

JOINT INTERNATIONAL TROPICAL MEDICINE MEETING 2018

"INNOVATION, TRANSLATION, AND IMPACT IN TROPICAL MEDICINE"

12 – 14 DECEMBER 2018 AMARI WATERGATE HOTEL, BANGKOK, THAILAND

ABSTRACTS

Oral Presentations





Opening Session 09.00-09.45 Watergate Ballroom



OPENING CEREMONY BY ORGANIZERS AND CO-ORGANIZERS

Report by:
Prof. Srivicha Krudsood
Chair, JITMM2018 Scientific Committee



WELCOME ADDRESS

Dr. Sombat ThanphasertsukSenior Expert in Prevention Medicine, Department of Disease Control, Thailand Ministry of Public Health



WELCOME ADDRESS

Mr. David BurtonChief Operating Officer, Mahidol-Oxford Tropical Medicine Research Unit (MORU)



OPENING REMARKS

Assoc. Prof. Pratap Singhasivanon *Chairman, JITMM2018 Organizing Committee*



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



AWARD RECIPIENTS:

Prof. Akira KanekoProfessor of Global Health, Department of Microbiology, Tumor and Cell biology, Karolinska
Institutet, Sweden



Prof. Dr. Tawadchai SuppaditVice President, Planning and Development Strategies, Walailak University, Thailand



Dr. Twatchai SrestasupanaDirector, Maesot General Hospital, Mae Sot, Tak, Thailand



09.45-10.30 Watergate Ballroom

SI: The 24th Chamlong-Tranakchit Lecture

Chairperson:

Pratap Singhasivanor



Keynote Speaker:



The safe and effective radical cure of malaria

Prof. Ric PriceMenzies School of Health Research, Darwin, Australia University of Oxford, United Kingdom

The safe and effective radical cure of malaria



Ric Price^{1,2}

 1 Centre for Tropical Medicine and Global Health, Nuffield Department of Clinical Medicine, University of Oxford, UK; 2 Global and Tropical Health Division, Menzies School of Health Research and Charles Darwin University, Darwin, NT, Australia

The leaders of 18 malaria endemic countries have set ambitious goals to eliminate malaria from the Asia Pacific region by 2030. Whilst there has been significant progress in reducing the burden of malaria, these gains are fragile. The ultimate goal of malaria elimination is threatened by a variety of challenges, particularly the spread of multidrug resistant *P. falciparum* and a rising proportion of infections due to non-falciparum malaria. These challenges highlight the importance of the main themes of this conference: innovation, translation, and impact. The timely elimination of malaria from the Asia Pacific will require expansion of malaria control activities to include active case detection and the widespread implementation of the effective radical cure of malaria, in which all stages of the parasite are targeted. Vivax's ability to form dormant liver stages (hypnozoites) and to recur weeks to months after a primary infection requires treatment of both the blood and liver stages of the parasite. Currently, the only widely available drug to eliminate hypnozoites from the human host is primaguine a drug that can cause significant risk of haemolysis in individuals with G6PD deficiency. The prolonged treatment course and requirement for G6PD testing are major obstacles to healthcare providers, who are often reluctant to prescribe PQ, and patients, who are reluctant to take a full course of treatment. New tools have been developed to overcome these, including novel point of care devices and short course treatment regimens. These innovations will be discussed with regard to their translation into policy and their impact upon the burden of disease.

Keyword: malaria, vivax, radical cure

11.00-12.30 Room A

S2: Ivermectin for malaria elimination

Chairpersons:

1 Kesinee Chotivanich





2. Joel Tarning

Invited Speakers:



Ivermectin for malaria elimination - clinical trials **Kevin Kobylinski**

Armed Forces Research Institute of Medical Sciences (AFRIMS)



Evaluating the effect of ivermectin B1a and B1b compounds against the malaria vector *Anopheles dirus*

Narenrit Wamaket

Armed Forces Research Institute of Medical Sciences (AFRIMS)



Ivermectin metabolites

Phornpimon Tipthara

Mahidol-Oxford Tropical Medicine Research Unit (MORU)



Ivermectin inhibits *P. cynomolgi* and *P. falciparum* liver stage development

John H Adams *University of South Florida*

Ivermectin for Malaria Elimination - Clinical Trials



Thailand

<u>Kevin C. Kobylinski</u>¹, Podjanee Jittamala², Borimas Hanboonkunupakarn^{3,4}, Sasithon Pukrittayakamee³, Kanchana Pantuwatana¹, Siriporn Phasomkusolsil¹, Silas A. Davidson¹, Markus Winterberg^{4,5}, Richard Hoglund^{4,5}, Mavuto Mukaka^{4,5}, Rob W. van der Pluijm^{4,5}, Arjen Dondorp^{4,5}, Nicholas P. J. Day^{4,5}, Nicholas J. White^{4,5}, Joel Tarning^{4,5}

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- ² Department of Tropical Hygiene, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand
 ³ Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok,
- ⁴ Mahidol-Oxford Tropical Medicine Research Unit, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand
- ⁵ Centre for Tropical Medicine and Global Health, Nuffield Department of Clinical Medicine, University of Oxford, Oxford, United Kingdom

Ivermectin mass drug administration is being evaluated as a potential new vector control tool to aid malaria elimination efforts around the globe. Two clinical trials have recently been completed investigating the safety, tolerability, mosquito-lethal pharmacokinetics, and effect of ivermectin dihydroartemisinin-piperaguine. A study in Kenya evaluated three day regimens of ivermectin at 300 or 600 µg/kg with dihydroartemisinin-piperaguine in Plasmodium falciparum infected persons, while a study in Thailand evaluated single dose administration of ivermectin at 400 µg/kg with dihydroartemisininpiperaguine and primaguine in healthy volunteers. In a few volunteers, there was an increase in liver enzymes when ivermectin and dihydroartemisininpiperaguine were co-administered which requires further investigation. Interestingly, both studies observed much higher than initially predicted ivermectin mosquito-lethal effects. Pharmacokinetic analyses demonstrated that ivermectin bioavailability was substantially increased when coadministered with dihydroartemisinin-piperaguine. Another contributing factor to increased mosquito lethality could be the possibility of ivermectin metabolites with mosquito-lethal effect. Several ivermectin mass drug administration field trials for malaria control are underway in Africa and Southeast Asia, each with their own unique approaches to control malaria which will be presented here.

Keyword: Ivermectin, *Plasmodium falciparum*, malaria, Africa, Southeast Asia

Evaluating the effect of Ivermectin B_{1a} and B_{1b} compounds against the malaria vector *Anopheles dirus*



Narenrit Wamaket ^{1,2}, Oranicha Khamprapa _{1,2}, Siriporn Phasomkusolsil ², Silas Davidson ², Patchara Sriwichai ³, Phornpimon Tipthara ⁴, Markus Winterberg ⁴, Joel Tarning ⁴, Nicholas White ⁴, Jetsumon Sattabongkot ¹, Kevin Kobylinski ²

- ¹ Mahidol Vivax Research Unit, Faculty of Tropical Medicine, Mahidol University
- ² Department of Entomology, Armed Forces Research Institute of Medical Sciences
- ³ Department of Medical Entomology, Faculty of Tropical Medicine, Mahidol University
- ⁴ Mahidol-Oxford Tropical Medicine Research Unit, Faculty of Tropical Medicine, Mahidol University

Ivermectin (IVM) is particularly potent against Anopheline *mosquitoes*, causing significant mortality, *delayed* re-*feeding*, and reduced fertility when ingested through a *blood meal*. In nature, IVM is a mixture of two homologs, 22, 23-dihydroavermectin B_{1a} (IVM B_{1a}) and 22, 23-dihydroavermectin B_{1b} (IVM B_{1b}) at a ratio of >90% and <10% respectively. Both structures are metabolized by similar pathways in the vertebrate. A recent study in snails demonstrated that the minor IVM B_{1b} is the lethal component, while the major IVM B_{1a} component had no effect. Here, IVM compounds *in vitro* activity was assessed by spiking human blood with various concentrations of IVM parent compound, IVM B_{1a} and IVM B_{1b} , blood feeding to *Anopheles dirus* and monitoring subsequent mortality to determine the lethal concentration that kills 50% (LC₅₀) of mosquitoes. This study present for the first time, the *in vitro* impact of IVM B_{1a} , and IVM B_{1b} on *An. dirus* survival. These results will be used to guide discovery of which IVM metabolites possess mosquito-lethal effect.

Keyword : Ivermectin B_{1a} , Ivermectin B_{1b} , metabolite, Anopheles dirus, lethal

Ivermectin metabolites



<u>Phornpimon Tipthara</u>¹, Siribha Apinan¹, Narenrit Wamaket^{2,3}, Oranicha Khamprapa^{2,3}, Nicholas J White^{1,4}, Kevin Kobylinski³, Markus Winterberg^{1,4}, Joel Tarning^{1,4}

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Ivermectin (IVM) mass drug administration (MDA) is used for control a number of neglected tropical diseases such as onchocerciasis, lymphatic filariasis, scables, and is now under consideration for malaria transmission suppression. A recent trial demonstrated the mosquito-lethal effect of human venous blood from IVM-treated volunteers active for several days beyond the expected halflife of the parent compound. This could be due to active IVM metabolites with mosquito-lethal effect. IVM is a nonpolar and lipophilic compound. It is semisynthesized from avermectin, a natural fermentation product of *Streptomyces* avermitilis. IVM parent compound is comprised of two fermentation products, a major (>90%) 25-secondary-butyl (IVM B_{1a}) and a minor (<10%) 25-iso-propyl (IVM B_{1b}) component. Separation of the two components is impractical on a large scale, therefore they are commercially sold as a mixture. Drug metabolite identification studies has increased significantly due to the use of high resolution mass spectrometry. In this study, a quadrupole time-of-flight (Q-ToF) mass spectrometer, coupled to ultra-performance liquid chromatography (UPLC) was used to identify IVM metabolites. The common IVM metabolites found both in vitro and in vivo will be further characterized. In the in vitro experiment, human microsome were treated with IVM parent compound, B1a and B1b. Metabolite fractions were collected within two hours. Incubation at zero minute, incubation without cofactor, and incubation without IVM were used as controls. For the *in vivo* study, plasma of volunteers who have ingested IVM were analyzed. Ten metabolites were identified from in vitro, including oxidation, dioxidation, and demethylation. Of these, two were found in the plasma of volunteers who had ingested IVM. To our knowledge, this is the first description of IVM metabolites in human.

Keyword: Ivermectin, Metabolite, LC-MS/MS, Malaria

Ivermectin inhibits *P. cynomolgi* and *P. falciparum* liver stage development



Alison Roth¹, Samantha O. Aylor², Brian Vesely², Ratawan Ubalee³, Kevin Kobylinski³, Silas Davidson³, Norman Waters², John H. Adams¹

¹Center for Global Health and Infectious Diseases Research, College of Public Health, University of South Florida, 3720 Spectrum Blvd STE 404 Tampa, Florida 33612, USA.

Plasmodium vivax is the most prevalent cause of malaria outside of sub-Saharan Africa with over 80 million clinical cases reported each year. Most vivax malaria cases are relapse infections that originate from a dormant stage, termed hypnozoite, residing in the liver of *P. vivax*-infected individuals. There is a critical need for new chemotypes of anti-relapse drugs since treatment options for clearing hypnozoites from the liver are limited and the primary antihypnozoite drug, primaguine, is toxic to individuals with G6PD-deficiencies found in malaria-endemic countries. The ability to screen for new anti-relapse drugs is limited by the variable availability of P. vivax-infected mosquitoes coming from human infections. To overcome this limitation, *Plasmodium* cynomolgi, a closely-related non-human primate model of relapsing malaria that provides highly-reproducible in vivo infections, can be utilized as an alternative for studying liver stage dormancy. This study demonstrates how the use of an innovative *P. cynomolgi* liver stage *in vitro* microscale culture system using primary macague hepatocytes can overcome current shortcomings related to *P. vivax* liver stage research. This novel in vitro culture system maintains stable metabolic activity for >30 days and supports P. cynomolgi liver-stage development with infection rates as high as 2.5%. This study also demonstrates killing activity of ivermectin, a well-established broad-spectrum anthelminthic drug, against P. cynomolgi as well as P. falciparum. Utilizing this system as a model for studying P. vivax liver stage development, as well as the discovery of ivermectin's antimalarial efficacy, are important breakthroughs for the development of new anti-relapse therapies.

Keyword : Ivermectin, *P. cynomolgi, P. falciparum, P. vivax,* malaria

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11.00-12.30 Room B

S3: Infections and parasitic diseases: put them on the map

Chairpersons:

1. Serge Morand





Paron Dekumyoy

Invited Speakers:



Evolution of public health prevention of leptospirosis in Mahasarakham Province (Thailand) in a One Health perspective **Jaruwan Viroj and Claire Lajaunie** *Montpellier University, Mahasarakham University; INSERM,*

Ceric-DICE CNRS, Aix-Marseille University, Marseille, France



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Mapping spatio-temporal spread of dengue in Delhi
Olivier Telle
Centre National de la Recherche Scientifique (CNRS)



From citizen science to laboratory verification: distribution of the newly invasive New Guinea flatworm *Platydemus manokwari* and its role in carrying *Angiostrongylus* nematode larvae in Thailand

Kittipong Chaisiri

Department of Helminthology, Faculty of Tropical Medicine, Mahidol University



Planetary changes: challenges for health forecasting

Serge Morand

CNRS-CIRAD, Department of Helminthology, Faculty of Tropical Medicine,

Mahidol University

Evolution of public health prevention of leptospirosis in Mahasarakham Province (Thailand) in a One Health perspective



Jaruwan Viroj¹, Claire Lajaunie²



¹Montpellier University, Mahasarakham University, ²INSERM, Ceric-DICE CNRS, Aix-Marseille University, Marseille, France,

Leptospirosis is an endemic disease with moderate incidence in Mahasarakham Province Thailand. The present study was designed to assess the policy implementation mission regarding leptospirosis prevention and control from the national level to the loca administrative levels, in Mahasarakham Province through a One Health perspective. We will present the existing framework of policy from the national to the local level and how the One Health perspective has been integrated. Then we will present the qualitative study conducted in the Province of Mahasarakham, using documentation review individual in-depth interviews and structured interviews of 26 persons (public healtl officers, local government officers, livestock officers) who developed policy implementation tools or have responsibilities in leptospirosis prevention and control. Before 2000, the policy implementation in this phase was not clearly framed at the local level. Between 2000 and 2003, Mahasarakham Provincial Public Health Office supported public healtl officers in their responsibility to control the disease and gave them a clearer role in the prevention of the disease. Between 2004 and 2010, leptospirosis prevention and contro have been enhanced at the district level. The cooperation between public health officer in the district is now clearly established. Between 2011 to 2014, the province o Mahasarakham has decided to foster cooperation in leptospirosis prevention and control a the local level between public health department, livestock department, and the sub district level, i.e. Tambon Administration Organization. However, some linkage gap between provincial departments and leptospirosis prevention were identified, concerning mainly patients and the whole population. In order to develop a clear and concrete cooperation between departments for a realistic leptospirosis guideline relying on the One Health concept several steps are necessary for improving and achieving more effectively the prevention and control of leptospirosis.

Keyword: leptospirosis, One Health, prevention and control, Thailand, policy implementation **common presentation with Dr.Claire Lajaunie

Mapping spatio-temporal spread of dengue in Delhi



Olivier Telle

Centre National de la Recherche Scientifique

Dengue is one of the major modern urban diseases that have swept through the tropics and subtropics over the last decades. In Delhi, epidemics are becoming more and more frequents with one epidemic every three years. In a recent research, we could estimate that nearly 40% of individual were at least infected once in their life. This disease provides us with a unique case with which to understand the link between intra-urban environmental disparities and emerging disease. To better tackle epidemic of dengue, we identify the spatio-temporal pattern of dengue diffusion and the relation between environmental heterogeneity of a city with mosquito abundance and incidence rate of dengue virus. If we couldn't detect a significant relation between quality of environment and dengue incidence, this does not mean that poverty associated with high density of population a major role in dengue attachment within cities.

Keyword : Dengue, health geography, spatio-temporal diffusion, social and environmental urban heterogeneity

From citizen science to laboratory verification: Distribution of the newly invasive New Guinea flatworm Platydemus manokwari and its role in carrying Angiostrongylus nematode larvae in Thailand



<u>Kittipong Chaisiri</u>, Sirilak Dusitsittipon², Nonn Panitvong³, Thawatchai Ketboonlue¹, Supaporn Nuamtanong¹, Urusa Thaenkham¹, Serge Morand^{1,4,5} and Paron Dekumyoy¹

Invasive species constitute one of the most serious threats to biodiversity and ecosystems, and they potentially cause economic problems and impact human health. The globally invasive New Guinea flatworm, Platydemus manokwari (Platyhelminthes: Geoplanidae), has been identified as a threat to terrestrial biodiversity, particularly soil-dwelling native species (e.g. molluscs, annelids and other land planarians), and is listed among 100 of the world's worst invasive alien species. We report here, for the first time, P. manokwari occurrences in many locations throughout Thailand, using voluntary digital public participation from the social network portals associated with the Thailand Biodiversity Conservation Group and collections of living flatworm specimens. Mitochondrial cytochrome c oxidase subunit I (COI) sequences confirmed that all collected flatworms were P. manokwari and placed them in the "world haplotype" clade alongside other previously reported specimens from France, Florida (USA), Puerto Rico, Singapore, French Polynesia, New Caledonia, and the Solomon Islands. In addition, infective stage larvae (L3) of the nematode Angiostrongylus malaysiensis were found in the flatworm specimens, with a 12.4% infection rate (15/121 specimens examined). Platydemus manokwari occurrence in Thailand and its capacity to carry L3 of Angiostrongylus should be of concern to biodiversity conservation and human health practitioners, because this invasive flatworm species may be involved in the life cycle of angiostrongylid worms in Thailand.

Keyword : Angiostrongylus; invasive species; New Guinea flatworm; *Platydemus manokwari*: Thailand

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⁴CIRAD ASTRE, Faculty of Veterinary Technology, Kasetsart University, 10900 Bangkok, Thailand and ⁵Intitut des Sciences de l'Evolution, CNRS, IRD, University of Montpellier, Montpellier 34290, France

Planetary changes: challenges for health forecasting



Morand Serge¹

¹CNRS-CIRAD, Department of Helminthology, Faculty of Tropical Medicine, Mahidol University.

The recent "Rockefeller Foundation - Lancet Commission on Planetary Health" highlights that global environmental change is a serious threat to human health. The Rockefeller Foundation - Lancet report, among many other reports, emphasizes the links between environmental health and human health. Models of climate changes have highlighted the need to built health scenarios. Here we will show how models of health risk scenarios, coupled with climate models, are becoming more complex and have gained predictive and heuristic power, moving from statistical models (such as distribution models based on the concept of environmental niche) to models including mechanisms or functional properties (such as epidemiological models integrating vector dynamics). The next phase of modeling will have to combine both climate change models. biodiversity change models (linked in particular to land use change) and models of health risks (infectious and non-infectious). Close collaboration between climatologists, ecologists, epidemiologists and social scientists will be necessary for their construction and validation. Retrospective analyses, comparative analyses based on phenomenological (statistical) models are a first step. However, scenarios should be produced from process - based models, using disease modeling and be policy-driven. Public policy and law can be integrated through their socio-ecological impacts.

Keyword: planetary changes, health forecasting, environmental change

11.00-12.30 Room C

S4: Universal influenza vaccine: where are we?

Chairpersons:

1. Bruce Innis





2. Punnee Pitisuttithum

Invited Speakers:



Thailand's influenza surveillance networks and response for pandemic influenza Malinee Chittaganpitch

National Institute of Health, Department of Medical Sciences, Ministry of Public Health, Thailand



Clinical development of universal influenza vaccines: a current perspective **Bruce L Innis**

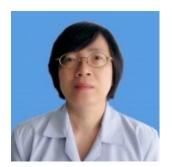
PATH, Center for Vaccine Innovation and Access, Seattle, WA, USA



Influenza pandemic preparedness: vaccine research and development **Punnee Pitisuttithum**

Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University

Thailand's influenza surveillance networks and response for pandemic influenza



Malinee Chittaganpitch¹, Sunthareeya Waicharoen¹, Thanutsapa Thanadachakul¹, Siripaporn Phuygun¹, Wandee Meechalad¹, Sirichol Kala¹, Busarawan Sirwanthana¹, Soawapak Hinjoy², Pawinee Doungngern², Somchai Sangkitporn ¹

¹National Institute of Health, Department of Medical Sciences, Ministry of Public Health, Thailand ²Bureau of Epidemology, Department of Disease Control, Ministry of Public Health, Thailand

Influenza surveillance in Thailand is continuously developed in the past decades. It has undertaken significant acceleration since 2004 with the US-CDC collaboration in response to the threats of avian influenza and the risk of pandemic influenza. Current influenza surveillance involves activities in public health and animal health sectors. Public health sector influenza surveillance has been developed and run under coordination and supervision by the Bureau of Epidemiology (BOE), Department of Disease Control (DDC) and the Department of Medical Science (DMSc). It's main component include routine disease reporting from health care facilities countrywide (506 reporting) which is mainly clinical based, whereas special sentinel-based surveillance for influenzalike illness (ILI) and severe acute respiratory infection (SARI), and event-based surveillance are supported by PCR testing, viral isolation and strain characterization, genome sequencing and antiviral drug sensitivity testing by the National Influenza Center (NIC) at the DMSc. For instance, NIC has been continued sharing influenza virus information to the global scientific community via WHO Flu-Net and Thai NIC website (www.thainihnic.org). Influenza virus shipment is annually sent to WHO CC for the selection of influenza vaccine strains composition. In 2015, one of virus strain in the WHO vaccine component. B/Phuket/3073/2013-like virus was detected from Thailand's influenza sentinel surveillance.

Keyword: influenza viruses, pandemic influenza, Flu-Net

Clinical development of universal influenza vaccines: a current perspective



Bruce L. Innis¹

There is wide interest in developing universal influenza vaccines to improve prevention and control of seasonal and pandemic influenza, especially in lowand middle-income countries (LMICs). The target product profile (TPP) for this transformative class of vaccines is: 1) broad protection against influenza A and B disease, 2) multi-year effect, 3) suitable for all ages including pregnant women, 4) affordability for LMICs. Several candidates are already in clinical development; currently, their ability to meet the TPP above is uncertain. Clinical development of a universal influenza vaccine will need to generate data supportive of two indications: 1) protection against seasonal influenza illness (A/H1, A/H3, B) and 2) active immunization against pandemic threat subtypes. The latter indication must rest on animal model studies. Vaccine development programs will require ≥10 years and be costly. Public-private partnerships offer one way to share cost and risk with manufacturers. Another is to qualify a candidate for clinical endpoint studies by first evaluating its efficacy against upper respiratory infection (while identifying immune markers predictive of protection) in a controlled human influenza virus infection model (CHIVIM). Thailand has critical capacity to do CHIVIM studies. Phase 3 development of a promising candidate will require large, multi-year studies to assess absolute and relative efficacy and safety, benchmarking against an approved influenza vaccines. These trials must be done where placebo controls are ethical due to absence of national influenza vaccine programs for targeted age groups. Thailand and its neighbors can play a vital role in development of universal influenza vaccines.

Keyword: Universal Influenza Vaccine, Development, Strategy

¹ PATH, Center for Vaccine Innovation and Access, Seattle, WA, USA

Influenza Pandemic Preparedness: Vaccine Research and Development



Punnee Pitisuttithum

Vaccine Trial Centre, Faculty of Tropical Medicine, Mahidol University

Pandemic influenza is a major health threat due to its potential of rapid global spread and devastating health and socioeconomic impacts. With the Emergence of highly pathogenic avian influenza H5N1 outbreaks in poultry in 2004 and pandemic spread of Influenza A H1N1 2009 around the globe including Thailand. There is a constant risk of the circulating avian influenza A viruses (eg. H5N1, H7N9) will lead to pandemics. One effective tool to stop the transmission is vaccine. WHO under Global Action Plan(GAP) has worked with developing country manufacturers to increase vaccine production capacity in the last nearly 10 years. Under WHO GAP, the monovalent live attenuated H1N1 2009 influenza vaccine have been developed, advanced to the clinical trial phase I and II. The LAIV H1N1 was proved to be safe and has received the Emergency Use Authorization (EUA) from Thai FDA1. The H5N2 LAIV vaccine was selected and manufactured thereafter as part of pandemic preparedness. As a results of phase I/II clinical trial in the isolation ward at the Vaccine Trial Center. The vaccine was safe, immunogenic, and was able to induce cross clade antibodies after receiving a booster dose of an inactivated H5N2 one year later2. The EUA was granted in 2015.

Although viruses of the A/ H5 and A/ H7 subtype are under the spotlight, prepandemic vaccine development is complicated by the continuous identification of novel zoonotic influenza virus. To cope with the antigenic diversity of A/ H5 GsGd viruses, the WHO has identified 38 vaccine candidates, of which 32 are already available for distribution. For A/ H7N9 viruses, three new candidate vaccines have been identified in 2017 to match the antigenic variation observed in recent A/ H7N9 viruses. There are remaining challenges in especially on vaccine strategies in preparation for next pandemic if occurs.

Keyword: influenza virus

11.00-12.30 Room D

\$5: Young Investigator Award

Chairpersons:

1. Saranath Lawpoolsri Niyom



2. Wirichada Pan-Ngum

Speakers:



A population dynamic model to assess and predict the burden of melioidosis in Thailand

Wiriya Mahikul

Department of Tropical Hygiene, Faculty of Tropical Medicine, Mahidol University



The role of cytokines and prediction of dengue complications

Hisham Imad

Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University



Broad-spectrum monoclonal antibodies targeted chikungunya virus structural proteins: promising candidates for rapid immunochromatographic kit development

Aekkachai Tuekprakhon

Mahidol-Osaka Center for Infectious Diseases (MOCID), Faculty of Tropical Medicine, Mahidol University



Mechanisms of diabetes mellitus and dengue fever co-morbidity revealed by integrated omics analysis

Nikhil Pathak

TIGP-Bioinformatics, Institute of Information Science, Academia Sinica, Taipei, Taiwan

A POPULATION DYNAMIC MODEL TO ASSESS AND PREDICT THE BURNEN OF MELIOIDOSIS IN THAILAND



Wiriya Mahikul,¹ Lisa J White,² Kittiyod Poovorawan,³ Ngamphol Soonthornworasiri,¹ Pataporn Sukontamarn,⁴ Phetsavanh Chanthavilay,¹ Graham F Medley⁵ & Wirichada Pan-ngum^{1,2*}

Thailand demography is in the transient phase with the aged population doubling within a decade. Melioidosis is a communicable disease, with transmission from environment, especially soil and water. Changes in the population structure and social impacts of life style changes reflecting in seasonal movement and underlying health status can influence the incidence of melioidosis. We examine changes in the age, sex, diabetes status, and seasonal movement on melioidosis using mathematical modelling. The model was fitted to the incidence of melioidosis reported by the national surveillance between 2008 and 2015. Our model predicted two-fold higher incidence rates of melioidosis compared with national surveillance data from 2015. The estimated incidence rates among males were two-fold greater than those in females. The melioidosis incidence rates in the Northeast region population, and among the transient population, were more than double compared to the non-Northeast region population. The highest incidence rates occurred in males aged 45-59 years old for all regions. The average incidence rate of melioidosis between 2005 and 2035 was predicted to be 10.78 to 12.04 per 100,000 population per year, with a slightly increasing trend. Overall, it was estimated that about half of all cases of melioidosis were symptomatic. The increasing trend of melioidosis incidence rates was significantly higher among working-age Northeast and transient populations, males aged ≥45 years old, and diabetic individuals. The model is useful to identify high risk groups and to guide targeted strategies to disease prevention and control.

Keyword: Melioidosis; dynamic model; diabetes; seasonal movement; aging

population; Thailand

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⁴ College of Population Studies, Chulalongkorn University, College of Population Studies, Chulalongkorn University, Bangkok, 10330, Thailand

⁵ Centre for Mathematical Modelling of Infectious Disease & Department of Global Health and Development, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, UK

The role of cytokines and prediction of dengue complications



Hisham Ahmed Imad¹, Weerapong Phumratanaprapin^{1*,} Benjaluck Phonrat¹, Prakaykaew Charunwatthana¹, Kesinee Chotivanich¹, Sant Muangnoicharoen¹, Srisin Khusmith², Terapong Tantawichien³, Eiji Konishi⁴ and Tatsuo Shioda⁵

Dengue is the most common mosquito-borne flaviviral infection in the world today. Several factors undoubtedly contribute to the developing of dengue complications. The plasma leakage mediated by the expressed cytokines, causes endothelial dysfunction, increasing vascular permeability and bleeding. We conducted a prospective study to elucidate the dynamic changes of cytokines during the acute phase in dengue infection to predict dengue complications. Dengue-infected adult patients admitted at the Hospital for Tropical Diseases were enrolled to this study.

