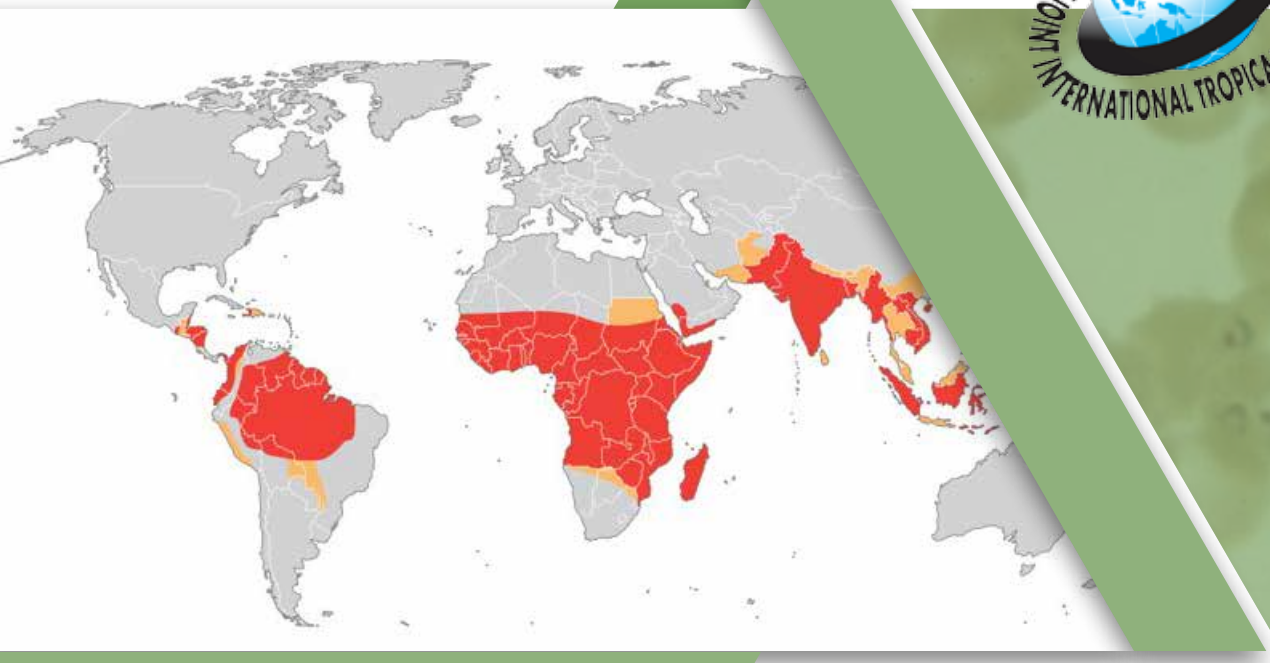
JOINT INTERNATIONAL TROPICAL MEDICINE MEETING 2017 **(JITMM 2017)**



Abstracts
ORAL PRESENTATIONS

"TROPICAL MEDICINE 4.0: EFFECTIVE COLLABORATION FOR AN IMPACT ON GLOBAL HEALTH"

6 – 8 DECEMBER 2017

AMARI WATERGATE, BANGKOK, THAILAND

Join the biggest conference on Tropical Medicine, hosted by the Faculty of Tropical Medicine, Mahidol University

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- Department of Disease Control Ministry of Public Health (MOPH)
- Mahidol - Oxford Tropical Medicine Research Unit (MORU)

Wednesday 6 December 2016

Opening Session

9.00-9.30

Watergate Ballroom

OPENING SESSION BY ORGANIZERS AND CO-ORGANIZERS

Report by Assoc. Prof. Dr. Pratap Singhasivanon
Chairman, Organizing Committee

WELCOME ADDRESS (CO-ORGANIZERS)

Dr. Tanarak Plipat
Deputy Director General, Department of Disease Control

Prof. Nicholas Day
Director, Mahidol-Oxford Tropical Medicine Research Unit (MORU)

OPENING REMARKS

Assoc. Prof. Soranit Siltharm
Permanent Secretary, Ministry of Science and Technology, Thailand

TROPMED Outstanding Alumni Award Presentation
Presented by Assoc. Prof. Supranee Changbumrung

AWARD RECIPIENT

Prof. Emeritus Arunee Sabchareon
Consultant, Faculty of Tropical Medicine, Mahidol University
Consultant, Tropical Medicine Alumni Association

9.30-10.15
Watergate Ballroom

S1: The 23rd Chamlong-Tranakchit Harinasuta Lecture

Chairperson

Pratap Singhasivanon

Keynote Speaker

COLLABORATION AND INNOVATION AT SCALE: MC'S EXPERIENCES WITH UPSCALE AND SMC

James Tibendarana [1]

[1] *Global Technical Director for Malaria Consortium*

Especially as countries around the world are aspiring towards Universal Health Coverage and reaching the SDGs, looking at effective models of partnership is key. Malaria Consortium believes that effective collaboration and innovation are important in delivering sustained programs that support different health and related objectives.

As a sub-goal of SDG 3, UHC has the potential to unify and bring harmony to a fragmented health agenda, and ensure that adequate attention is paid to equity and human rights. At the same time, to achieve the sub-goals for malaria, NTDs and child health, continued political commitment is needed to address the underlying social determinants of poor health and diseases.

Tenets of such partnership and collaboration include: a strong, efficient, well-run health system; mechanisms that bring the government, private sector and international partners together; model of financing health services; access to essential medicines and innovative technologies; and a sufficient number of well-trained and motivated health workers at all levels.

Since the path to UHC is highly complex and no single policy solution exists, putting resources in place (partnership, innovation, financing and health services) are key to ensure that services are accessible to all. There is also a need to look at promising practices from around the world to decide on models to adopt so as to use available resources as wisely as possible in partnership with stakeholders involved.

In this abstract, we will talk about two such practices; digital health strategies and seasonal malaria chemoprevention.

Digital health strategies can help governments manage malaria and disease control programs better. In the countries MC work in, we have explored areas where technology can play an important role, particularly to improve the motivation and supervision of community health workers, to provide effective diagnostic tools, and to strengthen surveillance and data management.

Encompassing Cambodia, Laos, Myanmar, Thailand and Vietnam and bordering China and India, the Greater Mekong Region holds a population that easily exceeds 200 million people. It is therefore critical for the region to capitalize on innovative digital strategies for addressing some ongoing challenges in health and socio-economic development. Thailand is one of the few low and middle-income countries (LMIC) which has achieved universal health coverage (UHC). The knowledge of how to achieve UHC and implement such a program is more valuable to many LMICs considering universal health coverage than the experiences of other developed countries. The process of trial and error in dealing with problems will also become knowledge that can be shared with other LMICs. In that sense, I hope that this presentation will generate discussions from which we can all benefit. Forms of partnership and collaboration that have produced concrete results in the region and beyond will be helpful to consider while looking at scalable models of large scale and national/regional programs that have provided proof of concept.

From 2009 to 2017, Malaria Consortium tested a number of interventions to improve the quality of care provided by community health workers in Mozambique, locally known as agentes polivalentes elementares (APEs), including a smartphone application introduced in Mozambique's Inhambane province through the inSCALE project. Building from this success and in order to link APEs with the national health information system, Malaria Consortium worked in collaboration with the Ministry of Health and UNICEF to develop the upSCALE platform – a digital strategy to strengthen health systems and community health delivery. The platform collects real time data entered by APEs who deliver health services in the remote areas in which they live. The remoteness of some regions of the GMS, particularly in view of the areas inhabited by the Mobile Migrants Ethnic Vulnerable Populations (MMEVs) who are in need of specific health services (for example Malaria programs) through extension health workers (VHVs, VMWs, HWs etc.) make the prospect of large scale and nationally adopted models of digital health strategies particularly attractive. Added to this, there is a need to harmonise the various pilots of digital strategies that are being run in various parts of the GMS in comparison with similar or different approaches from different parts of the world. The upSCALE platform which is implemented in the Mozambique provinces of Inhambane, Cabo Delgado and soon Zambezia to create a national mHealth system led by the Ministry of Health. This is the first country to scale up a digital health strategy to this extent.

upSCALE is DHIS2 compliant and helps visualise household indicators in real time, identifies stock-outs helps review APE performance and supports disease surveillance and response - including early detection of disease outbreaks.

In terms of collaboration and partnership at scale in delivering complex health interventions, another model worth sharing is the implementation of the seasonal malaria chemoprevention (SMC) across the Sahel region of Africa. Following World Health Organization (WHO)'s 2012 policy recommendation, Malaria Consortium has been leading seasonal malaria chemoprevention (SMC) interventions in seven Sahel countries of Burkina Faso, Chad, Guinea, Mali, Niger, Nigeria and The Gambia. With partnership approaches instilled to the core and mobilizing innovation at every opportunity, SMC has been highly effective intervention to prevent malaria in those children most vulnerable to the disease. Despite the challenges in administering up to four monthly doses of antimalarial drugs to children aged 3-59 months during peak malaria transmission season, which involves reaching out to as many as 3-6 million children in a given year, it was the focus on strengthened partnership and innovative approaches that resulted in the success of the program. For the same reasons, SMC has been shown to be cost effective and feasible for the prevention of malaria among children, preventing up to 85 percent of malaria cases.

The potential of replicating such partnerships across the borders of nation states is enormous. For example, there are opportunities in the GMS to effect regional approaches to consolidate partnerships in the delivery of critical services for Malaria and NTDs- potentially saving lives, reducing illness and boosting economic growth.

Wednesday 6 December 2017

10.45-12.15
Room A

S2: From Single Cell to Population: Impact of Whole-Genome Technology on Tropical Medicine

Chairpersons:

Chamnarn Apiwathanasorn

Arporn Wangwiwatsin

Invited Speakers

1. GWAS analysis of malaria drug resistance
   Olivo Miotto
   Nuffield Department of Medicine, University of Oxford

(No available abstract)

2. Genetics of antimalarial drug resistance in *Plasmodium* crosses
   Thomas E. Wellems
   National Institute of Allergy and Infectious Diseases

3. Single cell RNA-seq to show how parasite sexual determination
   Oliver Billker
   Wellcome Trust Sanger Institute

(No available abstract)

GWAS ANALYSIS OF MALARIA DRUG RESISTANCE

Olivo Miotto

Nuffield Department of Medicine, University of Oxford

(No available abstract)

GENETICS OF ANTIMALARIAL DRUG RESISTANCE IN *PLASMODIUM* CROSSES

Thomas Wellems

Laboratory of Malaria and Vector Research, National Institute of Allergy and Infectious Diseases, Bethesda, USA

Genetic crosses of *Plasmodium* parasites are powerful tools for research on mechanisms of antimalarial resistance. Crosses and their analysis have identified mutations that affect responses to such first-line drugs as chloroquine, pyrimethamine, amodiaquine and quinine, and they may be useful for insights into recrudescences after artemisinin treatment. In this presentation, I will discuss the use of genetic crosses and information they are providing about drug responses in malaria. Antimalarial chemotherapy and Progress in drug discovery and development, in conjunction with improvements in the quality, use, and availability of antimalarial combinations, are vital to the effectiveness of chemotherapy for malaria control.

Keyword: Combination chemotherapy, trait linkage analysis

SINGLE CELL RNA-SEQ TO SHOW HOW PARASITE SEXUAL DETERMINATION

Oliver Billker

Wellcome Trust Sanger Institute

Wednesday 6 December 2017

10.45-12.15
Room B

S3: Young Investigator Presentation Award

Chairperson:

Saranath Lawpoolsri Niyom

Wirichada Pan-Ngum

Speakers

1. An integrated analysis tool for analyzing hybridization intensities and genotypes using new-generation population-optimized human arrays
   Mei-Chu Huang
   Academia Sinica, Taipei

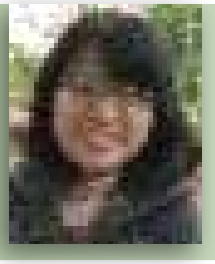
2. Protein Profiles of Female Salivary Glands of Three Human-biting Black Flies (*Diptera: Simuliidae*) in Thailand
   Chayanit Hempolchom
   Chiang Mai University

3. Anti-protozoan study of a medicinal herb, *Bidens pilosa*
   Meng-Ting Yang
   Academia Sinica, Taipei

4. Daily and seasonal dynamics of the house fly *Musca domestica L.* as revealed by semi-automatic trap collections
   Tunwadee Klongklaew
   Chiang Mai University

5. LATS2 gene as a modulator in the oxidative stress response induced by phytoagent deoxyelephantopin derivatives in breast cancer cells
   Yu-Ting Cheng
   Academia Sinica, Taipei

AN INTEGRATED ANALYSIS TOOL FOR ANALYZING HYBRIDIZATION INTENSITIES AND GENOTYPES USING NEW-GENERATION POPULATION-OPTIMIZED HUMAN ARRAYS



Tzu-Po Chuang [2], Chien-Hsiun Chen [3], Jer-Yuarn Wu [3], Yuan-Tsong Chen [3], Ling-Hui Li [3], Hsin-Chou Yang [4], Mei-Chu Huang [1]

[1] Institute of Biomedical Informatics, National Yang-Ming University, Taipei 112; Taiwan, Institute of Statistical Science, Academia Sinica, Taipei 115, Taiwan and Bioinformatics Program, Taiwan International Graduate Program, Institute of Information , [2] Taiwan International Graduate Program in Molecular Medicine, National Yang-Ming University and Academia Sinica, Taipei 115, Taiwan; Institute of Biochemistry and Molecular Biology, National Yang-Ming University, Taipei 112, Taiwan, [3] Institute of Biomedical Sciences, Academia Sinica, Taipei 115, Taiwan, [4] Bioinformatics Program, Taiwan International Graduate Program, Institute of Information Science, Academia Sinica, Taipei 115, Taiwan; Institute of Statistical Science, Academia Sinica, Taipei 115, Taiwan; Institute of Public Health, National Yang Ming

Affymetrix Axiom® single nucleotide polymorphism (SNP) arrays provide a cost-effective, high-density, and high-throughput genotyping solution for population- optimized analyses. However, no public software is available for the integrated genomic analysis of hybridization intensities and genotypes for this new-generation population-optimized genotyping platform. A set of statistical methods was developed for an integrated analysis of allele frequency (AF), allelic imbalance (AI), loss of heterozygosity (LOH), long contiguous stretch of homozygosity (LCSH), and copy number variation or alteration (CNV/CNA) on the basis of SNP probe hybridization intensities and genotypes. This study analyzed 3,236 samples that were genotyped using different SNP platforms. The proposed AF adjustment method considerably increased the accuracy of AF estimation. The proposed quick circular binary segmentation algorithm for segmenting copy number reduced the computation time of the original segmentation method by 30–67 %. The proposed CNV/CNA detection, which integrates AI and LOH/LCSH detection, had a promising true positive rate and well-controlled false positive rate in simulation studies. Moreover, our real-time quantitative polymerase chain reaction experiments successfully validated the CNVs/CNAs that were identified in the Axiom data analyses using the proposed methods; some of the validated CNVs/CNAs were not detected in the Affymetrix Array 6.0 data analysis using the Affymetrix Genotyping Console. All analysis functions that they can be efficiently implemented in parallel on multi-core devices are packaged into the ALICE (AF/LOH/LCSH/AI/CNV/CNA Enterprise) software. ALICE and the used genomic reference databases, which can be downloaded from http://hcyang.stat.sinica.edu.tw/software/ALICE.html, are useful resources for analyzing genomic data from the Axiom and other SNP arrays.

Keywords: microarray, single-nucleotide polymorphism (SNP), fluorescence intensity, allele frequency (AF), allelic imbalance (AI), loss of heterozygosity (LOH), long contiguous stretch of homozygosity (LCSH), copy number variation or alteration (CNV/CNA), circular binary segmentation (CBS), AF/LOH/LCSH/AI/CNV/CNA Enterprise (ALICE)

PROTEIN PROFILES OF FEMALE SALIVARY GLANDS OF THREE HUMAN-BITING BLACK FLIES (*DIPTERA*: SIMULIIDAE) IN THAILAND

Chayanit Hempolchom [1], Wichai Srisuka [2], Onrapak Reamtong [3], Nitat Sookrung [4], Yuwaporn Sakolvaree [5], Wanpen Chaicumpa [5], Kritsana Taai [6], Watcharatip Dedkhad [1], Hiroyuki Takaoka [7], Atiporn Saeung [1]

[1] Department of Parasitology, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand, [2] Entomology Section, Queen Sirikit Botanic Garden, Chiang Mai, Thailand, [3] Department of Molecular Tropical Medicine and Genetics, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand, [4] Department of Research and Development, Faculty of Medicine Siriraj Hospital, Mahidol University, Thailand, [5] Department of Parasitology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, [6] Faculty of Veterinary Medicine, Western University, Kanchanaburi, Thailand, [7] Institute of Biological Sciences, Faculty of Science, University of Malaya, Kuala Lumpur Malaysia

Black flies are small bloodsucking insects. Some species serve as vectors of filarial nematodes of the genus *Onchocerca* to humans and other vertebrates. The biting of female black flies can cause localized allergic reaction in human and animals. In Thailand, *Simulium asakoae*, *S. nigrogivum* and *S. nodosum* are human-biting species. Herein, the protein profiles of female salivary glands showed at least 6, 13 and 9 major protein bands for *S. asakoae*, *S. nigrogivum* and *S. nodosum*, respectively. The several minor protein bands have also been observed in all species. The SDS-PAGE gel of each species was excised for LC-MS/MS analysis and database search for protein identification. Interestingly, the LC-MS/MS analysis and protein identification derived from three species revealed some interesting proteins, i.e., putative 5' nucleotidase/apyrase, serine protease and erythema protein, which involved in blood-feeding process of black flies. Moreover, antigen 5-related proteins were only found in *S. nigrogilvum* and *S. nodosum* salivary glands. These results obtained in this study provide an initial step to understanding the role of salivary gland proteins in black flies and further study on pharmacological use and immunological applications for humans who are sensitive to black fly bites in Thailand and other countries.

Keywords: Simulium, black fly, salivary gland, SDS-PAGE, LC-MS/MS

ANTI-PROTOZOAN STUDY OF A MEDICINAL HERB, *BIDENS PILOSA*

Meng-Ting Yang [1], Tien-Fen Kuo [2], Yueh-Chen Wu [3], Lee-Tian Chang [4], Wen-Chin Yang [2]

[1] Agricultural Biotechnology Research Center, Academia Sinica, Taiwan; Molecular and Biological Agricultural Sciences Program, Taiwan International Graduate Program, National Chung-Hsing University, Taichung, Taiwan and Academia Sinica, Taipei, Taiwan;, [2] Agricultural Biotechnology Research Center, Academia Sinica, Taiwan, [3] Agricultural Biotechnology Research Center, Academia Sinica, Taiwan , [4] Graduate Institute of Biotechnology, National Chung-Hsing University, Taichung, Taiwan

Protozoan infections, very common tropical diseases in men and animals, tremendously impact human health and food animal production. Most of the poultry industry is now located in tropical countries with a yearly market value of 60 billion USD. Avian coccidiosis is a protozoan disease with serious infection in chickens, causing sick bird syndrome, bloody stools, gut lesions, and mortality. It causes an annual economic loss of 800 million USD worldwide. Moreover, intensive chicken farming in tropical countries accelerates coccidiosis development due to high stress and temperature. Due to the problems with anti-coccidial chemicals and vaccines, medicinal medicine has been emerging as an alternative approach to control chicken coccidiosis. We first studied a medicinal plant, *B. pilosa* (BP), for chicken coccidiosis. It was extremely effective against coccidiosis as evidences by survival rate, body weight, fecal oocysts and gut pathology in chickens. It also had little development of drug resistance in coccidia. Next, field trial of BP in chicken farms had the same outcomes. Next, mechanistic studies indicated that BP reduced coccidiosis through interfering with the protozoan life cycle. Metagenomics approach showed that BP regulated gut microbiota in chickens by increasing 7 probiotics and decreasing 15 harmful bacteria. Finally, a bioactivity-directed fractionation and isolation (BDFI) strategy was used for identification of anti-coccidial compounds from BP. Collectively, this study demonstrated that BP serves as a novel remedy for coccidiosis in chickens. Besides, BP has edges over anti-coccidial drugs in drug residue and drug resistance. Such study may be applicable to other protozoan diseases, e.g., malaria, leishmaniasis, etc.

Keywords: protozoan, coccidiosis, *Bidens pilosa*

DAILY AND SEASONAL DYNAMICS OF THE HOUSE FLY MUSCA *DOMESTICA L.* AS REVEALED BY SEMI-AUTOMATIC TRAP COLLECTIONS

Tunwadee Klongklaew [1], Narin Sontigun [2], Sangob Sanit [2], Chutharat Sameai [2], Kom Sukontason [2], Philip Koehler [3], Roberto M. Pereira [3], Theeraphap Chareonviriyaphap [4], Hiromu Kurahashi [5], Kabkaew L. Sukontason [2]

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Effective control of house fly, *Musca domestica L.*, a species of medical importance, requires information on daily and seasonal dynamics. Daily and seasonal activity patterns of *M. domestica* were studied in three different microhabitats (palm plantations, forest area and longan orchard) in the suburban area of Chiang Mai Province, northern Thailand. Investigations were conducted for 24-h/day using a semi-automatic trap and 1-day tainted beef offal (300 g) as an attractive bait. Collections were carried out twice a month for one year (July 2013 – June 2014). A total of 1,324 adult *M. domestica* were collected, with 64.8% being in the longan orchard. Peak activity was recorded in the rainy season. House flies were active during the day, with peak activity in late morning (9.00 AM – 12.00 noon). Numbers of collected flies were correlated negatively with relative humidity (r=-0.137, P=0.009). No correlation between trap catch and temperature was found (r=-0.054, P=0.304). Female flies were more abundant with a 0.3 male/female sex ratio. These results provided baseline information of daily and seasonal dynamic activity of *M. domestica* under natural conditions, which is a prerequisite for effective control measures.

Keywords: *Musca domestica*, collection, daily activity, seasonal activity, control

LATS2 GENE AS A MODULATOR IN THE OXIDATIVE STRESS RESPONSE INDUCED BY PHYTOAGENT DEOXYELEPHANTOPIN DERIVATIVES IN BREAST CANCER CELLS

Yu-Ting Cheng [1], Lie-Fen Shyur [2]

[1] Molecular and Biological Agricultural Sciences Program, Taiwan International Graduate Program, Academia Sinica, Taipei, Taiwan; Agricultural Biotechnology Research Center, Academia Sinica, Taipei, Taiwan; Graduate Institute of Biotechnology, National, [2] Agricultural Biotechnology Research Center, Academia Sinica, Taipei, Taiwan; Biotechnology Center, National Chung Hsing University, Taichung, Taiwan

Breast cancer is the most common cancer type in women worldwide, and the mortality rate is especially high in tropical area. Despite of current therapeutic approaches for breast cancer, complexities such as tumor recurrence and drug-resistance development are still encountered during disease treatment and patient follow-up. Lack of targeted therapy for specific subtype such as triple negative breast cancer (TNBC) (ER—, PR—, HER2—) is still a critical issue for cancer patients. Traditional herbal medicine provides a rich and sustainable source to develop bioactive phytochemicals for disease prevention and treatment. Elephantopus scaber (ES) is a tropical medicinal plant from the Asteraceae family that is anecdotally used in various disorders such as infection and hepatitis. In our previous study, we demonstrated that a bioactive plant sesquiterpene lactone deoxyelephantopin (DET) isolated from ES and its semi-organically synthesized derivative DETD-35 created in our laboratory showed potent anti-TNBC activity in vitro and in vivo. We observed that the anti-TNBC effect of DET and DETD-35 involved oxidative stress (OS)-mediated biological activities. In this work, we show that specific tumor suppressor gene, large tumor suppressor 2 (LATS2), may be involved in the OS-dependent activity of DET and DETD-35 in TNBC cells. Based on publically available database, LATS2 gene expression may positively correlate to breast cancer patient survival, and DET or DETD-35 induces its expression in TNBC cells OS-dependently. Our study not only provides the mechanistic insight of the anti-breast cancer activity of phytochemical DET and DETD-35, but also characterizes a novel role of LATS2 in the oxidative response in breast cancer cells.

Keywords: breast cancer, deoxyelephantopin, oxidative stress

Wednesday 6 December 2017

10.45-12.15
Room C

S4: Trans-National Research and Promoting Cross-Sector Collaboration and Socio-Ecological Systems and Resilience Approach to Vector-Borne and Parasitic Diseases

Chairpersons:

Hans Overgaard

Invited Speakers

1. Progress and Prospects for Application of Social-ecological Systems Approach for Vector Borne Diseases
   Bruce Wilcox

2. Social-ecological Systems approach to residual malaria transmission in the Greater Mekong Sub-region
   Jeffrey Hii
   Malaria Consortium

3. Prospects and challenges towards sustainable liver fluke control
   Pierre Echaubard
   Global Health Asia Institute

4. The Reality of Using Transdisciplinarity and Ecosystem Approaches for Vector Borne Diseases
   Jennifer Steele
   Infectious Disease Epidemiologist

5. Insecticide resistance mapping of *Anopheles* and *Aedes* species and opportunities for integrated vector management
   Melinda Hadi
   Vestergaard Frandsen (EA) Limited, Nairobi, Kenya

PROGRESS AND PROSPECTS FOR APPLICATION OF SOCIAL-ECOLOGICAL SYSTEMS APPROACH FOR VECTOR BORNE DISEASES

Bruce Wilcox [1]

[1] *Global Health Asia Institute, Integrative Research & Education Programme, Faculty of Public Health, Mahidol University, 420/1 Rajavithi RD, Rachathewi District, Bangkok 10400*

The social-ecological systems & resilience framework (SESR) developed on the basis of findings in ecology and environmental management has been suggested as applicable to vector borne diseases. As with environmental and natural resource management problem-solving, vector management requires taking into account natural and human ecological factors, systems thinking, and transdisciplinarity. The latter provides the philosophical and practical basis for local or community as well as cross-sectoral participation, consideration of socioeconomic factors, and gender equity as called for by various agencies sponsoring VBD programs. Application of SESR, which includes the so-called ecosystem approach to VBDs, remains at an early stage and comprehensive case examples are lacking. In this presentation we summarize based on our experience with specific projects the potential and limitations of SESR for VBD applications.

Keyword: Vector Borne Diseases

SOCIAL-ECOLOGICAL SYSTEMS APPROACH TO RESIDUAL MALARIA TRANSMISSION IN THE GREATER MEKONG SUB-REGION

Jeffrey Hii [1], Edwards H [1], Sattabongkot J [2], Sriwichai P [2], Kiattibutr K [2], Phuanukoonnon S [2], Chinh VD [3], Duy BL [3], Thang ND [3], Xa NX [3], Trang DM [3], Shafique M [1]

[1] Malaria Consortium, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand, [2] Mahidol Vivax Research Unit, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand, [3] National Institute of Malariology, Parasitology and Entomology (NIMPE), Hanoi, Vietnam

Thailand and Vietnam aims to eliminate malaria by 2024 and 2030 respectively. Elimination in many of the remaining districts and provinces is hindered by the continuing presence of malaria infections in workers with 'high risk' occupations, for example farming communities, rubber plantation, seasonal and forest workers. These groups often belong to migrant or mobile populations with lower access to health care and greater exposure to malaria vectors in forest/plantation areas. Sibling species of malaria vectors with different ecological traits and vector competencies further complicate transmission patterns. Poor understanding of the ecological and behavioural attributes of vector and human populations, and their interactions, in these localities makes focal vector control difficult to design. We combined entomological, epidemiological, geo-spatial and qualitative research methods to understand the bio-socio-ecological determinants of residual malaria transmission (RMT) in three ecological niches – village, farm huts, and forest. The magnitude of RMT comprised outdoor biting (49-90% of all night-biting) plus indoor biting that occurred outside of sleeping hours (24% of all-night biting indoors) if universal coverage and usage of insecticide-treated nets (ITNs) were achieved. Furthermore, ownership did not translate into usage. Many ITNs were old or damaged, therefore affecting the risk of biting exposure. Given the heterogeneity of human behaviour and the variation of vector densities and biting behaviours and the under-achievement of community level universal coverage of ITN, additional efforts in improving bednet use may take into account natural and human ecological factors, systems thinking, and transdisciplinarity.

Keyword: Malaria transmission

PROSPECTS AND CHALLENGES TOWARDS SUSTAINABLE LIVER FLUKE CONTROL

Pierre Echaubard [1], Bruce A. Wilcox [1]

[1] *Global Health Asia Institute, Faculty of Public Health, Mahidol University*

The liver fluke *Opisthorchis viverrini (*Ov*)* is endemic in Southeast Asia where more than 10 million people are estimated to be infected. The infection is associated with several hepatobiliary diseases including cholangiocarcinoma (CCA). Northeast Thailand is a hotspot of Ov transmission and despite extensive public health prevention campaigns led by the government, Ov infection prevalence is still high. The persistence of high Ov infection rates in the region is due to (1) cultural behaviors associated with fishing, food preparation, and eating uncooked fish, practices that are deeply embedded as part of the indigenous rice-fish culture of this region; (2) wetland ecosystem-dependent livelihood and an ancient co-evolutionary relationship of Ov, natural hosts and humans; (3) a parasite highly efficient in its transmission within this coupled human-natural system; (4) a complex set of pathological consequences associated with infection and treatment; (5) historically unprecedented environmental change, including those caused by regional and local water resources management and flood control projects that lead to the disruption of natural ecological regulatory mechanisms with consequences on hosts abundance and patterns of exposure ; and, (6) possibly the most important, lack of knowledge integration at the policy level, discontinuity in government support including reduction in geographic coverage and lack of community-based control activities. We review here the state of our knowledge regarding the social-ecological determinants of Ov transmission and we highlight the role of neglected social, ecological and complex system sciences in improving our understanding of the systems transmission dynamic. We then describe an integrative research rationale based on transdisciplinarity pointing to the needs to enhance collaborative research and education as well as provide a broader human health and sustainable development framework in the context of the rapidly changing Southeast Asia waterscape.

Keyword: *Opisthorchis viverrini*, Landscape Epidemiology, Disease ecology, Transdisciplinarity, Global health

THE REALITY OF USING TRANSDISCIPLINARITY AND ECOSYSTEM APPROACHES FOR VECTOR BORNE DISEASES

Jennifer Steele

Infectious Disease Epidemiologist

Though the concept and importance of using a transdisciplinary ecosystem approach for global health problems have been elaborated for over a decade, the practice of using them for real-world application to problems has been difficult. Issues including how to implement an ecosystem approach, how to evaluate its effectiveness, and how to overcome challenges encountered have not been adequately described, creating uncertainty amongst health professionals seeking to move from theory to action. Vector borne diseases present especially complex problems with intricate connections among the environment, vectors, pathogens, reservoirs, animal hosts, and human communities in affected areas. Problems involved in vector borne disease control span far outside of the overt human clinical medical realm, requiring transdisciplinarity to create sustainable, effective interventions. In this presentation we seek to provide our knowledge and experience with concrete examples for how to implement an ecosystem approach to problem, including the process of using transdisciplinarity, systems thinking, and adaptive management to guide action on vector borne disease problems.

Keywords: vector borne diseases

INSECTICIDE RESISTANCE MAPPING OF *ANOPHELES* AND *AEDES* SPECIES AND OPPORTUNITIES FOR INTEGRATED VECTOR MANAGEMENT

Melinda P. Hadi 1, Jeffrey Hii 2

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Vector borne diseases account for more than 700,000 deaths each year. The prevention of mosquito borne diseases relies heavily on insecticide based vector control tools and knowledge of the spatiotemporal distribution of insecticide resistance is essential. IR Mapper (www.irmapper.com) was launched in 2012 to map insecticide resistance in *Anopheles* species. In 2016, it was expanded to map insecticide resistance in *Ae. aegypti* and *Ae. albopictus*. As of September 2017, the *Anopheles* IR Mapper platform consisted of over 17,000 unique data points in 60 countries. Confirmed resistance to pyrethroids was reported in 96% of countries. The *Aedes* IR Mapper consisted of over 7,000 field records in 65 countries and territories. 75% of localities reported confirmed resistance to at least one class of public health insecticide. Insecticide resistance was more frequently investigated in *Ae. aegypti* (93% of localities) than in *Ae. albopictus* (16% of localities), and the majority of assays reported were on adult mosquitoes (80% of localities) compared to the larval stage (41% of localities). The majority of data were available from Asia followed by the Americas; very few data points were available from Africa. In the control and elimination of vector borne diseases, integrated vector management (IVM) can contribute to insecticide resistance management by reducing the selection pressure imposed by insecticides. IVM also takes an ecosystem perspective and examines the way land use can alter vector habitats and change disease risk. For example, intensive agriculture such as cotton growing in West Africa has contributed to insecticide resistance in mosquito vectors. In South Asia, irrigated rice ecosystems are breeding sites for a number of vectors that many transmit several diseases such as malaria and Japanese encephalitis. Factors such as urbanization also changes vector ecology and introduced new disease transmission risk. A range of both chemical and non-chemical intervention form IVM based control strategies, which contribute to addressing malaria, dengue, and other vector borne diseases. IR Mapper is a useful tool for visualizing insecticide resistance trends and identifying data gaps in both *Anopheles* and *Aedes* species, and can be used to assist in decision making for deployment of the most appropriate tools.

Keywords: *Aedes aegypti, Aedes albopictus*

Wednesday 6 December 2017

10.45-12.15
Room D

S5: Free Paper I: Travel Awardees Presentation

Chairperson:

Jaranit Kaewkungwal

Vicente Belizario

Speakers

1. Viral Etiology of Community-Acquired Sepsis in Vietnam: Unraveling the Unknown by Next-generation Sequencing Analysis
   Anh Nguyen To
   Oxford University Clinical Research Unit, Vietnam

2. Migration process, vulnerability and information and communication channels among migrant workers at remote sites in the context of malaria elimination: a qualitative strand
   Aung Ye Naung Win
   Department of Medical Research, Myanmar

3. The Unexpected Stability of Malaria Elimination: Research Needs The Feasibility of Malaria Elimination In Eastern Indonesia
   Jontari Hutagalung
   Universitas Gadjah Mada, Indonesia

4. Therapeutic potential of lymphatic endothelial progenitors as alternative treatment for filarial lymphedema
   Anand Setty Balakrishnan
   Madurai Kamaraj University, Madurai, India

5. Changing epidemiology and antimicrobial resistance in *Vibrio cholerae*: findings of a decade from national AMR surveillance
   Nisha Rijal
   National Public Health Laboratory, Nepal

6. Development of Monoclonal Antibodies Against Dengue NS1 Peptides
   Erandi Munasinghe
   University of Kelaniya, Sri Lanka

7. Viral Etiology of Acute Febrile Diseases from Archived Specimens Collected between 2012 to 2017 in Indonesia
   Chairin Nisa Ma'Roef
   Eijkman Institute for Molecular Biology, Indonesia

VIRAL ETIOLOGY OF COMMUNITY-ACQUIRED SEPSIS IN VIETNAM: UNRAVELING THE UNKNOWN BY NEXT-GENERATION SEQUENCING ANALYSIS

Anh Nguyen To [1], Nhu Le Nguyen Truc [1], Hong Nguyen Thi Thu [1], Thanh Tran Tan [1], H. Rogier van Doorn [2], Direk Limmathurotsakul [3], Chau Nguyen Van Vinh [4], Eric Delwart [5], Guy Thwaites [2], Motiur Rahman [1], Thuy Le [1], Tan Le Van [1]

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Background: Community-acquired (CA) sepsis is a major public-health problem worldwide. Yet despite extensive laboratory diagnosis, the etiology remains unknown in >50% of the patients. Improving our knowledge of the causative agents is essential for improving disease burden. Methods: A deep-sequencing based viral metagenomics approach was employed to analyze 493 clinical samples (384 plasma, 92 pooled nasal- and throat swabs, 10 stools and 7 CSF) from 392 undiagnosed CA sepsis patients (children and adults) recruited from 6 hospitals cross Vietnam in 2014-2015. Sensitive specific PCRs were used to confirm deep sequencing results. Finding: 21 viruses were detected in 51/493 samples (including 8 viruses in 28 plasma samples), corresponding to a detection rate of 11% (44/392). The detected viruses included enteroviruses (n=14), hepatitis B virus (10), rhinovirus (5), rotavirus A (3), measles virus, respiratory syncytial virus, parainfluenza virus, adenovirus, hepatitis C virus, dengue virus, influenza A/B virus, parechovirus 1/6 (2 each), metapneumovirus, human immunodeficiency virus, coronavirus, WU-polyomavirus, saffold virus, salivirus and a recently discovered human pegivirus 2 (HPgV2) (1 each). HPgV2 was subsequently detected by PCR in 1.5% (5/409) of plasma samples from patients with chronic hepatitis C virus infection. Whole-genome phylogenetic analysis illustrated a close relatedness between the 5 Vietnamese HPgV2 and the others strains from the US and the UK. Conclusion: Multiple viral pathogens were detected by deep sequencing in 44/392 (11%) undiagnosed sepsis patients. Metagenomics can be a sensitive pan-pathogen assay for unbiased/sequence-independent detection of known/unknown pathogens in clinical samples. This is the first report of HPgV2 in Asia. The results warrant further active surveillance for novel pathogens in Asia where there is a high risk of emerging infections.

Keyword: Metagenomics, virus, undiagnosed-patients, sepsis, deep-sequencing

MIGRATION PROCESS, VULNERABILITY AND INFORMATION AND COMMUNICATION CHANNELS AMONG MIGRANT WORKERS AT REMOTE SITES IN THE CONTEXT OF MALARIA ELIMINATION: A QUALITATIVE STRAND

Aung Ye Naung Win [2], Aung Ye Naung Win [1], Thae Maung Maung [2], Khin Thet Wai [2], Tin Oo [2], Aung Thi [3], Rungrawee Tipmontree [4], Ngamphol Soonthornworasiri [1], Mondha Kengganpanich [5], Jaranit Kaewkungwal [1]

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Background: Migrant workers as large clusters in transition in Regional as well as in Myanmar economy pose as a big challenge to meet Myanmar's malaria elimination target, 2030 in remote areas. Still, there are gaps between the interventions by the National Malaria Control Program and the extent of utilization of these services by mobile/migrant populations. This paper examines the complex migration process, vulnerability and challenges for early diagnosis and treatment (EDAT) of malaria by diverse groups of mobile/migrant workers in remote sites of Shwegyin Township, Bago Region, Myanmar linking to interventions for malaria elimination.

Method: This qualitative study was done in remote areas of Shwegyin Township, Bago Region, Myanmar. There were two FGDs each for migrant workers engaged in gold panning and rubber tapping and one FGD for farming groups (n=50) and five participants involved in in-depth interviews (n=5).

Results: Mobility patterns of migrant workers were variable and unable to anticipate their duration of stay in the particular worksite. Familiarity to malaria did not facilitate their awareness to confirm suspected fever by RDT and its availability at RHCs and malaria volunteers. Rather, they had expressed their trust, reliance and confidence in unlicensed practitioners/quacks due to readiness and accessibility. Gaps existed to acquire EDAT from well-equipped and skilled basic health staff and volunteers. Moreover, artemisinin tablets were widely available at drug shops nearby. They also relied on pre-packed drugs for self-medication which was a challenging practice in the prevention of drug resistant malaria. Their less frequent or no contact with health staff or malaria volunteers for EDAT led to the lack of or inadequate knowledge that might have an impact on their treatment-seeking preferences.

Conclusions: Limited information, inadequate exposure and poor access to EDAT amongst migrant workers at various less stable work sites in remote areas are still an impediment for malaria elimination strategy of NMCP in Myanmar. Frequent visits of health staff and malaria volunteers and close contact with managers or team leaders of the migrant work sites in remote areas are desirable to channel adequate information related to malaria. This approach may improve treatment seeking practices at the public sector inclusive of malaria check-points.

Keyword: Malaria, migrant workers, EDAT, qualitative study, Myanmar, elimination

THE UNEXPECTED STABILITY OF MALARIA ELIMINATION: RESEARCH NEEDS THE FEASIBILITY OF MALARIA ELIMINATION IN EASTERN INDONESIA

Jontari Hutagalung [1]

Center for Tropical Medicine-Faculty of Medicine-Universitas Gadjah Mada

Background: Currently MoH Indonesia announced to have reached the pre-elimination stage by 2020 and to be free of malaria transmission by 2025. Unfortunately, lacking real data real prevalence and API from different assignment of malaria and detailed maps of the epidemiological distribution are needed. The research required to support these objectives is critically evaluated here.

Methods: A survey of 555 people enrolled in this study who were systematically selected from healthy population from five districts in eastern Indonesia. Data was collected by standard questionnaire, physical examination and laboratory tests. All protocols of assignment followed manufactures manual. Confirmed cases of malaria are positive by nPCR and microcopis test. Univariate and bivariate statistical analysis (Odds Ratios, α= 0.05 with 95% CI) were performed with the SPSS 16.0 software package.

Result(s): Among the 555 samples, there were 1.6% samples (9/555) by microscopic and 32.6% (181/555) by nPCR positive for malaria respectively. *P. vivax* was the dominating species. Not using bed nets was the most significant risk factors with malaria prevalence (OR= 2.34 with 95% CI= 1.98-4.83). Mapping spatial analysis indicated three distinguish significant clusters (13 cases/7.2%, 54 cases/29.9% and 87 cases/48.1%). All malaria clusters were found in low cases incidence (LCI) malaria as per the standard classification.

Conclusions: Malaria pre-elimination in eastern Indonesia can proceed strategically using new evidence based practices that provide more reliable results. Routine treatment to stop silent transmission, outbreak control efforts and improved laboratory surveillance are needed to effectively meet the goals of malaria pre-elimination in eastern Indonesia.

Keyword: New evidence based, malaria pre-elimination programme, eastern Indonesia

THERAPEUTIC POTENTIAL OF LYMPHATIC ENDOTHELIAL PROGENITORS AS ALTERNATIVE TREATMENT FOR FILARIAL LYMPHEDEMA

Anand Setty Balakrishnan

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Lymphatic Endothelial progenitor cells are circulating adult progenitor cells capable of differentiating into mature lymphatic endothelial cells. They play an essential role in fluid homeostasis and immune surveillance. In secondary lymphedemic condition, caused by lymphatic filariasis, the adaptive ability of lymphatic vasculature to form new lymphatic vessels is greatly compromised. Currently available treatment strategies involve either the administration of chemotherapeutic agents or the use of growth factor (VEGF-C) is encouraging and promising in human application. Mesenchymal Stem cells based therapeutic lymphatic neovascularization has been used for the treatment of lymphedema. Similarly, LEPCs based revascularization therapies are still lacking for the treatment of secondary lymphedemic complications caused by lymphatic filariasis. Subjects with these complications suffer from wound healing, endothelial repair and associated endothelial dysfunction. The objective of our study is to evaluate the functional properties of lymphatic endothelial progenitors isolated from peripheral blood mononuclear cells (PBMCs). PBMCs were isolated from 10ml of peripheral blood sample after obtaining an informed consent from the study subjects as per ICMR guidelines. Flow cytometry was used to enumerate CD34+ and VEGFR3+ cells. Gene expression analysis through RT-PCR revealed significant changes in the expression of Prox-1, VEGFR3 and Podoplanin in PBMCs obtained from lymphedema subjects. Serum angiogenic markers like Angiopoietins and Tie-2 shows significant differences compare to controls. Transwell migration, adhesion and matrigel assays were employed to evaluate the migratory potential in response to SDF-1α, adherence to fibronectin and tube forming ability respectively. All these functions are altered in lymphedema subjects compared to healthy individuals.

Keyword: Lymphatic Filariasis Lymphedema

CHANGING EPIDEMIOLOGY AND ANTIMICROBIAL RESISTANCE IN *VIBRIO CHOLERAE*: FINDINGS OF A DECADE FROM NATIONAL AMR SURVEILLANCE

Nisha Rijal [1], Jyoti Acharya [1], Shailaja Adhikari [1], Palpasa Kansakar [2], Bishnu Prasad Upadhaya [1], Supriya Sharma [3], Tankeshwar Acharya [4]

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Background: In Nepal, *Vibrio cholerae* cases occur annually either as sporadic or as outbreaks claiming the lives of many in rural areas. The study aims to analyze the changing epidemiology and antimicrobial susceptibility trend of 836 *V. cholerae* strains isolated or referred to National Public Health Laboratory(NPHL) over a period of 11 years (2006-2016).

Methods: Specimens of fresh stool /rectal swab were received from outbreak areas to NPHL following appropriate transport condition. Suspected isolates were identified following standard techniques and confirmed by serotyping. Antimicrobial susceptibility testing was performed following Kirby Baeur disc diffusion method.

Results: Of the 836 confirmed isolates,87% (728/836) were *V.cholerae* O1 Ogawa ,12% (106/836) were *V.cholerae* O1 Inaba and only 2 isolates were *V.cholerae* O1 Hikojima. In 2006 all the isolates were of Inaba serotype, followed by all 3 serotypes during 2007, switched to only ogawa 2008 onwards till 2015 where upon few cases of Inaba were again reported. Resistance to ampicillin decreased from 93% in 2006 to 18% by 2010 and again raised to 100% by 2016. Cotrimoxazole resistance remained at constant range (77-100%) Nalidixic acid resistance was 100% since 2006. Ciprofloxacin and tetracycline resistance emerged in 2007, reached a peak during 2010-2012 and declined to 0 by 2016. Susceptibility to Furazolidone has re-emerged. 50% of the isolates were Multi drug resistant.

Conclusion: With changing epidemiology and antibiogram of *V.cholerae* in Nepal, the present study reflects the importance of continous monitoring, which could be used by policy makers and health professionals for better management in outbreaks.

Keyword: *V.cholerae*, antimicrobial resistance, Nepal, Antibiotics

DEVELOPMENT OF MONOCLONAL ANTIBODIES AGAINST DENGUE NS1 PEPTIDES

Erandi Munasinghe [1], Dimitris Korbakis [2], Eleftherios P. Diamandis [2], N. V. Chandrasekharan [3], Maheshi Athapaththu [4], W. Abeywickreme [1]

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Synthetic peptides have recently become essential as antigens for antibody production. Peptide immunogenicity is a critical factor for inducing strong immune response for the production of desired antibodies. These antibodies play a vital role in development of immunoassays and as therapeutic antibodies. Dengue virus (DENV) Non Structural 1 (NS1) protein is an important target antigen in production of Monoclonal Antibodies (MAbs) for the detection of dengue (DEN) infection. The objective of this study is to develop a MAb against NS1 protein of DENV. In this study, four serotype specific synthetic peptides were designed from DENV NS1 region considering the sequence of Sri Lankan isolates, abundance of Cysteine residues, solubility and length of the peptides. These peptides were used to immunize four, six weeks old female Balb/c mice and fusions were carried out for the production of hybridoma clones. Time-resolved fluorescent-Enzyme linked immunosorbent assay was developed to analyse the antibody response to the peptides. A total number of 28 IgG secreting hybridoma clones out of 1830 growing clones produced DENV specific monoclonal antibodies. The above clones were tested with peptides DEN1, 2, 3 and 4 with appropriate positive and negative controls. According to the results, MAb from clone DP1C18 resulted from the fusion of DEN1 immunized mice, showed promising antibody response for all four DEN serotypes. Thus, in this study, a monoclonal antibody was produced which can capture all four serotypes of dengue virus and this antibody can be used for further development of immunoassays for the detection of dengue infection.

Keyword: Dengue-NS1, Monoclonal -antibodies, Peptide antigens.

VIRAL ETIOLOGY OF ACUTE FEBRILE DISEASES FROM ARCHIVED SPECIMENS COLLECTED BETWEEN 2012 TO 2017 IN INDONESIA

Chairin Nisa Ma'Roef [1], Frilasita Aisyah Yudhaputri [1], Ageng Wiyatno [1], Ungke Anto Jaya [1], Rama Dhenni [1], Araniy Fadhilah [1], Adewantari Kresno [1], Tina Kusumaningrum [1], I Made Artika [1], R. Tedjo Sasmono [1], Din Syafrudin [1], Bachti Alisjahbana [2], Dewi Megawati [3], Sotianingsih Haryanto [4], Khin Saw Myint [1], Corina Monagin [5], Ann Powers [6], Dodi Safari [1]

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Viral etiology responsible for acute febrile illness (AFI) in Indonesia is obscure and poorly understood. Our goal is to have comprehensive information on viral agents causing AFI of unknown origin in humans on specimens archived from previous studies submitted to the Emerging Virus Research Unit (EVRU), Eijkman Institute; Indonesia, during the period of 2012-2017. A total of 2820 archived specimens from patients with AFI of unknown origin collected from over 40 health agencies, were retrospectively evaluated for viral causes. Specimens were from in- and outpatients, emergency and intensive care units and also outbreak specimens. Dengue had been excluded from most banked specimens either by molecular assays or rapid diagnostic test. Majority of specimens were submitted from Jakarta, West Java, Bali, North Sulawesi, Central Sumatera, South Kalimantan, and Papua. Specimens were propagated in VERO cell line and tested in parallel for the presence of 9 viral families by RT-PCR Assay, including flaviviruses, alphaviruses, hantaviruses, herpesviruses, coronaviruses, paramyxoviruses, filoviruses, enteroviruses, and henipaviruses. Serological assays for arboviruses were also conducted on paired samples when convalescent specimen was available. Next generation sequencing was successfully carried out on unique and emerging viruses. Among 2122 (23.6% children) serum, CSF, respiratory specimens submitted with undiagnosed AFI, only 17.8% (n=379) was confirmed as viral infection; 18.9% was from children and 81% from adults. The most common endemic and emerging viruses discovered were chikungunya, cytomegalovirus, measles, and enteroviruses. Emerging viruses such as zika, west nile and enterovirus 71 were also documented. Successful detection depends on early collection of specimen and cold chain maintenance. The compiled data provides relevant information on the endemic and emerging viruses in Indonesia from 2012 to 2017. This also highlights the importance of gold standard assays like virus isolation in addition to the molecular screening and deep sequencing as a useful tool for virus characterization.

Keyword: Acute febrile illness (AFI), Indonesia, Viral infection

Wednesday 6 December 2017

13.45-15.15
Room A

S6: Melioidosis Updates

Chairpersons:

Yuvadee Mahakunkijcharoen

Pornpan Pumirat

Invited Speakers

1. Evolution of *Burkholderia pseudomallei* and its disease dynamics
   Claire Chewapreecha
   King Mongkut's University of Technology Thonburi

2. Predicted global distribution of *Burkholderia pseudomallei* and burden of melioidosis
   Direk Limmathurotsakul
   Faculty of Tropical Medicine, Mahidol University

3. Host genetic variation: a tool to illuminate the host response in melioidosis
   T. Eoin West
   University of Washington

4. Why are people with diabetes so susceptible to melioidosis?
   Susie Dunachie
   Nuffield Department of Medicine, University of Oxford

EVOLUTION OF *BURKHOLDERIA PSEUDOMALLEI* AND ITS DISEASE DYNAMICS

Claire Chewapreecha

Department of Medicine, University of Cambridge, UK; The Wellcome Trust Sanger Institute, Hinxton, UK; King Mongkut's University of Technology Thonburi, Bangkok, Thailand

Burkholderia pseudomallei is a soil organism found in many parts of the world. Through direct contact with contaminated soil or water, humans acquire infection and develop melioidosis. The bacterium has a large and variable genome. Genomic analyses have revealed geographically distinct population structure of the bacterium, as well as strain-to-strain variation in virulence in experimental models. To explore the geographic structure and cross-continental transmission patterns, whole genome sequencing was performed on 469 isolates from 30 countries collected over 79 years. Our data point to Australia as an early reservoir, with transmission to Southeast Asia followed by onward transmission to South Asia and East Asia which supported previous delineation of two major lineages that segregate between Australia and Asia. We next tested the hypothesis that some strains of *B. pseudomallei* are more likely to cause human infection than others using genome samples from a case-control collection collected from circumscribed area in northeast Thailand (totaling 325 clinical and 428 environmental isolates). While no large-scale genetic differences could be observed between clinical and environmental isolates, small-scale nucleotide variations could be identified in 387 "disease clusters", which accounted for 2.57% of *B. pseudomallei* pan-genome pooled from northeast Thailand. The ratio of non-synonymous to nonsynonymous substitutions rates (dN/dS) for most disease cluster fell below 1 (median = 0.522), arguing against positive selection and towards genetic drift with relaxation of purifying selection for most disease genes. Thus the bacterium may not be evolutionarily selected to cause a human disease. These findings contribute to our understanding of disease pathogenicity.

Keyword: Melioidosis, Bacterial genomics

PREDICTED GLOBAL DISTRIBUTION OF *BURKHOLDERIA PSEUDOMALLEI* AND BURDEN OF MELIOIDOSIS

Direk Limmathurotsakul [1]

[1] *Department of Tropical Hygiene, Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand.; Mahidol-Oxford Tropical Medicine Research Unit, Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand.; Centre for Tropica*

Burkholderia pseudomallei, a highly pathogenic bacterium that causes melioidosis, is commonly found in soil in Southeast Asia and Northern Australia. Melioidosis can be difficult to diagnose due to its diverse clinical manifestations and the inadequacy of conventional bacterial identification methods. The bacterium is intrinsically resistant to a wide range of antimicrobials, and treatment with ineffective antimicrobials may result in case fatality rates (CFRs) exceeding 70%. The importation of infected animals has, in the past, spread melioidosis to non-endemic areas. The global distribution of *B. pseudomallei* and the burden of melioidosis, however, remain poorly understood. Here, we map documented human and animal cases and the presence of environmental *B. pseudomallei* and combine this in a formal modelling framework to estimate the global burden of melioidosis. We estimate there to be 165,000 (95% credible interval 68,000–412,000) human melioidosis cases per year worldwide, from which 89,000 (36,000–227,000) people die. Our estimates suggest that melioidosis is severely underreported in the 45 countries in which it is known to be endemic and that melioidosis is probably endemic in a further 34 countries that have never reported the disease. The large numbers of estimated cases and fatalities emphasize that the disease warrants renewed attention from public health officials and policy makers.

Keyword: melioidosis; *pseudomallei*; mortality; global; burden

HOST GENETIC VARIATION: A TOOL TO ILLUMINATE THE HOST RESPONSE IN MELIOIDOSIS

Eoin West

Division of Pulmonary, Critical Care & Sleep Medicine, Department of Medicine, University of Washington, USA

Human genetic variation occurs in all populations. Studying the association of specific genetic variants with disease can provide insights into pivotal mechanisms that underlie disease susceptibility or outcomes. Therefore, analysis of human genetic variation in infectious diseases is a powerfully informative scientific tool. Much of our work to date has involved study of host genetic variation in cohorts of patients with melioidosis. We have performed candidate gene studies to identify innate immune genes that are associated with susceptibility to or outcome from melioidosis. As a limitation to candidate gene studies is that they depend on a priori scientific knowledge, we have also performed unbiased whole-exome sequencing of patients with extreme phenotypes of melioidosis to identify novel genetic determinants of outcome. The function of genes pinpointed in these clinical studies can then be studied using in vitro and in vivo models of infection. Together, these results can advance our understanding of host biology in human melioidosis and may accelerate the development of new host-targeted therapies to prevent or treat infection.

Keywords: Human genetic variation, Melioidosis

WHY ARE PEOPLE WITH DIABETES SO SUSCEPTIBLE TO MELIOIDOSIS?

Kemajittra Jenjaroen[1], Barbara Kronsteiner-Dobramys[2], Manutsanun Sumonwiriya[1], Panjaporn Chaichana[1], Suchintana Chumseng[1], Pitchayanant Ariyaprasert[1], Prapit Teparrukkul[3], Paul Klenerman[4], Direk Limmathurotsakul[1,2,5], Nicholas PJ Day[1,2], Susanna Dunachie[1,2,4]

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Melioidosis is a grossly under-diagnosed sepsis caused by the Gram negative bacterium *Burkholderia pseudomallei* (Bp), with a mortality of 40% in Southeast Asia and an estimated 89,000 annual deaths worldwide. Type 2 Diabetes (T2DM) increases susceptibility to melioidosis and other intracellular pathogens such as tuberculosis. 77% of people with diabetes mellitus now live in low and middle-income countries, and understanding the collision of this non-communicable disease with global infections is a public health priority. This presentation will give an overview of how T2DM affects the human immune response to intracellular pathogens such as *B. pseudomallei* and *Mycobacterium tuberculosis*, focussing on our own experimental work in Thailand and Oxford.

A prospective longitudinal clinical and immunological study of 300 culture-confirmed patients with acute melioidosis and 400 endemic control subjects with and without T2DM was established at Sunpasitthiprasong Hospital, Ubon Ratchathani, Northeast Thailand. Immune parameters were measured, then evaluated by survival and T2DM status. Survival was associated with a non-functioning TLR5 variant, a reduction in IL-10 and with enhanced T cell immunity, especially CD8+ T cells, to whole heat-killed Bp. People with T2DM had a lower magnitude of cellular responses to Bp during acute melioidosis. Immunophenotyping of peripheral blood mononuclear cells (PBMC) from patients with acute melioidosis revealed mature CX3CR1+ type I innate lymphoid cells (ILC) were linked to survival in non-diabetics, whilst higher humoral responses were associated with survival in T2DM.

Characterisation of correlates of protection associated with survival during acute melioidosis offers an essential foundation for designing effective vaccines and therapeutics. Understanding the mechanisms of the unique susceptibility in T2DM to intracellular pathogens is key to tackling the accelerating interaction between diabetes and global infection.

