian and economic burden upon those least able to bear it. Infections comprise the majority of this burden, and three have been singled out for particular attention: HIV/AIDS, tuberculosis, and malaria. Of these, malaria is probably the easiest to attack. But how should we attack it? ∅

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MELIOIDOSIS: INSIGHTS INTO THE PATHOGENICITY OF *BURKHOLDERIA PSEUDOMALLEI*

W Joost Wiersinga[1], Tom van der Poll[1], Nicholas J White[2,3], Nicholas P Day[2,3] and Sharon J Peacock[2,3]

[1] *Academic Medical Centre, Centre for Infection and Immunity Amsterdam (CINIMA), Amsterdam, The Netherlands;*
[2] *Wellcome Trust, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand;*
[3] *Centre for Clinical Vaccinology and Tropical Medicine, Nuffield Department of Clinical Medicine, University of Oxford, Churchill Hospital, Oxford OX3 7LJ, UK*

Burkholderia pseudomallei is a potential bioterror agent and the causative agent of melioidosis, a severe disease that is endemic in areas of Southeast Asia and Northern Australia. Infection is often associated with bacterial dissemination to distant sites, and there are many possible disease manifestations, with melioidosis septic shock being the most severe. Eradication of the organism following infection is difficult, with a slow fever-clearance time, the need for prolonged antibiotic therapy and a high rate of relapse if therapy is not completed. Mortality from melioidosis septic shock remains high despite appropriate antimicrobial therapy. Prevention of disease and a reduction in mortality and the rate of relapse are priority areas for future research efforts. Studying how the disease is acquired and the host–pathogen interactions involved will underpin these efforts; this review presents an overview of current knowledge in these areas, highlighting key topics for evaluation. ∅

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MELLIOIDOSIS IN MYANMAR: FORGOTTEN BUT NOT GONE?

Vanaporn Wuthiekanun, Sayan Langla, Witaya Swaddiwudhipong, Wilarat Jedsadapanpong, Yingyot Kaengnet, Wirongrong Chierakul, Nicholas P Day, and Sharon J Peacock

The Wellcome Trust-Mahidol University-Oxford Tropical Medicine Research Program, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; Mae Sot General Hospital, Tak, Thailand; Center for Clinical Vaccinology and Tropical Medicine, Nuffield Department of Clinical Medicine, University of Oxford, Churchill Hospital, Oxford, United Kingdom

A serologic survey of adults resident in Myanmar was conducted to define the presence of antibodies to Burkholderia pseudomallei, the cause of melioidosis. Antibodies were detectable by indirect hemagglutination assay (IHA) in 757 (78%) of 968 adults, of whom 69 (7%) had an IHA titer ≥0. ∅

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DEVELOPMENT OF ANTIBODIES TO *BURKHOLERIA PSEUDOMALLEI* DURING CHILDHOOD IN MELIOIDOSIS-ENDEMIC NORTHEAST THAILAND

Vanaporn Wuthiekanun, Wirongrong Chierakul, Sayan Langla, Wipada Chaowagul, Chanathip Panpitpat, Penchan Saipan, Thaksinaporn Thoujaikong, Nicholas P Day, Sharon J Peacock

Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; Sappasithiprasong Hospital, Ubon Ratchathani Province, Thailand; Udon Thani Hospital, Udon Thani Province, Thailand; Center for Clinical Vaccinology and Tropical Medicine, Nuffield Department of Clinical Medicine, University of Oxford, Churchill Hospital, Oxford, United Kingdom

A cross-sectional serological survey of 2,214 children living in northeast Thailand was conducted to define the antibody response to *Burkholderia pseudomallei* from birth to 14 years. There was a sharp rise in detectable antibodies from birth to 4 years followed by reactivity in approximately 60-70% of children thereafter. ∅

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SEROLOGICAL EVIDENCE FOR INCREASED HUMAN EXPOSURE TO *BURKHOLDERIA PSEUDOMALLEI* FOLLOWING THE TSUNAMI IN SOUTHERN THAILAND

Vanaporn Wuthiekanun,[1] Wirongrong Chierakul,[1] Jurairat Rattanalertnavee,[2] Sayan Langa,[1] Damrong Sirodom,[2] Charnkij Wattanawaitunechai,[2] Wut Winothai,[2] Nicholas J White,[1,3] Nicholas Day,[1,3] and Sharon J Peacock[1,3]*