We performed cytokine analysis at three phases of infection for 96 dengue-confirmed hospitalized adult patients during the outbreaks of 2015 and 2016. All enrolled patients were performed PCR for dengue serotypes. The serial serum concentrations of 6 cytokines (IL-4, IL-6, IL-8, IL-10. TNFa, IFNg) were measured in duplicate using a commercial kit for Human Bio-6 plex (BioRad, USA).

All four dengue serotypes were identified in our study, with DENV-4 the predominant serotype detected, and almost all participants had secondary dengue infections with a type 2 immune response. The significant dynamic changes of IL-8 during dengue infection associated with hemorrhagic manifestations, hepatomegaly and increased transaminitis. Hemorrhagic patients with plasma leakage had significantly higher levels of IL-8 during both at the acute and defervescence phase. Pro-inflammatory cytokine, TNFa, was significantly higher level during the acute phase in DHF when compared to DF in DENV-1 infection. Both IL-6 and TNFa were significantly elevated in the patients with bleeding and increased transaminitis.

In this study, we demonstrated that secondary dengue infection causes a robust Type 2 response. Our results showed a trend of elevated cytokines were seen in DHF. The dynamic changes of IL-6, IL-8 are associated with bleeding presentations in dengue.

Keyword: Dengue, plasma leakage, transaminitis, bleeding, cytokines

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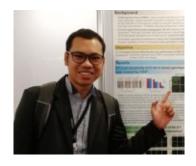
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Broad-spectrum monoclonal antibodies targeted chikungunya virus structural proteins: promising candidates for rapid immunochromatographic kit development



Aekkachai Tuekprakhon^{1,2}, Orapim Puiprom²¹, Tadahiro Sasaki²¹, Michael K. Meno², Emi E. Nakayama^{2,3}, Juthamas Phadungsombat², Koen Bartholomeeusen⁴, Ralph Huits⁵, Kevin K. Ariën^{4,6}, Natthanej Luplertlop¹, Tatsuo Shioda^{2,3*}, and Pornsawan Leaungwutiwong^{1*}

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In response to the aggressive global spread of the mosquito-borne chikungunya virus (CHIKV), an accurate and accessible diagnostic tool is of high importance. CHIKV, an arthritogenic alphavirus, comprises three genotypes: East/Central/South African (ECSA), West African (WA), and Asian. Although joint pain is the hallmark of this disease, accuracy of clinical diagnosis is limited due to the non-pathognomonic symptoms during acute phase of infection. A previous rapid immunochromatographic (IC) test detecting CHIKV E1 protein exhibited high performance for detection of ECSA genotype. Unfortunately, its performance was lower towards Asian genotype, currently in circulation in the Americas, reflecting the low avidity between one of the monoclonal antibodies (mAbs) in this IC kit and the variant E1-amino acid sequence of Asian genotype. To address this shortcoming, we aimed to generate a new panel of broad-spectrum mouse anti-CHIKV mAbs using hybridoma technology. Here, we report the successful generation of mouse anti-CHIKV mAbs targeting CHIKV E1 and capsid proteins. These mAbs possessed broad reactivity to all three CHIKV genotypes, with most mAbs lacking cross-reactivity towards Sindbis, Dengue, and Zika viruses. Accurate diagnosis is one of the keys to effective disease control and to date no antibody-based rapid IC platform for CHIKV is commercially available. Thus, the application of our characterized mAbs in the rapid diagnostic IC kit for CHIKV detection is highly prospective for clinical diagnosis and surveillance purposes

Keyword: Chikungunya virus, hybridoma technology, monoclonal antibody, antichikungunya virus E1 antibody, anti-chikungunya virus capsid antibody

¹These authors contributed equally to this work

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Mechanisms of diabetes mellitus and dengue fever comorbidity revealed by integrated omics analysis



Nikhil Pathak^{1,2}, Szu-Ying Wu^{3,4}, Yong-Chun Luo^{3,4}, Yen-Hsu Chen^{4,5}, Jinn-Moon Yang^{1,3,4}

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Recent clinical studies revealed that Diabetes mellitus (DM) patients co-infected with Dengue fever(DF) more likely progress to severe Dengue haemorrhagic fever (DHF) with blood plasma leakage and internal organ failure, which could lead to mortality. In the current work, we aimed to understand the underlying mechanisms of these DM-DF interactions during comorbidity using integrated "Disease-Gene-Pathway-miRNA Network" approach. First, we explored the gene expression data of DM and DF patients (public) to obtain the disease-associated significantly expressed geneset for each disease. We combined these genesets to obtain a "DM-DF associated geneset" representing the comorbidity. Most of these genes significantly related to the immune response, transcription and cell division processes. This geneset was then used to build a comprehensive DM-DF disease network exploring the pathways and the proteinprotein interactions involved. The pathways related to blood coagulation, wound healing, and viral processes were significantly affected. In the next step, significantly expressed DM-DF associated miRNAs obtained from miRNA omics data of DM and DF (public) were linked to the DM-DF gene network, resulting in a comprehensive "DM-DF Gene-Pathway-miRNA Network". This integrated network was used to identify potential biomarkers(miRNAs) for diagnosis or targets (genes) for therapy. To verify some of our findings, we analysed clinical blood samples (from DM-DF(DHF) comorbid vs DM, DF patients) using qRT-PCR to confirm some identified DM-DF miRNAs. Also, the DM-DF patient blood biochemical profiles verified the network findings. For ex., the modulation of blood coagulation and wound healing pathways in the network were directly reflected by the low white blood cells/platelets in DM-DF patient blood profiles, which could be a critical factor behind the DM-DF patient mortality. We thus believe that the comprehensive DM-DF network is critical in understanding the DM-DF mechanisms and for therapeutic interventions.

Keyword: DM-DF/DHF comorbidity; Significantly expressed genesets; Comprehensive integrated network; Blood Coagulation & wound healing; miRNAs

12.30-13.15 Room B

Lunch symposium: Tropmed Innovation: from research to products

Moderators:







2. Maneerat Ekkapongpisit

Panelists' discussion:



Translational research: from basic to rapid diagnostic kit for melioidosis

Narisara Chantratita

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

(No Abstract)



2. Young blood

Jetsumon Prachumsri and Wanlapa RoobsoongMahidol Vivax Research Unit (MVRU), Faculty of Tropical Medicine, Mahidol University

(No Abstract)



3. Development of Chikungunya virus-specific mouse mAb for advanced diagnosis **Pornsawan Leaungwutiwong**

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

(No Abstract)



4. Therapeutic human antibodies against dengue virus

Pongrama Ramasoota

Department of Social and Environmental Medicine, Faculty of Tropical Medicine, Mahidol University

(No Abstract)



5. Research to IMPACT: Bridging the GAP to Innovations

Maneerat Ekkapongpisit

Mahidol-Oxford Tropical Medicine Research Unit (MORU)

(No Abstract)

14.00-15.30 Room A

S6: Antimalarial Drug Discovery

Chairperson:

1. John Adams



2. Sasha Siegel

Invited Speakers:



Malaria egress as a drug target: progress and surprises

Michael Blackman

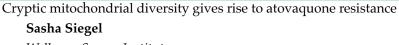
Department of Pathogen Molecular Biology, London School of Hygiene & Tropical Medicine



Structure of malaria parasite enzyme involved in folate synthesis

Amit Sharma

ICGEB, New Delhi, India



Wellcome Sanger Institute

Malaria egress as a drug target: progress and surprises



Michele SY Tan¹, James A Thomas^{1,2}, Christine R Collins¹, Fiona Hackett¹, Chrislaine Withers-Martinez¹, Claudine Bisson³, Trishant R Umrekar³, Aaron Borg⁴, Ambrosius P Snijders⁴, Gemma Vizcay-Barrena⁵, Roland A Fleck⁵, Helen R Saibil³, David A Baker² and **Michael J Blackman**^{1,2}.

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Clinical malaria requires replication of asexual blood stage malaria parasites, characterised by successive cycles of intraerythrocytic replication within a parasitophorous vacuole (PV), active egress of merozoites with associated host red blood cell destruction, and invasion of fresh red cells. Merozoite egress is tightly controlled by a parasite enzyme cascade in which activation of the single parasite cGMP-dependent protein kinase PKG triggers the discharge of a parasite serine protease called SUB1 into the lumen of the PV. SUB1 in turn activates a PV-located cysteine protease called SERA6 in *Plasmodium falciparum*. Whilst SUB1 is required for all the morphological changes that lead up to egress, including PV membrane rupture, SERA6 is essential only for the final step of red cell membrane rupture (Thomas, Tan et al. *Nature Microbiology* 2018). In this talk I will summarise this work and describe recent exciting and unexpected insights into the molecular mechanisms underlying egress as well as how ongoing attempts to target the egress pathway may provide new approaches to antimalarial drug discovery.

Keyword: malaria; egress; protease

Structure of malaria parasite enzyme involved in folate synthesis



Amit Sharma

ICGEB, New Delhi, India

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 and folate synthesis. 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. Using crystal structures of sulfadoxine drug target that catalyzes sequential metabolic reactions in the folate biosynthetic pathway, we will dissect the modes of action of some of the potent inhibitors.

Keyword: Drug, sulfadoxine, enzyme, structure

Cryptic mitochondrial diversity gives rise to atovaquone resistance



Sasha V. Siegel¹, Andrea Rivero², Swamy R. Adapa², ChengQi Wang², Roman Manetsch³, Rays H.Y. Jiang², Dennis E. Kyle⁴

¹Wellcome Trust Sanger Institute, Hinxton UK; ² Department of Global Health, College of Public Health, University of South Florida, Tampa, Florida, USA; ³College of Science and the Bouvé College of Health Sciences, Northeastern University, Boston, USA; ⁴Center for Tropical and Emerging Global Diseases, University of Georgia, Athens, GA, USA

Atovaquone (ATO) is a safe and effective antimalarial drug that acts on cytochrome b of the mitochondrial electron transport chain (mtETC) in Plasmodium falciparum. We phenotypically characterized P. falciparum isolates that failed in ATO phase II studies and found a surprisingly large spectrum of resistance (5-10,000-fold). The genetic mechanisms underlying the resistance spectrum is unknown because simple mutations in cyt. b cannot explain the large variation in phenotypes, and we hypothesized that heteroplasmy, the presence of multiple mitochondrial genomes, is responsible for this wide range of phenotypes. To discover pre-existing heteroplasmy at known drug resistance alleles we deep-sequenced paired admission and recrudescent isolates with high coverage (10-30,000x). Y268S heteroplasmy was detected at 1-2% frequency in pre-treatment (wild-type, ATO susceptible) patient isolates, which indicates that Y268S exists in parasites before drug pressure. In contrast, in ATO-resistant, drug-selected *P.falciparum*, a majority of mitochondrial copies were Y268S mutant, which indicates drug pressure increased Y268S copies due to mitochondrial heteroplasmy. To discover mitochondrial diversity globally, we analyzed publicly available P. falciparum genome data from the MalariaGEN Pf3K project to uncover heteroplasmic diversity in the ~2600 parasite collection. We estimated the mitochondrial copy number to be 20-26 copies, and found that diversity was underestimated at least 3-fold without considering heteroplasmy. Our study shows that ATO treatment failure in parasite populations can potentially be predicted with detection of low-level Y268S heteroplasmic alleles; the dynamics of heteroplasmy is important for the development of drug resistance to mitochondrial inhibitors.

Keyword : Atovaquone (ATO), *Plasmodium falciparum*, heteroplasmy

14.00-15.30 Room B

S7: Control of Parasitic Infections, from the Bench to the Field

Chairpersons:

1. Poom Adisakwattana





2. Aaron Je

Invited Speakers:



Taeniasis and cysticercosis in Asia: is chaotic situation through globalization or local? **Akira Ito**

Asahikawa Medical University, Asahikawa, Japan



'Omics approaches to understanding stress responses and metronidazole resistance in *Giardia*

Aaron Jex

The Walter and Eliza Hall Institute of Medical Research



Environmental DNA: a different approach for food/water-borne helminths studies

Marcello Otake Sato

Department of Tropical Medicine and Parasitology, Dokkyo Medical University



Back to the field: Ticks species distribution after half century of environmental changes and the risk for tick-borne diseases in Niigata Prefecture, Japan

Megumi Sato

Graduate School of Health Sciences, Niigata University



Effective, low-cost preservation of human stools for nucleic acid extraction, helminth detection and microbiome investigation

Katharina Stracke

The Walter and Eliza Hall Institute of Medical Research

Taeniasis and cysticercosis in Asia: Is chaotic situation through globalization or local?



Akira Ito¹, Tiaoying Li², Toni Wandra³, Kadek Swastika⁴, Umar Zein⁵, Paron Dekuymoy⁶, Kittipong Chaisiri⁶, Anu Davaasuren⁷, Tetsuya Yanagida⁸, Munehiro Okamoto⁹

¹Asahikawa Medical University, Asahikawa, Japan; ²Sichuan Centers for Disease Control and Prevention, Chengdu, Sichuan, China; ³Sari Mutiara Indonesia University, Medan, Indonesia; ⁴Udayana University, Denpasar, Indonesia; ⁵Islamic University of North Sumatra, Medan, Indonesia; ⁶University of Mahidol, Bangkok, Thailand; ⁷National Center for Communicable Diseases, Ulaanbaatar, Mongolia; ⁸Yamaguchi University, Yamaguchi, Japan; ⁹Kyoto University, Inuyama, Aichi, Japan

In Asian countries, three human Taenia species are known to be distributed mainly in remote and rural areas. The distribution is highly variable and often affected by the local traditional life styles including religions. Taeniasis is caused by ingestion of undercooked or uncooked pork (Taenia solium and Taenia asiatica) or beef (Taenia saginata and T. asiatica?). Detection of tapeworm carriers of T. saginaga and/or T. asiatica, compared with T. solium, is much easier, but microscopical detection of *Taenia* eggs is not so common as those of STHs, FBT or schistosomiasis in Asia. Without molecular identification of the species, it is impossible to differentiate which *Taenia* species are living in the carriers' intestines (*T. solium* vs two other *Taenia*). It had generally been conceived that taeniasis was very rare or eradicated from developed countries with better socioeconomic infrastructure by the end of 20th century. Almost all cases were believed as imported cases through visiting friends and relatives and tours to territories of ethnic people were living. However, through globalization with the increase in the number of laborers from endemic countries, the rebound of taeniasis, especially with *T. solium*, appears not to be rare with accidental confirmation of secondary cysticercosis. Among these three human Taenia species, T. solium is unique, since it exclusively causes cysticercosis by human to human transmission with eggs. No one knows T. solium until we face unexpected acute seizure attacks or confirm symptomatic NCC cases. As introduction of this session, the present situation of taeniasis/cysticercosis in Asia is overviewed.

Keyword : Taeniasis; Cysticercosis; *Taenia solium*; *Taenia asiatica*; *Taenia saginata*; Asia; Globalization

'Omics approaches to understanding stress responses and metronidazole resistance in *Giardia*



Aaron Jex1,2

- 1 Population Health and Immunity Division, the Walter and Eliza Hall Institute of Medical Research, Parkville, Australia
- 2 Faculty of Veterinary and Agricultural Sciences, the University of Melbourne, Parkville, Australia

Metronidazole is the frontline treatment for a range of anaerobes and microaerophiles, including Giardia. After decades of use, clinical resistance is reported for each of these important pathogens. Understanding the mode of resistance is central to developing methods to detect, monitor and control its spread and preserve this essential drug. As metronidazole is believed to function as a reactive metabolite causing widespread DNA, protein and lipid damage, metronidazole resistance is presumed to be multi-factorial and arising through multiple independent paths. In vitro studies to date support this, with little evidence of DNA encoded mutations or involvement of a single target or phenotypic change. Rather, these studies indicate multiple, divergent changes in the behaviour of core glycolytic and/or oxidative stress response genes associated with metronidazole activation and neutralization, which may be epigenetically regulated. We have adopted a varied 'omics-based approach to characterise metronidazole resistance in multiple Giardia isolates in vitro. We have compared these changes to responses to a variety of physiological stress conditions, including temperature, oxidative stress and protein misfolding. This work provides insight into the complexity of metronidazole resistance, identifies core changes that overlap with other microaerophiles and anaerobes and are likely most relatable to clinical resistance. I will discuss these findings, relate these to prospects for identifying clinically relevant mechanisms in Giardia and other microaerophiles and anaerobes and discuss advanced computation methods we are using to better understand the biology of infectious organisms.

Keyword : Giardia, metronidazole resistance, 'omics-based approach

Environmental DNA: a different approach for food/water-borne helminths studies



Marcello Otake Sato* ¹, Armand Rafalimanantsoa ², Megumi Sato ³, Tiengkham Pongvongsa ⁴, Toshifumi Minamoto ⁵, Jitra Waikagul ⁶, Tippayarat Yoonuan ⁶, Satoru Kawai ¹, Raffy Jay C. Fornillos ^{7,8}, Ian Kim B. Tabios ⁹, Lydia R. Leonardo ⁷, ¹⁰, Ian Kendrich C. Fontanilla ⁷, ⁸ & Yuichi Chigusa ¹

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Climate change, migrations, urbanization, and infrastructure construction are causes of landscape transformation, leading to environmental changes and creating emergent and reemergent challenges in infectious diseases, especially the neglected tropical diseases (NTDs) in ecotonal regions of the world. Among NTDs, opisthorchiasis causing cholangiocarcinoma and schistosomiasis causing chronic illness/liver fibrosis, are important food/water-borne diseases, their infective forms can be present in the daily life of everyone in endemic areas. Usually, the occurrence of NTDs is studied based on diagnosis in host materials, which provides data on disease status. However, information on environmental contamination with NTDs agents is a key in NTDs control programs, once with ecoepidemiology information, prophylactic measures can be taken to avoid infection. As a tool in NTDs' ecoepidemiology studies, we are using environmental DNA (eDNA) approach. Consisting of detecting specific DNA in water/soil samples. eDNA is currently used to investigate the diversity and distribution of organisms in ecology studies. We adapted the technique for studies in ecoepidemiology of parasites developing a system for eDNA detection of Opisthorchis viverrini, Schistosoma mansoni, S. japonicum and its hosts in water samples. We successfully detect O. viverrini and its fish hosts in endemic areas of Laos, S. mansoni in Madagascar, and S. japonicum/Oncomelania hupensis quadrasi in the Philippines, accurately determining their active transmission sites. The eDNA analysis, a new tool for surveillance/control of diseases in endemic areas, can point safe/unsafe sites in endemic areas, contributing to the water/food safety for the people and help to establish intelligent control programs for NTDs.

Keyword: one-health, eco-health, neglected tropical diseases, zoonosis, helminths, foodborne, waterborne, Southeast Asia, Africa, Madagascar

Back to the field: Ticks species distribution after half century of environmental changes and the risk for tickborne diseases in Niigata Prefecture, Japan



Megumi SATO¹, Marcello Otake SATO², Sumire IKEDA¹, Kozo WATANABE³, Maria Angenica F. REGILME³, Reiko ARAI⁴, Tsutomu TAMURA⁴

¹ Graduate School of Health Sciences, Niigata University; ² Department of Tropical Medicine and Parasitology, Dokkyo Medical University; ³ Department of Civil and Environmental Engineering, Ehime University; ⁴ Virology Division, Niigata Prefectural Institute of Public Health and Environmental Sciences

Ticks cause allergic reactions by feeding their hosts, but more importantly they are vectors of several infectious diseases transmitted to humans. There is a strict specificity of pathogen and tick species. Therefore, knowing the occurring tick species give us important hints on the tick-borne diseases of the region. Field surveys on ticks were conducted all over Japan until 1960's. The prevalent tick species were well understood. However, nowadays, tick research has been done based on tick-borne diseases occurrence (case-based research). In Niigata Prefecture, the last field study was done during 1956-57. After 60 year's blank period, we are returning to the field to determine tick species and their related pathogens occurrence. We collected 940 ticks in total, during April to December 2016 in 22 locations in Niigata Prefecture. The tick species occurrence in 1950's and 2016 were different. Species generally prevalent in warmer areas could be seen in Niigata's 2016 survey. This tick species swift might be influenced by environmental change such as global warming, migration of host species and land usage. Several important tick-borne infectious diseases agents are known in Japan, such as SFTS virus, Japanese spotted fever Rickettsia and Borrelia spp. Their occurrence was restricted mostly to western part of Japan, however recently this tendency is changing, and the cases start to spread to eastern part of Japan. Tick and pathogens have strict host specificity, then knowing tick species in the area is guite important to prevent/prepare for those infectious diseases in public health aspects.

Keyword: tick, tick born diseases, environmental change

Effective, low-cost preservation of human stools for nucleic acid extraction, helminth detection and microbiome investigation



Stracke K¹, Adisakwattana P², Phuanukoonnon S³, Yoonuan T², Poodeepiyasawat A², Roth Schulze A¹, Wilcox S¹, Karunajeewa H¹, Traub R⁴, Jex A^{1,4}

Molecular tools are a cornerstone of diagnostic and epidemiological studies. However, they are no better than the quality of samples they are used on. Studies of gastrointestinal infections and the impacts of infection or diet on gut microbial health require rapid sample processing and/or effective preservation of a range of molecular media, including DNA, RNA and proteins. This preservation must introduce minimal disruption or bias into the data. These challenges are particularly difficult in the field of neglected parasitic infections, which overwhelmingly affect impoverished populations in remote, tropical to subtropical, regions globally. Rapid refrigeration or freezing of samples upon collection is often not feasible and costs associated with commercial preservatives are prohibitive. We have investigated three low-cost preservation methods, DESS (DMSO, EDTA, NaCl), 2.5% potassium dichromate and rapid freezing at -80°C for nucleic acid and protein preservation, qPCR-based diagnosis of helminth infection and microbiome characterisation in a crosssectional study of pre-school and school-aged children from an endemic region in North-West Thailand. All three preservatives had similar performance in microbiome preservation, whereas DESS provided the best performance for helminth preservation. Currently, we are testing if faecal samples preserved in DESS can be used for extraction of high quality RNA and proteins.

Keyword : Soil-transmitted helminths, sample preservation, MT-PCR, fecal microbiome

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³Social and Environmental Medicine, Faculty of Tropical Medicine, Mahidol University, 420/6 Ratchawithi Road, Ratchathewi Bangkok 10400, Thailand;

^⁴Faculty of Veterinary and Agricultural Sciences, The University of Melbourne, Flemington Rd, Parkville, Victoria 3052, Australia

14.00-15.30 Room C

S8: Mycobacterium: Novel approaches for diagnosis and treatment

Chairpersons:

1. Wirongrong Chieraku





2. Narisara Chantratita

Invited Speakers



Blood transcriptomics for TB diagnosis and monitoring treatment-response **Jackie Cliff**

London School of Hygiene & Tropical Medicine



Diagnosis for adult-onset immunodeficiency with non-tuberculous mycobacterial Infections and autoantibodies against interferon-gamma

Ganjana Lertmemongkolchai

Department of Clinical Immunology, Khon Kaen University

(No Abstract)



Development of interferon gamma release assay for elephant TB Diagnosis

Tanapat Palaga

Faculty of Science, Chulalongkorn University



Antitubercular natural products and synthetic agents against clinical multidrug resistant isolates of mycobacterium tuberculosis

Prasat Kittakoop

Chulabhorn Research Institute

Blood transcriptomics for TB diagnosis and monitoring treatment-response



Jackie Cliff

London School of Hygiene & Tropical Medicine

The peripheral immune system is altered in tuberculosis patients compared to healthy control individuals, and this is reflected in different gene expression profiles in blood. Genes involved in inflammation and the innate interferon response exhibit upregulated expression, whereas adaptive immunity-related genes have reduced expression. Such alterations in gene expression might be developed into sensitive diagnostic markers for active tuberculosis. Furthermore, the blood transcriptome changes during successful tuberculosis drug treatment, with a rapid down-regulation of innate immunity gene expression and a slower resolution of the adaptive immune system gene expression. Measurement of these changes in gene expression could be used as host-based biomarkers of tuberculosis drug efficacy, facilitating and expediting clinical trials of new drugs and regimens.

Recently, we have found that the blood transcriptome is even further disturbed in people with tuberculosis and diabetes comorbidity, with an exacerbated proinflammatory response and a reduced interferon response, and with altered expression kinetics during treatment. These differences potentially contribute to the enhanced susceptibility to tuberculosis in people with diabetes, alongside poor tuberculosis treatment outcomes in this group. They also suggest the potential for host-directed therapy.

Keyword: Blood transcriptomics, TB diagnosis, monitoring

Development of interferon gamma release assay for elephant TB Diagnosis



Songkiat Songthammanuphap ¹, Wandee Yindeeyoungyeon ², Wanlaya Tipkantha³, Songchan Puthong ⁴ and **Tanapat Palaga** ¹

Tuberculosis is a serious disease for both human and some animals. Various wild animals in captivity including elephants have been reported to be infected with M. tuberculosis (MTB) complex, which can cause tuberculosis in animals. Elephants can be latently infected with the bacteria and often do not show clinical symptoms until the animals become ill at an active stage. Because elephants have a large and thick skin, the common diagnosis approaches used in human such as chest X-ray and tuberculin skin test are not applicable. Moreover, the bacteria culture from trunk wash, which is the current gold standard for tuberculosis diagnosis has low sensitivity, is timeconsuming and can only diagnose active tuberculosis. Specific antibody response, although easy to do, often yields results with low consistency and accuracy. Therefore, an accurate TB diagnosis in elephants is needed. Interferon gamma release assay (IGRA) is an alternative approach for tuberculosis diagnosis for latently infected individual. The assay detects the interferon gamma (IFNy) secreted from white blood cells stimulated with specific MTB antigens. In this study, a sandwich ELISA using inhouse polyclonal and monoclonal antibodies against elephant IFNy were developed. The developed IGRA was validated using PBMC from an elephant confirmed to be positive for MTB infection. The sensitivity of the IGRA assay is in the range of 0.16 - 10 ng/mL. PBMC from elephants from various regions were stimulated with PPD from M. bovis or M. avium or recombinant MTB antigens and the released IFNg were determined. Among 75 samples tested, 46 samples were found positive (61.3%) while the rest were found negative or indeterminated. Compared to the results obtained from commercially available DPP® VetTB Assay for elephants, our inhouse IGRA detected higher rate of immune positive response (76% vs 8%). Taken together, we believe that our elephant IGRA presents a more sensitive assay to detect latently infected TB in elephants. This test kit may be useful for future health management of elephants in captivities.

Keyword: tuberculosis, elephant IFNy, ELISA, IGRA

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²The National Center for Genetic Engineering and Biotechnology, National Science and Technology Development Agency

³Endangered Species Conservation & Research Institute, Zoological Park Organization

⁴Institute of Biotechnology and Genetic Engineering, Chulalongkorn University

Antitubercular Natural Products and Synthetic Agents against Clinical Multidrug Resistant Isolates of *Mycobacterium tuberculosis*



Prasat Kittakoop 1,2,3,*

¹Chulabhorn Graduate Institute, Chemical Biology Program, Chulabhorn Royal Academy, Kamphaeng Phet 6 Road, Laksi, Bangkok 10210, Thailand

World Health Organization (WHO) reveals that tuberculosis (TB) is one of the leading causes of death worldwide. In 2017, there were 10 million patients with TB; 1.6 million people infected with TB died in 2017. WHO reported that multidrug-resistant TB (MDR TB) has caused a major public health problem. Although there are increasing numbers of TB incidence rate worldwide, a few anti-TB drugs are currently available for first-line and second-line TB therapies. There has been only one new anti-TB drug (approved in 2012) since 1960s. Recently, there are increasing numbers of MDR TB, and this implies that Mycobacterium tuberculosis might rapidly resist the new drugs that are redesigned from the existing chemical scaffolds of the currently used anti-TB drugs. Therefore, there is an urgent need to find new chemical scaffolds with potent antimycobacterial activity; these new scaffolds could be useful for the development of effective anti-TB drugs. Antimycobacterial activity of both natural products and synthetic compounds against *M. tuberculosis*, as well as against MDR TB isolates of *M. tuberculosis*, is presented in this lecture. Some natural products and synthetic compounds were found to be potential anti-TB lead compounds.