Keyword: Melioidosis, diabetes, immunology

Wednesday 6 December 2017

13.45-15.15
Room B

S7: Malaria Elimination Towards Eradication in 21st Century

Chairperson:

Nicholas Day

Kesinee Chotivanich

Invited Speakers

1. Ivermectin mass drug administration for malaria elimination in the Greater Mekong Subregion
   Kevin C. Kobylinski
   Armed Forces Research Institute of Medical Sciences

2. Faculty of Tropical Medicine Mahidol University collaborative projects on the malaria elimination/eradication
   Borimas Hanboonkunupakarn
   Faculty of Tropical Medicine Mahidol University

3. Transmission blocking activity of Ivermectin on artemisinin resistant parasites
   Kesinee Chotivanich
   Faculty of Tropical Medicine Mahidol University

   (No available abstract)

4. New genetic approaches to identify antimalarial targets and measure parasite fitness
   Marcus Lee
   Wellcome Trust Sanger Institute

IVERMECTIN MASS DRUG ADMINISTRATION FOR MALARIA ELIMINATION IN THE GREATER MEKONG SUBREGION

Kevin Kobylinski

Armed Forces Research Institute of Medical Sciences: Department of Entomology; Walter Reed Army Institute of Research: Entomology Branch

Novel vector control tools are urgently needed for the malaria elimination and artemisinin resistance containment efforts in the Greater Mekong Subregion (GMS). These vector control tools must target outdoor-feeding malaria vectors and integrate with current malaria control efforts. Ivermectin mass drug administration (MDA) has been shown to reduce the survivorship, population age structure, and *Plasmodium falciparum* sporozoite rate of wild *Anopheles gambiae* in Senegal, Liberia, and Burkina Faso. Laboratory data demonstrates that important GMS vectors *An. dirus*, *An. minimus*, *An. campestris*, and *An. sawadwongporni* are susceptible to ivermectin at human relevant concentrations. Ivermectin MDA would make treated humans lethal to GMS vectors regardless of mosquito feeding location or time, thus directly targeting outdoor malaria transmission. Ivermectin at mosquito sub-lethal concentrations are sporontocidal to *P. vivax* in *An. dirus* and *An. minimus*. Ivermectin MDA could integrate with antimalarial drug MDAs, targeting both human and vector reservoirs. Clinical trials in Thailand and Kenya have assessed the safety, tolerability, pharmacokinetic interaction, and mosquito-lethal efficacy of ivermectin and dihydroartemisinin-piperaquine. Ivermectin MDA affects numerous neglected tropical diseases (NTDs) such as lymphatic filariasis, scabies, lice, gnathostomiasis, and soil-transmitted helminths. These effects on NTDs are noticeable during ivermectin MDAs in Africa, therefore if ivermectin were combined with antimalarial MDAs this may improve MDA compliance. Ivermectin MDAs for malaria parasite transmission control are planned for the GMS. The above evidence suggests that ivermectin MDA may be effective at reducing *Plasmodium* transmission in the GMS and thus has a potential role in malaria elimination in the region.

Keyword: Ivermectin *Anopheles Plasmodium* Asia

FACULTY OF TROPICAL MEDICINE MAHIDOL UNIVERSITY COLLABORATIVE PROJECTS ON THE MALARIA ELIMINATION/ERADICATION

Borimas Hanboonkunupakarn

Faculty of Tropical Medicine, Mahidol University

Malaria eradication is a renewed global ambition of the 21st century, half a century after the failure of the first mission. There are at least 35 countries including Thailand targeting to be free from malaria by 2030, meaning all related challenges could be rectified. The recent emergence of artemisinin resistance in *P. falciparum* is the main obstacles for the malaria elimination in Greater Mekong regions. The Faculty of Tropical Medicine Mahidol University, affiliated with Oxford University and other international organizations has conducted medical and public health research to support the global malaria control programs to date. There are 10 ongoing such projects including phases I, II and III clinical trials and in-depth pharmacological studies on drug-to-drug interactions of antimalarial drugs. Studies on ways to improve interruption of malaria transmission with Ivermectin and RTS,S vaccine. A pilot project on mass drug chemoprophylaxis has been initiated in Savannakhet Province, Lao PDR. These collaborative works are to support malaria elimination programs in Asia and beyond.

Keyword: Malaria, elimination, artemisinin, resistance

TRANSMISSION BLOCKING ACTIVITY OF IVERMECTIN ON ARTEMISININ RESISTANT PARASITES

Kesinee Chotivanich

Faculty of Tropical Medicine Mahidol University

(No available abstract)

NEW GENETIC APPROACHES TO IDENTIFY ANTIMALARIAL TARGETS AND MEASURE PARASITE FITNESS

Marcus Lee [1], **Manuela Carrasquilla** [1], **Julian Rayner** [1]

[1] *Wellcome Trust Sanger Institute*

The repeated emergence of antimalarial resistance underscores the importance of identifying new drug targets, as well as understanding the genetic architecture of current resistance pathways and any associated fitness costs. We are developing approaches that combine CRISPR-Cas9 genome editing of *P. falciparum* and next-generation sequencing to accelerate the validation of potential new targets identified from in vitro resistance evolution, to profile compound mode of action, and to address the impact of resistance mutations on parasite fitness. Parasite fitness is likely to play an important role in driving the epidemiology of drug resistance, but competitive head-to-head assays comparing fitness between strains are typically limited in throughput, and suffer from issues when comparing growth between parasites in different wells. We have used CRISPR-Cas9 to insert unique barcodes into multiple parasite lines of different genetic backgrounds or resistance profiles, allowing these parasites to be mixed and grown in a single culture, with relatively growth rates in the presence and absence of drug accurately quantified by next-generation sequencing of the barcodes. These approaches will ultimately allow us to examine the effects of parasite background on both drug response and potential fitness costs associated with resistance mutations.

Keyword: Malaria, Drug resistance, CRISPR-Cas9

Wednesday 6 December 2017

13.45-15.15
Room C

S8: Investigating Neglected Infectious Diseases at the Interface between Ecology and Anthropology

Chairpersons:

Serge Morand

Paron Dekumyoy

Invited Speakers

1. Helminths in pigs: the impact of *Taenia solium* and *Taenia asiatica* in Asia
   Akira Ito
   Asahikawa Medical University

2. Life of a pig among the Karen: from raising to sacrifice
   Abigael Pesses
   IRASEC

3. Wild rodents as research model for studying ecology of infectious pathogens in Southeast Asia
   Kittipong Chaisiri
   Faculty of Tropical Medicine, Mahidol University

4. Health risks and rodent bushmeat consumption an central Thailand: preliminary results and emerging questions
   Michel de Garine Wichatitsky
   Kasetsart University

5. From paratisosis to sacrifice; symbiosis complex in hunting and livestock farming
   Stephane Rennesson
   IRASEC

HELMINTHS IN PIGS: THE IMPACT OF *TAENIA SOLIUM* AND *TAENIA ASIATICA* IN ASIA

Akira Ito

Department of Parasitology, Asahikawa Medical University, Japan

Taenia solium is potentially one of the most pathogenic helminths in humans and distributed in developing countries worldwide. Cysticerci mature into adult tapeworms exclusively in the human intestine after uncooked pork contaminated with cysticerci are eaten (definitive host). Pigs in rural or remote areas in developing countries are free roaming and scavengers to get accidental ingestion of eggs in human feces. Oncospheres in eggs hatch in the small intestine, invade into the intestinal tissue and differentiate into cysticerci in the whole body and survive for long term without symptoms (intermediate host). Intestinal taeniasis in humans is basically asymptomatic. Humans are unique and serve the definitive and intermediate host. So, the highest risk of disseminated neurocysticercosis (NCC) is the tapeworm carriers themselves. NCC, the most neglected tropical disease (NTD) or zoonotic disease (NZD) is suddenly confirmed by seizure attack. From human side, detection of tapeworm carriers for deworming is essential mission for prevention of NCC in the community. However, taeniasis is caused not only by *T. solium* but also by other species, *Taenia saginata* and *Taenia asiatica*. The latter two species are the sister species and do not cause cysticercosis in humans. Pigs are the main intermediate hosts of *T. solium* and *T. asiatica.* The present situation of these human *Taenia* tapeworm infections in humans (three species) and in pigs (two species) in Asia will be overviewed to point out the difficulty in control of NCC in humans with traditional life style in Asia and the importance of One Health.

Keyword: taeniasis, cysticercosis, pigs, humans, Asia

LIFE OF A PIG AMONG THE KAREN: FROM RAISING TO SACRIFICE

Abigaël Pesses

Institute of Research on Contemporary Southeast Asia (IRASEC)

In Karen society, like in many other upland and lowland rice grower's societies of mainland Southeast Asia, rearing and sacrificing animals is part of a "ritual economy" engaging humans and nonhumans in the process of social life. The possession of livestock – pigs, buffaloes, chicken and cattle -, successful rice crop and numerous descendants, indicate the wealth of the people and contribute to enhance their prestige. In Karen society, the sacrifice of pigs plays a crucial role in the consolidation of human health (prevention and curing) and the maintenance of the socio-political order in connection with territorial spirits and ancestors. Considered as the gatekeepers of the social and moral order, these spirits need to be fed by sacrifice at important moments of the annual agricultural calendar as well as certain crucial steps of human life. If the sacrifice itself is a male prerogative, women raise and feed pigs all along their life. This presentation proposes to explore the intimate relation between men, women, spirits and pigs, looking at how their destiny are intertwined.

Keyword Pig, Karen, sacrifice, Southeast Asia, ritual

WILD RODENTS AS RESEARCH MODEL FOR STUDYING ECOLOGY OF INFECTIOUS PATHOGENS IN SOUTHEAST ASIA

Kittipong Chaisiri [1], **Serge Morand** [2]

[1] Department of Helminthology, Faculty of Tropical Medicine, Mahidol University, Thailand , [2] CNRS ISEM-CIRAD ASTRE, Faculty of Veterinary Technology, Kasetsart University, Bangkok 10220, Thailand

Rodents are certainly recognized as pests in human community, causing significant losses to agricultural products and household food. They also play an important role as reservoir of several pathogens of medical importance. Some rodent species in subfamily Murinae (Old World rats and mice) are hazardous as they can amplify pathogens from the environment and act as reservoirs of several neglected diseases. Over the past ten years, better knowledge on taxonomy, diversity and habitat preference of wild murine rodents in Southeast Asian mainland as well as pathogens carried by the rodents has been extensively revealed. Here, habitat associations with potential rodent-borne pathogens are highlighted and discussed. There were also evidences showing that human-modified habitats affected pathogen diversity by reducing species richness of both micro- and macro-parasite in rodents. The oriental house rat, *Rattus tanezumi* has been reported as habitat generalist species and highly abundant in this region. A number of pathogens were also detected from this rodent species. Therefore, *R. tanezumi* can be hypothesized as the 'bridge species' that links rodent-parasite communities from one habitat to the others, and potentially play important role in pathogen transmission to other rodent hosts or even humans and domestic animals. Although we are better understanding in ecology of some rodent-borne diseases, but epidemiological evidence to show the possible infection route and rate of pathogen transmission from rodents to human is still largely limited. Risk human population should be identified such as the people that live in a high rodent density area where human and rodent are really in close contact; or people who hunt, prepare or consume rodents as bush meat diet. Further research projects should be launched to investigate those risk populations to assess level of exposure and infection status in the communities.

Keywords: rodents, pathogen, rodent-borne disease, ecology, Southeast Asia

HEALTH RISKS AND RODENT BUSHMEAT CONSUMPTION IN CENTRAL THAILAND: PRELIMINARY RESULTS AND EMERGING QUESTIONS

Michel de Garine-Wichatitsky[1,2,3,*], Karnrawee Sratongno[1], Waraphon Pimpapai[1], Phitsanu Tulayakul[1], Serge Morand [1], Chalermkiat Saengthonpinit[1]

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Over the past decades, major concerns about the ongoing "bushmeat crisis" have been raised, especially in tropical forests of Asia and Africa. Initially focused mostly on environmental considerations and the conservation of hunted endangered species, the concerns have also grown regarding public and veterinary health risks associated with bushmeat, in the context of emerging diseases pandemics associated with wildlife. However, eating "wild food" remains a major component of man-nature relationships for numerous societies, with important cultural and symbolic values, often highly praised by local and urban consumers alike, and regarded as healthy food or even traditional remedies. Rodent meat consumption is fairly common in Thailand, related to traditions and culture, as well as social and economic status of households. We investigated the perceptions of rat meat by producers and consumers, including health risks, two rat species, *Bandicota indica* and *Rattus tanezumi*, sold at shops located along the major roads of the central provinces of Thailand. Samples collected from the two species were analysed at the laboratory for the following health hazards: bacterial contamination (total, *E. coli*, Salmonella), antibiotic resistance of *Salmonella spp* strains isolated, and concentrations of heavy metals (lead and cadmium). We report on the preliminary results of this survey and reflect on the practical and ethical implications raised regarding food safety, communication on health risks with bush-meat consumers and producers, pest control and biodiversity conservation in Thailand, and in SE Asia.

Keyword: bushmeat crisis

FROM PARATISOSIS TO SACRIFICE; SYMBIOSIS COMPLEX IN HUNTING AND LIVESTOCK FARMING

Stéphane Rennesson

IRASEC

On the basis of the different talks of the panel, I will try to assess up to what point the challenges posed by infectious diseases can be highlighted by the articulated perspective brought by various disciplines across the great divide between hard and social sciences. How ecology and anthropology for instance can work together on the deciphering of transformation cycles linking together micro organisms, animals, humans, social organisation, environmental management, technology, ritual activity and cosmolgies?

Wednesday 6 December 2017

13.45-15.15
Room D

S9: Turbo Talk I *(Plase find abstracts in the Poster Presentations book)*

Chairpersons:

John Adams

Srivicha Krudsood

Speakers

1. Biology of Zika Virus Infection in Human Skin Cells
   Rodolphe Hamel
   IRD, Faculty of Tropical Medicine, Mahidol University

↑ *(p. 20 Poster)*

2. C ross-neutralizing antibodies in Hand, Foot and Mouth Disease patients
   Nguyet Lam
   Oxford University Clinical Research Unit, Ho Chi Minh City, Vietnam

↑ *(p. 30 Poster)*

3. Assessment of factors associated with dengue mortality in Fiji, 2014: A case control study
   Aneley Getahun
   Fiji National University

↑ *(p. 9 Poster)*

4. Dengue and zika viral infections in patients with acute febrile illness in Northeastern Thailand
   Sirinart Aromseree
   Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand

↑ *(p. 24 Poster)*

5. The seroprevalence of neutralizing antibody against dengue virus in healthcare workers
   Warunee Punpanich Vandepitte
   Queen Sirikit National Institute of Child Health, Bangkok, College of Medicine, Rangsit University

↑ *(p. 10 Poster)*

6. Antiviral activity of bismuth derived chemical compound against dengue virus serotype 2
   Babu Ramanathan
   Department of Biological Sciences, Sunway University, Malaysia

↑ *(p. 11 Poster)*

7. Evolution of Coxsackievirus A6: an emerging pathogen of hand, foot and mouth disease
   Nhu Le Nguyen Truc
   Oxford University Clinical Research Unit

↑ *(p. 31 Poster)*

8. Development of the cost and time saving zika virus detection method by Real Time Rt-Pcr in response for 2016 outbreak in Thailand
   Pattara Wongjaroen
   Ministry of Public Health, Thailand

↑ *(p. 21 Poster)*

10.13.45-15.15
Room D

S9: Turbo Talk I *(Plase find abstracts in the Poster Presentations book)* (*Continued*)

Speakers

9. Immunological and entomological indices to evaluate the risk of dengue transmission in northeastern Thailand
   Benedicte Fustec
   Universite de Montpellier, France

↑*(p. 15 Poster)*

10. Dengue seasonal variation and prediction model in Khon Kaen Province, Thailand.
    Thipruethai Phanitchat
    Khon Kaen University, Khon Kaen, Thailand

↑*(p. 16 Poster)*

11. Knowledge and perception of malaria prevention measures among Tanzanian students and factors, associated with the ignorance of bed net use
    Zanda Bochkaeva
    University of Dodoma, Tanzania

↑*(p. 74 Poster)*

12. A longitudinal cohort study of infant anemia in a marginalized population at the Thailand-Myanmar border: onset, risk factors and recovery
    Hellen Barsosio
    KEMRI-Wellcome Trust

↑*(p. 115 Poster)*

13. Effectiveness of fipronil as a systemic control agent against Xenopsylla cheopis (*Siphonaptera: Pulicidae*) in Madagascar
    Dora Murielle Rajonhson
    Faculty of Tropical Medicine, Mahidol University

↑*(p. 103 Poster)*

14. Seroprevalence of syphilis, cytomegalovirus and rubella infections in waste-blood samples
    Nyein Ko Hein
    Defence Services Medical Research Centre, Myanmar

↑*(p. 33 Poster)*

15. Health Problems Among Thai Trekkers In Thailand: A Prospective Study
    Nujareenart Kuhakasemsin
    Faculty of Tropical Medicine, Mahidol University

↑*(p. 113 Poster)*

Wednesday 6 December 2017

15.45-17.15
Room A

S10: Antimicrobial Resistance

Chairpersons:

Direk Limmathurotsakul

Ben Cooper

Invited speakers

1. Epidemiology and Burden of Multidrug-resistant Bacterial Infection in a Developing Country
   Cherry Lim
   Mahidol-Oxford Tropical Research Unit

2. Whole genome sequencing of ESBL-producing *E. coli* isolated from patients, farm waste and canals in Thailand
   Chakkaphan Runcharoen
   Faculty of Tropical Medicine, Mahidol University

3. Impact of a multimodal hand hygiene improvement intervention in a 1000-bed hospital in NE Thailand: a stepped wedge clustered randomized controlled trial
   Maliwan Hongsuwan
   Mahidol-Oxford Tropical Research Unit

4. A spatial and temporal model for antibiotic resistance
   Mathupanee Oonsivilai
   Mahidol-Oxford Tropical Medicine Research Unit

5. Discriminating bacterial from viral causes of fever using the C-reactive protein (CRP): findings from a community-based clinical trial in Southeast Asia
   Thomas Althaus
   Mahidol-Oxford Tropical Medicine Research Unit

15.45-17.15
Room A

S10: Antimicrobial resistance *(Continued)*

Invited speakers

6. The impact of point of care CRP testing on antibiotic prescriptions and future studies in routing care
   Rachel Greer
   Mahidol-Oxford Tropical Medicine Research Unit

7. Model-based analytics for understanding the epidemiology and trends in multi-drug resistant bacteria in hospitalized patients in Thailand
   Jiraboon Tosanguan
   Mahidol-Oxford Tropical Medicine Research Unit

8. Surveillance for antimicrobial resistant *Neisseria Gonorrhea* globally and in Thailand
   Pachara Sirivongrangson and **Eileen F. Dunne**
   Thailand MOPH - U.S. CDC Collaboration

EPIDEMIOLOGY AND BURDEN OF MULTIDRUG-RESISTANT BACTERIAL INFECTION IN A DEVELOPING COUNTRY

Cherry Lim[1], Emi Takahashi[1], Maliwan Hongsuwan[1], Vanaporn Wuthiekanun[1], Visanu Thamlikitkul[2], Soawapak Hinjoy[3], Nicholas PJ Day[1,4], Sharon J Peacock[1,5,6], Direk Limmathurotsakul[1,4,7]

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[3]Bureau of Epidemiology, Department of Disease Control, Ministry of Public Health, Nonthaburi, Thailand
[4]Centre for Tropical Medicine and Global Health, Nuffield Department of Medicine, University of Oxford, Oxford, United Kingdom [5]London School of Hygiene and Tropical Medicine, London, United Kingdom
[6]University of Cambridge, Addenbrooke's Hospital, Cambridge, United Kingdom
[7]Department of Tropical Hygiene, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

Little is known about the excess mortality caused by multidrug-resistant (MDR) bacterial infection in low- and middle-income countries (LMICs). We retrospectively obtained microbiology laboratory and hospital databases of nine public hospitals in northeast Thailand from 2004 to 2010, and linked these with the national death registry to obtain the 30-day mortality outcome. The 30-day mortality in those with MDR community-acquired bacteraemia, healthcare-associated bacteraemia, and hospital-acquired bacteraemia were 35% (549/1555), 49% (247/500), and 53% (640/1198), respectively. We estimate that 19,122 of 45,209 (43%) deaths in patients with hospital-acquired infection due to MDR bacteria in Thailand in 2010 represented excess mortality caused by MDR. We demonstrate that national statistics on the epidemiology and burden of MDR in LMICs could be improved by integrating information from readily available databases. The prevalence and mortality attributable to MDR in Thailand are high. This is likely to reflect the situation in other LMICs.

Keyword: Antimicrobial resistant; bacteraemia; epidemiology; global health

WHOLE GENOME SEQUENCING OF ESBL-PRODUCING *E. COLI* ISOLATED FROM PATIENTS, FARM WASTE AND CANALS IN THAILAND

Chakkaphan Runcharoen[1], Kathy E. Raven[2], Sandra Reuter[2], Teemu Kallonen[4], Suporn Paksanont[1], Jeeranan Thammachote[3], Suthatip Anun[3], Beth Blane[2], Julian Parkhill[4], Sharon J. Peacock[1,2,4,5], Narisara Chantratita[1]

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[2] University of Cambridge, Department of Medicine, Box 157 Addenbrooke's Hospital, Hills Road, Cambridge CB2 0QQ, United Kingdom;
[3] Division of Clinical Microbiology, Medical Technology Department, Bhuddhasothon Hospital, Chachoengsao, 24000, Thailand;
[4] The Wellcome Trust Sanger Institute, Wellcome Genome Campus, Hinxton, Cambridge CB10 1SA, United Kingdom;
[5] London School of Hygiene and Tropical Medicine, London, WC1E 7HT, United Kingdom

Tackling multidrug-resistant *Escherichia coli* requires evidence from One Health studies that capture numerous potential reservoirs in circumscribed geographic areas. We conducted a survey of extended β-lactamase (ESBL)-producing *E. coli* isolated from patients, canals and livestock wastewater in eastern Thailand between 2014 and 2015, and analyzed isolates using whole genome sequencing. The bacterial collection of 149 isolates consisted of 84 isolates from a single hospital and 65 from the hospital sewer, canals and farm wastewater within a 20 km radius. *E. coli* ST131 predominated the clinical collection (28.6%), but was uncommon in the environment. Genome-based comparison of E. coli from infected patients and their immediate environment indicated low genetic similarity overall between the two, although three clinical-environmental isolate pairs differed by <5 single nucleotide polymorphisms. Thai *E. coli* isolates were dispersed throughout a phylogenetic tree containing a global *E. coli* collection. All Thai ESBL-positive *E. coli* isolates were multidrug resistant, including high rates of resistance to tobramycin (77.2%), gentamicin (77.2%), ciprofloxacin (67.8%) and trimethoprim (68.5%). ESBL was encoded by six different CTX-M elements and SHV-12. Three isolates from clinical samples (n=2) or a hospital sewer (n=1) were resistant to the carbapenem drugs (encoded by NDM-1, NDM-5 or GES-5), and three isolates (clinical (n=1) and canal water (n=2)) were resistant to colistin (encoded by mcr-1); no isolates were resistant to both carbapenems and colistin. Tackling ESBL-producing *E. coli* in this setting will be challenging based on widespread distribution, but the low prevalence of resistance to carbapenems and colistin suggests that efforts are now required to prevent these from becoming ubiquitous.

Keyword: *Escherichia coli*, ESBL, genome, sequence, phylogeny

IMPACT OF A MULTIMODAL HAND HYGIENE IMPROVEMENT INTERVENTION IN A 1000-BED HOSPITAL IN NE THAILAND: A STEPPED WEDGE CLUSTERED RANDOMIZED CONTROLLED TRIAL

Maliwan Hongsuwan [1], Maliwan Hongsuwan [1], Nantasit Luangasanatip [2], Direk Limmathurotsakul [3], Ben S. Cooper [4]

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Introduction: Improving hand hygiene (HH) compliance amongst healthcare workers (HCWs) is one of the simplest and most effective measures for preventing hospital-acquired infections (HAIs). However, only a few studies have evaluated the effectiveness of interventions for improving HH compliance using strong study designs, and almost all of these have been in high income countries.

Objectives: To evaluate the impact of a multimodal hand hygiene improvement strategy on directly observed hand hygiene compliance. Design: Prospective stepped wedge randomised controlled trial using 58 in-patient hospital wards (the study clusters) in a 1000-bed hospital located in Northeast Thailand. All wards received the intervention but the timing of the intervention in each ward was randomly selected using a computer generated sequence.

Intervention: The intervention was adapted from The World Health Organization's Hand Hygiene Improvement Strategy including five components with the aim of inducing behavioural and cultural change in relation to hand hygiene. A novel feature of the intervention is that staff on each ward were asked to actively decide how best to implement each of the five components of the WHO strategy.

Results: The intervention was associated with small increases in hand hygiene compliance (OR 1.12; 95% CI 1.01 to 1.24, p = 0.027), though lack of adherence to the intervention was a major problem. Larger improvements were seen in some units (obstetrics and gynecology: OR 3.96; 95% CI 1.88 to 8.31, p < 0.001) and for some types of opportunities (before patient contact: OR 1.72; 95% CI 1.32 to 2.25, p < 0.001).

Conclusion: The findings show that improvements in hygiene are possible, but multiple organizational factors need to be addressed to achieve acceptable hand hygiene levels in this setting.

Keyword: Hand hygiene, hospital-acquired infections

A SPATIAL AND TEMPORAL MODEL FOR ANTIBIOTIC RESISTANCE

Mathupanee Oonsivilai, Ben Cooper

Mahidol-Oxford Tropical Medicine Research Unit

Antibiotic resistance is amongst the world's most important public health problems: it threatens the safety of patients that undergo medical procedures, is associated with worse patient outcomes, and increases economic costs of treatment. Much research has been done to model the transmission dynamics of resistance, but existing models often struggle to sufficiently explain coexistence between antibiotic-sensitive and resistant phenotypes and our current understanding of how antibiotic usage patterns affect these is limited. A potentially important limitation of most models of spread of antibiotic resistance in the community is that they overlook spatial and temporal clustering of antibiotic treatment. We aimed to investigate the impact of spatial and temporal correlation in patterns of antibiotic usage on the spread and coexistence of susceptible and resistant bacteria strains using a simple model. We developed a spatial model for a bacterial pathogen following susceptible-infected-susceptible (SIS) dynamics. The model allows for two strains of this pathogen, one fully sensitive to antibiotics and one fully resistant. We use the model to explore how changing both the frequency of antibiotic use and the extent of spatial and temporal clustering affect the system dynamics and stability. We explore the sensitivity of our results to assumed contact patterns, comparing models with only local contacts between individuals, fully mass action models, and models with small-world like connection topologies. We argue that our simulator can help us better understand how antibiotics select for resistant phenotypes, while also providing a framework for thinking about potential interventions to combat the spread of resistance.

Keyword: antibiotics, resistance, spatial

DISCRIMINATING BACTERIAL FROM VIRAL CAUSES OF FEVER USING THE C-REACTIVE PROTEIN (CRP): FINDINGS FROM A COMMUNITY-BASED CLINICAL TRIAL IN SOUTHEAST ASIA

Thomas Althaus [1], Rachel Greer [1], Nick Day [1], Nick White [1], Frank Smithuis [2], NiNi Tun [3], Joshua Cohen [3], Myo Maung Maung Swe [3], James Heaton [3], Stuart Blacksell [1], Janjira Thaipadungpanit [4], Direk Limmathurotsakul [1], Tri Wangrangsimakul [1], Kyaw Soe [3], Narisara Chantratita [5], Sabine Dittrich [6], Khin Yupar Soe [7], Pieter Smit [8], Myo Nanda Aung [9], Kyi Kyi Nyein Win [9], Han Win [9], Clare Ling [10], Yoel Lubell [1]

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Investigating the causes of febrile illnesses is essential to inform up to date empirical treatment guidelines, as clinical diagnosis is unreliable because of overlapping presentations [1]. Health workers in most resource poor settings rely on patient history with or without physical examination findings for fever management, and even in well-resourced research contexts approximately 50% of the aetiologies remain unknown, despite extensive microbiological investigations [2-5]. Consequently, clinicians do not have access to updated information on local epidemiology to guide antibiotic prescription [1]. This problem is worse in the community context, where such data and human capacity are even more scarce and patient follow-up is often more challenging, worsening the consequences of missing a treatable infection [6]. We present the findings of a multi-site clinical trial in primary care investigating the causes of acute fever among children and adults from the community and the impact of a C-reactive protein (CRP) point-of-care test (POCT) on antibiotic prescription. Samples were collected from 2,400 children and adults from northern Thailand and Yangon suburbs, Myanmar, during a full calendar year. We tested for a broad range of pathogens by multiplex real-time PCR using the TaqManÒ array card (TAC) on both blood and nasopharyngeal samples. In addition, we serologically screened for melioidosis using ELISA and cultured throat swabs from patients presenting with a sore throat, specifically looking for group A streptococcus and determining the antibiotic susceptibility to these isolates. We evaluated the performance of C-reactive protein (CRP) POCT in differentiating bacterial from viral aetiologies, and provide evidence for its use in the tropical primary care setting.

Keyword: C-reactive protein Point-of-care testing Fever Bacterial infections

THE IMPACT OF POINT OF CARE CRP TESTING ON ANTIBIOTIC PRESCRIPTIONS AND FUTURE STUDIES IN ROUTINE CARE

Rachel Greer [1], Thomas Althaus [1], Supalert Nedsuwan [2], Daranee Intralawan [2], Myo Maung Maung Swe [3], Tri Wangrangsimakul [1], Marco J Haenssgen [1], Nutcha Charoenboon [4], Sabine Dittrich [5], Stuart Blacksell [1], Janjira Thaipadungpanit [4], Hlaing Myat Thu [6], Han Win [6], Pieter Smit [4], James Heaton [3], Mavuto Mukaka [1], Joshua Cohen [2], Nithima Sumpradit [7], Myo Nanda Aung [6], Kyi Kyi Nyein Win [8], NiNi Tun [3], Nicholas White [1], Nicholas Day [1], Frank Smithuis [3], Yoel Lubell [1]

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Antimicrobial resistance (AMR) is an increasing threat to global health. The World Health Organisation describe AMR as a 'burgeoning and often neglected problem' in the South-East Asia Region. Overuse and misuse of antibiotics has been linked to the development of AMR. This has led to various strategies to tackle AMR and target antimicrobial use. One such strategy is the use of biomarkers of infection to guide antibiotic prescriptions. C-reactive protein (CRP) is one of the few biomarkers available for use in primary care, where the majority of antibiotics are prescribed. A multi-site clinical trial was conducted in Thailand and Myanmar investigating the impact of CRP testing on antibiotic prescription in febrile patients attending primary care units. 2,410 children and adults were individually randomised into three arms; two intervention arms with CRP cut offs of 20mg/L and 40mg/L and a control arm. The interim analysis revealed a significant reduction in antibiotic prescriptions on day 0 for children in Thailand (49% controls, 32% CRP groups, OR 0.46 [0.25-0.87]) but a non-significant reduction in adults (39% controls, 31% CRP groups, OR 0.72 [0.43-1.2]). While in Myanmar there was a significant reduction in antibiotic prescriptions in adults (45.7% controls, 34.4% CRP groups, OR 0.61 [0.36-1.03]) but no difference in children (34.9% controls, 37.7% CRP groups, OR 1.11 [0.71-1.70]). This presentation of our final results will focus on the impact of CRP testing on antibiotic prescriptions and patient outcomes, as well as discussing healthcare workers' opinions on CRP testing.

Keyword: Antimicrobial resistance, biomarkers, primary care

MODEL-BASED ANALYTICS FOR UNDERSTANDING THE EPIDEMIOLOGY AND TRENDS IN MULTI-DRUG RESISTANT BACTERIA IN HOSPITALIZED PATIENTS IN THAILAND

Jiraboon Tosanguan [1], Esther Van Kleef [2], Maliwan Hongsuwan [1], Cherry Lim [1], Direk Limmathurotsakul [1], Ben Cooper [1]

[1] Mahidol-Oxford Tropical Medicine Research Unit, [2] Mahidol-Oxford Tropical Medicine Research Unit; Modelling and Economics Unit, National Infection Service, Public Health England, UK; Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, the Netherlands

Introduction & Objectives Antimicrobial resistance (AMR) is a major public health issue. In Thailand, 19,000 annual deaths are estimated to result from multidrug-resistant bacterial infections in hospitalised patients. In terms of the dissemination of clinically significant multidrug-resistant bacteria, major uncertainties exist about the relative importance of nosocomial transmission versus selection of pre-existing strains as a result of antibiotic therapy. We aimed to analyse a large volume of routinely collected hospital data from Northeast Thailand to determine the relative importance of these processes for different pathogens. Methods A population-based transmission model was developed to describe the spread of sensitive and resistant strains of bacteria within a hospital, incorporating both selection and transmission processes. Maximum likelihood estimation was used to fit models to bacteraemia data (years 2004 – 2010) from nine provincial hospitals in Northeastern Thailand for four organisms (*Escherichia coli* (EC), *Acinetobacter spp.* (AS), *Klebsiella pneumoniae* (KP), and *Staphylococcus aureus* (SA)). Results Analysis with the dynamic model indicated that both force of infection and selection periods varied between the species: the Gram-negative bacteria generally had lower forces of infection and shorter selection periods than *Staphylococcus aureus* suggesting that selection played a more dominant role. Over time, there was evidence of an increasing trend of carriage of resistant bacteria at the time of hospital admission. Models with both selection and transmission components gave better fits to the AS and SA data compared to models with just selection or just transmission. Conclusions This study has demonstrated the utility of routine hospital surveillance data and a novel analytic approach for making inferences about the drivers of the increasing prevalence of multidrug-resistant bacteria, and has highlighted important differences between bacterial species. These findings could potentially be used for informing future studies to evaluate the impact of interventions to reduce the burden of AMR.

Keyword: Antimicrobial Resistance, Infectious Disease Modelling

SURVEILLANCE FOR ANTIMICROBIAL RESISTANT (AMR) NEISSERIA GONORRHEA GLOBALLY AND IN THAILAND

Pachara Sirivongrangson [2], **Eileen Dunne** [1]

[1] *US CDC Collaboration* , [2] *Thailand Ministry of Public Health*

Neisseria gonorrhea (NG) infection is an important global public health threat, and emergence of antimicrobial resistance could hamper control efforts. In 2012, the World Health Organization (WHO) reported an estimated 78 million people were infected with NG around the world, and 11.4 million people in the WHO South-East Asian region. Strengthening NG AMR monitoring is important to provide valid and comparable data globally, which can be used to inform treatment practices, but also can be used to detect emergent resistance early. Because of the variability of methodologies for AMR NG surveillance, global AMR data are often not comparable. The Thailand Enhanced Gonococcal Antimicrobial Surveillance Programme (EGASP) was established by WHO in collaboration with the Thailand Ministry of Public Heath, and the Centers for Disease Control and Prevention, to strengthen the existing gonococcal antimicrobial resistance monitoring by augmenting the collection of clinical and behavioral information, and utilizing standardized protocols for data collection and laboratory testing. Antimicrobial susceptibility testing of NG isolates is sytematic and utilizes Etest. The capacity of participating laboratories to perform NG culture and AMR testing is improved through training and internal and external laboratory quality assurance systems. The experience in the establishing this surveillance activity informs expansion of EGASP to other countries and settings. In this session we will provide an overview of global surveillance for AMR NG and Thailand EGASP.

Keyword: AMR *Neisseria gonorrhea*, Surveillance, Thailand

Wednesday 6 December 2017

15.45-17.15
Room B

S11: Free Paper II: Tropical Medicine I

Chairpersons:

Srisin Khusmith

Poom Adisakwattana

Speakers:

1. Different Mode of Induction of Galectin-9 and Osteopontin In THP-1 Cells Upon Dengue Virus Infection
   Toshio Hattori
   KIBI International University

2. Incidence of Traveler's Diarrhea Among Adult Foreign Travelers in Thailand: A Prospective Study
   Chollasap Sharma
   Faculty of Tropical Medicine, Mahidol University

3. SITE 1 protease (S1P) inhibitor, PF-429242 suppress dengue virus propagation *in vitro*
   Leo Uchida
   Nagasaki University

4. The Characterisation of B Cell Epitopes and The Prediction of three Dimensional Ns1 Protein structure of Japanese Encephalitis virus
   Wipa Tangkananond
   Thammasat University

5. Immunopathological study of scrub typhus in rhesus macaques following intradermal inoculation of *Orientia tsutsugamushi* Karp and Gilliam strains
   Piyanate Sunyakumthorn
   Armed Forces Research Institute of Medical Sciences

6. How the Schistosomiasis Control Initiative tracks value for money across sub-Saharan African national preventive chemotherapy programmes for schistosomiasis
   Roya Karimnia
   Imperial College London

7. Incidence and Risk Factors of *Opisthorchis viverrini* Infection in a Rural Area of Central Thailand: Mixed-method Approach
   Saruttaya Wongsuwanphon
   Phramongkutklao College of Medicine

DIFFERENT MODE OF INDUCTION OF GALECTIN-9 AND OSTEOPONTIN IN THP-1 CELLS UPON DENGUE VIRUS INFECTION

Toshio Hattori [1], Dyshelly Nurkartika Pascapunama [2], Isolde C Dapat [2], Haorile Chagan-Yasutan [1], Shinichi Egawa [2]

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Introduction: Matricellular proteins (MCPs) play essential roles for dynamisms of pathological changes in infectious diseases. We have previously clarified both osteopontin (OPN) and galectin-9 (Gal-9) were correlated with the severity of the dengue patients. Gal-9 levels were higher in dengue hemorrhagic fever patients than dengue fever patients (J Clin. Virol 2013). The elevated OPN levels were involved in coagulopathy (Thromb. Res 2014). To better understand their roles, we have observed their induction in THP-1 (human monocytic cell line) cells infected with dengue virus (DENV) in vitro.

Results: Different dosages of DENV-3 (MOI 0.01, 0.03 and 0.1) were infected with THP-1 cells at varying time points (Day 1- 3). Results showed augmentation of gal-9 levels in the supernatant, reduction of gal-9 levels in the cells and decreased expression of LGALS9 mRNA, while DENV-3 mRNA copies for all three doses remained stable. The results implicated gal-9 as a potential DAMP (IJMS, 2017) and that gal-9 could limit further viral replication. On the contrary THP-1 constitutively expressed OPN mRNA which was enhanced by DENV-3 infection. Brefelamide and its derivative isolated from slime mold fruiting bodies suppressed OPN production in DENV-3 infected THP-1 cells. The effective dosages of these compounds had no effect on uninfected cells. (Front. Microbiol. 2017).

Discussion: These results indicate that monocyte/macrophages are the source of MCPs in infected individual and the different systems were operating in induction. Gal-9 may be able to limit virus replication in the first line. Brefelamide may have therapeutic effects in preventing inflammation and coagulopathy caused by OPN upregulation.

Keyword: Galectin-9, Osteopontin, Dengue virus, THP-1

INCIDENCE OF TRAVELER'S DIARRHEA AMONG ADULT FOREIGN TRAVELERS IN THAILAND: A PROSPECTIVE STUDY

Chollasap Sharma [1], Kittiyod Poovorawan [1], Watcharapong Piyaphanee [1], Ngamphol Soonthornworasiri [2], Piyada Angsuwatcharakon [3], Weerapong Phumratanaprapin [1], Wattana Leowattana [1], Polrat Wilairatana [1]

[1] Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Thailand, [2] Department of Tropical Hygiene, Faculty of Tropical Medicine, Mahidol University, Thailand, [3] Queen Saovabha Memorial Institute, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

Traveler's diarrhea (TD) is a common health problem, and the current incidence of traveler's diarrhea in Thailand is yet to be determined. We performed a clinic-based prospective cohort study to determine the incidence of traveler's diarrhea. Adult international travelers who had arrived in Thailand within the previous week were invited to join the study. Demographic data, travel plans, and health history, were collected. Follow-up questionnaires were collected on days 7, 14, and 28 from day of arrival. A total 349 participants met the criteria for analysis. The median age of the participants was 29 years; 55.58% were male. Most were from North America (40.1%) and Europe (38.3%). The cumulative incidences of the participants developing TD were 13.18% (46/349), 22.63% (79/349), and 32.37% (113/349) at 7, 14, and 28 days, respectively. The median time to develop TD was 9.5 days (IQR 5-18 days) post-arrival. Among the participants with TD, 37.2% (42/113) concurrently had fever with diarrhea; the median duration of diarrhea was 2 days (IQR 1-3.5 days). Of 113 participants with TD, 75 (66.38%) consulted a physician, while 2 were hospitalized. 11.5% of participants with TD needed to change their travel plans. Factors significantly associated with TD were age (youth), allergy (OR = 1.90, 95% CI: 1.07-3.39), not routinely washing hands after using the toilet (OR = 1.80, 95% CI: 1.09-2.96), consuming street food (OR = 2.25, 95% CI: 1.05-4.83), travel to the countryside (OR = 1.79, 95% CI: 1.01-3.18), and having recently visited other South-East Asia countries or traveled abroad during the follow-up period (OR = 2.01, 95% CI: 1.24-3.26). In conclusion, TD occurred in about one-third of adult foreign travelers in Thailand and occasionally had a negative impact on their travel. A campaign to improve the awareness and practices of travelers might help to reduce the incidence of TD.

Keyword: Traveler

SITE 1 PROTEASE (S1P) INHIBITOR, PF-429242 SUPPRESS DENGUE VIRUS PROPAGATION IN VITRO

Leo Uchida[1, 3], Shuzo Urata[2], Gianne Eduard L. Ulanday[3], Yuki Takamatsu[3], Jiro Yasuda[2], Kouichi Morita[3], Daisuke Hayasaka[3]

[1] Laboratory of Zoonotic Diseases, School of Veterinary Medicine, Rakuno Gakuen University, [2] Department of Emerging Infectious Disease, Institute of Tropical Medicine, Nagasaki University, [3] Department of Virology, Institute of Tropical Medicine, Nagasaki University

Background: Dengue virus (DENV) infection causes one of the most widespread mosquito-borne diseases in tropical and subtropical regions of the world. Despite the great need, effective and practical antiviral therapies are still under development. Intracellular lipid levels are regulated by sterol regulatory elements-binding proteins (SREBPs), which are activated by serine protease, site 1 protease (S1P). Small compound PF-429242 is known as a S1P inhibitor and the antivirus effects have been reported in some viruses.

Methods: Anti-DENV effects of PF-429242 was evaluated by using all four serotypes of DENV and several primate-derived cell lines. Moreover, emergence of drug-resistant DENV mutants was assessed by sequential passages with the drug. DENV dependency on intracellular lipids during their infection was also evaluated by adding extracellular lipids.

Results: The addition of PF-429242 showed suppression of viral propagation in all DENV serotypes. We showed that drug-resistant DENV mutants are unlikely to emerge after five times sequential passages through treatment with PF-429242. Although the levels of intracellular cholesterol and lipid droplets were reduced by PF-429242, viral propagations were not recovered by addition of exogenous cholesterol or fatty acids, indicating that the reduction of LD and cholesterol caused by PF-429242 treatment is not related to its mechanism of action against DENV propagation.

Conclusion: We showed an evidence that PF-429242 could be a potential candidate for an anti-DENV drug, although the mechanism of the inhibitory effects are still unclear.

Keyword: Dengue virus, Antivirus drug, Site 1 protease, and PF-429242

THE CHARACTERISATION OF B CELL EPITOPES AND THE PREDICTION OF THREE DIMENSIONAL NS1 PROTEIN STRUCTURE OF JAPANESE ENCEPHALITIS VIRUS

Wipa Tangkananond [1,2], Panusorn Hunsub [1]

[1] Department of Biotechnology, [2] Industrial Science and Management, International Program, Faculty of Science and Technology, Thammasat University, Rangsit Center, THAILAND

The non-structural protein 1 (NS1) of Japanese encephalitis virus (JEV) contributes to viral replication and elicits protective immune responses during infections. The phylogenetic tree was generated with the whole NS1 amino acid sequences of 7 species of genus Flavivirus. Their 21 samples showed that the JEV and Murray Valley encephalitis virus were more closely related while Tick-borne encephalitis virus was classified as basal taxon. In addition, the NS1 proteins was predicted by using Bepipred, Ellipro and SVMTrip. Their 17 epitopes were predicted by these tools and the 16 epitopes were retrieved from IEDB (Immune Epitope Database and analysis resource). The analysis homologous regions on B-cell epitopes of NS1 proteins among 7 species of genus Flavivirus were depicted the non-cross-reactivity regions. The 176 JEV strains were analysed with Epitope Conservancy Analysis tool available at IEDB and MEGA 7.0 program.Â It was depicted that the high levels of conservation and without cross-reactivity of 9 B-cell epitopes as follows, DENGIVLD, RDELNVL, KTQNQGPWDENGIVLD, PKRLSMTQEKFEMGWK, RYKYLPETPRSLAKIV, STFVVDGPETKECPDE, KYLPETPRS, PKRLSMTQEKFEMGWKAWGKSILFAPELANST and EDFGFGITS. In addition, the three dimensional (3D) of NS1 protein homo-dimer structure was built by Swiss-Model program, evaluated by VADAR 1.8 program and showed the standard value range of that model. It depicted that the amino acids were fallen within the acceptable 99 % with the great quality of 3D NS1 protein. These specific linear B-cell epitopes of NS1 would benefit for the development of diagnostic assays and new vaccines of JEV in the future.

Keyword: JEV, non-structural protein 1, B-cell epitope

IMMUNOPATHOLOGICAL STUDY OF SCRUB TYPHUS IN RHESUS MACAQUES FOLLOWING INTRADERMAL INOCULATION OF *ORIENTIA TSUTSUGAMUSHI* KARP AND GILLIAM STRAINS

Piyanate Sunyakumthorn [1], Tippawan Anantatat [2], Rawiwan Im-erbsin [1], Manutsanun Sumonwiriya [2], Kesara Chumpolkulwong [1], Sirima Wongwairot [2], Ajchara Vongsawan [2], Susanna Dunachie [3], Matthew Wegner [1], Christine Ege [1], James Jones [1], Brett Swierczewski [4], Allen Richards [5], Nicholas Day [3], Carl Mason [1], Daniel Paris [6]

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Emerging evidence from several studies has shown high genetic diversity of *O. tsutsugamushi*, which may be reflected in different immunopathophysiology of infections caused by different strains. In this study we compared bacterial dissemination, clinical manifestations and immune responses in a rhesus macaque scrub typhus model using two different *O. tsutsugamushi* strains: Karp (highly mouse pathogenic) and Gilliam (intermediate mouse pathogenic) strains. Both strains are highly pathogenic for humans. Two groups of animals were intradermally inoculated with either Karp or Gilliam strains. Blood samples were collected for bacterial quantitation and immunological bioassays until day 28 post inoculation (pi) when the animals were treated with doxycycline. Macaques infected with Gilliam strain demonstrated more pronounced eschars and earlier onset of bacteremia (Day 3 pi), while in the Karp-infected group bacteremia was detected later on Day 6 pi. Cellular immune responses in the Karp-inoculated macaques as determined by ex-vivo IFN-γ ELISPOT were higher than in the Gilliam group on days 12 and 28. At day 80 pi, tissue samples were collected for pathology and long-term immune responses. Interestingly, the Gilliam-inoculated macaques showed more pronounced cellular immune responses in blood and skin. Long-term memory of cellular immune responses was detected in both skin and lymph nodes tissues. Compared to Karp strain, the Gilliam strain caused more severe clinical signs and overall induced more pronounced immune responses similar to human scrub typhus. Therefore, *O. tsutsugamushi* Gilliam strain should be evaluated further in the rhesus macaque scrub typhus model for future drug and vaccine development.

Keyword: Scrub typhus, rhesus macaques, *Orientia*

HOW THE SCHISTOSOMIASIS CONTROL INITIATIVE TRACKS VALUE FOR MONEY ACROSS SUB-SAHARAN AFRICAN NATIONAL PREVENTIVE CHEMOTHERAPY PROGRAMMES FOR SCHISTOSOMIASIS

Roya Karimnia [1], **Fiona Fleming** [1]

[1] *Schistosomiasis Control Initiative*

The Schistosomiasis Control Initiative (SCI), at Imperial College London, works to help those who suffer from and are at risk of schistosomiasis by supporting governments in 18 sub-Saharan African countries and Yemen to create or scale up deworming programmes. SCI is currently funded by multiple public and private donors including the End Fund and the UK Department for International Development (DFID). As part of SCI's monitoring and evaluation of schistosomiasis control, value for money is tracked across SCI's country programmes. Value for money triangulates direct sources of data to understand if good quality programmes are affordable with strong impact as a result of appropriate resources and their use. DFID defines value for money as the four 'E's' of (i) economy, (ii) efficiency, (iii) (cost-)effectiveness and (iv) equity. Following on from the DfID framework, SCI has developed VfM metrics to capture the four 'E's in the context of a national schistosomiasis control programme with examples being (i) costs and quality of programme inputs (ii) cost per person trained and treatments delivered per trainee (iii) cost per treatment delivered and cost per disability adjusted life-years averted, (iv) gender equity in coverage and reaching >75% coverage in non-attending school age children. This presentation will provide more detail of SCI's VfM metrics including presenting VfM results for Cote d'Ivoire, which SCI has been working with since 2010, for financial year 2016-17.

Keyword: Schistosomiasis, Deworming programmes, Value for money

INCIDENCE AND RISK FACTORS OF *OPISTHORCHIS VIVERRINI* INFECTION IN A RURAL AREA OF CENTRAL THAILAND: MIXED-METHOD APPROACH.

Picha Suwannahitatorn [1], Saruttaya Wongsuwanphon [1], Siraphop Malairat [1], Mathirut Mungthin [1]

[1] *Phramongkutklao College of Medicine*

Opisthorchis viverrini (OV) infection is acknowledged as a major public health concern in the North and Northeastern of Thailand where the disease is endemic. Chronic infection could progress to a fatal complication, cholangiocarcinoma. Baseline survey using a cross-sectional study in 2016 showed prevalence of OV infection was 12.9% which was higher than regional and national average. A follow-up study was conducted to assess incidence of the infection. Moreover, qualitative study was used to determine risk factors in social aspects. Study design was a mixed-method conducted in Baan Sai Thong Community, Khao Chakan District of Sra Kaew Province. Stool examination was performed in baseline population from 2016 survey to assess incidence of the infection using a community-based cohort design. Focus group discussion was used to study the behavioral and social factors. Enrolled participants were 524 with average follow-up time of 10 months. The incidence of OV infection was 12.3/100 person-years. Mixed-method approach showed that alcohol consumption and agriculturist were risk factors for acquiring the infection from both multivariate analysis and content analysis from focus-group discussion. Majority of population are descendant of the Northeastern which traditional way of life is still well-preserved. Mixed-method approach helps to understand the association between biological, behavioral and social factors; when farmers work in the field, it is more convenient to catch fish from the natural waterbody and consume it as raw food. In the celebration party, raw fish is likely to be served as festive menu eaten with alcoholic drinks. In conclusion, robust results would be resourceful to design precise intervention for target-population.

Keyword: *Opisthorchis*, OV, Incidence Risk factors, Mixed-method

Wednesday 6 December 2017

15.45-17.15
Room C

S12: Surveillance-response Approaches for Effective Elimination and Prevention of Reintroduction of Malaria
(Sponsored by Vysno a Partners, Inc)

Chairpersons:

Mallika Imwong

Nicholas Day

Speakers

1. Surveillance-response approaches for effective elimination and prevention of reintroduction of malaria
   Marcel Tanner
   Swiss Tropical and Public Health Institute

2. A spatial decision support system approach to implementing malaria surveillance as a core intervention activity in high priority Vietnam
   Sara Canavati
   Mahidol-Oxford Tropical Research Unit

3. Targeted-Reactive Investigation of Remote Area Sleeping Sites to Interrupt Malaria Transmission in Vietnam
   Nguyen Quy Anh
   National Institute of Malaria, Parasitology, and Entomology

4. Clinical and sub-clinical malaria in overseas laborers returning to Vietnam
   Nicholas J. Martin
   The Naval Medical Research Center-Asia

CLOSING REMARKS AND WAY FORWARD BY CHAIRS

SURVEILLANCE-RESPONSE APPROACHES FOR EFFECTIVE ELIMINATION AND PREVENTION OF REINTRODUCTION OF MALARIA

Marcel Tanner [1]

[1] *Director, The Swiss Tropical and Public Health Institute, Basel, Switzerland*

The concept of surveillance and response evolved from the original vision of the general term "surveillance". Surveillance is the ongoing systematic collection, analysis, and interpretation of health data and is aimed at discovery, investigation, and elimination of continuing transmission, the prevention and cure of infection and final substantiation of claimed eradication. Assuming the timely dissemination of the results, it can improve the planning, implementation, and evaluation of public health practice. In contrast, we now promote the surveillance and response approach to more effectively link the activities to detect, report, analyze and interpret with the public health action through integrated packages tailored to the specific setting with the prime aim– to stop transmission in pockets of transmission and to treat all infected people. Surveillance response systems are essentially based on the concept of minimal essential data to capture foci/pockets of transmission or reintroduction. This approach is different to the classical monitoring and evaluation based on maximal possible data and leading too often to information overflow with no feedback and thus no rapid effective public health action. While surveillance has always been a major cornerstone of the initial GMEP, GTS builds now on surveillance-response as one of the key determinants for elimination and the prevention of reintroduction. Currently all efforts are made to operationalize surveillance-response approaches fully into the national malaria control and elimination programs. We shall discuss and propose how effective surveillance-response approaches can be tailored to and integrated into the ongoing malaria elimination efforts in the Greater Mekong Subregion to make elimination and therefore also the elimination of artemisinin-resistant *P. falciparum* a reality.

A SPATIAL DECISION SUPPORT SYSTEM APPROACH TO IMPLEMENTING MALARIA SURVEILLANCE AS A CORE INTERVENTION ACTIVITY IN HIGH PRIORITY VIET NAM

Sara Canavati [1]

[1] *Vysnova Partners, Inc. Under contract to the Naval Medical Research Centre-Asia*

A customized SDSS was developed for three communes in Phu Yen. Village health workers conducted household geographic reconnaissance (GR) operations to map and enumerate all households in the study site. Detected malaria cases were recorded in the SDSS from 2015–2016 and auto-georeferenced to household residence locations. Case data were utilized in the SDSS to guide and map village level targeted response interventions. Remote area sleeping site surveys were also conducted during the study period and analyzed in the SDSS. User acceptability survey and in-depth interviews were conducted with SDSS stakeholders in March 2017. A total of 4,667 households with 17,563 people were mapped during baseline GR operations. During the study period, 128 malaria cases were reported and automatically mapped in the SDSS. Twelve village level targeted response interventions were conducted, testing a total of 872 people. Of those, 361 were investigated during remote-area sleeping site assessments. Intervention and remote-area sleeping site data were mapped and analyzed in the SDSS. Overall, very high acceptability (100%) of the SDSS was reported by Vietnamese malaria personnel (n=16). Key areas identified for improvement included data collection form standardization and further training and support. The pilot SDSS provided an effective and acceptable operational tool for Vietnam's malaria personnel to implement the surveillance. Study findings call for further operational research, streamlining and wider rollout of SDSS surveillance approaches throughout Vietnam and the GMS.

TARGETED-REACTIVE INVESTIGATION OF REMOTE AREA SLEEPING SITES TO INTERRUPT MALARIA TRANSMISSION IN VIETNAM

Quy Anh Nguyen

Vice-head of Epidemiology, The National Institute for Malaria, Parasitology and Entomology, Hanoi, Vietnam

In settings where malaria transmission is known to occur outside of the residential home, standard interventions such as reactive case detection have limited cost-effective impact. In Vietnam, over 60% of malaria cases sleep in forests or on farms. This study applied a targeted-reactive investigative approach to capture information from participants at remote area sleeping sites in three mountainous communes in Phu Yen Province, Central Vietnam. Aims were to identify associated malaria prevention and risk behaviors of individuals frequenting these areas. An analytical cross-sectional study of forest and farm goers was conducted between April and September 2016. Forest and farm going malaria patients were identified from health facilities and followed to their remote-area sleeping sites. Cases (n=110) and neighbors (n=197) within 500m of index camps were interviewed. Logistic regression models were used to calculate prevalence odds ratios (PORs) and 95% confidence interval (CI) for risk factors after adjusting for socio-demographic characteristics. 82% of cases were males with a mean age of 36.6 years. Forest-going cases were less likely to use treated nets (adjusted-POR=0.10; 95% CI 0.02–0.58); and more likely not to use any net (POR=2.95; 95% CI 1.26–6.92), sleep in huts without walls or outdoors (POR=44.0; 95% CI 13.0–148), and work after dark (adjusted POR=6.33; 95% CI 1.92–20.9) than neighbors. A significantly higher proportion of farm-going index cases were involved in planting or logging (POR=2.74; 95% CI 1.27–5.91). Results from this study suggest targeted education and malaria prevention strategies can be developed to address the specific risk factors identified for those sleeping in farms and forests.

CLINICAL AND SUB-CLINICAL MALARIA IN OVERSEAS LABORERS RETURNING TO VIETNAM

Lieutenant Commander Doctor Nicholas J. Martin

Naval Medical Research Center-Asia

Malaria morbidity in Vietnam has been significantly reduced, declining from >1.6 million cases in 1991 to <5,000 in 2016. However, challenges to malaria elimination remain including the potential importation of malaria from outside of Vietnam. To better understand the impact of imported malaria records from 2014-2016 for malaria patients seen at two referral medical facilities in Ha Noi were reviewed to identify individuals recently returned from work or travel outside of Vietnam. During the study's timeframe 298 malaria patients returned from abroad and *Plasmodium falciparum* was the cause of 86% of the malaria infections in these patients. Most patients reported staying abroad for >1 year (median time 13.5 months; IQR 6-33) with the vast majority returning from work in Angola (83%). Of the 196 *P. falciparum* cases identified in this study, 87% were still parasitaemic on Day 3. The interval between returning to Vietnam and seeking care was significantly higher in these patients than those cleared of parasites suggesting delayed clearance was related to treatment seeking behavior. However it was not possible to conduct molecular analysis or survival assays to confirm this finding. The importation of malaria by Vietnamese nationals returning from work abroad warrants research to understand the impact on elimination efforts. The introduction of malaria species not typically reported in Vietnam or parasites resistant to treatment or invisible to current screening techniques could impact elimination efforts in Vietnam. Detailed clinical studies of recently returned patients is being conducted to evaluate transmission potential of imported malaria and identify any presence of artemisinin-resistant genes; together with in-depth interviews (IDIs) and focus group discussions (FGDs) with selected patients to gain an understanding on migration, treatment seeking behavior and knowledge of migrant workers. Preliminary results will be presented.