[1] *Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand;*
[2] *Takuapa General Hospital, Phangnga, Thailand;*
[3] *Center for Clinical Vaccinology and Tropical Medicine, Nuffield Department of Clinical Medicine, University of Oxford, Churchill Hospital, Oxford OX3 7LJ, United Kingdom*

A serological study was performed to determine recent human exposure to Burkholderia pseudomallei (the cause of melioidosis) in residents of southern Thailand affected by the tsunami of 26 December 2004. The findings were suggestive of increased recent exposure in both tsunami survivors and uninjured bystanders. Survivors of the Thailand tsunami may be at increased risk of melioidosis. ∅

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MANAGEMNT OF MELIOIDOSIS

Wuthiekanun V, Peacock SJ

Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

Melioidosis is a serious human infection caused by the environmental Gram-negative bacterium Burkholderia pseudomallei. Outcome following melioidosis remains poor despite 20 years of clinical research. Overall mortality is 50% in north-east Thailand (35% in children) and 19% in Australia. Relapse is common (13% over 10 years), and results from failure to eradicate the organism. Treatment is required to complete 12-20 weeks, or longer if clinically indicated. This is divided into intravenous and oral phases. Clinical trial evidence supports the use of ceftazidime or a carbapenem antibiotic for initial parenteral therapy, which should be administered for at least 10-14 days. This is followed by a prolonged course of oral antimicrobial therapy with trimethoprim-sulfamethoxazole (TMP-SMX) with or without doxycycline. Amoxicillin-clavulanate is an alternative for children, pregnant women and for patients with intolerance to first-line therapy. Resistance of B. pseudomallei to these drugs is rare, with the exception of TMP-SMX; resistance rates are approximately 2.5% in Australia and 13-16% in Thailand. There is a lack of evidence for the value of adjunctive therapies in the treatment of melioidosis. Future studies aim to address whether meropenem is superior to ceftazidime during parenteral therapy, and whether doxycycline is a necessary component of oral treatment. ∅

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LONG LASTING PROTECTIVE IMMUNE RESPONSE TO 19 kDa CARBOXY-TERMINAL FRAGMENT OF *PLASMODIUM YOELII* MEROZOITE SURFACE PROTEIN 1 ($MSP1_{19}$) IN MICE

Pimmada Jeamwattanalert,[1] Yuvadee Mahakunkijcharoen,[2] Leera Kittigul,[1] Pakpimol Mahannop,[3] Sathit Pichyangkul,[4] and Chakrit Hirunpetcharat[1*]

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

MSP1 is the major protein on the surface of plasmodial merozoite and its carboxy-terminus, the 19kDa-fragment ($MSP1_{19}$), is highly conserved and effective in induction of a protective immune response against malaria parasite infection in mice and monkeys. However, the duration of the immune response has not been elucidated. As such, we immunized BALB/c mice with a standard four-dose injection of recombinant *P. yoelii* $MSP1_{19}$ formulated with Montanide ISA51 and CpG oligodeoxynucleotide (ODN) and monitored the $MSP1_{19}$-specific antibody levels for up to 12 months. The antibody titers persisted constantly over the period of time without significant waning, in contrast to the antibody levels induced by immunization with Freund's adjuvant, where the antibody levels gradually declined to significantly lower levels 12 months after immunization. Investigation of IgG subclass longevity revealed that only the IgG1 antibody level (Th2 type driven response) decreased significantly by 6 months while the IgG2a antibody level (Th1 type driven response) did not change over the 12 months post immunization but that the boosting effect was seen in the IgG1 but not in IgG2a antibody responses. After challenge infection, all immunized mice survived with negligibly patent parasitemia. These findings suggest that protective immune responses to $MSP1_{19}$ following immunization using oil-based Montanide ISA51 and CpG ODN as adjuvant are very long-lasting and encourage clinical trials for malaria vaccine development. ∅

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BEYOND DEWORMING: THE PROMOTION OF SCHOOL-HEALTH-BASED INTERVENTIONS BY JAPAN

Kobayashi J, Jimba M, Okabayashi H, Singhasivanon P, Waikagul J

Bureau of International Cooperation, International Medical Centre of Japan (IMCJ), Ministry of Health, Labor and Welfare, 1-21-1 Toyama, Shinjuku-ku, Tokyo 162-8655, Japan