Keyword: Natural Products, MDR TB, Mycobacterium tuberculosis

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Wednesday 12 December 2018

14.00-15.30 Room D

S9: Helminthiases: rare, ancient and common helminthes

Chairpersons:

1. Chen Jia-Xu





2. Paron Dekumyoy

Invited Speakers:



Cerebral toxocariasis and neurodegenerative diseases

Chia-Kwung Fan

College of Medicine, Taipei Medical University

Speakers:



Community-based intervention using PRECEDE-PROCEED model framework for controlling *Opisthorchis viverrini* infection: a propensity score matching analysis

Picha Suwannahitatorn

Phramongkutklao College of Medicince



Dioctophyma renale, the biggest, the oldest and still the most neglected zoonotic nematode

Yukifumi Nawa

Tropical Diseases Research Center, Faculty of Medicine, Khon Kaen University

Status of food-borne parasitic diseases in China



Jia-Xu Chen

National Institute of Parasitic Diseases, China

Food-borne parasitic diseases have become one of the public health problems for social economy, health care and food safety. In this presentation, we will give an overview on the epidemiological information of some major foodborne parasitic diseases, such as clonorchiasis, taeniasis/cysticercosis, trichinosis and toxoplasmosis, etc. in China, and summarize their emerging characteristics and epidemiological trends. Research on the prevention techniques and pathogenesis of the diseases is reviewed as well. Finally, perspectives are given on the diagnosis/detection, basic mechanisms of the diseases, and the strategies for prevention and transmission interruption. This chapter summarizes information on the epidemic features, diagnosis, and technologies of food-borne parasitic diseases in China. Meanwhile, perspectives are given on the strategies for prevention of food-borne parasitic diseases, combined with foreign management and regulation. The major food-borne parasites are divided into seven groups, including meat-borne, plant-borne, shellfish-borne, fish-borne, mollusc-borne, water-borne, and reptile- and amphibian-borne parasites. Diagnostic methods for food-borne parasites rely on the use of morphological identification and remain highly dependent on light or electron microscopy, which can provide a useful confirmation of clinical infection, and can also be used in surveys of food-borne parasites in endemic regions. Surveillance for parasitic diseases is complicated by the often prolonged incubation periods, sub-clinical nature and unrecognized, chronic sequelae. Education and increasing awareness were identified as important components of foodborne parasite control and, in some cases, may be the only feasible options available.

Keyword: food-borne, parasites, China

Cerebral toxocariasis and neurodegenerative diseases



Chia-Kwung Fan

Department of Molecular Parasitology and Tropical Diseases, School of Medicine, College of Medicine, Taipei Medical University, Taipei, TAIWAN

Toxocara canis and T. cati are highly prevalent nematode infections of the intestines of dogs and cats. In paratenic hosts, larvae do not mature in the intestine but instead migrate through the somatic tissues and organs of the body. The presence of these migrating larvae can contribute to pathology. Toxocara larvae can invade the brains of humans, and while case descriptions of cerebral toxocariasis (CT) are historically rare, improved diagnosis and greater awareness have contributed to increased detection. Despite this, CT remains a poorly understood phenomenon. Furthermore, our understanding of cognitive deficits due to CT in human populations remains particularly deficient. From murine studies, our findings indicate although there were insignificant differences in learning and memory function between the experimental mice and uninfected control mice, possibly because the site where T. canis larvae invaded was the surrounding area but not the hippocampus per se. Nevertheless, enhanced expressions of neurodegeneration-associated factors (NDAFs), including transforming growth factor (TGF)-\(\theta\)1, S100B, glial fibrillary acidic protein (GFAP), transglutaminase type 2 (TG2), claudin-5, substance P (SP) and interleukin (IL)-1β, persistent impairment of ubiquitin-proteasome system (UPS) and excess amyloid β (Aβ) accumulation concomitantly emerged in the experimental mice hippocampus at 8, 16 and 20 weeks post-infection. We thus postulate that progressive CT may still progress to neurodegenerative diseases e.g., Alzheimer's disease due to enhanced NDAF expressions, persistent UPS impairment and excess AB accumulation in the hippocampus.

Keyword : *Toxocara canis, T. cati, c*erebral toxocariasis, neurodegenerative diseases

Human fascioliasis in China



<u>Lin Ai</u>

National Institute of Parasitic Disease Control, China

Fascioliasis has emerged as a significant public health problem among ruminants and humans. Human fascioliasis is a neglected food-borne parasitic disease, which has emerged or reemerged in more than 60 countries worldwide. In China, the first case of human fascioliasis was reported in 1921 in Fujian Province. The first major outbreak of this parasitic disease in 29 patients occurred in 2012 in Yunnan Province. Nonetheless, the prevalence of fascioliasis in China is probably underestimated due to poor sensitivity of diagnostic tests, limited epidemiological data, and a poor understanding of the impact of subclinical illness. Herein, we summerized the prevalence of fascioliasis in China in order to improve the prevention and control of this disease.

Keyword: fascioliasis, human, food-borne, China

Prevalence, intensity and spatial distribution of soil transmitted helminthiasis and water, sanitation and hygiene resource in Ogun State, Nigeria



<u>**Hammed M**</u>^{1,2}, Gabriel D³, Babatunde B³, Samuel B³, Uwem E^{1,3}

¹Spatial Parasitology and Health GIS group, Abeokuta, Nigeria; ²Federal Univ. Oye-Ekiti, Ekiti, Nigeria, ³Federal Univ. of Agriculture Abeokuta, Ogun State, Nigeria

Soil Transmitted Helminthiasis (STH) is one of the major public health problem in Nigeria. Efforts channeled towards complimenting preventive chemotheraphy with provision WASH resources have been hampered by lack of empirical evidence on transmission hotspots. To this end, a cross-sectional study involving 1,499 households across 33 communities was conducted in Ogun State. Field visitations were made to recruited households and condition of WASH resources were assesed using WHO/UNICEF set standards. 1027(68.5%) of the sampled households provided feacal samples for laboratory examinations for STH ova using ether concentration. The WASH and STH data were compiled into a GIS database and subjected to preliminary descriptive statistic. Spatial Maps were constructed using ArcGIS software. Of the 20 LGAs examined, 19(95.0%) were endemic for one or more kind of the three main STH species (except ljebu-Ode). Ascaris lumbricoides infections are the most geographically distributed species, found in 28/33(84.8%) locations and in 19LGAs. Hookworm was present in 19/33(57.6%) locations and in15LGAs. Trichuris trichiura infection was found in 9/33(27.3%) locations and in 7LGAs. An overall cumulative score of 52.9% was recorded for WASH resource conditions. The percentages score ranges between 65.7% and 38.6% across the LGAs. By categories, cumulative scores of 64.1%, 32.8%, 69.0% and 49.3% was recorded for water, sanitation, household hygiene and individual hygiene respectively. Findings from this study will serve as decision-support visual tool for Ogun State programme managers to help facilitate integration of STH control into WASH resource programming efforts.

Keyword : Soil Transmitted Helminthiasis, WASH, Prevalence

Community-based intervention using PRECEDE-PROCEED model framework for controlling *Opisthorchis viverrini* infection: a propensity score matching analysis



Suwannahitatorn P

Phramongkutklao College of Medicince

Fieldworks conducted in Ta-Kadarn Subdistrict located in Chachoengsao Province indicated that prevalence and incidence of *Opisthorchis viverrini* (OV) infection were high considering the studied areas were outside the endemic Northeastern Thailand and there was significant association of *Koi pla* consumption, an uncooked fish menu, with increased risk for acquiring infection. The PRECEDE-PROCEED model framework was applied to the community to systematically engage the problem with the aim of reducing the incidence of OV infection through behavioral modification by decreasing *Koi pla* consumption.

Intervention and control groups were matched by propensity score matching. The intervention group participated in community-derived mutual agreement to discontinue *Koi pla* consumption. After the 17-month study period, both groups were evaluated for OV infection by stool examination and *Koi pla* consumption was assessed by questionnaire.

The results indicated that community intervention could significantly reduce incidence of OV infection by 63% (95% CI: 7 - 85), p = 0.03 and reduce *Koi pla* consumption by 46% (95% CI: 1 - 71), p = 0.04.

Consumption behaviors were complex involving traditional beliefs, attitudes and diverse cultural backgrounds. Following the PRECEDE-PROCEED framework, community participatory action including community-derived intervention was considered adaptive and practically suited to villagers' lifestyles. Local health volunteers were originally community members and could play an important role as a reinforcing factor. The PRECEDE-PROCEED model framework also provided a comprehensive approach for intervention/evaluation planning.

Keyword : PRECEDE-PROCEED; propensity score matching; intervention;

community; Opisthorchis viverrini

Dioctophyma renale, the biggest, the oldest and still the most neglected zoonotic nematode



<u>Yukifumi Nawa</u>¹, Jorge Costa Eiras², Xin-Quan Zhu³, Natalia Yulrova⁴, Masahide Yoshikawa⁵

Diocophyma renale, also known as the "giant kidney worm" is a nematode parasite of canines. As its name, this nematode parasitize in the kidney of dogs for many years and become extremely large, sometimes reach 1 m in length. It was first described by Francesco Redi in 1645 in his famous book of "Osservazioni intorno agli animali viventi che si trovano negli animali viventi" as an extraordinary huge worm in the kidney of a dog. The lifecycle of this parasite is simple; the earth worms as the intermediate host and the canine or some other carnivorous mammals as the final host. Eggs produced by mature female worms in the kidney are shed in urine and embryonated in water, ingested by intermediate host earthworms. The infective larvae in earthworms are often ingested by paratenic hosts such as fish or frog in that the larvae encyst and do not develop any further. When humans ingest raw or undercooked fish meat containing larvae, they migrate into the kidney to become mature worms. Human infection is extremely rare but sporadically distributed worldwide. In recent English literature, human cases are estimated to be around 20. However, when we have conducted extensive literature survey, over 70 cases were recorded. Before the 1960s, most of cases were found in Europe and guite few in Asia. However, after the 1970s, large number of cases were reported in China in local journals. Some mysterious epidemiology of this nematode parasite will be discussed in detail.

Keyword: Dioctophyma renale, zoonosis, fish-borne nematodiasis, human cases, literature review

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Wednesday 12 December 2018

16.00-18.00 Room A

S I 0: Malaria Elimination Task Force, Malaria Elimination on the frontline, Impact and Challenges (Organized by SMRU)

Chairpersons:

1. Gilles Delmas



2. Lorenz von Seidlein

Speakers:



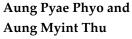
Introduction to, strategy of METF and impact on malaria elimination: A regional *P. falciparum* elimination program in Eastern Kayin State, Myanmar: impact of generalized access to early diagnosis and treatment and targeted mass drug administration

Gilles Delmas

Shoklo Malaria Research Unit (SMRU)



Trends of artemisinin-combination therapy resistance on the Thailand-Myanmar border



Shoklo Malaria Research Unit (SMRU)



Community engagement in malaria elimination

Ladda Kajeechiwa

Shoklo Malaria Research Unit (SMRU)



Importance of monitoring and evaluation to frontline structures

Suphak Nosten

Shoklo Malaria Research Unit (SMRU)



Entomological determinants of malaria elimination

Victor Chaumeau

Shoklo Malaria Research Unit (SMRU)

(No Abstract)



Malaria elimination task force *in silico* (Modelling)

Lisa White

Mahidol-Oxford Tropical Medicine Research Unit (MORU)



Scaling up targeted malaria elimination: opportunities and challenges

Lorenz von Seidlein

Mahidol-Oxford Tropical Medicine Research Unit (MORU)

Introduction to, strategy of METF and impact on malaria elimination: A regional *P. falciparum* elimination program in Eastern Kayin State, Myanmar: impact of generalized access to early diagnosis and treatment and targeted mass drug administration



Jordi Landier¹, Daniel M Parker¹, Aung Myint Thu¹, Khin Maung Lwin¹, **Gilles Delmas**^{1,2}, François Nosten^{1,2} for the Malaria Elimination Task Force Group.

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 2018, 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 58 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 48 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: METF, malaria elimination, Kayin State, Myanmar, mass drug administration

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² Centre for Tropical Medicine and Global Health, Nuffield Department of Medicine, University of Oxford, Oxford, UK.

Trends of Artemisinin-Combination Therapy resistance on the Thailand-Myanmar border



Aung Pyae Phyo¹, Aung Myint Thu², Tim J C Anderson³, Zbynek Bozdech⁴, Stephan Proux², Kanlaya Sriprawat², Mallika Imwong^{5,6}, Jordi Landier², Charles J Woodrow^{5,7}, Rose McGready^{2,5,7}, Khin Maung Lwin², Verena Ilona Carrara², Elizabeth Ashley^{1,5,7}, Nicholas J White^{5,7}, Nicholas P J Day^{5,7}, Francois Nosten^{2,5,7}

Global malaria burden has significantly declined chiefly due to the highly efficacious Artemisinin Combination Therapy (ACT). ACT had been deployed at Thailand-Myanmar border since 1990s\' and was a principal determinant for malaria elimination. However, artemisinin resistance had emerged on the Thai-Cambodia border and now parasites with K13 molecular markers (of artemisinin resistance) are wide-spread in the Greater Mekhong Sub-region. The prevalence of wild-type genotype for K13 was significantly declined on the Thailand-Myanmar border (over 90% in 2003 to 16% in 2014). Between 2014 and 2017, a scaled-up programme (Malaria Elimination Task Force) was implemented in Southeastern Myanmar to eliminate the drug reistant *P. falciparum* malaria preventing the further spread. The prevalence of wild-type genotype for K13 molecular markers was not increased over the three years in malaria elimination project area. In Myanmar, the therapeutic efficacy of ACT\'s are still high above 90% in the country though continuing vigilance is necessary, as the K13 mutations associated with artemisinins resistance has reached the Myanmar-India/China border.

Keyword: artemisinin, ACT, artemisinin resistance, Kelch, K13

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Community engagement in malaria elimination



Ladda Kajeechiwa

Shoklo Malaria Research Unit, Mae Sot, TAK, Thailand

Following a pilot phase, the METF has launched an ambitious malaria elimination project in Karen state (Myanmar). From the onset, community engagement emerged as the most important determinant of success. In this rural, remote population, affected by decades of conflict and political instability, gaining the trust and the support of the communities is complex and difficult. Given the absence of a conceptual framework adapted to this population, we developed our own approach and we determined some key basic notions such as the history of the people, their space and work, their knowledge of the world their believes, their relationship with health care structures but also their migration patterns, their economic systems and most importantly the power relations

Keyword: Community engagement, malaria elimination, Karen Myanmar

Importance of monitoring and evaluation to frontline structures



Jade D. Rae¹, **Suphak Nosten**¹, Stéphane Proux¹, Aung Myint Thu¹, Naw Win Cho Cho¹, Naw K'Nyaw Paw¹, Naw Eh Shee Paw¹, Naw Paw Bway Shee¹, Saw Aye Be¹, Saw Hsa Dah¹, Saw Ku Ler Moo¹, Saw Myo Chit Minh¹, Paw Wah Shee¹, Jacher Wiladphaingern¹, Saw Win Tun¹, Ladda Kajeechiwa¹, May Myo Thwin¹, Gilles Delmas^{1,2}, François H. Nosten^{1,2}, Jordi Landier¹.

Background

Improving access to early diagnosis and treatment (EDT) is increasingly proven to be a major contributor to decreasing malaria incidence in low-transmission settings. The Malaria Elimination Task Force has deployed malaria posts set up in Eastern Myanmar, providing free uninterrupted community-based access to EDT in more than 1200 villages. This aims to determine the functionality of the malaria posts in this program.

Methods

We analysed routinely collected data (weekly reports, individual consultation, and data collected specifically during monitoring and evaluation visits). The presence of major or minor dysfunctions and the ability to anticipate dysfunctions through analysis of weekly reports were assessed.

Results

A total of 64.60% of malaria posts had no major dysfunction identified during monitoring and evaluation visits, while 85.69% of malaria posts were fully stocked with tests and treatments. Knowledge of treatments by malaria post workers showed few gaps, mostly in the treatment of more complex presentations. Malaria posts were well utilized in the population, with 94% of consultations occurring within the first 3 days of fever. Reported stock-outs and delayed reports were associated with observed dysfunctions in M&E visits, emphasizing the need to reinforce support to malaria post supervisors, responsible for the local logistics of supply, data transmission and day-to-day supervision.

Conclusion

The malaria posts operating under the METF program perform to a high standard, and high service uptake in the villages serviced by the program. However, program operations can be strengthened through improvements to the frequency of malaria post supervisor visits and in the re-training of malaria post workers.

Keyword: Malaria elimination, Falciparum, Monitoring, Myanmar

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Malaria Elimination Task Force in silico



<u>Lisa White</u> and Ricardo Aguas¹

Mathematical and Economic Modelling (MAEMOD), Mahidol-Oxford Tropical Medicine Research Unit, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

A mathematical model was developed to simulate the Malaria Elimination Task Force (METF) activities in Myanmar. The model created a synthetic population of individuals clustered within villages. The villages were linked in a similar way to those in the study area in terms of *P.falciparum* malaria transmission. The purpose of the model was to reproduce the observed decreases in malaria infection, to explore the relative contribution of the activities (early clinical case detection and treatment, mass drug administration) and to simulate alternative designs for both future trials and programmatic implementation.

Keyword: malaria; elimination; mathematical model

Scaling up targeted malaria elimination: opportunities and challenges



Lorenz von Seidlein

Targeted malaria elimination includes generalized access to early diagnosis and treatment, long lasting insecticide treated bednets, and targeted mass drug administration. Much progress has been made using targeted malaria elimination in select areas of the Greater Mekong Subregion (GMS) which creates opportunities to replicate this success in other regions. Yet there remain challenges including appropriate investments and political will. There are also technical guestions which require future research. Which drug regimens are must suitable for mass drug administrations. The preferred antimalarial drug, dihydroartemisinin+piperaquine (DHA/pip) is becoming increasingly compromised by multidrug resistance. Other antimalarials such as artemether+lumefantrine or artesunate+pyronaridine have a distinctly shorter half-life than DHA/pip which make them less suitable for mass drug administrations. Second the success of mass drug administrations depends not only on the drug regimen but also on the coverage. Factors influencing populations to participate in interventions such as mass drug administrations are difficult to understand. Third the lifestyle of the main disease vectors, daytime outdoor biting makes bednets much less effective in the GMS compare to subSaharan Africa. Novel research approaches address these challenges and may allow us to adapt targeting malaria elimination to the regions aiming to eliminate malaria by 2030.

Keyword: Mass drug administration, Greater Mekong Subregion, Community engagement, Politics, Governance

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Wednesday 12 December 2018

16.00-17.30 Room B

SII: Updates on Dengue and Zika virus infections

Chairpersons:

1. Toshio Hattori





2. Pornsawan Leaungwutiwong

Invited Speakers:



Detection of degraded form of matricellular proteins in vitro and in vivo. **Toshio Hattori** *KIBI International University*



Performance of a rapid diagnostic test using the single-tag hybridization chromatographic printed array strip format in the detection of dengue infection in the emergency room

Maria Luisa Daroy

St. Luke's Medical Center College of Medicine



Two ways that non-coding DENV RNA enhances mosquito transmission **Julien Pompon**

Duke-National University of Singapore Medical School



A multiplex diagnostic platform for detection of Zika virus infection in a cohort of febrile patients from Thailand

Lauren Ching

University of Hawaii at Manoa, Honolulu, Hawaii

Detection of degraded form of matricellular proteins in vitro and in vivo.



<u>Toshio Hattori</u>¹, Gaowa Bai¹, Hirotoshi Motoda¹, Takashi Matsuba² and Toishiro Niki³

- 1: Graduate School of Health Science Studies, Kibi International University
- 2: Division of Bacteriology, Department of Microbiology and Immunology, Faculty of Medicine, Tottori University, Yonago, Tottori, Japan
- 3: Department of Immunology, Faculty of Medicine, Kagawa University

Introduction:We have previously reported that both osteopontin (OPN) and galectin-9 (Gal-9) were correlated with the severity of the dengue patients (J Clin. Virol 2013;Thromb. Res 2014). Because both proteins have protease cleavage site, we investigated if the cleaved product have different functional roles. Results: OPN: Various forms of OPN were identified in human monocytic THP-1 cells stimulated by phorbol 12-myristate 13-acetate (PMA). The antibody specific to thrombin-cleaved site of OPN (34E3) detected a distinct band corresponding to 18 kD, indicating that OPN cleavage occurred by endogenous proteases in the PMA-stimulated THP-1 cells. The cleavage was enhanced by BCG infection.

Gal-9: By comparing two elisa system (The R&D and GalPharma) the former showed a 50-fold higher median concentration of plasma Gal-9 than that shown by the latter in normal individuals. This variation is due to aberrantly enhanced reactivity of the R&D Systems' ELISA to degraded Gal-9 present in small quantities in the plasma. The GalPharma ELISA could detect only intact Gal-9 and its results correlated well with the plasma Gal-9 level obtained by western blotting. ELISA kits from R&D Systems reacts aberrantly higher against degraded product.

Discussion: These results indicate that matricellular proteins represented by OPN and Gal-9 are cleaved and generate new cleaved form. The OPN is known to facilitate the proliferation of dengue or HCV and the inhibition of the synthesis may be the therapeutic target. We have previously shown that the levels of full length Gal-9 reflect disease severities of dengue and malaria. It should also be clarified whether the cleaved form also correlate to them or not.

Keyword : Dengue, malaria, osteopontin, galectin-9, proetase

Performance of a rapid diagnostic test using the single-tag hybridization chromatographic printed array strip format in the detection of dengue infection in the emergency room



Maria Luisa G. Daroy¹, Maria Terrese A. Dimamay¹, Veni R. Liles¹, Lady-Anne S. Pangilinan¹, Rachel S. Reyes¹, Mick Kelvin Bulusan¹, Mark Pierre S. Dimamay¹, Paolo Antonio S. Luna², Abigail Mercado², Haorile Chagan-Yasutan³, Yutaka Takarada⁴, Mitsuo Kawase^{3,4}, and Toshio Hattori^{3,5}

¹Research and Biotechnology Group, and ²Department of Emergency Medicine, St. Luke's Medical Center, Philippines; ³ Japan Graduate School of Biomedical Engineering, Tohoku University, Japan; ⁴Tohoku Bio-Array Co., Ltd., Japan; ⁵KIBI International University

Introduction: A novel rapid diagnostic test for dengue, the DENV Nucleic Acid Chromatography Universal Primer Kit and Single-Tag Hybridization – Printed Array Strip system was evaluated for its analytical and clinical performance in the early detection of dengue from peripheral blood.

Methods: The analytical performance of the test method was determined in a retrospective study using stored RNA samples previously identified to carry all 4 serotypes of dengue virus, chikungunya virus and influenza virus. Clinical performance was also assessed in a prospective study using plasma from febrile cases presenting at the Emergency Room for medical assistance, and 30 afebrile normal healthy volunteers. A Tagman real-time RT-PCR assay and a rapid dengue test, SD Dengue Bioline Duo, were used as comparator tests. Results and Discussion: Analytical performance of the DENV Nucleic Acid Chromatography Universal Primer Kit and Single-Tag Hybridization - Printed Array Strip System exhibited 100% sensitivity, 93.75% specificity, and a diagnostic accuracy of 97.84%. On samples taken from febrile cases at the Emergency Department, it showed 100% sensitivity and 88.9% and 86.6% specificities, compared to the Tagman real-time RT-PCR and SD Dengue Duo NS1 test, respectively. This report on the highly sensitive STH-PAS system for the rapid detection of dengue in stored and freshly collected clinical samples may serve as a basis for its selection as a laboratory assay to confirm the clinical diagnosis of dengue. Further evaluation of its performance in the field may give important data to extend its usefulness for surveillance and epidemiological research in outbreak situations.

Keyword: dengue, rapid diagnostics, laboratory assay, STH-PAS, RT-PCR

Two ways that non-coding DENV RNA enhances mosquito transmission



Shih-Chia Yeh¹, Wei Lian Tan¹, Menchie Manuel¹, Benjamin Wong¹, Arthur Chain¹, Mariano Garcia-Blanco^{1,3}, **Pompon Julien**^{1,2}

Dengue viruses (DENV) produce a non-coding subgenomic flaviviral RNA (sfRNA) in mosquito and human. Previously, we revealed that sfRNA enhances mosquito transmission by increasing saliva infection rate, therefore augmenting epidemiological potential. We linked two sfRNA substitutions, present in epidemic isolates, to higher sfRNA quantity in salivary glands and determined that this higher sfRNA quantity inhibited components of the antiviral Toll pathway. Immune inhibition resulted in higher virus production in salivary glands and infection rate of saliva. Because our results also showed a high production of sfRNA in salivary glands, we next hypothesized that sfRNA was secreted in saliva along with the virus. The known immune inhibitory capacity of sfRNA in human would provide a crucial time advantage to the virus over the immune response in skin. For the first time, we discovered sfRNA in infected saliva and showed that it enhances infection to skin cells. Furthermore, we searched for a regulator of saliva sfRNA quantity. Using RNA chromatography, we identified 14 sfRNA-interacting proteins in mosquitoes. Using in vivo RNAi, we showed that one of them, Staufen, reduces sfRNA in salivary glands and saliva. Altogether, we discovered two transmission-enhancing functions for DENV sfRNA: increase of virus particle production and enhancement of infection initiation in skin cells. These studies suggest that monitoring sfRNA sequence would inform about newly-introduced virus epidemiological potential and that secreted sfRNA is a candidate target for transmission-blocking tools.

Keyword: Dengue, sfRNA, in vivo, mosquito

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A multiplex diagnostic platform for detection of Zika virus infection in a cohort of febrile patients from Thailand



Lauren Ching¹, Akanitt Jittmittraphap², Siriporn Chattanadee², Jasmine Padamada¹, Narin Thippornchai², Madhuri Namekar¹, Axel Lehrer¹, Vivek R. Nerurkar¹, and Pornsawan Leaungwutiwong²

¹Department of Tropical Medicine, Medical Microbiology, and Pharmacology, John A. Burns School of Medicine, University of Hawaii at Manoa, Honolulu, Hawaii, USA; ²Department of Microbiology and Immunology, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

Thailand is endemic for dengue virus (DENV), with serological evidence of Zika virus (ZIKV) as early as 1954 and epidemiological evidence for human transmission since 2011. In this study we employed an in-house developed flavivirus multiplex microsphere immunoassay (MIA) using color-coded fluorescent microspheres covalently coupled with ZIKV, DENV and Japanese encephalitis virus (JEV) nonstructural protein 1 (NS1), and human IgG conjugated to streptavidin peroxidase. Selected serum samples collected in 2017 were sequenced and a phylogenetic tree based on the ZIKV envelope gene was constructed. The flavivirus serological assay was conducted on serum samples from two Thai cohorts of patients who presented with DENV-like symptoms, however, were DENV negative by PCR. The first cohort included archival samples collected from hospitals in rural northeast Thailand between 2002-2004 (n=300). The second cohort of serum samples was collected at the Hospital for Tropical Diseases in urban Bangkok, between 2014-2017 (n=58). In these settings of high DENV endemicity, we detected 3% (n=11) serum samples reactive for only ZIKV NS1 antibodies as early as 2002. Overall ZIKV NS1 antibodies were detected in 40% (n=143) of the serum samples, which were also positive for DENV (90%; n=128) and JEV (34%; n=49) NS1 antibodies. When stratified by geographic location, ZIKV seropositive serum samples were found more frequently in the rural cohort, 41% (n=124), as compared to the urban cohort, 33% (n=19). Furthermore, the rural cohort had fewer, 6% (n=7), samples that were positive for ZIKV NS1 antibodies, as compared to the urban cohort in which 21% (n=4) of the samples were positive. Sequencing data indicated that the circulating 2017 ZIKV strains in Thailand clustered with the Asian linage of ZIKV, specifically those isolated from Singapore in 2016. These data suggest transmission of ZIKV in Northeastern Thailand as early as 2004 and warrants further surveillance of ZIKV across Thailand.

Keyword: Zika Virus, Multiplex Diagnostic Platform, Thailand

Wednesday 12 December 2018

16.00-17.30 Room C

S I 2: Melioidosis: Epidemiology, diagnostics and vaccine development

Chairpersons:

1. Yuvadee Mahakunkijcharoer





2. Narisara Chantratita

Invited Speakers:



Presence of environmental *Burkholderia pseudomallei* and burden of melioidosis in Thailand

Viriya Hantrakun

Mahidol-Oxford Tropical Research Unit (MORU)



Detection and quantification of capsular polysaccharide of *Burkholderia pseudomallei* in melioidosis patient urine samples

David AuCoin

Department of Microbiology and Immunology, University of Nevada Reno School of Medicine, USA



Identification of antigens for the development of melioidosis vaccines and diagnostics

Mary Burtnick

Department of Microbiology and Immunology, University of Nevada Reno School of Medicine, USA

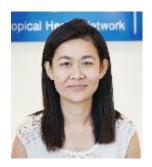


Optimization of glycoconjugate vaccines for immunization against melioidosis

Paul Brett

Department of Microbiology and Immunology, University of Nevada Reno School of Medicine, USA

Presence of environmental *Burkholderia pseudomallei* and burden of melioidosis in Thailand



Viriya Hantrakun¹, Patpong Rongkard¹, Somkid Kongyu², Preeyarach Klaytong¹, Sittikorn Rongsumlee¹, Punnarai Smithsuwan², Rungrueng Kitphati², Nicholas PJ Day^{1,3}, Vanaporn Wuthiekanun¹, Sharon J. Peacock^{1,4,5}, Soawapak Hinjoy², Direk Limmathurotsakul ^{1,3,6}

Melioidosis is an infectious disease with high fatality rate of 40%, caused by an environmental *Burkholderia pseudomallei*. Knowledge of the bacterium distribution and disease morbidity are limited to the Northeast Thailand, but not nationwide. Thirty-four deaths of melioidosis reported by national surveillance system (Report 506), whilst researchers estimated >1000 deaths in 2012-2015. Risk and burden of melioidosis are officially under-recognized.