Wednesday 6 December 2017

15.45-17.15
Room D

S13: Turbo Talk II

Chairperson:

Jetsumon Prachumsri

Ashley Vaughan

Speakers

1. Haemolysis in G6PD heterozygous females treated with primaquine for *Plasmodium vivax malaria*: a nested cohort in a trial of radical curative regimens
   Cindy Chu
   Mahidol-Oxford Tropical Medicine Research Unit; Shoklo Malaria Research Unit

↑ *(p. 64 Poster)*

2. Determination of organic acids produced by *Plasmodium falciparum* using liquid chromatography - mass spectrometry
   Parsakorn Tapaopong
   Mahidol Oxford Research Unit

↑ *(p. 56 Poster)*

3. Exploring Pancreatic Pathology in Severe *Plasmodium falciparum*
   Supattra Glaharn
   Faculty of Tropical Medicine, Mahidol University

↑ *(p. 57 Poster)*

4. Significance of characterizing microclimate conditions to derive extrinsic incubation period of malaria parasites in an urban malaria transmission setting in Chennai, India
   Alex Eapen
   ICMR - National Institute of Malaria Research, Chennai, India

↑ *(p. 68 Poster)*

5. Malaria Case-Based Reporting mobile application: collaborative effort towards malaria elimination
   Su Yee Mon
   Save the Children International

↑ *(p. 69 Poster)*

6. Variability in Antimalarial Drug Sensitivities across Regions in Cambodia may Pose Unique Challenges to National Malaria Program
   Chatchadaporn Thamnurak
   Department of Immunology and Medicine, AFRIMS

↑ *(p. 71 Poster)*

7. Genetic Polymorphisim and Natural Selection in the C-Terminal 42-Kda Region of Merozoite Surface Protein-1 in *Plasmodium falciparum* Myanmar Isolates
   Thi Lam Thai
   Gyeongsang National University School of Medicine, Republic of Korea

↑ *(p. 58 Poster)*

8. Molecular Characterization of G6PD Deficiency in Malaria-Endemic Northeastern Region of India
   Ram Suresh Bharti
   ICMR-National Institute of Malaria Research, New Delhi, India

↑ *(p. 72 Poster)*

15.45-17.15
Room D

S13: Turbo Talk II *(Continued)*

Speakers

9 Community Based Intervention towards Malaria and Dengue Fever Prevention and Control among Ethnic Minority Groups in Ratanakiri and Mondolkiri Province
Ratana Somrongthong
College of Public Health Sciences, Chulalongkorn University
↑ *(p. 73 Poster)*

10. Trafficking of merozoite adhesive erythrocyte binding-like protein in the human malaria parasite, *Plasmodium falciparum*
Serena Shunmugam
University of the Witwatersrand, National Health Laboratory Service, Johannesburg, South Africa
↑ *(p. 59 Poster)*

11. Zoonotic Helminths in Okinawa Main Island, Japan
Sumire Ikeda
Graduate School of Health Sciences, Niigata University, Niigata, Japan
↑ *(p. 96 Poster)*

12. Determination of the association between *Opisthorchis viverrini* infection and type 2 diabetes mellitus: an 8-year retrospective cohort study
Napatsorn Jaruratmongkol
Phramongkutklao College of Medicine
↑ *(p. 91 Poster)*

13. Species Diversity and Natural *Plasmodium* Infections in *Anopheles* Mosquitoes in a Malaria Endemic Area of Na Chaluai District, Ubon Ratchathani Province
Petchaboon Poolphol
Chiang Mai University, Chiang Mai, Thailand
↑ *(p. 55 Poster)*

14. Dynamics of *Aedes aegypti* Larvae in a Rural Area of Rattankiri and Mondukiri Provinces, Cambodia
Wannapa Suwonkerd
Office of Disease Prevention and Control No 1, Department of Disease Control, MoPH, Thailand
↑ *(p. 99 Poster)*

15. Effect of 350th amino acid substitution of Chikungunya virus 6K-E1 protein on its sensitivity in a rapid E1-antigen test
Aekkachai Tuekprakhon
Faculty of Tropical Medicine Mahidol University
↑ *(p. 25 Poster)*

16. UPLC-MSMS method development and validation of Atovaquone in human plasma for pharmacokinetic study
Winita Ta-aksorn
Department of Immunology and Medicine, AFRIMS
↑ *(p. 111 Poster)*

17. Most patients in Cambodia with treatment failure post atovaquone-proguanil lack cytb mutations in Y268 locus by Sanger sequencing
Mariusz Wojnarski
US Armed Forces Research Institute of Medical Sciences, Bangkok, Thailand
↑ *(p. 112 Poster)*

9.00-10.30
Room A

S14: The Challenge of Rabies Elimination: How to Get Success?

Chairpersons:

Sopon Iamsirithaworn

Invited Speaker

1. Animals Free of Rabies: Human Are Safe From The Disease Project Under The Wish of Her Royal Highness Princess Chulabhorn
   Khongsak Thiangtum
   Kasetsart University, Thailand

   (No available abstract)

2. Strategy in Rabies Control and People Behavior
   Sopon Iamsirithaworn
   Department of Disease Control, MOPH

   (No available abstract)

3. Animal Rabies: Is it possible to get rid?
   Wirongrong Hoonsuwan
   Department of Livestock Development

   (No available abstract)

ANIMALS FREE OF RABIES: HUMAN ARE SAFE FROM THE DISEASE PROJECT UNDER THE WISH OF HER ROYAL HIGHNESS PRINCESS CHULABHORN

Apinan Suprasert

Department of Disease Control, MOPH

(No available abstract)

STRATEGY IN RABIES CONTROL AND PEOPLE BEHAVIOR

Sopon Iamsirithaworn

Department of Disease Control, MOPH

(No available abstract)

ANIMAL RABIES: IS IT POSSIBLE TO GET RID?

Wirongrong Hoonsuwan

Department of Livestock Development

(No available abstract)

Thursday 7 December 2017

9.00-10.30
Room B

S15: Update on Malaria Research, (Sponsored by CIDR)

Chairpersons:

Jetsumon Prachumsri

Sebastian Mikolajczak

[Speaker

1. New tools for the generation of genetically attenuaed *Plasmodium falciparum* for vaccine development
   Ashley Vaughan
   Center for Infectious Disease Research

2. An improvement of hepatocyte cell line for a robust *in vitro* drug screening assay for exoerythrocytic stage of *P. vivax*
   Wanlapa Roobsong
   Mahidol Vivax Research Unit

3. Perturbation of *Plasmodium vivax* hypnozoite formation, growth and reactivation *in vivo* in a human-liver chimeric mouse
   Erika Flannery
   Center for Infectious Disease Research

4. Plasmepsin V is essential for malaria parasite development in the liver
   Justin Boddey
   Walter and Eliza Hall Institute of Medical Research

5. Cross-invasion inhibitory of *Plasmodium vivax* antibodies of monkey and human-adapted *P. knowlesi* parasites into host erythrocytes
   Eun-Taek Han
   Kangwon National University, republic of Korea

4. Toward rational vaccine design for pre-erythrocytic malaria vaccines
   Noah Sather
   Center for Infectious Disease Research

NEW TOOLS FOR THE GENERATION OF GENETICALLY ATTENUATED *PLASMODIUM FALCIPARUM* FOR VACCINE DEVELOPMENT

Ashley M. Vaughan [1]

[1] *Debashree Goswami, Navin Locham, Nelly Camargo and Stefan H. I. Kappe*

An effective vaccine against malaria will be a crucial component in our efforts to eradicate this devastating disease. It has been shown in rodent models of malaria and that genetically attenuated parasites (GAP) that are unable to complete liver stage development can act as powerful immunogens and provide sterile protection from a sporozoite challenge. Furthermore, GAP created in the human malaria parasite *Plasmodium falciparum* are both safe and immunogenic and will be entering clinical trials to test for efficacy in 2017. Research carried out in the rodent malaria parasite *P. yoelii* has shown that GAP that arrest late in liver stage development are more powerful immunogens than early liver stage-arresting parasites and can protect mice from not only a sporozoite challenge but also a blood stage challenge (thus providing cross-stage immunity) and a *P. berghei* challenge (thus providing cross-species immunity). To date however, efforts to create late liver stage-arresting *P. falciparum* GAP for pre-clinical testing have failed. Here we show that CRISPR/Cas9 gene editing can be applied to *P. falciparum* transgenesis to quickly create GAP for phenotypic testing. We have used this technology to delete the ATP binding cassette (ABC) transporter ABCC2 and this knockout parasite is attenuated but persists in the liver for up to five days, demonstrating that late liver stage-arresting GAP can be created. We are continuing our studies and will present evidence for the creation of further late liver stage-arresting GAP that we hope can soon be used in pre-clinical testing for safety profiling.

Keyword: Malaria, vaccine, *Plasmodium*, genetically attenuated parasite, sporozoite, liver stage

AN IMPROVEMENT OF HEPATOCYTE CELL LINE FOR A ROBUST *IN VITRO* DRUG SCREENING ASSAY FOR EXOERYTHROCYTIC STAGE OF *P. VIVAX*

Wanlapa Roobsoong [1], Ubonwan Jaihan [1], Sittinont Chainarin [1], Jetsumon Sattabongkot [1]

[1] *Mahidol Vivax Research Unit (MVRU), Faculty of Tropical Medicine, Mahidol University*

Plasmodium vivax is the most widely distributed human malaria parasite. Due to its ability to stay dormant in the liver, hypnozoite, it can cause relapse of the disease in months of years after primary attacked causing a major problem in the disease management and control program. Even though Primaquine is currently and effectively use to kill liver stage but cannot be used in G6PD deficiency due to its side effect in causing hemolysis in G6PD deficient patient. In addition, 14 days' regimen is also long. Therefore, there is a need of new drug that could effectively kill the liver stage of *P. vivax* especially hypnozoite. Exo-erythrocytic invasion assay using HCO4 cell line can be used as a platform for drug screening against *P. vivax* but it hardly provide solid data due to low infection rate. Therefore, the improvement of the platform to yield high infection rate is needed. Our studied aim to improve the drug screening platform by targeting the host HCO4 cell. The EphA2 has been strongly shown to involve with the invasion of *Plasmodium sp*'s sporozoite, *P. yoelii*, *P. falciparum*. By modification of the HCO4, the infection rate was increased by 2-4 times compared to original HCO4 control. This strategy can be used to improve the infection rate in the drug screening platform and also indicate the important role of EphA2 in the invasion of *P. vivax* sporozoite.

Keywords: *Plasmodium vivax*, exoerythrocytic stage, hypnozoite, drug screening, HCO4 cell

PERTURBATION OF *PLASMODIUM VIVAX* HYPNOZOITE FORMATION, GROWTH AND REACTIVATION IN VIVO IN A HUMAN-LIVER CHIMERIC MOUSE

Erika L. Flannery [1], Vorada Chuenchob, Niwat Kangwanrangsan, Wanlapa Roobsong, Matt Fishbaugher, Mary Jane Navarro, Brice Campo, Stefan H.I. Kappe, Jetsumon Sattabangkot, Sebastian A. Mikolajczak

[1] *Center for Infectious Disease Research, Seattle WA*

Plasmodium vivax eradication will necessitate an additional set of interventions to prevent and cure latent liver infection. Unlike *P. falciparum, P. vivax* can remain dormant in an infected persons' liver for months to years before the parasite reactivates and causes clinical disease. While it is recognized that drugs, vaccines and mosquito interventions are all necessary to eradicate malaria, the eradication of *vivax* malaria will require not only preventing the formation of latent liver hypnozoites, but will also demand inactivation or removal of hypnozoites in persons presently infected. A better understanding of hypnozoite formation, persistence and reactivation will be needed to achieve this task. Here we show for the first time *in vivo* the effect of prophylactic antimalarials on *P. vivax* liver stage development to begin to understand the biology of hypnozoite growth and maturation. Using the liver-chimeric humanized mouse model, we show that treatment with primaquine during early liver stage development prevents hypnozoite formation and a treatment time-course highlights the point of true hypnozoite maturation, as latent parasites are refractory to absolute clearance in the liver. Hypnozoites continue to expand in size while the ER and apicoplast become larger, albeit without DNA replication. Treatment with MMV048, a pre-clinical candidate, is able to selectively kill and clear replicating schizonts from the liver when administered during the pre-erythrocytic growth cycle which allowed us to demonstrate the reactivation and blood-stage relapse of *P. vivax* hypnozoites. Using this model we are investigating transcriptional responses during the switch from early to mature hypnozoite, and persistent to reactivated, in an effort to identify potential drug targets and biomarkers of latent infection.

Keyword: *Plasmodium vivax*

PLASMEPSIN V IS ESSENTIAL FOR MALARIA PARASITE DEVELOPMENT IN THE LIVER

Pravin Rajasekaran [1], Bethany Davey [1], Matthew T. O'Neil [2], Sash Lopaticki [2], Annie SP Yang [1], Sara M. Erickson [1], Alan F. Cowman [1], Justin A. Boddey [1]

[1] The Walter and Eliza Hall Institute of Medical Research, Parkville 3052, Victoria, Australia; Department of Medical Biology, The University of Melbourne, Parkville 3052, Victoria, Australia, [2] The Walter and Eliza Hall Institute of Medical Research, Parkville 3052, Victoria, Australia

Malaria parasites export proteins into the infected erythrocyte that extensively remodel the cell. Protein export involves proteolytic cleavage of the *Plasmodium* export element (PEXEL) by the aspartyl protease plasmepsin V (PMV), which licenses the cargo for translocation across the parasitophorous vacuole membrane. Attempts to genetically disrupt the PMV gene using conventional and CRISPR-based methods have failed. PEXEL-proteins and PMV are conserved in all *Plasmodium* species and are expressed in multiple lifecycle stages. Prior to blood stage infection, malaria parasites infect hepatocytes of the liver. Protein export may be involved in subverting hepatocyte responses to infection but, so far, little evidence has been accumulated supporting PEXEL-dependent export to the infected hepatocyte. Here, we use the rodent malaria Flp-FRT system to conditionally delete the PMV locus from parasites during passage through mosquitoes. Injection of ΔPMV sporozoites into mice reveals that they readily invade the liver but are cleared from this organ and no patent infections occur in vivo. Mice infected with ΔPMV parasites are protected from a lethal dose of wildtype sporozoites. Immunofluorescence microscopy reveals that export of a PEXEL-containing effector protein is blocked in hepatocytes containing ΔPMV parasites. Biochemical analyses show that PMV cleaves the PEXEL sequence of this exported protein with the same substrate specificity as needed for blood-stage effector export. This study provides the first genetic deletion of PMV and demonstrates that it is essential in pre-erythrocytic stages and is involved in export to hepatocytes. This suggests PMV is a dual liver and blood stage drug target.

Keyword: Malaria, liver, hepatocyte, PEXEL, export

CROSS-INVASION INHIBITORY OF *PLASMODIUM VIVAX* ANTIBODIES OF MONKEY AND HUMAN-ADAPTED *P. KNOWLESI* PARASITES INTO HOST ERYTHROCYTES

Eun-Taek Han [1], Seong-Kyun Lee[1], Jin-Hee Han[1], Ji-Hoon Park[1], Mohammad Rafiul Hoque[1], Nam-Hyeok Kim[1], Moh. Egy Rahman F.[1], Takafumi Tsuboi[2], Osamu Kaneko[3] and Eun-Taek Han[1]

[1] Department of Medical Environmental Biology and Tropical Medicine, School of Medicine, Kangwon National University, Chuncheon, Gangwon-do, Republic of Korea
[2] Proteo-Science Center, Ehime University, Matsuyama, Ehime, Japan
[3] Department of Protozoology, Institute of Tropical Medicine, Nagasaki University, Japan

Invasion process in *Plasmodium* species is very rapid and complex process which involved several ligands and receptors interaction. Several ligands have been well identified in *Plasmodium vivax* and *P. knowlesi*, but extensive molecular machinery in invasion makes vaccine development hampered. Hence, a vaccine targeting different species which enable to block the invasion of blood-stage parasites will enormously affect to elimination program. Thus, this study revealed the importance of finding in possibility of cross-protection from *vivax*- and/or *knowlesi*-infection. Several candidates have been selected as potential enormous cross-vaccine development based on identical amino acids domain and B-cell epitope recognition. Cross-reactivity was proved by using *P. vivax* antibodies with *P. knowlesi* parasite by immunofluorescence assay, western blotting, and protein microarray. Cross-invasion inhibition for target antibodies was investigated in monkey and human-adapted *P. knowlesi* parasites. *P. vivax* specific target antibodies successfully recognized *P. knowlesi* parasite which specifically localized in the different subcellular organelles of parasites such as surface, microneme, and rhoptry. Also, antibodies from *vivax*- and *knowlesi*-infected patient serum samples recognized common and shared epitope by using specific target recombinant prot! eins. The most unique of this finding is some *P. vivax* antibodies could be able to block the merozotie invasion of monkey and human-adapted *P. knowlesi* into erythrocytes in concentration dependent manner. Our findings might highlight the notion of cross-protection among *vivax*- and *knowlesi*-infected malaria patients. As future direction, this study will facilitate the containment of *P. vivax in vitro* culture, and to get attention of broadly vaccine development among *Plasmodium* species.

Keyword: *Plasmodium* species

TOWARD RATIONAL VACCINE DESIGN FOR PRE-ERYTHROCYTIC MALARIA VACCINES

Noah Sather [1]

[1] *Center for Infectious Disease Research*

Our focus is on the development of pre-erythrocytic vaccine antigens to elicit protective antibodies against malaria. For some antigens we have observed partial protection in our vaccine efficacy studies, rather than sterilizing protection. Typical vaccine analyses rely on assessing polyclonal immune serum to quantify vaccine efficacy. However, polyclonal serum is a mix of many different antibodies, some of which are likely to be functional and some that are not. Thus, in cases in which partial protection is observed, it may be that highly functional antibodies are in the minority, or that non-functional epitopes are immunodominant. Thus, a thorough, detailed dissection of vaccine elicited antibodies is warranted to advance further vaccine development. Here we report on our progress with the antigen PfTRAP. Using advanced monoclonal antibody isolation techniques, we have begun to map functional antibody activity to specific domains within PfTRAP, and have mapped neutralizing activity to a specific domain. These efforts are the first steps toward the realization of second generation, rationally designed pre-erythrocytic vaccines.

Keywords: malaria, vaccines, PfTRAP

Thursday 7 December 2017

9.00-10.30
Room C

S16: Antibodies Against Arboviruses

Chairpersons:


Tatsuo Shioda


Pongrama Ramasoota

Invited Speaker

1. A single amino acid substitution in dengue virus envelope protein suppressed induction of infection-enhancing antibody in a mouse-DNA vaccine model
   Atsushi Yamanaka
   Osaka University

2. Antibody Engineering at Fc Region to Diminish Antibody Dependent Enhancement of Cross-Neutralizing Human Monoclonal Antibody Against Dengue Virus
   Pannamthip Pitaksajjakul
   Faculty of Tropical Medicine, Mahidol University

3. The dynamics of disease progression in severe dengue
   Takeshi Kurosu
   National Institute of Infectious Diseases, Japan

4. Evaluation of immunochromatography rapid diagnosis kit strip for detection of chikungunya virus antigen in clinical samples of India
   Tamaki Okabayashi
   University of Miyazaki, Japan

5. Improving malaria rapid diagnostic using shark VNAR antibody
   Chiuan Herng Leow
   Institute for Research in Molecular Medicine Thursday 7 December 2017

A SINGLE AMINO ACID SUBSTITUTION IN DENGUE VIRUS ENVELOPE PROTEIN SUPPRESSED INDUCTION OF INFECTION-ENHANCING ANTIBODY IN A MOUSE-DNA VACCINE MODEL

Atsushi Yamanaka [1], Tatsuo Shioda [2], Eiji Konishi [3]

[1] Research Institute for Microbial Diseases, Osaka University, [2] Mahidol-Osaka Center for Infectious Diseases (MOCID), Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; Department of Viral Infections, Research Institute for Microbial Diseases, Osaka University, Osaka, Japan, [3] BIKEN Endowed Department of Dengue Vaccine Development, Research Institute for Microbial Diseases, Osaka University, Osaka, Japan

Dengue fever and dengue hemorrhagic fever are the most important mosquito-borne flaviviral diseases worldwide. Four serotypes of dengue virus (DENV-1 to DENV-4) are the causative agents. Heterotypic secondary infection potentially induces antibody-dependent enhancement of infection. There is a concern that vaccine-induced infection-enhancing antibodies. Here, we identified an epitope for enhancing antibody induction and evaluated modified dengue vaccine antigens which do not induce enhancing antibody using a mouse-DNA vaccine model. Mouse monoclonal antibody against DENV-1 (D1-V-3H12), originally of IgG1 subclass displaying only enhancing but not neutralizing activity, was engineered by using pFUSE vectors to generate an IgG2b subclass antibody (3H12-IgG2b) showing neutralizing activity. DENV-1 Mochizuki strain was cultivated in the presence of 3H12-IgG2b. BALB/c mice were immunized three times with DNA plasmid expressing pre-membrane and envelope (E) proteins of DENV. To measure the balance of enhancing and neutralizing antibodies, semi-adherent FcγR-bearing K562 cells were used. An antigen epitope recognized by D1-V-3H12 antibody was identified on the fusion loop of E protein domain II. Mice immunized with a DNA vaccine containing the corresponding single amino acid substitution induced neutralizing antibody, which did not show enhancing activity in the present assay system. In contrast, the original DNA vaccine without any epitope modification induced enhancing antibody. The present study demonstrated that epitope manipulation by substituting a single amino acid on the fusion loop suppressed induction of enhancing antibodies. This specific amino acid substitution working in a DNA vaccine system can be probably applied to other dengue vaccine strategies.

Keyword: Dengue, Vaccine

ANTIBODY ENGINEERING AT FC REGION TO DIMINISH ANTIBODY DEPENDENT ENHANCEMENT OF CROSS-NEUTRALIZING HUMAN MONOCLONAL ANTIBODY AGAINST DENGUE VIRUS

Pannamthip Pitaksajjakul [1], Subenya Injampa [2], Chonlatip Pipattanaboon [2], Surachet Benjathummarak [2], Khwanchit Boonha [2], Pongrama Ramasoota [1]

[1] Center of Excellence for Antibody Research, Mahidol University, Bangkok, Thailand and Department of Social and Environmental Medicine, Mahidol University, Bangkok, Thailand, [2] Center of Excellence for Antibody Research, Mahidol University, Bangkok, Thailand

Dengue is one of the most important mosquito-borne disease in the tropics and subtropics. Severe dengue cases usually occur among patients secondarily infected with different serotypes. This is believed to be derived from antibody-dependent enhancement (ADE). In our previous study, strong neutralizing HuMAb (NHuMAb) was successfully generated (D23-1B3B9) by hybridoma technology. This NHuMAbs showed neutralizing activity against all 4 serotypes of dengue virus higher than 85%. However, this antibody still showed ADE activity at sub-neutralizing concentration. To eliminate this ADE phenomenon, variable heavy (VH) chain and variable light (VL) chain genes were isolated from antibody-secreting hybridoma cells of clone B3B9 NHuMAb. Both VH and VL gene were subcloned into mammalian expression plasmid containing CMV promoter, and expressed in Human Embryonic Kidney (HEK) 293T as wildtype B3B9. Substitution of antibody heavy chain at position N297Q and L234A/L235A (LALA) were created by site-directed mutagenesis. Those 2 modified HuMAbs namely N297Q_B3B9, and LALA B3B9 were also produced from HEK293T cells. The neutralizing activity of the 3 HuMAbs were tested on Vero cells. K562 cells containing FcγRII was used to analyse the ADE activity. It was found that those 3 HuMAbs showed comparable neutralizing activity to all 4 DENV serotype. Fortunately, those 2 modified HuMAbs (N297Q_B3B9 and LALA B3B9) showed critical reduction of ADE activity in all antibody concentration. The effector function that involved with Fc region of antibody molecule will be further characterized. After thoroughly characterizations, these 2 modified HuMAbs can be a promising therapeutic candidates for Dengue treatment.

Keyword: Dengue virus, Neutralizing activity, Antibody Dependent Enhancement, Fc gamma receptor

THE DYNAMICS OF DISEASE PROGRESSION IN SEVERE DENGUE

Takeshi Kurosu [1], Daisuke Okuzaki [2], Kriengsak Limkittikul [3], Masayuki Shimojima [1], Shuetsu Fukushi [1], Shumpei Watanabe [1], Masayuki Saijo [1]

[1] National Institute of Infectious Diseases, [2] Research Institute for Microbial Diseases, Osaka University, [3] Tropical Pediatrics, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

Background: We reported that the dengue virus (DENV) type 3 DV3P12/08 caused a lethal systemic infection in mice due to severe vascular leakage. Treatment with a neutralizing anti-TNF-α antibody (Ab) efficiently protected mice and suppressed vascular leakage in mouse liver and intestine. We aimed to understand the disease progression toward death by using this model.

Materials and Methods: IFN-α/β/γR KO mice infected with DV3P12/08 were treated with normal serum IgG or anti-TNF-α antibody. The mRNA were extracted from livers and intestines at different time points, and analyzed for microarray. Genes with expression level of at least ±2.0-fold change and a Student's t-test $P<0.05$ were defined statistically significant. Functional analysis and pathway enrichment analyses of the expressed genes were performed using the Ingenuity Pathway Analysis (IPA).

Results: The following events occurred in liver and intestine. 1) At the early stage, an abnormal activation of macrophage occurred, mainly through TLR4, and specific scavenger receptors were possibly involved in it. 2) Secondly, inflammatory cytokines, such as TNF-α, were produced. 3) Next, a battle between protective and exacerbation factors, such as matrix metalloproteases (MMPs), began probably at endothelium. 4) These events resulted in a multiple organ failure at the terminal stage. Dynamic changes of cell death-related genes and estrogen-related factors as well as IL-6 were highly produced. Anti-inflammatory cytokine, IL-10 were drastically induced in liver but not intestine.

Discussion: Across the entire process, expression of protective factors to endothelial and organs are drastically increased. However, they failed to protect mice against lethality. Once pro-inflammatory cytokines were excessively produced, it might be difficult to protect mice form suffering multiple organ damage.

Keyword: Dengue, hemorrhagic fever, virus infection, animal model

EVALUATION OF IMMUNOCHROMATOGRAPHY RAPID DIAGNOSIS KIT STRIP FOR DETECTION OF CHIKUNGUNAY VIRUS ANTIGEN IN CLINICAL SAMPLES OF INDIA

Tamaki Okabayashi [1,2,3]

[1] *Department of Veterinary science, Faculty of Agriculture, University of Miyazaki, Japan.*
[2] *Center for Animal Disease Control, University of Miyazaki, Japan*
[3] *Mahidol Osaka Center for Infectious Diseases, Osaka University, Japan*

Background: Chikungunya virus (CHIKV) and dengue virus (DENV) are arboviruses that share the same *Aedes* mosquito vectors, and there is much overlap in endemic areas. In India, co-infection with both viruses has been often reported. Clinical manifestations of CHIK fever are not specific and are difficult to differentiate from other febrile illnesses, especially dengue fever. We have previously developed the CHIKV antigen detection IC kit using monoclonal antibodies against CHIKC ECSA genotype isolated in Thailand, 2010, for early diagnosis (Okabayashi et al., 2015). The current study examined the efficacy of IC kit using patients sera in India where CHIKV ECSA outbreak occurred in 2016.

Materials and Methods: A hundred twenty three sera, including 104 CHIK positive sera quantitative RT-PCR (qRT-PCR) positive, qRT-PCR and IgM positive, and IgM positive sera collected and 19 control samples, other febrile samples and health samples, were examined. Twenty patients were co-infection with CHIKV and DENV.

Results: Compared to the diagnosis by qRT-PCR, the sensitivity, specificity and over all agreement with qRT-PCR were 93.7%, 95. 5% and 94.3%, respectively. Besides, a statistical significant strong positive correlation was found between IC kit device score and CHIKV RNA copy number. Our IC kit effectively detected CHIKV antigen even in-co-infected patients sera and did not cross-react with DENV-infected sera. Discussion: The results of this studies suggested that the IC kit can be useful for rapid, bedside and semi-quantification of CHIKV in endemic area, circulating both CHIKV and DENV, such as India.

Keyword: Chikungunay virus

IMPROVING MALARIA RAPID DIAGNOSTIC TESTS USING SHARK VNAR ANTIBODY

Chiuan Herng Leow [1], Katja Fischer [2], Qin Cheng [3], James McCarthy [2]

[1] Institute for Research in Molecular Medicine (INFORMM) Universiti Sains Malaysia, Penang, Malaysia, [2] QIMR Berghofer Medical Research Institute, Australia, [3] Australian Army Malaria Institute, Australia

Monoclonal antibody technology has been widely deployed for clinical diagnostic and therapeutic uses. Malaria rapid diagnostic tests (RDTs) represent an important antibody based immunoassay platform, and are being increasingly deployed for early diagnosis and prevention of the spread of anti-malarial drug resistance. However, conventional monoclonal antibodies are subject to degradation at high ambient temperatures, resulting in potentially catastrophic false negative diagnosis. To overcome this limitation, we sought to investigate new binders derived from shark antibodies, so called variable new antigen receptors (VNARs). VNARs are known to have excellent heat-stability, and their unique structure entails an extraordinarily long CDR3 permits it penetration into cleft region of antigen. Following immunization of a wobbegong shark (*Orectobolus ornatus*) with three malaria biomarkers (HRP2, LDH and Aldolase), and ensuring a positive antibody response was present, a single domain antibody (sdAb) library was constructed from splenocytes using a T7 phage vector system. VNAR cDNA was cloned into the library by PCR, and screened by biopanning against the target malaria biomarkers. The results indicated that the primary library titre of shark VNAR phage display library was 1.16 x 106 pfu/ml, with 60% appearing to be the appropriate size (~ 450 bp). After six rounds of biopanning, 27 clones were selected and verified by DNA sequence analysis. Recombinant clonal VNARs were generated using an E. coli expression system. Further biological characterization of these clones will be presented. The outcome of this work has the potential to significantly improve malaria RDTs, and also suggest that VNARs may represent an alternative sdAb for other applications.

Keyword: Monoclonal antibody technology, malaria, rapid diagnostic tests

Thursday 7 December 2017

9.00-10.30
Room D

S17: Research Update on Mekong Schistosomiasis (PTAT)

Chairperson:

Padet Siriyasatie

Sonthaya Tiawsirisu

Invited Speaker

1. Sex-specific genes of *Schistosoma mekongi*, target for drug and vaccine development
   Poom Adisakwattana
   Faculty of Tropical Medicine, Mahidol University

(No available abstract)

2. Development of diagnostic and vaccine for *Schistosoma mekongi* using proteomics approach
   Onrapak Reamtong
   Faculty of Tropical Medicine, Mahidol University

3. An update of distribution, habitats and densities of *Neotricula aperta*, snail intermediate host of blood fluke, *Schistosoma mekongi*, in Thailand
   Yanin Limpanont
   Faculty of Tropical Medicine, Mahidol University

SEX-SPECIFIC GENES OF *SCHISTOSOMA MEKONGI*, TARGET FOR DRUG AND VACCINE DEVELOPMENT

Poom Adisakwattana

Faculty of Tropical Medicine, Mahidol University

(No available abstract)

DEVELOPMENT OF DIAGNOSTIC AND VACCINE FOR *SCHISTOSOMA MEKONGI* USING PROTEOMICS APPROACH

Onrapak Reamtong [1]

[1] *Department of Molecular Tropical Medicine and Genetics, Faculty of Tropical medicine, Mahidol University*

Schistosomiasis is one of the most important human parasitic diseases caused by schistosoma blood flukes. To date, many researches focus on *Schistosoma haematobium, S. japonicum*, and *S. mansoni*, the three main species infecting humans. Since *S. mekongi* is endemic only in South-east Asia which is more localized geographically. Very few studies have been done on this parasite. Diagnostics, vaccines and biological knowledge of *S. mekongi* need to be explored. Microscopic identification of eggs in patient stool is common method for diagnosis. In addition, antibody detection using circumoval precipitin test is also applied for indicating schistosome infection. However, the test is time consuming, complicated to execute and difficult to interpret. In our study, important *S. mekongi* proteins were discovered using mass spectrometry based proteomics. Protein profiling of *S. mekongi* crude egg and worm secretome were investigated. The data provided more understanding of biological basic knowledge. Moreover, whole *S. mekongi* antigens was detected by immunoblotting using IgG and IgM of uninfected and infected mouse sera at 2, 4 and 8 weeks. Our finding is the first report of *S. mekongi* antigens which can be a potential library for further diagnostic and vaccine development.

Keyword: *Schistosoma mekongi*, Proteomics

AN UPDATE OF DISTRIBUTION, HABITATS AND DENSITIES OF *NEOTRICULA APERTA*, SNAIL INTERMEDIATE HOST OF BLOOD FLUKE, SCHITOSOMA MEKONGI IN THAILAND

Yanin Limpanont [1], Phiraphol Chusongsang [1], Yupa Chusongsang [1], Jareemate Limsomboon [1], Prasasana Charoenjai [1], Songtham Kiatsiri [1], Saiyud Padungcheep [1], Suthep Numnual [1], Kantee Tanasarnprasert [1], Suwalee Worakhunpiset [1], Wanchai Maleewong [2]

[1] Southeast Asian Center for Medical Malacology, Department of Social and Environmental Medicine, Faculty of Tropical Medicine, Mahidol University, Thailand, [2] Department of Parasitology, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand

Schistosomiasis is an important global, public health important parasitic disease cause by Schistosoma trematode. *Schistosoma mekongi* is found along Mekong River and some of its tributaries in Cambodia and Lao PDR. The freshwater snail, *Neotricula aperta* (Pomatiopsidae) is intermediate host for human blood fluke *Schistosoma mekongi*. In Thailand, the former known habitat of *N.aperta* was in Mun and Mekong River in Ubon Ratchatani. Until 2010 survey, we reported a new population and habitat type in Nong Khai upstream from the previously known site of this species. In 2014-2015 more intensive survey of N.aperta along Mekong River was conducted and total of 18 *N.aperta* habitats were identify along Mekong River in Ubon Ratchathani, Amnat Charoen, Nakhon Panom, Nong Khai and Loei. The habitats of *N.aperta* in most sampling sites were in the islet of Mekong River. The bottom of the river or the islet type included bedrock, rock, pebble, sand, sandy soil, silt and muddy bottom. *N.aperta* needs substrate (rock) to attach. In some sampling sites, not only the natural rock was found, but also the rock that use for making river bank protection. The habitat of *N.aperta* in Mun River was known from the lower Mun River, Ubon Ratchatani Province. The survey in 4 rapids of Phibun Mungsahan district, Ubon Ratchatani during 2009, found 2 of 4 habitats of *N.aperta*. From recent malacological survey in Mekong and Mun River during 2015-2017, we update the distribution, habitats and densities of *Neotricula aperta* in Thailand and identified the habitat where the occasion of human-*N.aperta* inhabited water can occur. This study was supported by Research Grant from the Faculty of Tropical Medicine, Mahidol University, Fiscal Year 2013 and Mahidol University, Fiscal Year 2016-2017.

Keywords: *Neotricula aperta,* habitats, distribution, Mun River, Mekong River, Thailand

11.00-12.30
Room A

S18: M/XDR-TB in Thailand: The Real Threat? (Sponsored by MOPH)

Chairperson:

Petchawan Pungrassami

Invited Speaker

1. Updated M/XDR-TB situation and control strategy in Thailand
   Phalin Kamolwat
   Department of Disease Control, Ministry of Public Health

   (No available abstract)

2. Advanced laboratory tests for M/XDR-TB control and outbreak investigation
   Surakameth Mahasirimongko
   Department of Disease Control, Ministry of Public Health

   (No available abstract)

3. Clinical management of M/XDR-TB
   Charoen Chuchottaworn
   Department of Disease Control, Ministry of Public Health

   (No available abstract)

4. Active drug safety monitoring for M/XDR-TB treatment
   Thidaporn Jirawattanapisal
   Department of Disease Control, Ministry of Public Health

   (No available abstract)

UPDATED M/XDR-TB SITUATION AND CONTROL STRATEGY IN THAILAND

Phalin Kamolwat

Department of Disease Control, Ministry of Public Health

(No available abstract)

ADVANCED LABORATORY TESTS FOR M/XDR-TB CONTROL AND OUTBREAK INVESTIGATION

Surakameth Mahasirimongko

Department of Disease Control, Ministry of Public Health

(No available abstract)

CLINICAL MANAGEMENT OF M/XDR-TB

Charoen Chuchottaworn

Department of Disease Control, Ministry of Public Health

(No available abstract)

ACTIVE DRUG SAFETY MONITORING FOR M/XDR-TB TREATMENT

Thidaporn Jirawattanapisal

Department of Disease Control, Ministry of Public Health

(No available abstract)

11.00-12.30
Room B

S19: Ethical Issues in Human Subject Studies: a Views from four sides (Panel Discussion)

Chairpersons:

Jaranit Kaewkungwal

Saranath Lawpoolsri Niyom

Invited Speaker

1. View from Ethics Committee
   Tada Sueblinvong

(No available abstract)

2. View from Investigator
   Direk Limmathurotsakul
   Faculty of Tropical Medicine, Mahidol University

(No available abstract)

3. View from Community Member
   Udom Liknhitwonnawut
   NCAB

(No available abstract)

4. Ethical Issues in issues in studies involving human subjects: View from Sponsor
   Carina Frago
   Sanofi-Aventis Singapore Pte Ltd

VIEW FROM ETHICS COMMITTEE

Tada Sueblinvong

(No available abstract)

VIEW FROM INVESTIGATOR

Direk Limmathurotsakul

Faculty of Tropical Medicine, Mahidol University

(No available abstract)

VIEW FROM COMMUNITY MEMBER

Udom Liknhitwonnawut

NCAB

(No available abstract)

ETHICAL ISSUES IN STUDIES INVOLVING HUMAN SUBJECTS: VIEW FROM SPONSOR

Carina Frago [1]

[1] *Sanof-Aventis Singapore Pte Ltd*

Clinical research studies should adhere to the ICH-Good Clinical Practice guidelines and uphold the principles of Helsinki declaration. Researchers, sponsors and other stakeholders in human health research should actively work together for proper implementation. Complexities may arise if there is lack of harmonization and absence of a coherent integrated approach.

Keywords: clinical research studies, ethical issues

Thursday 7 December 2017

11.00-12.30
Room C

S20: Current Research on Microbial Infections in the Tropics

Chairpersons:

Narisara Chantratita

Pornsawan Leaungwutiwong

Invited Speaker

1. Development of a multivalent subunit vaccine that provides sterilizing immunity against melioidosis

   Paul J. Brett

   University of Nevada, Reno School of Medicine, USA

2. Imipramine Inhibits Chikungunya Virus Replication in Human Skin Fibroblasts through Interference with Intracellular Cholesterol Trafficking

   Sineewanlaya Wichit

   Faculty of Medical Technology, Mahidol University

3. Hepatitis E: A silent infection in Thailand

   Yong Poovorawan

   Faculty of Medicine, Chulalongkorn University

DEVELOPMENT OF A MULTIVALENT SUBUNIT VACCINE THAT PROVIDES STERILIZING IMMUNITY AGAINST MELIOIDOSIS

Paul Brett [1]

[1] *Department of Microbiology and Immunology, University of Nevada, Reno School of Medicine, USA*

Burkholderia pseudomallei, the etiologic agent of melioidosis, is a CDC Tier 1 select agent that causes severe disease in both humans and animals. Diagnosis and treatment of melioidosis can be challenging and in the absence of optimal chemotherapeutic intervention, acute disease is frequently fatal. Melioidosis is an emerging infectious disease for which no licensed vaccine currently exists. Due to the potential misuse of *B. pseudomallei* as a biothreat agent, as well as its impact on public/animal health in endemic regions, there is significant interest in developing vaccines for immunization against diseases caused by this bacterial pathogen. Several studies have demonstrated that *B. pseudomallei* expresses a number of structurally conserved protective antigens. Included amongst these are multiple surface exposed polysaccharides and a variety of cell-associated/secreted proteins. Based on this information, these antigens have become important components of the multivalent subunit vaccine candidates that we are developing in our laboratory. We propose that an efficacious vaccine for immunization against melioidosis can be developed by combining polysaccharide-based conjugates with specific *B. pseudomallei* protein(s) to produce a single, antigenically-defined formulation. Using murine models of acute melioidosis, our current research is focused on evaluating the protective capacity of these vaccine preparations with the goal of identifying suitable candidates for clinical development. Collectively, it is anticipated that our studies will provide valuable insights towards the rational design of a safe, affordable and effective vaccine to combat melioidosis.

Keyword: *Burkholderia pseudomallei*, melioidosis, polysaccharide, protein, vaccine

IMIPRAMINE INHIBITS CHIKUNGUNYA VIRUS REPLICATION IN HUMAN SKIN FIBROBLASTS THROUGH INTERFERENCE WITH INTRACELLULAR CHOLESTEROL TRAFFICKING

Sineewanlaya Wichit

Department of Clinical Microbiology and Applied Technology, Faculty of Medical Technology, Mahidol University

Chikungunya virus (CHIKV) is an emerging arbovirus of the *Togaviridae* family that poses a present worldwide threat to human in the absence of any licensed vaccine or antiviral treatment to control viral infection. Here, we show that compounds interfering with intracellular cholesterol transport have the capacity to inhibit CHIKV replication in human skin fibroblasts, a major viral entry site in the human host. Pretreatment of these cells with the class II cationic amphiphilic compound U18666A, or treatment with the FDA-approved antidepressant drug imipramine resulted in a near total inhibition of viral replication and production at the highest concentration used without any cytotoxic effects. Imipramine was found to affect both the fusion and replication steps of the viral life cycle. The key contribution of cholesterol availability to the CHIKV life cycle was validated further by the use of fibroblasts from Niemann-Pick type C (NPC) patients in which the virus was unable to replicate. Interestingly, imipramine also strongly inhibited the replication of several *Flaviviridae* family members, including Zika, West Nile and Dengue virus. Together, these data show that this compound is a potential drug candidate for anti-arboviral treatment.

Keyword: Chikungunya virus, Imipramine, Human skin

HEPATITIS E: A SILENT INFECTION IN THAILAND

Yong Poovorawan [1]

[1] *Center of Excellence in Clinical Virology, Faculty of Medicine, Chulalongkorn University*

Hepatitis E virus (HEV) is a public health problem in developing countries and an increasing as a problem in developed countries. HEV infection also causes a high mortality rate among pregnant women. Clinical manifestations of the disease can range from asymptomatic or mild to fulminate hepatic failure. Based on molecular characterization, human HEV can be divided into four genotypes. Thailand is an endemic area for hepatitis B (HBV), and nowadays has deceasing trended due to universal immunization program. Hepatitis C is also reduced due to effective blood screening program, health education and reduced number of IVDUs. Hepatitis A is decreasing due to improved sanitation and hygiene. Although sporadic, acute and symptomatic hepatitis E virus infections are more common than previously recognized particularly in adults, the elderly and immunocompromised individuals. Most infections caused by HEV genotype 3, which is similar and closely related to swine HEV circulating in Thailand. The seroprevalence of hepatitis E virus was lower in children than in adults, suggesting that increasing age is a risk factor. Specifically, the seroprevalence in Narathiwat province, which is 85% Muslim, was lower than Lop Buri province (a mostly Buddhist population which consumes pork). The possibility that swine is a major source of HEV. We investigated the potential zoonosis of HEV from dietary consumption of pork and variety meats sold in fresh markets; we found approximately 0.3 % in liver and pork. However, the HEV RNA was detectable 3-5% in bile and feces of pig from the slaughterhouse. We also studied the prevalence of HEV among healthy blood donors in Thailand in which we screened 5,020 pooled blood samples representing 30,115 individual blood donors for HEV RNA using a one-step real-time reverse-transcription polymerase chain reaction (RT-PCR). HEV RNA was found in 9 healthy individuals or approximately 1 in 3,000 blood donors. The cost-benefit for screening in the blood donors should be evaluated. Data regarding the prevalence of HEV in healthy adults have important implications in ensuring the safety of donated blood. Currently, a promising vaccine produced from the viral capsid protein of HEV genotypes 1 and 4 is available in China. The efficacy of this vaccine would require evaluation in HEV genotype 3 prevalent areas.

Keywords: Hepatitis E, infection, Thailand

Thursday 7 December 2017

11.00-12.30
Room D

S21: Challenges: Academia-Industry Collaborations in Development of Drugs and Vaccines

Chairperson:

Nares Damrongchai

Thanat Chookajorn

Invited Speaker

1. Challenges in implementing clinical R&D road map to achieve Thailand 4.0 national plan: investigator perspective

   Punnee Pitisuttithum

   Faculty of Tropical Medicine, Mahidol University

(No available abstract)

2. Open innovation at DDW: current and future perspectives of our collaboration model between pharmaceutical and academic research

   Francisco Javier Gamo

   GlaxoSmithKline, Tres Cantos, Spain

3. Public Private Partnership in HIV vaccine Research and Development

   Nelson Michael

(No available abstract)

CHALLENGES IN IMPLEMENTING CLINICAL R&D ROAD MAP TO ACHIEVE THAILAND 4.0 NATIONAL PLAN: INVESTIGATOR PERSPECTIVE

Punnee Pitisuttithum

Faculty of Tropical Medicine, Mahidol University

(No available abstract)

OPEN INNOVATION AT DDW: CURRENT AND FUTURE PERSPECTIVES OF OUR COLLABORATION MODEL BETWEEN PHARMACEUTICAL AND ACADEMIC RESEARCH

Javier Gamo [1]

[1] *Tres Cantos Medicines Development Campus. Diseases of the Developing World (DDW). GlaxoSmithKline, Tres Cantos, Spain; fjg19447@gsk.com*

The Diseases of the Developing World (DDW) facility is located at the Tres Cantos Medicines Development Campus (TCMDC) and is fully focused on the discovery of novel and differentiated treatments for Kinetoplastids, Tuberculosis and Malaria disease. Since 2010, GlaxoSmithKline TCMDC has adopted an open innovation strategy that fosters collaboration and transfer of knowledge with academia and biotech, with the final aim to deliver new and affordable effective medicines for DDW (malaria, tuberculosis and kinetoplastid diseases). As part of this open innovation strategy DDW has made public different compound boxes containing information on hits found from phenotypic screens against malaria, tuberculosis and some relevant kinetoplastids. Furthermore, innovative collaboration approaches such as the Open Lab (www.openlabfoundation.org) at TCMDC provides visiting scientists funding and access to GSK facilities, compound collections and drug discovery expertise, in an attempt to exploit a novel model of collaboration for DDW medicine discovery and development. In this communication we´ll highlight some of our successful collaboration approaches and we´ll be a call to new drug discovery collaborative opportunities with the aim of filling neglected diseases portfolio and guarantee a sustainable pipeline. "The human biological samples were sourced ethically and their research use was in accord with the terms of the informed consents."

Keyword: Partnership, Drug-Discovery, Open-Innovation;

PUBLIC PRIVATE PARTNERSHIP IN HIV VACCINE RESEARCH AND DEVELOPMENT

Nelson Michael

(No available abstract)

12.00-13.15
Room C

Grantsmanship: The Art of Obtaining Grant for Research

Moderators:

Jetsumon Prachumsri

Aaron Jex

Invited Speaker

1. Tips for a successful fellowship application to the Wellcome Trust

   Michael Chew

   Science Portfolio Advisor, Wellcome Trust, UK

2. TBA

   Aaron Jex

   Watter and Eliza Hall Institute of Medical Research

(No available abstract)

TIPS FOR A SUCCESSFUL FELLOWSHIP APPLICATION TO THE WELLCOME TRUST

Michael Chew

Infection and Immunobiology Science Division, Wellcome Trust

The Wellcome Trust is one of the largest independent biomedical research charities in the world. One way we support tropical medicine research is to provide fellowships to scientists in order to pursue research training and an independent research career. Obtaining a Wellcome Fellowship in Public Health and Tropical Medicine, at all levels, is a highly competitive process. Funding committees look for certain qualities in a grant proposal. Are you the right person? Is the project important, interesting and achievable? Are you working in the best place? In this talk I will share some tips that will maximise your chances of success.

Keyword: Wellcome Trust, application

TBA

Aaron Jex

Watter and Eliza Hall Institute of Medical Research

(No available abstract)

Thursday 7 December 2017

14.00-15.30
Room A

S22: Involving the Community is Key to Effective Research: The HIV Prevention Research Experience

Chairpersons:

Anupong Chitwarakorn

Chaiwat Ungsedhapand

Invited Speaker

1. The importance of the Community Advisory Board (CAB)
   Rapeepun Jommaroeng
   Multiple Sexuality Community Advisor Board (M-CAB

(No available abstract)

2. Community Engagement from the Researcher's Perspective
   Anchalee Varangrat
   Thailand MOPH – U.S. CDC Collaboration

(No available abstract)

3. How to Begin Community Engagement?
   Wipas Wimonsate and Ms. Farida Langkafah
   Thailand MOPH - US CDC Collaboration

(No available abstract)

4. Is CAB effective in community engagement? Confession of an optimist
   Udom Likhitwonnawut
   NCAB

THE IMPORTANCE OF THE COMMUNITY ADVISORY BOARD (CAB)

Rapeepun Jommaroeng

Multiple Sexuality Community Advisor Board (M-CAB

(No available abstract)

COMMUNITY ENGAGEMENT FROM THE RESEARCHER'S PERSPECTIVE

Anchalee Varangrat

Thailand MOPH – U.S. CDC Collaboration

(No available abstract)

HOW TO BEGIN COMMUNITY ENGAGEMENT?

Wipas Wimonsate and Ms. Farida Langkafah

Thailand MOPH - US CDC Collaboration

(No available abstract)

IS CAB EFFECTIVE IN COMMUNITY ENGAGEMENT? CONFESSION OF AN OPTIMIST

Udom Likhitwonnawut [1]

[1] *NCAB*

The presentation summarizes the history of community involvement in HIV clinical research in Thailand which started with an HIV efficacy trial. CAB was and still is the most popular mechanism for including community in HIV clinical research. The presentation describes structural and cultural flaws of CAB. Unclear role and responsibility compromises CABs' ability in providing relevant inputs to the design and implementation of a study. Lack of systematic capacity training for CAB members compromises the ability of CAB members to involve meaningfully in HIV research. Power imbalance between researchers, doctors and CAB members inhibits frank discussions. As the result, CAB's role is reduced to primarily providing comments and suggestions for informed consent documents. Furthermore, the engagement is mostly with research team, not with the communities that CABs supposedly represent. The presentation concludes with suggestions for improving CAB effectiveness.

Keyword: Community Advisory Board (CAB)

Thursday 7 December 2017

14.00-15.30
Room B

S23: Progress towards Developing Vaccines against *Plasmodium vivax*

Chairperson:

John Adams

Invited Speakers

1. Rational development of *Plasmodium vivax* pre-erythrocytic vaccines: towards better efficacy using Virus-Like Particles
   Arturo Reyes-Sandoval
   The Jenner Institute / University of Oxford

2. A PfRH5-like protein in *P. vivax*?
   Wang Nguitragool
   Faculty of Tropical Medicine, Mahidol University

3. Long-term memory B cell responses in Thai patient to *P. vivax* Duffy binding protein
   Patchanee Chootong
   Faculty of Medical Technology, Mahidol University

4. An engineered vaccine of the *Plasmodium vivax* Duffy binding protein enhances induction of broadly neutralizing antibodies
   John Adams

5. Transferrin receptor 1 is a reticulocyte-specific receptor for *Plasmodium vivax*
   Wai-Hong Tham
   The Walter and Eliza Hall Institute

RATIONAL DEVELOPMENT OF *PLASMODIUM VIVAX* PRE-ERYTHROCYTIC VACCINES: TOWARDS BETTER EFFICACY USING VIRUS-LIKE PARTICLES

Arturo Reyes-Sandoval [1]

[1] *The Jenner Institute / University of Oxford*

The development of a protective and broad-acting vaccine against the most widely distributed human malaria parasite, *Plasmodium vivax*, is considered important to achieve malaria elimination. The most of Vaccine candidates expressing the *P. vivax* circumsporozoite protein (CSP) because it has been shown to induce potent immune responses. At the moment, the scarcity of pre-clinical models to test protective efficacy and define surrogates of protection limits the effective comparison between vaccine candidates.

We report the rational development to obtain a highly protective *P. vivax* vaccine by using newly developed rodent challenge models to assess various *P. vivax* CSP (PvCSP) vaccine candidates. To this end, we generated two transgenic rodent *P. berghei* parasite lines, where the P. berghei csp gene coding sequence has been replaced with either full-length *P. vivax* VK210 or VK247 csp. sporozoites of these transgenic parasites were used to challenge mice that were immunized with viral vectors (ChAd63, MVA) or virus-like particles (Rv21) vaccines expressing or presenting various versions of the PvCSP protein.

While protective efficacy using viral vectors was low, immunization with Rv21, that display in a kind of viral surface a chimeric PvCSP protein (VK210/247), in Matrix M adjuvant induced 100% sterile protection in mice that are highly sensitive to malaria infection and for which previous attempts to protect against a *P. berghei* pre-erythrocytic challenge had failed. The higher IgG total antibody levels induced by Rv21 vaccine correlated with protection. Our results demonstrate that the antibody response (Th2) induced by the Rv21 and Matrix M is important in protection against vivax malaria infection, in addition, the presence of adjuvant, for a certain time, produce Th1 response.

We confirm the high protective efficacy induced by a chimeric CSP antigen presented in a VLP platform and the description of a model for a parasite challenge in rodents.

Keywords: *Plasmodium vivax*, malaria, vaccines

A PFRH5-LIKE PROTEIN IN *P. VIVAX*?

Wang Nguitragool [1], Anongruk Chim-Ong [1], Thitiporn Surit [1]

[1] *Faculty of Tropical Medicine; Mahidol University*

The number of vaccine candidates against *Plasmodium vivax* is highly limited. For blood stage vaccine, *Plasmodium vivax* Duffy Binding Protein (PvDBP) has historically been the only protein that receives in-depth attention. But the difficulty in achieving cross protection due to the high degree of polymorphism, and the existence of *P. vivax* lines that apparently do not need PvDBP for invasion, indicate that additional candidates are needed. Over the past 5 years, several lines of investigation have identified PfRH5 as a promising protein for the blood stage *P. falciparum* vaccine. PfRH5 is essential for parasite invasion of the erythrocyte and antibodies against the proteins are associated with protection. We asked whether there is a functional homolog of PfRH5 in *P. vivax*. We have analyzed the *P. vivax* gene database and identified a protein that shares several properties with PfRH5. The protein binds erythrocytes but the binding is differentially affected by pretreatment of erythrocytes with enzymes. Importantly, the level of human antibody to this protein is associated reduced parasitemia in patients. Asymptomatic carriers of *P. vivax* also have a heightened level of antibody to this protein.

Keywords: malaria, *Plasmodium vivax*, invasion, vaccine

LONG-TERM MEMORY B CELL RESPONSES IN THAI PATIENT TO *P. VIVAX* DUFFY BINDING PROTEIN

Patchanee Chootong [1]

[1] *Department of Clinical Microbiology and Applied Technology, Faculty of Medical Technology, Mahidol University, Thailand*

The major challenge in designing a protective Duffy binding protein region II (DBPII) based vaccine against blood-stage *vivax* malaria is the high number of polymorphisms in critical residues targeted by binding-inhibitory antibodies. The polymorphic patterns of DBPII vary geographically from region to region. In Thailand, there are 12 polymorphic DBPII haplotypes (DBL-TH1, -TH2, -TH3, -TH4, -TH5, -TH6, -TH7, -TH8, -TH9, -TH10, -TH11 and -TH12) among Thai *vivax* isolates. Here, longevity of antibody and memory B cell response (MBCs) of polymorphic DBL-TH haplotypes were analyzed in *P. vivax*-exposed individuals living in a malaria endemic area in southern Thailand. The result showed that DBL-TH was immunogenic during infection and sufficient to produce a positive anti-DBL-TH antibody response for up to 9 months post-infection. Seropositive in some individuals were able to maintain inhibitory antibody against the binding of DBL-TH to erythrocytes after recovery from infection. Interestingly, the persistence of anti-DBL-TH responses at recovery phase was associated with the expansion of activated and atypical memory B cells and a positive DBL-TH-specific MBCs response by ELISPOT. These data demonstrate that patients can produce antibody and memory B cells in natural *P. vivax* exposure. Both antibody and memory B cells response to DBL-TH antigen is stably maintained in the absence of reinfection. More knowledge of immunity to DBPII variants which are common in malaria-endemic areas will enhance development of a DBPII-based vaccine.

Keyword: Memory B cell responses

AN ENGINEERED VACCINE OF THE *PLASMODIUM VIVAX* DUFFY BINDING PROTEIN ENHANCES INDUCTION OF BROADLY NEUTRALIZING ANTIBODIES

John Adams [1], Francis B Ntumngia[1], Camilla V Pires[2], Samantha J Barnes[1], Miriam T George[1], Richard Thomson-Luque[1], Flora S Kano[2], Jessica RS Alves[2], Darya Urusova[3], Dhelio B Pereira[4], Niraj H Tolia[3], Christopher L King[5], Luzia H Carvalho[2], John H Adams[1*]

[1]Center for Global Health and Infectious Diseases Research, Department of Global Health, College of Public Health, University of South Florida, Tampa, 33612, USA; [2]Centro de Pesquisas René Rachou/ FIOCRUZ, Belo Horizonte, 30190, Brazil; [3]Departments of Molecular Microbiology & Microbial Pathogenesis, and Biochemistry & Molecular Biophysics, Washington University School of Medicine, Saint Louis, 63130, USA; [4]Centro de Pesquisa em Medicina Tropical de Rondonia-CEPEM, Porto Velho, 76812-245, Brazil; [5]Center for Global Health and Diseases, Case Western Reserve University, Cleveland, 44106, USA

Plasmodium vivax invasion into human reticulocytes is a complex process. The Duffy binding protein (DBP) dimerization with its cognate receptor is vital for junction formation in the invasion process. Due to its functional importance, DBP is considered a prime vaccine candidate, but variation in B-cell epitopes at the dimer interface of DBP leads to induction of strain-limited immunity. We believe that the polymorphic residues tend to divert immune responses away from functionally conserved epitopes important for receptor binding or DBP dimerization. As a proof of concept, we engineered the vaccine DEKnull to ablate the dominant Bc epitope to partially overcome strain-specific immune antibody responses. Additional surface engineering on the next generation immunogen, DEKnull-2, provides an immunogenicity breakthrough to conserved protective epitopes. DEKnull-2 elicits a stronger broadly neutralizing response and reactivity with long-term persistent antibody responses of acquired natural immunity. By using novel engineered DBP immunogens, we validate that the prime targets of protective immunity are conformational epitopes at the dimer interface. These successful results indicate a potential approach that can be used generally to improve efficacy of other malaria vaccine candidates.