Deworming bestows a variety of health and socioeconomic benefits and has been embraced by developing countries. To extend the beneficial impact of deworming, the Asian Centre of International Parasite Control (ACIPAC) project has carried out activities to link deworming with health-promoting school programs in the Greater Mekong Subregion (Cambodia, Laos, Myanmar, Thailand and Vietnam). ACIPAC has also conducted an integrated school-health-based program, including deworming and malaria education, under the umbrella of the health-promoting schools initiative. Implementing "beyond-deworming" efforts is now a practical challenge in the subregion. ∅

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IN VITRO ANTIMALARIAL ACTIVITY OF AZITHROMYCIN, ARTESUNATE, AND QUININE IN COMBINATION AND CORRELATION WITH CLINICAL OUTCOME

Noedl H, Krudsood S, Leowattana W, Tangpukdee N, Thanachartwet W, Looareesuwan S, Miller RS, Fukuda M, Jongsakul K, Yingyuen K, Sriwichai S, Ohrt C, Knirsch C

Department of Specific Prophylaxis and Tropical Medicine, Center for Physiology and Pathophysiology, Medical University of Vienna, Kinderspitalgasse 1 5, A-1090 Vienna, Austria. harald.noedl@meduniwien.ac.at

Azithromycin when used in combination with faster-acting antimalarials has proven efficacious in treating *Plasmodium falciparum* malaria in phase 2 clinical trials. The aim of this study was to establish optimal combination ratios for azithromycin in combination with either dihydroartemisinin or quinine, to determine the clinical correlates of in vitro drug sensitivity for these compounds, and to assess the cross-sensitivity patterns. Seventy-three fresh *P. falciparum* isolates originating from patients from the western border regions of Thailand were successfully tested for their drug susceptibility in a histidine-rich protein 2 (HRP2) assay. With overall mean fractional inhibitory concentrations of 0.84 (95% confidence interval [CI] = 0.77 to 1.08) and 0.78 (95% CI = 0.72 to 0.98), the interactions between azithromycin and dihydroartemisinin, as well as quinine, were classified as additive, with a tendency toward synergism. The strongest tendency toward synergy was seen with a combination ratio of 1:547 for the combination with dihydroartemisinin and 1:44 with quinine. The geometric mean 50% inhibitory concentration (IC(50)) of azithromycin was 2,570.3 (95% CI = 2,175.58 to 3,036.58) ng/ml. The IC(50)s for mefloquine, quinine, and chloroquine were 11.42, 64.4, and 54.4 ng/ml, respectively, suggesting a relatively high level of background resistance in this patient population. Distinct correlations (R = 0.53; P = 0.001) between quinine in vitro results and parasite clearance may indicate a compromised sensitivity to this drug. The correlation with dihydroartemisinin data was weaker (R = 0.34; P = 0.038), and no such correlation was observed for azithromycin. Our in vitro data confirm that azithromycin in combination with artemisinin derivatives or quinine exerts additive to synergistic interactions, shows no cross-sensitivity with traditional antimalarials, and has substantial antimalarial activity on its own. ∅

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INTRAHOST SELECTION OF *PLASMODIUM FALCIPARUM* pfmdr1 ALLELES AFTER ANTIMALARIAL TREATMENT ON THE NORTHWESTERN BORDER OF THAILAND

Uhlemann AC, McGready R, Ashley EA, Brockman A, Singhasivanon P, Krishna S, White NJ, Nosten F, Price RN

Centre for Infection, Division of Cellular and Molecular Medicine, St. George's, University of London, London, United Kingdom

Background: Increased pfmdr1 copy number is associated with reduced susceptibility to structurally unrelated antimalarial drugs. We assessed how administration of different antimalarial drugs altered pfmdr1 polymorphism in parasites from patients who experienced treatment failure.

Methods: In studies conducted on the northwestern border of Thailand, amplifications and single-nucleotide polymorphisms in pfmdr1 were compared before and after antimalarial drug treatment.

Results: Intrahost changes in pfmdr1 copy number were observed in 20% (26/132) of patients with recurrent infections. Among infections that recrudesced after mefloquine-containing regimens, increases in pfmdr1 copy number occurred in 68% (95% confidence interval [CI], 46%-85%), and decreases occurred in 2% (95% CI, 0.4%-11%) of isolates; corresponding proportions after artemether-lumefantrine were 25% (2/8) and 11% (2/19); after quinine, 50% (1/2) and 40% (4/10); and after artemisinins alone, 0% (0/10) and 19% (3/16) of isolates (overall P<.001).

Conclusions: Intrahost selection based on pfmdr1 copy number occurs frequently in parasite populations within individual patients. Amplification confers multidrug resistance but probably imposes a significant fitness cost to the parasites. ∅

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