Soil sampling was conducted in 61 rice fields in East, Central, and Northeast Thailand. We obtained the microbiology and hospital database of hospitals in Thailand, and the Report 506 (2012 to 2015). The national death registry in 2012 was obtained from the Ministry of Interior, Thailand to evaluate 30-day mortality. *B. pseudomallei* was isolated from 12/21 (57%), 13/19 (68%) and 5/21 (24%) rice fields in the Northeast, East and Central Thailand, respectively. Prevalence of the organism in the East was as high as in the endemic Northeast. Total of 7,126 culture-confirmed melioidosis were identified in 71/96 regional or general hospitals. The incidence rate was highest in Northeast, followed by East, North, Central, South and West Thailand. In 2012, 30-day mortality was 40% (696/1,735), while 4 deaths of melioidosis were reported to the Report 506 of MoPH.

Risk and burden of melioidosis is beyond the Northeast region, and is an important cause of death in Thailand. Data from the national surveillance system in resource-limited settings should be verified by integrating available databases. Improving estimates of melioidosis burden is crucial in shaping national health policies and a reduction of deaths.

Keyword: Melioidosis, *B. pseudomallei*, disease-surveillance, burden of disease

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⁵ Department of Medicine, University of Cambridge, Cambridge, United Kingdom

⁶ Department of Tropical Hygiene, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

Detection and quantification of capsular polysaccharide of *Burkholderia pseudomallei* in melioidosis patient urine samples



DeMers H¹, Green HR¹, Kanneganti V², Hau D¹, Thorkildson PN¹, Woods K³, Boutthasavong L, NicFhogartaigh C³, Lee SJ³, Davong V, Dance DAB^{3,4}, McLarty M¹, Chung C¹, Gates-Hollingsworth MA¹, **AuCoin DP**¹

¹Department of Microbiology and Immunology, University of Nevada Reno School of Medicine, USA; ²DxDiscovery, Inc., Reno NV, USA; ³Lao-Oxford- Mahosot Hospital-Wellcome Trust Research Unit, Microbiology Laboratory, Mahosot Hospital, Vientiane, Lao PDR; ⁴Centre for Tropical Medicine and Global Health, University of Oxford, UK

Burkholderia pseudomallei is the causative agent of melioidosis, a lifethreatening disease prominent in Southeast Asia and Northern Australia. The gold standard for diagnosis of melioidosis is culturing the bacteria. However, this process can take up to seven days and sensitivity for this method is low. Receiving adequate antibiotic treatment relies on correct diagnosis. The Active Melioidosis Detection (AMD) lateral flow immunoassay (InBios) detects the capsular polysaccharide (CPS) of *B. pseudomallei*. Previously, it has been shown that CPS is a good candidate biomarker of melioidosis due to its presence in patient urine and serum samples, most notably in urine. CPS appears to be cleared rapidly from blood into urine. The presence of CPS in either urine or serum is a good indicator of an active infection. Urine is a non-invasive sample, which makes it easier to collect than other sample types. In this study patient samples were analyzed for the presence and concentration of CPS by AMD lateral flow immunoassay and quantitative antigen-capture enzyme-linked immunosorbent assay (ELISA). Disease status was blinded before testing. We determined that CPS concentration is highly variable between patients. Some patient samples had low concentrations of CPS that are currently below the limit of detection for these assays. Collecting antigens from larger volumes may allow for higher sensitivity detection. This could be done by enriching samples through immunoprecipitation with CPS-specific antibodies conjugated to magnetic particles in combination with a lateral flow immunoassay. This could lead to earlier and more accurate diagnosis of melioidosis.

Keyword: melioidosis, diagnosis, lateral flow immunoassay

Identification of antigens for the development of melioidosis vaccines and diagnostics



Burtnick MN

Department of Microbiology and Immunology, University of Nevada, Reno, USA

Burkholderia pseudomallei is a facultative intracellular, Gram-negative bacterium that causes melioidosis in humans and animals. Diagnosis and treatment of this emerging infectious disease can be challenging and no licensed vaccines currently exist. This important pathogen survives and replicates in the cytosol of eukaryotic cells, uses actin-based motility to spread intracellularly and induces host cell fusion resulting in the formation of multinucleated giant cells. Several factors expressed by B. pseudomallei are known to influence key processes during interactions of the organism with phagocytic cells. Included amongst these are a Type III secretion system (T3SS-3), a Type VI secretion system (T6SS-1), a deubitiquitinase (TssM), an actin motility protein (BimA) and the VirAG two-component regulatory system. Previous work in our laboratory and others has demonstrated that expression of these proteins/systems is tightly regulated and only occurs following contact of B. pseudomallei with or internalization by host cells. Recently, we have identified growth conditions that activate the expression of these intracellular virulence factors in vitro. Specifically, when B. pseudomallei was grown in minimal media lacking iron, T6SS-1, bimA and tssM were expressed suggesting that these media conditions mimicked the intracellular environment. It is anticipated that these "in vivo-like" growth conditions will facilitate further characterization of the functions of these important virulence factors as well as aid in identification of new antigens to develop novel melioidosis vaccines and diagnostics.

Keyword: B. pseudomallei, melioidosis, antigens, diagnostics, vaccines

Optimization of glycoconjugate vaccines for immunization against melioidosis



Brett PJ

Department of Microbiology and Immunology, University of Nevada, Reno, 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. Several studies have shown that B. pseudomallei expresses a number of structurally conserved protective antigens that include cell-surface polysaccharides and cell-secreted proteins. Based on this, such antigens have become important components of the subunit vaccine candidates that we are currently developing in our laboratory. Recently, we demonstrated that immunization of C57BL/6 mice with CPS-CRM197 produced high-titer IgG and opsonizing antibody responses against the capsular polysaccharide (CPS) component of the glycoconjugate while immunization with hemolysin coregulated protein 1 (Hcp1) produced high titer IgG and robust IFN-y secreting T cell responses against the protein. Extending upon these studies, we found that when vaccinated with a combination of CPS-CRM197 plus Hcp1, 100% of the mice survived a lethal inhalational challenge of B. pseudomallei and that 70% of the survivors had no culturable bacteria in their lungs, livers or spleens. Based on these results, studies in our laboratory are currently focused on optimizing the immunogenicity and protective capacity of our lead vaccine candidate as well as investigating novel approaches for producing a safe, effective and lowcost formulation that could be broadly used to immunize humans and animals against melioidosis in endemic regions.

Keyword : *B. pseudomallei*, melioidosis, polysaccharide, protein, subunit vaccine

Wednesday 12 December 2018

16.00-17.30 Room D

S13: Free paper: Malaria

Chairpersons:







2. Rapatbhorn Patrapuvich

Speakers:



Drug quantification using dried blood spots – advantages and challenges

Daniel Blessborn

Mahidol-Oxford Tropical Medicine Research Unit (MORU)



Eponemycin *in silico*: a potential antimalarial candidate by inhibiting ubiquitin proteasome system of *Plasmodium falciparum*

Kana Mardhiyyah

Faculty of Medicine, Universitas Brawijaya



Artemisinin resistance in *Plasmodium falciparum* in malaria endemic areas, Lao PDR

Sengdeuane Keomalaphet

Institut Pasteur du Laos



The role of AcylCoA binding proteins (ACBPs) and lysophopholipases (LPLs) in lipid recycling and trafficking for membrane biogenesis, and remodelling in Apicomplexa parasites and their host cell

Serena Shunmugam

Université Grenoble Alpes, France

Drug quantification using dried blood spots - advantages and challenges



<u>Daniel Blessborn</u>^{1,2}, Karnrawee Kaewkhao^{1,3}, Joel Tarning^{1,2}

Dried blood spot (DBS) sampling techniques were developed in the 1960s as a screening method for phenylketonuria (PKU) in newborn infants. Since then, DBS techniques have gained in popularity and have been implemented in several different research fields. This sample collection technique is rather simple; blood from a finger or heal stick is collected and placed on a filter paper, and allowed to dry in open air. In our laboratory, a small disc is punched through the filter paper and the drug molecule is extracted using a suitable solvent in order to allow drug analysis quantification. Only 30 - 100 µL of blood per spot is needed for the analysis and the finger/heal stick blood collection require only minimal training to perform, allowing for pharmacokinetic sampling in vulnerable populations such as young children. These methods are particularly advantageous in rural areas where resources are limited for sampling, cold storage and shipping of venous samples. However, there are several factors to consider when using the DBS technique and here we describe some of those challenges regarding sample collection, drying, storage and what impact they may have on the final analysis of drug levels in blood spots.

Keyword: DBS, method development, method validation, LC-MS/MS

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³ Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

Eponemycin *in silico*: a potential antimalarial candidate by inhibiting ubiquitin proteasome system of *Plasmodium falciparum*



Kana Mardhiyyah^{1,2}, Rivo Yudhinata Brian Nugraha³, Sri Winarsih⁴, Loeki Enggar Fitri³

¹ Doctoral Program in Medical Sciences, Faculty of Medicine Universitas Brawijaya; ² Department of Biochemistry and Biomolecular, Faculty of Medicine Universitas Brawijaya; ³ Department of Parasitology, Faculty of Medicine Universitas Brawijaya; ⁴ Department of Pharmacy, Faculty of Medicine Universitas Brawijaya

Drug resistance in malaria treatment becomes major problems all over the world. Finding a novel potent antimalarial candidate is mandatory. Previous study proved that secondary metabolite of Streptomyces hygroscopicus significantly Hygroscopicus containing eponemycin inhibits Proteasome System (UPS) of *Plasmodium* in vivo. The aims of this study are to know toxicity profile of eponemycin and its potency as Ubiquitin Proteasome System inhibitor of *Plasmodium falciparum*. The methods of this study were ADMET SAR Toxicity (ACD/LABS), Protein Modelling (SWISS), and Molecular Docking (AUTODOCK VINA PYRX). The result Absorption, Distribution, Metabolism, Excretion and Toxicity profiles (ADMET) of Eponemycin was absorbed 83.5% via intestinal route. This is based on Lipinski\\\'s rule of five. Eponemycin belonged to Category 4 of toxicity. Smaller toxicity category means the compound has higher toxicity. Several possible drug targets within Plasmodium UPS were 26S Proteasome, PfhsIU/pfhsIV proteasome complex, E3 ligases, E3 target substrates, and DUBs. E3 is a potential drug target because of its different structure to that of the human. The E1 and E2 are proteins that conserved in eukaryotic. The C-score (confidence score of the prediction) of the active side E3 was 0.06 and E2 was 0.45 (COACH ZHANG LAB). Eponemycin had the ability to bind to E3 and E2 with an affinity score binding of -3.8 and -4.1. The more negative the affinity binding value the easier the compound binds to the target protein. Based on this in silico study, eponemycin has potential effect as antimalaria by inhibiting Ubiquitin Proteasome System of Plasmodium falciparum.

Keyword: in silico, eponemycin, antimalaria, ubiquitin proteasome system

Artemisinin resistance in *Plasmodium falciparum* in malaria endemic areas, Lao PDR



<u>Sengdeuane Keomalaphet</u>^{1,2}, Phonepadith khattignavong^{1,2}, Pheovaly Soundala^{1,2}, Lavy Lorphachan^{1,2}, Masami Nakatsu^{1,3}, Moritoshi Iwagami^{1,2,3}, Bouasy Hongvanthong^{1,4}, Paul T. Brey^{1,2}, Shigeyuki Kano^{1,2,3}

Background: Despite the fact that malaria morbidity and mortality have decreased in Laos, artemisinin-resistant *Plasmodium falciparum* has been reported since 2013, which is now threatening malaria elimination in the country by 2030. The objective of the study was to assess the distribution of the k13-mutations in Laos, which are reported to be responsible gene mutations for artemisinin-resistance of the parasite.

Method: Blood samples of malaria patients were collected in 160 health care facilities in 5 southern provinces from October 2015 to November 2016, where over 90% of malaria cases in Laos were reported. The blood collection was also conducted in the northern-most province, Phongsaly, from November-December 2017. Real-time PCR was performed to identify *Plasmodium* species and direct DNA sequencing was performed to detect the *k13*-mutations.

Results: In the 5 southern provinces, a total of 1,553 cases of *P. falciparum* were detected, in which, 52.8% had nonsynonymous mutations in the k13-mutations, precisely, Attapeu (107 cases which occupied 76.9% of the samples); Champasak (n=384, 67.7%); Sekong (n=72, 48.3%); Salavan (n=150, 53.2%); Savannakhet (n=107, 24.9%). The C580Y was the most predominant mutation in the k13, followed by R539T, Y493H and P574L. In Phongsaly, there were 8 malaria cases including 3 *P. falciparum*, 3 *P. malariae* and 2 *P. vivax*. All the 3 *P. falciparum* possessed the C580Y mutation.

Conclusion: The C580Y was the predominant mutation among the 4 mutations in these 6 provinces. The high rate of the k13-mutations highlights the importance of surveillance of artemisinin-resistance to achieve the elimination of malaria in Laos, as well as in the Greater Mekong Subregion.

Keyword : *P. falciparum*, *k13* gene, Artemisinin-resistance, malaria elimination, Laos

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³Department of Tropical Medicine and Malaria, Research Institute, National Center for Global Health and Medicine, Tokyo, Japan

⁴Center of Malariology, Parasitology and Entomology, Vientiane, Lao PDR

The role of AcylCoA binding proteins (ACBPs) and lysophopholipases (LPLs) in lipid recycling and trafficking for membrane biogenesis, and remodelling in Apicomplexa parasites and their host cell



<u>Serena Shunmugam</u>¹, Yoshiki Yamaryo-Botté¹ and Cyrille Botté¹

¹Apicolipid group, Institut Albert Bonniot UMR5309, CNRS, Université Grenoble Alpes, INSERM, Domaine de la Merci, 38700, La Tronche, France

Apicomplexa parasites cause major human diseases affecting hundreds of millions and killing scores every year. They include *Plasmodium falciparum* and *Toxoplasma* gondii, causative agents of malaria and toxoplasmosis, respectively. The prevalence and drug resistance of these parasites emphasize the need to identify novel drug targets. Current evidence shows that lipid synthesis and trafficking are pertinent drug targets. During the life cycle of Apicomplexa pathogens, a large amount of lipids is needed for the generation of membrane compartments for newly formed cells. Membrane biogenesis is achieved by de novo lipid synthesis mainly from the apicoplast or by scavenging host lipids. The function and integration of each pathway in the parasite remains unknown. This project aims to understand the lipidprocessing pathway involved in the transfer of fatty acids from the host and within the parasite and their recycling into lipids. This PhD project focuses on a group of uncharacterized proteins, putatively important for parasite membrane dynamics and remodelling, namely Acyl-CoA binding proteins (ACBPs) and (lyso)phospholipases ((L)PLs). We will be able to decipher the roles of these proteins during intracellular development in both Apicomplexa models. For each model, it is proposed to epitopetag and disrupt each candidate using CrispR-Cas9-based knock outs and inducible knock-downs to localize and determine the function of each protein. Putative binding partners will be identified by co-immunoprecipitation methods. The role of these proteins for membrane biogenesis will be determined using mass spectrometrybased lipidomic and fluxomic approaches. This project will generate data on how the parasite transports and recycles lipids for membrane biogenesis in Apicomplexa parasites and potentially contribute to identifying new drug targets and developing new therapeutic approaches to fight malaria and toxoplasmosis.

Keyword: Apicomplexa, Malaria, Toxoplasmosis, Lipidomics



Thursday 13 December 2018

07.30-08.55 Room B

Workshop: How to Write Great Papers

From title to references, from submission to publication

An overview of scientific publishing including the latest trends in e-publishing, and content innovation within manuscripts. What are the things that an editor looks out for?



Speaker:

Andrew Thompson

Editor-in-Chief, International Journal for Parasitology: Parasites and Wildlife

Thursday 13 December 2018

09.00-10.30 Room A

\$14: Current status of antimalarial resistance and its impact on clinical practice (Sponsored by MORU)

Chairpersons:

1. Mallika Imwong





2. Arjen Dondorp

Speakers



Update on antimalarial drug resistance in the Greater Mekong Subregion

Arjen Dondorp

Mahidol-Oxford Tropical Medicine Research Unit (MORU)

(No Abstract)



Seasonal malaria shifting trends and implications for malaria elimination program in Thailand

Prayuth Sudathip

Bureau of Vector-Borne Diseases, Disease Control Department Ministry of Public Health



Triple artemisinin-based drug combinations to combat multi-drug resistant *P. falciparum* malaria

Mehul Dhorda

Tracking Resistance to Artemisinins Collaboration



Molecular and *in vitro* surveillance of artemisinin combination therapy (ACT) partner drug efficacy in the Greater Mekong Subregion

Suttipat Srisutham

Mahidol-Oxford Tropical Medicine Research Unit (MORU)

Seasonal malaria shifting trends and implications for malaria elimination program in Thailand



International Development, Bangkok, Thailand

Julien Zwang¹, Richard Reithinger¹, David Sintasath², Preecha Prempree³, and **Prayuth Sudathip³**

Between October 2012 and September 2017, 94,486 malaria cases occurring in Thailand (37% Plasmodium falciparum, 61% P. vivax, and 2% of mixed and other spp.) were analyzed. Logistic regression was used to measure adjusted odd ratios (AORs) for the explanatory variables. Trend analyses showed a significant reduction of malaria: 90% in Pf from (21 to 2/100,000), 54% in Pv from (25 to 11/100,000), 62% in mixed infection, and 40% in other *Plasmodium* spp. cases. The reduction of *Pf* cases was significantly greater during the rainy season (May to October) than during the dry season (November to April) with 93% and 85% reduction, respectively, as well as for Pv cases showing a 61% and 44% reduction, respectively (p=0.001, for all comparisons). After a malaria outbreak during the rainy season in 2015 in Yala province, the ongoing transmission resulted in an increased number of cases during the following dry season, especially in rubber farm workers. This increase corresponded to the optimal time for latex collection between September (end of rainy season) and February. As a result, rubber farm workers accounted for 30% of cases in 2016 and likely contributed to the reduction of seasonal malaria usually observed. Using multivariate analysis, malaria cases occurring during the rainy season decreased significantly faster (AOR = 0.92, p=0.001) than in the dry season; people working and living in rubber plantations were at significantly greater risk for malaria (AOR = 1.12, p=0.001) compared to other occupations, as well as subjects from Yala province (AOR = 1.16, p=0.001) compared to other provinces. Our results showed that malaria has been decreasing rapidly over the study period and has reached low levels of incidence in Thailand. Malaria seasonality seems to be mitigated because of the general decrease in incidence and sporadic outbreaks reported among workers and their families living in rubber plantations and related lifestyle (collecting/hunting in the forest). This finding has implications for malaria elimination program implementation, including management of outdoor transmission, timing of bednet distribution, and targeting active case detection in identified high-risk groups.

Keyword: Malaria elimination, program implementation

¹ Inform Asia: USAID's Health Research Program, RTI International, Research Park Triangle, NC, USA ² U.S. President's Malaria Initiative, Regional Development Mission for Asia, United States Agency for

³ Bureau of Vector Borne Diseases, Department of Disease Control, Ministry of Public Health, Bangkok, Thailand

Triple artemisinin-based drug combinations to combat multi-drug resistant *P. falciparum* malaria



Mehul Dhorda

Tracking Resistance to Artemisinins Collaboration

The spread of artemisinin (ART) 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 5 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 ACT with two longer-acting partner drugs.

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, tolerability and safety of TACTs in 18 hospitals in 7 countries in Asia and 1 in Africa. In this presentation, we will present the final results of this large-scale initiative.

Keyword: TRAC II, artemisinin resistance, ACT

Molecular and *in vitro* surveillance of artemisinin combination therapy (ACT) partner drug efficacy in the Greater Mekong Subregion



Suttipat Srisutham¹, Nguyen Than Thuy-Nhien², Ranitha Vongpromek³, Kanokon Suwannasin¹, Teeradet Khomvarn³, Mayfong Mayxay⁴, Olivo Miotto^{5,6,7}, Francois Nosten^{7,8}, Frank Smithuis^{7,9}, Rob van der Pluijm⁵, Lorenz von Seidlein⁵, Carol H Sibley¹⁰, Philippe J. Guérin^{7,10}, Nicholas P. J. Day^{5,7}, Arjen Dondorp^{5,7}, Mehul Dhorda^{3,5,7}, Mallika Imwong¹

¹Department of Molecular Tropical Medicine and Genetics, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; ²Oxford University Clinical Research Unit, Ho Chi Minh, Viet Nam; ³WorldWide Antimalarial Resistance Network - Asia Regional Centre, Bangkok, Thailand; ⁴Laos Oxford Mahosot Wellcome Research Unit, Vientiane, Lao PDR; ⁵Mahidol-Oxford Tropical Medicine Research Unit, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; ⁶Wellcome Sanger Institute, Hinxton, UK; ⁷Centre for Tropical Medicine and Global Health, University of Oxford, Oxford, UK; ⁸Shoklo Malaria Research Unit, Mae Sot, Thailand; ⁶Myanmar-Oxford Clinical Research Unit, Yangon, Myanmar; ¹⁰WorldWide Antimalarial Resistance Network, Oxford, UK

Artemisinin combination therapies (ACTs) are the recommended treatment for falciparum malaria worldwide, including in the countries of the Greater Mekong Subregion (GMS, Thailand, Cambodia, Laos, Vietnam and Myanmar). In the context of spreading artemisinin resistance in the Greater Mekong Subregion (GMS), parasite susceptibility to partner drugs in artemisinin-based combination therapies (ACTs) becomes a critical determinant of ACT efficacy. Molecular markers of resistance to the ACT partner drugs mefloquine and piperaquine have been identified. Real-time polymerase chain reaction (qPCR) based assays to detect gene amplifications of *P. falciparum multi-drug resistance 1* gene (*pfmdr1*) and plasmepsin 2 (pfplasmepsin2) were performed. Results were summarised by location and year of specimen collection for upload on to open access maps [http://www.wwarn.org/molecular/surveyor/]. 2,474 specimens collected in 2016-17 at sites across the GMS were tested (1,800 for pfmdr1, 2,319 for pfplasmepsin2) resulting in an overall assay success rate of 79.55% for at least one marker. All results from dried blood spots (DBS) samples were uploaded on to web-based maps within 4 months from the time of specimen reception. These results represent the demonstration of the feasibility of near-real time molecular surveillance for resistance to ACT partner drugs support to policy-makers and researchers, thereby enhancing malaria control and elimination.

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

09.00-10.30 Room B

\$15: Foods for Health and Prevention

Chairpersons:

1. Karunee Kwanbunjan





2. Pattaneeya Prangthip

Invited Speakers:



Foods and nutrition in health promotion and chronic disease prevention **Karunee Kwanbunjan**

Department of Tropical Nutrition and Food Science, Faculty of Tropical Medicine, Mahidol University



Current status of genetic improvement for Low GI/GL and insulin insensitivities in rice

Apichart Vanavichit

Rice Science Center, Kasetsart University



Thai rice and Non-communicable diseases prevention

Ratchanee Kongkachuichai

Institute of Nutrition, Mahidol University

(No Abstract)

Foods and nutrition in health promotion and chronic disease prevention



Karunee Kwanbunjan

Department of Tropical Nutrition and Food Science, Faculty of Tropical Medicine, Mahidol University

Foods and nutrition are important factor in promotion and maintenance of good health throughout entire life. During the past decade, rapid expansion in a number of relevant scientific evidences has helped to clarify the role of diet in preventing and controlling morbidity and premature mortality resulting from non-communicable diseases. Chronic diseases are largely preventable diseases. Metabolic syndrome associated with the risk of developing cardiovascular disease and type 2 diabetes, resulted from unhealthy diets and physical inactivities. Promote an appropriate diets and healthy lifestyle is significant manage of prevention and reduce risk of chronic disease.

Keyword: Foods and nutrition

Current status of genetic improvement for Low GI/GL and insulin insensitivities in rice



Apichart Vanavichit^{1, 2, 3}

¹Rice Science Center, Kasetsart University, Khamphangsean, Nakornpathom ²Rice Gene Discovery, BIOTEC, Kasetsart University, Khamphangsean, Nakornpathom ³□Agronomy Department, Faculty of Agriculture Khamphangsaen, Kasetsart University, Khamphangsean, Nakornpathom

Type II Diabetes (T2D) is one of the most common non-communicable disease (NCD). Recently, 415 million people or one on every 11 persons are identified as T2D. The disease prevalence in Thailand was one on every 10 persons or 3.2 million people aged from 35 years old. T2D patients are also affected by chronic kidney disease (CKD), coronary heart disease, and obesity. In particular, 57% of the T2D had high risk of amputation and blindness due to hyperglycemia. The causes of T2D are complex involving genetic, foods, and stagnant habit. Imbalance diet high in rapidly available glucose (RAG) carbohydrate is the major cause. As the major source of daily calories intake for Asian, rice is the main target of genetic improvement for slowly glucosereleasing carbohydrate or low glycemic index (GI) and low glycemic load (GL). Genetic factors determining GI/GL are amylose (AM) content, amylopectin (AP) structure, resistant starch (RS), alpha glucosidase inhibitor (AGI), and dietary Successful rice cultivars with low GI (GI<55) was reported in Doonggara rice from Australia and parboiled-polished Basmati rice from India. In Thailand, there were three periods of breeding rice for low GI/GI. In the early stage, aromatic, low amylose, intermediate GI rice varieties named Sinlek (GI=58) and Riceberry (GI=62) were reported. In the second period, breeding for high yielding, low GI with high AM, resistance to biotic and abiotic stresses resulted in releasing Pinkaset +4 (PinK4). In the third step, clinical screening of 15 existing cultivars from Thailand Rice Department resulted RD43 as an intermediate GI with aromatic grains. In the next step, developing low GI food products from low GI rice is very challengig on-going project in Thailand

Keyword : Glycemic index and glycemic load, Type 2 diabetes, Rapid available glucose, Dietary fiber, alphs glucosidase inhibitor

09.00-10.30 Room C

\$16: Biology and interventions for pre-erythrocytic stages (Sponsored by SCRI)

Chairpersons:

1. Steffan Kappe





2. Jetsumon Prachumsri

Speakers:



Ferroptosis-like signaling facilitates a potent innate defense against *Plasmodium* infection

Alexis Kaushansky

Seattle Children's Research Institute



Human PDGFR-beta is a new host receptor interaction for *Plasmodium falciparum* protein PfTRAP

Noah Sather

Seattle Children's Research Institute



Towards generating a genetically-engineered replication-competent whole *Plasmodium falciparum* parasite vaccine that confers broad and durable protection against infection

Stefan Kappe

Seattle Children's Research Institute



Discovery of radical cure drugs for P. vivax latent infection

Erika L. Flannery

Novartis Institute for Tropical Diseases, Novartis Institute for Biomedical Research, USA

Ferroptosis-like signaling facilitates a potent innate defense against *Plasmodium* infection



Heather S. Kain, Nadia Arang, Elizabeth K. Glennon, Alyse N. Douglass, Chelsea L. Fortin, Denali R. Dudgeon, Jarrod S. Johnson, Peter D. Crompton, Kelly R. Stevens, Alan Aderem, Tuan M. Tran and <u>Alexis</u> **Kaushansky**

Seattle Children's Research Institute, Seattle, WA 98109, USA

The facets of host control during Plasmodium liver infection remain largely unknown. We find that the SLC7a11-GPX4 pathway, which has been associated with the production of reactive oxygen species and a form of cell death called ferroptosis, plays a critical role in control of Plasmodium liver stage infection. Specifically, blocking GPX4 or SLC7a11 dramatically reduces Plasmodium liver stage parasite infection. In contrast, blocking negative regulators of this pathway, NOX1 and TFR1, leads to an increase of infected hepatocytes. We have shown previously that increased levels of P53 reduces Plasmodium LS burden in an apoptosis-independent manner. Here, we demonstrate that increased P53 is unable to control parasite burden during NOX1 or TFR1 knockdown, or in the presence of ROS scavenging. Additionally, SLC7a11 inhibitors Erastin and Sorafenib reduce infection. Interestingly, preliminary analysis indicates that that individuals with differential susceptibility to malaria in Mali exhibit differentially regulated levels of ferroptosis-related genes, suggesting that this pathway might serve not only to regulate malaria in a mouse model of malaria, but also might regulate susceptibility to disease in humans in the field. These findings suggest that the SLC7a11-GPX4 pathway serves to selectively elevate ROS in infected cells and may, in turn, may promote ferroptosis of infected cells. This raises the possibility that ferroptosis operates as an axis of the innate immune system to defend against intracellular pathogens.