Keyword: malaria, vaccine, *Plasmodium vivax*

TRANSFERRIN RECEPTOR 1 IS A RETICULOCYTE-SPECIFIC RECEPTOR FOR *PLASMODIUM VIVAX*

Wai-Hong Tham [1]

[1] *The Walter and Eliza Hall Institute*

Plasmodium vivax is the most widely distributed malaria parasite that infects humans. This parasite shows a strict host tropism for reticulocytes. We identify transferrin receptor 1 (TfR1), a known receptor for New World hemorrhagic fever arenaviruses, as the target for stable engagement by the *P. vivax* reticulocyte-binding protein 2b (PvRBP2b) invasion ligand. We show that these divergent pathogens bind the apical domain of TfR1. The structure of the N-terminal domain of PvRBP2b involved in red blood cell binding was determined, elucidating the molecular basis for TfR1 recognition. TfR1 was validated as the biological target of PvRBP2b engagement by TfR1 expression knockdown analysis. TfR1 mutant cells were refractory to invasion of *P. vivax*, but not to invasion of *P. falciparum* which is not reticulocyte restricted. Using Brazilian and Thai clinical isolates, we show that PvRBP2b monoclonal antibodies that inhibit reticulocyte binding also block *P. vivax* entry into reticulocytes. These data show that TfR1-PvRBP2b invasion pathway is critical for the selective recognition of reticulocytes during *P. vivax* invasion.

Keyword: *Vivax*, malaria, invasion, antibodies

Thursday 7 December 2017

14.00-15.30
Room C

S24: Research Data Sharing Controversy

Chairperson:

Phaik Yeong Cheah

Mehul Dhorda

Invited Speakers

1. Population Pharmacokinetic Properties of Piperaquine in *Falciparum* Malaria: An Individual Participant Data-level Meta-analys

   Joel Tarning

   Mahidol-Oxford Tropical Research Unit

2. Real-time data sharing

   Suttipat Srisutham

   Mahidol-Oxford Tropical Research Unit

3. Data sharing – current practices and guidelines

   Phaik Yeong Cheah

   Mahidol-Oxford Tropical Research Unit

4. Data sharing: case studies and current practices (panel discussion)

   Mehul Dhorda

   Worldwide Antimalarial Resistance Network

POPULATION PHARMACOKINETIC PROPERTIES OF PIPERAQUINE IN *FALCIPARUM* MALARIA: AN INDIVIDUAL PARTICIPANT DATA-LEVEL META-ANALYSIS

Richard M. Hoglund [1], Lesley Workman [2], Michael D. Edstein [3], Nguyen Xuan Thanh [4], Nguyen Ngoc Quang [5], Issaka Zongo [6], Jean Bosco Ouedraogo [7], Steffen Borrmann [8], Leah Mwai [9], Christian Nsanzabana [10], Ric N. Price [11], Prabin Dahal [10], Nancy C. Sambol [12], Sunil Parikh [13], Elizabeth A. Ashley [14], Aung Pyae Phyo [14], Khin Maung Lwin [14], Rose McGready [15], Nicholas P.J. Day [16], Philippe J Guerin [10], Nicholas J. White [16], Karen I. Barnes [2], Joel Tarning [1]

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Artemisinin-based combination therapies (ACTs) are the mainstay of the current treatment of uncomplicated *P.falciparum* malaria, but ACT resistance is spreading across Southeast Asia. Dihydroartemisinin-piperaquine is one of the five ACTs currently recommended by the World Health Organization. Previous studies suggest that young children (< 5 years) with malaria are under-dosed. The aim of the following study utilised a population-based pharmacokinetic approach to optimise the antimalarial treatment regimen of piperaquine. Published pharmacokinetic studies on piperaquine were identified through a systematic literature review of articles published between January 1960 and February 2013. Individual plasma piperaquine concentration-time data from eleven clinical studies (8,776 samples from 728 individuals) in both adults and children with uncomplicated malaria or healthy volunteers were collated and standardised by the WorldWide Antimalarial Resistance Network. Data were pooled and analysed using nonlinear mixed-effects modelling. Piperaquine pharmacokinetics were described successfully in all patient groups, resulting in lower piperaquine exposures in young children compared to older children and adults. The derived population pharmacokinetic model was used to develop a revised dose regimen of dihydroartemisinin-piperaquine that is expected to provide equivalent piperaquine exposures safely in all patients, including in young children with malaria. This should prolong the useful therapeutic life of dihydroartemisinin-piperaquine by increasing cure rates and thereby slowing resistance development. This work was part of the evidence that informed the World Health Organization Technical Guidelines Development group in the development of the recently published treatment guidelines (2015).

Keyword: Malaria, Piperaquine, Pharmacometrics

REAL-TIME DATA SHARING

Suttipat Srisutham [1]

[1] *Mahidol Oxford Tropical Medicine Research Unit (MORU)*

Artemisinin combination therapies (ACTs) are the first-line treatment for falciparum malaria worldwide, including five countries in the Greater Mekong Subregion (GMS)--Thailand, Cambodia, Lao PDR, Vietnam, and Myanmar. Each contains an artemisinin drug, with either piperaquine (DP), mefloquine (AM), amodiaquine (ASAQ), or lumefantrine (AL). Molecular markers have been identified that correlate with resistance to each of the partner/combination drugs. The principal aim of the project was to inform *P. falciparum* treatment policies for intensified malaria control and malaria-elimination efforts in the GMS by defining the prevalence and distribution of molecular markers of partner drug resistance and sharing data in real time. The updated data will be presented promptly on an open-access tool (http://www.wwarn.org/tracking-resistance/act-partner-drug-resistance-surveyor). This system provides timely data support to policy-makers and researchers, thereby enhancing malaria control and elimination.

Keyword: Real-time data sharing, drug resistance, malaria

DATA SHARING – CURRENT PRACTICES AND GUIDELINES

Phaik Yeong Cheah [1]

[1] *Mahidol Oxford Tropical Medicine Research Unit*

My talk will be about the current international guidelines and requirements for data sharing including the CIOMS 2016 guidelines. It will also include the experience of our Data Access Committee in managing data requests as well as data from our recently completed qualitative study.

Keyword: Data sharing

DATA SHARING: CASE STUDIES AND CURRENT PRACTICES (PANEL DISCUSSION)

Mehul Dhorda [1]

[1] *WorldWide Antimalarial Resistance Network*

Data sharing is now a fundamental part of clinical research throughout the world, but it requires an ethical and responsible approach to safeguard patient confidentiality and credit data contributors. The WorldWide Antimalarial Resistance Network (WWARN)'s innovative approach to data sharing and pooled analyses is enabling the malaria community to ask practical and life-saving research questions. Working with research partners we are able to perform cross-disciplinary analyses that help to identify important treatment trends and information gaps that affect vulnerable populations such as pregnant women and small children. As well as the many positive attributes associated with data sharing, we still face many challenges such as the complex issues of participant consent, equity and reciprocity and the distribution of credit and reward, especially highlighted in lower and middle income countries. This symposium will provide an opportunity to address both the opportunities and challenges that arise from data sharing and begin to articulate responses to assure that responsible data sharing will benefit the whole malaria research community.

Keyword: data sharing, malaria, clinical research

Thursday 7 December 2017

14.00-15.30
Room D

S25: Red Queen's Race: Malaria Drug Resistance vs. Drug Development

Chairpersons:

Prapon Wilairat

Rapatbhorn Patrapuvich

Invited Speakers

1. Advances on the development of next generation differentiated antimalarial drugs
   Francisco Javier Gamo
   GlaxoSmithKline, Tres Cantos, Spain

2. Membrane transport proteins as antimalarial drug targets
   Kiaran Kirk
   Australian National University

3. Protein translation enzymes as druggable targets in malaria parasites
   Amit Sharma
   International Centre for Genetic Engineering and Biotechnology

4. Mutability of malaria parasites
   Pradipsinh Rathod
   University of Washington

ADVANCES ON THE DEVELOPMENT OF NEXT GENERATION DIFFERENTIATED ANTIMALARIAL DRUGS

Javier Gamo [1]

[1] *Tres Cantos Medicines Development Campus. Diseases of the Developing World (DDW). GlaxoSmithKline, Tres Cantos, Spain.*

The Diseases of the Developing World (DDW) facility is located at the Tres Cantos Medicines Development Campus (TCMDC) and is fully focused on the discovery of novel and differentiated treatments for Kinetoplastids, Tuberculosis and Malaria disease. Since 2010, GlaxoSmithKline TCMDC has adopted an open innovation strategy that fosters collaboration and transfer of knowledge with academia and biotech, with the final aim to deliver new and affordable effective medicines for DDW (malaria, tuberculosis and kinetoplastid diseases). As part of this open innovation strategy DDW has made public different compound boxes containing information on hits found from phenotypic screens against malaria, tuberculosis and some relevant kinetoplastids. Furthermore, innovative collaboration approaches such as the Open Lab (www.openlabfoundation.org) at TCMDC provides visiting scientists funding and access to GSK facilities, compound collections and drug discovery expertise, in an attempt to exploit a novel model of collaboration for DDW medicine discovery and development. In this communication we´ll highlight some of our successful collaboration approaches and we´ll be a call to new drug discovery collaborative opportunities with the aim of filling neglected diseases portfolio and guarantee a sustainable pipeline.

Keywords: malaria, Drug-Discovery, antimalarials

MEMBRANE TRANSPORT PROTEINS AS ANTIMALARIAL DRUG TARGETS

Kiaran Kirk [1]

[1] *Australian National University*

High-throughput whole-cell phenotypic screens have led to the identification of a raft of potential new antimalarial agents. Using a range of physiological and biochemical assays we have tested the effects of several collections of such compounds on parasite ion homeostasis. The assays have revealed that a significant proportion of the antimalarial agents identified in phenotypic screens against the human malaria parasite, *Plasmodium falciparum*, inhibit membrane transport proteins in the parasite plasma membrane. In particular, the data are consistent with a structurally diverse range of compounds sharing a common mechanism of action, exerting their antimalarial effect via an interaction with the parasite's putative Na+-efflux ATPase, PfATP4. The parasite's lactic acid efflux transporter, PfFNT, has also emerged as a candidate antimalarial drug target.

Keywords: malaria, transporter

PROTEIN TRANSLATION ENZYMES AS DRUGGABLE TARGETS IN MALARIA PARASITES

Amit Sharma [1]

[1] *International Centre For Genetic Engineering And Biotechnology*

Our laboratory has made contributions to understanding of structural principles that underlie molecular function of malaria parasite proteins. Over the past decade, the laboratory has studied parasite proteins involved in various crucial processes including in protein translation. These proteins have been studied using multi-disciplinary approaches including bioinformatics, structural biology, biological assays, parasite biology and inhibitor development. These studies together provide specific targets for structure-based design of inhibitors against malaria and some of the projects are poised for collaboration with pharmaceutical partners. We have therefore highlighted the importance of protein translation motors as new targets for discovery of novel anti-malarials. We have also underpinned these studies with a basic biology understanding of malarial tRNA synthetases. Using case studies, we will discuss how several members of the *P. falciparum* tRNA synthetase enzyme family have been successfully targeted with small molecular inhibitors. Using crystal structures of protein-drug complexes, we will dissect the modes of action of some of the potent inhibitors, and their potential as leads against the malaria parasite.

Keywords: complex, drug, inhibitor, malaria, protein

MUTABILITY OF MALARIA PARASITES

Pradipsinh K. Rathod [1]

[1] *Professor of Chemistry University of Washington Seattle, WA, USA*

Drug resistance in *P. falciparum* has threatened the effectiveness of global malaria control programs for over half-a-century. The best understood traits involve decreased effectiveness of antimalarials such as antifolates and chloroquine. More recent concerns revolve around decreasing potency of Artemisinin Combination Therapies (ACTs). Formal descriptions of how haploid blood-stage parasites arrive at beneficial mutations, without large collateral damage in the rest of the genome, is of interest.

In vitro selection for resistance to experimental antimalarials, and a detailed characterization of genomic DNA in early and late resistance outcomes, capture intermediate gene amplification steps that eventually lead to pure point mutations in the parasite genome. In a population-based strategy, mutations arise where needed and only where needed.

Here we describe newer selection experiments which show a shared mutagenesis strategy with a variety of compounds, each leading to successful mutations against very different targets. Importantly, such capabilities are enhanced in a subset of recent parasite isolates from Southeast Asia and from South Asia. These phenotypic approaches offer new tools to characterize mutating potential of distinct global parasite populations.

Supported by a US NIH ICEMR (South Asia) grant AI089688.

Keyword: *P. falciparum*

Thursday 7 December 2017

16.00-17.30
Room A

S26: Helminthology

Chairpersons:

Dorn Wathanakulpanich

Windell Rirera

Invited Speakers

1. The role of domestic dogs in the transmission of zoonotic helminthes in a rural area of Mekong river basin
   Megumi Sato
   Graduate School of Health Sciences, Niigata University

2. Environmental DNA as a tool for surveillance and control of NTDs and its application in opisthorchiasis and schistosomiasis endemic areas
   Marcello Otake Sato
   Dokkyo Medical University, Japan

3. Transmission of *Opisthorchis viverrini, Schistosoma mekongi* and soil-transmitted helminthes on the Mekong Islands, Southern Lao PDR.
   Youthanavanh Vonghachack
   University of Health Sciences, Vientiane, Lao PDR

4. Intestinal Parasitic Infections in School-aged Children and Molecular Speciation of Hookworms, and *Strongyloides sp.*, and Genotyping of *Giardia intestinalis* in East Sikkim, India
   Shantikumar Singh Takhellambam
   Department of Microbiology, Sikkim Manipal Institute of Medical Sciences, Gangtok, Sikkim, India

THE ROLE OF DOMESTIC DOGS IN THE TRANSMISSION OF ZOONOTIC HELMINTHES IN A RURAL AREA OF MEKONG RIVER BASIN

Megumi Sato [1]

[1] *Graduate School of Health Sciences, Niigata University*

Dogs have been bred since ancient times for companionship, hunting, protection, shepherding and other human activities. Some canine helminth parasites can cause significant clinical diseases in humans such as *Opisthorchis viverrini* causing cholangiocarcinoma in Southeast Asian countries. In this study, socio-cultural questionnaire, canine parasitological analysis, necropsy, parasite molecular confirmation and dog roaming data were evaluated in Savannakhet, Lao PDR, a typical Mekong Basin area. Dog owners comprised 48.8% of the studied population, with 61.2% owning one dog, 25.1% 2 dogs, 8.5% 3 dogs and 1.8% owning more than 4 dogs. Data from GPS logger attached to dogs showed they walked from 1.4 to 13.3 km per day, covering an area of 3356.38m2 average, with a routine of accessing water sources. Thirteen zoonotic helminth species were observed. Causative agents of visceral and cutaneous larva migrans occurred in 44.1% and 70% of the samples respectively. *Spirometra erinaceieuropaei* was detected in 44.1% of samples. Importantly, *O. viverrini* was found in 8.8% of samples. Besides the known importance of dogs in the transmission of *Ancylostoma spp*., *Toxocara spp*. and *S.erinaceieuropaei*, the observed roaming pattern of dogs confirmed it as an important host perpetuating *O. viverrini* in endemic areas; their routine access to waterbodies may spread *O. viverrini* eggs in a favorable environment for the fluke development, facilitating the infection of fishes, and consequently infecting humans living in the same ecosystem. Therefore, parasitic NTDs control programs in humans should be done in parallel with parasite control in animals, especially dogs, in the Mekong River basin area.

Keywords: eco-health, helminth zoonosis, GIS, NTDs, Laos, canines

ENVIRONMENTAL DNA AS A TOOL FOR SURVEILLANCE AND CONTROL OF NTDS AND ITS APPLICATION IN OPISTHORCHIASIS AND SCHISTOSOMIASIS ENDEMIC AREAS

Marcello Otake Sato [1], Armand Rafalimanantsoa-Solofoniaina [2], Megumi Sato [3], Tiengkham Pongvongsa [4], Toshifumi Minamoto [5], Jitra Waikagul [6], Satoru Kawai [1], Yuichi Chigusa [1], Kazuhiko Moji [7]

[1]Department of Tropical Medicine and Parasitology, Dokkyo Medical University, Mibu, Tochigi, Japan., [2]Unité de Recherche sur les Helminthiases, Institut Pasteur de Madagascar, Antananarivo, Madagascar, [3]Graduate School of Health Sciences, Niigata University, Niigata, Japan, [4]Station of Malariology, Parasitology, and Entomology of Savannakhet Province, Savannakhet, Lao PDR, [5]Graduate School of Human Development and Environment, Kobe University, Kobe, Japan, [6]Department of Helminthology, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand, [7]Graduate School of International Health Development, Nagasaki University, Nagasaki, Japan

Foodborne and waterborne diseases are major threats to human health once those agents are present in the daily life of everyone. In southeast Asian countries, the liver fluke *Opisthorchis viverrini* (Ov) is a major public health problem as the liver fluke cause cholangiocarcinoma in chronic infections. Opisthorchiasis is highly prevalent in Laos and it is a foodborne zoonosis transmitted by fish. Blood flukes, the most important parasitic disease of Madagascar is caused by Schistosoma mansoni (Sm) and *S. haematobium* (Sh) infecting people by skin penetration of metacercaria in water sources. The infection by those blood flukes causes granulomatous reactions and fibrosis in the affected organs, resulting in severe clinical manifestations. Usually the diagnosis of Ov, Sm and Sh is done by the detection of the parasite in host material; fecal examination, copro DNA, serology and so on. However, even those methods provide us important information in individual samples, the range of the disease in the environment and the impact it can cause in endemic areas is difficult to predict, especially in the case of zoonotic diseases. To fill the lack of eco-epidemiology information we developed a system for detection of Ov, Sm and Sh based on environmental DNA (eDNA) detection enabling us to determine risky and safe spots in 2 endemic areas: Ov in Laos and Sm in Madagascar. Application of eDNA detection may provide a highly accurate surveillance technology to be applied in NTDs, helping to establish intelligent control programs of NTDs and contributing to food and water safety for the people in living in endemic areas.

Keyword: zoonosis; helminth; eco-epidemiology; ecohealth

TRANSMISSION OF OPISTHORCHIS VIVERRINI, SCHISTOSOMA MEKONGI AND SOIL-TRANSMITTED HELMINTHES ON THE MEKONG ISLANDS, SOUTHERN LAO PDR

Youthanavanh Vonghachack [1]

[1] *Unit of Parasitology, Faculty of Basic Sciences, University of Health Sciences, Vientiane, Lao PDR*

Background: Prevalence of *Opisthorchis viverrini*, *Schistosoma mekongi* and soil-transmitted helminths (STH) remains high in Lao People's Democratic Republic (Lao PDR), despite control efforts including mass-drug administration, education and communication campaigns. New approaches are required to advance helminth control.

Methodology: An ecohealth study was conducted on two Mekong islands in southern Lao PDR. Demographic and behavioural data were collected by questionnaire. Human and animal reservoir stools were examined. *Bithynia spp.* and *Neotricula aperta* snails were examined using shedding. Freshwater fish were examined using digestion technique. Multivariate random-effects analysis was used to find risk factors associated with helminth infections.

Principal findings: Human infection rates with *O. viverrini*, hookworm, *S. mekongi*, *Trichuris trichiura*, *Ascaris lumbricoides* and *Taenia spp.* were 60.7%, 44.1%, 22.2%, 4.1%, 0.6% and 0.1%, respectively. Heavy intensity infections were 4.2%, 3.6% and 1.8% for *O. viverrini*, *S. mekongi* and hookworm, respectively. *O. viverrini* infection rate among dogs and cats were 25.0% and 53.1%, respectively. *S. mekongi* infection rates among dogs were 14.7%. Prevalence of *O. viverrini* and *S. mekongi* in snails was 0.3% and 0.01%, respectively. Overall prevalence of *O. viverrini* infection in fresh water fish was 26.9%, with the highest infection rates occurring in *Hampala dispar* (87.1%), *Cyclocheilichthys apogon* (85.7%) and *Puntius brevis* (40.0%). Illiteracy and lower socioeconomic status increased the risk of *O. viverrini* infection, while those aged 10–16 years and possessing latrines at home were less likely to be infected. Household dogs and cats that consumed raw fish were significantly and positively associated with *O. viverrini* infection of the household members. For *S. mekongi*, children under 9 years old were exposed significantly to this infection, compared to older age groups.

Conclusions/Significance: There is a pressing need to design and implement an integrated helminth control intervention on the Mekong Islands in southern Lao PDR. Given the highly dynamic transmission of *S. mekongi*, *O. viverrini*, STH and extended multiparasitism, annual mass-drug administration is warranted along with environmental modifications, health education and improved access to clean water and adequate sanitation to consolidate morbidity control and move towards elimination.

Keywords: *Opisthorchis viverrini*, *Schistosoma mekongi*, animal hosts, *Bithynia sp.*, *Neotricula aperta*, Cyprinidae fish, southern Lao PDR, Laos.

INTESTINAL PARASITIC INFECTIONS IN SCHOOL-AGED CHILDREN AND MOLECULAR SPECIATION OF HOOKWORMS, AND *STRONGYLOIDES SP.*, AND GENOTYPING OF GIARDIA INTESTINALIS IN EAST SIKKIM, INDIA

Shantikumar Singh Takhellambam [1], **Onila N.** [1], **Sunu Hangma Subba** [1]

[1] *Department of Microbiology, Sikkim Manipal Institute of Medical Sciences, Gangtok, Sikkim, India*

Intestinal parasitic infections (IPIs) are common public health problem of school–aged children affecting about 2 billion people worldwide, especially in the developing countries. Studies have shown that IPI is endemic in many parts of India; however, no data is available from Sikkim. In order to plan treatment, preventive and control strategies knowledge of prevalence of intestinal parasites is essential. Prevalence of IPIs in school-aged children in East Sikkim. 2. Morphological identification of intestinal parasites. 3. Molecular identification of hookworms, *Strongyloides sp.* and genotyping of *Giardia intestinalis*. A total 700 stool samples, 300 from children of four schools and 400 samples from two tertiary care hospitals in East Sikkim were collected between January 2015 and December 2016. Saline and iodine wet mounts of stool samples were examined microscopically for parasite ova and cysts. Formol-ether concentration technique was employed to concentrate the stool samples. Conventional PCR and PCR-RFLP were carried out using kits from HELINI biomolecules, Chennai, India for species identification of hookworms and *Strongyloides* eggs, and genotyping of *Giardia intestinalis* cysts, respectively. Of the total 700 children 24.7% were found infected with intestinal parasites from the highest to lowest, *G.intestinalis* 8.9%, *Entamoeba histolytica / dispar / moshkovskii sp.* (8.2%), and *A. lumbricoides* (2.3%), *Taenia sp.* (2.1%), Hookworm sp. (2%), *H.nana* (0.7%) *T .trichiura* (0.3%), *E.vermicularis* (0.1%) and *S. stercoralis* (0.1%) Among the hookworms, *N.americanus* was 64% (9/14) and *A.duodenale* was 36% (5/14). The genotypes of *G.intestinalis* were B IV (54.5%), A II and B (38.2%) and B III (7.3%) assemblages, of which the most prevalent genotype was B IV. The occurrence of IPIs is moderately high among school- aged children in East Sikkim. Higher rate of Taenia infection than most of the soil-transmitted helminths (STH) may be due to non-vegetarian diet habit of people in Sikkim. Infection with STH is still a problem in Sikkim despite mass albendazole prophylaxis. High prevalence of *G. intestinalis* B IV indicates humans as the major mode of transmission. Personal hygiene, safe drinking water supply, proper sanitation and regular deworming of schools children may significantly reduce IPIs.

Keywords: parasitic infections, hookworms, *Strongyloides sp, Giardia intestinalis*

16.00-17.30
Room B

S27: Antimalarial Drug Discovery and Resistance

Chairpersons:

John H Adams

Chairat Uthaipibull

Invited Speakers

1. MMV portfolio of drug discovery projects with academic and pharma partners
   Javier Gamo
   Medicines for Malaria Venture

2. Drug target prioritization for *Plasmodium falciparum* by whole-genome saturation mutagenesis
   John Adams
   University of South Florida

3. Experimental systems to validate targets and study of antimalarial drug resistance mechanisms
   Chairat Uthaipibull
   National Center for Genetic Engineering and Biotechnology (BIOTEC)

4. Optimising dosing of antimalarials to prevent drug resistance
   Ric Price
   Menzies School of Health Research

MMV PORTFOLIO OF DRUG DISCOVERY PROJECTS WITH ACADEMIC AND PHARMA PARTNERS

Javier Gamo [1]

[1] *Visiting Senior Director, Drug Discovery. MMV*

Working together with partners, Medicines for Malaria Venture (MMV), a not-for-profit product development partnership (PDP), have established a strong anti-malarial drug pipeline with over 15 compounds in clinical development. The presentation will discuss some of the challenges and opportunities in antimalarial drug discovery with particular focus on case histories from MMV's successful collaboration with both academic and pharma partners. The requirements for delivering the next generation of antimalarial medicines will also be discussed, with an emphasis on developing drugs that provide the tools necessary for the move towards malaria elimination. Particular areas of interest are anti-relapse agents for *P. vivax* malaria, compounds that kill hepatic schizonts and protect against the onset of symptoms, and gametocytocidal compounds to block transmission. Finally MMV's work to explore new open models for drug discovery will be reviewed

Keywords: Drug-Discovery, malaria; antimalarials, partnership

DRUG TARGET PRIORITIZATION FOR *PLASMODIUM FALCIPARUM* BY WHOLE-GENOME SATURATION MUTAGENESIS

Min Zhang [1], Chengqi Wang [1], Jenna Oberstaller [1], Thomas D. Otto [2], Swamy R. Adapa [1], Xiangyun Liao [1], Justin Swanson [1], Suzanne Li [1], Kenneth Udenze [1], Julian C. Rayner [2], Rays H. Y. Jiang [1], John H. Adams [1]

[1] Center for Global Health and Infectious Diseases, Department of Global Health, University of South Florida, Tampa, Florida, USA, [2] Malaria Programme, Wellcome Trust Sanger Institute, Genome Campus Hinxton Cambridgeshire, United Kingdom

Malaria caused by *Plasmodium falciparum* remains a major global health problem, with hundreds of thousands of deaths each year. Recent reductions in disease intensity made in part through concerted recent use of artemisinin combination therapies are now threatened as ACT resistance spreads across South East Asia, requiring new drugs with distinct mechanisms of action. However, the genetic basis of many of its unique biological properties and important metabolic pathways remains unknown hampering drug discovery efforts. In this study, we fulfill the critical need for a robust analytical method to systematically define the genes and pathways indispensable for in vitro survival of asexual blood-stage *P. falciparum* NF54 at a whole-genome scale. This study exploits the efficiency of the piggyBac transposon method to achieve for the first saturation-level mutagenesis of *P. falciparum*. Even at this high density of mutagenesis, no piggyBac insertions were recovered from half of the genes in *P. falciparum* genome and so disruption of the ORF of these genes was presumed deleterious to parasite survival. Therefore, the genes without insertions disrupting their ORFs are considered essential for asexual blood-stage growth. Examples of essential genes includes K13 implicated in ART-R, the essential egress kinase gene CDPK5, and the primary drug target gene DHFR. Overall, saturation-level, whole-genome coverage of unique piggyBac insertions discerns genes and pathways most important for asexual intraerythrocytic growth of *P. falciparum* NF54 under ideal in vitro culture conditions. Our study provides the robust genomic tool needed to accelerate progress to identify and validate essential candidate targets to develop the most effective new antimalarial therapies.

Keyword: *Plasmodium falciparum*

EXPERIMENTAL SYSTEMS FOR TARGET VALIDATION AND STUDY OF ANTIMALARIAL DRUG RESISTANCE MECHANISMS

Chairat Uthaipibull [1], Parichat Prommana [1], Navaporn Posayapisit [1], Jutharat Pengon [1], Aiyada Aroonsri [2], Philip J Shaw [1], Sumalee Kamchonwongpaisan [1], Yongyuth Yuthavong [1]

[1] National Center for Genetic Engineering and Biotechnology (BIOTEC), Thailand Science Park, Pathum Thani, Thailand, [2] National Center for Genetic Engineering and Biotechnology (BIOTEC), Thailand Science Park, Pathum Thani, Thailand

The increasing number of reports on artemisinin-resistant *Plasmodium falciparum* from Southeast Asia are alarming signals for the malaria control and treatment. Therefore, there is an urgent need for discovery of new and effective antimalarials that cannot be tolerated by the parasites. To achieve this ultimate goal, we will need to understand the mechanisms of drug resistance which will lead to the design of new antimalarial drugs that can counteract the resistance. Identification of new and potential drug targets is a necessary process for the discovery of new drugs to fight the parasites. In our laboratory, various genetic tools have been used for dissecting gene functions with the aims to validate new drug targets and to study drug resistance mechanisms. The glmS riboswitch gene attenuation system has been used to control the expression of genes in the process of target identification and validation, as well as for chemogenomic profiling to identify new antimalarial compounds. CRISPR/Cas9 gene editing tool has been used to dissect the drug resistance mechanisms. The results from these experimentation systems will be presented and discussed to guide researchers in selecting genetic tools for their studies.

Keywords: malaria, target validation, drug resistance

OPTIMISING THE DOSING OF ANTIMALARIALS TO PREVENT DRUG RESISTANCE

Ric Price [1]

[1] *Menzies School of Health Research, Darwin, Australia*

The clinical management of patients with an infectious disease is based on two fundamental elements: making the diagnosis and prescribing the correct dose of treatment. Once antimalarials are prescribed the therapeutic response is influenced by a range of factors that can be broadly classified into those pertaining to the host, the parasite and the drug. Drug resistance is driven by inadequate treatment, which is sufficient to kill the drug sensitive parasites, but not the resistant parasites. Under this selective drug pressure resistant parasites emerge and spread. In this presentation, the factors determining the therapeutic response to malaria will be reviewed, with particular attention to the dosing recommendations. Specific patient populations are vulnerable to being exposed to subtherapeutic drug concentrations – these will be explored in those infected with either *P. falciparum* or *P. vivax*. The implications of subtherapeutic dosing will be reviewed and suitable strategies proposed to overcome these.

Keywords: malaria, falciparum, vivax, antimalarials, drug resistance å

Thursday 7 December 2017

16.00-17.30
Room C

S28: Free Paper III: Tropical Medicine II

Chairpersons:

Aongart Mahittikorn

Wanlapa Roobsoong

Speakers

1. Novel animal models to identify PK/PD relationships for gut localized pathogens
   Samuel L. Arnold
   University of Washington

2. Biogents Sweetscent lure increases the collection rate of *Aedes aegypti* and *Aedes albopictus* in commercially available homeowner mosquito traps
   Ingeborg Schleip
   Biogents AG

3. Two Plus One: The Combination of Two Passive and One Active Mosquito Traps May Well Be an *Aedes* (*Stegomyia*) Control Tool Worthy of Attention
   Martin Geier
   Biogents AG

4. *Anopheles* Species Diversity and Biting Behavior of Incriminate as Malaria Vectors in a High Prevalence Malaria Area of Tak Province, Western Thailand
   Chatchai Tananchai
   Kasetsart University

5. Making Automatic Mosquito Monitoring Smarter: Counting and Identifying Mosquito Species Using the New BG-Counter
   Jennifer McCaw
   Biogents AG

6. A 3-year regional *P. falciparum* elimination program in Eastern Kayin State, Myanmar: impact of generalized access to early diagnosis and treatment and of hotspot-targeted mass drug administration
   Jordi Landier
   Shoklo Malaria Research Unit

NOVEL ANIMAL MODELS TO IDENTIFY PK/PD RELATIONSHIPS FOR GUT LOCALIZED PATHOGENS

Samuel Arnold [1], **Wesley Van Voorhis** [1], **Molly McCloskey** [1]

[1] *University of Washington*

Shigellosis and cryptosporidosis are generated by oral ingestion of the bacteria *Shigella* or protozoan parasite *Cryptosporidium*, respectively. Symptoms include severe diarrhea and dysentery, and their impact disproportionately affects children and those in low-income countries such as sub-Saharan Africa and Asia. The only drug for cryptosporidiosis, nitazoxanide, has only a 30% response rate in malnourished children and no efficacy in HIV infected individuals. Therapeutic options for shigellosis are limited and globally emerging drug resistance to sulfonamides, tetracyclines, ampicillin, and TMP-SMX has been reported. A major hurdle in drug development for each illness is the lack of a readily available mouse model. Therefore, we have worked on the development of mouse models that are suitable for testing small molecule therapeutics and for identifying PK/PD relationships. An additional challenge for drug development is the gastrointestinal localization of the parasites, as not only are we unsure which PK/PD index should be used for predicting in vivo efficacy, it is also unclear which tissue drug concentration will provide the information required for predicting the desired in vivo response. We have used our mouse model of *Cryptosporidium* infection and PBPK modeling to identify an association between the gastrointestinal drug concentration and *in vivo* efficacy. The PBPK/PD models generated for our anti-*Cryptosporidium* drugs have allowed us to select efficacious dosing regimens prior to *in vivo* studies. The information on the importance of gastrointestinal drug exposure for anti-*Cryptosporidium* will be valuable for the entire research community currently engaged in the development of therapeutics for enteric diseases.

Keyword: *Shigella Cryptosporidium* PK/PD

BIOGENTS SWEETSCENT LURE INCREASES THE COLLECTION RATE OF *AEDES AEGYPTI* AND *AEDES ALBOPICTUS* IN COMMERCIALLY AVAILABLE HOMEOWNER MOSQUITO TRAPS

Ingeborg Schleip [1], Martin Geier [1], Daniel Kline [2], Scott Willis [3], Joyce Urban [2], Scott Gordon [1]

[1] Biogents AG, [2] United States Department of Agriculture, [3] Calcasieu Mosquito Control

A wide variety of mosquito traps designed for homeowner use are available in the marketplace today. We tested seven commercially available mosquito traps that were available from local home improvement stores or from online merchants ranging in price from $49 to $140. Tests were conducted in the USA using a modified Latin square design to assess the collection efficacy of the traps with and without Biogents Sweetscent Lure. Sweetscent Lure contains a chemical blend designed to simulate human skin emissions and is effective for two months after opening. In Florida, the MosClean, Dynatrap XL, Bite Shield Protector, Flowtron Galaxie and Skeetervac Bite-Guard were tested. All traps with Sweetscent Lure showed an increase in the number of *Ae. albopictus* collected (between 2.1 and 4.5 times) compared to the traps without the lure. *Aedes aegypti* was collected in higher rates (between 1.5 to 9.7 times) in all traps with Sweetscent except the Flowtron, which was also the poorest performing trap overall. In Louisiana, the Black Flag, Skeetervac Bite-Guard and the Dynatrap were tested and between 1.9 and 3.8 times more *Ae. albopictus* were collected in traps baited with Sweetscent Lure. These results demonstrate that using Biogents Sweetscent Lure can greatly increase the catching success for *Ae. aegypti* and *Ae. albopictus* when using off the shelf mosquito traps. For mosquito control programs using CO2 baited CDC light traps, the addition of BG-Sweetscent can dramatically increase collections of *Ae. albopictus.* Additionally, in most traps tested, adding BG-Sweetscent also increased overall mosquito collections.

Keyword: mosquito attractant

TWO PLUS ONE: THE COMBINATION OF TWO PASSIVE AND ONE ACTIVE MOSQUITO TRAPS MAY WELL BE AN *AEDES* (*STEGOMYIA*) CONTROL TOOL WORTHY OF ATTENTION

Martin Geier [1], Jennifer McCaw [1], Alvaro Eiras [2], Scott Ritchie [3]

[1] Biogents AG, [2] Universidade Federal de Minas Gerais, [3] James Cook University

Source reduction, traps for host-seeking females, or traps for gravid females may each significantly reduce mosquito populations. We argue that a combination of these methods would provide a robust and sustained vector control program. Recent years have seen the establishment of a highly efficient trap for host-seeking *Aedes (Stegomyia) spp*., the BG-Sentinel (BGS). Originally used in surveillance and monitoring, research has also demonstrated its potential as a control tool, showing a significant reduction in Stegomyia abundance in intervention sites. The BG-Bowl is a novel BGS-type trap with the same efficacy, but made to be constantly deployed in a household. It is cheaper, smaller, sturdy, and silent, with an energy consumption of less than 2.5 W. The development of improved passive traps for oviposition site-seeking Stegomyia females has been equally successful, resulting in various new trap types, one being the Gravid Aedes Trap (BG-GAT). The BG-GAT can be a useful tool for capturing adult *Ae. aegypti* and *Ae. albopictus*. The low cost, practicality of operation and the high catch rates make the BG-GAT suitable for vector surveillance and projects requiring monitoring of mosquitoes for arboviruses, especially in developing countries. In Brazil, studies showed significant reduction abundance of gravid *Ae. aegypti* by BG-GAT. It has also outperformed the CDC's Autocidal Gravid Ovitrap (AGO) in Australian field comparisons. We propose an area-wide *Aedes (Stegomyia) spp*. control strategy, based on an initial source reduction and a subsequent and permanent mass trapping using one active mosquito trap and two lethal ovitraps per household.

Keywords: mosquito traps, gravid control, aedes

ANOPHELES SPECIES DIVERSITY AND BITING BEHAVIOR OF INCRIMINATE AS MALARIA VECTORS IN A HIGH PREVALENCE MALARIA AREA OF TAK PROVINCE, WESTERN THAILAND

Chatchai Tananchai [1], Sylvie Manguin [2], Theeraphap Chareonviriyaphap [3]

[1] Departmentof Entomology, Faculty of Agriculture, Kasetsart University, [2] 2Institut de Recherche pour le Développement, UMR-MD3, Montpellier 34093, France, [3] Department of Entomology, Faculty of Agriculture, Kasetsart University, Bangkok 10900 Thailand

The species diversity, trophic behavior and host preference studies of Anopheles mosquitoes were conducted in a malaria endemic area of Umphang District, Tak Province during a two-year period. Adult Anopheline mosquitoes were collected using a standard collection technique, indoor and outdoor human-landing captures and outdoor cattle-baited collection. Mosquitoes were primarily identified using morphological characters and followed by the appropriate multiplex AS-PCR assay for the identification of species within Anopheles complexes and groups present. From a total of 16,468, 2723 were collected from human-landing method. All three malaria vector complexes, Dirus, Minimus, Maculatus and one putative malaria vector group of Hyrcanus group were detected in areas. Six important malaria vectors were identified, including *An. dirus*, *An. baimaii*, *An. minimus*, *An. aconitus*, *An. maculatus* and *An. sawadwongporni*. Trophic behavior of *An. minimus*, *An. dirus*, *An. baimaii*, *An. maculatus*, and *An. sawadwongporni* were described. In addition, the Anopheles densities and seasonal abundance were more prevalent during the wet periods (June-September) of both years.

Keywords: Anopheles, species diversity, malaria, Umphang, biting behavior

MAKING AUTOMATIC MOSQUITO MONITORING SMARTER: COUNTING AND IDENTIFYING MOSQUITO SPECIES USING THE NEW BG-COUNTER

Jennifer McCaw [1], Martin Geier [1], Michael Weber [1], Andreas Rose [1], Ilyas Potamitis [2], Pancraç Villalonga [3], João Encarnação [3]

[1] Biogents AG, [2] Technological Educational Institute of Crete, [3] Irideon S.L.

As part of an autonomous mosquito trapping station, the BG-Counter automatically differentiates mosquitoes from other insects captured in mosquito traps, counts them, and wirelessly transmits these results together with environmental data to a cloud server for further analysis. This device can also be used to remotely control the run times of mosquito traps and the emission times of carbon dioxide from gas cylinders and the data can be exchanged and analyzed through the internet on the PC, tablet or smart phone. The collected data can give insights into variables that influence mosquito activity, supporting research into the development of more efficient and environmentally friendly mosquito control techniques. In our presentation, we describe the technical background of the BG-Counter and show examples of data sets generated in the field. We also present initial results from our research into advanced versions of the BG-Counter, which are planned to be able to identify and differentiate species of special interest. The development of the BG-Counter was partly supported by the EU's 7th Framework Programme (grant 306105, acronym MCD), the continuation of the development is being supported by the EU's Horizon 2020 programme (grant 691131, acronym REMOSIS).

Keywords: mosquitoes, monitoring, counter, remote, autonomous

A 3-YEAR REGIONAL *P. FALCIPARUM* ELIMINATION PROGRAM IN EASTERN KAYIN STATE, MYANMAR: IMPACT OF GENERALIZED ACCESS TO EARLY DIAGNOSIS AND TREATMENT AND OF HOTSPOT-TARGETED MASS DRUG ADMINISTRATION

Jordi Landier [1], Aung Myint Thu [2], Daniel Parker [3], Gilles Delmas [2], Khin Maung Lwin [2], Francois Nosten [4]

[1] Mahidol Oxford Tropical Medicinie Research Unit ; Shoklo Malaria Research Unit, [2] Mahidol Oxford Tropical Medicine Research Unit ; Shoklo Malaria Research Unit, [3] Mahidol Oxford Tropical Medicine Research Unit; Shoklo Malaria Research Unit, [4] Mahidol Oxford Tropical Medicine Research Unit; Shoklo Malaria Research Unit; Centre for Tropical Medicine and Global Health, Nuffield Department of Medicine, University of Oxford

In the Greater Mekong Sub-region, elimination *P. falciparum* (PF) malaria is of particular interest and urgency because of the threat of spreading artemisinin resistance. In coordination with community-based health organizations and the Myanmar National Malaria Control program, the Malaria Elimination Task Force was set up to develop strategies and to implement a regional approach towards PF elimination in 4 districts of Eastern Myanmar. Malaria Posts (MP) were deployed in each community of the target area to provide access to early diagnosis and treatment of malaria. MP reported PF and *P. vivax* (PV) case data weekly. Malaria prevalence was measured by surveys analyzed by ultrasensitive qPCR. Hotspots of asymptomatic malaria prevalence were defined by malaria prevalence > 40% with PF representing >20% of all malaria infections. Hotspots were addressed by 3 rounds of mass drug administration (MDA) using dihydroartemisin-piperaquine. From May 2014 to April 2017, 1220 villages were equipped with MP and reported weekly data. Out of 272 surveys performed, 70 hotspots were identified and 61 were addressed with 3 consecutive months of TMT between January 2015 and August 2017. The incidence of PF episodes decreased rapidly after opening of a MP (Incidence rate ratio(IRR)=0.75; 95%CI=0.73-0.77) per quarter of MP activity). The decrease was slower in hotspots (IRR=0.81; 95%CI=0.75-0.87), which also had a higher baseline incidence compared to non-hotspot neighbor villages (IRR=2.9; 95%CI=1.9-4.3). In 40 villages surveyed again 12 months after MDA, median PF prevalence had decreased by 92% (interquartile range: 81-100%) compared to baseline. A similar impact was observed on PF incidence. Over 24 months of follow-up, the deployment of an MP network in 4 districts showed a strong decrease of PF incidence rate. MDA proved to accelerate the decrease in high prevalence villages.

Keyword: *Falciparum malaria* elimination Myanmar artemisinin-resistance

Thursday 7 December 2017

16.00-17.30
Room D

S29: Free Paper IV: Tropical Medicine III

Chairpersons:


Wirongrong Chierakul


Muthita Vanaporn

Speakers


1. Six years of quality improvement in clinics in remote areas of Myanmar
   Andrew Silver
   Karen Department of Health and Welfare

2. Incidence and risk factors for acute mountain sickness among Thai travelers to high-altitude areas.
   Akkavich Harnnavachok
   Faculty of Tropical Medicine, Mahidol University


3. Compliance and reported adverse effects of malaria chemoprophylaxis among travelers: a prospective study
   Jitfa Loorungroj
   Faculty of Tropical Medicine, Mahidol University


4. Triple ACTs for the treatment of uncomplicated *Falciparum malaria*
   Rob van der Pluijm
   Mahidol-Oxford Tropical Research Unit


5. CRI*S*PR-Cas9 in *P. knowlesi* enables rapid, iterative and scalable targeted modification of the parasite genome
   Robert Moon
   London School of Hygiene and Tropical Medicine


6. Factors affecting diphtheria-Tetanus toxoid mass campaign vaccination among upper northeastern population
   Kanlaya Skulthai
   Silpakorn University


7. Five-Year Antibody Persistence following a Booster Dose of Live-Attenuated Japanese Encephalitis Vaccine (Imojev®) in Children
   Danaya Chansinghakul
   Sanofi Pasteur


8. Progress in Takeda's Tetravalent Dengue Vaccine Candidate Development
   Vianney Tricou
   Takeda Vaccines Pte Ltd, Singapore

SIX YEARS OF QUALITY IMPROVEMENT IN CLINICS IN REMOTE AREAS OF MYANMAR

Andrew Silver [1]

[1] *Karen Department of Health and Welfare*

The Karen comprise about 15% of the population of Burma. Since 1997 the Karen Department of Health and Welfare (KDHW), from its office in Mae Sod, Thailand, has operated clinics in remote areas of southeastern Burma where mortality rates are among the highest in the world. Leading causes of death, after childbirth, are diarrhea, acute respiratory infections, and malaria. Health workers are trained in refugee camps, Mae Tao Clinic, or at KDHW clinics. Annual logbook review instigated by the international Rescue Committee and conducted by KDHW for the three infectious diseases found correct diagnoses and treatments based on signs and symptoms in the range 11-62% for diarrhea and respiratory infections. The quality improvement project was launched in 2012 in 7 of nearly 50 clinics. Flip chart checklists for diagnosis and treatment were given to the 7 clinics. Volunteer QI coordinators send logbook review data to QI staff in Mae Sod. The QI staff send back charts showing rates of correct resonses on several quality measures for each disease. Clinic staff can see whether they are improving month to month. QI and non-QI clinics had similar rates of correct resonses in 2012 in logbook review. By 2014, continuing through 2016, quality measure scores for diarrhea were significantly better in QI clinics than in other clinics. In 2015 and 2016 QI clinics scores were significantly better for respiratory infections. All clinics improved to nearly 100% for malaria.

Keyword: Karen Myanmar "quality improvement" clinics

INCIDENCE AND RISK FACTORS FOR ACUTE MOUNTAIN SICKNESS AMONG THAI TRAVELERS TO HIGH-ALTITUDE AREAS.

Akkavich Harnnavachok [1]

[1] *Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University*

Introduction: We aimed to determine the incidence and risk factors for acute mountain sickness (AMS) among Thai travelers visiting high-altitude areas.

Method: A prospective cohort study was conducted and the study population comprised Thai travelers seeking pre-travel counseling at the Travel Clinic of the Hospital for Tropical Diseases, Faculty of Tropical Medicine, Mahidol University, 2017. Baseline characteristics, incidence of acute mountain sickness, and ascent rate, were prospectively collected and analyzed. Results: A total of 353 participants were eligible for analysis. The mean age was 35.2±9.3 years (range 20-65 years); 80% of participants were female. Leh, in Ladakh, northern India, at an altitude of ~3,500 meters, was the most commonly visited high-altitude place. The overall incidence of AMS was 17.80% (69/353), where 2 had to delay, and another 4 had to cancel, their trips. The median time for developing AMS was 2 days (range 1-12 days); 36.23% (25/69) of the participants developed AMS on 1st day in the high-altitude area. Cox regression analysis showed that pre-exposure prophylaxis with acetazolamide (Diamox) tended to reduce AMS (HR = 0.62; 95% CI 0.34-1.13). Travelers with asthma had significantly increased the risk of AMS (HR 4.23; 95% CI 1.54-11.94). Gender, age, BMI, dehydration, rapid-ascent profile, and previous medical condition (hypertension, allergic rhinitis, dyslipidemia) were not contributing factors.

Conclusion: The overall incidence of AMS was 17.80%; the most significant risk factor was asthma. High-risk travelers should be aware of the early signs and symptoms of AMS and seek pre-travel counseling before going to high-altitude areas.

Keyword: AMS

COMPLIANCE AND REPORTED ADVERSE EFFECTS OF MALARIA CHEMOPROPHYLAXIS AMONG TRAVELERS: A PROSPECTIVE STUDY

Jitfa Loorungroj [1], Watcharapong Piyaphanee [2], Udomsak Silachamroon [2], Sant Muangnoicharoen [2], Natthida Sriboonvorakul [2], Wattana Leowattana [2], Suda Punrin [3], Polrat Wilairatana [2], Pornthep Chanthavanich [4]

[1] Hospital for Tropical Diseases, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand, [2] Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand , [3] Queen Saovabha Memorial Institute, The Thai Red Cross Society, Bangkok, Thailand, [4] Department of Tropical Pediatrics, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

Background: The number of International travelers to malaria endemic area has increased in recent years. Many studies from European countries have been conducted to determine compliance of antimalarial prophylaxis and adverse effects of the drug. However, there are no previous studies in Thai travelers whose practices may be different from European counterpart. This study aims to determine the compliance of malaria chemoprophylaxis and find the incidence of Mefloquine, Atovaquone-Proguanil and Doxycycline adverse effects among Thai and Foreign travelers. Methods: This study focuses on Thai and foreign travelers who attend travel clinic and plan to travel in malaria endemic area less than 3 months. Pre-travel questionnaire was collected at the first time of their visit. Either post-travel electronic questionnaire or telephone interview was implemented within 7 days after they completed the medication. Results: This preliminary result, which can be followed up, consists of 130 participating travelers with 79% of Thai participants and 21% of other nationals. Mean age was 42 years, and median trip duration was 10 days. Africa was the most popular destination. Malarone was the most commonly proscribed drugs, followed by Doxycycline and Mefloquine. Overall, 75% of participants had good compliance to chemoprophylaxis. 23% of travelers displayed adverse effects. The most common side effect was GI symptoms (14.5%). Among those taking Malarone and Doxycycline there was no difference in side effect reported between 2 groups(19% vs 32%,p=0.15). This may be because of the small number of participants. No serious adverse effect was detected in this preliminary result. Conclusion: About a quarter of travelers did not complete chemoprophylaxis course. Most travelers can tolerate with the adverse effects. To raise awareness of adhering to the drug in pre-travel counseling is of essence.

Keyword: Malaria chemoprophylaxis, Compliance, Adverse effects

TRIPLE ACTS FOR THE TREATMENT OF UNCOMPLICATED *FALCIPARUM MALARIA*

Rob van der Pluijm [1]

[1] *Mahidol Oxford Research Unit*

The spread of artemisinin resistance, and subsequent ACT partner drug resistance, threatens malaria control in the Greater Mekong Subregion (GMS) and beyond. The efficacies of dihydroartemisinin-piperaquine (DHA-PPQ) and artesunate-mefloquine (AS-MQ) have declined dramatically in the GMS. The spread of multidrug-resistant *P. falciparum* to Africa, where most of the world's malaria transmission, morbidity, and mortality occur, would be disastrous. Since new drugs are years away, there is an urgent need to evaluate alternative treatments using existing drugs. A promising novel approach is the use of Triple ACTs (TACTs), which combine a short-acting artemisinin with two longer-acting partner drugs. TACTs can potentially exploit fortuitous inverse relationships between susceptibility to paired partner drugs, such as amodiaquine and lumefantrine, or piperaquine and mefloquine. A large multinational study, the "Tracking Resistance to Artemisinin Collaboration II" (TRAC II) was initiated to map the current spread of resistance and assess the efficacy and safety of TACTs in 18 hospitals in 7 countries in Asia and 1 in Africa. Dr. Rob van der Pluijm will present the near-final results of the large multinational, multicenter randomized clinical TRAC II trial, evaluating two TACTs (DHA-piperaquine-mefloquine, and artemether-lumefantrine-amodiaquine, compared to standard ACTs, and an update on the current geographical extent of artemisinin and partner drug resistance.

Keyword: *Falciparum malaria* resistance TripleACTs

CRISPR-CAS9 IN *P. KNOWLESI* ENABLES RAPID, ITERATIVE AND SCALABLE TARGETED MODIFICATION OF THE PARASITE GENOME

Robert Moon [1], Franziska Mohring [1], Melissa Hart [1], Thomas Rawlinson [2], Simon Draper [2]

[1] Faculty of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, [2] Jenner Institute, University of Oxford

Plasmodium knowlesi causes malaria in humans by zoonotic transmission from monkeys in South-East Asia. We have previously adapted a *P. knowlesi* line to *in vitro* culture with human red blood cells. Whilst transfection efficiencies are high, genomic modifications are constrained by the number of drug selection markers available, construct size and potential for reversion to wild type. The CRISPR Cas9 system uses a targetable nuclease to drive site-directed mutations or homologous recombination in a range of host genomes. Its adoption in *P. falciparum* has revolutionised genome editing in the species and greatly improved modification efficiency. In current work, we have adapted the CRISPR-Cas9 system to use in *P. knowlesi* using a range of *P. knowlesi* specific vectors. Modifications are made using marker free donor DNA, and the episomal vectors driving integration can be readily recycled for iterative modification of the genome. Our system is compatible with gene knock-outs/tagging and we have generated marker free lines expressing a variety of different fluorescent protein markers, as well as allelic exchanges of genes more than 3.5kb in size. We have also adapted a PCR method for donor DNA constructs, which permits complex modifications containing >3kb inserts, allowing scalable construct generation. This work has enabled us to create vital new tools to study the process of red blood cell invasion in *P. knowlesi* and critically has enabled us to study unique biology of the closely related parasite *P. vivax* – which currently cannot be grown in continuous culture.

Keyword: Malaria, CRISPR-Cas9, *knowlesi*, *vivax*

FACTORS AFFECTING DIPHTHERIA-TETANUS TOXOID MASS CAMPAIGN VACCINATION AMONG UPPER NORTHEASTERN POPULATION

Kanlaya Skulthai [1]

[1] *Silpakorn University*

There were an outbreak of diphtheria occur among adult population in the northeastern and lower northern of Thailand. The study on diphtheria immunization level among general Thai population show the decreasing trend of immunization level in increasing age, especially in the adult aged between 20 - 50 years old. This situation led to the mass campaign vaccination of Diphtheria-Tetanustoxoid (dT) for diphtheria prevention and control in the area which the outbreak occur among the adult population. In 2014, Department of Disease Control, implemented the dT vaccination mass campaign among adult aged 20-50 years old who live in the northeastern in 20 province target 5,735,562vaccine recipients had 4,953,578people (86.37%). The Office of Disease Prevention and Control, 6th Region (ODPC 6) Khon Kaen, which has the area responsibility in 9 provinces target 2,579,013 vaccine recipients had 2,450,171 people(88.81%), completely implemented this vaccination campaign. This is a survey study, Multi-Stage cluster random sampling includes 692 participants. The sample are knowing about this dT mass vaccination campaign (45.31%).The are many channel of information that they received, including their local staff (60.94%). There are 84.38% of total participants who have vaccinated with dT. The vaccinated participants mostly because of awareness of diphtheria (92.22%).The factors affecting the vaccination of the people are dT vaccination information obtaining, because the most likely cause of unvaccination is unknown of this mass vaccination campaign in their local area. To increase accessibility for target population, the relevant agencies might develop communication channel, covering all target population, for planning the next vaccination campaign in the future.

Keyword: Diphtheria-Tetanus toxoid mass campaign vaccination , Factors affecting vaccine

FIVE-YEAR ANTIBODY PERSISTENCE FOLLOWING A BOOSTER DOSE OF LIVE-ATTENUATED JAPANESE ENCEPHALITIS VACCINE (IMOJEV®) IN CHILDREN

Danaya Chansinghakul[1, 2], Emmanuel Feroldi[3], Maria Rosario Capeding[4], Thelma Laot[5], Celine Monfredo[3], Alain Bouckenooghe[6]

[1] Sanofi Pasteur, Thailand, [2] Authors: Chansinghakul Danaya, MD1 (Sanofi Pasteur, Thailand); Feroldi Emmanuel, MD2 (Sanofi Pasteur, France); Capeding Maria R, MD3 (Research Institute of Tropical Medicine, Muntinlupa City, Philippines); Laot Thelma, MD4 (Sanofi Pasteur, Philippine, [3] Sanofi Pasteur, France, [4] Research Institute for Tropical Medicine, Muntinlupa City, Philippines, [5] Sanofi Pasteur, Philippines, [6] Sanofi Pasteur, Singapore

Background: A live attenuated Japanese encephalitis vaccine (JE-CV, IMOJEV®, Sanofi Pasteur, Lyon, France) is now licensed recommended as single-dose primary and booster vaccination in pediatric populations from 9 months. Trials in children receiving a JE-CV booster dose shown seroprotection rates of 100% 28 days after vaccination. Objective: To document in children the persistence of the antibody response up to 5 years after a JE-CV booster vaccination. Material and Method(s): In an open Phase III trial in the Philippines, 349 children who had received a first dose of JE-CV 2 years previously (NCT 00735644) received a JE-CV booster. JE neutralizing antibody titres using PRNT50 were assessed before, 7, 28 days, and yearly for 5 years after booster. Children with titres ≥10 (1/dil) were considered seroprotected. Results: Before boosting, 80.3% (95% CI: 75.7; 84.4) of children remained seroprotected; GMT was 39.3 (33.7; 45.8). Seven days after boosting, the seroprotection rate was 96.2% (93.6; 98.0) and GMT was 233 (193; 281). These values increased to 100% (98.9; 100.0) and 2,259 (1,930; 2,645) by Day 28. Five years after boosting 98.2% (96.2; 99.3) of subjects were still seroprotected with GMT of 161 (141; 184). Conclusions: A single-dose primary JE-CV (IMOJEV®) immunization in 12-18 month-olds elicited a strong anamnestic response upon IMOJEV® boosting 2 years later; the booster response to IMOJEV® was robust and persisted in almost all children for at least five year. An IMOJEV® booster vaccination in JE-CV primed children induces long-lasting protection. (240 words) ClinicalTrials.gov: NCT 01190228 WHO UNT: U1111-1113-3629

Keyword: JE-CV, IMOJEV®, live attenuated Japanese encephalitis vaccine, Philippines, Japanese encephalitis

PROGRESS IN TAKEDA'S TETRAVALENT DENGUE VACCINE CANDIDATE DEVELOPMENT

Vianney Tricou [1], Xavier Sáez-Llorens [2], Delia Yu [3], Luis Rivera [4], José Jimeno [5], Ana Cecilia Villarreal [5], Epiphany Dato [3], Sonia Mazara [4], Maria Vargas [4], Manja Brose [6], Martina Rauscher [6], Suely Tuboi [7], Astrid Borkowski [6], Derek Wallace [6]

[1] Takeda Vaccines Pte Ltd, Singapore, [2] Hospital del Niño Dr. José Renán Esquivel, Panama City, Panama; Sistema Nacional de Investigación, SENACYT, Panama City, Panama, [3] De La Salle Health Sciences Institute, Cavite, Philippines, [4] Hospital Universitario Maternidad Nuestra Señora de la Altagracia, Santo Domingo, Dominican Republic, [5] Centro de Vacunación Internacional S.A. (Cevaxin), Panama City, Panama, [6] Takeda Pharmaceuticals International AG, Zurich, Switzerland, [7] Takeda Pharmaceuticals Ltd., Rio de Janeiro, Brazil

Takeda's live attenuated tetravalent dengue vaccine candidate (TDV) contains a molecularly characterized dengue serotype 2 virus (TDV-2), and three recombinant viruses expressing the pre-membrane (prM) and envelope (E) structural genes for serotypes 1, 3, and 4 in the attenuated TDV-2 backbone. Clinical development of TDV has followed the WHO guidelines for dengue vaccine development. Takeda has investigated different formulations, routes of administration, dosage schedules, and vaccine presentations, in several phase 1 and phase 2 studies in more than 3500 participants who were adults and children living in dengue endemic and non-endemic countries. In an ongoing phase II placebo-controlled, multi-centre trial (ClinicalTrials.gov: NCT02302066), the safety and immunogenicity of different TDV vaccination schedules is being evaluated in ~1800 participants from 2 to < 18 years of age, living in dengue endemic areas of the Dominican Republic, Panama, and the Philippines. Here we present 18-month safety and immunogenicity results, including febrile illness surveillance, in which all reported febrile illnesses were investigated and DENV infections were laboratory-confirmed by serotype-specific RT-PCR and non-structural protein 1 ELISA. Progress of the phase 3 pivotal efficacy trial will also be presented.