Keyword: Ferroptosis-like signaling, *Plasmodium* infection

Human PDGFR-beta is a new host receptor interaction for *Plasmodium falciparum* protein PfTRAP



Ryan W. J. Steel¹, Vladimir Vigdorovich¹, Nicholas Dambrauskas¹, Brandon Wilder¹, Silvia A. Arredondo¹, Sara Carbonetti¹, Kristian Swearingen^{1, 2}, Robert Moritz², Thao Nguyen¹, Will Betz¹, Nelly Camargo¹, Stefan H.I. Kappe^{1, 3,}, <u>D. Noah Sather^{1, 3,}</u>

Plasmodium falciparum Thrombospondin-Related Anonymous Protein (PfTRAP) has been extensively pursued as a vaccine candidate against pre-erythrocytic malaria infection due to its exposure on the surface of the sporozoite and its essential role in motility and invasion. Viral-vectored PfTRAP has shown some promise in clinical trials, but recombinant protein-based PfTRAP vaccines have failed to show any protection. PfTRAP's critical roles in the life cycle of the sporozoite make it a priority vaccine target, despite these setbacks, and it is possible that a greater understanding of its role and host-pathogen interactions could guide the design of a more effective vaccine. Our goal was to better characterize the biology underlying PfTRAP's role in infection, and to harness that information to understand how to induce better immunity. By screening a library of human surface proteins, we identified a potential binding partner, PDGFRB, which we found was expressed in the skin and liver around vascular tissue. Further, we found that the VWA and TSR domains were critical for this interaction. In parallel, we immunized animals with recombinant PfTRAP and isolated monoclonal antibodies. Intriguingly, we found that that mAbs that map to the VWA and TSR domains also interrupted PfTRAP-PDGFRB interactions in vitro. Thus, it is possible that targeting this interaction between the VWA/TSR domains of PfTRAP and PDGFRB may be a viable pathway forward for vaccine design. Our future efforts will focus on rational design efforts against the binding region of PfTRAP.

Keyword: Human PDGFR-beta, *Plasmodium falciparum* protein PfTRAP

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³ Department of Global Health, University of Washington, Seattle, WA, USA

Towards generating a genetically-engineered replicationcompetent whole *Plasmodium falciparum* parasite vaccine that confers broad and durable protection against infection



Debashree Goswami, Navinder K. Locham, Sean C. Murphy, Ashley M. Vaughan, **Stefan H.I. Kappe**

Seattle Children's Research Institute, 307 Westlake Avenue North, Suite 500, Seattle, WA 98109, USA

Whole sporozoite immunogens constitute the most promising avenue to create a highly protective malaria vaccine. Previous studies in models of rodent malaria provide conclusive evidence that a late liver stage-arresting (LA) genetically attenuated Plasmodium parasite (GAP) vaccine acts as a superior immunogen compared to radiation-attenuated sporozoites, thereby laying the translational foundation for an efficacious late-arresting GAP vaccine against human malaria. One such LA-GAP candidate gene to target for attenuation is plasmei2, the Plasmodium ortholog of the eukaryotic RNA-binding protein (RBP) Mei2 that is conserved across the Plasmodium species and exclusively expressed in liver stages. We have previously shown that a P.yoelii plasmei2 (Py plasmei2) knockout (KO) parasite is arrests late in liver stage development and immunization with Py plasmei2 sporozoites confers complete sterile protection against infectious sporozoite challenge. Herein, we report for the first time the successful generation of a LA-GAP in *Plasmodium falciparum* by gene deletion of *Pf plasmei2*. We found that Pf plasmei2 is dispensable for asexual blood stages, for gametocyte formation and for developmental stages in the mosquito vector. Infection of human liver-chimeric FRG huHep mice with Pf plasmei2 KO sporozoites did not impair either initial hepatocyte infection or growth to late liver stage parasites. However, Pf plasmei2 KO liver stages had discernible defects in late schizogony, aberrant DNA segregation, and did not form exo-erythrocytic merozoites. When FRG-huHep mice infected with *Pf plasmei2* KO sporozoites were infused with human red blood cells (RBCs) on Day 7 after infection, they did not show blood stage infection, in contrast to mice infected with WT NF54 sporozoites that all transitioned to blood stage infection. Generation of such a replication-competent, yet fully attenuated late liver stage-arresting GAP is a significant advance towards generating an efficacious anti-malarial vaccine.

Keyword : genetically-engineered replication-competent, whole *Plasmodium falciparum*, parasite vaccine

Discovery of radical cure drugs for *P. vivax* latent infection



Erika L. Flannery

Novartis Institute for Tropical Diseases, Novartis Institute for Biomedical Research, USA

Latent Plasmodium vivax infections contribute to over 90% of vivax malaria blood stage disease. This latent, asymptomatic, hypnozoite-reservoir in the liver, which can relapse months to years after the initial infection, is a challenge to the goal of malaria eradication. NITD is dedicated to discovering novel therapies to eradicate this latent malaria reservoir through a variety of approaches including high-throughput phenotypic screening, target-based biochemical assays and furthering the fundamental knowledge of the biology of this organism. Recently, the liver-chimeric humanized mouse model has allowed us to discover properties of the *P. vivax* hypnozoite that had remained elusive. We show the dormant parasite becomes mature and thus refractory to drug treatment three days post infection. While the parasite remains single nucleate and non-replicating, the mitochondria and apicoplast appear to gain complexity over time suggesting several metabolic pathways can be targeted to cure this sleeping parasite. Using the knowledge gained from this model, we are developing models with the monkey malaria parasite, P. cynomolgi, to increase the throughput of screening and biological assays. We will use this model to study the biology of hypnozoite relapse and persistence as well as screen large chemical libraries to identify novel small molecule inhibitors of P. *vivax* relapse.

Keyword : NITD, *P. vivax* latent infection

09.00-10.30 Room D

\$17: Vivax malaria elimination: a real possibility

Chairperson:

Srivicha Krudsood



Invited Speakers:



Primaquine resistance situation

Srivicha Krudsood

Department of Tropical Hygiene, Faculty of tropical Medicine, Mahidol University

(No Abstract)



The potential contribution of tafenoquine to radical cure in *vivax* malaria elimination **Andy Walker** *Global Health, GSK*



Quantitative POC testing for G6PD deficiency to support vivax malaria elimination **Germana Bancone**

Shoklo Malaria Research Unit (SMRU)

The potential contribution of tafenoquine to radical cure in vivax malaria elimination



Andy Walker

Scientific Director, Global Heath, GSK, Brentford, UK

Plasmodium vivax accounts for about half of malaria cases outside sub-Saharan Africa, often in countries that are close to eliminating malaria. Around 8.5 million clinical infections every year are caused by *P. vivax*. Many of these are relapses from existing infections that occur in the absence of new infective mosquito bites. This occurs because *P. vivax* parasites can lie dormant in the liver as hypnozoites, reactivating weeks, months or even years after initial infection.

Until recently primaquine (PQ) was the only available treatment for liver-stage *P. vivax* malaria. However, as per the PQ label and WHO recommendations, it is administered once daily for 14 days – a regimen that is hard for patients to comply with, meaning that many are not cured. A single-dose treatment with the potential to improve patient compliance could positively impact *P. vivax* control and elimination efforts.

For this reason, MMV and GSK have partnered to develop tafenoquine (TQ) – a new single-dose cure for the liver-stage treatment of *P. vivax* malaria currently approved for use in the USA and Australia. TQ reduces the risk of relapses by 70% as compared to chloroquine (CQ) alone.

Feasibility studies, to assess the operational feasibility of introducing a quantitative G6PD test before appropriate radical cure at various levels of the health services, are being planned for Brazil, Thailand and Ethiopia in 2019-2020. These studies will help to inform potential adoption of TQ in other countries affected by *P. vivax* malaria.

Keyword : Malaria, Vivax, Tafenoguine, Primaguine, Relapse

Quantitative POC testing for G6PD deficiency to support vivax malaria elimination



<u>Germana Bancone</u>^{1,2}, Gonzalo J. Domingo³, Cindy S. Chu^{1,2}, Mutsumi Metzler³, Gornpan Gornsawun¹, Emily Gerth-Guyette³ and Francois Nosten^{1,2}

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the most common enzymopathy in the human population affecting an estimated 8% of the world population, especially those living in areas of malaria endemicity. Decreased G6PD enzymatic activity is associated with drug-induced hemolysis, even in women with intermediate G6PD activity. 8-aminoquinolines (such as primaguine and tafenoguine) are the only drugs able to kill the dormant liver stages (hypnozoites) of *Plasmodium vivax*. In vivax endemic areas of South-East Asia relapses originating from hypnozoites are considered to cause up to 80% of the overall malaria episodes contributing enormously to malaria morbidity and mortality. Wide use of 8-aminoquinolines in those areas is hindered by the associated hemolytic risk in G6PD deficient patients and by the lack of suitable G6PD field testing. Several laboratory-based diagnostic assays can be used to assess the G6PD status of a person but they are complex, require equipment and are not readily accessible to clinicians at the point-of-care (POC). In recent vears some qualitative and quantitative POC tests have been developed. validated and marketed. Current G6PD qualitative rapid tests can diagnose deficiency under the 30% threshold, are easy to use and appropriate for treatment in males using primaguine or tafenoquine. Quantitative POC tests can assess G6PD enzymatic activity especially in women with intermediate activity allowing for treatment with tafenoquine in both males and females with >70% G6PD activity. Reliable G6PD POC tests that show good technical performances and good usability by health workers are important tools for vivax malaria elimination.

Keyword: G6PD deficiency, POC testing, elimination, vivax, malaria

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³ Diagnostics Program, PATH, 2201 Westlake Ave, Suite 200, Seattle, WA 98121, USA

09.00-10.30

Room E

\$18: Thai-cave flooding rescue, emergency public health response and infection control (Sponsored by MOPH)

Chairperson:

Pornpitak Panlar

S	p	ea	ık	e	rs	:

An overview of Thai-cave flooding rescue, emergency public health response

Pramote Imwattana

Armed Forces Research Institute Of Medical Sciences (AFRIMS)

(No Abstract)

Medical operation in Thailand cave rescue: navy medicine perspective

Natthasak Woracharonesri

Somdej Pranangchao Sirikit Hospital (Naval Medical Department)

(No Abstract)

Experience of EID management from the cave to hospital, Chiangrai Prachanukroh Hospital

Supalert Nedsuwan

Chiangrai Prachanukroh Hospital

(No Abstract)

Infectious control and disease: lessons learned from Thailand cave rescue

Visal Moolasart

Department of Disease Control, Ministry of Public Health (MOPH)

(No Abstract)

11.00-12.30 Room A

\$19: Genomes, phenotypes and populations in malaria

Chairpersons:

1. Jaranit Kaewkungwal





2. Charin Modchang

Invited Speakers:



Immunogenetics: Studying host-malaria parasite genetic interactions using transspecies expression quantitative trait loci (Ts-eQTL) analysis

Su Xinzhuan

National Institutes of Allergy and Infectious Diseases, National Institutes of Health, USA



Drug resistance mediated by the CRT genes of Plasmodium species

Thomas E. Wellems

National Institutes of Allergy and Infectious Diseases, National Institutes of Health, USA



From Patient to Policy: Genetic surveillance as a tool for malaria control and elimination

Christopher Jacob

Wellcome Sanger Institute

(No Abstract)

Immunogenetics: Studying host-malaria parasite genetic interactions using trans-species expression quantitative trait loci (Ts-eQTL) analysis



Xin-zhuan Su

National Institutes of Allergy and Infectious Diseases, National Institutes of Health, USA

Malaria infections trigger vigorous host immune responses, including changes in expression of a large number of genes. Identification of parasite elements that stimulate host gene expression will provide important information for understanding host-parasite interaction and disease mechanism. Using Plasmodium yoelii-mouse models, we have performed several P. yoelii genetic crosses to identify parasite genetic loci linked to host genes. In one study, we developed a method called trans-species expression quantitative trait locus (tseQTL) analysis using genotypes of *P. yoelii* parasites and phenotypes of mouse gene expression. We significantly linked >1,000 host genes to nearly 100 parasite genetic loci (LOD score ³ 3.0). We also used genome-wide LOD score patterns (GLSPs) to cluster host genes. We showed that host genes clustered in the same GLSP group largely functioned in related pathways, allowing functional prediction of unknown genes. Many genes grouped with known interferonstimulated gene (isg) were functionally shown to be regulators of type I interferon (IFN-I) responses. This analysis demonstrates that malaria parasites are powerful models for studying host genes in response to infections, including genes uniquely stimulated by malaria parasites. At the same time, parasite loci significantly linked to IFN-I response and hematopoiesis are being investigated in order to identify parasite genes affecting the host responses. A better understanding of the mechanisms of host-parasite interaction will facilitate development of effective measures to prevent and better manage malaria infections.

This research was supported by the Intramural Research Program of the National Institute of Allergy and Infectious Diseases, National Institutes of Health, USA

Keyword : Immunogenetics, host-malaria parasite, trans-species expression quantitative trait loci (Ts-eQTL) analysis

Drug resistance mediated by the *CRT* genes of *Plasmodium* species



Thomas E. Wellems

Laboratory of Malaria and Vector Research, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland

Genes in the chloroquine (CQ) resistance transporter (CRT) family mediate resistance to a variety of compounds, including such major antimalarial drugs as chloroquine, amodiaguine, quinine, and piperaguine. Understanding the resistance conferred by these genes will inform programs of drug discovery and provide diagnostic markers in support of malaria epidemiology and control programs. Although there are extensive sequence similarities among members of the CRT family, important differences are present in the evolution and mechanisms of CQR among major *Plasmodium* species. For example, CQR arose in Southeast Asian and South American strains of *Plasmodium falciparum* in the 1960s and then entered Africa in the late 1970s, whereas CQR in Plasmodium vivax was not reported until the late 1980s - from Papua New Guinea. CQR in P. falciparum results from mutations in PfCRT, including a charge-change mutation in position 76 that protects the parasite against CQ accumulation and damage. In contrast, P. vivax CQR could not be attributed to amino acid changes PvCRT, the *P. vivax* ortholog of PfCRT: in various studies, any PvCRT mutations observed were independent of CQ treatment failures in humans and P. vivaxinfected monkeys. These findings leave open the possibility that increased pvcrt expression can contribute to CQR in *P. vivax*. Recent genetic studies have strengthened this hypothesis. Drawing from various lines of evidence including biophysical findings, we suggest that net transport of CQ may be an inherent property of PvCRT, in contrast to PfCRT. Structural explanations of the properties of PfCRT and PvCRT will have broad implications for our understanding of the CRT family of carriers, the natural functions of which remain unknown.

Keyword : Drug resistance, *CRT* genes, *Plasmodium*

11.00-12.30 Room B

S20: Plasmodium knowlesi: case study from Thailand (Presentation in Thai) (MOPH)

Chairpersons:

1. Kesinee Chotivanich





2. Wang Nguitragool

Panelists' discussion:



Tips and tricks in microscopic diagnostic of *Plasmodium knowlesi* **Wanlapa Roobsong**

Mahidol Vivax Research Unit, Faculty of Tropical Medicine, Mahidol University

(No Abstract)



Update on molecular diagnostic of Plasmodium knowlesi

Wang Nguitragool

Molecular Tropical Medicine and Genetics Department, Faculty of Tropical Medicine, Mahidol University

(No Abstract)

Case study of patients from Uthai Thani Province

Office of Disease Prevention Control 3, Nakhonsawan (สคร.3)

(No Abstract)

Case study of patients from Songkhla Province

Office of Disease Prevention Control 12, Songkhla (สคร.12)

(No Abstract)

11.00-12.30 Room C

S21: Illnesses associated with caves (Organized by PTAT)

Chairpersons:

1. Padet Siriyasatien





2. Alongkot Ponlawat

Invited Speakers:



Cave diving

Chamchan ChanchangNaval Medical Department



Cave bats and viruses

Supaporn Wacharapluesadee

WHO Collaborating Centre for Research and Training on Viral Zoonoses, King Chulalongkorn Memorial Hospital, Faculty of Medicine, Chulalongkorn University



Arthropod borne infections associated with cave

Pathamet Khositharattanakool

School of Medicine, Mae Fah Luang University, Chiang Rai, Thailand

Cave diving



Chamchan Chanchang¹

¹Naval Medical Department, Royal Thai Navy

Diving has become a well known sport and recreational activity for many years. Breathing underwater with compressed gas can cause various illnesses to a diver including decompression illness, gas toxicity, technical and equipment failure.

Cave diving is a form of technical diving in a natural overhead environment with lack of independent emergency ascent. Cave divers must manage significantly greater risks than those they experienced in open water.

Therefore, they require specific diving equipments, skills and training.

Apart from general health problems of scuba diving, cave diving is more vulnerable for accidents due to restricted space, visibility and increased risk of panic attack. Cave diver certification is available only through specific organizations. Highly specialized gas delivery system and equipments should be well prepared. Moreover, the divers demand special training in guideline and reel use, advanced buoyancy control and equipment modification.

Evacuation and resuscitation of an injured diver is technically limited. Thus, medical concern of cave diving should be emphasized on illness prevention with readiness evaluation and appropriate dive safety planning.

Keyword: Cave diving, evacuation

Cave bats and viruses



Supaporn Wacharapluesadee

Thai Red Cross Emerging Infectious Diseases - Health Science Centre and WHO Collaborating Centre for Research and Training on Viral Zoonoses , King Chulalongkorn Memorial Hospital, Faculty of Medicine, Chulalongkorn University

Bats are important to ecosystems, and many bat species rely on cave habitat for survival. On the other hand, bats are also natural reservoirs for several lifethreatening viruses such as Ebola, Nipah, SARS coronavirus (CoV) and MERS CoV. Rousettus, fruit eating bats, were reservoirs for the Ebola virus found in Africa. SARS CoV has been found in Hipposideros bats in China. Tylonycteris and Pipistrellus bats harbor group C MERS CoVs, which was first detected in China in 2006 before the outbreak in humans reported in Middle East in 2012. In Thailand, several groups of CoVs have been found from cave bats including SARS, MERS and potentially a new CoV. Staying in a cave for long time increases the risk of infection from viral pathogens from bats, both known and novel viruses. Testing assays which detect both known and novel is crucial to identifying new emerging viruses from cave bats in a timely manner. The viral family-wide PCR concept was used for testing specimens from wild boar soccer players after they were rescued from the Tham Luang cave in Chiang Rai, Thailand in July 2018. Fortunately no bat viruses were detected.

Keyword: cave, bats, viruses

Arthropod borne infections associated with cave



Phumee A¹, **Khositharattanakool P**², Somwang P², Boonsriwong W³, Boonserm R¹, Samung Y⁴, Payakkapol A⁴, Loyer M⁵, Augot D⁵, Gay F⁶, Depaquit J⁵, Siriyasatien P¹

¹Department of Parasitology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand ²School of Medicine, Mae Fah Luang University, Chiang Rai, Thailand ³Faculty of Medical Technology, Western University, Watcharaphol Campus, Pathumthani, Thailand ⁴Department of Medical Entomology, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand ⁵Université de Reims Champagne Ardenne, ANSES, SFR Cap santé, EA 4688 - USC « Transmission Vectorielle et Épidémiosurveillance de Maladies Parasitaires (VECPAR) », Reims, France ⁶Université Pierre et Marie Curie-Paris 6, CHU Pitié-Salpêtriere, AP-HP, Groupe Hospitalier Pitié-Salpêtriere, Service Parasitologie-Mycologie, Paris, France

Arthropod, especially insects and arachnids, are predominant creatures living as part of the ecology of caves. In the recent past, caving has become increasingly popular, due to the challenges of the complete darkness and the peace and beauty of the surroundings. This caving activity may increase risks of exposure to cave-dwelling arthropods that can cause direct trauma through envenomation. Also hematophagous insects in caves may play a key role as vectors of many pathogens. Phlebotomine sand flies are able to transmit leishmaniasis, which is an emerging disease in Thailand. Cases of Leishmaniasis, in either immunocompromised or immunocompetent patients, have been reported sporadically in Chiang Rai, Northern Thailand. Our study, surveying cave-dwelling insects in Chiang Rai, showed that the majority of hematophagous insects, captured by CDC miniature light traps, were sand flies. A total of 824 female sand flies were collected. Four genera (Sergentomyia, Phlebotomus, Idiophlebotomus and Chinius) including 13 species of sand flies were morphologically identified. Sergentomyia anodontis (Se. anodontis) was the most abundant species (comprising 33.37% of the collected females), followed by Sergentomyia sp. (25.85%), Se. sylvatica (9.35%), Phlebotomus barguesae (8.01%) and Idiophlebotomus longiforceps (Id. longiforceps) (8.01%). DNA of Leishmania spp. was detected in Se. anodontis and Id. longiforceps by DNA sequence analysis of ITS1. However, the ecology of cave-dwelling arthropods in Thailand remains poorly known. Therefore, studies on cavedwelling arthropods and experiments to confirm that Sergentomyia and Idiophlebotomus are biological vectors of leishmaniasis are still needed.

Keyword: Arthropod, Sand fly, Cave, *Leishmania*

11.00-12.30 Room D

\$22: Medical entomology impacts in tropical medicine

Chairpersons:







2. Jiraporn Ruangsittichai

Invited Speakers:



Breeding site of *Schoengastia* chigger mites as potential vector of scrub typhus in Vientiane (Lao PDR)

Rawadee Kumlert

Department of Disease Control, Ministry of Public Health, Thailand



 306° Vector Control: Tools and Engagement, imperative steps for combatting emerging tropical diseases

Su Yee Lim

Bayer Thai Co., Ltd.



Geometric Morphometrics: a quantitative tool for modern taxonomists **Suchada Sumruayphol**

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



Insecticide resistance of *Aedes aegypti* in Singapore – a comprehensive study **Sin Ying KOOU**

Department of Environmental Health Institute, National Environment Agency, Singapore

Breeding site of *Schoengastia* chigger mites as potential vector of scrub typhus in Vientiane (Lao PDR)



Rawadee Kumlert¹, Pathomporn Prikchoo¹, Paul Newton², Daniel H Paris^{3,4,5}, Anchana Prasartvit⁶, Serge Morand⁷, Sungsit Sungvornyothin⁸

- 1. The Office of Disease Prevention and Control 12 (Songkhla Province), Department of Disease Control, Ministry of Public Health, Thailand
- 2. The Lao-Oxford-Mahosot Hospital-Wellcome Trust Research Unit (LOMWRU), Lao PDR
- 3. Mahidol-Oxford Tropical Medicine Research Unit, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand
- 4. Swiss Tropical and Public Health Institute, Basel, Switzerland
- 5. University Basel, Basel, Switzerland
- 6. Department of Disease Control, Ministry of Public Health, Thailand
- 7. Institut des Sciences de l'Evolution de Montpellier (ISEM), Université de Montpellier, France
- 8. Department of Medical Entomology, Faculty of Tropical Medicine, Mahidol University, Thailand

Orientia tsutsugamushi, the causative agent of scrub typhus, is endemic in rural areas in the tropical zone, particularly in Asia Pacific. More than 1 billion of the world population lives in high risk areas, especially in agricultural sectors. The pathogen is spread by species of Trombiculid mites. The tissue-feeding larval stage, known as chigger mite, is the only stage related to O. tsutsugamushi transmission to vertebrate hosts, including human. Chigger mites inhabit "hot spot areas" known as "mite islands", where high numbers of chigger mites are present. Contact with these areas increases the risk of acquiring scrub typhus, leading to local outbreaks. In this study, we conducted surveys of chigger mite habitats in areas with reported scrub typhus cases. Survey areas covered houses and areas frequently visited by scrub typhus patients, including shades, high humidity zones, rodent holdings and water sources. Chigger mites were collected using black plates and identified morphologically by species identification keys. Additionally, we also used molecular methods and geometric morphometric technique to confirm species identification of chigger mites. Study site data were also gathered. We found 109 Schoengastia chiqger mites. Ninety percent of them inhabit shaded water source margins, 7% in rice fields near water sources, 2% around huts in rice field and 1% in shaded lowlands. Most chigger mite habitats were humid agricultural areas. By having a holistic understanding of scrub typhus and its transmission-risk areas, we expect to provide a practical surveillance system for more effective prevention and control programs.

Keyword: chigger mite, breeding site, scrub typhus

360° Vector Control: Tools and Engagement, imperative steps for combatting emerging tropical diseases



Su Yee Lim

Bayer Thai Co., Ltd.

Many of the common vector borne tropical diseases in the Southeast Asia are well known amongst its community. Despite this, transmission details, and/or prevention techniques are not often well understood by the public at large. Malaria, Dengue, Chikungunya, and Zika are some of the main vector-borne diseases that have taken center stage in the public health arena in recent years as their spread increase. With global efforts and ambitious goals for the elimination of these diseases, stronger collaboration and partnerships will be vital towards achieving these goals. At Bayer, we strongly back these initiatives, and believe there are five (5) key areas identified as part of the 360° Vector Control holistic approach; namely 'Expertise, Education, Partnerships, Advocacy, and Solutions'. We will discuss on-going efforts focused on 'Education' and 'Solutions' in this paper.

Keyword : 360° vector control, training & education, innovation, community engagement, Fludora, Mosquito Learning Lab

Geometric Morphometrics: a quantitative tool for modern taxonomists



Suchada Sumruayphol¹, Jean-Pierre Dujardin², Chamnarn Apiwathnasorn¹, Jiraporn Ruangsittichai¹, Patchara Sriwichai¹, Yudthana Samung¹, Ronald Enrique Morales Vargas¹, Sebastien Dujardin²

Correct identification of insect vector is an important work for vector surveillance and control which is mainly based on traditional taxonomy. Traditional taxonomy is a qualitative morphological characters. Modern taxonomy makes use of quantitative morphological characters. Geometric Morphometrics is a modern quantitative technique. GM, therefore is accurate and powerful tool for rapid low-cost identification by quantifying size and shape of many organisms. GM provides 3 types for taxonomic data collection, analysis and classification: landmark, semi landmark and outline. Landmark-based and outline-based GM are much more study. Landmark-based GM is popular approach and more wildly applied in variety of organisms. Recently, outline-based GM has been increasing interested from taxonomists.

There are many publications studying the power of these 2 techniques to differentiate closely related species including *Aedes*, *Stomoxys*, Chigger mites, *Anopheles*, and *Fasciola*.

Keyword: Geometric morphometrics

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Insecticide resistance of *Aedes aegypti* in Singapore - a comprehensive study



<u>Sin-Ying Koou</u>¹, Chee-Seng Chong ¹, Chow-Yang Lee², Indra Vythilingam³, Sook-Cheng Pang¹, Cheong-Huat Tan¹, Lee-Ching Ng^{1,4}

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In Singapore, environmental management and source reduction of mosquito vectors are the cornerstones of vector control programme. The use of insecticides is an integral component of the vector control programme, particularly in outbreak and dengue cluster management. However, the primary dengue vector in Singapore, Aedes aegypti has shown resistant to pyrethroids. Previous bioassay studies have reported development of insecticide resistance in some areas in Singapore. This study involved the classical WHO bioassay method, the use of synergists, biochemical assays and molecular technique to determine the insecticide susceptibility in seven field populations of Ae. aegypti in Singapore, and to investigate its underlying mechanisms involved. Bioassays revealed different levels of resistance to pyrethroids (deltamethrin, cypermethrin, permethrin and etofenprox) and susceptibility to organophophates (temephos and pirimiphosmethyl), Bacillus thuringensis israel (Bti) and pyriproxyfen. The insecticide susceptibility profile of Ae. aegypti was found to be homogeneous among different study sites. The addition of synergists generally failed to enhance the toxicity of the insecticides investigated, suggesting an insignificant role of metabolic-based resistance. Further biochemical investigation of specific metabolic enzyme activities suggested that detoxifying enzymes (mono-oxygenases, esterases, glutathione Stransferases and altered acetylcholinesterases) generally did not contribute to the resistance observed. The prevalence of pyrethroid resistance in Ae. aegypti populations is significantly inferred by the knockdown resistance (kdr) mechanism. Molecular assay revealed the presence of kdr mutations, S989P, V1016G and F1534C in resistant-strains of Ae. aegypti. Most (77%) individuals possessed F1534C mutation, reflecting the wide distribution of this mutation in field populations of Ae. aegypti. These data help to guide the use of chemicals for operational control of Ae. aegypti in Singapore.

Keyword: insecticide, resistance, bioassay, *Aedes*, Singapore

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11.00-12.30 Room E

\$23: Integration of Disease Control in Prison: Experience from Thailand (Sponsored by MOPH)

Chairperson:

Nakorn Premsri

Speakers:



General Health Problem in Thai Prison

Chutarut Chintakanont

Bureau of Penology, Department of Corrections

(No Abstract)



Review of disease outbreaks in prisons for prevention and control measures

Nakorn Premsri

Bureau of Epidemiology, Department of Disease Control, Ministry of Public Health (MOPH)

(No Abstract)



Success story of prevention and control in prison

Phalin Kamolwat

Bureau of Tuberculosis, Department of Disease Control, Ministry of Public Health (MOPH)

(No Abstract)



Development of integrated screening system for identification of important communicable and non-communicable diseases among prisoner inmates at admission, transfer, and release

Arjin Cholapand

Rajprachasamasai Institute, Department of Disease Control, Ministry of Public Health (MOPH)

(No Abstract)

14.00-15.30 Room A

\$24: Genome Editing of Malaria Parasites

Chairpersons:

1. John Adams





2. Nonlawat Boonyalai

Invited Speakers:



Recent advances in conditional gene disruption in *Plasmodium falciparum*: new insights into new and old targets

Michael Blackman

Department of Pathogen Molecular Biology, London School of Hygiene & Tropical Medicine



Molecular epidemiology of *Plasmodium falciparum* drug resistance in the Greater Mekong Subregion

Liwang Cui

University of South Florida



Validation of *Plasmodium falciparum* deoxyhypusine synthase as an antimalarial target **Philip Shaw**

National Center for Genetic Engineering and Biotechnology (BIOTEC)

Recent advances in conditional gene disruption in Plasmodium falciparum: new insights into new and old targets.