Keyword: Live-attenuated tetravalent dengue vaccine, paediatric study, immunogenicity, safety, febrile illness surveillance

9.00-10.30
Room A

S30: Extending the Frontiers of Vector Control

Chairpersons:

Ronald Enrique Morales Vargas

Narumon Komalamisra

Invited Speakers

1. WIN: The Worldwide Insecticide resistance Network
   Waraporn Juntarajumnong
   Kasetsart University

2. Assessing durability of long-lasting insecticidal mosquito nets in Tanzania 3 years after distribution: preliminary results
   Hans J. Overgaard
   Norwegian University of Life Sciences

3. Entomological observations surrounding a mass drug administration trial against lymphatic filariasis in Papua New Guinea
   Stephan Karl
   Walter and Eliza Hall Institute of Medical Research

4. Reproductive biology and mating behavior of the dengue vector, *Aedes aegypti*: potential targets for vector control
   Laura C. Harrington
   Northeast Regional Center for Excellence in Vector Borne Diseases

WIN: THE WORLDWIDE INSECTICIDE RESISTANCE NETWORK

Waraporn Juntarajumnong [1]

[1] *Department of Entomology, Faculty of Agriculture, Kasetsart University, Bangkok, Thailand*

The Worldwide Insecticide resistance Network (WIN) initiated by the WHO-TDR and NTD proposes to bring together internationally recognized institutions in vector research, providing a unique framework for tracking insecticide resistance in mosquito vectors of arboviruses around the world. The network aims at identifying the particular countries/regions where resistance could challenge vector control interventions and to provide the WHO and member states with key recommendations for improvement of insecticide resistance surveillance and deployment of alternative vector control tools. The outcomes of the WIN are to provide stakeholders with strong evidence for the development of strategic plans for vector control and sound management of pesticide use in public health.

Keywords: insecticide, resistance, arbovirus, vector

ASSESSING DURABILITY OF LONG-LASTING INSECTICIDAL MOSQUITO NETS IN TANZANIA THREE YEARS AFTER DISTRIBUTION: PRELIMINARY RESULTS

Hans J. Overgaard[1], Sarah J. Moore[2], Dennis Massue[3], Zawadi Mageni[4], Renata Mandike[5], Jason D. Moore[4], William Kisinza[3], John Bradley[6], Lena M. Lorenz[6]

[1]Norwegian University of Life Sciences, Norway. [2]Swiss Tropical and Public Health Institute, Switzerland. [3]National Institute for Medical Research, Tanzania. [4]Ifakara Health Institute, Tanzania. [5]National Malaria Control Programme, Tanzania. [6]London School of Hygiene & Tropical Medicine, United Kingdom.

Global malaria mortality declined by 60% between 2000 and 2015. The reduction was attributed to upscaling of malaria control measures, including vector control such as Long-Lasting Insecticidal Nets (LLINs). Although universal LLIN coverage is recommended, there is still limited knowledge of the durability and effective life of nets under user conditions. Increasing LLIN durability will have large impacts on the cost of malaria prevention. We present results from one of the largest net studies carried out. The aim was to investigate net durability of three LLIN products during three years under user conditions by assessing attrition (net loss), biological efficacy, chemical residue, physical degradation, and risk factors for LLIN degradation and loss. Innovative, novel and reproducible methods were developed for counting holes in nets and testing whole net bioefficacy. These methods will be essential for future operational research. About 10,600 nets of three different brands were distributed to 3,420 households in 76 villages in October-December 2013. Nets were still effective in killing mosquitoes and inhibiting blood feeding after 2 years in the field. The effectiveness of nets in different physical conditions and chemical content is being investigated. After 3 years, 30.6% of nets were lost, 85% had holes, but 68% were still serviceable. Damage of nets differs between net products. Median survival time of these net brands is 2-3 years. The project has validated international durability monitoring tools, which governments can use to select net types with the longest effective life and estimate the correct timing of repeated distribution campaigns.

Keywords: malaria, vector control, attrition, bioefficacy

ENTOMOLOGICAL OBSERVATIONS SURROUNDING A MASS DRUG ADMINISTRATION TRIAL AGAINST LYMPHATIC FILARIASIS IN PAPUA NEW GUINEA

Stephan Karl [1], Lincoln Timinao [2], Michelle Katusele [2], Livingstone Tavul [2], Samuel C. Howard [3], Daniel Tisch [3], Moses Laman [2], Leanne J Robinson [4], Christopher L King [3]

[1] Walter and Eliza Hall Institute of Medical Research; Papua New Guinea Institute of Medical Research, [2] Papua New Guinea Institute of Medical Research, [3] Case Western Reserve University, [4] Burnet Institute

Lymphatic filariasis (LF) caused by *Wuchereria bancrofti* (Wb) is present at high prevalence in some parts of Papua New Guinea. Here, we describe preliminary results from a series of entomology surveys on the North Coast of PNG, in Bogia district, which were conducted alongside a mass drug administration (MDA) study aimed at investigating the safety of a triple drug regimen (Albendazole + diethylcarbamazine + ivermectin, IDA) against LF and assessing the potential of IDA for LF elimination on the community level as part of a global set of similar trials. The study was conducted in 4 villages. Two of these villages were treated with the double drug regimen of Albendazole+diethylcarbamazine, while the other 2 villages were treated with triple drug (Albendazole + diethylcarbamazine +ivermectin). Average treatment coverage reached 70-80%. A total of 27,141 anopheline mosquitoes were collected before and after the MDA in a total of 2562 person-hours. There were 2 collections in each village, one before and one shortly after the MDA Mosquitoes were analysed by microscopy for species and feeding status at the time of collection. A subset of pooled (n=1302 pools) of unfed mosquitoes (n=7520 mosquitoes) was subjected to PCR analysis for *Wuchereria bancrofti* (Wb) infection. Prevalence of mosquitoes carrying Wb was determined from the pooled data by using Bayesian MCMC estimation. As subset of mosquitoes was also tested for *Plasmodium* infection. Anopheline biting density was very heterogeneous and localised in the 4 villages ranging from an average of 28 bites per person night to an average of >200 per person night. Similarly Wb infection rate ranged from 0.1% - 4.8% in the tested mosquito population depending on village. Wb infection rate in the mosquito population was significantly reduced after the MDA (overall decrease in all 4 villages from 2.3% to 0.1%.

Keywords: Papua New Guinea, Lymphatic filariasis

REPRODUCTIVE BIOLOGY AND MATING BEHAVIOR OF THE DENGUE VECTOR, AEDES AEGYPTI: POTENTIAL TARGETS FOR VECTOR CONTROL

Laura C. Harrington [1]

[1] *Cornell University and Director of the Northeast Regional Center for Excellence in Vector Borne Diseases*

A solid understanding of mosquito mating behavior and reproductive fitness is essential for developing new control strategies, yet our understanding of these fundamental life history events is incomplete. An overview of our recent efforts to understand the mating system and fitness of the global dengue vector, *Ae. aegypti*, will be presented. Recent work on the role of male seminal fluid proteins as modulators of female behavior and disease transmission reveal potentially powerful targets for vector population control. Pre-copulatory acoustic mating interactions in *Ae. aegypti* and their potential role as indicators of fitness, as well as assortative mating by phenotype and genotype will be presented. In addition, a discussion of important unanswered questions and considerations for genetic mosquito control including variation across geographic ranges, local adaptation, effect of mass rearing on fitness, and optimal approaches for measuring fitness and reproductive success will be presented.

Keywords: *Ae. aegypti*, vector control

Friday 8 December 2017

9.00-10.30
Room B

S31: Environmental Health, Toxicology, and Biotechnology

Chairpersons:


Pongrama Ramasoota


Kraichat Tantrakarnapa

Invited Speakers

1. Assessing the Health Impacts from Air Pollution in Thailand
   John Cherrie
   Institute of Occupational Medicine and Heriot Watt University

2. Potential impact of climate change on the formation of brominated trihalomethanes in water supply systems in central Thailand
   Suthirat Kittipongvises
   Environmental Research Institute, Chulalongkorn University

3. Health Risk and Health Care Access: Research Experiences among Cambodian Fruit Farm Workers in Eastern Thailand
   Anamai Thetkathuek
   Faculty of Public Health, Burapha University

4. The domino effect: correct identification of introduced freshwater snails and implications for future research
   Ting Hui Ng
   Faculty of Science, Chulalongkorn University

5. Organic Antimicrobial products from Sea shells and Mangosteen peels extract
   Pongrama Ramasoota
   Faculty of Tropical Medicine, Mahidol University

ASSESSING THE HEALTH IMPACTS FROM AIR POLLUTION IN THAILAND

John Cherrie [1]

[1] *Institute of Occupational Medicine and Heriot Watt University*

The health impacts from outdoor and indoor air pollution are important societal concerns. The Global Burden of Disease (GBD) project has estimated that around 6% of all Disability Adjusted Life Years (DALYs) lost in Thailand are due to air pollution, mostly from airborne particulate pollution from motor vehicles and indoor combustion sources. Like many developing nations, outdoor pollution concentrations continue to rise over time, which contrasts with developed nations where concentrations are declining. Understanding the magnitude of the health impacts from pollution provides better opportunities to intervene to reduce future risks. The GBD analysis provides a good basis for international comparisons, but it lacks a detailed evaluation for individual countries and it provides impacts for a limited range of health outcomes. The Thai Air Pollution Health Impact Assessment (TAPHIA) project is a collaborative research initiative involving researchers in Thailand and the UK. The project will collect new data on indoor air pollution concentrations and produce refined estimates of outdoor air pollution concentrations using the available measurements and appropriate mathematical modelling. Health impacts will be provided in terms of mortality and morbidity for a range of plausible outcomes. The first health impact projections will be available in 2018. The project aims to provide information to aid people in Thailand to discuss interventions to reduce the impacts of air pollution in the future.

Keywords: air pollution, chronic health impacts

POTENTIAL IMPACT OF CLIMATE CHANGE ON THE FORMATION OF BROMINATED TRIHALOMETHANES (BR-THMS) IN WATER SUPPLY SYSTEM IN CENTRAL THAILAND

Suthirat Kittipongvises [1,2], Athit Phetrak [3]

[1] Environmental Research Institute, Chulalongkorn University (ERIC), Bangkok 10330, Thailand
[2] Research Program of Toxic Substance Management in the Mining Industry, Center of Excellence on Hazardous Substance Management (HSM), Thailand
[3] Department of Social and Environmental Medicine, Faculty of Tropical Medicine, Mahidol University, Thailand

Observed sea-level rise is in fact one of the most serious consequences of global climate change. Between 1993 and 2010, in Thailand, the rate of sea level rise was about 3-5 mm per year compared to the global average of 1.7 mm per year from 1901 to 2010. Impact of climate change particularly on sea level rise presents some challenges for sustainable water quality management. As one of the most pressing public health concerns, the continued rise in sea level is expected to increase the occurrence of seawater intrusion that is potentially associated with the formation of brominated trihalomethanes (Br-THMs). This study aimed to investigate the relationship between total dissolved solid (TDS) concentration and the bromine incorporation factor (BIF) of trihalomethanes in Bangkok water supply systems from the period 2015 to 2017. The results revealed that high concentrations of TDS (> 500 mg/L) were obviously detected during a 3-month period from late May to end of July. An elevated TDS concentration led to enhance the occurrence of Br-THMs formation in treated water and subsequently increase the BIF value. These increases could pose a possible risk of causing cancer in human. Crucially, as the intrusion of seawater becomes more prominent, water treatment utilities should be aware of changes in certain water quality induced by seawater. Selections of alternative drinking water sources and appropriate technologies are needed to effectively control the formation of Br-THMs in drinking water.

Keywords: climate change impact, sea-level rise, seawater intrusion, Thailand, water supply

HEALTH RISK AND HEALTH CARE ACCESS: RESEARCH EXPERIENCES AMONG CAMBODIAN FRUIT FARM WORKERS IN EASTERN THAILAND

Anamai Thetkathuek [1], Parvena Meepradit [1], Wanlop Jaideeb [1], Patchana Jaidee [1]

[1] *Faculty of Public Health, Burapha University*

Objectives: In this study, we examined the effects of pesticides, work-related musculoskeletal disorders as well as elucidate factors that influenced access to health care for migrant farm workers from Cambodia employed on fruit plantations in eastern

Methods: We studied 891 migrant farm workers employed on pineapple, durian, and rambutan plantations in Thailand. Data were collected via a detailed questionnaire survey, measurements of serum cholinesterase level (SChE) and the Nordic Musculoskeletal Questionnaire, Rapid Upper Limb Assessment, and Hazard Zone Jobs Checklist techniques.

Results: Only 4.4% had normal levels of cholinesterase activity. The OR for farm migrant workers who worked on larger plantations of more than 39.5 acres (95% CI) was 2.69 (1.51, 4.82). For musculoskeletal disorder, the data showed that men who had been working for >10 years were more at risk of neck pain than those working for <1 year with adjusted odds ratio (aOR) 1.66, 95% confidence interval (CI) (1.90, 14.5). In case of access to health care, most of the workers (89.8%) received health care services at a nearby government health promotion hospital (THPH). The differences between those who reported significant minor illnesses and serious illness were important, as workers with significant complaints were 3.17 and 4.85 times more likely, respectively, to have sought medical treatment than those not reporting illness.

Conclusions: These results suggest that health screening should be provided to migrant farm workers.

Keywords: health care access, Cambodia

THE DOMINO EFFECT: CORRECT IDENTIFICATION OF INTRODUCED FRESHWATER SNAILS AND IMPLICATIONS FOR FUTURE RESEARCH

Ting Hui Ng [1], Yanin Limpanont [2], Somsak Panha [1]

[1] Animal Systematics Research Unit, Department of Biology, Faculty of Science, Chulalongkorn University, 10330 Bangkok, Thailand, [2] Department of Social and Environmental Medicine, Faculty of Tropical Medicine, Mahidol University, 10400 Bangkok, Thailand

Invasive species are key threats to native fauna and ecosystems, and can cause economic losses and impact human health. Only four species of freshwater snails have been recorded as being introduced to Thailand, out of the almost 300 species that are known from the country. The most notorious introduced species are the South American apple snails *Pomacea canaliculata* and *Pomacea maculata* (*Ampullariidae*), which were the focus of intensive research in the 1990s because of the damage caused by these snails to rice fields. Based on examination of museum records and fresh collections conducted in 2017, we present an update of the introduced freshwater snails in Thailand, including a new record of a non-native species that was previously misidentified. We discuss the consequences of taxonomic confusion in freshwater gastropods, and its domino effect on managing the impact of invasive species, and understanding the spread of zoonotic diseases.

Keywords: non-marine gastropods, invasive species, distribution, taxonomy

ORGANIC ANTIMICROBIAL PRODUCTS FROM SEA SHELLS AND MANGOSTEEN PEELS EXTRACT

Pongrama Ramasoota[1, 2], Pannamthip Pitaksajjakul[1, 2], Surachet Benjathummarak[1], Khwanchit Boonha[1], Isao Miyazaki[3]

[1]Center of Excellence for Antibody Research, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; [2]Department of Social and Environmental Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; [3]Biomedical Research Institute (BMRI), Chiba, Japan

Human are risky living their everyday life with dangerous micro-organisms that existed in the environment such as indoor air pathogens like *M. tuberculosis*, highly pathogenic Influenza virus, Severe acute respiratory syndrome (SARS) virus and also with directed contacted dangerous micro-organisms such as *Salmonella typhimurium*, Methicillin resistant *Staphylococcus aureus* (MRSA). Even-though various antimicrobial products were established and available in the market but most of them were produced from chemical substance which is irritant to human skin and not suitable for used in everyday life. So more effective antimicrobial product produced from organic substance is needed. In this study, antimicrobial products like antimicrobial air spray, air filter and mouth wash were produced from organic wastes like Sea shell and Mangosteen peel extracts. Sea shell and Mangosteen peel extracts powder were commercially produced. Then the antimicrobial solution was produced by dissolve sterile mineral water with different concentration of Sea shell and Mangosteen peel extracts powder, respectively. Then its antimicrobial activities was tested with the following bacteria; *Mycobacterium tuberculosis*, *Klebsiella pneumoniae*, *Salmonella typhimurium*, and *Pseudomonas aeruginosa*. The antimicrobial activity against aerosol bacteria were specifically tested in our in-house developed aerosol chamber model with 42 inch long, 32 inch width and 25 inch high. The 10 8 bacilli solution of each bacteria was prepared and aerosolize sprayed in to the aerosol chamber model, then each antimicrobial spray was spray in to the same chamber to kill aerosol bacteria. The amount of surviving bacilli were cultured from five bacterial culture plates that place in 4 corners and 1 center of the chamber and also cultured from water in air impinger which an indoor air was collected by using air impinger at the same time as the bacterial spray and the antimicrobial spray. It was found that the organic antimicrobial solution dissolved from Sea shell could kill each bacteria up to 10 8 bacilli. Our organic antimicrobial aerosol spray and antimicrobial mouth wash will be shortly launched to the market.

Keywords: organic, antimicrobial products, sea shells, mangosteen peel extract, antimicrobial spray, antimicrobial mouth wash

Friday 8 December 2017

9.00-10.30
Room C

S32: Drug Resistance (Sponsored by MORU and Royal Society of Tropical Medicine and Hygiene)

Chairpersons:

Tamar Ghosh

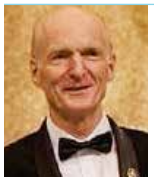
Nicholas Day

Invited Speakers

1. Royal Society of Tropical Medicine and Hygiene - alignment, allegiance and impact over the next 5 years

   Tamar Ghosh

   Royal Society of Tropical Medicine & Hygiene



2. Drug resistant malaria – a risk assessment

   Nicholas White

   Mahidol-Oxford Tropical Research Unit

   (No available abstract)

3. Antibiotic footprint of human and chicken meat in Thailand

   Direk Limmathurotsakul

   Mahidol-Oxford Tropical Research Unit

4. Epidemiology of drug resistant malaria

   Richard Maude

   Mahidol-Oxford Tropical Research Unit

   (No available abstract)

5. Two physiological origins of malaria artemisinin resistance in the Greater Mekong Sub-region

   Zbynek Bosdech

   School of Biological Sciences, Nanyang Technological University, Singapore

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE - ALIGNMENT, ALLEGIANCE AND IMPACT OVER THE NEXT 5 YEARS

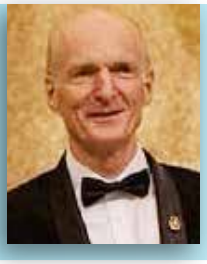
Tamar Ghosh

Royal Society of Tropical Medicine and Hygiene

This year the Royal Society of Tropical Medicine and Hygiene celebrates its 110th year. As support for science and scientific research is under threat, the Society lauches a new 5-year strategy based on utilising its independent platform and voice to strengthen partnerships, networks and relationships, across countries, sectors and disciplines. Setting priority areas and audiences, and with clear goals, you will hear how it is aiming to step up its work to deliver more impact in tropical medicine and global health. It is calling for researchers and health profesionals at the Meeting and in the region to join in.

Keyword: tropical disease imact partnership

DRUG RESISTANT MALARIA – A RISK ASSESSMENT



Nicholas White

Mahidol-Oxford Tropical Research Unit

(No available abstract)

ANTIBIOTIC FOOTPRINT OF HUMAN AND CHICKEN MEAT IN THAILAND

Direk Limmathurotsakul [1]

[1] *Department of Tropical Hygiene, Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand.; Mahidol-Oxford Tropical Medicine Research Unit, Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand.; Centre for Tropica*

Methods. In a single province, we surveyed farms in which chickens were raised for meat and interviewed the farms' owners. The antibiotic footprint of each chicken was defined as the amount of antibiotic given to the chicken over its entire life pre-slaughter divided by the target weight of the chicken at the time of its slaughter. Assuming that the results were nationally representative, we roughly estimated annual antibiotic use on all Thai chickens raised for meat. An on-line pilot survey was conducted to evaluate antibiotic usage in human. The data from the survey and a review was used to estimate antibiotic footprint in human in Thailand, which was primarily defined as the amount of antibiotic directly consumed individually over his or her entire life. Findings. A proportion of chicken farms reported routine use of antibiotics for prophylaxis. Per kg final weight, each chicken raised for company B was estimated. A number of antibiotics considered medically important for human were observed to be routinely used. The total amount of antibiotic used on all Thai chickens raised for meat in 2016 was extrapolated. Antibiotic footprint for Thai people was estimated. Conclusion. Each year in Thailand, many tonnes of antibiotics are probably routinely used in raising chickens for meat. Labels on retail packs of meat should include data on antibiotic use in the production of the meat. These measures may encourage a reduction in antibiotic use globally and lead to a reduction in human mortality from infections with drug-resistant bacteria.

Keyword: AMR

EPIDEMIOLOGY OF DRUG RESISTANT MALARIA

Richard Maude

Mahidol-Oxford Tropical Research Unit

(No available abstract)

TWO PHYSIOLOGICAL ORIGINS OF MALARIA ARTEMISININ RESISTANCE IN THE GREATER MEKONG SUB-REGION

Zbynek Bozdech [1], Lei Zhu [1], Frances Rocamora [1], Olivo Miotto [2], Rob van der Pluijm [3], Arjen Dondorp [3]

[1]School of Biological Sciences, Nanyang Technological University, Singapore, [2]University of Oxford, UK, [3]Mahidol-Oxford Research Unit, Thailand

Artemisinin resistance of *Plasmodium falciparum* has been firmly established in several countries of the Greater Mekong Subregion (GMS), and is currently threatening all malaria control programs around the world. Recently completed Genome- and Transcriptome-wide association studies (GWAS[1] and TWAS[2]) have identified several genetic markers and cellular physiological features that underline the artemisinin resistance phenotype in a *pfk13*-dependent manner. However, the causative elements of artemisinin resistance remain unknown. Here we utilized the GWAS and TWAS results from 818 *P. falciparum* GMS isolates collected during the Tracking Artemisinin Resistance Collaboration (TRACI) project[3] for expression quantitative trait loci (eQTL) analysis. In total, we identified over 5000 SNP-transcript association pairs involving >1000 *Plasmodium* genes and close to 3500 SNPs in both *cis* and *trans* position. Overall we identify a set of 898 genes whose transcription is associated with artemisinin sensitivity ($pValue<10^{-4}$) and are enriched for genes encoding proteins related to endoplasmic reticulum stress, ubiquitin-related protein metabolism, DNA damage but also cytoadhesion, Maurer's clefts-linked functions and gametocytogenesis. Crucially, using PCA-based normalized TWAS data, we identified two distinct sets of genes/transcripts and corresponding eQTLs that associate with artemisinin resistance in the eastern part of GMS (Cambodia, Vietnam and Laos) and the western part (western Thailand, Myanmar and Bangladesh), respectively. This strongly suggests two origins of the emergence of artemisinin resistance involving distinct parasite physiologies as well as genetic backgrounds. We will discuss the utility of the novel genetic variants as factors of the putative genetic background(s) of the *pfk13*-dependent or -independent phenotype of malaria parasite artemisinin resistance.

References: 1 Miotto, O. *et al.* Genetic architecture of artemisinin-resistant Plasmodium falciparum. *Nat Genet* 47, 226-234, doi:10.1038/ng.3189 (2015). 2 Mok, S. *et al.* Drug resistance. Population transcriptomics of human malaria parasites reveals the mechanism of artemisinin resistance. Science 347, 431-435, doi:10.1126/science.1260403 (2015). 3 Ashley, E. A. *et al.* Spread of artemisinin resistance in *Plasmodium falciparum* malaria. *N Engl J Med* 371, 411-423, doi:10.1056/NEJMoa1314981 (2014).

Friday 8 December 2017

11.00-12.30
Watergate Ballroom

S33: Closing Session

Sornchai Looareesuwan Medal Lecture

Chairperson:

Pratap Singhasivanon

Keynote Speaker:

"The Induced Blood Stage Malaria Model: A Tool to Accelerate The Development of New Interventions Against Malaria"

James McCarthy
QIMR Berghofer Medical Research Institute, Brisbane, Australia

THE INDUCED BLOOD STAGE MALARIA MODEL: A TOOL TO ACCELERATE THE DEVELOPMENT OF NEW INTERVENTIONS AGAINST MALARIA

Keynote Speaker:

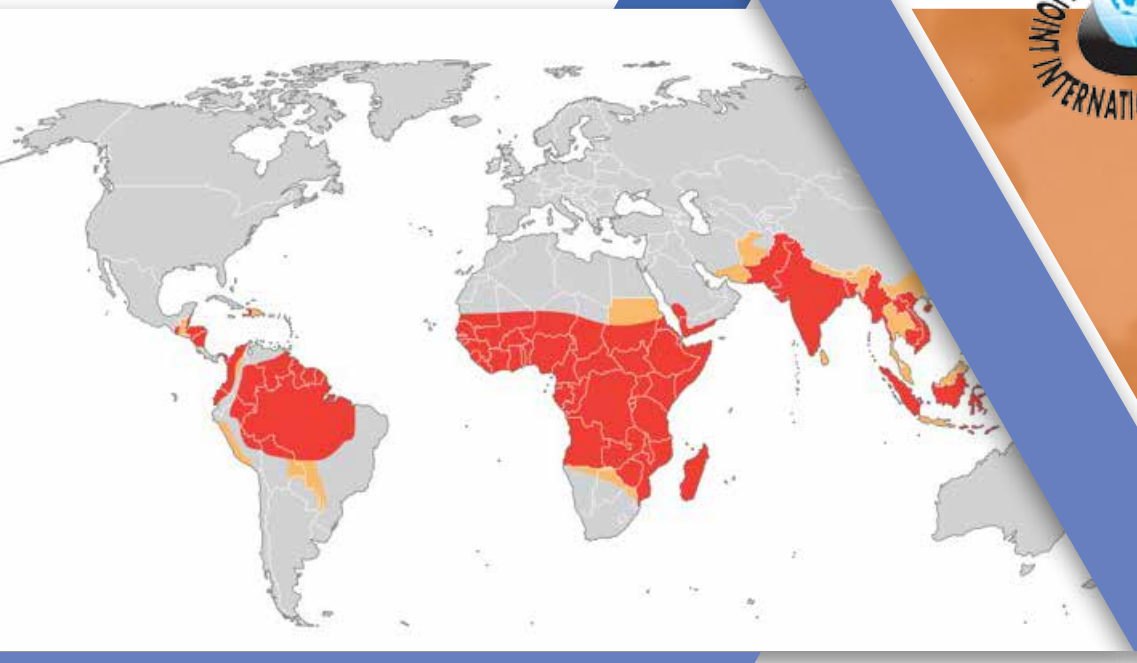
James S. McCarthy [1]

[1] *QIMR Berghofer Medical Research Institute, Brisbane, Australia*

Over the last 15 years the number of deaths caused by malaria has fallen by 63% globally as a result of better access to medicines and the deployment of insecticide-treated bed-nets. This has led to the more ambitious goal of the eventual elimination of malaria. However, progress achieved towards malaria elimination is challenged by the development of resistance to ACTs in the Greater Mekong Subregion. Paradoxically, the fall in the incidence of malaria is significantly hampering the clinical testing of new antimalarial drugs and vaccines. Over the past 7 years, the QIMR Berghofer team has developed a human malaria challenge model, the induced blood stage malaria (IBSM) model. This builds on the pioneering work of Professor Sornchai Looareesuwan where he tested experimental drugs in natural infection. We have used the IBSM system to undertake early phase clinical trials of 7 novel antimalarial drugs, 4 of which have progressed to Phase IIb field trials. As well, we have developed a clinical trial system for experimental *Plasmodium vivax* infection, the commonest species of malaria in the Asia-Pacific, and have developed in vivo systems to explore transmission of malaria from experimentally infected humans to mosquitos; this enables testing of transmission-blocking interventions. Results of these studies will be reviewed and future directions of this system will be discussed.

Keywords: malaria, IBSM model

JOINT INTERNATIONAL TROPICAL MEDICINE MEETING 2017 **(JITMM 2017)**



Abstracts
Poster PRESENTATIONS

"TROPICAL MEDICINE 4.0: EFFECTIVE COLLABORATION FOR AN IMPACT ON GLOBAL HEALTH"

6 – 8 DECEMBER 2017

AMARI WATERGATE, BANGKOK, THAILAND

Join the biggest conference on Tropical Medicine, hosted by the Faculty of Tropical Medicine, Mahidol University

CHARACTERISTICS OF DENGUE HEMORRHAGIC FEVER PATIENTS IN HAJI ADAM MALIK HOSPITAL MEDAN

Poster No. 1

Rina Yunita, MD, Clin.Microbiologist [1], Grace Thangamani [2], Ayodhia Pitaloka Pasaribu, MD, Pediatrician, PhD [3]

[1] Faculty of Medicine, Universitas Sumatera Utara, [2] Medical Student, Faculty of Medicine, Universitas Sumatera Utara, [3] Department of Pediatric Faculty of Medicine Universitas Sumatera Utara

Background: Dengue Hemorrhagic Fever (DHF) is caused by dengue virus. It is transmitted from person to person by the *Aedes aegypti* mosquito bites and became endemic in tropic and subtropic country including Indonesia.

Method: This is a descriptive study using retrospective data DHF cases in Haji Adam Malik Hospital in 2015-2016 by taking secondary data derived from medical records. There were 106 eligible medical records which being analized using 11 variables.

Result: Based on the results of the data, it was found that number of male patients is almost equal to female patients (51,8 % and 48,2%, respectively). The largest age group is 15-59 year old (62,2%). Highest incidence occurred in period April-June (33%), followed by period October-December. Proportion of patient with fever was similar with patient without fever when admitted to the hospital. More patients had bleeding manifestation with platelet counts < 50.000 u/L at the first measurement. From serological testing, it was found that Ig M (-) and IgG (+) was predominant. The most severity level is DHF grade 2 (49%) and most patients recovered before leaving the hospital.

Discussion: DHF is still a major health problem. It impacts the productive age group and for young children it could give serious outcome. Similar with many report showed that mostly secondary infection attribute clinical manifestation in dengue infection. Dengue infection can occur every time in year, not only in rainy season. Prevention and vector eradication must be reinforced in order to reduce the incidence of DHF.

Keyword: Dengue Hemorrhagic Fever, Characteristics, Haji Adam Malik Hospital

ASSESSMENT OF FACTORS ASSOCIATED WITH DENGUE MORTALITY IN FIJI, 2014: A CASE CONTROL STUDY

Poster No. 2

Aneley Getahun [1]

[1] *Fiji National University*

Background: Fiji experienced a dengue serotype 2 outbreak in 2013-14 with significantly increased number of dengue related deaths compared to an earlier outbreak of similar intensity. This study determines the sociodemographic and clinical factors associated with dengue mortality during the 2014 outbreak.
Methods: A retrospective matched case control study was conducted. Cases were confirmed or presumed dengue deaths and controls were dengue patients who required hospital admission and who survived. A standardized data collection form was used to gather relevant information from patients' medical folders. Data was analyzed using Statistical Package for the Social Sciences software version 22.

Results: A total of 48 dengue death were reported with overall mortality of 5.6/100,000 population. Mortality rate was higher among males (6.8/100,000) and patients above 55 years of age (12.7/100,000). A total of 32 cases and 94 cases were included in this study. Cases and controls were comparable in terms of sex (p=0.900), ethnicity (p=1.00) and mean age (0.888). The commonly reported symptoms included fever (88.9%), body pain (63.5%), headache (39.7%), any loose bowel motion (38.1%), loss of appetite (34.9%) and vomiting (31.0%). Factors associated with mortality included abdominal pain (p=0.044), haemorrhagic manifestations (p=0.010), tachycardia (p=0.001), tachypnoea (p=0.018), conjunctival pallor (p=0.039), haemoglobin <12mg/dl (p=0.030), serum creatinine > 150mg/dl (p=0.013), low sodium (p=0.031), ICU admission (p<0.001), shock (p<0.001) and organ failure (p=0.001).

Conclusion: Study findings can benefit clinical decision making for the management of severe dengue in Fiji and provide valuable information for public health measures to reduce dengue related mortality.

Keyword: Dengue, Severe dengue, Mortality, Risk factors

THE SEROPREVALENCE OF NEUTRALIZING ANTIBODY AGAINST DENGUE VIRUS IN HEALTHCARE WORKERS

Poster No. 3

Warunee Punpanich Vandepitte [1]

[1] *Queen Sirikit National Institute of Child Health, Bangkok, College of Medicine, Rangsit University*

Recent epidemiological studies from Southeast Asia demonstrated an increased incidence of dengue disease and a predominantly adult age distribution. Population density/urbanization is known as important risk factor for the increase burden of dengue infection. Nevertheless, little is known about dengue serostatus among Thai adults in an urban setting. The aims of this study were to determine dengue seroprevalence and factors affecting dengue serostatus among healthcare workers (HCWs) aged 21-60 years in Bangkok. To achieve these objectives, we conducted a cross-sectional survey among 400 HCWs (with relatively equal distribution among the 4 age groups: 21-30, 31-40, 41-50, and 51-60 years) during routine annual health check-up. Additional blood samples were sent for antibody of the 4 dengue serotypes using plaque reduction neutralization test (PRNT). The results show that 95% of participants had positive dengue serology. 20.1% of these individuals, however, reported having been diagnosed with dengue infection. 88.8% of our sample (n=355) has antibody against all 4 serotypes. The PRNT levels were highest among serotype 1 and lowest among serotype 4 with geometric mean (standard deviation) titer against serotype 1, 2, 3, and 4 of 678.14 (677.22), 449.92 (429.80), 431.92 (474.22), and 102.04 (92.90), respectively. Logistic regression analysis indicated that youngest age group (21-30 years) is associated with negative dengue serostatus for serotype 2, 3, and 4 with adjusted odds ratios and 95% confidence intervals of 2.69 (1.18–6.14), 2.28 (1.03–5.05), and 2.41 (1.20–4.83), respectively. In summary, dengue seroprevalence in Thai HCWs in urban Bangkok is very high. Most individuals had been exposed to all 4 serotypes. The older the age, the higher the dengue seropositive prevalence.

Keyword: Dengue, seroprevalence, adults, healthcare, Thailand

ANTIVIRAL ACTIVITY OF BISMUTH DERIVED CHEMICAL COMPOUND AGAINST DENGUE VIRUS SEROTYPE 2

Poster No. 4

Babu Ramanathan [1], Sie Yeng Wong [1], Chit Laa Poh [2], Edward Tiekink [3]

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Dengue is an arthropod-borne viral disease that has become endemic and a global threat in over 100 countries. To date, there is no universal vaccine nor an effective antiviral agent against this life-threatening disease. Bismuth derived chemical compounds have been showed to inhibit the helicase activity of SARS coronavirus in vitro. In this study, we have investigated the antiviral activity of bismuth compounds against dengue virus serotype 2. Evaluation of the antiviral activity was performed with three different assay conditions; attachment, post attachment and cidal assay that was determined through foci forming reduction assay and quantitative realtime RT-PCR. The results have revealed that the bismuth compound have potential antiviral activity against DENV2 by inhibiting 89.7% of viral RNA copy number. The findings of the present study may exploit inherent towards the development of a future antiviral agent against dengue.

Keyword: Dengue virus, bismuth, helicase activity, RT-PCR, foci forming reduction assay

CURRENT GENOTYPE DISTRIBUTION OF DENGUE VIRUSES IN THAILAND

Poster No. 5

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Dengue is a mosquito-borne disease spreading over 100 countries. Dengue is caused by dengue virus which belongs to the genus flavivirus of the family *Flaviviridae*. Dengue virus comprises of 4 serotypes (DENV-1 to DENV-4) and each serotype is divided into distinct genotypes. Thailand is an endemic area where all 4 serotypes of dengue virus are co-circulating. To know current genotype distribution of dengue viruses in Thailand, we enrolled 100 cases of fever with dengue suspected symptoms in Bamrasnardura Infectious Diseases Institute during 2016-2017. Among them, 37 cases were shown to be dengue positive by real-time PCR. There were 2 DENV-1, 16 DENV-2, 7 DENV-3, and 12 DENV-4. To investigate the divergence of the viruses, RNA was extracted from supernatant of isolated virus and the viral whole genome sequences were determined. The phylogenetic analysis of the obtained viral sequences revealed DENV-2 genotype Cosmopolitan was co-circulating with DENV-2 genotype Asian-I, a previously predominant genotype in Thailand. Furthermore, DENV-3 genotype III was found instead of DENV-3 genotype II. DENV-2 Cosmopolitan and DENV-3 genotype III found in Thailand were closely related to respective strains in nearby countries. These results indicated that dengue viruses in Thailand have increased in genotype diversity, and suggested that the dengue virus genotype shift observed in other Asian countries might be taking place also in Thailand.

Keyword: Dengue virus, Genotype shift, Thailand, Phylogeny

EVALUATION OF A RAPID DIAGNOSTIC TEST FOR DENGUE VIRUS INFECTION IN BALI, INDONESIA

Poster No. 6

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Introduction: Dengue virus (DENV), a vector-borne disease, remain a huge public health problem in Indonesia. Clinical diagnosis is challenging as clinical manifestations can resemble other viral infections. There is a need for reliable screening tests to diagnose DENV infection, especially in regions without adequate laboratory capacity. We evaluated a rapid diagnostic test (RDT) based on NS1 DENV antigen detection during acute febrile illness studies involving both adults and children in three Regencies in Bali where DENV is endemic.

Methodology: From 2015-2017, a total of 403 samples were collected from Sanjiwani, Wangaya and Tabanan Hospital, Bali. Acute serum samples were screened for DEN with a SD Bioline NS1 rapid test (Alere, Australia). Confirmatory molecular assays for DENV infection were conducted at the Eijkman Institute by either DEN-specific or pan-flavivirus RT-PCR or Simplexa Dengue (Focus Diagnostics, Cypress, USA).

Result and Discussion: Out of 199 DENV RDT-positive samples from the three hospitals, 188 were confirmed as positive, while out of 208 DENV RDT-negative samples 23 were confirmed positive DENV infection by at least one of the assays. The diagnostic performance of the DENV RDT was evaluated in relation to onset of illness. The sensitivity and specificity of the DENV RDT was 89.1% and 94.9%, respectively. The positive predictive value using DENV RDT was 94.5% while the negative predictive value was 89.1%.

Conclusion: Our preliminary findings indicate that the DENV NS1 antigen RDT can be reliably used to confirm and exclude early DEN infection. Delineation of results distinguishing between primary and secondary infections should also be further evaluated.

Keyword: Dengue, DENV-RDT, RT-PCR, Indonesia, NS1-antigen

A SURVEY OF KNOWLEDGE, ATTITUDES, PRACTICES AND BELIEFS ON THE APPLICATION OF INDOOR RESIDUAL SPRAYING (IRS) FOR DENGUE CONTROL IN PENANG, MALAYSIA

Poster No. 7

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Indoor residual spraying (IRS) is not recommended for dengue control but it is likely to impact on dengue vectors during malaria control in the past. The effectiveness of IRS for dengue control was conducted in a small community of residential houses located in Bagan Dalam, Penang, Malaysia. To evaluate the community understanding on the prevention and control of dengue, surveys of knowledge, attitudes, practices and beliefs (KAPB) were conducted during baseline study, 3 months post-intervention and 6 months post-intervention to assess their knowledge, practise of preventive methods and response of community towards IRS. In this study, a total of 123 participants were interviewed from the selected households. At baseline study, 93.5% of householders stated that mosquitoes were a problem in the house while for peak biting time, 43.5% mentioned that mosquitoes bite during the day and night, whereas 39.4% stated that mosquitoes bite at any time during the day. To prevent being bitten, 59.4% of the householders used mosquito coils at home, 13.8% used aerosol can, electric mat and liquid vaporizer, and 26.8% used fan, blanket and bed nets. The most useful preventive method as perceived by this community was insecticide usage which contributes of 75.6%. The results indicated that the application of IRS for dengue control was highly accepted in the study area. The participants mostly satisfied with the insecticides used for IRS as compared to the conventional space-spraying interventions. Surveys of KAPB for vector control should be carried out consistently within householders to evaluate the effectiveness of dengue preventive and control activities in the future.

Keyword: IRS, dengue, vector, mosquito, control

IMMUNOLOGICAL AND ENTOMOLOGICAL INDICES TO EVALUATE THE RISK OF DENGUE TRANSMISSION IN NORTHEASTERN THAILAND

Poster No. 8

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Dengue fever is a fast spreading mosquito-borne disease threatening about 2.5 billion people. Despite efforts made worldwide, dengue incidence raises and outbreaks periodically occur in endemic countries. Dengue prevention and control are mainly based on vector surveillance and control. However, infestation indices currently used lack of constancy to assess dengue transmission and predict outbreaks. This study aims to identify immunological and entomological indices that accurately discriminate between dengue positive and negative households. These indices will be used to evaluate dengue transmission and thresholds values will be proposed as early warning tools. Data collections started in June 2016, from a prospective hospital-based case-control study including nine district hospitals in northeastern Thailand. Febrile patients were tested for dengue infection using commercial rapid diagnosis test. Both dengue positive and negative patients were included at ratio 1:3, to reach 370 samples. Dengue infection was later confirmed and virus serotyped. Blood samples were collected on filter paper for immunological study of human exposure to *Aedes* mosquito bites, using a salivary peptide. Adult and immature mosquito collections were performed in patient and surrounding households within the day of enrolment. At the abstract submission, a total of 49 dengue cases and 101 controls were sampled. Preliminary analysis of the available data (n= 581 houses, n= 1115 containers) shows that mosquito infestation was higher in dengue positive than in dengue negative households. Dengue incidence was low the first year of the study and only few cases were sampled. We expect more sample which will strength the trend observed and will assist our work to propose indices and thresholds that accurately evaluate dengue transmission.

Keyword: Dengue, *Aedes*, Immunological & entomological indices

DENGUE SEASONAL VARIATION AND PREDICTION MODEL IN KHON KAEN PROVINCE, THAILAND

Poster No. 9

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Objective: Dengue is an important mosquito-borne disease endemic in most tropical countries, including Thailand. Considering the increasing amount of disease surveillance data available, predictive modelling of transmission dynamics becomes increasingly accurate, and as such can be a tool for dengue prevention and control. Accordingly, the objectives of this study were to determine dengue seasonal variation and predict its incidence in KhonKaen province accounting for incident dengue cases and climate data using time-series predictive modelling.

Methodology: This retrospective study analyzed the number of dengue cases recorded from all hospitals in KhonKaen Province during 2006-2016. Weekly incidence, including severe dengue (DHF and DSS) infections, and climate data (temperature, rainfall, relative humidity) from KhonKaen meteorological station were collected. Multiple regression and SARIMA models were used to analyze the time series. For validation of dengue prediction, we constructed models using the 2006-2014 data, and subsequently used lags of weekly data to forecast 2015-2016.

Results: There were 7,706 reported dengue cases during the study period. More symptomatic cases were observed in 2013 and 2015, with peaks during the wet season (July). An exponential smoothing model was robust to predict in first 15 week of disease incidence posterior to the last case recorded. Mean weekly maximum temperature at a 6-11 weeks lag, rainfall at a lag of a week and current relative humidity were significant predictors of dengue disease occurrence.

Conclusion: Combining climate data to epidemiological surveillance data in predictive models appears to be a promising strategy towards the development of more accurate early warning systems.

Keyword: Dengue, climate, prediction, model

IMMUNOLOGICAL CHARACTERISTICS ON DENGUE VIRUS INFECTED PATIENTS AT NATIONAL HOSPITAL OF TROPICAL DISEASES

Poster No. 10

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Introduction: Dengue hemorrhagic fever is an acute disease caused by dengue virus. Early diagnosis based on immunological results have important role in treatment and prognosis.

Objective: Evaluation of Dengue virus infection through serological survey in patients with dengue fever/dengue hemorrhagic fever.

Methods: Cross-sectional description of 1417 samples, from outpatients or inpatients at the National Hospital for Tropical Diseases, who diagnosed as Dengue fever and/or Dengue hemorrhagic fever, had Dengue NS1/antidengue IgM positive, from 10/2010 to 10/2011.

Results: Mean age was 29.17 ± 12.26, 54% male. Dengue NS1-positive was observed in 91.02%, antidengue IgM positive in 46.96% and antidengue IgG positive in 51.54%. Dengue NS1 presented at highest level on the first 3 days and no positive case after 6th day after onset. Anti dengue IgM antibody was detectable at highest level on the 7th day of onset (88.98%). On the 9th day after onset the positive rate of anti dengue IgG antibody was 42.9%. In 29 cases NS1, IgM and IgG were positive, 9/29 samples were taken on 5th day of fever.

Conclusion: The diagnosis of dengue fever/dengue hemorrhagic fever can be based on the immunological results, depends on the time collecting samples.

Keyword: Dengue virus, NS1, Anti-dengue IgM antibody, Anti-dengue IgG antibody

ASSOCIATION BETWEEN ADIPOSITY AND DENGUE SEVERITY: A SYSTEMATIC REVIEW AND META-ANALYSIS

Poster No. 11

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Introduction: Severe dengue infection often has unpredictable clinical progression and outcome. Adiposity defined as the state of being obese, may play a role in the deterioration of dengue infection due to stronger body immune responses. Several studies found that dengue patient with obese/overweight have more severe presentation and poorer prognosis. However, the association is still inconclusive due to the variation in results.

Aim: To explore the association between adiposity and dengue severity.

Methods: We performed a systematic search of Ovid (MEDLINE), EMBASE, the Cochrane Library, Web of Science, Scopus and grey literature databases. Meta-analysis using random-effects model was conducted to compute the pooled odds ratio with 95% confidence intervals (CI).

Results: A total of 13,333 articles were obtained from the search. Fifteen studies were included in the final analysis. All studies were conducted among pediatric patients. Three cohorts, two case-control, and one cross-sectional studies found an association between adiposity and dengue severity. In contrast, six cohorts and three case-control studies found no significant association between adiposity and dengue severity. Our meta-analysis revealed that there are 20% higher odds (Odds Ratio=1.20; 95% CI:1.01, 1.43) of dengue severity among adiposity children compared to non-adiposity children. No heterogeneity was found between studies and its association was not modified by classification of adiposity, study design, study quality, nor multivariable adjustment for confounders.

Conclusion: This review found that adiposity is a risk factor for dengue severity among children. The results highlight and improve our understanding that obesity might influence the severity of dengue infection.

Keyword: Dengue, severe dengue, adiposity, obesity

KNOWLEDGE, ATTITUDE AND PREVENTIVE BEHAVIORS REGARDING DENGUE INFECTION AMONG LOCAL POPULATION IN AO NANG, KRABI PROVINCE, SOUTHERN THAILAND.

Poster No. 12

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Dengue fever is one of the major vector borne disease in Thailand and continues to be a public health concern. Dengue virus infection still causes significant morbidity and mortality in most tropical and sub-tropical countries of the world. There are a lot of tourist attraction places in Thailand but there is no information on the local knowledge, attitudes, and preventive behaviors regarding dengue fever exist although such information is necessarily required for prevention and control measures. The objective is to study the knowledge, attitude and preventive behaviors regarding dengue infection among the local population in Ao Nang, Muang district of Krabi Province, and southern part of Thailand. Ao Nang is one of the famous places where the high dengue transmission always occurs during the rainy season. This study conducted a community based cross-sectional survey in Ao Nang during May to July 2017. A structured questionnaire was conducted to collect information on the socio-demographic characteristics of the respondents and their knowledge, attitude and preventive behaviors regarding Dengue infection. One hundred respondents were purposely selected from 350 households with the mean age of 41 years. Three questionnaires were used for data collection and descriptive statistics, percentage, mean and standard deviation were employed for data analysis. The results showed that 88% of respondents had heard of dengue infection and 79% understood the cause of dengue infection. There were 75% could relate the key containers and *Aedes* mosquito breeding places to the transmission risk of dengue fever. This study also revealed that 96% of people had good attitude about the mosquito bites could spread dengue infection. Both knowledge and attitude of the respondents were positively related whereas 50% reported had low preventive behavior and awareness of dengue infection. Most of the respondents had a low perception of susceptibility to dengue fever. However, the community involvement in the prevention and control of dengue is very essential while strengthening the awareness of people regarding dengue infection urgently need to be done to protect the health of people from dengue and to limit its further spread throughout the country.

Keyword: Dengue, knowledge, attitudes and practices

BIOLOGY OF ZIKA VIRUS INFECTION IN HUMAN SKIN CELLS

Poster No. 13

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Zika virus (ZIKV) is an emerging arbovirus of the *Flaviviridae* family that includes Dengue, West Nile, Yellow Fever and Japanese encephalitis viruses, causing a mosquito-borne disease transmitted by the *Aedes* genus, with recent outbreaks in the South Pacific and South America. Here, we determine the importance of the human skin in the entry of ZIKV and its contribution to the induction of anti-viral immune responses. We show that human dermal fibroblasts, epidermal keratinocytes and immature dendritic cells are permissive to the most recent ZIKV isolate, responsible for the epidemic in French Polynesia. Several entry and/or adhesion factors permitted ZIKV entry with a major role for the TAM receptor AXL. ZIKV permissiveness of human skin fibroblasts was confirmed by the use of a neutralizing Ab and specific RNA silencing. ZIKV induced the transcription of TLR-3, RIG-I and MDA5, as well as several interferon-stimulated genes, including OAS2, ISG15 and MX1, characterized by a strongly enhanced interferon-b gene expression. ZIKV was found to be sensitive to the antiviral effect of both type I and type II interferons. Finally, infection of skin fibroblasts resulted in the formation of autophagosomes whose presence was associated with enhanced viral replication, as shown by the use of Torin 1, a chemical inducer of autophagy or the specific autophagy inhibitor 3-Methyladenine. The results presented herein permit to gain better insight in the biology of ZIKV and to devise strategies aiming to interfere with the pathology caused by this emerging Flavivirus.

Keyword: Zika, Arbovirus, Skin, Antiviral-Response

DEVELOPMENT OF THE COST AND TIME SAVING ZIKA VIRUS DETECTION METHOD BY REAL TIME RT-PCR IN RESPONSE FOR 2016 OUTBREAK IN THAILAND

Poster No. 14

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Zika virus is the important tropical disease which has big 2016 outbreak in South America and Asia. Zika virus infection diagnosis needs laboratory testing because of similar symptoms to dengue and chikungunya infections. The most useful detection method for Zika virus is real time RT-PCR. Because of the large amount of samples in 2016 Zika outbreak in Thailand, the original testing protocol is not suitable due to expensiveness and takes much time. This study aimed to develop the cost and time saving Zika virus detection method for using in Thailand. Real time RT-PCR for Zika virus detection was developed based on US-CDC's method with modification. Viral RNA was extracted from 150 ml of sample then tested simultaneously with two sets of primer/probe targeting E and NS2b gene of Zika virus. The developed method can detect Thai isolate Zika virus spiked in urine and serum at least 0.15 PFU/ml. No false positive result occurred with Dengue, Chikungunya, Japanese encephalitis and West Nile viruses. The developed method showed satisfactory result with good limit of detection and no false positive with other viruses. Cost and time consuming was at 25% and 50% from the original method respectively. At Thai NIH, more than 10,000 samples had been tested with this method since 2016.

Keyword: Zika virus, real time RT-PCR, urine

THE INFECTIVITY OF ZIKA VIRUS IN SWINE SPERM

Poster No. 15

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Nowadays, the spreading of Zika virus has been a severe impact on human health in tropical regions. Contrary to other *Aedes* borne viruses, sexual transmission of Zika virus has been reported. Therefore, in the present study, we investigated the infectivity of Zika virus in swine sperm. The sperm were collected from healthy swine. The swine sperm were infected with Zika virus, and the viral RNA and morphologic alteration were observed at different time point of infection. Zika virus infection was confirmed by transmission electron microscopy. The viral RNA was performed by Real time RT-PCR. The results demonstrated that viral RNA markedly decrease as the time post-infection increased, without any evidence of virus replication. The sperm showed no significant changes in morphology. Virus infected sperm have not been seen by Transmission electron microscopy, implying that Zika virus cannot replicate in swine sperm. We suggest the possible reasons correlated with this phenomenon might be, the spermatozoa of swine might not be the target of Zika virus, and Zika virus may not be tropic for spermatozoa. This pilot study used as a platform to investigate the sexual transmission of Zika virus in other longer-lasting cells.

Keyword Zika virus, swine sperm, sexual transmission, flavivirus

CONSTRUCTION OF THE RECOMBINANT ANTIGEN FOR THE IMMUNODIAGNOSIS OF ZIKA VIRUS INFECTION

Poster No. 16

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Zika virus is a mosquito-borne virus related to Dengue virus (DENV) and other flavivirus. It is transmitted by *Aedes sp*. mosquitoes. Zika fever often cause no or only mild symptoms, similar to a very mild symptom of dengue fever. However, a neurological effect, such as microcephaly and Guillain-Barre syndrome (GBS), has been concerned. Serological diagnosis of flavivirus infections is difficult to distinguish due to the extensive antigenic cross-reactivity among these viruses, especially, DENV and ZIKV infection. The domain III of envelope glycoprotein (E), the virus receptor-binding site and highly antigenic, is recognized by virus-neutralizing monoclonal antibodies. Some studies have reported that domain III is a useful antigen target for diagnostic assays. In this study, the specific recombinant ZIKV E domain III antigen was constructed to discriminate the antibody of ZIKV and DENV infection. The ZIKV E domain III gene was amplified with specific primer by PCR. Then, PCR fragment was ligated to pRSET B vector and transformed into *BL21 (DE) pLysS*. Protein expression was induced by addition of IPTG. Thereafter, we have successfully achieved a 25 kDa of ZIKV E domain III with 6x His-tagged. Purified ZIKV E domain III protein will be used as antigen and examined with mouse antibodies in near future. We expect that the recombinant antigen can differentiate between Zika virus and Dengue virus infection to solve the difficulty of interpretation due to their cross-reactivity. Moreover, serological laboratory diagnosis is important to confirm the etiology and prevalence of Zika virus infection in the endemic area

Keyword: ZIKV, Recombinant protein, E Domain III

DENGUE AND ZIKA VIRAL INFECTIONS IN PATIENTS WITH ACUTE FEBRILE ILLNESS IN NORTHEASTERN THAILAND

Poster No. 17

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Introduction: Dengue viruses (DENV) and Zika virus (ZIKV) are naturally transmitted to humans via infective *Aedes* mosquitoes. As DENV and ZIKV infections share common clinical symptoms, differential diagnosis is difficult without laboratory support. This study investigated the prevalence of DENV and ZIKV infections as well as DENV-ZIKV co-infection in acute febrile illness (AFI) patients in northeastern Thailand.

Materials and Methods: One-hundred and forty-three whole blood samples were collected from AFI patients who presented at participating hospitals between June 2016 and June 2017. DENV NS1 antigen and IgM/IgG antibodies were initially screened by commercial rapid diagnostic test (RDT). Blood was tested by RT-PCR for detection of DENV and ZIKV RNA and dengue serotyping. ZIKV infection was confirmed by DNA sequencing of the envelope gene region.

Results: From tested blood samples, 32.9% (47/143) were DENV positive by RDT and/or RT-PCR. Thirty-eight samples were used for DENV serotyping. DENV-4 was the most common serotype detected (55.3%, 21/38). Monotypic DENV-3, DENV-2 and DENV-1 infections were 5.3% (2/38), 2.6% (1/38), 10.5% (4/38), respectively. Multiple DENV serotypes represented 26.3% (10/38) of virus positive samples. ZIKV infection was detected in six samples (4.2%) collected during August-September 2016. Two cases of ZIKV were co-infected with DENV and four samples were ZIKV-infected only. Clinical features and severity of co-infected patients did not differ significantly from mono-infections of either virus.

Conclusion and Discussion: During a 13-month study period, DENV-4 was predominant. ZIKV was also co-circulating in a DENV endemic region. Surveillance of arboviral infections, especially DENV and ZIKV in AFI patients presenting dengue-like symptoms is required to assess relative transmission risk to local populations in northeastern Thailand.