Christine R Collins¹, Abigail J Perrin¹, Konstantinos Koussis¹, Michele SY Tan¹, Abhinay Ramaprasad¹, Fiona Hackett¹, Chrislaine Withers-Martinez¹, James A Thomas^{1,2}, Emma S Sherling¹, and <u>Michael J</u> **Blackman**^{1,2}.

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The available genome sequences of *Plasmodium falciparum* and several other malaria parasite species have highlighted the abundance of parasite-specific genes (including so-called hypothetical genes) that have no obvious orthologues in other genera. Many of these genes could encode potential targets for drug or vaccine development; consistent with this, genome-wide gene disruption approaches have indicated that many of these *Plasmodium* genes are essential for parasite viability. However, their functions are largely unknown. For detailed insights into gene function, conditional gene modification methodologies are essential, but development of such tools has long been a major technical hurdle in malaria research. In this talk I will summarise the work of our group and our collaborators towards developing and refining such technologies, including recently-published and unpublished examples in which we have combined cutting-edge approaches to uncover new insights into parasite biology. I will also discuss the development and continuing urgent need for new phenotypic screens to decipher gene function and essentiality in P. falciparum and other human malaria pathogens.

Keyword: Plasmodium falciparum, new insights, malaria, genome editing

Molecular epidemiology of Plasmodium falciparum drug resistance in the Greater Mekong Subregion



Liwang Cui

University of South Florida

The Greater Mekong Subregion (GMS) of Southeast Asia is a hotspot for multidrug resistant (MDR) malaria parasites. Especially the recent emergence and spread of parasites resistant to the artemisinin family drugs are a major concern. Active research is targeted to understand the underlying mechanisms and strengthened control efforts are aimed to mitigate this urgent problem, along with the ultimate goal of regional malaria elimination by 2030. We have been closely monitoring the epidemiology of MDR parasites in this region, determining the mechanisms of resistance, and following the evolution and spread of resistant parasites. Our longitudinal monitoring of the kelch 13 (K13) gene involved in artemisinin resistance in the northeastern Myanmar identified an increasing trend of parasites with a predominant K13 gene mutation F446I, which is further associated with day 3 slide positivity in clinical efficacy studies and increased ring survival in an in vitro assay. We genetically confirmed the association of several K13 mutations that were prevalent in the China-Myanmar border area with increased ring survival rates. In addition, our study also suggested the involvement of a key hemoglobin digestion enzyme falcipain 2A in artemisinin resistance. Increased prevalence of multiple mutant genotypes of falcipain 2A in the GMS Plasmodium falciparum populations suggests that this gene might be under drug selection. Parasites having these mutant genotypes have impaired hemoglobin digestion, reduced parasite fitness, but higher ring survival rates. Furthermore, we try to identify additional molecular markers that are associated with drug resistance through procurement of field parasite isolates, in vivo drug efficacy studies, in vitro drug assays, and genome-wide association studies. These studies identified additional markers that are associated with stress responses in the parasite, which may also contribute to drug resistance. Taken together, we are using a combination of clinical, epidemiological and genetic tools to tackle the problem of drug resistance in the GMS.

Keyword: Plasmodium falciparum, drug resistance, Greater Mekong Subregion

Validation of *Plasmodium falciparum* deoxyhypusine synthase as an antimalarial target



Aiyada Aroonsri¹, Navaporn Posayapisit¹, Jindaporn Kongsee², Onsiri Siripan^{1,3}, Sugunya Utaida², Chairat Uthaipibull¹, Sumalee Kamchonwongpaisan¹ and **Philip J. Shaw**¹

Hypusination is an essential post-translational modification in eukaryotes. The two enzymes required for this modification, namely deoxyhypusine synthase (DHS) and deoxyhypusine hydrolase are also conserved. *Plasmodium falciparum* human malaria parasites possess genes for both hypusination enzymes, which are hypothesized to be targets of antimalarial drugs.

Transgenic *P. falciparum* parasites with modification of the PF3D7_1412600 gene encoding PfDHS enzyme were created by insertion of the glmS riboswitch or the M9 inactive variant. Attenuation of PfDHS expression for 72 h led to a significant reduction of hypusinated protein; however, global protein synthesis was unaffected. Parasites with attenuated PfDHS expression showed a significant growth defect, although their decline was not as rapid as parasites with attenuated dihydrofolate reductase-thymidylate synthase (PfDHFR-TS) expression. PfDHS-attenuated parasites showed increased sensitivity to N^1 -guanyl-1,7-diaminoheptane, a structural analog of spermidine, and a known inhibitor of DHS enzymes.

Loss of *Pf*DHS function leads to reduced hypusination, which may be important for synthesis of some essential proteins. The growth defect in parasites with attenuated <u>Pf</u>DHS expression implies that this gene is essential. However, the slower decline of *Pf*DHS mutants compared with *Pf*DHFR-TS mutants in competitive growth assays suggests that *Pf*DHS is less vulnerable as an antimalarial target. Nevertheless, the data validate *Pf*DHS as an antimalarial target which can be inhibited by spermidine-like compounds.

Keyword : deoxyhypusine synthase; *Plasmodium falciparum*; malaria; *glmS* riboswitch; hypusination

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14.00-15.30 Room B

\$25: Entrepreneurship in Diagnostic, Pharmaceutical and Healthcare

Chairpersons:

1. Santi Maneewatchararangsri





2. Supachai Topanurak

Invited Speakers:



Therapeutic human monoclonal antibodies against Dengue virus; Towards the industrial production and commercialisation

Pongrama Ramasoota

Department of Social and Environmental Medicine, Faculty of Tropical Medicine, Mahidol University

Cancer precision medicine in Thailand

Manop Pithukpakorn

Faculty of Medicine Siriraj Hospital, Mahidol University



Lateral flow test kits for small molecules and viruses: an example work from basic research to innovation

Kiattawee Choowongkomon

Faculty of Science, Kasetsart University



Combination of PCR and dual nanoparticles for malaria detection **Kulachart Jangpatarapongsa**

Faculty of Medical Technology, Mahidol University

Therapeutic human monoclonal antibodies against Dengue virus; Towards the industrial production and commercialisation



Pongrama Ramasoota¹, Pannamthip Pitaksajjakul¹, Tadahiro Sasaki², Kazuyoshi Ikuta²

Dengue hemorhagic fever (DHF) cause by the mosquito borne Dengue virus (DENV) has become the world public health problem due to global warming and globalization. Each year, 100 million Dengue cases required hospitalization. World Health Organization aim to reduce Dengue mortality to be at 50% in the year 2020. But until present, there is no specific drug for Dengue treatment. By using SPYMEG myeloma cell fused with pheriperal blood mononuclear cell (PBMC) obtained from Dengue patients, the hybridoma cell producing neutralizing human monoclonal antibodies (NhuMAbs) anti envelope protein against 4 serotypes of DENV has been the world's first time established at CEAR. Two candidates NhuMAb (1B3B9 and 1G7C2) were successfully preclinically tested in vitro by 95-100 % neutralized all 4 serotypes of 20 clinical isolates DENV and in vivo tested by significantly decreased mortality of DENV intra-cranially mice and eliminated DENV (from 10¹⁰ to be 0) in blood of DENV challenged Marmoset monkeys within 2 days. For further used in human, large scale production of NhuMAb using the Food and drug administration (FDA) accepted method namely Stable Chinese Hamster Ovary (CHO) cell expression, has been prepared. Until present 120 ng/cell NhuMAbs from the stable expressed CHO cell has been prepared, that aiming for further safety and toxicity test and followed by Phase 1 clinical trial. We are calling for collaboration with GMP Biologics production plants and also with venture drugcompany to make happen the world first Biologics drug for Dengue treatment in human.

Keyword: Neutralizing, human monoclonal antibodies, Dengue virus, 4 serotypes, envelope protein

¹Center of excellence for antibody research (CEAR), Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

²Research Institute for Microbial Diseases, Osaka University, Osaka, Japan

Cancer precision medicine in Thailand



Manop Pithukpakorn

Faculty of Medicine Siriraj Hospital, Mahidol University

Precision medicine is an emerging paradigm for disease diagnosis, treatment and prevention that takes individual genetic and molecular variability, environmental and lifestyle difference of each person into account. Contrary to "one-size-fits-all" approach, precision medicine will allow doctors and researchers to predict more accurately which treatment and prevention strategies for a particular disease will work in which patients.

Cancer is the best example to demonstrate the benefit of precision medicine. It has been universally accepted that cancer is a genetic disorder that results in abnormal cell growth and the invasiveness and spreading potential to other parts of the body. Better understanding in cancer genetics leads to new types of cancer diagnostic tests and several novel drugs which are designed to target specific genetic abnormalities in

The unprecedented throughput, speed and cost of next generation sequencing (NGS) enables researchers to investigate genetic contribution of cancer and implement this technology to the real world medical practice. We currently see widespread use of NGS to discover genetic alterations in each patient, to identify potential treatment target, and to predict response of medical treatment. In clinical practice, oncologists could select the best and most appropriate treatment for each patient, based on the patient's genetic data. Precision medicine widely becomes a standard approach in cancer diagnosis and treatment. Patients with lung or breast cancers with specific genetic alterations could get significant benefit from novel targeted therapies that specifically act on certain molecular pathway. Precision medicine also predict what medication would not work and that treatment could be avoided. This novel approach would improve cancer treatment efficacy, patient outcome, quality of life, reduce healthcare cost and overall social and economic burden.

Many studies have shown that genetic diversity plays role in phenotypic differences among various ethnic groups with the same diseases. Some cancer types are significantly more prevalent in Asian than in Western population. Same cancers display difference in subtypes among countries. Many similar cancers from various ethnic groups also have different treatment outcome and prognosis. To be able to determine the role of genetic diversity in Thai cancer patients, as well as development and implementation of cancer precision medicine in Thailand, a multi-institute research collaboration was established under the 'Research University Network' (RUN). The research network aims to study genetic alterations in Thai cancer patients, develop a study platform for cancer biology and cancer treatment, apply clinical genetic testing for Thai cancer patients and develop precision medicine guidelines for cancer diagnosis and treatment. Since the inception, the network has established a collection of clinical data and bio-specimens from more than 1,500 cancer patients as well as several hundreds of cancer genome data. The research team has also developed the threedimensional model of cancer cell culture and collection of primary cancer 'organoids' for high-throughput cancer drug testing platform.

In conclusion, cancer precision medicine research network has established databases of Thai cancers and generated vast amount of the clinical and genomic data, which could propel cancer researches in various aspects. The research has also led to several Thailand's first successes including integrated genetic diagnostic laboratory for cancer diagnosis, patient-derived three-dimensional cancer cell cultures (cancer avatar), cancer drug testing system, cancer cell culture in zebrafish. The research can be translated to a comprehensive cancer diagnosis and treatment of cancer. In addition, Thai cancer patients could also benefit from widespread use of genetic testing and precision medicine approach for cancer care, which could result in an increased treatment effectiveness and improved quality of life.

Keyword: Cancer, precision medicine, Thailand

Lateral flow test kits for small molecules and viruses: an example work from basic research to innovation



Kiattawee Choowongkomon¹

In my laboratory, we have been studied on protein based drug design in both computational and experimental works focusing mainly in cancer and virus based diseases. My interest has been focused on DNA aptamer screening biotechnology. The specific DNA sequences from random DNA library can be identified to bind with any target molecules with high affinity. These DNA aptamers can use to as inhibitors against target molecules or detection kits. We are able to screen the biomolecules bind specifically to target protein in cancer, insecticides (eg. Paraguat, organophosphate), antibiotic (eg. Nitrofulan, tetracycline, oxycline), and porcine reproductive and respiratory syndrome virus (PRRSV). We are using these technologies on development new inhibitors against target proteins and also detection kits by colorimetric method or the lateral flow technology to detect pesticides, antibiotics and viruses. These works seem to be promising for me to further developing a startup company,"BioXcreen" in the future.

Keyword: Lateral flow test kits, paraguat, organophosphate, antibiotics, virus, aptamer

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Combination of PCR and dual nanoparticles for malaria detection



Kulachart Jangpatapongsa

Center for Research and Innovation, Faculty of Medical Technology, Mahidol University

The detection based on nanoparticle-DNA amplification technique was developed for the detection of asexual and sexual stage of malaria infection. The functional magnetic latex particles (MLPs) and quantum dots encapsulated polymer particles (QDs-PPs) was designed and synthesized. MLPs were prepared from the precipitation of iron oxide, polymerization using initiator, and adsorption of aminodextran (AMD) so as to provide amino-functionalized MLPs. Aminocontaining polymer particles (PPs) were prepared by emulsifier-free polymerization and encapsulated with fluorescent quantum dots (QDs) for use as a signaling support. Subsequently, poly(maleic anhydride-alt-methyl vinyl ether) (PMAMVE) copolymer was effectively used for rapid and simple grafting of amino-modified DNA primers onto the surface of amino-functionalized particles thereby providing a promising method for particle immobilization. Herein, Pfg377 specific primer-grafted particles were applied in the amplification of the Pfg377 gene. After amplification, PCR products containing PMAMVE-grafted MLPs and QDs-PPs were separated using a magnet and examined via a fluorescence microscope. PMAMVE-grafted particles were facilitated efficient fluorescent signal detection of the PCR product. Results showed high sensitivity and specificity for the detection of amplified Pfg377 gene among malaria blood sample containing sexual stage, and asexual stage presenting in some blood sample within only a few steps. This procedure represents a novel improvement to the post-amplification analysis and could be potentially used as rapid detection test for malaria surveillance in endemic countries.

Keyword: PCR, malaria, dual nanoparticles

Thursday 13 December 2018

14.00-15.30 Room C

\$26: Free Paper: Microbiology and immunology

Chairpersons:







2. Nathamon Kosoltanapiwat

Speakers:



Safety and immunogenicity of AGS-v, a mosquito saliva peptide vaccine: a randomized, double-blind, placebo-controlled Phase 1 trial

Jessica Manning

National Institute of Allergy and Infectious Diseases, National Institutes of Health, USA



Molecular detection and characterization of serotypes and virulence factors of *Klebsiella pneumoniae* from mastitic dairy cattle of Batangas, Philippines

Flor Marie Immanuelle Pilapil-Amante

College of Veterinary Medicine, University of the Philippines, Los Baños



Anti-fungal study of a medicinal compound from *Bidens pilosa*, cytopiloyne **Meng-Ting Yang**

Agricultural Biotechnology Research Center, Academia Sinica, Taiwan



Antibiotic resistance, biofilm formation and virulence factors among enterococci clinical isolates collected from two tertiary care hospitals, Thailand

Seinn So Lwin

Faculty of Science, Prince of Songkla University, Thailand



Structural basis for DNA recognition and transduction activation by the response regulator OmpR

Sushant Sadotra

Chemical Biology and Molecular Biophysics, Taiwan International Graduate Program, Academia Sinica, Taipei, Taiwan



Gayan Parakrama Wijayapala Kombala Withanage

Molecular Medicine Unit, Faculty of Medicine, University of Kelaniya, Sri Lanka



Safety and immunogenicity of AGS-v, a mosquito saliva peptide vaccine: a randomized, double-blind, placebocontrolled Phase 1 trial



Jessica E. Manning¹, Fabiano Oliveira¹, Iliano V. Coutinho-Abreu¹, Samantha Herbert¹, Claudio Meneses¹, Shaden Kamhawi¹, Holly Ann Baus², Alison Han², Lindsay Czajkowski², Luz Angela Rosas², Adriana Cervantes-Medina², Rani Athota², Susan Reed², Ana Fernandez³, Olga Pleguezuelos³, Gregory Stoloff³, Jesus G. Valenzuela¹, Matthew I. Memoli²

¹Laboratory of Malaria and Vector Research, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland, USA; ²Laboratory of Infectious Diseases Clinical Studies Unit, Viral Pathogenesis and Evolution Section, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland, USA; 3SEEK, PepTcell Limited, London, United Kingdom

A novel approach to mosquito-borne disease prevention focuses on arthropod salivary-mediated transmission of pathogens. Parasites and viruses carried within mosquito saliva appear to initiate or enhance severity of host infection by taking advantage of saliva-human host interactions. This leads to alteration of the cutaneous environment and modulation of the host's innate and adaptive immune responses, thereby providing a rationale for creating vaccines against mosquito salivary proteins rather than the pathogens contained within the saliva, or a combination of both. AGS-v is a vaccine composed of four salivary peptides isolated from *Anopheles gambiae* salivary glands, but that are common across a number of mosquitoes. In this first-in-human study, we enrolled and randomized 49 healthy adult participants to receive the AGS-v vaccine with and without adjuvant (Montanide ISA 51) versus placebo. Vaccinations occurred at Day 0 and Day 21 followed by a clean Aedes aegypti mosquito feeding at Day 42. Primary objectives are: 1) to assess safety via incidence of adverse events and 2) to evaluate humoral and cellular immunity by respectively measuring total AGS-v specific immunoglobulins and Th1-associated cytokine release after incubation of peripheral blood mononuclear cells (PBMCs) with AGS-v antigens. Secondary objectives are post-mosquito feeding measures of AGS-v specific immunoglobulins and Th1-related cytokine release, mosquito survival and fecundity, as well as the effects of immunized individuals' peripheral blood mononuclear cells on Zika virus after stimulation with Aedes aegypti saliva. Results are pending until data blind is lifted October 2018, but will be available

for presentation at the conference.

Keyword: mosquito, saliva, Zika, vaccine

Molecular Detection and Characterization of Serotypes and Virulence Factors of *Klebsiella pneumoniae* from Mastitic Dairy Cattle of Batangas, Philippines



Flor Marie Immanuelle R. Pilapil¹; Loinda R. Baldrias²; Antonio A. Rayos³; & Billy P. Divina²

Klebsiella pneumoniae is an opportunistic pathogen both shared by humans and animals. Adhesins, siderophore (Koczura and Kaznowski, 2003), lipopolysaccharide (LPS), and the capsular polysaccharide (CPS) are factors adding to its virulence (Brisse, et al., 2009; Younes., 2010). This study was conducted to determine the molecular serotypes and to understand the virulence factors of Klebsiella pneumoniae isolates from bovine milk. California mastitis test (CMT) was done on 2,406 teats coming from 624 milking cows in 12 dairy cattle farms in Batangas, Philippines last June 2016. Individual quarter milk samples of CMT scores 3 and 2 (n=230) were collected aseptically and cultured in McConkey agar. Bacterial growths were subcultured in McConkey-inositol-potassium tellurite agar. Colony morphology, biochemical testing and molecular detection were performed and yielded only six isolates resulting to a confirmed prevalence rate of 2.6% (6/230). Molecular serotyping of K1, K2, K5 and non-K1/K2 isolates were done through Polymerase Chain Reaction (PCR) by determination of the prevalence of virulence gene magA (1283 bp), wzy (641 bp), K5wzx (280bp) and rmpA (516 bp) respectively. Molecular serotyping for K20, K54 and K57 and virulence gene wcaG (169 bp) were also determined. The subclinical mastitis rate was at 9% from 93 milking cows while the clinical mastitis rate was at 19% from 228 milking cows. Only one isolate belonged to the capsular serotype K57 which means that the remaining isolates could belong to the other 71 serotypes such as K3, K4, K6, and K52. K57 is often involved with invasive pyogenic liver abscess, septicaemia and pneumonia (Turton et al., 2008). Therefore, its presence in food poses a potential public health risk (Zhang et al., 2018) and it being isolated in bovine milk marks the high risk of this food type. K1 and K2 serotypes are more related to human disease (Osman et al., 2014) which can possibly explain why the isolates of this study were not of K1 and K2 serotype and possibly note that the origin of the infection was non-human. Furthermore, since there were no virulence genes detected even on the K57 isolate, it could be noted that the infections brought about by these isolates are not that severe.

Keyword : bovine mastitis, food-borne, *Klebsiella pneumoniae*, molecular serotyping, virulence genes

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Anti-fungal study of a medicinal compound from Bidens pilosa, cytopiloyne



Meng-Ting Yang^{1,2,3}, Chih-Yao Chung⁴, Chih-Lung Liang⁵, Hsien-Yueh Liu ⁴, Shih-Kai Lai ⁴, Cicero Lee-Tian Chang ⁴, Wen-Chin Yang^{1,2,3}

¹Agricultural Biotechnology Research Center, Academia Sinica, Taiwan;²Molecular and Biological Agricultural Sciences Program, Taiwan International Graduate Program, National Chung-Hsing University, Taichung, Taiwan and Academia Sinica, Taipei, Taiwan; Graduate Institute of Biotechnology, National Chung-Hsing University, Taichung, Taiwan; Department of Veterinary Medicine, National Chung-Hsing University, Taichung, Taiwan; Department of Microbiology and Immunology, Institute of Microbiology and Immunology, Chung Shan Medical University, Taichung, Taiwan

Fungal infections, very common tropical diseases worldwide, have the profound impact on human health. Candida species, the major cause of fungal infections, are a tremendous threat to immunocompromised persons such as infants, pregnant women, elders, and patients with cancers and HIV/AIDS. Candidiasis can result in a mortality rate up to 71%. Currently, anti-fungal drugs market will rise to \$17,718 million by 2023; however, anti-fungal drug resistance is emerging as a burning issue. Therefore, a novel strategy to treat fungal infection without drug resistance is important. One approach is to boost antifungal immunity using herbal plants and their compounds.

Here, we first test the anti-fungal activity of *Bidens pilosa*, a plant with diverse anti-microbial activities. Using a bioactivity-directed strategy, we identified cytopiloyne (CP) from Bidens pilosa and studied its anti-fungal function. The in vitro assays showed that CP increased killing of Candida by macrophages. Next, in vivo study in Candida-infected mice revealed that CP protected the mice from death via reduction of Candida dissemination and inflammatory organs by macrophage modulation, including the augmentation of phagolysosomal fusion, phagolysosomal acidification, and lysosomal enzyme activity. Finally, a mechanistic study indicated that CP activated phagocytosis of macrophage via the PKC pathway. This study could be applied to other fungal infections in the immunocompromised hosts, such as Aspergillosis and Cryptococcosis.

Keyword: Candida species; immunity; Bidens pilosa; cytopiloyne

Antibiotic resistance, biofilm formation and virulence factors among enterococci clinical isolates collected from two tertiary care hospitals, Thailand



<u>Seinn So Lwin</u>¹, Kanitta Muangngam¹, Nurihan Yusoh¹, Pimonsri Mittraparp-arthorn¹, <u>Wipawadee Sianglum</u>¹*

Department of Microbiology, Faculty of Science, Prince of Songkla University, Thailand ^{1*} corresponding author

Objectives: This study evaluated vancomycin-resistant enterococci (VRE), multidrug resistance and the possible association of antimicrobial resistance with biofilm and virulence factors activity among enterococci isolates.

Methods: Enterococci clinical isolates collected from the laboratories of Sunpasitthiprasong Hospital (Northeastern Thailand) and Hat Yai Hospital (Southern Thailand). The susceptibility of 11 commonly used antibiotics in all isolates and 4 additional antibiotics in VRE isolates were determined using disk diffusion method. MIC of vancomycin were examined using broth microdilution method. *Enterococcus* species and vancomycin-resistant genes were identified using multiplex PCR. Biofilm formation was observed using crystal violet assay and caseinase, gelatinase, haemolysin, and lipase productions were determined phenotypically.

Results: Among 765 isolates, *E. faecalis* (72.3%), *E. faecium* (23.7%), *E. casseliflavus* (1.6%), *E. gallinarum* (1.3%) and *Enterococcus* spp. (1.2%) isolated from urine, pus, blood, body fluid and sputum. The most resistant antibiotics observed as erythromycin (81.7%), tetracycline (76.9%) and ciprofloxacin (71.9%). Multidrug resistance (MDR) and high-level aminoglycosides resistance (HLAR) exhibited from 77.9% and 43.7% of isolates. The incidence of MDR and HLAR were significantly lower in biofilm and virulence factors producers than non-producers (p<0.001). All 30 VRE isolates revealed *vanA* gene in genotype and one VRE showed the susceptibility to teicoplanin in phenotype as vanA genotype-vanB phenotype. Although all VRE isolates were MDR, chloramphenicol (90%), linezolid (100%) and tigecycline (100%) were most active against VRE. There was no significant association between VRE and virulence factors activities (p>0.05). Overall, 33.6%, 39.8%, 52.4%, 17.9% and 5.6% of isolates produced biofilm, gelatinase, caseinase, β -haemolysin, and lipase. Caseinase and gelatinase production exhibited the correlation with biofilm formation (p<0.01) but β -haemolysin and lipase productions were no effect on biofilm formation (p>0.05).

Conclusion: This study may support as an evaluation of the importance of multidrug resistance and virulent determinants of enterococci in hospitalized patients.

Keyword: antibiotic resistance, biofilm formation, *Enterococcus*, vancomycin-resistant enterococci, virulence factors

Structural Basis For DNA Recognition And Transduction Activation By The Response Regulator OmpR



<u>Sushant Sadotra</u>^{1,2,3}, Yuan-Chao Lou², Chun-Hua Hsu⁴ and Chinpan Chen²

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OmpR, an OmpR/PhoB family response regulator, has an evident regulatory role in controlling transcription of at least 125 genes that include both housekeeping and virulence genes; thus, is highly responsible for bacterial pathogenesis. During signal transduction, OmpR undergoes phosphorylation at its conserved Asp residue in the N-terminal receiver domain and recognizes promotor DNA from its variable C-terminal effector domain/DNA-binding domain (OmpRc) to elicit an adaptive response. However, an elaborate picture of this DNA binding mechanism of OmpR is still not fully clear until date. To gain insights, we determined the crystal structure of OmpRc in complex with OmpF1 promotor DNA, and report two different crystal structures of OmpRc-apo form in different crystallization conditions. Our structural analysis suggest that OmpRc can bind to its cognate DNA as a homodimer, in Head-to-Tail orientation, only in its traditional monomeric form but not in domain-swapped dimeric form. We observed the low solubility of full-length OmpR (OmpR-FL) upon activation through BeF, phosphate analog that clearly indicates OmpR-FL dimerizes on phosphorylation. The HSQC NMR spectra of both ¹⁵N-Labelled OmpR-FL (unphosphorylated) and ¹⁵N-Labelled OmpRc showed a significant chemical shift perturbation upon titration with DNA. Furthermore, our fluorescent polarization experimental data show that OmpR FL has weaker binding affinity with DNA as compared to OmpRc, specifying that phosphorylation may only enhance but not require for DNA binding. Taken together, our results provide a clear depiction of how OmpRc recognizes the target DNA, reveal a unique domain-swapped dimeric state of OmpRc, and identify the potential for this "druggable" target.

Keyword: bacterial signal transduction, response regulator, OmpR, DNA binding domain, X-ray crystal structure, NMR

Molecular approach to identify mosquito species in Sri Lanka



Withanage GP¹, Piyadasa TA¹, Koo C², Yeo Huiqing², Gunawardena YINS¹, Ng LC^{2,3}, Lam-Phua SG², Hapuarachchi CH² and Hapugoda MD^{1*}

¹Molecular Medicine Unit, Faculty of Medicine, University of Kelaniya, Ragama, Sri Lanka; ²Environmental Health Institute, National Environment Agency, 11 Biopolis Way, Helios Block, #06-05/08, Singapore 138667, Singapore; ³School of Biological Sciences, Nanyang Technological University, 60 Nanyang Drive, Singapore 637551, Singapore

Mosquitoes are one of the most medically important arthropod vectors of human pathogens. Even though the use of taxonomic keys is the gold standard methodology to identify mosquito species, morphology-based identification is challenging when there is a lack of required expertise and well-preserved specimens. Cytochrome C oxidase subunit1 (COI)-based DNA barcoding is a recently developed complementary tool to taxonomy and has achieved great success in mosquito identification. In the present study, we generated complete 'Folmer region' barcodes for 47 mosquito specimens belonging to 21 species of six genera in Sri Lanka and compared the morphological identification with COI barcodes utilizing distance and phylogenetic methods. COI sequences were highly AT rich and the Automatic Barcode Gap Discovery analysis indicated a clear barcode gap between inter- and intra-specific distances. Mean interspecies Kimura-2-parameter pairwise divergence ranged from 7.0% to 25.4%, while that for intra-species ranged from 0.0% to 1.4%. Purifying selection was observed with 5.116 overall transition: transversion bias of COI sequences. The index of substitution saturation (Iss) was significantly lower than critical Iss (p<0.05), suggesting that the study sequences were neither too diverged nor too conserved, illustrating the appropriateness of COI sequences for DNA barcoding of mosquito species. In the study, we report the presence of *Culex* pipiens for the first time in Sri Lanka. We conclude that COI barcodes can be used to complement the taxonomy-based identification of mosquito species and still there is a prime requirement of COI based DNA barcodes of curated mosquito specimens from geographically different locations globally.