Keyword: Dengue virus, Zika virus

EFFECT OF 350TH AMINO ACID SUBSTITUTION OF CHIKUNGUNYA VIRUS 6K-E1 PROTEIN ON ITS SENSITIVITY IN A RAPID E1-ANTIGEN TEST

Poster No. 18

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Chikungunya virus (CHIKV), East/Central/South/Africa (ECSA), West Africa (WA), and Asian genotype, caused sporadic outbreaks worldwide. A novel rapid Immunochromatographic kit detecting CHIKV E1-protein had been innovated. Although it showed high performance in specimens containing CHIKV ECSA genotype, low performance found in specimens with Asian genotype virus which currently broadened from Southeast Asia to the American continents. To understand factors affecting performance of this rapid kit towards Asian genotype virus, an interaction between anti-CHIKV monoclonal antibodies (mAbs) used in kit assembly, CK47 and CK119, and envelope proteins of three CHIKV genotypes was explored. We found that the reactivity of CK47, but not CK119, was lower towards Asian genotype virus compared to ECSA virus in Immunofluorescence test. Amino acid variations of envelope proteins (6K-E1) among genotypes provided a clue; ECSA viruses during outbreaks of 2005-2011, one of which was used to generate CK47 and CK119, possessed glutamic acid (E) at position 350, in contrary to other ECSA, WA, and Asian viruses, which possess aspartic acid (D). Site-directed mutagenesis confirmed that mutation at this position affected the reactivity of CK47, since E-to-D amino-acid substitution at position 350 in ECSA 6K-E1 reduced its reactivity, while D-to-E substation at this position in Asian and WA dramatically increased it. Taken together, these results unequivocally indicated that amino-acid position 350 of CHIKV 6K-E1 envelope protein is a key element affecting the performance of this kit. To overcome the huge challenges caused by viral mutations, further development is needed to construct a broadly reacting CHIKV-detection kit to accurately detect all three CHIKV genotype.

Keyword: Chikungunya virus, amino acid variation, rapid Immunochromatographic kit, monoclonal antibody

THE COMPARISON OF VECTOR COMPETENCE BETWEEN *AEDES AEGYPTI* AND *AEDES ALBOPICTUS* MOSQUITOES FOR CHIKUNGUNYA VIRUS

Poster No. 19

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Chikungunya virus (CHIKV) is an important mosquito-borne virus in Thailand. However, the study about vector competence for CHIKV in Thailand is limited. CHIKV infections in *Ae. aegypti* and *Ae. albopictus* were investigated in this study to indicate the competent vectors of these mosquitoes. Five groups of *Ae. aegypti* and *Ae. albopictus* were allowed to feed on different levels of CHIKV which were 102, 103, 104, 105, and 106 TCID50/ml. CHIKV infection, dissemination, and transmission were assessed by ICC staining on whole body, legs, and saliva samples on day 14 post blood feeding, respectively. Percent infection, dissemination, and transmission in *Ae. albopictus* were 83, 71, and 42%, respectively while the results in *Ae. aegypti* were 25% after taking the blood meal with 102 TCID50/ml of CHIKV. Percent infection, dissemination, and transmission in *Ae. albopictus* were 90, 87, and 70%, respectively while the results in *Ae. aegypti* were 29% after taking the blood meal with 103 TCID50/ml of CHIKV. Percent infection, dissemination, and transmission in *Ae. albopictus* were 100% but the results in *Ae. aegypti* were 33% after taking the blood meal with 104 TCID50/ml of CHIKV. Percent infection, dissemination, and transmission in *Ae. albopictus* were 100, 90, and 90%, respectively while the results in *Ae. aegypti* were 43% after taking the blood meal with 105 TCID50/ml of CHIKV. Percent infection, dissemination, and transmission in *Ae. albopictus* were 100%, but the results in *Ae. aegypti* were 42% after taking the blood meal with 106 TCID50/ml of CHIKV.

Keyword: Chikungunya virus, *Aedes*, infection, transmission

QUALITY OF LIFE OF PATIENTS LIVING WITH HUMAN IMMUNODEFICIENCY VIRUS INFECTION – EVIDENCE FROM SOUTH INDIA

Poster No. 20

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Introduction: With anti-retroviral therapy (ART) for human immunodeficiency virus infection (HIV) coming into picture, quality of life (QOL) has gained importance. Knowledge on the factors affecting QOL would be helpful in making important policy decisions and health care interventions. The aim of this study is to assess the quality of life of people living with HIV (PLWH) and to identify the factors influencing their QOL.

Materials and Methods: The study was done among 100 PLWH attending a tertiary care hospital, and three Non-Governmental Organizations at Calicut, Kerala, India, from June 2011 to May 2014. QOL was assessed using HIV specific World Health Organization Quality Of Life scale (WHOQOL-HIV) – BREF questionnaire which has six domains (physical, psychological, level of independence, social relationships, environment and spirituality/religiousness/personal belief). Social support and stigma were measured using "Multidimensional Scale of Perceived Social Support" and "HIV Stigma Scale," respectively, using Likert Scale. Factors influencing QOL were identified using backward stepwise multiple linear regression with the six domain scores as the dependent variables.

Results: Male: Female ratio was 1:1 and 58% were in early stage of the disease (stage I/II). Psychological and SRPB (Spirituality Religiousness and Personal Beliefs) domains were the most affected domains. All the regression models were statistically significant ($P<0.05$). The determination coefficient was highest for the social relationship domain (57%) followed by the psychological domain (51%). Disease stage and perceived social support significantly influenced all the domains of WHOQOL. Younger age, female gender, rural background, shorter duration of HIV, non-intake of ART and greater HIV related stigma were the high risk factors of poor QOL.

Conclusion: Interventions such as ART, family, vocational and peer counselling would address these modifiable factors influencing QOL, thereby improving the QOL of PLWH.

Keyword: Human immunodeficiency virus, HIV related stigma, India, people living with HIV, quality of life, social support, WHOQOL-HIV

MOTHER TO CHILD HIV&AIDS TRANSMISSION OCCURENCE IN REGIONAL PUBLIC HOSPITAL MERAUKE DISTRICT, PAPUA IN 2010-2014

Poster No. 21

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Background: HIV (Human Immunodeficiency Virus) and AIDS (Acquired Immunodeficiency Syndrome) is rapid growing infection globally, especially in Indonesia. Based on data issued by Indonesian Health Ministry, until 2015 the accumulation of HIV infection case is 184.929. Cumulative number of AIDS case per 100.000 population (case rate) until September 2015 shows that Papua is on first rank (378,14). Furthermore, accumulation of AIDS case in Indonesia for housewives is 9.906 cases. Merauke is one of the districts in Papua that has problems with HIV. The result of Voluntary Counselling Test (VCT) conducted in the period January - July 2007 in Merauke district showed 11 out of 380 positive housewives contracted HIV &AIDS. If there is housewife that has HIV&AIDS, it can cause risk of virus transmission to the child.

Aims: This study aims to know mother to child HIV&AIDS transmission occurrence number and mother involvement in PMTCT on Regional Public Hospital Merauke District, Papua in 2010-2014. Results: There are 31 HIV positive mothers that have child with non-reactive HIV diagnosis. Negative diagnosis can be acquired by taking PMTCT program. The PMTCT program in this study is limited on ARV therapy, Caesarean Section labor, no history of infection when pregnant, no breastfeeding, well-nourished and didn't smoke. In this study, all mother only take 3 of 6 PMTCT program.

Conclusion: There is no HIV&AIDS transmission occurrence from mother to child that caused by taking PMTCT, where 2 main preventive factors is breastfeeding and Caesarean Section labor.

Keyword HIV&AIDS, mother to child virus transmission, risk factor

HEPATITIS C ASSOCIATED ORAL LICHEN PLANUS MANAGEMENT USING DIRECT-ACTING ANTIVIRALS

Poster No. 22

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Objectives: Oral Lichen Planus is one of the extraneous manifestation of hepatitis C infection. Traditionally pegylated-interferon-alpha (PEG-IFN) in combination with ribavirin was used but lately direct-acting antivirals (DAAs) which are specifically designed to target various stages of HCV life cycle. The DAAs are well tolerated and with lesser adverse effects.

Methods: Lichen Planus refractory to conventional steroid treatment was considered as an oral manifestation of HCV and it was confirmed by anti-HCV by ELISA (third generation) and reverse transcription polymerase chain reaction (RT-PCR) for HCV-RNA. Nine patients with HCV-related OLP received Ledipasvir/sofosbuvir for 12 weeks. Out of nine, five were males with a mean age of 64. The patient response were assessed before and after treatment.

Results: Sustained virological response was observed in all patients and there was no worsening of lichen planus in any of the treated patients. Clinically refractory lichen planus resolved with DAAs treatment.

Conclusion: We have reported a case series of successful management of interferon free treatment in HCV associated oral lichen planus. Given the strong association, screening for HCV should be considered in patients with oral lichen planus.

Keyword: HCV, Lichen Planus

CROSS-NEUTRALIZING ANTIBODIES IN HAND, FOOT AND MOUTH DISEASE PATIENTS

Poster No. 23

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Background: Hand, Food and Mouth Disease (HFMD) is a major public-health problem in the Asia-Pacific region with global pandemic potential. Antiviral drugs are not available to treat the infected patients. While enterovirus A71 (EV-A71), coxsackievirus A6 (CV-A6), CV-A10 and CV-A16 are the most common causes, only EV-A71 vaccine was successfully developed and has recently been licensed in China. Scarce information exists whether infection with one enterovirus serotype could induce antibodies cross-neutralizing other serotypes. Yet such knowledge is essential to guide the development of effective HFMD vaccines.

Materials and Methods: 67 convalescent sera collected between day 8 and 14 after admission from patients with laboratory confirmed HFMD (including CA6 (n = 17), CA10 (19), CA16 (13) and EV71 (18)) enrolled in an ongoing HFMD research program in Vietnam since 2013 were selected and tested for the presence of cross-neutralizing antibodies against these 4 serotypes by micro-neutralization assay. A titer of 1:16 or above was considered as protective (cross-neutralization/cross-protection).

Results: 100% of the tested sera had neutralizing antibodies at a titer beyond the protective level (≥1:32) for homologous serotypes. Only some EV-A71 infected patients' sera showed cross-neutralisation against CV-A6 (4/18, 22%), CV-A10 (8/18, 44%) and CV-A16 (4/18, 22%). Likewise, among CV-A6, CV-A10 and CV-A16, cross-protection was recorded in 5%-38% of the patients' sera. In contrast CV-A6 and CV-A16 infection did not cause cross-neutralisation against EV-A71.

Discussion: Our study represents the first investigation into the presence of cross-neutralizing antibodies in patient sera for the 4 most common causes (EV-A71, CV-A6, A10 and A16) of HFMD. The results point out multivalent vaccine is needed to control HFMD.

Keyword: Cross-neutralizing, antibodies, Hand, Foot and Mouth

EVOLUTION OF COXSACKIEVIRUS A6: AN EMERGING PATHOGEN OF HAND, FOOT AND MOUTH DISEASE

Poster No. 24

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Background: Hand, foot and mouth disease (HFMD) is a major public health issue across the Asia-Pacific region. While enterovirus A71 and coxsackievirus A16 (CV-A16) are regarded as the most common causes, CV-A6 has recently emerged and become the most common virus causing HFMD outbreaks worldwide. Improving our knowledge about the evolution of this emerging pathogen and associated clinical phenotypes is essential to the development of intervention strategies.

Materials and methods: Consecutive CV-A6-positive swabs were collected between 2011 and 2015 and were subsequently whole-genome sequenced. The obtained sequences were analyzed to determine their genetic relationship with global strains, origin, divergence time and relative genetic diversity over time using phylogenetic methodologies available in IQ-TREE and Bayesian Evolutionary Analysis by Sampling Tree (BEAST).

Results: Between 2011 and 2015, CV-A6 was detected in 514/1877 (27.4%) of HFMD patients. 93 (18%) patients had moderately severe or severe HFMD. 100 complete genome sequences were successfully recovered. Phylogenetic analysis revealed that all of the Vietnamese CV-A6 belonged to genogroup A, and were likely imported into Vietnam around 2010, two years prior to its perceived emergence. Transmission of CV-A6 between localities within Vietnam frequently occurred, whilst movement of CV-A6 across international borders appeared rare. Skyline plots identified fluctuations in the relative genetic diversity of CV-A6 corresponding to large HFMD outbreaks caused by genogroup A of CV-A6 worldwide.

Conclusions: We present a comprehensive investigation into the molecular epidemiology and evolution of CV-A6 at both local and global scales. These data show that CV-A6 is an emerging pathogen with the capacity to cause severe HFMD, and highlight the importance of active molecular surveillance, and understanding the underlying mechanisms that shape pathogen evolution and emergence, which is essential for development and implementation of intervention strategies.

Keyword: CoxsackievirusA6, evolution, whole genome sequencing

ROLE OF MYCOVIRUS IN *BIPOLARIS MAYDIS*

Poster No. 25

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The mycoviruses have been known as fungal viruses. Most of them are RNA genome, either double or single-stranded RNA. However, the circular DNA has been reported. Generally, the mycovirus have no specific effect on their infected host, but some of them can reduce the virulence of fungi, fungal hypovirulence effects. The *Bipolaris maydis* was one of the most important causative agent of Southern corn leaf blight. This study aimed to characterize the role of mycovirus in *Bipolaris maydis* (5-1 strain) isolated from corn leaves compared with Thai isolated strain (mycovirus negative). We confirmed the mycovirus infection by Real time RT-PCR with inhouse primers, fungal growth kinetics and stress response test. We found that mycovirus RNA had been found in 5-1 strain only. Fortunately, the growth rate of 5-1 strain was slower than Thai isolated strain. The mycovirus infected strain cannot grow in low pH, high temperature and hyperosmotic condition. These phenomena imply that mycovirus might be influence on fungal virulence; hypovirulent property. Further investigation such as other stress condition, biofilm formation, drug susceptibility and fungal ultrastructure will be evaluated.

Keyword: Mycovirus, *Bipolaris maydis*, hypovirulence, Southern corn leaf blight

SEROPREVALENCE OF SYPHILIS, CYTOMEGALOVIRUS AND RUBELLA INFECTIONS IN WASTE-BLOOD SAMPLES

Poster No. 26

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Syphilis, cytomegalovirus (CMV) and rubella infections usually cause asymptomatic or mild infection in children and adults. But they can cause serious consequences in fetus such as congenital anomalies and intrauterine fetal death. Moreover, these infections may lead to significant morbidity and mortality in immunosuppressed or immunocompromised patients. In Myanmar, there has been no study for seroprevalence of syphilis, CMV and rubella in relatively low risk population such as patients with non-communicable diseases. Therefore, this study was carried out to determine the seroprevalence of syphilis, CMV and rubella infections in waste-blood samples tested for non-communicable diseases from July to October 2016. In this hospital-based, cross-sectional descriptive study, 500 waste-blood samples were collected from No.(2) Defence Services General Hospital (1000-beds), No.(2) Defence Services Obstetric, Gynaecology and Children Hospitals (300-beds), Pobba Thiri Retired Services Personnel Hospital and Zabu Thiri Specialist Hospital. Serological examination was done at Defence Services Medical Research Centre. In this study, overall seroprevalence rate was syphilis (0.6%), CMV immunoglobulin G (IgG) (72.4%), rubella IgG (70.0%), CMV-rubella co-infection (57.0%), syphilis-rubella co-infection (0.2%) and syphilis-CMV-rubella co-infection (0.4%). The highest rate for CMV (IgG) and rubella (IgG) was found in age group older than 60 years (96.07% and 94.11% respectively) whereas lowest rate was found in 2-10 years (36.73% and 34.69% respectively). Seroprevalence in reproductive age groups 21-30 and 31-40 years for female showed that CMV (IgG) was 86.84% and 90.48% respectively while rubella (IgG) was 84.21% and 92.86% respectively. Therefore, this study showed high seroprevalence of cytomegalovirus and rubella infections.

Keyword: Seroprevalence, Syphilis, CMV, Rubella

JAPANESE ENCEPHALITIS AMONG PEDIATRIC PATIENTS IN NUEVA ECIJA, PHILIPPINES: A CROSS-SECTIONAL, ANALYTICAL STUDY

Poster No. 27

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Objective: To determine the demographic profile, common clinical manifestations and laboratory findings with Japanese Encephalitis (JE) patients confirmed by JE IgM by ELISA.

Setting: The researchers conducted the study at Dr. Paulino J. Garcia Memorial Research and Medical Center, a tertiary training hospital in the Nueva Ecija, Philippines, from April 2015-March 2016.

Study population. All pediatric patients 1-12 years old who met the criteria of Acute Encephalitis Syndrome and who resides in Nueva Ecija, were included in study.

Methodology: All patients with Acute Encephalitis Syndrome (AES) underwent lumbar tap. Acute Encephalitis Syndrome (AES) is defined as a person with acute onset of fever and at least one of the following: 1) Change in mental status such as confusion, disorientation, coma or inability to talk 2) New onset of seizures which excludes simple febrile seizures. Cerebrospinal fluid and serum samples were sent to the Research Institute for Tropical Medicine for Japanese Encephalitis and also Dengue Virus-specifc IgM ELISA test.

Results: Among patients with IgM positive Japanese Encephalitis, 91.18% had exposure to rural environment, mean age is 5.78 +/- 2.81 years and male-to-female ratio is 1.2. The incidence and case fatality rate are 5/100,000 and 7.35%, respectively. It is somewhat surprising that co-infection with Dengue and Japanese Encephalitis virus exhibited cross-protection to severe Japanese Encephalitis.

Conclusion: The findings about patients who are diagnosed with Acute Encephalitis Syndrome, with rural exposure, fever, altered sensorium, meningeal irritation and normal reflexes, with cerebrospinal fluid analysis of low-normal sugar, normal to high protein, and normal to lymphocytic results has important implications for developing clinical criteria for diagnosing Japanese Encephalitis, since screening test of Japanese Encephalitis is not readily available in the different parts of the Philippines.

Keyword: Japanese Encephalitis, Philippines, incidence, isolation

PREVALENCE OF LATENT TUBERCULOSIS INFECTION AMONG SCHOOLCHILDREN BY TUBERCULIN SKIN TEST AND RADIOLOGICAL METHOD

Poster No. 28

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The tuberculin skin test (TST) is one of the available screening tests for the diagnosis of Mycobacterium Tuberculosis infected subjects. The next steps for confirmation are Chest X Ray (CXR), Gene X pert, Culture and Next Generation Sequencing technique. The aim of this study is to find out the prevalence of latent tuberculosis infection (LTBI) among schoolchildren by Tuberculin Skin Test and Radiological Method. This is cross sectional descriptive study. The parents and guardians of the children provided their consent prior to the whole procedures. All 300 children of age between 5 years and 12 years underwent tuberculin skin test with one TU of purified protein derivative. A total of 39 children had a positive tuberculin skin test. These children were taken CXR for confirmation. Among them, both tuberculin skin test and CXR positive were found in only five children. The tuberculin skin test positive subjects were 13% after screening test. According to the result of TST and CXR, 1.67% of subjects were positive results. While the evidence for targeted tuberculosis testing exists and benefits of screening programs are clear, administrative logistics are of greater concern. This study provided that it is possible to reduce morbidity and mortality associated with latent tuberculosis infection if case detection is improved and preventive therapy and curative treatment are made more accessible globally.

Keyword: TST, CXR, LTBI

THE FACTORS RELATED TO DEFAULT AND FAILURE TREATMENT OF MDR-TB PATIENT IN THE LOWER PART OF NORTHEAST, THAILAND

Poster No. 29

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This research aimed to study the factors related to default and failure treatment of MDR-TB patient in the lower part of the north-eastern Thailand. The study area was 7 provinces in the Lower Part of Northeast, Thailand. 70 patients who laboratory showed drug resistant to INH and Rifampicin, diagnosis MDR-TB by the physician, registered as MDR-TB patient, and treatment during the year 2002-2014 were include to study. The tools were questionnaires and semi-structure interview guide. Data was analyzed by Binary logistic regression. The most of patient were male (75.5%), age 40-49 year (60.5%), outcome treatment was default and failure treatment (50.0%), cured and complete of treatment (50%). The factor of the perception on risk and utilities of care and treatment about MDRTB, access to services, social support, self-care and prevention of MDRTB, and income during treatment of MDRTB were predict 20.7% of the default and failure treatment of MDRTB. The accuracy of the prediction was 67.1%. The factor of non-income during treatment of MDRTB was related significantly (at 0.05) to default and failure treatment. The portion of default and failure treatment between the patient who have no income and who have income during treatment was 2.88. The economy was the most important factor effecting to the default and failure treatment of the MDRTB patient. Hence the care and treatment of MDRTB patient should be comprehensive and specific to the socio-economic problems and provided the service from the integrated health professional care team with strongly DOT method.

Keyword: Default, Failure, Treatment, MDR-TB

MYCOBACTERIUM TUBERCULOSIS DRUGS RESISTANCE PROFILE ALONG THE THAILAND-MYANMAR BORDER

Poster No. 30

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Since 2009, the Shoklo Malaria Research Unit (SMRU) has been providing comprehensive tuberculosis (TB) services to a migrant population located on the Thailand-Myanmar border, Tak Province. Thailand and Myanmar are two of the 14 countries that appear in all three TB high burden country list: TB Incidence, multi-drug resistant TB (MDR-TB) and TB/HIV. SMRU program components include TB case detection, diagnosis and treatment, with provision of care and directly observed treatment for both drug sensitive and drug resistant TB, with patient`s close monitoring and follow up. Clinical diagnoses have been supported by laboratory testing composed of microscopy, solid/liquid culture and phenotypic DST (provided by International Organization for Migration, IOM), and GeneXpert testing introduced in 2013. The results obtained for 1245 patients with bacteriologically confirmed samples (either microscopy or GeneXpert) were reviewed. From these patients 199 had *Mycobacterium tuberculosis* (Mtb) isolates with resistance to one or more of the tested drugs (1st line and 2nd line). Of these 76 presented with rifampicin resistance alone or in combination with other drug resistances. During the review characteristics, including outcome, of these groups of patients with different resistance profiles are compared together and to the characteristics of TB patients with fully susceptible strains. In addition, the challenges and issues of different diagnostic strategies and results are considered. Findings of this review highlight the need to increase our understanding of TB drug pharmacokinetics, acquisition of resistance and impact on outcomes.

Keyword: Tuberculosis, Drug Resistance, Migrants

EVALUATION OF THE GENXPERT MTB/RIF IN PRESUMPTIVE TUBERCULOUS MENINGITIS PATIENTS

Poster No. 31

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Background: Meningitis caused by *Mycobacterium tuberculosis* is a major cause of morbidity and mortality worldwide. We evaluated the performance of GeneXpert for detection of *M. tuberculosis* in cerebrospinal fluid (CSF) compared with conventional microbiological tests and clinical assessment.

Methods: Participants were adults (n=37) presenting with suspected tuberculous meningitis (TBM) to the Hospital Nacional Dos de Mayo, Lima, Peru, during 12 months until 1st January 2015. CSF specimens were tested for *M. tuberculosis* using GeneXpert, Ziehl-Neelsen smear and culture on solid and liquid media. Drug susceptibility testing used Mycobacteria Growth Indicator Tube (MGIT 960) and the proportions method.

Results: 81% (30/37) of participants had clinically-diagnosed TBM, of whom 63% (19/30, 95% confidence intervals, CI: 44-80%) were HIV-positive. 19% (7/37), of participants had microbiologically-confirmed TBM, also had clinically-diagnosed TBM. Compared to clinical diagnosis, all laboratory tests had 100% specificity and diagnostic sensitivity was 23% (7/30, 95%CI: 9.9-42%) for GeneXpert and 18% (16/73, 95%CI: 11-28%) for culture; significantly greater than 7% (2/30, 95%CI: 0.82-22%) for microscopy (P<0.001). GeneXpert and microscopy provided same-day results, whereas culture took 20-56 days. GeneXpert provided same-day rifampicin-susceptibility results, whereas culture-based testing took 32-71 days. 43% (3/7, 95%CI: 9.9-82%) of microbiologically-confirmed participants with data had evidence of drug-resistant TB, but 81% (30/37, 95%CI: 65-92%) of clinically-diagnosed participants had no interpretable drug-susceptibility results available.

Conclusions: Compared with traditional culture-based methods of CSF testing, GeneXpert had similar yield and faster results for both the detection of *M. tuberculosis* and drug-susceptibility testing. However, most clinically-diagnosed participants lacked microbiological confirmation and drug-susceptibility results.

Keyword: Tuberculous meningitis, laboratory diagnostics, GeneXpert

THERAPEUTIC RESPONSE: A DIAGNOSTIC CRITERION IN CUTANEOUS TUBERCULOSIS

Poster No. 32

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Tuberculosis is a global problem. The is an estimated 10.4 million new cases of tuberculosis worldwide, extrapulmonary cases accounting for 15% of the global burden. Further, less than half of new cases are bacteriologically-confirmed, proving the difficulty in diagnosing tuberculosis in many cases. An 11 year-old girl presented with a gradually enlarging verrucous plaque on the left knee. The lesion started as a solitary slightly erythematous papule which developed a few days after sustaining a minor injury. She noted peripheral expansion of the lesion in the span of 3 years without accompanying systemic symptoms. Physical examination revealed a solitary, erythematous, scaly, verrucous plaque on the left knee measuring about 1.5 cm x 2 cm. Complete blood count and routine biochemical examinations were normal. Chest radiography revealed hazy infiltrates in the lower and middle lung fields and retrocardiac spaces. Tuberculin skin test was positive (20 mm) at 48 hours. Biopsy of the lesion showed presence of dense inflammatory infiltrates in the upper dermis and granulomatous foci with rare multinucleated giant cells in the mid-dermis. Based on clinical presentation and histopathologic findings together with high prevalence of tuberculosis in our region, anti-tuberculosis therapy was initiated with fixed dose combination of isoniazid, pyrazinamide, rifampicin and ethambutol for two months, followed by isoniazid and rifampicin for 4 months. Complete resolution after 6 months of therapy confirms our diagnosis.

Keyword: tuberculosis verrucosa cutis, cutaneous tuberculosis, anti-tuberculosis therapy, therapeutic response

DISTRIBUTION PATTERN OF AEROSOLIZED *MYCOPLASMA BOVIS* WITH ENVIRONMENTAL AEROSOLS UNDER DIFFERENT HUMIDITY LEVELS

Poster No. 33

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Introduction: *Mycoplasma bovis* (*M.bovis*) is a pathogen affecting cattle to causes pneumonia, mastitis, and more, causing a significant economic loss for the livestock industry. However, *M.bovis* infection with airborne route has not been well understood. This study investigated the potential risk of airborne *M.bovis* to be suspended in the air under the different relative humidity (RH) levels and effect of dust present in the same environment.

Materials & Methods: A 128L Teflon sheet chamber with two separate rooms was employed. After the stable conditions on both side of the chamber rooms with *M.bovis* and sawdust were verified by Optical Particle Counter (OPC), two aerosol components were mixed. The aerosols from the chamber were sampled by a cascade impactor (cut off size: 0.25 to 2.5μm). A Real time-PCR was employed to quantify the amount of *M. bovis* DNA in each of aerosol cut off sizes.

Results & Discussion: From the cumulative *M. bovis* DNA quantitative analyses with different RH conditions, the 80 % RH showed less amount of airborne DNA. These result suggested that airborne *M. bovis* behave differently under the different RH conditions. The presence of environmental dust enhanced the diminishing trend with high RH condition. These results may contribute to having a further understanding of the airborne transmission of *M. bovis* with different climate scenarios.

Keyword: *M. bovis*, bioaerosols, climate condition

PROTEOMIC STUDY OF *BURKHOLDERIA PSEUDOMALLEI* AFTER SERIAL PASSAGES IN LURIA-BERTANI MEDIUM

Poster No. 34

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Burkholderia pseudomallei is Gram-negative bacteria that cause melioidosis, leads to fatal death in human. This bacteria is capable of survival and adaptation in a wide range of niches, both in the environment and in an infected host. However, mechanisms for its adaptation during serial passages remain totally unknown. In the present study, we employed a proteomics approach to examine alteration of *B. pseudomallei* proteins after serial passages in Luria-Bertani (LB) medium. *B. pseudomallei* strain K96243 was daily subcultured 1:10 into LB broth and grown at 37 oC for 5 days. Bacterial cells of the first and fifth passages were collected and lysed. Protein lysates were separated with two-dimensional electrophoresis in triplicate and visualized protein spots with SYPRO Ruby fluorescent stain. Protein spots were differentially analysed with ImageMaster 2D Platinum version 5.0. Analyses indicated that 21 protein spots were identified as altered proteins after the fifth passage, in comparison to the first passage. Among these proteins, 6 were up-regulated, while 15 were down-regulated. These proteins will be further characterized by mass spectrometry for more understanding about *B. pseudomallei* adaptive mechanisms. This study will provide the first dataset of *B. pseudomallei* proteome after serial passages in LB medium and its alteration, which may lead to novel insights into adaption of *B. pseudomallei* passages.

Keyword: *Burkholderia pseudomallei*, serial passage, proteomics

PATHOGENESIS IN HUMAN SKIN FIBROBLAST ; A TRUELY SKIN INFECTION MODEL OF *BURKHOLDERIA PSEUDOMALLEI*

Poster No. 35

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Burkholderia pseudomallei is a gram-negative intracellular bacterium with causes fatal melioidosis. The disease is endemic in South East Asia and northern Australia. *B. pseudomallei* is a tier 1 select agent that can transmit to human by inhalation, inoculation through skin abrasion, and ingestion. Once entry, *B. pseudomallei* can invade and damage many cell types including respiratory eepithelial and phagocytic cells. Although, some studies in fibroblast were documented but they are not exactly human skin cell representatives. In this study, we demonstrated *B. pseudomallei* invasion to human fibroblast and intracellular survival. Co-culture assays between human skin fibroblast and *B. pseudomallei* K96243 were performed at multiplication of infection of 1:20 at37 °C with 5% CO2. Infected cells were lysed with 0.1% Triton-X 100, diluted in PBS and inoculated onto LB agar plate for colony count. The result showed *that B. pseudomallei* can invade to human skin fibroblast, and replicate inside for at least 24 hours after infection. This work expands our understanding of *B. pseudomallei* infecton in skin fibroblast of the host. Confirmation of invasion by microscopic technique and virulence factors involved in the pathogenesis *of B. pseudomallei* in human skin fibroblast cells are being investigated.

Keyword: melioidosis, skin abrasion, fibroblast, invasion

FUNCTIONAL CHARACTERIZATION OF SHORT-CHAIN DEHYDROGENASE/ OXIDOREDUCTASE (SDR) FROM *BURKHOLDERIA PSEUDOMALLEI*

Poster No. 36

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Burkholderia pseudomallei is the causative agent of melioidosis, a severe infectious disease endemic in tropical and subtropical areas. In Thailand, *B. pseudomallei* is commonly present in the northeast region, where saline soil and water are abundant. It has been suggested that high salt condition is associated with survival and invasion of *B. pseudomallei*. Previously, it was reported that the expression of bpss2242 gene was significantly up-regulated when *B. pseudomallei* was cultured under salt stress. Moreover, the invasion efficiency as well as the ability to survive and replicate inside host cells were significantly impaired in *B. pseudomallei* lacking bpss2242. This suggested that bpss2242 might play important role in adaptive response and pathogenesis of this pathogen. BPSS2242 protein was categorized into short-chain dehydrogenase/oxidoreductase (SDR) superfamily. It was revealed by bioinformatics analysis that BPSS2242 contained NAD(P)+ binding domain with catalytic triad active site. However, the authentic function of this protein is still unknown. In the present study, the functional role of BPSS2242 was investigated. The recombinant BPSS2242 from *B. pseudomallei* was constructed, expressed, and purified to homogeneity. Finally, purified BPSS2242 was biochemically characterized. The results obtained from this study provides useful information regarding adaptive response to salt stress and pathogenesis of *B. pseudomallei*. In addition, information of properties and function of BPSS2242 might be useful for developing a new strategy for melioidosis treatment.

Keyword: *Burkholderia pseudomallei*, melioidosis, function, short-chain dehydrogenase/ oxidoreductase

INNOVATION FOR DIAGNOSIS OF MELIOIDOSIS

Poster No. 37

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Melioidosis is an infectious disease that is highly endemic in Asia and northern Australia. The disease is caused by a Gram-negative bacterium, *Burkholderia pseudomallei*, which is commonly found in soil and water in these regions. Diagnosis of melioidosis is difficult because the disease has a wide range of clinical manifestations. The current standard method for laboratory diagnosis is bacterial culture. This method is time-consuming and requires biosafety level 3 (BSL-3) facility which is not available in rural areas. There is currently no reliable rapid serological test for melioidosis. Indirect haemagglutination assay (IHA) has been widely used but several reports have shown that it is neither sensitive nor specific when used in endemic areas. We previously established rapid enzyme-linked immunosorbent assays (ELISA) based on several purified antigens for antibody detection. In comparison with other antigens, we found that Hcp1-ELISA showed the highest performance with the areas under receiver operator characteristics (AUROCCs) for diagnosis of melioidosis in Thailand of 0.95. To further improve the speed for diagnosis, we have developed an Immunochromatographic test (ICT) based on the Hcp1. ICT is a simple device for point-of-care (POC) serological testing. The results can be read visually within 15 minutes after sample loading. Positive results show red color on the strip at test and control lines. Negative results show red color at only control line. We evaluated the ICT to detect antibody in 4 groups of sera: 141 serum samples from culture-confirmed melioidosis patients, 188 serum samples from Thai healthy donors, 90 serum samples from healthy U.S. donor and 60 serum samples from Thai patients with other bacterial infections including tuberculosis, scrub typhus and leptospirosis (20 patients for each disease). The sensitivity of the ICT was 90% when compared to positive culture results and the specificities for Thai donors, U.S. donors and other infection patients were 87%, 100%, and 98%, respectively. The result of ICT assay for these samples was 92% in agreement with Hcp1-ELISA with kappa value of 0.81. We conclude that an ICT assay based on the use of Hcp1 is a promising POC test for rapid diagnosis of melioidosis. Prospective evaluation of the ICT as an early diagnostic tool in several hospitals in Thailand is ongoing.

Keyword: *Burkholderia pseudomallei*, Immunochromatographic test, Melioidosis

CORRELATION OF CLINICAL AND ENVIRONMENTAL ISOLATES OF *CRYPTOCOCCUS NEOFORMANS* IN URBAN AREA, INDONESIA

Poster No. 38

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Cryptococcus neoformans is a pathogenic fungus that causes life-threatening meningeal cryptococci, mainly in immunocompromised individuals, such as HIV/AIDS infected patients. From 21 isolates were collected, 7 isolates were from clinical samples and 14 isolates from environmental samples. Of the clinical isolates, 100% were from men with an average age of 29.71 years. All *C. neoformans* clinical isolates were from HIV-positive patients (100%) and were found from liquor cerebrospinal fluid (100%). Clinical isolates were collected from Jakarta and surrounding areas with most isolates from Jakarta (57.14%), Depok (28.57%), and Bekasi (14.29%). Environmental isolates, 35.71% were obtained from pigeon droppings, 14.29% from dust house, 28.57% from the soil, and 21.43% from decaying wooden. PCR-fingerprinting, using (GACA)4 as a primer, discriminated 21 clinical and environmental isolates into 2 groups (group A and B). Seven clinical and 12 environmental isolates were group A, which had two major specific bands of approximately 1,250 and 960 base pairs. Two environmental isolates, one from pigeon excreta and the other one from decaying wood sample were group B, which had two major specific bands of approximately 1,180 and 554 base pairs. Genetic correlation between the majority of clinical and environmental isolates is consistent with the hypothesis that human cryptococcosis is acquired from spora exposure in the nature.

Keyword: *Cryptococcus neoformans*, clinical isolate, environment isolate

LEPTOSPIROSIS : AN EMERGING CAUSE OF FEBRILE ILLNESS IN NEPAL

Poster No. 39

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Background: Leptospirosis is an emerging zoonotic disease, with major burdens in tropical regions and is often overlooked in the differential diagnosis of febrile illnesses. Agronomy and farming being the major profession in Nepal facilitates leptospirosis transmission. However, the disease is under reported in Nepal due to lack of awareness and diagnostic facilities. Failure to recognize these cases could lead to serious morbidity and mortality.

Methods: A cross sectional study was conducted among 300 patients visiting National Public Health Laboratory suspected of leptospirosis. Demographic and clinical data from these patients were collected and their serum samples were processed for rapid detection test and qualitative detection of leptospiral IgM antibody by ELISA.

Results: A total of 300 serum samples from patients referred to NPHL for laboratory diagnosis of leptospirosis were analyzed. All these patients were febrile. Other symptoms reported were headache, myalgia, abdominal pain, vomiting, jaundice, and diarrhea. Among them 60% were male and 40% were female with majority in the age group 20-40 years (43%). Of the 300 serum samples tested, seropositivity was seen in 60 samples (20%) by IgM ELISA, with high incidence during autumn season.

Conclusion: This study showed high prevalence of leptospirosis, indicating need to consider leptospirosis in the differential diagnosis of febrile patients. Awareness and knowledge regarding this disease should be strengthened among health care personnel as the clinical symptoms of leptospirosis overlaps with many other tropical diseases.

Keyword: Leptospirosis; Febrile illness, IgM ELISA, Nepal

MOLECULAR DETECTION OF LEPTOSPIRA IN ENVIRONMENTAL SAMPLES COLLECTED FROM REGIONS WITH HIGH INCIDENCE OF HUMAN LEPTOSPIROSIS IN THE PHILIPPINES

Poster No. 40

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Leptospira is the causative agent of leptospirosis, one of the prevalent infectious diseases affecting the Philippines. Since the disease is usually acquired upon exposure to contaminated environment, it is important to identify the most likely sources for human infections. In this study, a total of 54 soil and water samples were collected and screened for Leptospira. Samples were obtained from ponds, rivers, agricultural fields, flood waters, canals, and waterways housing informal settlers where high incidences of human leptospirosis were reported this year. Compared to microscopic examination which detected 23 Leptospira-positive cultures, PCR-based detection targeting the 23S rRNA gene confirmed 19 samples positive for Leptospira. Sequencing of the 16S rRNA gene identified the species of Leptospira present in the samples. Most positive samples were obtained from the National Capital Region and Region 1 where there is high risk of infection due to population overgrowth and poor sanitary conditions. Further investigations are necessary to determine potential sources of human leptospirosis in the country to understand disease transmission.

Keyword: Leptospira; environment samples; 23S; 16S

DEVELOPMENT OF MONOCLONAL ANTIBODY-BASED DOT-BLOT ELISA FOR THE DETECTION OF LISTERIA MONOCYTOGENES IN FOOD

Poster No. 41

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Major outbreaks of listeriosis, with high morbidity and mortality, have been caused by a variety of *Listeria monocytogenes* contaminated foods, including undercooked/raw meat, vegetable, soft cheese, milk and ready-to-eat products. Standard culture method for detection of *L. monocytogenes* in foods is laborious, expensive, and requires 4-5 days for completion of the whole procedure. Therefore, more rapid and sensitive method for the detection of *L. monocytogenes* in various kinds of samples is needed. This study aims to produce recombinant intanalin A (inlA) protein of *L. monocytogenes* by using genetic engineering and molecular cloning and develop monoclonal antibody (MAb)-based dot-blot ELISA for the detection of *L. monocytogenes* in food sample. Recombinant InlA protein was produced, purified and used as an antigen for mice immunization. Mouse has high antibody titer to inlA was selected as splenocyte donor for cell fusion. The spleen cells of immune mouse were fused with myeloma cells by hybridoma technique. Monoclone that secrete specific MAb from hybrid was selected by limiting dilution. The specific MAb to inlA was characterized and used as detection reagent in MAb-dot ELISA. The MAb-dot ELISA was calculated sensitivity and specificity of *L. monocytogenes* detection with 33 food samples by compared with conventional bacterial culture and DNA amplification. The results showed 5 positive-*L. monocytogenes* food samples by MAb-dot ELISA which correlated to the conventional method and PCR results. The MAb-dot ELISA have high sensitivity, specificity and change the detection format to plate ELISA and read optical density (OD) by spectrophotometer in future.

Keyword: *Listeria monocytogenes*, intanalin A, MAb-dot ELISA

NATIONWIDE SEROPREVALENCE OF SCRUB TYPHUS AMONG YOUNG THAI MEN, 2007–2008

Poster No. 42

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Scrub typhus is a zoonotic disease caused by *Orientia tsutsugamushi*, transmitted to humans by the bite of larval trombiculid mites (chiggers). Common clinical symptoms of scrub typhus include fever, headache, body aches, and rash, which usually begin within 10 days of being bitten. Scrub typhus is an acute febrile illness that is endemic to Northern Australia and East and Southeast Asia, including Thailand. Annual case reports of scrub typhus in Thailand have increased over a 10 year period, from 5.21 per 100,000 people in 2006 to 16.99 per 100,000 people in 2013. While the scrub typhus incidence declined in 2014-2015, case fatality rates increased. The combination of nonspecific clinical symptoms, a lack of laboratory confirmation, and disease underreporting places scrub typhus into a neglected disease status. The overall status and distribution of scrub typhus in the Thai population remains a critical public health concern. This study conducted a retrospective scrub typhus seroprevalence on repository serum specimens obtained from young Thai men entering the Royal Thai Army during 2007-2008 to better understand the distribution of scrub typhus exposure in Thailand. The overall nationwide scrub typhus IgG seroprevalence was 12% (95% confidence interval = 11%-13%) and the range by province was 5%-26%, confirming scrub typhus as an endemic disease throughout Thailand. Seroprevalence was highest in individuals with the lowest education from rural areas; however, a high seroprevalence was also found in the South regions, which is contrary to current morbidity reports. Improvement in diagnostics and reporting, as well as continued surveillance efforts, will increase scrub typhus awareness and enable more effective public health interventions.

Keyword: Scrub typhus, seroprevalence, Thailand, endemic, zoonotic disease

CLONING PEAQ-HT-ZIKV-SP IN *ESCHERICHIA COLI* FOR TRANSIENT EXPRESSION IN TOBACCO PLANTS

Poster No. 43

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Zika virus is a mosquito borne virus which is responsible for ongoing epidemics in the Americas. It belongs to the flavivirus family and is transmitted to humans by *Aedes aegypti* mosquitoes from the bite. In this paper, we cloned the Zika virus's structural protein (Zika-sp) into pEAQ-HT vector for transient expression in *Nicotiana benthamiana*. The resulting vector was first cultured in *Escherichia coli*, then it will be introduced into *Agrobacterium tumefaciens*. The processes including plasmid extraction, gel purification, ligation and transformation were necessary for transforming recombinant plasmid into *E. coli* competent cells. The used coding region revealed to be toxic for *E.coli* and *A. tumefaciens* respectively, which mad adjustments during bacteria transformation necessary. In summary, the expected bands could not be presented in this work and the design of a new coding region is necessary.

Keyword: Zika virus, pEAQ-HT, Transformation, Cloning

A SEROLOGIC SURVEY USING ELISA TO DETERMINE THE PREVALENCE OF Q FEVER AMONG ROYAL THAI ARMY RECRUITS, 2012

Poster No. 44

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Sera (n = 6,627) collected in 2012 from enlisted Royal Thai Army recruits, ages 21 – 24 years, were evaluated for antibodies against *Coxiella burnetii*, the causative agent for Q fever, using the PanBio commercial ELISA kit. IgG phase II antibodies against *C. burnetii* were detected in 1.9% of the sera (95% CI: 1.5 - 2.2%), and prevalence and demographic variables were correlated. Recruits from the North-east region had the highest prevalence (2.6%, with a 95% CI: 2.0 - 3.2%), followed by the North (1.7%; CI: 0.9 – 2.4%), Central (1.5%; CI: 1.0 – 2.0%), and South (1.1%; CI: 0.4 – 1.7%), respectively. Farmers, agriculturist, and livestock workers demonstrated higher antibody titers (2.6%; CI: 1.8 - 3.4%) compared to non-agricultural occupations (1.6%; CI: 1.3 - 2.0%). Minimal variation was linked to marital status (married - 2.2%; single - 1.8 %) or to residential area (rural - 2.0%; urban - 1.8%). For education level, seroprevalence ranged between 1.2 - 2.3% (primary school or lower - 2.3%, junior high school - 2.2%, senior high school/vocational - 1.2%, and diploma/high vocational or higher degree - 1.6%). Q fever antibody prevalence in the general Thai adult population is low; however, this rate is elevated in individuals from the North-east region and in agricultural workers. This data suggests active surveillance and preventative measures of *C. burnetii* infections in Thailand is important to minimize future Q fever outbreaks.

Keyword: Q fever

ASSOCIATION OF BIOFILM AND SECRETED PROTEINASE IN *CANDIDA ALBICANS* CLINICAL ISOLATES

Poster No. 45

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Candida albicans is the most common opportunistic fungus causing candidiasis in the immunocompromised individuals. *C. albicans* possess several virulence factors that effectively contribute pathogenicity such as biofilm formation and several hydrolytic enzyme production. In this research, we aimed to study the ability of biofilm formation and secreted proteinase production in *C. albicans* including association of biofilm capacity and secreted proteinase production. A total of 73 clinical isolates of *C. albicans* from patients hospitalized at Thammasat University Hospital were used. The biofilms of the isolates were formed in 96-well microtiter plate and quantified by staining with 0.1% crystal violet. The production of secreted proteinase was examined by spotting assay on agar containing bovine serum albumin (BSA). Precipitation zone (Pz) was calculated after amino black dye staining. Regardless to source of isolation, the ability of biofilm formation and proteinase secretion in *C. albicans* isolates were highly variable. No correlation between biofilm formation and secreted proteinase was found (correlation coefficient, r = -0.1462).

Keyword: *Candida albicans*, biofilm, proteinase

EFFECT OF ULTRAVIOLET LIGHT TYPE C ON *SCEDOSPORIUM SPP.*

Poster No. 46

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Scedosporium spp. are important fungal species isolated from immunocompromised and immunocompetent patients. The filamentous fungi exist as saprophytes in the soil and showed the highest minimum inhibitory concentration to several drugs has been reported. This study aimed to examine how UVC affects the cells of both *Scedosporium apiospermum* and *Lomentospora prolificans* by investigating the role of UVC on growth, apoptosis induction by ethidium bromide (EB)/acridine orange (AO) staining, and transcriptomic study of caspase recruitment domain family, member 9 (CARD-9) gene. The results demonstrated that 15 minute of UVC exposure significantly reduced the growth to both fungi and induce the alteration of colony morphology, color and hyphal germination pattern. Moreover, the percentage of *S. apiospermum* and *L. prolificans* apoptosis were 96.06% and 28.30%, respectively. The expression of CARD-9 gene was induced in both fungi after UVC treatment. Our study suggested that UVC could be inactivated *S. apiospermum* and *L. prolificans*.

Keyword: *Scedosporium* spp., Ultraviolet type C, *Scedosporium apiospermum, Lomentospora prolificans*

NOSOCOMIAL INFECTION RELATED WITH OUTCOME IN PATIENT WITH ACUTE STROKE IN BETHESDA HOSPITAL, YOGYAKARTA, INDONESIA

Poster No. 47

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Background and Purpose: Infection, as a complication of acute stroke, contributes to mortality and functional outcomes. The most common infections in acute stroke patients are pneumonia and urinary tract infection (UTI). This study aims to explore the outcomes of acute stroke patients with pneumonia and UTI in Bethesda Hospital, during 2010 -2016.

Methods: 2010 – 2016 Bethesda Hospital stroke registry of 5,005 stroke patients admitted during January 2010 to December 2016 were retrieved, and analyzed. Outcome as discharge was measured using a modified Rankin score: 3 – 6 was categorized as "poor" outcome, whilst 0 – 2 was categorized as "good" outcome. A multivariable logistic regression model was applied to explore the association between UTI and pneumonia with outcomes at discharge. Variables included in the model are age groups, length of stay, sex, and type of stroke.

Results: Pneumonia was more common among haemorrhagic stroke patients compared to those with ischaemic stroke (6.8% vs 4.2%, p0.05). In our fully adjusted model, getting infected with UTI and pneumonia were positively associated with poor outcomes. The OR to have poor outcomes among those who got infected with UTI and pneumonia were 2.90 (95% CI=1.80-4.67), and 14.28 (95% CI=8.71-23.40).

Conclusions: In our single-center study, UTI and pneumonia were associated with poor outcomes in acute stroke patients. This highlights the importance of nosocomial infection control among stroke patients in addition to stroke therapy in optimizing post-stroke patients' functionality outcomes.

Keyword: nosocomial infection, patient outcomes, stroke

SPECIES DIVERSITY AND NATURAL PLASMODIUM INFECTIONS IN ANOPHELES MOSQUITOES IN A MALARIA ENDEMIC AREA OF NA CHALUAI DISTRICT, UBON RATCHATHANI PROVINCE

Poster No. 48

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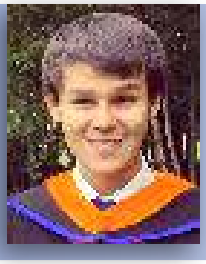
There was recently an outbreak of malaria in Ubon Ratchathani Province, northeastern Thailand. In the absence of information on malaria vector transmission dynamics, this study aimed to identify the anopheline vectors and their role in malaria transmission. Adult female *Anopheles* mosquitoes were collected monthly by human-landing catch in Na Chaluai District of Ubon Ratchathani Province during January 2014-December 2015. Field-captured mosquitoes were identified to species using morphology-based keys and molecular assays (allele-specific polymerase chain reaction, AS-PCR), and analyzed for the presence of *Plasmodium falciparum* and *Plasmodium vivax* using an enzyme-linked immunosorbent assay (ELISA) for the detection of circumsporozoite proteins (CSP). A total of 1,229 *Anopheles* females belonging to 13 species were collected. Four anopheline taxa were most abundant: Members of the *Anopheles barbirostris* complex comprised 38.41% of the specimens, species of the *Anopheles hyrcanus* group (17.66%), *Anopheles nivipes* (17.49%) and *Anopheles philippinensis* (11.72%). *Plasmodium* infections were detected in two of 668 pooled samples of heads/thoraces, *Anopheles dirus* (1/29) and *An. philippinensis* (1/97). The *An. dirus* pool had a mixed infection of *P. vivax*-210 (Pv-210) and *P. vivax*-247 (Pv-247), whereas *An. philippinensis* was positive for Pv-247. Both positive ELISA samples were confirmed by Nested PCR. Both positive samples were captured outdoors between 2300–2400 hours. This study is the first to incriminate *An. dirus* and *An. philippinensis* as natural malaria vectors in the area where the outbreak occurred. This information can assist in designing and implementing more effective malaria control program in the province.

Keyword: *Anopheles dirus, Anopheles philippinensis*, malaria transmission, circumsporozoite protein, AS-PCR

DETERMINATION OF ORGANIC ACIDS PRODUCED BY *PLASMODIUM FALCIPARUM* USING LIQUID CHROMATOGRAPHY - MASS SPECTROMETRY



Poster No. 49

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Lactic acid (LA) levels are usually measured in patients with acidosis. LA is a major product of the malaria parasite's consumption of glucose to meet its energy requirements. Previous studies have determined other organic acids, in addition to LA, and examined their roles in the pathogenesis of severe malaria patients. This study aimed to determine the source of the organic acids commonly found in patients, focusing on parasite-released products.

P. falciparum strain TM267 samples were synchronized with 5% D-sorbitol to yield a high percentage of ring-stage samples. Supernatants from malaria culture were collected from 4 stages--ring form, trophozoite, schizont, and post-schizont rupture. Mass spectrometer (MS) tuning was performed to acquire the target mass (m/z) of 4 acids and internal standards. Also, Liquid chromatography (LC) conditions were tested to determine the optimum pattern of chromatogram and retention time (tR). The organic acids detected were quantitated by establishing a calibration curve from standard solutions. Samples were prepared by solid phase extraction (SPE) in order to remove unwanted impurities, which might influence the LC-MS system.

LA was found to be a statistically significant ($P < 0.05$) parasite product in every stage. No statistically significant traces of other acids were found with this specific LC-MS method even when using isolated parasites and higher parasitaemia levels. The LC-MS method was shown to be sensitive, reproducible, and appropriate for small sample volumes. However, full validation methods are needed to improve the accuracy of acid quantitation. The use of a culture medium with amino acid depletion is an alternative for further study, to avoid the competition between amino acids and candidate acids at ion exchange sites during the SPE process. Acid fragility and lability are also important topics for further investigation. LA was found to be a *P. falciparum* product at different concentrations in each stage, while p-hydroxyphenyllactic acid (pHPLA), α-hydroxybutyric acid (aHBA), and β-hydroxybutyric acid (bHBA) were not detectable at significant levels using this specific LC-MS method. Amino acid depletion of culture medium and acid stability should be further investigated to achieve other aspect for future studies.

Keyword: *P.falciparum*, Organic acids, Acidosis, LC-MS, Malaria culture

EXPLORING PANCREATIC PATHOLOGY IN SEVERE *PLASMODIUM FALCIPARUM* MALARIA

Poster No. 50

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Hypoglycemia is an important complication of severe *Plasmodium falciparum* malaria, which can be lethal if not treated. The study aimed to explore the relationship between pancreatic pathology, including the expression of insulin and glucagon in the islets of Langerhans and blood sugar (BS) level in *P. falciparum* malaria patients. Malarial pancreatic tissues were divided into 3 groups, namely P. falciparum malaria patients with BS ≤ 40 mg/dl, BS = 40-120 mg/dl, and BS > 120 mg/dl. Immunohistochemical technique was used to study insulin and glucagon expressions in pancreatic tissues. Histopathological findings of pancreatic tissue showed numerous parasitized red blood cells (PRBCs) in the capillaries, edema, acinar necrosis and fibrosis. The islet cell size was significantly increased in P. falciparum malaria with BS < 40 mg/dl, and significantly decreased in *P. falciparum* malaria with BS > 120 mg/dl, compared with islet cells of the control group (all $p < 0.05$). The size of islet cells showed negative correlation with BS level ($r_s = -0.846$, $p=0.000$). Increased expression of insulin was observed in malaria patients with BS < 40 mg/dl and BS = 40-120 mg/dl, compared to the control group (all $p < 0.05$). The size of islet cells was significantly correlated with insulin expression ($r_p = 0.596$; $p=0.035$), and negatively correlated with BS level (mg/dl) ($r_p = -0.680$; $p=0.005$). This pioneer study documented an increase in insulin expression and increase in islet cell size in hypoglycemic patients of severe *P. falciparum* malaria, which could be a possible cause of hypoglycemia in malaria infection. The study highlights awareness for clinicians and prompt treatment of the hypoglycemic condition in severe *P. falciparum* malaria.

Keyword: Malaria, pancreas, *Plasmodium falciparum*, insulin, glucagon

GENETIC POLYMORPHISIM AND NATURAL SELECTION IN THE C-TERMINAL 42-KDA REGION OF MEROZOITE SURFACE PROTEIN-1 IN *PLASMODIUM FALCIPARUM* MYANMAR ISOLATES

Poster No. 51

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Malaria is one of the most important health burdens in worldwide, especially in tropical and subtropical countries. The C-terminal 42-kDa region of *Plasmodium falciparum* merozoite surface protein-1 (PfMSP-142) is considered as a promising candidate antigen for blood stage malaria vaccine. However, genetic polymorphisms encoding this region, within and among *P. falciparum* population, are one of the critical impeding factors for effective vaccine development. This study aimed to analyze genetic polymorphism and the effect of natural selection in PfMSP-142 among Myanmar *P. falciparum* isolates. A total of 69 P. falciparum isolates from Myanmar malaria patients were used in this study. The PfMSP-142 region was amplified by PCR, cloned and sequenced. The genetic structure and natural selection of the region were analyzed by MEGA4 and DnaSP programs. Sequence analysis of the Myanmar PfMSP-142 showed that three different genotypes, 3D7 (53.6%), K1 (26.1%) and RO33 (20.3%), were identified with different prevalence. Myanmar PfMSP-142 displayed genetic diversities and most polymorphisms were scattered throughout block 15 to block 17. The overall pattern of genetic polymorphisms identified in Myanmar PfMSP-142 was similar to other global isolates, but several novel amino acid changes were also found in Myanmar PfMSP-142. Compared to PfMSP-142 sequences from other geographical regions, genetic diversity of Myanmar PfMSP-142 was relatively lower, but evidences for natural selection were found. These results extend our understanding of the nature of the Myanmar *P. falciparum* population and have significant implication for the development of PfMSP142 based vaccine.

Keyword: *P.falciparum*, Myanmar, genetic polymorphism, PfMSP

TRAFFICKING OF MEROZOITE ADHESIVE ERYTHROCYTE BINDING-LIKE PROTEIN IN THE HUMAN MALARIA PARASITE, *PLASMODIUM FALCIPARUM*

Poster No. 52

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Malaria parasites require complex transport mechanisms to traffic proteins within the cell and to export proteins to extracellular compartments. Synthesized invasion proteins are translocated to the Golgi by an N-terminal signal peptide and other domains are responsible for trafficking to apical organelles in the parasite. MAEBL (merozoite adhesive erythrocyte binding protein) is stored in the rhoptries and plays a role in invasion of erythrocytes. The internal trafficking mechanism of MAEBL has not been fully elucidated, but the cysteine rich C-terminal domain (*Pf*CCys) is important. The aim of this study is to identify escorter proteins of MAEBL that participate in trafficking. The 348 bp *Pf*CCys sequence was cloned into the pET-15b vector. The recombinant His-tagged 13 kDa protein was purified with Ni-coated magnetic beads. SDS-PAGE and immunoblotting revealed 5 µg of protein from a 20 ml *E. coli* culture. The sequence for a sortilin-like receptor, which is essential in rhoptry trafficking in *Toxoplasma gondii*, was used to conduct a protein BLAST search against *Pf*Sortilin and showed a 50% sequence identity. The EMBL SMART programme identified a common VPS-10 domain, which is a transmembrane cargo receptor in *T. gondii* and responsible for endosomal protein-sorting. Modelling in the Phyre2 programme showed a similar predicted tertiary structure for both proteins. The 1632 bp *Pf*VPS-10 sequence was cloned into the pEX-4T-2 vector. The recombinant GST-tagged 83 kDa protein was purified with magnetic GSH beads. SDS-PAGE and immunoblotting revealed 2.5 µg of protein from a 200 ml *E. coli* culture with >70% purity. The purified proteins will be used for binding studies to determine if they interact. Future studies include identifying other escorter proteins of MAEBL, which may reveal a common trafficking mechanism and provide clues for novel therapeutic strategies.