Keyword: DNA barcoding, COI, mosquitoes, phylogeny

Thursday 13 December 2018

14.00-15.30 Room D

\$27: Protozoa

Chairpersons:

1. Aongart Mahittikorn





2. Supaluk Popruk

Invited Speakers:



Trichomonas vaginalis Infections in the Philippines

Windell Rivera

Institute of Biology, College of Science, University of the Philippines, Diliman

Speakers:



Trypanosomes and biosecurity

RC Andrew Thompson

Veterinary and Life Sciences, Murdoch University, Perth, Western Australia



Effect of *Toxoplasma gondii* profilin exposure on high density lipoprotein (HDL) level in normal and hypercaloric diet induced *Rattus norvegicus* wistar strain rats

Yulia Dwi Setia

Faculty of Medicine, Universitas Brawijaya, Indonesia



Difference in the infection pattern of two transgenic *Trypanosoma cruzi* strains, Tulahuen *luc*2 and Y02 *luc*2, detected by *in vivo* imaging and blood parasite monitoring in murine model

Eleonor Cervantes

Research Institute for Tropical Medicine, Department of Health, Philippines

Molecular detection of *Leishmania donovani* in blood samples collected from program and non-program districts of Nepal



Nepal Academy of Science and Technology, Khumaltar, Lalitpur, Nepal



Trichomonas vaginalis Infections in the Philippines



Windell L. Rivera^{1,2}

Trichomonas vaginalis is the causative agent of trichomoniasis, the most prevalent sexually-transmitted infection (STI) in the world. The prevalence of trichomoniasis in the Philippines is low as compared to the other countries. However, our studies showed an increasing trend in the prevalence of this STI in the Philippines. This can be attributed to the use of nucleic acid amplification techniques (NAATs) which are more sensitive and rapid than the traditional methods of detecting this protozoon. T. vaginalis parasitizes the urogenital tract of human, however, infection in other cell types, like the lung cells, was also observed. Infection with *T. vaginalis* may cause inflammation and this effect was associated with the presence of a virus in inside the cell called Trichomonas vaginalis virus (TVV). There are four species of TVV and all were detected in T. vaginalis isolated from Pampanga, Philippines. Another issue that must be of concern is the occurrence of drug-resistant T. vaginalis especially that only two drugs, metronidazole and tinidazole, have the approval for use in treatment of the infection. This is even aggravated by the higher risk of acquiring human immunodeficiency virus (HIV) when one has trichomoniasis. Our country is now challenged by an HIV epidemic and it is indeed high time that we look into other agents of STI that aid in the spread of HIV.

Keyword: trichomoniasis, STI, HIV, Philippines

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Trypanosomes and biosecurity



Murdoch University

RC Andrew Thompson

In recent years trypanosomes have emerged as growing threats to the biosecurity of countries in Southeast Asia and Australia. Recent discoveries concerning Leishmania and other trypanosomes have demonstrated that we must not become complacent and reliant on dogma when considering the potential emergence of new threats. This applies to public health, livestock industries and conservation. The demonstration of novel indigenous species of trypanosomes and vectors, particularly those associated with wildlife, and an increase in introductions of exotic pathogenic species with the potential to establish reservoirs in wildlife, has demonstrated the urgent need for further research. However, with such a dearth of information, it is important to keep an open mind in future investigations. This particularly applies to determining the vectorial capacity of native arthropods. For example, several new species of Trypanosoma have been described recently from Australian indigenous mammals, along with other unnamed isolates and genotypes. However, we know little about how they are transmitted due to difficulties relating to the confirmation of cyclical and mechanical vector candidates. Current biosecurity issues will be discussed with significant importance placed on the close phylogenetic and phenotypic relationship shared between Trypanosoma cruzi and some Australian trypanosomes.

Keyword: Trypanosomes; biosecurity; wildlife; transmission

Effect of Toxoplasma gondii Profilin Exposure on High Density Lipoprotein (HDL) Level in Normal and Hypercaloric Diet Induced *Rattus norvegicus* wistar Strain Rats



Setia YD¹, Poeranto S¹, Mohan K², Endrawati H¹, Mayashinta DK¹, Iskandar A¹, , Sudjari¹

Toxoplasma gondii, a protozoa causes toxoplasmosis. It is produces in cats, stray cats and domestic is the definitive host. It has been known for some time that T.gondii is not capable of synthesizing cholesterol (Chl), and thus depends on uptake of host Chl for its development. Chl metabolism in mammalian cells involves direct transport of preformed sterol from the liver in the form of very low density lipoprotein (VLDL) and low density lipoprotein (LDL) to the pheriphery. In fact, it has been shown that T. gondii acquires host Chl via endocytosis mediated by the LDL receptor or the LDL receptor-related protein. This shows that *Toxoplasma* depends on the host for ChI and uptaking it via LDL receptor. This may explain the fact that, the endocytosis causing the LDL level to increase, directly causing the HDL level to decrease. This study was conducted to determine the effect of *Toxoplasma gondii* profilin exposure on HDL levels in normal and hypercaloric induced Rattus norvegicus strain wistar rats. The research is a experimental study in the laboratory with true experimental-post-test- control-group design only. Result of Kruskal Walis test (p =0.252; $\alpha \ge 0.05$) shows that therewere not any significant difference on HDL levels in all groups. The result of correlation coeficient shows the majority of groups, show a weak correlation between *Toxoplasma gondii* profilin exposure HDL level with negatif direction. It can be concluded that, Toxoplasma gondii profilin does not influence the HDL level in Rattus norvegicus wistar strain rats.

Keyword : *Toxoplasma gondii,* profilin, HDL level, rat

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²Program Study of Medicine, Faculty of Medicine, Universitas Brawijaya/ Saiful Anwar General Hospital Malang

Difference in the infection pattern of two transgenic Trypanosoma cruzi strains, Tulahuen luc2 and Y02 luc2, detected by in vivo imaging and blood parasite monitoring in murine model



Eleonor A. Cervantes^{1,2}, Mahamoud Sama Cherif¹, Tetsuo Yanagi³, Takeshi Nara⁴, and Kenji Hirayama¹

Chagas disease is caused by the protozoan parasite Trypanosoma cruzi (T. cruzi). New therapeutics is necessary due to limited efficacy of known drugs Benznidazole (BNZ) and Nifurtimox. However, drug development has been impeded partly because of the lack of standardized method for the in vivo detection of parasitological cure in small animal model. Here, we aimed to develop and established an in vivo monitoring tool where we used three methodology namely in vivo whole body imaging system (IVIS), peripheral blood parasite count by hematocrit centrifuge technique (HCT) and by quantitative PCR (gPCR). After challenge infection, disease progression and treatment efficacy were assessed in BALB/c mouse model. IVIS has allowed long-term evaluation of systemic parasite burden and in addition with the other two methods that detected circulating parasite more sensitively. Taken together the observation of the three methodology used, we found a clear difference in the infectivity of the two strains and the sensitivity against BNZ treatment. Tulahuen *luc2* strain peaked infection at 14 days post-infection (dpi) as inferred by IVIS and peripheral blood parasite counting while Y02 *luc2* peaked infection at 7dpi and was found to be less sensitive to BNZ treatment. Our findings underscore the eventual usage of transgenic parasites for monitoring parasitological cure in mouse model with emphasis on the use of a particular T. cruzi strain in combination to an in vivo assessment method.

Keyword: Trypanosoma cruzi, strain difference, in vivo imaging system

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² Research Institute for Tropical Medicine, Department of Health, Philippines

³ NEKKEN Bio-Resource Center (NBRC), Institute for Tropical Medicine, Nagasaki University, Japan

⁴ Department of Molecular and Cellular Parasitology, Juntendo University, Japan

Molecular detection of Leishmania donovani in blood samples collected from program and non-program districts of Nepal



Mitesh Shrestha¹, Jyoti Maharjan¹, Prakash Nidhi Tiwari², Krishna Das Manandhar³, Basu Dev Pandey⁴, Sher Bahadur Pun⁵. Kishor Pandev¹

¹Nepal Academy of Science and Technology, Khumaltar, Lalitpur, Nepal; ²Kanti Children Hospital, Kathmandu, Nepal; 3Central Department of Biotechnology, Tribhuvan University, Nepal; 4Leprosy Control Division, Kathmandu, Nepal; 5Sukraraj Tropical and Infectious Disease Hospital, Kathmandu, Nepal

Leishmaniasis has been classified as one of the Neglected Tropical Diseases caused by an intracellular protozoan parasite, Leishmania. The vector-borne disease is transmitted by the infected female sandfly, *Phlebotomus argentipes*. The Nepalese government has designated 12 endemic districts as program districts where constant monitoring is conducted. For this study, a total of 37 suspected samples collected from both program and non-program districts were analyzed for presence of the parasite using Polymerase Chain Reaction (PCR) amplifying the kinetoplast region of the parasite. Out of the 37 samples, six samples gave positive result showing band length of approx. 720 bp confirming the presence of parasite in the blood samples. A significant result was obtained from one of the positive sample that had been collected from a patient residing at a high altitude region of Nepal (>5000 m) and had no prior travel history to either endemic places or to places from where sporadic cases had been reported. The selected positive samples were further used for sequencing. The sequencing results confirm that the positive samples were Leishmania parasites. This study along with the emerging case reports has led us to conclude that the disease is slowly progressing towards higher altitudes and could pose a tremendous hurdle for the concerned authorities planning to eliminate the disease from the country by 2020.

Keyword: Leishmaniasis, *Leishmania donovani*, Nepal, *Phlebotomus* argentipes, Visceral Leishmaniasis

Thursday 13 December 2018

14.00-15.30 Room E

S28: Turbo Talk I

Chairpersons:







2. Mathirut Mungthin

Speakers:



Parasite clearance and post-treatment submicroscopic parasitemia in patients treated with Atovaquone-Proguanil in combination with Artesunate

Panita Gosi

Armed Forces Research Institute of Medical Science, Bangkok, Thailand

(See Poster No 1 on pages 175)



Spatiotemporal modeling of relative risk of malaria infection along Thailand-Myanmar border: the Hlaingbwe Township and Tha-Song-Yang District

Aung Minn Thway

Department of Tropical Hygiene, Faculty of Tropical Medicine, Mahidol University

(See Poster No 2 on pages 176)



Relapse pattern in vivax malaria in nepal

Komal Raj Rijal

Central Department of Microbiology, Tribhuvan University, Nepal

(See Poster No 3 on pages 177)



How are the Village Health Volunteers delivering malaria testing and treatment services and what are the challenges they are facing? – a mixed methods study in Myanmar

Nay Yi Yi Linn

Vector Borne Disease Control Program, Ministry of Health and Sports, Nay Pyi Taw, Myanmar

(See Poster No 4 on pages 178)

14.00-15.30 Room E

\$28: Turbo Talk I (Continued)

Speakers:



FTY720 restores endothelial cell permeability induced by malaria sera **Supattra Glaharn**

Department of Tropical Pathology, Faculty of Tropical Medicine, Mahidol University

(See Poster No 5 on pages 179)



Spatio-temporal analysis of malaria cases along China-Myanmar border

Xiaotao Zhao

Faculty of Tropical Medicine, Mahidol University; Yunnan Institute of Parasitic Diseases, Puer China

(See Poster No 6 on pages 180



Antimicrobial susceptibility patterns of *Salmonella* species in a tertiary care hospital of Western Nepal: Are first line antibiotics still effective?

Dharm Raj Bhatta

Manipal College of Medical Sciences, Pokhara, Nepal

(See Poster No 7 on pages 181)



Investigating of knockdown resistance (Kdr) mutation in dengue vector Aedes aegypti cypermethrin resistant from dengue endemic area in Medan City, North Sumatera Province, Indonesia

Ledy Afrida Sinaga

Faculty of Medicine, Public Health, and Nursing, Gadjah Mada University, Indonesia
(See Poster No 8 on page 182)

Thursday 13 December 2018

16.00-17.30 Room A

\$29: Tackling Malaria Transmission and Infection

Chairperson:

Wai-Hong Tham



Invited Speakers:



Glycobiology of malaria parasite host infection

Justin Boddey

Walter and Eliza Hall Institute of Medical Research, Victoria, Australia

(No Abstract)



Identifying cases of malaria and asymptomatic infections along the Vietnam-Cambodia border using loop-mediated isothermal amplification (LAMP) and geospatial localization

Ricardo Ataíde

Burnet Institute, Victoria, Australia

The dynamic nature of malaria transmission in Papua New Guinea

Leanne Robinson

Burnet Institute, Victoria, Australia



Combatting residual malaria transmission on islands in Vanuatu

Akira Kaneko

Karolinska Institutet, Stockholm, Sweden

Identifying cases of malaria and asymptomatic infections along the Vietnam-Cambodia border using loop-mediated isothermal amplification (LAMP) and geospatial localisation



Ataide R^{1,2}, Surrao LD ^{1,3}, Irani V ^{1,4}, Vo DT^{1,5}, Thang NX ⁶, Nguyen HN ⁶, O'Donnell JJ ^{1,4}, Le A ^{1,2}, Kelly GC¹, Canavati SE¹, Tram I¹, Piedrafita DM ³, Greenhill AR ³, Dahl G ⁷ Vazquez MV ⁷, Hopper JM ⁸, Hopper WR ⁸, Ding XC 9, Bui DV 5, Thang ND 6, Duong TT 6, Richards IS 1,2,4

¹Burnet Institute Burnet Institute for Medical Research and Public Health, Melbourne, Australia; ²Department of Immunology, Monash University, Melbourne, Australia; Federation University Australia, Churchill, Australia;⁴Department of Medicine, University of Melbourne, Melbourne, Australia; ⁵Ca Mau General Hospital, Ca Mau, Vietnam; ⁶National Institute of Malariology, Parasitology, and Entomology, Hanoi, Vietnam; ⁷Health Poverty Action, London, United Kingdom; ⁸Axxin Pty Ltd, Fairfield, Australia; ⁹FIND, Geneva, Switzerland

Vietnam is pushing towards the elimination of malaria by the year 2030, with 40 of its 58 provinces currently malaria-free. Despite this, and an 88% reduction in cases from 2015 to 2016, malaria elimination will require local and national authorities to have detailed maps of where malaria cases are reported and devise mass-screening strategies to locate asymptomatic individuals. These data will identify transmission enable interventions tailored for specific provinces subpopulations. With this in mind, we conducted a Regional Artemisinin-resistance Initiative (RAI) project in 5 Communes of Binh Phuoc and Dak Nong Provinces. This included mapping of >11,000 households on the Vietnam-Cambodia border. Data on demographics and malaria preventive strategies were collected. Individuals presenting with symptomatic malaria to Commune Health Clinics (CHCs) were geolocated back to their primary residence using a mHealth digital data entry form designed in Epicollect5. This data produced detailed information on potential hotspots of transmission. Additionally, we sampled 5,424 asymptomatic individuals using a mass-screening survey for low-density Plasmodium infection using loopmediated isothermal amplification (LAMP) at each of the CHCs. We detected a total of 103 asymptomatic individuals that were below the detection threshold of regular malaria RDTs. This was a prevalence of 1.6 % across the whole cohort (range 0.54%-2.56% across 5 communes). We were able to show that simple mHealth forms with geolocation ability and large-scale sampling and testing efforts using LAMP at the community level are feasible and help determine potential hotspots of malaria transmission in remote areas as part of an intensified malaria elimination strategy.

Keyword: Malaria, Elimination, GIS, LAMP

The dynamic nature of malaria transmission in Papua New Guinea



Leanne J Robinson^{1,2,3,} Maria Ome-Kaius1, Johanna H. Kattenberg¹, Cristian Koepfli², Natalie E. Hofmann⁴, Daniela Rodriguez⁴, John Bosco Keven¹, Daisy Mantila¹, Benishar Kombut¹, Samuel Maripal¹, Shadrach Jally¹, Elisheba Malau², Thomas Obadia⁶, Alyssa Barry², Manuel Hetzel⁴, Ingrid Felger⁴, James Kazura⁵, Ivo Mueller²,5

¹Papua New Guinea Institute of Medical Research, Papua New Guinea, ²Walter and Eliza Hall Institute of Medical Research, Parkville, Australia, ³Burnet Institute, Melbourne, Australia, ⁴Swiss Tropical & Public Health Institute, Basel, Switzerland, ⁵Case Western Reserve University, Center for Global Health and Diseases, Cleveland, USA, ⁶Institut Pasteur, Paris, France

A scale-up of malaria control in Papua New Guinea (PNG) in 2008 resulted in a significant overall reduction in the prevalence and incidence of malaria. However, these reductions were not uniform in all areas and recent data demonstrates a resurgence in some locations. A suite of health facility surveillance, community cross-sectional surveys, longitudinal child cohorts and vector collections undertaken throughout the past decade, combine sensitive serological and molecular diagnosis of infections (multiplicity of infection (MOI), molecular force of blood-stage infection (moIFOB) and gametocyte-specific RT-qPCR) with operational, demographic, human and vector behavioural and spatial data, providing the opportunity to examine the key drivers of ongoing transmission in different settings and identify the barriers/enablers to achieving further reductions.

Across all sites and surveys, the reduction in transmission between 2005 and 2014 has been very pronounced for *P. falciparum*, with qPCR prevalence declining from >50% to <10% and molFOB declining from 5.9/child/year (2006) to 1.6 /child/year (2013) in 1-5 year old children. For *P. vivax*, the decline was more gradual, from 40% to 7-13% in the general population and 60% (2006) to 65% (2008) to 18% (2013) in 1-5 year old children, with molFOB dropping from 14.0/child/year (2006) to 2.4/child/year (2013) in East Sepik. Parasite densities decreased 5-fold, with 72% of *P. falciparum* and 87% of *P. vivax* infections submicroscopic in 2014. More recent 2016/17 surveys demonstrate a resurgence in many coastal areas with qPCR prevalence as high as 40%. The detectability of infections and gametocytes with different molecular and point of care approaches will be presented, as well as a detailed analysis of the relationship between host and vector behavior and infection status.

Understanding the highly dynamic nature of malaria transmission in PNG and the driving factors is critical to inform appropriate surveillance and intervention strategies to get malaria control back on track in PNG.

Keyword: malaria transmission, Papua New Guinea

Combatting residual malaria transmission on islands in Vanuatu



Akira Kaneko^{1,2}, Wataru Kagaya², Chim Chan¹, Morris Kalkoa³, Kalo Kalkoa³, James Yaviong³, Sam lamar³, Peter Kalsei³, George Taleo³

¹Karolinska Institutet, Sweden, ²Osaka City University, Japan ³Ministry of Health, Vanuatu

Vanuatu is an archipelago of 68 inhabited islands with a high linguistic diversity in Remote Oceania, where anopheline presence and malaria roughly correspond to the Buxton line. The transmission was generally more intense in the northern islands than in the south. There was a seasonal fluctuation of *Plasmodium* falciparum incidence, whereas the P. vivax incidence was rather stable. A positive rank-order correlation was found between malaria incidence and G6PD deficiency rate on the different islands. The southernmost Aneityum island has demonstrated a proof of the long-term sustainability of malaria elimination, and invigorates the recently renewed international commitment to global malaria eradication.

In the late 1980s, annual parasite incidence per one thousand population (API) was around 180. With the mass distribution of insecticide-treated bed nets since 1992, malaria burden in Vanuatu has decreased substantially. Nationally, API declined from 74 in 2003 to 13.2 in 2012, ranging from 0.4 in the south to 38.2 in the north.

Our malaria prevalence surveys on 16 main islands showed overall prevalence by microscopy decreased from 11.9% in 1988-1992 (N=14476) to 6.1% in 1996-2002 (N=16472). During this period about 57% of positives were *P. vivax*. Recent surveys on 10 islands in 2011-2017 showed overall prevalence by microscopy (N=13879) and by PCR (N=13121) were 0.55% and 2.6%, respectively, and 96% of positives by PCR were P. vivax. P. falciparum was detected only on Epi island in 2011. Distribution of positives was not even. All positives were detected in 5 northern islands (N=5548) except for one in southern Futuna island in 2011. Even though an outbreak risk surfaced on the southern islands after Tropical Cyclone Pam in 2015, surveys on 3 southern islands revealed no infection by PCR three months after the cyclone, in contrast to the sharp increase after Cyclone Uma in 1987. However many island communities in the north still hold substantial P. vivax prevalence by PCR ranging 2-20%. The full evacuation of the northern island of Ambae as a volcano eruption in September 2017 represents a major risk of malaria resurgence and threatens the national eradication target of Vanuatu in 2025.

Keyword: malaria transmission, Vanuatu

Thursday 13 December 2018

16.00-18.00 Room B

\$30: Accelerating access to existing new and old technologies for vector-borne disease elimination in Asia-Pacific (Sponsored by Malaria Consortium)

Chairpersons:

1. James Tibenderana



2. Jason Nash

Speakers:



Wolbachia establishment: its potential for dengue blocking and its risk on mosquito fitness

Eggi Arguni

World Mosquito Project (WMP) in Yogyakarta



Challenges facing vector-borne disease control, collaboration, and the role of the private sector

Jason Nash

Bayer (Southeast Asia) Pte Ltd



Challenges and opportunities in reaching remote and mobile populations with malaria services in Cambodia

Yves Bourny

Malaria Consortium



Impacts of existing vector control tools in Africa in the context of expanding insecticide resistance: findings from studies in Uganda

Tarekegn Abeku

Malaria Consortium

Wolbachia establishment: its potential for dengue blocking and its risk on mosquito fitness



Eggi Arguni, Warsito Tantowijoyo, Ranggoaini Jahja, Citra Indriani, Riris Andono Achmad, Adi Utarini, World Mosquito Project (WMP) in Yogyakarta Team.

Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, Yogyakarta, Indonesia

Wolbachia is common bacteria in insects. Wolbchia has successfully established in Aedes aegypti, which in laboratory it has proven for blocking dengue. World Mosquito Project in Yogyakarta has been developing a research using Wolbachia to control dengue from 2012. Release of Wolbachia has been done in 2014-2015 in four small isolated areas and 2016-2017 in half of Yogyakarta city. The current result indicates that Wolbachia has established and stable in all release area. Impact of Wolbachia in ecological aspect routinely done, and concluded that Wolbachia doesn't influence Aedes aegypti fitness and insecticide resistant.

Keyword: wolbachia, world mosquito program, yogyakarta, aedes aegypti

Challenges facing vector-borne disease control, collaboration, and the role of the private sector



Jason Nash

Bayer (South East Asia) Pte Ltd.

As we strive towards malaria elimination and to contain the growing incidence of arboviral diseases such as dengue, chikungunya and Zika, vector control continues to face challenges. Limited resources, capacity, and tools, restrict our ability to implement sufficiently effective control programs, but on the positive side there are a number of promising new technologies emerging. To accelerate and make best use of these new technologies, collaboration between the public, private and non-government bodies is crucial. It will also require a more open mindset, a change of approach, as well as a greater tolerance of risk and potential failure - in order to succeed.

It is estimated that currently US\$ 0.3 billion is spent annually on vector control globally, but at least US\$ 0.2 billion more is required. But even if this additional funding was available, we don't have the physical capacity and human resources to implement the required programs in most countries.

What is needed are new technologies that can enable vector control programs to not only be more effective, but also more efficient. Fortunately, several new technologies are now emerging that can address these issues. These technologies include development of new vaccines, surveillance and control tools.

But, none of these technologies is sufficient on their own, they must be used as part of an integrated approach. Similarly no institution can be successful in adopting these technologies alone, we must collaborate.

The private sector has an important role to play here as a source of new technologies, as well as bringing different perspectives, extended networks and expertise.

Keyword: collaboration, challenges, private, technologies, role

Challenges and opportunities in reaching remote and mobile populations with malaria services in Cambodia



Yves BOURNY

Malaria Consortium

on:

As growing evidences are suggesting that malaria transmission is happening only in forested areas, the national program in Cambodia is requesting partners to now deploy community services to reach forest-goers.

Malaria Consortium has been working with communities living in forested areas along the border regions of Cambodia since 2013. Our program which first started out as a research project quantifying Plasmodium infection among border-crossing populations and the value of malaria posts at border crossings has since been scaled up to a large operational program that services Mobile Migrant Population, ethnic groups and forest goers who remain the most difficult to reach populations and those most vulnerable to infection .

Border populations and MMPs are at high risk of malaria infection due to their itinerant lifestyles, difficulty in reaching them for diagnostic, treatment and preventive interventions, and occupational and behavioural factors that bring them in close contact to the forest. Due to difficulty in access, populations in remote forested regions rely on local community health volunteers as opposed to public health facilities.

Since 2016 Malaria Consortium has successfully deployed a network of mobile malaria posts and mobile malaria workers to provide package of malaria services to this key population in three border provinces in the North-East of Cambodia. Using the knowledge of our target communities and surveillance data from the national malaria program our services are located in areas where they have the greatest chance of reaching those most at risk and with the least access to the public health services. Based on the experiences in implementing forest activities this presentation will focus

- Summarising the key lessons learned and challenges faced when establishing a large scale programme targeting potential high-risk populations living or going to forest.
- Developing targeted interventions for forest goers in remote and hard-toreach locations

Keyword: remote and mobile populations, malaria services, Cambodia

Impacts of existing vector control tools in Africa in the context of expanding insecticide resistance: findings from studies in Uganda



Tarekegn Abeku¹

¹Malaria Consortium, The Green House, 244-254 Cambridge Heath Road, London E2 9DA, United Kingdom

The scale-up of insecticide-treated nets (ITNs) and indoor residual spraying (IRS) had substantial impacts on malaria in Africa. Malaria indicator surveys in 2014-15 in Uganda showed that prevalence decreased by more than half in under five children compared to rates recorded in a similar survey in 2009, from 42% to 19%, while during the same period percentage of households with at least one ITN grew from 47% to 90%. In the northern part of the country where IRS has been in use, prevalence rate of 7% was reported, substantially lower than the national average. However, insecticide resistance is now widespread in major malaria vectors. Resistance against IRS insecticides has necessitated switching to more expensive chemicals, affecting coverage. Nevertheless, studies in Uganda and other countries have concluded that despite pyrethroid resistance, sleeping under long-lasting insecticidal nets (LLINs) provides individual protection against malaria infection, although community level protection remained less well understood. Possible explanations include the impact of delayed mortality of resistant mosquitoes after exposure to pyrethroids and a potential effect of pyrethroids on the sporogonic development of the malaria parasite. LLINs with piperonyl butoxide (PBO) have become available for potential use in areas with moderate levels of pyrethroid resistance, alongside other new generation LLINs. A recent trial in Tanzania demonstrated that PBO LLINs are more effective than standard LLINs against malaria infection and transmission, and provided evidence of the negative effect of resistance on malaria. Malaria transmission has become increasingly heterogeneous, while deployment of expensive tools has become necessary due to resistance. Careful targeting of locally appropriate tools, including new and existing ones, will be essential to achieve the highest possible impact with available resources.

Keyword: malaria, vector control, insecticide-treated nets, indoor residual spraying, insecticide resistance

Thursday 13 December 2018

16.00-17.30 Room C

S31: Antimicrobial Resistance

Chairpersons:

1. Direk Limmathurotsakul





2. Ben Cooper

Invited Speakers:



Antibiotic knowledge, attitudes, and practices: new insights from representative social surveys in low- and middle-income Southeast Asia

Marco J Haenssgen

Mahidol-Oxford Tropical Medicine Research Unit (MORU)



Generating isolate-based, specimen-based and case-based antimicrobial resistance surveillance reports from readily available data sets using an open-access, offline and easy-to-use application

Cherry Lim

Mahidol-Oxford Tropical Medicine Research Unit (MORU)

Global antimicrobial resistant Neisseria gonorrhea. Is the cat out of the bag?



Thailand MOPH - U.S. CDC Collaboration



Applications of causal inference to hospital epidemiology

Yin Mo

Mahidol-Oxford Tropical Medicine Research Unit (MORU)

16.00-17.30 Room C

\$31: Antimicrobial Resistance (Continued)

Invited Speakers:



Modelling the nosocomial transmission of multi-drug resistant *Enterobacteriaceae*Thomas Crellen

Mahidol-Oxford Tropical Medicine Research Unit (MORU)



Upper respiratory tract infections among febrile patients attending primary care in Southeast Asia

Thomas Althaus

Mahidol-Oxford Tropical Medicine Research Unit (MORU)



Modelling the selection of AMR at multiple scales

Ben Cooper

Mahidol-Oxford Tropical Medicine Research Unit (MORU)



How people are measuring global and national burden of antimicrobial resistance. Do we need a better model?