Keyword: Parasitology, *Plasmodium falciparum*, Malaria, Invasion proteins

GENETIC POLYMORPHISM OF CIRCUMSPOROZOITE PROTEIN IN *PLASMODIUM FALCIPARUM* FIELD ISOLATES FROM MYANMAR

Poster No. 53

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Circumsporozoite protein of *Plasmodium falciparum* (PfCSP) is a major surface protein of sporozoites, which plays a critical role in the invasion by sporozoites of hepatocytes. PfCSP is one of the leading malaria vaccine candidates, but a comprehensive genetic polymorphism of the protein among global isolates of *P. falciparum* is a critical hurdle for effective vaccine development. In this study, we investigated the genetic diversity and natural selection of PfCSP among 51 Myanmar *P. falciparum* field isolates. Our result revealed that the central repeat region of PfCSP was highly polymorphic among Myanmar PfCSP with 23 different haplotypes, in which 14 haplotypes had non-synonymous amino acid changes. Meanwhile, low levels of polymorphisms were found in both the N-terminal and the C-terminal non-repeat regions of Myanmar PfCSP with 1 haplotype and 3 haplotypes, respectively. Positive natural selection was observed within the C-terminal non-repeat region. Comparative analysis of the central repeat region of Myanmar PfCSP to those from different geographic regions demonstrated that most Asian PfCSP had NANP repeats ranged from 38 to 43. However, 36 and 37 NANP repeats were mainly observed in the African and Venezuela PfCSP. Comparison of the C-terminal non-repeat region between Myanmar PfCSP and global PfCSP indicated that they shared similar nucleotide diversity patterns, in which most nucleotide diversity was found at Th2R/Th3R epitope regions. Our results contribute to the understanding of genetic nature of global PfCSP and may provide valuable information for development of effective vaccine based on PfCSP.

Keyword: *Plasmodium falciparum*, Circumsporozoite protein (CSP), Genetic polymorphism, Myanmar

POPULATION GENETIC STRUCTURE AND NATURAL SELECTION OF *PLASMODIUM FALCIPARUM* APICAL MEMBRANE ANTIGEN-1 IN MYANMAR ISOLATES

Poster No. 54

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Plasmodium falciparum apical membrane antigen-1 (PfAMA-1) is a leading candidate antigen for blood stage malaria vaccine. However, antigenic variation is a major obstacle in the development of an effective vaccine based on this antigen. In this study, the genetic structure and the effect of natural selection of PfAMA-1 among Myanmar *P. falciparum* isolates were analysed. Blood samples were collected from 58 Myanmar patients with falciparum malaria. The entire PfAMA-1 gene was amplified by PCR, cloned and sequenced. The polymorphic characteristics and effect of natural selection in PfAMA-1 were analysed using the DNASTAR, MEGA4, and DnaSP programs. Thirty-six haplotypes of PfAMA-1 were identified in the 58 Myanmar *P. falciparum* isolates. Most of amino acid changes identified in Myanmar PfAMA-1 were found in domains I and III, but they were also found in domain II as well as 5′-terminal and 3′-terminal regions. The overall patterns of amino acid changes in PfAMA-1 were similar among global isolates, but the frequencies of each amino acid changes differed by region. Novel amino acid changes were also identified in Myanmar PfAMA-1. Evidences for natural selection and recombination event were observed, which are likely to play important roles in generating genetic diversity across the PfAMA-1. Among the 51 commonly identified amino acid changes in global PfAMA-1 sequences, 43 amino acid changes were found in predicted RBC-binding sites, B-cell epitopes or IUR regions, which suggest a close association between natural selection and host immune pressure. These results extend our knowledge for the genetic nature of global PfAMA-1.

Keyword: *P.falciparum*, AMA-1, Myanmar

STUDYING THE FUNCTION OF KEY MITOCHONDRIAL PROTEINS OF *PLASMODIUM FALCIPARUM* IN SACCHAROMYCES CEREVISIAE

Poster No. 55

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Plasmodium falciparum contains a minimalistic, but essential mitochondrion in all stages of its life cycle. Several mitochondrial processes such as division, genome replication, membrane biogenesis that are very well understood in higher eukaryotes are very unclear in *Plasmodium*. Furthermore, very little is known about the regulation of mitochondrial structure and function. Understanding the molecular mechanisms of some of these essential processes would require functional studies of the key proteins. Even with the recent advancements in gene manipulation techniques in *Plasmodium*, it is still not easy to study the function of critical molecules *in vivo*, especially if they are essential. Functional complementation of *Plasmodium* proteins in a heterologous system such as *Sacchromyces cerevisiae* is an established method to study the function of putative orthologs. Here we use the yeast heterologous system to understand the function of three putative mitochondrial proteins that may be involved in key processes. We show that PfSURF1, the putative orthologue of human and yeast SURF1/SHY1, involved in cytochrome c oxidase assembly, partially complements a haploid *S. cerevisiae* strain harboring the null allele SHY1. Prohibitins (PHB1 and PHB2) are mitochondrial proteins, and have been shown to regulate the structure and function of mitochondria in other eurkaryotes. Using the yeast two hybrid system, we show that putative *Plasmodium* prohibitins (PfPHB1 and PfPHB2) interact with each other which suggests that they could form supercomplexes of heterodimers in *Plasmodium*, the functional form required for optimum mitochondrial function.

Keyword: Mitochondrial proteins, *Plasmodium falciparum, Saccharomyces cerevisiae*

EFFECTS OF HYPO AND HYPER BODY TEMPERATURE (37°C) ON THE ERYTHROCYTIC STAGE DEVELOPMENT OF *PLASMODIUM FALCIPARUM*

Poster No. 56

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Plasmodium falciparum is one of leading causes of child death from malaria worldwide. The basics of hypothermia resuscitation might help patients with severe and cerebral malaria by reducing death from severe malaria. In this study, development of asexual blood stage of *P.falciparum* was investigated at different condition 32°C, 34°C, 35°C, 38°C, 39°C, and 40°C. Parasite culture was separated into 2 experiments 1) incubate at different temperature for 2 hr and then return to 37°C for 72 hr (short term exposure) 2) incubate at different temperature for 72 hr (long term exposure). Parasite culture was sampling every 24 hr for 72 hr. Thick-thin blood films were prepared and stained with Field's stained for microscopic examination. Data were calculated by counting number of the infected red blood cells (iRBCs)/5,000 red blood cells (RBCs). In addition, the rosette formation; two or more uninfected red cells bound to iRBCs which cultured at different temperature was counted/100 iRBCs. All experiments were performed starting with 3 differences stages; ring, trophozoite, and schizont. The results showed that only growth rate of schizont stage was decreased significantly ($p<0.01$). Growth rate is defined as; percent of iRBCs/5,000 RBCs of dayn/percent parasitemia of daybefore day n at hypothermia condition (short term exposure) at 34°C-35°C. The growth rate of ring and trophozoite stage was significantly decreased at hyperthermia condition (long term exposure) ($p<0.01$). Rosette formation was reduced both hyperthermia (84.68%) and hyperthermia (27.87%) ($p<0.01$). This study highlights the hypo-hyperthermia can inhibit growth rate and decrease rosette formation of *P.falciparum*.

Keyword: *Plasmodium falciparum*, Hypothermia, Hyperthermia, Rosette formation

HAEMOLYSIS IN G6PD HETEROZYGOUS FEMALES TREATED WITH PRIMAQUINE FOR *PLASMODIUM VIVAX* MALARIA: A NESTED COHORT IN A TRIAL OF RADICAL CURATIVE REGIMENS

Poster No. 57

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Background: The radical curative efficacy of the 8-aminoquinolines in vivax malaria has been recognized for over 75 years. However, treatment with 8-aminoquinolines against the hypnozoites of *Plasmodium vivax* malaria is complicated by haemolysis in individuals with glucose-6-phosphate dehydrogenase (G6PD) deficiency. G6PD heterozygous females may have low G6PD activity levels, yet are usually reported as G6PD "normal" by current phenotypic screening tests. Their haemolytic risk when treated with 8-aminoquinolines has not been well characterized.

Methods and Findings: In a randomised clinical trial comparing different treatment regimens in *Plasmodium vivax* malaria, patients with a normal G6PD fluorescent spot test (≳30%–40% of normal G6PD activity) were randomised to receive 3 days of chloroquine or dihydroartemisinin-piperaquine in combination with primaquine, either the standard high dose of 0.5 mg base/kg/day for 14 days or a higher dose of 1 mg base/kg/day for 7 days. Within a subgroup of females, patterns of haemolysis were compared between G6PD wild-type and G6PD heterozygous participants.

Results: Between 21 February 2012 and 04 July 2014, 241 female participants were enrolled, of whom 34 were heterozygous for the G6PD Mahidol variant. Haemolysis was substantially greater in G6PD heterozygotes taking the higher (7 days) primaquine dose (9/17 [53%]) compared with G6PD heterozygotes taking the standard high (14 days) dose (2/16 [13%]; p= 0.022). In heterozygotes, the mean fractional haematocrit reductions were correspondingly greater with the higher primaquine dose (7-dayregimen): −20.4% (95% CI −26.0 % to −14.8%) compared with the standard high (14 days) dose: −13.1% (95% CI−17.6%to −8.6%). Two heterozygotes taking the higher (7 days) primaquine dose required blood transfusion. In wild-type participants, mean haematocrit reductions were clinically insignificant and similar with both doses: −5.8 (95% CI −7.2%to −4.4%) compared with −5.5% (95% CI −7.4%to −3.7%), respectively.

Conclusion: Higher daily doses of primaquine greater than 0.5mg/kg/day are potentially dangerous in G6PD heterozygous females who screen as "normal" with current point of care tests.

Keyword: *Plasmodium vivax*; Primaquine; G6PD deficiency

PLASMODIUM VIVAX INVASION LIGAND DIVERSITY IN LOW ENDEMIC AREAS OF SOUTH AMERICA

Poster No. 58

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Ecuador is focusing in elimination of malaria; nevertheless, outbreaks and cases of malaria persist in the Coast and Amazon of the country. *P. vivax* is the most prevalent malaria parasite in Ecuador it is endemic in the coast and Amazon regions. However, very little is known about the diversity and evolution of *P. vivax* in Latin America and no data has been reported in Ecuador. Invasion ligand diversity can give important information about the evolution of the parasite and the variety of invasion pathways. Regions of important invasion genes (Pvmsp1-19, Pvdbp RII and Pvrbp-1a) were sequenced and compared in 90 *P. vivax*-infected blood samples collected in 3 areas of Ecuador (two in the Amazon and one in the coast) from 2013 to 2015. Only one non synonymous polymorphism was identified in Pvmsp1-19. This mutation differs from previously reported polymorphisms in the same area. There was very low genetic variability for Pvmsp1-19 (Hd= 0.028 and π= 0,00009). On the other hand PvdbpII was highly polymorphic, 45 polymorphic sites were found, 35 sustitutions were non synonymous and 28 haplotypes were identified. There was a very high genetic variability for Pvdbp RII (Hd= 0.940 ± 0.019) while nucleotide diversity was low (π= 0.00736 ± 0,00059). Most haplotypes were unique for each locality. Pvrbp1a was also highly polymorphic: 56 polymorphic sites were identified, 47 of which were non synonymous. A total of 31 haplotypes were found. Haplotypic diversity was very high while nucleotide diversity was low (Hd= 0.924 ± 0.018, π= 0.00747). Most haplotypes were unique to each locality. As expected, the Amazon region (where more cases are reported) was more diverse for *P. vivax* than the Coast for all the studied genes. Even though the number of reported cases in Ecuador is low, there is important differentiation in some merozoite invasion ligands. These results provide insights into merozoite vaccine candidates in South America. Polymorphisms in merozoite ligands in low endemic areas should be considered when designing vaccines.

Keyword: Malaria, *Plasmodium vivax*, Ecuador, diversity

IDENTIFICATION OF MUTATIONS IN PFMDR-1, PFATP6, PVMDR-1 AND PVCRT(O) GENES IN *PLASMODIUM FALCIPARUM* AND *PLASMODIUM VIVAX* FROM NORTHERN INDIA

Poster No. 59

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Introduction: We tried to explore whether any anti-malarial drug resistance markers exist in our population.

Methods: Of 2186 febrile patients with clinical suspicion of malaria screened between Jul-2013 to Feb-2015, 561 patients fulfilled inclusion criteria. Microscopy, nested PCR, and sequencing were performed.

Results & Conclusions: *Plasmodium* was detected in 78/561 (13.90%) cases using either microscopy or PCR. 47/78 (60.25%) were *Plasmodium falciparum*, 28/78 (35.89%) were *Plasmodium vivax* and 3/78 (3.84%) were mixed infections. All strains had wild-type Y184 (100%), N1042 (100%), A630 (100%) and I898 (100%) polymorphisms. No allelic variations (either 630S or 898I mutations) in Pfatp6 gene were observed. Pvmdr-1 sequence analysis showed the presence of 958M, 976F and 1076L mutations, F979, M980, L1022 and S1080 wild-type SNPs. Wild-type codon for all the above-mentioned SNPs was present in 2/31 (6.45%) samples of *Plasmodium vivax*. A 958m mutation was present in 26/31 (83.87%) samples; majority showed multiple mutations. Pvmdr1-976 mutation (976F) was identified only in 6/31 (19.35%) isolates. Interestingly, a Pvmdr1-976 mutation was found only in those isolates which harbored 958M and 1076L mutations together. Thus, triple mutations (958M, 976F, and 1076L) were found in 6/31 (19.35%) samples. Double mutants of 1076L with 958M were present in 19/31 (61.29%) samples. However, Pvmdr1-1076 (1076L) mutation was observed with the highest prevalence i.e. 27/31 (87.09%). We observed that 8/31 (25.8%) *Plasmodium vivax* samples had K10 insertion (AAG codon for lysine) at the 10th position of the first exon and wild-type Pvcrt(o) samples without K10 insert were 23/31 (74.2%).

Keyword: Single nucleotide polymorphism, allelic variation

THE FIRST CASE INVESTIGATION OF *PLASMODIUM KNOWLESI*, SARABURI PROVINCE, THAILAND, JUNE 2017

Poster No. 60

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Background: *Plasmodium knowlesi* is a simian malaria parasite. In May 2017, the ODPC 4 received the first *P.knowlesi* patient case notification living in Village Z, Mittrapap Sub-District, Muaklek, Saraburi. He admitted in hospital of Tropical Medicine, Mahidol University.

Methods: The investigation team had interviewed patient, reviewed malaria cases (ICD-10: B50-B54) in Muaklek and private hospitals Y in Saraburi from 2008 to 2017. Then, the active case finding was defined as person living in Village Z who developed fever, chill and history of wandering around the forest or malaria infected areas since December 1, 2016. We collected blood sampling by thick and thin blood smears and PCR for *P.knowlesi*. The entomologic study was classified and identified mosquitoes to determine potential of risk factor.

Results: On January 23, 2016, the 46-year-old Thai male patient developed symptom as fever, chill, myalgia, fatigue and syncope. Also, Septic shock with *P.vivax* was diagnosis and admitted ICU for early treatment by Chloroquine Primaquine and Artesunate at hospital Y. Then, the hospital referred him to Hospital of Tropical Medicine and the PCR testing was positive for *P.knowlesi*. He had the history in visiting the monkeys in the forest. All 37 malaria cases reviewed in both hospitals, the sex ratio (F:M) was 2.4:1, average age was 29±15.04. Most nationality was Thai (68.0%), *P. vivax* and unspecified malaria were 78.4 and 13.5%, respectively. All 96 persons do not infect of malaria. Meanwhile, *Annopheles sawadwongporni*, a non-vector *P. knowlesi*, was found in mosquitoes' collections. Thus, *P.knowlesi* case may be infected from the above environment. Hence, we should strengthen surveillance and investigation for prevention and control malaria effectively.

Keyword: Malaria, *Plasmodium knowlesi*, Saraburi

SIGNIFICANCE OF CHARACTERIZING MICROCLIMATE CONDITIONS TO DERIVE EXTRINSIC INCUBATION PERIOD OF MALARIA PARASITES IN AN URBAN MALARIA TRANSMISSION SETTING IN CHENNAI, INDIA

Poster No. 61

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Emerging insecticide resistant mosquitoes, drug resistant parasites and changing environmental conditions complicates the understanding of the vector-host-parasite relationship and the transmission mechanism which in turn hinders malaria control. Environmental factors such as temperature, relative humidity and their daily variation influence a range of mosquito life history traits and hence, malaria transmission. A longitudinal study was conducted in Chennai, India to characterize local temperature and relative humidity (RH). Microclimate parameters were taken hourly to estimate mean temperature and RH, along with daily temperature range (DTR) and daily relative humidity range (DRHR). The temperature data were used to explore the predicted variation in extrinsic incubation period (EIP) of *Plasmodium falciparum* and *P. vivax* between microhabitats and across the year. Mean daily temperatures within the indoor settings were significantly warmer than those recorded outdoors. Differences in EIP between microhabitats were most notable during the hottest summer months of April-June, with parasite development predicted to be impaired for tiled houses and overhead tanks. Overall, the prevailing warm and stable conditions suggest rapid parasite development rate regardless of where mosquitoes might rest. Taking account of seasonal and local environmental variation, the predicted EIP of *P. falciparum* varied from 9.1 to 15.3 days, while the EIP of *P. vivax* from 8.0 to 24.3 days. The study provides a detailed picture of the actual microclimates experienced by mosquitoes in an urban setting. Properly characterizing local microclimate conditions would be the key to fully understand the effects of environment on local transmission ecology and efforts to eliminate malaria.

Keyword: Microclimate, Extrinsic incubation period

MALARIA CASE-BASED REPORTING MOBILE APPLICATION: COLLABORATIVE EFFORT TOWARDS MALARIA ELIMINATION

Poster No. 62

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As Myanmar moves towards Malaria Elimination, real-time reporting of malaria cases is becoming an important component of the Malaria Program. Current paper-based reporting often takes weeks to reach township offices where it takes a considerable amount of time for processing to be analyzable. To fill this gap, Save the Children assessed malaria mobile tools in use in the region and started a project after finding a possible solution being implemented by Population Service International (PSI) Cambodia and communicating with them. Save the Children modified the application and named it Malaria Case-Based Reporting (MCBR) to be used by Village Health Volunteers (VHVs) to report case-based data. MCBR feeds data into DHIS2 server, which will be customized for easy analysis by different levels of the National Malaria Control Program (NMCP) and partner organizations. Besides enabling real-time reporting, the application helps the program in many different ways; by providing geographic information of place of data entry, by providing guidance to VHVs, and helping volunteers keep track of their medical stock. The NMCP and our partner organizations all contributed to MCBR since prototype development till implementation. As a result of early information sharing and collaboration, the mobile application is broadly accepted and has been blessed by the NMCP and other stakeholders with the prospect of becoming a national reporting tool. All the actors using the same reporting tool means that the data collected from various actors will be consistent and can be compiled easily. As program implementation will be similar for the same mobile application, it will let us share experiences and help out each other.

Keyword: MCBR, Mobile Reporting, Malaria, Myanmar

ACTIVE SURVEILLANCE MALARIA IN SRISAKET PROVINCE ALONG THAI – CAMBODIA BORDERS

Poster No. 63

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An active Surveillance Malaria in Srisaket province along Thai – Cambodia Borders between October, 2012 to September, 2017. The vectors survey was in 3 districts: Kantharalak , Khun Han and Phu sing and was found mosquitoes 5 species *Anopheles dirus* , *An. minimus, An. aconitus* , *An barbirostris and An. Philippinensis*.

The results of susceptibility testing *An. philippinensis* from Kantharalak to Deltametrin 0.05%, Permetrin 0.07% showed up to 42.5, 40% mortality by WHO test kit, both resistance according to WHO standards.

The results of susceptibility testing *An barbirostris* from Khun Han to Deltametrin 0.05%, Permetrin 0.07% showed up to 70, 51% mortality by WHO test kit, both resistance trend according to WHO standards.

The results of susceptibility testing from Phu sing: *An. philippinensis* showed up to 70, 51% mortality by WHO test kit to Deltametrin 0.05% and Permetrin 0.07%, both thus no resistance according to WHO standards. But the testing of *An barbirostris* to Deltametrin 0.05% and Permetrin 0.07% both resistance trend according.

The residual spraying inside huts and households in Kantharalak , Khun Han and Phu sing were 3,630 , 4,209 , and 2,028 respectively. The chemical nets were distributed to Kantharalak, Khun Han and Phu sing amount 1,717, 2,049, 1,501 mosquitoes net respectively.

The *Plasmodium* infected patient in Kantharalak were 1,404: *Plasmodium falciparum* 50, *P. vivax* 807 , Khun Han were 1,985: *P. falciparum* 689 *P. vivax* 1,030 and Phu sing were 945: *P. falciparum* 209 *P. vivax* 684

Keyword: Active Surveillance Malaria

VARIABILITY IN ANTIMALARIAL DRUG SENSITIVITIES ACROSS REGIONS IN CAMBODIA MAY POSE UNIQUE CHALLENGES TO NATIONAL MALARIA PROGRAM

Poster No. 64

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Recently Cambodia adopted a single fixed-dose combination drug regimen, artesunate-mefloquine, for the treatment of malaria in the entire country due to high rates of Dihydroartemisinin-Piperaquine (DHA-PPQ) failure in the treatment of uncomplicated *Plasmodium falciparum* in multiple provinces. We have analyzed drug sensitivities of parasites from 2 distinct sites in Cambodia with suspected risk differences for drug resistance, one in the northwest (Anlong Veng) and another site in the eastern part of Cambodia (Kratie). Approximately 70% of 219 fresh pf-isolates could be interpreted after testing ex vivo HRP-2 assay against standard antimalarials with the median IC50s in Anlong Veng (AV) significantly higher than those from Kratie (KT) for PPQ (87.4 vs. 29.1 nM), ATQ (4.35 vs. 3.17 nM), and doxycycline (18701 vs. 12826 nM). The pfmdr1 copy number was higher in KT than AV (1 vs. 1.94) suggesting lower mefloquine sensitivity in KT. 50% of samples could be evaluated by ex vivo ring-stage survival assay (RSA) for DHA and showed the median % survival rate of 11.7% vs. 6.6% in KT and AV respectively, suggesting widespread artemisinin resistance (p= 0.09). Observed parasite clearance time (PCT) between sites was longer in Anlong Veng (AV) over Kratie (KT) but this was not statistically significant (72 vs 56 hr). The PCT was significantly different between patients treated with atovaquone-proguanil and artesuante atovaquone-proguanil in KT site (64 vs. 56 hr, p-value=0.04) but with no difference observed in AV. The differences observed between northern and eastern parts of Cambodia underscore the importance of conducting therapeutic efficacy studies with multiple drug regimens across multiple regions and clinical sites as we try to better understand the factors that drive antimalarial drug resistance across different regions.

Keyword: antimalarial drug, sensitivity, Cambodia, RSA

MOLECULAR CHARACTERIZATION OF G6PD DEFICIENCY IN MALARIA-ENDEMIC NORTHEASTERN REGION OF INDIA

Poster No. 65

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Objectives: Glucose-6-phosphate dehydrogenase (G6PD) is a housekeeping and rate limiting enzyme in the pentose phosphate pathway, generating reducing power in the form of NADPH. The National drug policy recommends primaquine for the radical cure of malaria, however, the dose and duration varies with the type of species. Primaquine and other 8-aminoquinoline based antimalarials may trigger haemolysis in G6PD deficient individuals. The present study was aimed to characterize G6PD deficiency in a malaria-endemic northeastern region of India.

Methods: A total of 1, 015 patients were screened for a G6PD deficiency from four states, namely Lunglei, Mizoram (n=214), Gomati, Tripura (n=304), Tura, Meghalaya (n=230) and Changlang, Arunachal Pradesh (n=267) using Beutler fluorescence spot test. Blood spots were also obtained on filter paper for molecular studies. Mutation analysis was carried out using PCR-RFLP and validated through DNA sequencing. Informed consent was obtained from the patients prior to sample collection.

Result: Among 1015 patients, 55 patients were found to be G6PD deficient. Of 55 deficient patients, mutation analysis was carried out in 54 samples. Interestingly, two novel G6PD mutations were observed; a novel variant was predominant and present in >80% samples while another is present in < 4% samples and both have been observed for the first time in the country.

Conclusion: Radical cure of malaria depends on drugs, which kills mature gametocyte stage of *Plasmodium falciparum* and relapse stage of *Plasmodium vivax* malaria parasites. Surveillance of G6PD through mutation analysis highlights the presence of novel mutations which could be useful for guiding the national treatment guidelines.

Keyword: G6PD, Primaquine, NADPH, Malaria

COMMUNITY BASED INTERVENTION TOWARDS MALARIA AND DENGUE FEVER PREVENTION AND CONTROL AMONG ETHNIC MINORITY GROUPS IN RATANAKIRI AND MONDOLKIRI PROVINCE

Poster No. 66

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Background: The Cambodia-Thailand Malaria Control project, was launched in 2007 in two eastern Cambodian provinces, Ratanakiri and Mondolkiri. It aimed at malaria control among indigenous people belonging to several ethnic minorities. The Community Life Competence Process (CLCP) was introduced to enhance ownership of malaria and dengue fever aspects and response by the community in 6 villages. The CLCP including; Ways of Thinking (believing in people capacity), Ways of Working (SALT:Stimulate/Support/Share, Appreciate, Listen/Learn/Link, Transfer/Team), and the Steps of working (dream building, self-assessment, resource mapping, action planning and self-measurement of progress).

Objective: This report aims to share the progress and lessons learned of the CLCP implementation.

Findings: After two years implementation of the CLCP, several improvements were found in those villages. Ratanakiri, three villages had shown some progress on their priority dreams (in 2015, a new primary school some toilets were built. In Mondolkiri, community leaders and volunteers had reviewed the progress of their dengue and malaria programs and other community development plans. All communities have conducted several activities, including training about Dengue and Malaria to the villagers, mobilizing villagers and school students to clean up and burn trashes around the community, and blood testing for Malaria suspected patients. The three villages had made quite significant progress on their priority dreams identified in 2015, which is to build identified number of toilets for families needed and ready to have one.

Conclusion: In conclusion, through the community life competence process communities now felt ownerships of their dreams and action plans. However, communities need regular coaching and support to ensure the progress and sustainability.

Keyword Community Based Intervention, Malaria

KNOWLEDGE AND PERCEPTION OF MALARIA PREVENTION MEASURES AMONG TANZANIAN STUDENTS AND FACTORS, ASSOCIATED WITH THE IGNORANCE OF BED NET USE

Poster No. 67

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University campuses are potential reservoirs of infectious diseases, but they are out of research focus. University of Dodoma, being the largest University of Tanzania, hosts about 20,000 students all over the country. It is obvious, that use of malaria preventive tools is extremely necessary in campus conditions. This study is the first malaria survey, conducted in University campus in Tanzania. Our investigation uncovered surprisingly high prevalence of malaria history among students: 89,4% of 246 random respondents assume, they have malaria in history, among them 145 (58,9%) suffered from the disease during last year. Consequently, they were potential carriers of the infection while living in the campus. The knowledge, attitude and practice study showed, that students are relatively confident about the vector, parasite and prevention measures of the disease, 98%, 65,8% and 87,8% of students, respectively, demonstrated understanding of the problem. Nevertheless, unfortunately, only 44,7% of students use bed nets, and 13,4% use body spray or ointment daily. The others use spray or ointment seldom, or don't care about problem at all. The first factor, associated with ignorance of malaria prevention, is financial - all these respondents have monthly income less than 200,000 Tshs (about 90$), OR=19.03 (95% CI: 9.55-38). The second factor is the opinion, that Dodoma is almost free from the disease, 64% of ignoring students are sure, that they are not in risk, OR=22.64 (95% CI: 10.17-50.4). Additionally, although major of students are relatively confident about preventive tools, 8,1% of respondents believe that only anti-malarial can protect them from the infection. Current results show that students are relatively educated about malaria, but don't follow the malaria prevention guidance. The knowledge about malaria is likely to be memorized by students, but they are not conscious of the fact that the disease prevention is a personal issue. It is clear, that at least proper informational propaganda of bed net use is required in University campuses in Tanzania. And student community should be investigated further, as many white spots have still remained.

Keyword: malaria, prevention, students, Dodoma, Tanzania

NATURAL MALARIA VECTOR STATUS IN THE HOT SPOT VILLAGES OF WESTERN THAILAND AND IMPLICATION FOR CONTROL OF MALARIA TRANSMISSION

Poster No. 68

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Cross-sectional entomological and epidemiological study was conducted in four malaria hot spots of western Thailand between February to November 2016 in Kanchanaburi province and the other area focused on two months of the malaria high transmission periods in Ratchaburi, Phetchaburi, and Prachuapkhilikhan provinces. The study was to determine vector abundance, biting behavior and parity rate in relation to malaria cases, demographic and climate variables. Malaria incidence rate varied from 0.1 to 0.6 cases per 1,000 population. Transmission varied throughout the year depending on the locations. *Anopheles minimus* sensu lato (s.l.) was the dominant species of malaria vectors combination of the varied other anopheline by locality and preferred exophilic behavior. Three positive ELISA infective stage in *Anopheles* mosquitoes were detected with high infective rate during the peak of transmission period. In Ratchaburi province during hot season, there were 2 infective *An. minimus* s.l. with total 11.7% infection rate (2/17) susceptible to *Plasmodium vivax* and *P. falciparum* collecting from indoor human landing catch at 22.00 and 23.00 and from indoor light trap, respectively. The mean indoor biting of infective *An. minimus* of *Plasmodium vivax* or *P. falciparum* per person per night or Entomological inoculation rate (EIR) was 2.54 infective bite per person per night with the high percentage of parous rate up to 40-60%. Moreover, five percent *P. falciparum* infection rate was found from *An. maculatus* group captured by outdoor light trap in the wet season in Petchaburi province. Even it had low outdoor biting rate but the parous rate was peak up to 80% (4/5) during this time. Noticeably, the pattern of highly peak indoor and outdoor biting rate in *An. minimus* s.l. up to 5.9 and 11.8 bites/person/night were changed and peaked in the early morning (5.00 to 6.00) with 40-60% parous rate in wet season of Kanchanaburi province where had the high malaria proportion of migrant patient (M1) in the specific cluster area. Therefore, the high potential of vector capacity with 92% *An. minimus* s.l. dominant species provided to enhance of cases by the temporal time. Changeable in malaria vector behavior, human-vector contact time and the migrant proportion of malaria cases may contribute for malaria transmission in the individual pattern of cluster areas. Identification of these area, associate the malaria control program including vector control will have to be specific planned accordingly and may considerably decrease the costs of control efforts.

Keyword: mosquito vector, malaria, transmission, hot spot area

INDIVIDUAL AND HOUSEHOLD FACTORS ASSOCIATED WITH VILLAGE MALARIA INCIDENCES IN XEPON DISTRICT, SAVANNAKHET PROVINCE, LAO PDR.

Poster No. 69

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Background: In the Lao PDR, malaria incidence greatly differs among villages even within a sub-district, and the reasons for this difference are poorly understood. The objective of this study was to identify differences in the behavior of villagers and the household environment between villages with high incidences and those with low incidences, in a rural district of the Lao PDR.

Methods: A case-control study was conducted in 12 villages. The case was a village with a high incidence and the control was a village with a low incidence. The data collection consisted of an interview survey and an observation survey in-and-around house. Logistic regression was used to assess the association between the case-control status and individual-level behavioral factors and household-level environmental factors.

Results: Compared to the household members in the control villages, the case villages were more likely to work at night in the forest (adjusted OR 1.95; 95% CI 1.28 to 2.98) and more likely to sleep overnight in the forest (adjusted OR 1.94; 95% CI 1.13 to 3.33). Additionally, the households in the case villages were more likely to have an open space on house surface than control village (adjusted OR 3.64; 95% CI 1.68 to 7.84).

Conclusions: There were significant differences in night-time working and sleeping behavior in the forest and the presence of an open space on house surface. Recommend villagers to use personal protection when working and sleeping in the forest and to reduce an open space on house surface.

Keyword: Malaria, incidence, risk factor, behavior and Laos

THE INTEGRATED ACTION PLANS OF NATIONAL MALARIA ELIMINATION IN THAILAND: THE AREA STUDIED IS IN THE NORTH EAST AND THE EAST OF THAILAND

Poster No. 70

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In 2024, the National Malaria Elimination Strategy proposed to eliminate indigenous malaria cases in all districts and expected that Thailand would be certified as malaria-free areas before 2026. Even though the national malaria elimination policy obviously focused on Strategy 1—To accelerate malaria elimination in Thailand by improving diagnosis and treatment, intensify active case detection, increase ITN coverage and ensure DOTs and follow up and Therapeutic Efficacy Surveillance, there were three supported strategies consisted of Strategy 2—To develop technology, innovation, measures and models that were appropriate for malaria elimination; Strategy 3—To develop partnerships among stakeholders at national and international level in order to enable malaria elimination; Strategy 4—To promote and empower community in taking care of themselves from malaria. The study stressed on Strategy 3—to develop partnerships among stakeholders at national level. Especially, in communities, there were significant partners namely Health Promoting Hospital, Local Administrative Organization and Communicable Disease Control Unit. The objective is to convince all partnerships to make integrated action plans by sharing related malaria elimination activities. Methodology of the study preferred all provinces in the Northeast and the East of Thailand selected significant partnerships in transmission areas working together. Through the community participation and strategic planning workshops, an integrated process of data collection and analysis was undertaken and descriptively presented. Findings showed that there were practically integrated action plans from significant partnerships in each transmission area. Twenty seven action plans of all provinces might be presented to their provincial level for approval before being launched in their communities. Some outcomes from strongly launched action plans have been obviously regarded as the best practices of each province. Conclusion and recommendation: The study suggested that in order to manage how to convince some key partners to join relevant malaria elimination activities. This could be empowered by regular active participation at the national level, provincial level and community level by specifically focusing on sustainably maintaining malaria-free areas. The government would like to seek support and integrative collaboration from Local Administrative Organization, Communicable Disease Control Unit, Health Promoting Hospital and private sector which directly leaded to its Sustainable Development Goal. The implementation of the action plans in each area will be strengthening for sustainably the maintaining malaria-free areas in Thailand.

Keyword Malaria, elimination, integrated action plan

DIFFERENTIAL DETECTION OF BLASTOCYSTIS SUBTYPE IN HUMAN STOOL SAMPLES BY A MULTIPLEX PCR ASSAY

Poster No. 71

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Blastocystis is a unicellular protozoan most commonly found in fresh stool samples in numerous forms (vacuolar, amoeboid, granular and cyst) and size. Infections occurs worldwide but is frequently found in the tropics and developing countries. Epidemiological Blastocystis studies are often limited by the poor sensitivity of standard parasitological assays for its detection. Thus, a multiplex PCR assay was developed for detection and differential diagnosis of the two Blastocystis subtypes commonly found in humans, subtypes 1 and 3 that are morphologically indistinguishable. Conserved forward and reverse primers were designed from signature sequences specific to each of these two Blastocystis subtypes found in GenBank, using PerlPrimer and Oligo Analyzer software. PCR generate a 138-bp product of subtype 1 and a 233-bp product with subtype 3 DNA. Two hundred fifty three stool samples were examined and the subtypes present were successfully detected and differentiated using this assay. It was possible to detect 7 ng/µl of subtype 1, while for subtype 3 the sensitivity was about 70 ng/µl of DNA. Testing with DNA from different pathogens, including bacteria and other protozoan confirmed the high specificity of the assay. In conclusion, the present study propose the use of this PCR assay as an accurate, rapid and effective diagnostic method for the detection and discrimination of these two morphologically indistinguishable Blastocystis subtypes in both routine diagnosis of blastocystosis and epidemiological surveys.

Keyword: Blastocystis; subtype; PCR; stool; Malaysia

EPIDEMIOLOGICAL STUDY OF BLASTOCYSTIS INFECTION IN A RURAL COMMUNITY, THAILAND

Poster No. 72

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Blastocystis infection is one of the most common intestinal protozoal infections in humans. The infection may cause a wild range of clinical outcomes from asymptomatic to nonspecific gastrointestinal symptoms including abdominal pain and diarrhea. A few modes of transmission including waterborne, foodborne, zoonotic and person-to-person have been documented. Our research aimed to identify the incidence and the risk factors of *Blastocystis* infection in a rural community, Central Thailand. In addition, we also determined persistent/reinfection rate and clearance rate of *Blastocystis* infection. The prospective cohort study was conducted in Phraploeng community, Khao Cha Kan District, Sakaeo Province, Thailand from February to December 2016. Short term cultivation of stool samples using Jone's medium was performed to detect *Blastocystis* sp. The incidence of *Blastocystis* infection in this community was 8.97 per 100 person-years. The persistent/reinfection rate was 46.41 per 100 person-years. The clearance rate was 75.73 per 100 person-years. Survival analysis showed that median time to clearance of *Blastocystis* infection was 10 months. Multivariate analysis using Poisson regression, drinking unboiled water was significantly related with *Blastocystis* infection (IRR = 8.07, 95% CI = 1.12 - 8.47). Our information indicates waterborne transmission of *Blastocystis* sp. in this community which should draws attention to public health policy to improve the quality of water in rural communities. Spontaneous clearance of *Blastocystis* infection may occur. However, the time to clearance of *Blastocystis* infection was relatively long which could keep the infection circulate in this population.

Keyword: *Blastocystis*, Intestinal protozoa, Waterborne transmission

SUBTYPE DISTRIBUTION OF *BLASTOCYSTIS* SPP. IN DOMESTIC ANIMALS OF COMMUNITIES LIVING ALONG CHAO PHRAYA RIVER, AYUTTHAYA PROVINCE

Poster No. 73

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Blastocystis is a common zoonotic enteric protozoan that has been classified into 17 distinct subtypes (STs). In Thailand, the prevalence and subtype distributions of *Blastocystis* in villagers living along the Chao Phraya River, Ayutthaya Province were present in 5.9% and ST3 was the predominant subtype, indicating a zoonotic risk. Therefore, this study was conducted to identify the prevalence and the genotype distribution of *Blastocystis* in goats and cattle in communities living along Chao Phraya River, Ayutthaya Province, Thailand for proving whether animals are the reservoirs of *Blastocystis* in these communities. In total, 150 stool samples from goats and cattle were collected and the DNA extracted. PCR and sequencing were performed with primers targeting the small-subunit ribosomal RNA (SSU rRNA) genes. The prevalence of *Blastocystis* infection was 80.0% (120/150), and ST10 (33.3%; 50/150) was the predominant subtype, followed by ST12 (26.7%; 40/150) and ST14 (20.0%; 30/150). Therefore, the results from such study can support, improve and promote the better health and quality of life as well as interaction among host and animals in these communities.

Keyword: *Blastocystis*, zoonotic risk, Chao Phraya River

MOLECULAR CHARACTERIZATION OF *BLASTOCYSTIS* SP. IN CANE TOADS (*RHINELLA MARINA*) AND COCKROACHES (*PERIPLANETA AMERICANA*) FROM THE PHILIPPINES

Poster No. 74

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Blastocystis sp. is a gastrointestinal protozoan commonly encountered in humans and animals. Its pathogenicity and host-specificity remains unclear and may be related to subtype (ST) identification of the organism based on SSU rRNA sequences. Current work on ST identification in zoo animals identified 8 STs in non-mammalian and avian hosts (NMAST) designated as NMAST I-XIII. There are still no published data on *Blastocystis* sp. in amphibian and insect hosts in the Philippines. In this study, NMAST I was identified in 9 out of 10 toads (*Rhinella marina*) and NMAST IV in a cockroach. Interestingly, NMAST I has also been identified in previous studies in a box turtle (*Terrapene carolina*), a Philippine macaque (*Macaca fascicularis*), and a duck (*Anas platyrhynchos domesticus*). The host range of NMAST I possibly extends to mammals and birds.

Keyword: *Blastocystis*, subtyping, toad, cockroach

COMPARISON OF DNA EXTRACTION METHODS FROM STOOL SAMPLES FOR PCR DETECTION OF *BLASTOCYSTIS* SPP.

Poster No. 75

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Blastocystis spp. is one of the most common protozoa distributed worldwide and found to be associated with various GI symptoms. PCR has more role than parasitological methods, since it is capable for *Blastocystis* subtyping for further studies. However, detection rates by PCR are usually lower than culture methods. In this study, we compared 3 methods of DNA extraction from stool samples, including phenol-chloroform technique, QIAamp Stool Mini Kit, and modified QIAamp Stool Mini Kit with glass beads. Total of 82 stool samples were collected and investigated for *Blastocystis* spp. by parasitological methods. Genomic DNA were extracted from 82 samples with 3 methods and processed for detections of *Blastocystis* spp. by SSU rDNA PCR. While 22 samples were positive by LES cultivation, only 10 samples were positive by PCR. Phenol-chloroform technique showed the highest DNA yield. However, none of DNA extracted by phenol-chloroform technique were positive by PCR while other 2 kit-based methods were positive for 7 samples each. Stool debris and PCR inhibitors might be still problematic to DNA quality despite well-controlled practice in DNA extractions. Therefore, spike test using plasmid harboring SSU rDNA fragments of *Blastocystis* spp. was conducted in 20 samples that positive for cultivation but negative for PCR. After plasmid spike, 16 samples from modified QIAamp with glass beads were positive while only 3 samples from phenol-chloroform were positive. These results indicated that DNA extracted by phenol-chloroform technique showed the highest PCR inhibitor contamination. However, modified QIAamp with glass beads gave the highest efficiency of PCR inhibitor removal.

Keyword: *Blastocystis* spp. DNA Extraction, Stool, Polymerase Chain Reaction (PCR), PCR inhibitor

GENOTYPING OF *CRYPTOSPORIDIUM MELEAGRIDIS* FROM EDIBLE BIVALVES OBTAINED FROM LAS PIÑAS PARANAQUE CRITICAL HABITAT AND ECOTOURISM AREA, PHILIPPINES

Poster No. 76

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The Las Piñas Paranaque Critical Habitat and Ecotourism Area (LPPCHEA) in the Philippines is recognized as a wetland of international importance because of the critical role it plays in the survival of threatened, restricted-range and congregatory bird species. In fact, in Metropolitan Manila, it is the only resting and refueling stop for migratory birds. These birds may come from other countries like China, Japan and Siberia, among others. However, these birds may carry zoonotic pathogens like *Cryptosporidium meleagridis*, which is the only known *Cryptosporidium* species that infects both avian and mammalian hosts and is responsible for some cases of human cryptosporidiosis especially in immunocompromised individuals. The pathogen might be dispersed around the area and accumulated in bivalves which depend on filter feeding for survival. In this study, *C. meleagridis* oocysts were present in 4 out of 40 edible bivalve samples. Oocysts were isolated using sucrose flotation and immunomagnetic separation (IMS). They were detected using direct fluorescent antibody (DFA) test while species identification was done using sequence analysis of 18S rRNA gene. Genotyping and subgenotying were done using analyses of their gp60 gene sequences. This study shows the presence of different genotypes and subgenotypes of *C. meleagridis* in edible bivalves obtained from LPPCHEA. This is the first report of the presence of the parasite in bivalves from the Philippines.

Keyword *Cryptosporidium meleagridis*, LPPCHEA, Philippines, bivalves

VISION THREATENING AMOEBA: MORPHOLOGICAL AND MOLECULAR BASED EVIDENCE FROM CORNEAL SPECIMENS ISOLATED IN MALAYSIA

Poster No. 77

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Acanthamoeba keratitis is a serious eyes infection among contact lens wearers and it is caused by an opportunistic free living amoeba known as *Acanthamoeba* spp. Trophozoite and cyst of this parasite can be found ubiquitously in the environment. Therefore, the aim of this study was to characterize the morphology and genotypes the species of *Acanthamoeba* from keratitis patients in Malaysia. Two clinical samples in the form of cyst culture were obtained from private hospital. Sub-cultured was done on non-nutrient agar seeded with heat-killed Escherichia coli and incubated at 30°C (±2oC) for 10 days. Morphological identification was performed using methylene blue stain based on shape and size of the endocyst and ectocyst. Observation was made under an inverted microscope (x40). Genomic DNA samples were extracted and PCR assay was conducted for amplification of the *Acanthamoeba*-specific amplimer (ASA.S1) region of the 18S ribosomal RNA gene. The phylogenetic analysis was carried out using Unipro UGENE software. It was observed that both clinical isolates have cyst sizes £18 µm with wrinkled exocyst and stellate endocyst. This morphological characterization demonstrated that the isolates belonged to Group II (Polyphagids). Product of approximately 464-bp was obtained using JDP1 and JDP2 primers. Phylogenetic analysis revealed that it belongs to genotype T4. In conclusion, the presence of *Acanthamoeba* Group II with genotype T4 resembled with previous studies that shown the major *Acanthamoeba* keratitis cases are associated with this genotype. Thus, *Acanthamoeba* infection is no more a rarity and can be a public health issue among the Malaysian community.

Keyword: *Acanthamoeba*, keratitis, polymerase chain reaction, contact lens, Malaysia

CUTANEOUS LEISHMANIASIS – DIAGNOSTIC AND THERAPEUTICAL CHALLENGES IN AN OLD DISEASE

Poster No. 78

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Introduction: Analysis of the literature on cutaneous leishmaniasis (CL) and mucosal leishmaniasis (ML) suggests an increase in imported cases in non-endemic countries that is attributable to the growing phenomenon of international tourism, migration, the refugee crisis in the Middle East and Africa and military operations in highly endemic regions. Cases of imported CL and ML are often missed initially and should be considered in all patients presenting slow healing ulcers. Moreover treatment of CL and ML is still controversial and challenging.

Case presentations: We present 8 cases with different CL and ML, seen and treated in our clinic from 2012-2017 (5 cases caused by *Leishmania infantum*, 1 case by *Leishmania braziliensis*, 1case by *Leishmania major*, 1 case by *Leishmania tropica*). The latest treatment recommendations for imported CL and ML from an European expert group "LeishMan" -from a "wait and see"-strategy until systemic therapies like intravenous liposomal amphotericin B or oral miltefosine - with regard to our patients will be discussed.

Conclusion: Polymerase chain reaction techniques using skin scrapings or biopsies of lesions can provide a rapid diagnosis and determination of the species by genotyping. Treatment recommendations can now be made species based rather than based on geographical exposure substantially improving treatment efficacy and patient outcomes.

Keyword: cutaneous leishmaniasis, miltefosine, *L.infantum*

ANTIGENICITY OF *TRICHINELLA SPIRALIS* GLYCOPROTEINS

Poster No. 79

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Trichinellosis is caused by trichinella nematodes. Specially, *T. spiralis* is the most recognized specie due to it distributes worldwide in many animals. Human can be infected by the ingestion of undercooked meat containing encysted larvae. After larvae are released, the parasites invade host intestinal wall and develop into adult worms which can release larvae to encapsulate within host muscle. Eventually, the larvae migration can lead to death of host due to heart, respiratory or kidney malfunction. Diagnosis is usually based on clinical symptoms and serology while biopsy is less recommended. However, vaccine are not available for trichinellosis. To develop a vaccine, knowledge of antigen-antibody response of trichinellosis is crucial to be explored. Glycoproteins are proteins containing glycans covalently attached to polypeptide side-chains. Since glycoproteins play an important role in host-pathogen interactions, they are important keys for vaccine development. In this research, trichinella adult worm was enriched their glycoproteins using ConA, LCH, GNA, WGA, SNA, MAL, AIL and PNA lectins. The separation relied on different carbohydrate structures. Each enriched samples were then measured protein concentration to indicate the abundance of each type of glycoproteins. Moreover, mass spectrometry was also introduced to identify glycoproteins in each fractions. To access antigenicity of each type of glycoproteins, individual healthy and *T. spiralis* infected patient sera were used for immunoblotting. The finding may lead to better understanding of antigen-antibody interaction and indicate major carbohydrate structure which is importance for host antibody response.

Keyword: *Trichinella spiralis*, Glycoprotein

EPIGENETIC AND GENETIC VARIATION IN STRONGYLOIDES IN RELATION TO DIFFERENT CONDITIONS OF HOSTS AND DRUG RESISTANCE

Poster No. 80

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Resistance to ivermectin (IVM) and related drugs is an increasing problems worldwide. Multiple mechanisms such as genetic and epigenetic variations in ABC transporter genes play an important role in parasitic susceptibility and resistance to anthelmintic drugs. However, the information of genetic and epigenetic variations in *Strongyloides spp.* is still limited. The objective of this research was to establish and investigate the genetic and epigenetic variations in in vivo established *S. ratti* drug-resistant strains. Experimental rats were divided into four groups: i) *S. ratti* infected only (C), ii) *S. ratti* infected and treated with IVM (I), iii) *S. ratti* infected and treated with ethylmethane sulfonate (EMS) (E), and iv) *S. ratti* infected and treated with IVM and EMS (IE). *S. ratti* adults and larvae were collected at 2-week post infection for *in vivo* and *in vitro* anthelminthic resistant tests. Additionally, genetic and epigenetic variations also will be studied in adults and larvae for ABC transporter genes expression and polymorphism. For the results by using larval migration assay, larvae in I group were still actively movement when treated with up to 50 ug/ml of ivermectin. For C, E and IE groups, worm movement was observed when treated with up to 25 ng/ml of ivermectin. Moreover, fecal culture in nematode growth media containing IVM also revealed the same trend of IVM concentration on the growth and survival rate of *S. ratti* among each experiment groups. The data observed in this study indicate that treatment with sub-therapeutic dose of IVM might result in ivermectin resistant in *S. ratti*.

Keyword: ABC transporter, Anthelminthic resistant, Ethylmethane sulfonate, Ivermectin

PREVALENCE AND RISK FACTORS OF SOIL-TRANSMITTED HELMINTH INFECTIONS AMONG SCHOOL-AGE CHILDREN IN NARATHIWAT PROVINCE

Poster No. 81

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Soil-transmitted helminths (STHs) are various species of nematodes which are transmitted by contaminated soil containing eggs or parasite larva. STH Infection in school-age children could play an important role in nutritional problem leading to delayed growth and development. Natathiwat is a southernmost province where STHs are endemic. A school-based control program had been implemented in some areas in Narathiwat Province from 2007-2016. Thus, the situation of STH infection in this area should be re-evaluated.

The fieldwork was conducted in 6 elementary schools in Tak Bai and Yee Ngor Districts of Narathiwat Province aimed to assess prevalence and risk factors for STHs using questionnaires and stool examination with direct simple smear and modified Kato-Katz methods.

Result showed that 1,084 subjects were enrolled and 664 (61.3%) participants completed the study. Age ranged from 6 to 12 years. Prevalence of STHs was 34.0%. STHs including *Trichuris trichiura* (24.4%), *Ascaris lumbricoides* (15.8%) and hookworms (1.7%) were identified. 8.1% of students carried multiple STHs infections. Multivariable analysis showed that untreated drinking water, always eating food by hands and poor clothe hygiene significantly increased risk for acquiring infections. Infected cases were statistically associated with short statue defined by height by age, OR = 2.95 (95% CI, 1.29 – 6.74). The study reveals a burden of STHs infection which reflects hygiene and sanitation problems. Growth might also be affected by the infection which immediate action is strongly suggested. Specific health promotion related to these risk behaviors should be performed.

Keyword: STHs, *Ascaris, Trichuris,* Hookworms, School-age children

NATURAL INFECTION WITH A FILARIAL LARVA OF A MAN-BITING BLACK FLY, SIMULIUM NIGROGILVUM (DIPTERA: SIMULIIDAE), IN CHIANG MAI PROVINCE, NORTHERN THAILAND

Poster No. 82

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Natural filarial infections of adult black flies were investigated at Ban Lek (elevation 1,500 m), Doi Pha Hom Pok National Park, Chiang Mai Province, northern Thailand. Female adult flies flying around a human were collected during the daytime from 06.00 to 18.00 hours on 18 May 2016. A total of 90 females were collected, and all were identified as *Simulium (Simulium) nigrogilvum*. One of 90 females dissected was naturally infected with one third-stage filarial larva (1.1%). The measurement of an unknown infective larva was 1,185 µm long by 25 µm wide, esophagus shorter than half of the body length. It was tentatively identified as *Onchocerca sp*. In order to clarify its taxonomic status, the PCR-based assay will be further conducted for molecular species identification.

Keyword: black fly, filaria, natural infection, *Onchocerca, Simuliidae*

KNOWLEDGE, ATTITUDE AND PRACTICE SURVEY ON SCHISTOSOMIASIS AMONG PUPILS IN MBITA, WESTERN KENYA

Poster No. 83

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In Kenya, prevalence of *Schistosoma mansoni* remains high, especially in lake region, despite of preventive measures such as mass drug administration. This study aims to clarify the knowledge, attitude and practice toward schistosomiasis among pupils in this area.

Four primary schools were randomly selected and pupils in class six and seven were recruited as study samples. Paper based knowledge, attitude and practice test toward schistosomiasis was administered. To understand the situation of *Schistosoma mansoni* prevalence, stool samples from same pupils were examined by Kato-Katz 3-day method.

Total 274 pupils were participated this study. 69% of pupils chose a correct answer for mode of transmission. 50% of pupils answered that they think they do not have any opportunity to be infected by schistosoma. 72% of pupils answered that bath in Lake Victoria causes schistosoma infection. 72%, 85% and 71% of pupils bathe, fetch water or wash clothes, respectively in Lake Victoria everyday or sometimes. The prevalence of *Schistosoma mansoni* was 36%.

Pupils in Mbita recognized that Lake Victoria is a source of schistosomiasis. However, most of them do not think that they have an opportunity to infect with schistosoma, even though they bathe, fetch water, wash clothes in the lake. This contradiction may come from the situation that health education succeed to input correct information, but daily life activities are too much "matter of course", thus those information may not link each other. Comprehensive approach, such as health education, provision of infrastructure and mass drug administration, is needed to prevent schistosomiasis.

Keyword: Schistosomiasis, school health

DETERMINATION OF THE ASSOCIATION BETWEEN *OPISTHORCHIS VIVERRINI* INFECTION AND TYPE 2 DIABETES MELLITUS : AN 8-YEAR RETROSPECTIVE COHORT STUDY

Poster No. 84

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Background: Type 2 diabetes mellitus(T2DM) is an increasing health burden worldwide. Many factors can be the cause of this rise including diet, physical activity and inflammation. A previous study in mice showed that chronic *Opisthorchis felineus* infection causing hepatic dicarbonyl stress which resulted in insulin resistance. In Thailand, *Opisthorchis viverrini*(OV) infection and T2DM share the same endemic area. Therefore, epidemiological investigation is needed to determine whether chronic OV infection contributes to the development of T2DM.

Objectives: The aim of present study was to determine the association between OV infection and T2DM.

Methods: The study employed a retrospective cohort design comprising 336 people from Ban-Nayao, Chachoengsao Province, Thailand who was previously non-diabeteic (Fasting plasma glucose(FPG)

Results: Of 336, 83(32.8%) were positive for OV infection. The incidence rate of T2DM in OV infection group and control group were 12.1/1,000 person-year and 13.4/1,000 person-year, respectively. An adjusted incidence rate ratio(IRR) is 0.917 (95%CI=0.4-2.1, p=0.834). Risk factors for T2DM incuded body mass index (adjusted IRR=2.5, 95%CI=1.2-5.2, p=0.016), age (adjusted IRR=2.4, 95%CI=1.1-5.3, p=0.022), male(adjusted IRR=2.2, 95%CI=1.0-4.6, p=0.038), dyslipidemia (adjusted IRR=2.6, 95%CI=1.2-5.9, p=0.018) and statins administration (IRR=3.5, 95%CI=1.3-8.3, p=0.0.009).

Conclusion: Our information shows that OV infection was not a contributing factor to T2DM over an 8-year follow-up study.

Keyword: *Opisthorchis viverrini*, type2diabetes mellitus, incidence, risk factor

AN INVESTIGATION OF TREMATODE METACERCARIAE INFECTION IN CYPRINOID FISH FROM A FRESH WATER RESERVOIR IN UDON THANI, THAILAND

Poster No. 85

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Food borne trematode species have been associated with public health problems. Approximately 6 million Thai people have been infected (Sripa et al., 2007). The major causative species of trematode are Haplorchoides and *Opisthorchis viverrini*. The parasites are transmitted to humans by the consumption of traditional dishes that are prepared from raw Cyprinoid fish. In this study, the trematode metacercariae in Cyprinoid fish were identified, all fish obtained from Huai Luang reservoir in Udon Thani Province of Thailand during May to October 2015 and May to November 2016. A total of 823 cyprinoid fish samples consisting of 9 species and 1 genus namely; *Systomus rubripinnis, Osteochilus vittatus, Henicorhynchus siamensis, Hampala dispar, Hypsibarbus malcolmi*, *Henicorhynchus sp., Cyclocheilichthys repasson, Gymnostomus siamensis, Labiobarbus siamensis* and *Barbonymus gonionotus* were analyzed for trematode infection. The fish samples of all species were digested in 0.25% pepsin-HCl solution and the resulting mixture was then filtered through different size of sieves. The metacercariae in fish samples were observed and identified using stereo and compound microscopes. In 2015, the cyprinoid fish, *Barbonymus gonionotus* was infected with the highest number of metacercariae (~19 metacercariae/fish) and *Cyclocheilichthys repason* was infected with the lowest number of metacercariae (~1 metacercariae/fish). The Trematode species, *Opisthorchis viverrini* was found with the largest number of total metacercariae (26.85%). In 2016, only two species were infected, *Labiobarbus siamensis* and *Cyclocheilichtys repasson* which the average numbers were less than one metacercariae per fish. *O. viverrini* was found with the largest number of total metacercariae (20.68%).

Keyword: Trematode, Metacercariae, Cyprinoid fish

TREMATODE INFECTION AMONG THE INTERMEDIATE HOST AT NAM-PHEE DAM PROJECT UNDER THE ROYAL PROJECTS

Poster No. 86

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The objective of this survey of trematode infection among intermediate hosts at the Nam-Phee dam was to investigation of trematode infection in intermediate hosts and to identify the species diversity of cercarial and metacercarial at the water shed and impact area at the Nham-Phee dam. Snails were collected from 15 locations. Shedding and crushing technique were applied for study the cercarial infection among the fresh water snails while pepsin digestion were used for study metacercarial infection in fresh water fishes that collected from the local markets. The result showed the infection rate in fresh water snail were 4.85% (32/659) classified into 5 species. They are *Centrocestus formosanus, Stictodora tridactyla, Apophallus muehlingi, Echinoparyphium recurvatum* in 6 species of fresh water snail. They were *Tarebia granifera* 12.63% (25/198), *Thiara scabra* 25% (3/12), *Melanoides tuberculata* 1.59% (2/126), *Filopaludina sumatrensis peninsularis* 16.67% (1/6) and *Mekongia swinsoni* 0.70% (1/142). The result of study in fishes showed 2 species were trematode infection, they are *Barbonymus gonionotus* 100% (17/17) and *Puntius orphoides* 25 % (34/136). The metacercarial were classified into 2 species. They are *Haplorchis taichui* and *Haplorchoides sp*.

Keyword: Trematode, infection, cercaria, metacercaria

MOLECULAR IDENTIFICATION OF VIRGULATE CERCARIA FROM SNAILS IN FAMILY BITHYNIIDAE, THAILAND

Poster No. 87

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The prevalence of trematode infection in the snails of family Bithyniidae was conducted in July 2015 to July 2016 in the reservoirs of dams, ditches, rice paddle fields, and waterfalls, Thailand. The snails were manually collected or scoop from seventeen Provinces of Udon Thani, Khon Kaen, Kalasin, Nong Khai, Maha Sarakham, Nong Bua Lam Phu, Bangkok, Ayutthaya, Suphan Buri, Chai Nat, Nakhon Sawan, Sing Buri, Non Thaburi, Nakhon Pathom, Chiang Mai and Pathum Thani Thailand. In the present study, six snail species *of B. siamensis goniomphalos, B. siamensis siamensis, B. funiculata, Hydrobioides nassa, Gabbia wykoffi* and *Wattebledia crosseana* were found. Snails were morphologically identified and examined for trematode infection by cercarial shedding. Seven hundred and eight (708) out of 28,119 snails were infected with trematode. Eight types of cercariae were identified as virgulate, monostome, furcocercous, amphistome, armatae, cystocercous, pleurolophocercous, and *O. viverrni*. The highest prevalence of trematode infection was virgulate of 2.05% and following cystophorous, armatae, furcocercous, amphistome, *O. viverrini*, monostome and pleurolophocercous about 0.31%, 0.20%, 0.18%, 0.11%, 0.10%, 0.06% and 0.03, respectively. Several types of cercariae were found in *B. siamensis goniomphalos*. Moreover, molecular analysis of 10 virgulate cercarial specimens indicated that they had a different mitochondrial cytochrome c oxidase 1 (COI) sequence which is discriminate those sequences in each Province. These results suggested that the molecular sequencing analysis has a highly effective to identify cercariae in the infected snails.

Keyword: prevalence, molecular identification, trematode, cercaria

GASTROINTESTINAL INFECTIONS IN DEPLOYED US MILITARY PERSONNEL TO THAILAND (COBRA GOLD-2015)

Poster No. 88

Patchariya Khantapura, Nattaya Ruamsap, Siriphan Gonwong, Paphavee Ketwalha, Woradee Lurchachaiwong, Oralak Serichantalergs, Apichai Srijan, Nuanpan Khemnu, Wirote Oransathid, Dilara Islam, Brett E. Swierczewski

Armed Forces Research Institute of Medical Sciences Afrims

Diarrheal disease remains a global health problem and a risk to travelers and military personnel deployed to developing regions. The isolation of enteric pathogens from diarrheal cases collected during earlier Cobra Gold exercises indicated Campylobacter was the leading cause of diarrhea. However, in this study a diarrheagenic *Escherichia coli* (DEC) was identified as a leading cause of diarrhea at 34%, *Salmonella* at 24%, Campylobacter (80% *C. jejuni*) at 12%, and viral species at 12%. Additionally, we identified enteric pathogens by conventional culture methods, multiplex RT-PCR, multiplex PCR of DEC, ELISA, TaqMan® Array Card (TAC), and xTAG® Gastrointestinal Pathogen Panel (GPP). Among the 18 enrolled diarrheal cases, 39% presented with loose stool, 28% with soft stool, and 16.5% with watery stool and formed stool. From the diarrheal cases with loose stool, enteric pathogens were detected in 58%. No relation between clinical symptoms and the pathogens detected in stools was found. No enteric pathogen was identified in two of three cases reporting formed stool, whereas C. jejuni was isolated from the third patient whose sole clinical symptom was pyrexia. The multiplex panels TAC and xTAG® GPP detected pathogens in 56% and 41% of the samples, respectively, whereas cultures, RT-PCR, PCR for DEC, and ELISA methods detected 66%. Consequently, these results indicate that currently available multiplex molecular assays cannot detect all circulating enteric pathogens from a single fecal sample. This further emphasizes the need for a more rapid, sensitive, and simple procedure to improve the diagnostic yield.

Keyword: Gastrointestinal, diarrhea, Cobra Gold

ZOONOTIC HELMINTHS IN OKINAWA MAIN ISLAND, JAPAN

Poster No. 89

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Trichostrongylus spp., gastrointestinal parasites of different animal species, including goats, are reported to be zoonotic causing clinical disease in human. The infection occurs orally by ingestion of L3 in contaminated food. Okinawa prefecture is the main goat breeder of Japan with 7518 heads and has human trichostrongylosis cases reported. However, the infection status *Trichostrongylus spp*. In goats and its relationship with human cases have never been studied. To evaluate the situation of trichostrongylosis in Okinawa main Island goats, 53 fecal samples were examined by parasitological and molecular techniques. Coproculture of goat feces found *Trichostrongylus spp*., *Haemonchus spp*., *Cooperia spp*. and *Oesophagostomum spp*. by morphology of L3. *Trichostrongylus spp*. genus specific PCR was positive for 14/53 samples. The zoonotic species, *T. colubriformis* (11/14) and *T. axei* (3/14) were confirmed by DNA sequencing. To understand the destination of goat fecal material by goat breeders, a survey was conducted at the meat inspection procedures. From 28 questionnaires received, 13 owners' answers indicated goat feces were used as fertilizer without the necessary procedures to assure parasite decontamination. Additionally, to assess the parasite contamination in food, 53 vegetable samples acquired in 11 local markets were examined for parasites. Larvae were detected in 13.2% of the samples presenting *Trichostrongylus spp*. (3/53), *A. cantonensis* (1/53) and *S. stercoralis* (3/53). In conclusion, human trichostrongylosis is likely to be occurring in Okinawa because of three main factors: 1) Zoonotic *Trichostrongylus spp*. were detected in goats' feces, 2) Procedures to decontaminate the fecal material for use in agriculture might be inefficient and 3) Three species of zoonotic helminths were detected in vegetables. Expand the study area to different islands and prophylactic measures for risk management are issues to be addressed in further studies.

Keyword: *Trichostrongylus spp*., zoonosis, goat, vegetable

BIOSURVEILLANCE OF ZOONOTIC DISEASES USING qPCR IN TANZANIA

Poster No. 90

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Tanzania Veterinary Laboratory Agency (TVLA) is an Executive Agency of the Ministry of Agriculture, Livestock and Fisheries Development (MALFD), one of its mandates is to conduct livestock and wildlife animal disease surveillance in Tanzania. In 2014 a molecular detection methodology was emphasized where TVLA started conducting biosurveillance for priority zoonotic diseases in Livestock and wildlife animals. Blood, sera and placental tissue samples were collected from January 2015 on seasonal bases annually and the collected samples were tested by screening test and then confirmed by real time qPCR methodology available at Central Veterinary Laboratory and satellite TVLA centres in Tanzania. Seven hundred and ninety three samples have already been collected from livestock and wildlife animals. Results indicate 11 suspect samples of anthrax were confirmed positive for *Bacillus anthracis* while 106 samples were positive against *Brucella spp* tested prior by Rose Bengal plate test and ELISA tests. Other diseases detected were *Yersinia pestis* (4), *Vibrio cholera* (5) and zero report for Rift Valley Fever and Avian Influenza. Real time qPCR methodology proved to be fast, reliable and convenient for zoonotic diseases surveillance.

Keyword: Biosurveillance, Zoonotic, Biodetector, real time qPCR.

SURVEY OF HELMINTH INFECTION IN KAREN POPULATION NA KIAN COMMUNITY, OMKOI DISTRICT OF CHIANG MAI PROVINCE.

Poster No. 91

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A survey was conducted under colloration of Chiang Mai Provincial Public Health Office, Office of Disease Prevention and Control 1 Chiang Mai and Phramongkutklao College of Medicine in karen population reside in mountain area. The community is lack of transportation access and healthcare infrastructure is still limited.

Survey team collected 425 stool specimens from students in Na Kian Non- Formal and Informal Education Centre and surrounded villages of Na Kian Community, Omkoi District of Chiang Mai Province, Northern Thailand. Specimens was examined with modified kato-katz technique aimed to diagnose intestinal helminth infection.

The results showed that 54.8% of participants were *Ascaris lumbricoides* (15.8%) and *Trichuris trichiura* (10.1%). Prevalence of helminth infection was significantly higher in
Study results are valuable for further prevention and control planning. Survey team is anticipating expanding the fieldwork by incorporating more participants, diagnostic technique to cover protozoa infection and assess for risk factors.

Keyword: Helminth, STHs, Trematode, Survey

DYNAMICS OF *AEDES AEGYPTI* LARVAE IN A RURAL AREA OF RATTANKIRI AND MONDUKIRI PROVINCES, CAMBODIA

Poster No. 92

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Aedes aegypti, the major vector of dengue, breeds in water storage containers and man-made waste-containers thus affecting dengue risk. A Visual Larval survey were performed by Bare foot Entomologist (Village Malaria Workers and Village Volunteer) who were trained to perform a task, all Larval containers were evaluated in wet and dry seasons from 2014 to July 2017. Immature mosquitoes were identified to species. The larval indices like house index, container index, breteau index varied from 26.1-91.11,7.45-52.98 and 20.0-315.56 in Ratanakiri and 16.33-94.12,4.78-55.68 and 23.81-397.65 in Mondulkiri province, respectively. The results showed that two species of *Aedes* mosquitoes were abundantly distributed and expanded their range in all the study areas of Rattanakiri and Mondulkiri. More recently, *Aedes aegypti* was found at 3.54 times in Rattanakiri, predominantly higher abundance than usual, while *Aedes albopictus* showed more abundance in Mondulkiri province. Larval Indices were seasonally different among localities. To reduce dengue risk and to achieve control of these mosquitoes, the integration of different methods with community participatory should be used.

Keyword: *Aedes aegypti*, larval indices. Household water container

STUDY OF BIOLOGICAL BEHAVIOUR OF MOSQUITO BITES OF *ANOPHELES SP.* AS MALARIA VECTOR IN BANJARMANGU SUB-DISTRICT, BANJARNEGARA DISTRICT, CENTRAL JAVA, INDONESIA

Poster No. 93

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Malaria is one of infectious diseases causing by *Plasmodium sp*. parasite and transmitted by the bites of mosquitoes vector *Anopheles sp.* Banjarnegara district is one of district in Central Java Province as endemic area of malaria. Recently, in 2015 – 2016 was reported malaria cases by Banjarmangu Public Health Center with Annual Parasite Rate (API) is 11.1%. One of the factor was affect the cases is biological behavior of mosquito vector there was mosquito bites of *Anopheles sp*. The aim of this research is to describes the bites behavior and blood feeding preferences of Anopheles sp. which were caught in the Banjarmangu area. This is descriptional research used cross sectional method. The sampling of mosquitoes catching was started at 6 pm until 6 am and continued catched of the resting mosquitoes in the outside were started at 6 am until 8 pm in Sigeblog Village. The mosquitoes criteria were blood feeding mosquitoes and used as sample for precipitin test. The mosquitoes were successfully identified is *An. vagus* with precipitin test result were 47.6% are zoophilic, 28.6% are zoo-antrophophilic, and 23.8% are antrophophilic. This result recommend that preventing method were by avoid the bites of *Anopheles sp*. mosquito and control the cattle cages did not associated with the houses of recidents.

Keyword: Malaria, Banjarnegara, *Anopheles*, antrophophilic, zoophilic

DIFFERENTIAL GENE EXPRESSION OF THE *PLASMODIUM*-INFECTED AND NON-INFECTED *ANOPHELES* MOSQUITOES AT 18 HOURS POST FEEDING

Poster No. 94

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Malaria disease is one of the major health problems in Thailand and elsewhere. This study aimed to investigate the *Anopheles* genes that respond to *Plasmodium* infection at 18 hours post blood feeding. The total RNA of female mosquitoes fed with *P. vivax*-infected and non-infected blood was extracted and submitted for RNA-seq. The total reads of both conditions were at least 9 gigabases. The percentages of the number of reads mapped to the *An. dirus* reference genome were 85% and 64% for the infected and non-infected samples, respectively. Of the total 13,420 known transcripts in the mosquito genome, 3,360 were up-regulated and 539 down-regulated upon *Plasmodium* infection. In gene ontology of molecular function, the highest numbers of modulated genes were found to have a binding function. In biological process gene ontology, altered genes were most abundant in transportation. From cellular component gene ontology category, the highest number of modulated genes encoded integral membrane proteins. These genes will be further analyzed for their biological functions associated with *Plasmodium* development in the mosquito.

Keyword: *P. vivax*, *An. dirus*, RNA-seq, gene ontology

EXCITO-REPELLENCY PROPERTIES OF ESSENTIAL OIL FROM MICROMELUM MINUTUM WIGHT & ARM. AGAINST LABORATORY POPULATION OF *AEDES AEGYPTI* AND *AE. ALBOPICTUS* (DIPTERA:CULICIDAE)

Poster No. 95

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The essential oil extracted from *Micromelum minutum* leaves at 3 different concentrations (0.5%, 1.5% and 2.5%v/v) were investigated for their repellency properties against laboratory strains of *Aedes aegypti* and *Ae. albopictus* using an excito-repellency test system. The results showed that both *Ae. aegypti* and *Ae. albopictus* exhibited vary escape rates after affected by the different concentrations of the oil. The best escape rate of *Ae. aegypti* was observed in both contact and non-contact chambers at the lowest concentration (50%escape), whereas the other two concentrations provided the low level escape rates. Meanwhile, the high escape rate was found in *Ae. albopictus* in all tested concentrations of the oil (41.7-66.7%contact, 60-70%non-contact). The greatest knockdown rate was found in *Ae. aegypti* and *Ae. albopictus* after exposure with the oil at concentration of 2.5% (25% contact, 36.7% non-contact) and 1.5% (23.3%contact, 20%non-contact), respectively. Moreover, the mortality rate of non-escaped *Ae. aegypti* after the 24h-holding period in both contact and non-contact were observed in 2.5% oil concentration (8.3-25%). GC-MS analysis revealed that the component of *M. minutum* leaves oil were caryophyllene (26.6%), alpha-selinene (14.4%) and 1,4,7,-cycloundecatriene, 1,5,9,9-tetramethyl-, Z,Z,Z- (8.1%). This is the first study of the irritancy and repellency activities of *M. minutum* leaves essential oil against *Ae. aegypti* and *Ae. albopictus*. Further studies, the protection times assay will be performed in order to develop the appropriate formulation of new herbal-base repellent.

Keyword: Excito-repellency, Essential oil, *Aedes aegypti, Ae. albopictus*, GC-MS analysis

EFFECTIVENESS OF FIPRONIL AS A SYSTEMIC CONTROL AGENT AGAINST *XENOPSYLLA CHEOPIS* (SIPHONAPTERA: PULICIDAE) IN MADAGASCAR

Poster No. 96

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Plague vector control in Madagascar is mainly carried out by insecticides, either sprayed in powder form or kept inside Kartman-box containing bait. However, current plague control methods are not efficient enough, as the country still reports a new case of plague every year. Therefore, in order to enhance the vector control program in Madagascar, the use of systemic insecticide, fipronil, was assessed as an alternative vector control method against the rat flea *Xenopsylla cheopis*, (Rothschild), the main vector of *Yersinia pestis* (Yersin), the causative agent of plague, in Madagascar. The effectiveness of fipronil as a systemic control agent against *X. cheopis* was assessed by determining the toxicity values of the "Lethal Dose 50" (LD50). Rodents bioassays, using rodent hosts, *Rattus norvegicus* (Berkenhout) and *Rattus rattus* (L.), which fed on fipronil-treated bait and then from which *X. cheopis* were fed were the technique used to evaluate the systemic action of the insecticide on the vector. As a standardized control method, the susceptibility of *X. cheopis* to fipronil was evaluated by exposure to impregnated paper following World Health Organization (WHO) insecticide test protocol to compare its effect to the systemic activity of the studied insecticide. Results showed that when administered in a systemic way, fipronil appears to be more effective: the toxicity level was evaluated to be ninefold higher compared with the WHO test. Compared with other methods, which require indiscriminate dusting of rodent burrows and human dwellings, fipronil applied in a systemic way enables the direct targeting of the plague vector. However, field tests need to be further carried out to confirm its suitability on large scales.

Keyword: plague, fipronil, *Xenopsylla cheopis, Rattus sp*, systemic insecticide

DETECTION OF HUMAN INTESTINAL PARASITES FROM SYNANTROPIC FLIES IN KLONG LUANG DISTRICT, PATHUM THANI PROVINCE

Poster No. 97

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Synanthropic flies are one of the most important mechanical vector of protozoa and helminthic parasites. This survey was performed to determine the parasite and protozoa from synanthropic flies in Klong laung district, Pathum Thani province. The adult flies were collected in various areas such as cafeterias, fresh-food markets, garbage piles, hospital and chicken slaughterhouse. The sweeping net was used for fly collections from study sites. A total of 1,449 flies were captured, primarily consisting of 6 species and the 2 dominant species were *Chrysomya megacephala* and *Musca domestica. C. megacephala* was predominant in garbage piles at cafeterias and market, while *M. domestica* was numerically dominant in fresh-food markets and chicken slaughterhouse. The other flies including *M. sorbens, Sarcophaga spp., Lucilia spp*. and *C. rufifacies* were found. All adult flies were examined for intestinal parasites by Formalin-ethyl acetate concentration technique and modified Ziehl–Neelsen. The results were negative for parasites. Although, the current survey have not been found intestinal parasites but the adult flies can be vector of other pathogens. The improved sanitation and proper garbage management can be used to control fly and other pathogenic organism in the area.

Keyword: syantropic flies, Pathum Thani, parasite

A MODIFIED CMU FLY TRAP TO CONTROL POPULATIONS OF MEDICALLY IMPORTANT BLOW FLIES

Poster No. 98

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Necrophagous blow flies are medically-important in Thailand. They are commonly found around human dwelling (e.g., house, market and garbage) and can act as vectors for human pathogens. Strategies to control the fly population are necessary, and bait-traps have been a useful method for control fly populations. The first aim of this study was to modify a semi-automatic funnel trap (Klong-Klaew et al. 2017). The modified CMU fly trap consists of two parts: 1) the trap base 2) the collecting bag which is designed to be easy removed. Compared to the previous trap, the new improved trap has many advantages because it is small and easy to regulate. In addition, the modified trap is more efficient in catching blow flies compared with the previous trap ($p<0.05$), highly efficient for catching flies. To prove the efficiency of the modified fly-trap, the total fly numbers collected by the improved trap, sticky traps, and the sweeping net method were compared. Each collection method was tested for 1-day and tainted beef mixed with offal was used as bait. Fly samples were conducted once every 2 weeks for 12 months (Apr 2015-Mar 2016). During the study, a total of 29,308 flies were captured, containing *Chrysomya megacephala* (60.25%), *Chrysomya rufifacies* (36.60%), *Lucilia cuprina* (0.60%), *Hemipyrellia ligurriens* (0.54%), *Ceylonomyia nigripes* (0.13%), *Chrysomya villeneuvi* (0.04%), *Chrysomya chani* (0.01%), *Chrysomya pinguis* (0.01%), *Hemipyrellia pulchra* (0.01%), *Stomorhina discolor* (0.01%) and *Subfamily Chrysomyinae* (1.79%). The results indicate that the sticky trap (7,256 flies; 25%) was the least efficient for collecting blow flies and the modified fly-trap (12,629 flies; 43%) was similar to the sweeping nets (9,433 flies; 32%) ($p>0.05$). The modified fly-trap is an effortless method which is useful not only for fly population control, but also for monitoring purposes.

Reference: Klong-klaew T., Sontigun N., Sanit S., Samerjai C., Sukontason K., Kurahashi H., Koehler PG., Pereira RM., Limsopatham K., Suwannayod S., Thanapornpoonpong S., Chareonviriyaphap T, Sukontason KL. Field evaluation of a semi-automatic funnel trap targeted the medically important non-biting flies: Acta Trop. 176; 2017, 68–77

Keyword: blow-fly, Fly trap, bait-trap

DNA-BASED IDENTIFICATION OF FORENSICALLY IMPORTANT FLESH FLIES (DIPTERA: SARCOPHAGIDAE) IN THAILAND

Poster No. 99

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Flesh flies (Diptera: Sarcophagidae) are forensically important, as their larvae are found in human corpses and the species specific developmental time can be used to estimate the post-mortem interval (PMI_{min}). For this reason, accurate species identification of specimens is a crucial step in forensic entomology. However, it is difficult to distinguish flesh flies using morphological identification, due to the similarity among the species, especially larvae and females. Although there are identification keys of flesh fly species, it is sometime difficult for the non-expert taxonomist to use them and/or identify damaged specimens. Therefore, molecular identification may help to overcome these problems. The mitochondrial gene has been used widely for species-level identifications. In this study, cytochrome oxidase subunits I (COI) was employed to differentiate nine species of forensically important flesh flies in Thailand; *Boettcherisca nathani, Liopygia ruficornis, Lioproctia pattoni, Lioproctia saprianovae, Parasarcophaga dux, Sarcorohdendorfia antilope, Sarcorohdendorfia inextricata, Sarcorohdendorfia seniorwhitei* and *Seniorwhitea princeps*. This data will be useful for accurate identification of flesh fly specimens that are found from a corpse, not only in Thailand, but also other countries where these species exist.

Keyword: Flesh fly, *Sarcophagidae*, molecular identification, Forensic entomology

EFFECTS OF HUMAN AND RHESUS MACAQUE BLOOD MEAL SOURCES FOR OPTIMIZATION OF REPRODUCTION AND ADULT SURVIVORSHIP OF MOSQUITOES UNDER LABORATORY CONDITIONS

Poster No. 100

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Production of over 100,000 female mosquitoes per month as required to fulfil research studies is a technically challenging endeavor at the Department of Entomology, Armed Forces Research Institute of Medical Sciences (AFRIMS) insectary. Mass rearing of mosquitoes requires modified strategies that will increase populations, such as type of blood meal. Five species of laboratory-colonized mosquitoes; *Anopheles cracens, An.dirus* (2 strains consisting of forced mate and free mating groups), *An.minimus, An.sawadwongporni*, and *Aedes aegypti* were fed blood meals from human and rhesus macaque using an artificial membrane feeder. The effects of different blood meal sources were evaluated with respect to rate of blood feeding, mortality and reproduction (fecundity and hatching rates). Adult survival was monitored at days 7, 14 and 21 post blood feeding. Except for *An.cracens* and *An.dirus* (forced mate strain), there were significant differences in feeding rates between blood sources.

Keyword: *Anopheles, Aedes*, Human, Rhesus macaque, Reproduction

DIVERSITY OF MOSQUITO SPECIES IN THE *PLASMODIUM GALLINACEUM* ENDEMIC AREA OF NAKHON SRI THAMMARAT PROVINCE, SOUTHERN THAILAND

Poster No. 101

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The avian malaria species, *Plasmodium gallinaceum*, is an important parasitic disease in poultry, and can be transmitted via bites from various species of infected mosquitoes. In southern Thailand, sporadic infection of the disease has been reported in Nakhon Sri Thammarat province by blood smears examined under light microscope. The objective of this study was to investigate the diversity of mosquitoes in a *P. gallinaceum* endemic area in a layer farm in Nakhon Sri Thammarat province. The mosquitoes were collected monthly on two consecutive days from February 2016 to January 2017. A sweeping insect net and aspirators around chicken-bait were used by day at collection times of 07.00-10.00 hrs and 15.00-18.00 hrs., whereas, CDC-type light traps were adjusted for approximately 12 hours at night (18.00-06.00 hrs). Climatic data also were recorded, i.e. average temperature, humidity and rainfall information. Subsequently, the mosquitoes were identified by using morphological characteristics. A total of 4100 mosquitoes of 18 species were collected and identified. The 5 most abundant species were *Culex gelidus* (35.85%) followed by *Aedimorphus vexans* (11.76%), *Aedes albopictus* (11.46%), *Mansonia uniformis* (9.90%) and *Armigeres theobaldi* (5.78%). Furthermore, the vector competence of laboratory raised colony by the artificial membrane feeding technique, and amplifying the mtDNA genome of the parasite from all wild caught mosquitoes will be performed for further analysis.

Keyword: *Plasmodium gallinaceum*, mosquitoes, layer farm, southern Thailand

FIVE NEW SPECIES OF BLACK FLIES (DIPTERA: SIMULIIDAE) IN THAILAND

Poster No. 102

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Black flies belonging to the family Simuliidae of the order Diptera, are an important medical and veterinary group of small bloodsucking insects. Some species can transmit pathogens to humans, livestock and poultry, and bites from adult females cause a wide range of problems for humans and animals. In Thailand, a total of 93 species of black-fly fauna, comprising 6 subgenera, i.e., *Asiosimulium, Daviesellum, Gomphostilbia, Montisimulium, Nevermannia* and *Simulium* s. str. in the genus *Simulium* Latreille s.l. were recognized between 1984 and 2014. During 2016-2017, we discovered five new species of black flies in the country, i.e., *Simulium (Gomphostilbia) maleewongae* Takaoka, Srisuka & Saeung sp. nov., *Simulium (Simulium) umphangense* Takaoka, Srisuka & Saeung sp. nov., *Simulium (Simulium) srisukai* Takaoka & Saeung sp. nov., *Simulium (Simulium) kiewmaepanense* Takaoka, Srisuka & Saeung sp. nov. and *Simulium (Gomphostilbia) fukudae* Takaoka, Srisuka & Saeung sp. nov., by comparative morphological investigations of the collected larvae, pupae and adult associated pupal skins from previously known species and DNA sequences were analysed based on the mitochondrial COI gene to confirm new species status.

Keyword: *Simulium*, black fly, new species, COI gene, Thailand

DEVELOPMENT OF HEALTH EDUCATION PROGRAM ON PEDICULOSIS IN GIRL SCHOOL CHILDREN AT AMPHOE MUANG, KHON KAEN PROVINCE, THAILAND

Poster No. 103

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Pediculosis, caused by head lice (*Pediculus humanus capitis*), is still an important health problem in female schoolchildren worldwide, including in Thailand. Molecular studies have classified head lice into three clades, A, B and C. Moreover, louse-borne pathogens have been detected in head lice and these agents can probably also be transmitted to humans. The prevalence of pediculosis in Thailand is still re-infestation and incomplete elimination, thus, prevention is an important strategy for sustainable control. The objectives of this study were, 1) to investigate the prevalence and intensity of head lice infestations in girl schoolchildren in Amphoe Muang, Khon Kaen Province, Thailand, 2) to increase knowledge, change attitudes and promote preventive practices among schoolchildren, and 3) to identify genetic diversity among head lice and the presence of louse-borne pathogens using PCR approach. The schoolchildren in Amphoe Muang Khon Kaen were randomly selected and a total 397 children obtained from six schools were allocated into intervention and control groups. The Knowledge, Attitude and Practice (KAP) questionnaire, consent forms and health education materials were constructed and tested of validity content and reliability with experts and school pilot before investigation. The prevalence and intensity of head lice infestation were investigated and the head lice were collected to identify clade and bacterial transmission. The health education package were provided only in intervention group. The KAP questionnaire was re-evaluated at two months after intervention. Principal findings, the overall prevalence of head lice infestation at base line was 58.16%, which was not different between in intervention (59%) and control (56%) groups. The KAP scores had no significant differences before intervention in both intervention and control groups. By contrast, after intervention, the KAP scores was significantly increased in intervention group. Moreover, the infestation rate in intervention group was significantly decreased. This finding indicated that schoolchildren in Amphoe Muang, Khon Kaen Province was still high prevalence of head lice infestation and the health education program was demonstrated a significant impact to reduce head lice infestation. The health education package should be provided to Thai schoolchildren in the future.

Keyword: Health education, Head lice infestation, Genetic diversity, Louse born pathogen

UPLC-MSMS METHOD DEVELOPMENT AND VALIDATION OF ATOVAQUONE IN HUMAN PLASMA FOR PHARMACOKINETIC STUDY

Poster No. 104

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Atovaquone-proguanil is one of the few remaining anti-malarials that is still efficacious against *Plasmodium falciparum* infection. A simple, sensitive, selective, and specific ultra-performance liquid chromatography (UPLC) coupled with tandem mass spectrometer (MS/MS) was developed and validated for determination of Atovaquone levels in human plasma using carboxymefloquine as internal standard. Chromatographic separation was performed on Waters Acquity UPLC® BEH C18, 2.1 x 50 mm, 1.8 µm column with a gradient mobile phase of 5 mM ammonium acetate in water with pH 7.0 and 5 mM ammonium acetate in acetonitrile, at a flow-rate of 0.4 ml/min over the 5-min run-time. The plasma samples were extracted by protein precipitation using acetonitrile with known concentrations of carboxymefloquine. The clear supernatants were transferred to UPLC vials after mixing with vortex and centrifugation for 10 minutes. Selective mass/charge (m/z) transitions were monitored for atovaquone (365.04 to 337.02) and for carboxymefloquine (307.94 to 223.93). The method is being fully validated based on US FDA guidance and demonstrates linear response over a concentration range from 3.00 to 180 ng/ml with a correlation coefficient (r^2) of 0.998 and a limit of detection of 0.5 ng/ml. Analyte recovery was typically greater than 90% with high intra- and inter-day accuracy and precision with less than 4% CV. The 3 cycles of freeze-thaw, short and long term stability, are ongoing. This method will be applied into pharmacokinetic study of atovaquone-proguanil against malaria.

Keyword: Atovaquone, LCMS, Pharmacokinetic

MOST PATIENTS IN CAMBODIA WITH TREATMENT FAILURE POST ATOVAQUONE-PROGUANIL LACK CYTB MUTATIONS IN Y268 LOCUS BY SANGER SEQUENCING

Poster No. 105

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Atovaquone-proguanil (AP) is an attractive treatment option as it is effective against *Plasmodium falciparum* resistant strains. However, there are concerns over rapid development of resistance due to point mutations in codon 268 in the cytochrome b gene (cytb). Data on atovaquone resistance from Cambodia remains limited. We have analyzed atovaquone and cycloguanil markers of resistance in parasite isolates from 205 patients with uncomplicated *P. falciparum* or mixed *P.falciparum/P. vivax* malaria infections who participated in a therapeutic efficacy study of AP with or without oral artesunate (AS) in Cambodia. At enrollment, all 205 samples evaluated at the Pfcytb Y268 locus by Sanger sequencing were wild type. Of 14 recrudescences, only one carried the Y268C mutation. Amplicon deep sequencing targeting cytb did not detect the mutation pre-treatment or 24 hours into treatment, even at a minor allele frequency down to 0.25%. This suggests de novo development of atovaquone resistance in one volunteer rather than expansion of a pre-existing parasite subpopulation. All isolates from the Anlong Veng and Kratie sites had normal atovoquone IC50 but with significant elevation of the cycloquanil IC50 (2,987 nM, 95% CI = 2415 – 3559) in the 44 isolates tested to date, consistent with high prevalence of DHFR mutations in the region. There was no efficacy benefit from adding AS to AP and nearly all isolates carried K13 mutations. Analysis of pharmacokinetics data and its contribution to treatment failures will also be presented. Better understanding of host and parasite factors leading to treatment failure will aid in appropriate implementation of AP in the malaria treatment policy guidelines.

Keyword: Malaria, malarone, cytb, *P. falciparum*, resistance

HEALTH PROBLEMS AMONG THAI TREKKERS IN THAILAND: A PROSPECTIVE STUDY

Poster No. 106

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Background/Objectives: Trekkers are group of travellers who may face with high risk of injury and illness during trekking. The numbers of Thai travellers to all national parks has been increasing year by year. In Thailand, unfortunately, there is no study about health problems among trekker. This study aimed to determine the incidence of health problems among Thai trekkers.

Method: This study focus on Thai trekkers who visited Phukradueng national park. Questionnaires were collected at the national park after they finished their trips. Either electronic questionnaires and telephone interview was implemented on day 14(+5) after the trip regarding their health problems.

Results: 342 Thai travellers consented and participated in this study. 51.5% were male. Median age was 27 (range 13-59). The average trip duration was 2.76 days. Overall 91.8% of all participants reported some health problems within 19 days after trip ending. 90.9% experienced health problems within last day of trip. Common health problems were muscle ache (83.3%), followed by runny nose (21.6%) and abdominal bloating (9.6%). 11.7% of participants did not prepare themselves before travel.270 participants can be followed. 19 participants reported additional health problems after return, 7 of them had URI symptom, 3 had fever and 2 had GI symptoms. 27.7% of sick travellers need some treatment. Average duration of the most common health problems; muscle ache was 2.88 days.

Conclusion: Many Thai trekkers experience some health problems during trekking. Proper pre-travel management to specific national park is important to prevent potential health problems.

Keyword: Trekker, thai, health problem

BEEDI ROLLING ON ORAL HEALTH OF WOMEN BEEDI ROLLERS OF MANGALORE- A CROSS SECTIONAL STUDY

Poster No. 107

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Background: The Beedi market in India is huge and highly competitive. A large part of this industry is highly unregulated and home based. Beedi rolling is an important occupation for a lot of women in Mangalore. Since women Beedi rollers have easier access to tobacco, they may be more predisposed to tobacco habits. Due to exposure to raw tobacco, habits, neglect of oral health due to their poor standard of living, lack of time, financial instability and lack of access to health care facilities they are predisposed to oral diseases. Though studies have found that Beedi rollers suffered from health problems, information about their oral health is lacking.

Objective: This study was conducted to assess tobacco habits, oral mucosal conditions and periodontal status among women Beedi rollers.

Methodology: The sample size was determined to be 550 women Beedi rollers. After obtaining informed consent, their tobacco habits, oral mucosal conditions and periodontal status was recorded. Pearson's correlation and chi square tests were used to analyse the data.

Results: Prevalence of Oral mucosal conditions was present in 4.4% of them. Calculus was present in 85.3% of study subjects and loss of attachment of 4-5 mm in 7.1% of them. Duration of Beedi rolling in years was found to have a weak correlation on the Oral mucosal conditions and periodontal status. Prevalence of smokeless tobacco use was 21.5%. Prevalence of oral mucosal conditions and periodontal diseases were significantly higher among smokeless tobacco users.

Conclusion: Tobacco use, Oral mucosal conditions and periodontal diseases were found to be high among Beedi rollers.

Keyword: Oral mucosal conditions, tobacco use, periodontal diseases

A LONGITUDINAL COHORT STUDY OF INFANT ANEMIA IN A MARGINALIZED POPULATION AT THE THAILAND-MYANMAR BORDER: ONSET, RISK FACTORS AND RECOVERY

Poster No. 108

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Background: Sub-Saharan Africa and South East Asia carry the heaviest global burden of anaemia. Infant anaemia is associated with neonatal mortality and impaired cognitive development. Little is known about the timing of onset of infant anaemia in South East Asia. This is the first study at the Thailand-Myanmar Border that aims to describe the timing of onset anaemia in the first year of life and investigate factors associated with anaemia and recovery from anaemia.

Methods: Retrospective analysis of a longitudinal birth cohort of infants born between 2012 and 2015, followed up from birth to their first year of life at the Shoklo Malaria Research Unit (SMRU). Anaemia was defined as haematocrit level of less than 33% inclusive at the anytime point in the first year of life.

Results: Out of the 1449 infants in the cohort, 65.9 % (955/1449) developed infant anaemia. Of these, 79.7% (761/955) went on to recover from infant anaemia within the first year of follow up. Median time to recovery from anaemia was 8.4 weeks. Infant anaemia occurred early in life, with 52.6% (502/955) of infants developing anaemia within 3 months of birth. Factors related to increased risk of anaemia: preterm birth (aHR 1.65(1.33-2.05), p<0.001), small for gestational age (aHR 1.64(1.22-2.21), p=0.001), malaria infection during follow up (aHR 5.21(1.36-19.92), p=0.016), maternal anaemia (aHR 1.32(1.13-1.55), p=0.001) and smoking in pregnancy (aHR 1.23(1.00-1.52), p=0.048). Factors related to reduced risk of anaemia: female gender (aHR 0.83(0.73-0.94), p=0.003), delayed cord clumping at delivery (aHR 0.76(0.65-0.89), p<0.001) and Karen ethnicity (aHR 0.77(0.63-0.933), p=0.008).

Conclusions: Infant anaemia is frequent and occurs early in infancy in this population, but the majority go on to recover. Risk factors associated with anaemia in this cohort are consistent with other studies investigating anaemia in children under 5 years old. Our results contribute to recommendations for prophylactic management of anaemia in at-risk populations.

Keyword: Infant anemia, marginalized populations

FACTORS RELATED TO NUTRITIONAL STATUS OF UNDER-FIVE-YEAR RURAL CHILDREN IN MINE-MAW STATION, MANDALAY REGION, MYANMAR

Poster No. 109

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Malnutrition remains one of the most common causes of morbidity and mortality among children throughout the world, especially in developing countries. This is community based cross- sectional descriptive study. Data were collected by using face-to-face interviewer method to mothers of children and anthropometric measurements to total of 280 children. Anthropometric measurements were analyzed by z score of weight-for-height, weight-for-age and height-for-age. Data were analyzed by using SPSS and Anthro software. The prevalence of wasting was 20.4%, underweight was 32.9% and stunting was 52.5%. In multiple logistic regression analysis, wasting was significantly associated with main meal per day above 2 times (AOR=0.002, 95% CI=0.001 to 0.017), children with no deworming (AOR= 8.458, 95% CI=1.428 to 6.889). Underweight was significantly associated with per capita per income above 32000 kyats (AOR= 0.589, 95% CI=0.346 to 0.894), main meal per day above 2 times (AOR= 0.300, 95% CI= 0.174 to 0.518) and diarrhea above 3 times (AOR= 6.672, 95% CI= 1.274 to 34. 454). Stunting was significantly associated with incomplete or no immunization (AOR= 3.689, 95% CI= 1.539 to 8.842). Community participation and intersectional appreciation were needed to modify these factors. Stakeholders should collaborate with community to increase participation. To have a sustained action, nutritional problems should be defined by community and local authority. It should be strengthened to existing programs of adequate, safe water supply and food safety. Early diagnosis and prompt treatment of infections should be promoted through health education to community and basic health care services.

Keyword: Anthropometric measures, wasting, stunting, underweight

ROLE OF CONDITIONED NATURAL KILLER CELLS IN CANCER IMMUNOLAGY

Poster No. 110

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Natural killer (NK) cells are CD3-NK1.1+ lymphocyte in mouse, and the earliest identified member of innate lymphoid cell 1 (ILC1). NK cells exert anti-tumor function through direct killing of tumor cells and indirect modulation of the function of other immune cells, such as T cells, dendritic cells and macrophages. However, the therapeutic effect of adoptive NK cell transfer on human and in mouse solid tumors are limited, which may be due to functional heterogeneity of NK cells and the immunosuppressive tumor microenvironment. We established culture conditions to generate murine NK cells with anti-tumor activity. The conditioned NK cells express NK cell receptors NKG2A, NKG2D and Ly49D, and maturation marker CD11b and CD27. In addition, conditioned NK cells also express MHC class I, MHC class II and CD86, which indicate antigen presentation function. The conditioned NK cells produced inteferon-gamma (IFN-g) and killed EO771 and B16F10 tumor cells directly in vitro. In the orthotopic EO771 breast cancer model, transfer of conditioned NK cells to early stage tumor-bearing mice caused tumor regrssion and altered the composition of immune cells in tumor, including CD8+ T cell, myeloid-derived suppressor cell (MDSC) and macrophage. To better imitate clinical condition, we transferred conditioned NK cells into EO771-resected mice, and found the therapy reduced tumor recurrence rate and improved survival rate. In elucidating the anti-tumor mechanism, my preliminary results indicate that the conditioned NK cells trafficked into draining lymph node, spleen and tumor in 24 hours. And CXCR3 is critical for the conditioned NK to migrate to dLN and tumor. For future work, we aim to investigate the machanism of how the conditioned NK cells affect myeloid cells and T cell response to exert anti-tumor function.

Keyword: Natural killer cell, cancer

IDENTIFICATION OF SPECIFIC BIOMARKER GENES FOR SEPARATING INTRAHEPATIC CHOLANGIOCARCINOMA SUBTYPE USING QUANTITATIVE REAL-TIME REVERSE TRANSCRIPTION POLYMERASE CHAIN REACTION

Poster No. 111

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Cholangiocarcinoma (CCA) is a deadly epithelial cancer originating from biliary system. CCA is classified into intrahepatic cholangiocarcinoma (ICC) and extrahepatic cholangiocarcinomas (ECC). ICC is grossly classifiable into mass forming (MF), periductal infiltrating (PI), and intraductal growth (IG) types. ICC arising in the intrahepatic small bile ducts or bile ductules is usually of the MF type while ICC arising in the intrahepatic large bile ducts (perihilar ICC) can be of the PI, MF or IG type. Therefore, it is quite difficult to separate among them. This study aims to investigate the association between gene expression in PI and IG types. Top five of up-regulated genes from PI (C19ORF33, UPK1B, CTHRC1, GREM1, KLK11) and IG type (CFTR, SLC5A1, MUC17, BDKRB2, CCL18) were validated by Real-Time PCR using SYBR assay. Those up-regulated genes were previously detected by Affymetrix Microarray in patients with CCA. The result showed that overexpression of CTHCR1 was found in 73% of PI type and 27% in IG (P-value<0.05), whereas up-regulate of CFTR was present in 73% of IG case and 9% PI (P-value<0.5). These results present that CTHRC1 and CFTR genes overexpression may be a biomarker for distinguish between PI and IG type of ICC.

Keyword: Intrahepatic Cholangiocarcinoma-Biomarker-PI type-IG type

TINY BEASTS IN SEEDS WITH KILLING EFFECTS!!

Poster No. 112

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Introduction: Indian restaurants offer fennel seeds as mouth freshener at the end of the meal. These are either offered in an open container with or without spoon or in a closed container with a lid. This study is aimed at the assessment of the microbial contamination of fennel seeds offered as mouth freshener in the restaurants of Mangalore city.

Methodology: This study was conducted in Mangalore city where samples of fennel seeds were collected from 40 different restaurants. Each sample was collected directly into a sterile container and soon after its collection; it was transported to the Microbiology Lab for microbial analysis. Bacterial growth was identified by Gram staining, colony morphology and biochemical tests. Bacterial count was done by manually counting the colonies and multiplying with dilution factor. The fungi were identified by tease mount with lactophenol cotton blue and slide culture.

Results: Only 12 samples of fennel seeds were not contaminated. Many samples contained multiple microorganisms. *Klebsiella species, Genus Bacillus, Citrobacter species, EColi, Pseudomonas species, Staphylococus aureus, Actinobacter species* were found in 4,2,2,10,6,2,4 and 4 of the samples respectively. Four samples had isolates of *Aspergillus Flavus* and *Aspergillus Fumigatus*.

Conclusion: The results highlight the importance of good hand hygiene practices to avoid contamination with pathogenic microorganisms. People should be provided with knowledge about hand washing, hand sanitizing and toilet facilities as contaminated fennel seeds are of unacceptable risk and are unsafe.

Keyword: Fennel seeds, Microbial contamination, Hygiene

THE DRIVEN MECHANISM DEVELOPMENT OF THE INTEGRATED NCD (NON COMMUNICABLE DISEASE) QUALITY CLINIC OF THE ACADEMIC CENTER NETWORK IN THE AREA RESPONSIBILITY OF THE OFFICE OF DISEASE PREVENTION AND CONTROL REGION 10, UBON RATCHATHANI

Poster No. 113

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This action research was aim to develop the driven mechanism of the Integrated NCD (Non Communicable Disease) Quality Clinic of the Academic Center Network in the Area Responsibility of the Office of Disease Prevention and Control Region 10th Ubon Ratchathani under the concept of NCD quality Clinic and management. Target group were the health working group board on driven and quality assurance of NCD, Health service provider board office 8th and 10th, and the NCD's board of district level in 45 districts. Data was collected by brainstorming and in-depth interview by self-assessment form of integrated NCD quality Clinic and documentary review. Data was analyzed by content analysis for qualitative data and descriptive statistics for quantitative data. The process of driven mechanism were; (1) Network's context was found the problem of manpower and budget; (2) Planning were divided in the plan of network of health working group board, plan and the driven NCD quality Clinic of province and district level, and model of quality assurance on NCD clinic; (3) The practicing driven by the integrated network with the method of teaching the guidance, the goals, and the model of practicing. The provincial and district driven as well as self-evaluation; and (4) 45 districts (100%) were evaluated and assurance and 44 districts (97.78) were reached to the criteria of NCD quality Clinic. This integrated driven mechanism was obviously on the mission and the goal whereas the problem of manpower of some offices were solving by man supporting from other offices within network.

Keyword: Driven mechanism, NCD Quality Clinic, integrated

IS THE HEALTH SYSTEM READY TO RESPOND TO THE BURDEN OF NON-COMMUNICABLE DISEASES (NCDS)? HEALTH FACILITY ASSESSMENT IN MYANMAR (2015)

Poster No. 114

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NCDs accounts for 59% mortality mainly due to cardiovascular diseases (CVD), diabetes, cancer and chronic respiratory diseases (CRD) in Myanmar in 2014 according to WHO estimates. This study aims to identify service availability and readiness of NCDs by assessing the critical inputs (guidelines, trained staff, equipment, diagnostic capacity, medicines and commodities) in public and private health facilities. This study was conducted in randomly selected 201 health facilities by using pretested WHO Service Availability and Readiness Assessment (SARA) questionnaire. Most hospitals, rural health centers (RHCs) and sub-RHCs offered CVD and CRD services. Most facilities except Sub-RHCs (48%) could offer diabetes services. Availability for cervical cancer diagnosis was highest among general to district hospitals (77%) and lowest at township-level hospitals (12%). NCD guidelines and trained staff were generally non-existent in all facilities except for cervical cancer in which service availability was highest in township-level hospitals (60%) and lowest in private hospitals (5%). Concerning diabetes, the hospitals had better capacities for blood glucose testing and metformin availability than the RHCs and sub-RHCs. The majority of the hospitals had injectable insulin except township-level hospitals. For CVD, availability of different tracer equipment except oxygen were 5% in RHCs and the most available medicine was calcium channel blocker and the least was hydrochlorothiazide tablets in all facilities. Regarding CRD, the availability of equipment, drugs and commodities were higher in hospitals than in other health facilities. However, specialized and private hospitals did not have peak flow meter, spacers, and salbutamol inhalers. Overall readiness scores calculated as weighted values to represent the country level are 48% (Diabetes), 48% (CVD), 50% (Ca Cervix) and 39% (CRD) respectively. This study highlighted that health facility enhancement is needed concerning NCDs as part of health system strengthening in Myanmar to fulfil the sustainable development goal in health sector.

Keyword: NCDs, Health Facility, Health System

KNOWLEDGE, ATTITUDES, PRACTICES, AND SELF-TREATMENT OF SICK INTERNATIONAL TRAVELERS REGARDING COMMUNICABLE AND NON-COMMUNICABLE DISEASES

Poster No. 115

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Background: A number of international travelers has been increasing every year. Even careful prevention, some travelers developed illness. The objectives of this study were to assess the prevalence of self-treatment of sick international travelers and to compare knowledge, attitudes, and practices between non-westerner and westerner travelers.

Methods: Sick international travelers visited at the Hospital for Tropical Diseases and Queen Saovabha Memorial Institute during 2016 to 2017 were invited to participate, and asked to complete a questionnaire regarding demographic data, self-treatment, knowledge, attitudes, and practices. The follow up was done for all participants approximately 1-6 weeks by email or telephone after enrolment. We also compared the differences between non-westerners and westerners using SPSS statistics software version 18.

Results: Three hundred twenty two sick international travelers were enrolled and eligible for analysis. The majority of participants was from Asia (64.9%), followed by Europe (17.1%) and North America (12.4%). Most of participants were university graduates (60.2%). The common health problems were tropical infection (32%) and rabies post-exposure prophylaxis (18.3%). From all participants, 24.8% sought pre-travel advice, 30.4% bought travel health insurance, and 37% tried self-treatment before visiting medical service (40% in non-westerners and 28.7% in westerners, $p = 0.063$). The percentage of self-treatment (65.6%) was highest in the travelers presenting with upper respiratory tract infection. There was a significant difference in scores of the attitudes and knowledge between non-westerners and westerners (72.8% vs 94.8% and 59.2% vs 70.6%, $p < 0.001$, respectively). According to practice part, non-westerners sought for pre-travel advice less than westerners significantly (11.5% vs 60.9%, $p < 0.001$).

Conclusions: Thirty-seven percent of sick international travelers tried to treat themselves before visiting medical service. Westerner travelers had a significantly higher score of knowledge, attitudes, and practices compare to non-westerner travelers.

Keyword: Knowledge, attitudes, practices, self-treatment, travelers

CARE FOR UNDER 5-YEARS OLD CHILDREN BY THE CAREGIVERS IN PALU CITY, INDONESIA: EXPLORING THE PRACTICE AND ITS POTENTIAL AFFECTING FACTORS

Poster No. 116

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Background: Diarrhoea and pneumonia remains frequent and are amongst the leading causes of child mortality in Indonesia. In addition to the quality of health service provision, care for childhood illness at the household level plays an important role in determining the diseases outcome.

Objective: To explore caregivers' practice in care for childhood illness, and its potential influencing factors

Method: This is a qualitative study conducted in Palu City, Indonesia. Data were collected through interview and group discussion involving caregivers, health workers, and health program managers.

Results: Diarrhoea, cough with breathing difficulties (which indicate childhood pneumonia), and high fever are considered to be common by the caregivers. Hence, they did not feel it is necessary to consult to health professionals immediately. First home care mostly includes traditional herbs and over the counter medicine, with some still prefer to take their children to traditional healer or have traditional ceremony to cure sick children. In addition to poor knowledge on the emergency sign, poor living condition has becoming a great barrier in providing nutritious meals for children – which at the end leads to increased risk to suffer from infectious disease.

Conclusion: Urgent action is required to improve care for child illness among caregivers in Palu, particularly in recognizing the emergency sign. The findings also emphasized that care for illness is greatly influenced by individual, interpersonal, environmental and societal factors, which are all intertwining and equally important to be addressed.

Keyword: Childhood illness, infectious disease, caregivers

THE EFFECTIVITY OF HAND WASHING METHOD IN REDUCING TOTAL BACTERIA COLONY AMONG NURSES IN SUMATERA UTARA UNIVERSITY HOSPITAL

Poster No. 117

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Background: Hospital acquired infection (HAI) is a major problem for patients health care and may impact the duration of treatment even increasing the risk of mortality. Hand hygiene is a simple procedure but giving good prevention usually done among nurses at the hospital. The objective of the study is to determine the effectivity of hand washing method compared to hand rub in order to eliminate microorganisms on nurse's hands at Sumatera Utara University Hospital.

Method: This is an analytic experimental study using random sampling technique. There were 16 nurses enrolled in this study. There were 2 groups involved; first group using hand washing with soap and the other one using hand rub. The swabs were taken from each hands from both groups before and after washing their hands. Moreover, the swabs directly sent to Microbiology Laboratory of Sumatera Utara University to identify bacteria which colonize the hand.

Result: There were no significant differences between using handwashing method compared to hand rub in reducing total bacterial colony on hands (p=0.088). The average of total colony decreased by using handwashing method is 59.5% and by using hand rub is 47.2%.

Discussion: Hand hygiene method using alcohol-based hand rub liquid has been recommended by WHO and can replace hand washing method in particular situation. It suggest that hand hygiene method using hand rub liquid could be choosen in hand hygiene method.

Conclusion: There was no significant difference between handwashing and handrub in reducing bacteria colonized nurse's hand in this study.

Keyword: Keywords: handwashing, handrub, total bacterial colony

PATTERN OF DRUG USE AND SEXUAL BEHAVIOR AMONG YOUNG MALES 15-24 YEARS OLD IN QUANGNINH PROVINCE, VIETNAM

Poster No. 118

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Objective: To describe the pattern of drug use and sexual behavior and identify factors related to drug use among young males in Quangninh, during the period 2003-2009.

Method: During 2003-2009, three repeated cross-sectional surveys were conducted every three years among the same population (young males aged from 15-24 years old, currently living in one commune). They were interviewed regarding their sexual behaviors and drug use behaviors. The prevalence of drug use and incidence of new drug users were estimated retrospectively. Z-test for proportions was used to measure absolute change between baseline and follow-up surveys, and to discover the trends of drug use and sexual behavior over time. Multiple logistic regression analysis was used to determine factors associated with drug use for each of the three surveys.

Results: Heroin was the major drug of use in 2003, and marijuana was the major drug of use in 2009; the type of drug changed from an injecting drug to a non-injecting drug over time. The proportions of new drug users increased, from 1% (2003) to 3.5% (2009), but the proportion of current drug users decreased over time. The prevalence of having ever had sexual contact increased over time, from 18.6 % (2003) to 36.8% (2009). Analysis of factors associated with drug use suggested the strong predictors were: smoking, drinking, and having friends/relatives who were drug users. The finding of this study also indicated that current drug use was associated with HIV infection, although few HIV-infected individuals were detected among the study population

Keyword: Drug use, young male, sexual behaviors, Vietnam, survey

METHOD OF STOOL PRESERVATIONS FOR DNA ISOLATION

Poster No. 119

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The storage of stool is one of the crucial factor in DNA isolation. So far the stool samples used for the PCR method are fresh or stored in the frozen refrigerator. To analyze fresh stool sample sometimes is difficult to do especially when it needs to be done in large quantities with limited facilities and infrastructure. Therefore, the method of storage or preservation of faeces with tools or materials that are easy to obtain is needed so that DNA isolation can be done successfully. The aim of this study is to compare various ways of preservations e.g. ethanol 70% and 2.5% potassium dichromate before DNA isolation. A total of 46 stool samples were soaked in liquid nitrogen until it is frozen and crushed, were washed with distilled water twice, sentrifuged and then the pellets were taken and weighed as much as needed to do the DNA isolation. Then proceed with the examination of the concentration and purity of DNA with nanodrop. After that 23 stool samples were preserved in ethanol 70% and 23 others in 2.5% potassium dichromate for 2 months in room temperature. Then proceed with DNA isolation and examination in nanodrop. All the preserved stool samples had various DNA concentration but all shows a decreased purity in DNA samples if compared with fresh stool. This indicates the best stool sample specimen for DNA isolation is the fresh ones.

Keyword: Stool preservation, DNA isolation, PCR

THE INFLUENCE OF FACTORS ON BEHAVIOR TOWARD SMOG PROBLEM MANAGEMENT OF PEOPLE IN COMMUNITY: A CASE STUDY OF BAN HONG LUANG, LUMPHUN PROVINCE

Poster No. 120

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The aims of this survey research were to (1) examine the behavior toward smog problem management, (2) to investigate the power of personal characteristics, knowledge, attitude, awareness and participate to behavior of people in Ban Hong Luang community, Ban Hong district, Lamphun province. The samples were 392 people, selected through the systematic random sampling method. The research instrument used in the study was questionnaire. The participatory action research were 3 phases as follows: 1) Pre-Research Phase 2) Research Phase and 3) Reflex Phase. The 40 key informants were selected by purposive sampling. The reliability of questionnaires was 0.86. Data were computed by computer program. The result of this study found that gender, knowledge, attitude, awareness and participation of people in Ban Hong Luang community of people in Ban Hong Luang community with 79.59%. The people is aware that Haze negatively effects their people's health.

Keyword: Knowledge, attitude, perception, smog problem management, Ban Hong Luang community

SUPPRESSORS SPECIFIC FOR HER2/4 (HUMAN EPIDERMAL GROWTH FACTOR RECEPTOR 2/4): A NEW FAMILY OF ANTI-TOXOPLASMIC AGENTS

Poster No. 120

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The effects of tyrosine kinase inhibitors (TKIs) were evaluated on growth inhibition of intracellular *Toxoplasma gondii* in host ARPE19 cells. The number of tachyzoites per parasitophorous vacuolar membrane (PVM) was counted after treatment of TKIs. *T. gondii* protein expression was assessed by western blot. And immunofluorescence assay was performed using PDCD4 and GRA3 antibodies. The TKIs were divided into three groups; the TKIs of non-EGFR, anti-HER2, and anti-HER2/4, respectively. Group I TKIs (nintedanib, AZD9291, sunitinib) were unable to inhibit proliferation without destroying host cells. Group II TKIs (lapatinib, gefitinib, erlotinib, AG1478) inhibited proliferation up to 98% equivalent to control pyrimethamine (5 μM) at 20 μM and higher, without affecting host cells. Group III TKIs (neratinib, dacomitinib, afatinib, pelitinib) inhibited proliferation up to 98% equivalent to pyrimethamine at 1-5 μM, but host cells were destroyed at 10-20 μM. In Group I, TgHSP90 and SAG1 inhibition were weak, and GRA3 expression was moderately inhibited. In Group II, TgHSP90 and SAG1 expression seemed to be slightly enhanced, while GRA3 showed none to mild inhibition, but AG1478 inhibited all proteins moderately. Protein expression was blocked in Group III, comparable to pyrimethamine. PDCD4 and GRA3 were well localized inside the nuclei in Group I. Mild disruption of PDCD4 was observed in Group II. PDCD4 and GRA3 were completely disrupted in Group III. This study suggests the possibility of a vital *T. gondii* TK as potential HER2/4 properties, thus anti-HER2/4 TKIs may inhibit intracellular parasite proliferation with minimal adverse effect on host cells.

Keywords: *Toxoplasma gondii*, intracellular, growth, inhibition, TKIs, HER2, HER2/4