Direk Limmathurotsakul

Mahidol-Oxford Tropical Medicine Research Unit (MORU)

Antibiotic knowledge, attitudes, and practices: new insights from representative social surveys in low- and middle-income Southeast Asia



Haenssgen, MJ^{1,2,3,4}, Charoenboon, N⁴, Zanello, G^{5,6}, Mayxay, M^{7,8}, Reed-Tsochas, F^{2,3,9,10}, Lubell, Y^{1,4}, Wertheim, HFL^{11,12}, Lienert, J^{3,12,13}, Xayavong, T^{7,14,15}, Khine Zaw, Y^{4,16}, Thepkhamkong, A⁷, Sithongdeng, N⁷, Khamsoukthavong, N⁷, Phanthavong, C⁷, Boualaiseng, S⁷, Vongsavang, S⁷, Wibunjak, K⁴, Chai-In, P⁴, Thavethanutthanawin, P⁴, Althaus, T^{1,4}, Greer, RC^{1,4}, Wangrangsimakul, T^{1,4}, Limmathurotsakul, D⁴, Elliott, E^{17,18}, Ariana, P¹

¹Centre for Tropical Medicine and Global Health, University of Oxford, UK; ²Saïd Business School, University of Oxford, UK; ³Green Templeton College, UK; ⁴Mahidol Oxford Tropical Medicine Research Unit, Thailand; ⁵School of Agriculture, Policy and Development, University of Reading, UK; ⁶Leverhulme Centre for Integrative Research on Agriculture and Health, UK; ⁷Lao Oxford Mahosot Wellcome Trust Research Unit (LOMWRU), Lao PDR; ⁸Faculty of Postgraduate Studies, University of Health Sciences, Lao PDR; ⁹Oxford Martin School, University of Oxford, UK; ¹⁰Department of Sociology, University of Oxford, Oxford, UK; ¹¹Oxford University Clinical Research Unit (OUCRU), Viet Nam; ¹²Medical Microbiology Department, Radboudumc, Netherlands; ¹³National Human Genome Research Institute, National Institutes of Health, US; ¹⁴Department of Peace and Conflict Studies, University for Peace, Costa Rica; ¹⁵Department of Political Science, School of Social Science, Ateneo de Manila University, Philippines; ¹⁶Department of Global Health and Development, London School of Hygiene & Tropical Medicine, UK; ¹⁷UCL Anthropology, University College London, UK; ¹⁸Institut de recherche pour le développement, Lao PDR

Background: Antimicrobial resistance (AMR) is a global health priority, but the narrow approach to behaviour change through education and awareness raising threatens to frustrate global commitments, waste enormous resources, and delay the search for complementary or more effective social solutions. Our objective is to inform antibiotic education and awareness-raising from an interdisciplinary perspective, thereby aiding to "burst the biomedical bubble" that continues to dominate global health policy.

Methods: We conducted representative rural surveys in Chiang Rai (Thailand) and Salavan (Lao PDR) between 11/2017 and 05/2018, whereby our 2,141 respondents represented 712,000 adult villagers. We used descriptive statistical analysis and hypothesis testing to compare antibiotic-related knowledge, attitudes, and practices across sites and across people who accessed antibiotics from public/private/informal healthcare channels.

Findings: Notions surrounding antibiotic use were diverse and context specific. The use of official terms for "antibiotics" was dwarfed by vernacular expressions like "anti-inflammatory medicine" (Chiang Rai) and specific antibiotic names like "ampi" and "amok" (Salavan). Antibiotics were not deemed a cure-all but typically used for specific conditions. Informal antibiotic access was generally low (4% of treatments received in Chiang Rai; 8% in Salavan), while desirable attitudes were associated with disproportionately higher consumption of antibiotics from formal sources.

Interpretation: Our novel survey data challenges the assumptions of the global AMR awareness-raising agenda. Locally specific, diverse, and contradictory notions of antibiotics and drug resistance complicate communication efforts and require intimate local understanding. Furthermore, the link between knowledge, attitudes, and practices is weak and counterintuitive, which invites potentially harmful but typically unmeasured side-effects in global awareness-raising efforts. Global health policy requires urgent disciplinary diversification to explore alternative mechanisms to address social dimensions of AMR.

Keyword: Antimicrobial resistance, antibiotics, awareness, treatment-seeking behaviour, survey, social sciences, development studies, interdisciplinary research, Thailand, Lao PDR

Generating isolate-based, specimen-based and case-based antimicrobial resistance surveillance reports from readily available data sets using an open-access, offline and easy-to-use application



<u>Cherry Lim</u>^{1,2}, Prapit Teparrakkul³, Viriya Hantrakun¹, Sharon Peacock^{1,4,5}, Nicholas PJ Day^{1,2}, Ben Cooper^{1,2}, Direk Limmathurotsakul^{1,2,6}

Background

Quantification of health burdens attributable to antimicrobial resistance (AMR) is difficult due to lack of data. Both isolate-based and sample-based surveillance reports are based on microbiology database and rarely stratified by infection origin. Case-based surveillance report and mortality rates attributable to AMR per infection origin are important to understand the burden of AMR. However, the case-based surveillance report requires a complicated data processing and analysis procedure.

Methods/Principal finding

We are developing an offline, open-access and easy-to-use application that allows a hospital to independently perform data analysis and generate isolate-based, sample-based, and case-based surveillance reports from their routinely collected electronic databases. The application was built in R, which is a free software environment. The application will import raw data files in a local computer upon double-clicking on the application icon. Data analysis and reports generation will be then performed automatically. The raw data files required included hospital admission and microbiology databases. The application will firstly clean raw microbiology database and produces isolates-based and sample-based surveillance reports. Then, the application will automatically merge the microbiology and hospital admission database, analyzed merged data, and produce a case-based surveillance report. The final part will perform statistical analysis to estimate all-cause mortality of patients with AMR infection and mortality attributable to AMR, and add those parameters into the case-based surveillance report. The application will be tested using a retrospective data from a provincial hospital in Thailand.

Conclusions

The newly developed and open-access application could be an important tool to generate AMR surveillance reports and parameters required for quantifying AMR burden in resource-limited settings.

Keyword: antimicrobial-resistance, surveillance, offline application, attributable mortality

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Global Antimicrobial Resistant *Neisseria gonorrhea*. Is the Cat out of the Bag?

Eileen Dunne

Thailand MOPH - U.S. CDC Collaboration

Neisseria gonorrhoeae (NG) is a gram-negative diplococci bacteria, which causes urethritis but also can lead to infertility, pelvic inflammatory disease and ectopic pregnancy. Gonorrhea is a major public health concern with over 106 million infections each year. NG antimicrobial resistance has increased in recent years and has reduced the options for treatment. Gonococcal resistance to third-generation cephalosporins has emerged in Japan, Norway, Australia, Canada and the UK. This session will highlight the emergence of antimicrobial resistant NG, describe the important surveillance efforts underway globally and in Thailand, discuss evaluation and control steps needed to contain the spread of resistant infections, and clinical trials to increase the available treatment options.

Keyword: Global, Antimicrobial Resistant, *Neisseria gonorrhea*

Applications of causal inference to hospital epidemiology



Mo Yin

- 1. Division of infectious disease, University Medicine Cluster, National University Hospital, Singapore
- 2. Department of Medicine, National University of Singapore
- 3. Mahidol-Oxford Tropical Medicine Research Unit, Faculty of Tropical Medicine, Mahidol University, Banakok, Thailand
- 4. Centre for Tropical Medicine, Nuffield Department of Medicine, University of Oxford, Oxford, United Kingdom

Causal inference methods underscore the paradigm shift from traditional statistical analyses, which are limited to establishing associations, to causal analysis of multivariate data. In this talk, we will introduce the basic concepts of causal inference, construction of a directed acyclic graph (DAG) and discuss the application these techniques to examples of clinical trials and observational data concerning infectious disease and bacterial antimicrobial resistance, with a special focus on the issue of duration of antibiotics on emergence of resistance. First, we demonstrate the strengths and weaknesses of conventional intentionto-treat and per-protocol analyses compared with instrumental variable estimation and propensity score matching in the analysis of a non-inferiority trial with non-compliance. Second, we discuss how to overcome immortality bias using causal inference techniques to estimate the effect of antibiotic treatment duration on clinical outcomes using observational data.

Keyword: Causal inference, antimicrobial resistance

Modelling the Nosocomial Transmission of Multi-drug Resistant *Enterobacteriaceae*



<u>Thomas Crellen</u>^{1,2}, Paul Turner^{1,2,3,} Sreymom Pol^{1,3,} Stephen Baker^{2,4,} To Nguyen Thi Nguyen⁴, Nicole Stoesser², Nicholas P.J. Day^{1,2}, and Ben S. Cooper^{1,2}

¹Mahidol-Oxford Tropical Medicine Research Unit, Faculty of Tropical Medicine, Mahidol University, 60th Anniversary Chalermprakiat Building, 420/6 Rajvithi Road, Bangkok 10400, Thailand

Widespread resistance to antibiotics is among the gravest threats to modern medicine, and controlling the spread of multi-drug resistant Enterobacteriaceae has been given priority status by the World Health Organization. We analyse data from a one year prospective carriage study in a neonatal intensive care unit in Cambodia using Bayesian hierarchical models to estimate the daily probability of acquiring multi-drug resistant organisms, while accounting for patient-level timevarying covariates, including interactions between species, and interval-censoring of transmission events. We estimate the baseline daily probability for becoming colonised with third generation cephalosporin resistant (3GC-R) Klebsiella pneumoniae as 0.142 (95% credible interval [Crl] 0.066, 0.27), nearly ten times higher than the daily probability of acquiring 3GC-R Escherichia coli (0.016 [95% Crl 0.0038, 0.049]). Prior colonization with 3GC-R K. pneumoniae was associated with a greatly increased risk of a patient acquiring 3GC-R E. coli (odds ratio [OR] 6.4 [95% Crl 2.8, 20.9]). Using 317 whole-genome assemblies of K. pneumoniae, we determined putatively related clusters and used a range of models to infer transmission rates. Model comparison strongly favored models with a time-varying force of infection term that increased in proportion with the number of colonized patients, providing evidence of patient-to-patient transmission, including among a cluster of Klebsiella quasipneumoniae. Our findings provide support for the hypothesis that K. pneumoniae can be spread person-to-person within ward settings. Subsequent horizontal gene transfer within patients from K. pneumoniae provides the most parsimonious explanation for the strong association between colonization with 3GC-R K. pneumoniae and acquisition of 3GC-R E. coli.

Keyword : Transmission, Multi-drug Resistant, *Enterobacteriaceae*

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Upper respiratory tract infections among febrile patients attending primary care in Southeast Asia



Thomas Althaus^{1,2}; Janjira Thaipadungpanit¹; Yoel Lubell^{1, 2}

Acute upper respiratory tract infections (URTI) represent a major cause of primary healthcare consultation. In Southeast Asia, 80% of acute consultations are due to URTI, with common cold and acute pharyngitis being the leading symptoms among febrile patients attending primary care. While multi-pathogen assays have recently extended the range of bacteria and viruses identified for URTI, demonstrating the causative role of these pathogens as independent or co-infectors remains challenging.

We prospectively collected 807 nasopharyngeal swabs among febrile children and adults attending primary care in Chiangrai, Northern Thailand, and Hlaing Tha Yar, Yangon, Myanmar. Using a validated multiplex real-time PCR assay, the Tagman Array Card (TAC), we measured the pathogen spectrum and its relative quantification. We compared these results with clinical presentations and outcomes, in particular in patients with and without respiratory symptoms. Antibiotic prescription at the health facility was analysed in light of the clinical presentations and the microbiological results.

Keyword: Primary care; Upper respiratory tract infections (URTI); Tagman Array Card (TAC); Southeast Asia

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Modelling the selection of AMR at multiple scales



Ben S Cooper^{1,2}

Mathematical and statistical models have become essential tools in planning and evaluating interventions to control the spread of communicable diseases and are routinely used to inform national and international policy decisions. This presentation will consider the ways in which such models are being used to help understand the spread of antimicrobial resistance at multiple scales: withinhost; within small populations (hospitals wards and households), and within larger populations (hospitals, networks of hospitals, and whole communities). This will include consideration of the use of models to provide broad epidemiological insights as well their use in evaluating the likely effectiveness and cost-effectiveness of potential interventions to control antimicrobial resistance including antimicrobial stewardship and hand hygiene.

Keyword: modelling, antimicrobial resistance, hospital, hand hygiene, antibiotic stewardship

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How people are measuring global and national burden of antimicrobial resistance. Do we need a better model?



<u>Direk Limmathurotsakul</u>^{1,2}, Susanna Dunachie^{1,2}, Keiji Fukuda³, Nicholas A. Feasey⁴, Iruka N. Okeke⁵, Alison H. Holmes⁶, Catrin E. Moore⁷, Christiane Dolocek², H. Rogier van Doorn^{2,8}, Nandini Shetty⁹, Carmem L. Pessoa Da Silva¹⁰, Jean Patel¹¹, Alan D. Lopez¹², Sharon J. Peacock¹³, Surveillance and Epidemiology of Drug Resistant Infections Consortium (SEDRIC)

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 m 6}$ Imperial College London, Hammersmith Campus, Du Cane Road, London, W12 0HS, UK
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Estimating premature mortality and the burden of disease due to infections caused by pathogens that have acquired antimicrobial resistance (AMR) is critical, both to decide on resource allocation for interventions against AMR and to inform the implementation of action plans at global and national levels. With robust methods and reliable estimates, individual countries could track trends, determine the impact of actions on AMR, and compare these with others. It is also crucial for policy-makers to be able to compare the impact of AMR infections with other major communicable diseases such as HIV/AIDS, malaria and tuberculosis, as well as non-communicable diseases with a large global impact, including heart disease and cancer.

The Review on AMR, chaired by Jim O'Neill, estimated that around 700,000 deaths each year globally may be from infections with drug-resistant bacterial infections and multidrug-resistant and extensively drugresistant tuberculosis. The Global Burden of Disease (GBD) study published in 2017 estimated that around 126,000 people died of multi-drug resistant and extensively drug-resistant tuberculosis in 2016, but the number of people who died of other drug-resistant bacterial infections, malaria and HIV were not estimated separately. National estimates of mortality from AMR infections have also been published for the United States (US), Europe and Thailand, among others. A direct comparison of these estimates is not possible because each used different methodology and data sources, including which types of infections were considered, when preparing the estimates.

Despite the importance of AMR as a public health threat, the lack of a robust and accepted methodology to assess its health and socioeconomic burden is widely acknowledged. Here, we compare and discuss the underlying assumptions, characteristics, limitations and comparability of the methods that have been used to quantify disease burden and mortality from AMR, and propose general guiding principles and potential approaches for improving these estimates in the future.

Keyword: AMR, antimicrobial-resistant, burden, mortality, attributable mortality

Thursday 13 December 2018

16.00-17.30 Room D

\$32: Environmental Health and Toxicology

Chairpersons:

1. Kraichat Tantrakarnapa





2. Suwalee Worakhunpiset

Invited Speakers:



Health impact assessment from long-term exposure to outdoor air pollution in Thailand

William Mueller

Research Division, Institute of Occupational Medicine, Edinburgh, UK



Impact of Biomass Combustion on Indoor Air Quality in Developing Countries **Kiyoung Lee**

Graduate School of Public Health and Institute of Health and Environment, Seoul National University, Seoul, Korea



Heavy metals; a possible health risk through free grazing duck farm in Thailand **Phitsanu Tulayakul**

Department of Veterinary Public Health, Faculty of Veterinary Medicine, Kasetsart University



Air quality forecasting system for haze episode in the upper north of Thailand **Kraichat Tantrakarnapa**

Department of Social and Environmental Medicine, Faculty of Tropical Medicine, Mahidol University

Health impact assessment from long-term exposure to outdoor air pollution in Thailand



William Mueller¹, Susanne Steinle¹, Miranda Loh¹, Sotiris Vardoulakis¹, Nopadol Precha², Wissanupong Kliengchuay², Narut Sahanavin³, Ratthaphol Sillaparassamee⁴, Kanchana Nakhapakorn⁵ Kraichat Tantrakarnapa², John W. Cherrie^{1,6}

Background: Air pollution is an important preventable cause of illness and premature mortality around the world.

Objective: To assess outdoor air pollutant trends in Thailand across three decades and to make a preliminary assessment of associated health impacts from long-term exposures.

Methods: We collected data on CO, NO₂, O₃, PM₁₀, PM_{2.5}, and SO₂ from 68 automatic monitoring stations across Thailand over 1996 to 2017. We combined historic exposure to PM_{2.5} and O₃ with mortality from lung cancer and chronic lower respiratory diseases to conduct a health impact assessment (HIA) for the projected population of adults aged 30+ in Thailand in 2020.

Results: Reductions in annual mean concentrations in the monitoring data from 1996 to 2017 were observed for CO (0.77 to 0.63 ppm; -19%), SO₂ (5.0 to 2.3 ppb; -54%), NO₂ (15.0 to 12.0 ppb; -20%), PM₁₀ (72.5 to 39.5 μ g/m³; -46%), and $PM_{2.5}$ (41.5 to 18.5 $\mu g/m^3$; -56%). Increases were apparent for O_3 (32.4 to 47.3) ppb; +46%). For the year 2020, we estimate 2593 lung cancer (9-18% of baseline provincial rates) and 228 chronic lower respiratory disease deaths (0-6% of provincial rates) attributed to long-term exposure to PM_{2.5} and O₃, respectively.

Conclusion: Ambient pollutant concentrations in Thailand are higher than in Europe and North America, with rising levels of O₃. Historic levels of PM_{2.5} and O₃ are estimated to lead to thousands of attributable deaths annually. We will extend the HIA to further health outcomes and indoor pollution contributions, as well as examine uncertainties involved in the assessment.

Keyword: health impact assessment (HIA), Air pollution

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⁶Institute of Biological Chemistry, Biophysics and Bioengineering, Heriot Watt University, Edinburgh, UK

Impact of biomass combustion on indoor air quality in developing countries



Kiyoung Lee

Graduate School of Public Health and Institute of Health and Environment, Seoul National University, Seoul, Korea

INTRODUCTION: Combustion of biomass fuel can generate high levels of indoor air pollutants including particulate matter (PM) and volatile organic compounds (VOCs). The purpose was to determine the size distributions of PM and the specific VOCs emitted from cow dung and unprocessed coal combustion in controlled experiments.

METHODS: Dried dung from grass-fed cows and three unprocessed coal samples from Mongolia were combusted. The dual cone calorimeter (Fire Testing Technology, East Grinstead, West Sussex, UK) was used to observe the generation of PM and VOCs. A dust spectrometer (1.108; Grimm, Ainring, Germany) with a 16-channel decomposition capacity was used for PM measurement. Air sample was collected by silicon canister and analyzed by GC/MS.

RESULTS: PM₁₀ emission factors of cow dung were 3,477 \pm 1594, 589 \pm 170, and 43 \pm 13 mg/kg at heat flux of 15 kW/m², 25 kW/m² and 50 kW/m², respectively. Particle concentrations were highest in the 0.23-0.3-µm size range at heat fluxes of 25 kW/m² and 50 kW/m². The high benzene emission factor has significant implication due to its carcinogenic potential.

 PM_{10} emission factors for coal were 1,122.9 \pm 526.2, 958.1 \pm 584.0, and 472.0 ± 57.1 mg/kg for coal samples 1, 2, and 3, respectively. PM with a diameter of 0.35-0.45 µm was dominant and accounted for 41, 34, and 48% of the total PM for coal samples 1, 2, and 3, respectively.

CONCLUSIONS: PM and VOCs emission factors from cow dung and coal were high enough to cause extremely high indoor air pollution.

Keyword: cow dung, coal, emission factor, PM and VOC

Heavy Metals: a possible health risk through free grazing duck farm in **Thailand**



Phitsanu Tulayakul

Department of Veterinary Public Health, Faculty of Veterinary Medicine, Kasetsart University, Kamphaeng Saen campus, Nakhon Pathom, 73140, Thailand

The number of duck is 2nd largest production next to broiler amongst livestock production in Thailand. The database from Department of Livestock Development reported that the number of duck was about 13,548,366 ducks and about 7,027,178 ducks were egg duck type. The free range production owner was about 3, 300 families of the total number of 94,459 families in the duck production system. Since the health effects from heavy metals has not much been focused in livestock production system and duck production having freely range type of duck production system. Therefore, the study of heavy metal contamination in duck production system including their feeds, drinking water in raising environment and its products such as meat, eggs and internal organs were carried on. In the first study, it was found that duck liver tissue contaminated with Pb for 93.61% (88/94) of the samples, whereas Cd contamination was 100% (100/100). The maximum levels of Pb and Cd in the duck liver tissues were 606.16 and 22,946.20 ng q−1, which was higher than those in the eggs. Pb contamination in the water from rice paddy fields after grazing was significantly higher than that in water samples taken before grazing. This is the first report of Pb and Cd contamination in blood, egg, and liver samples of free grazing ducks in Thailand.

The second studied of this project, it was found that Zn, Co, Mn, Fe, and Cr in yolks were found significantly higher than in albumen, whereas the levels of Cd and Cu contaminations in egg albumen were significantly higher than in yolks. It can be concluded that consumers may be at risk of Pb, Cd, and Cu contamination if they consume contaminated duck eggs. Moreover, Pb, Cd, and Cr levels were distinguished above the ILCR limit of (10⁻⁴) in both children and adult. In particularly, calculated of carcinogenic risk in children revealed the set of data of (Pb; 0.0116, Cd; 0.0421 and Cr; 0.0503) were higher than in adult (Pb; 0.0030, Cd; 0.0109 and Cr; 0.0130). These results can be concluding that children were at risk of cancer if having chance to receive contaminated such metals in eggs. Whereas, the estimation of THQ of consuming duck egg in 70 year olds Thai population showed that Pb>Co >Cr>Cd, respectively. Nevertheless, it stills be safe for consumer since the calculated of TTHQ of Pb was 0.58 which a half below the standard limit of 1.00.

The third study of the project in comparison of the three types of duck farms system in Thailand. It was found that the levels of Pb, Cd, Cr and Cu in eggs from large-scale farms were significantly higher than small farms and free grazing farms at P < 0.001. Zn in eggs from free grazing farms was higher than in the small farms and large-scale farms sampled. The contamination of Pb in eggs from all types of farms were exceeded the standard limits of ACFS 6703-2005. The average levels of Pb in the eggs from small-scale farms significantly correlated with the level of Pb found in the feed at P < 0.05, while the average levels of Pb in eggs from free grazing duck farms correlated significantly with the levels of Pb found in the drinking water at P < 0.05.

Last project was the study of heavy metals contamination in duck meat and its organs. It was found that the average concentrations of Pb in duck meat and liver samples from large scale farms and Cd levels in duck liver samples from free grazing farm also exceeded FAO/WHO and Codex Alimentarius limits of 100%(55/55), 100%(54/54) and 67.64% (23/34), respectively. In conclusion, heavy metals contamination could be passing through the food chains via the contaminated environment-animals-human-environment pathway and may cause health risk both in human and animal. Therefore, long term monitoring of inconsiderable heavy metals contamination into duck production system must be carried on.

Keyword:

Air quality forecasting system for haze episode in the upper north of Thailand



Kraichat Tantrakarnapa¹, Chakrit Chotamonsak²

The HAZE episode is one aspect of the environmental problem of the Southeast Asia countries, it has been detected for more than 10 years. It is an additional burden affecting human health, socio-economic and social activities. The haze is one important environmental problem in Thailand, it has happened in the different period depends upon the topography and location. For example of haze episode in the upper north of Thailand, normally, it has been found during the dry season. This research aims to gain insights into the haze situation and influencing factors. The forecasting system was developed for prediction, the forecasting can be illustrated for three days from the existing date. The R code (open-air package) was used to analyze the data and STELLA was used for understanding the behaviour of haze. The WRF-Chem was employed to develop the forecasting system. The system can predict both pollution and climate factors. The pollutants consist of particulate matter (pm2.5 and pm10), air quality index (AQI) and the climate factors consist of temperature, relative humidity, pressure and wind direction and wind speed, the results of the first year prediction system indicated that the AQI (Air Quality Index) generated from the model is similar to the monitoring data obtained from the Pollution Control Department. The correlation coefficients with values generated from the developed model, we found that the correlation coefficient was in the moderate to high level (from 0.7 - 0.9). However, the modeling is also needed for further development to get the better results.

Keyword: Haze episode, Upper North of Thailand, Particulate Matters, Forecasting system

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Thursday 13 December 2018

16.00-17.30 Room E

S33: Turbo Talk II

Chairpersons:

1. Srivicha Krudsood





2. Mathirut Mungthin

Speakers:



Knowledge, attitude and stigma of leprosy: a community based cross-sectional study in Nepal

Rakesh Singh

Patan Academy of Health Sciences

(See Poster No 9 on pages 183)

Prevalence and associated factors of *Enterobacteriaceae* producing extended spectrum beta-lactamase carriers in Thai rural area, 2018.

Rinrada Vanavanitkun

Phramongkutklao College of Medicine

(See Poster No 10 on pages 184)



Development of dengue virus serotype specific Non-structural protein 1(NS1) capture immunochromatographic assay

Emi Nakayama

Osaka University

(See Poster No 11 on pages 185)



Expression of gene encoding merozoite surface protein 1 *Plasmodium falciparum* (PfMSP1-19kDa) in *Escherichia coli* BL21 (DE3)

Tanti Rahayu

Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada

(See Poster No 12 on pages 186)



Malaria case investigation review in Thailand, 2012-2017

Julien Zwang

Inform Asia: USAID's Health Research Program, RTI International, Research Park Triangle, NC, USA

(See Poster No 13 on pages 187)

16.00-17.30 Room E

\$33: Turbo Talk II (Continued)

Speakers:



Health problems among Myanmar and Laos workers in Samut Sakhon, Thailand **Peyawadee Petchprapakorn**

Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University

(See Poster No 14 on page 188)

Optimal target concentrations of piperaquine against placental malaria

Palang Chotsiri

Mahidol-Oxford Tropical Medicine Research Unit (MORU)

(See Poster No 15 on pages 189)



Susceptible status and resistance mechanism of *Aedes aegypti* to malathion and cypermetrin in endemic dengue area from Palu City, Central Sulawesi, Indonesia

Purwaningsih Binti Sapar

Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada

(See Poster No 16 on pages 190)



Human population movement patterns in malaria hotspots on the Thai-Myanmar border

Sayambhu Saita

Department of Tropical Hygiene, Faculty of Tropical Medicine, Mahidol University

(See Poster No 17 on pages 191)



Expression, purification and activity assay of trehalose phosphate phosphatase from *Burkholderia pseudomallei*

Sarocha Suthisawat

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

(See Poster No 18 on pages 192)



JITMM 201



Friday 14 December 2018

07.30-08.55 Room B

Controlled Human Infection Studies in LMICs: Opportunities to Accelerate Vaccine Development

Chairperson:

Pratap Singhasivanon



Invited Speakers:



PV CHIM in Thailand

Nicholas PJ Day and Jetsumon Prachumsri Mahidol-Oxford Tropical Medicine Research Unit (MORU) and Faculty of Tropical Medicine Mahidol, University

(No Abstract)



Community Engagement: how important for the vaccine?

Phaik Yeong Cheah

Mahidol-Oxford Tropical Medicine Research Unit (MORU)

(No Abstract)



Perspective from EC on controlled human infection study Jaranit Kaewkungwal

Faculty of Tropical Medicine, Mahidol University

(No Abstract)

Friday 14 December 2018

09.00-10.30 Room A

S34 Dengue: Clinical presentation, vector situation, and the role of implementation research in control program (Sponsored by Universitas Gadjah Mada)

Chairpersons:

1. Elsa Herdiana Murhandarwati



2. Ida Safitri Laksono

Speakers:



Organ dysfunction in dengue infection

Ida Safitri Laksono

Master Program of Tropical Medicine; Department of Child Health, FK-KMK UGM, Indonesia



Insecticide resistance in mosquito vectors of dengue virus in Indonesia

Tri Baskoro Tunggul Satoto

Master Program of Tropical Medicine; Department of Parasitology, FK-KMK UGM, Indonesia



Implementation research in dengue control

Riris Andono Ahmad

Implementation Research Program (WHO-TDR), Department of Public Health, FK-KMK UGM, Indonesia



The implementation research on tropical diseases in South East Asia: Lessons learnt and way forward

Ari Natalia Probandari

Implementation Research Program (WHO-TDR), Department of Public Health, FK-KMK UGM, Indonesia

Organ dysfunction in dengue infection



Ida Safitri Laksono^{1,2}

Department of Child Health, Faculty of Medicine, Public Health and Nursing Universitas Gadjah Mada/ Dr Sardjito Hospital¹, Postgraduate program in Tropical Medicine - Faculty of Medicine, Public Health and Nursing -Universitas Gadjah Mada²

Dengue is one of the most prevalent arboviral disease in the world. The disease is endemic in tropical and subtropical countries. The clinical spectrum covers both—severe and non-severe clinical manifestations. After the incubation period, in symptomatic disease the illness begins with abrupt onset of febrile followed by critical and recovery phases.

Many studies suggest the three organ systems play an important role in the pathogenesis of DHF/DSS: the immune system, the liver, and endothelial cell (EC) linings of blood vessels. The degree of liver dysfunction in dengue infection varies from mild injury with elevation of transaminases to severe injury with jaundice and liver cell failure. Multi organ dysfunction may results from a progressive dysfunction of two or more organs or systems after an acute alteration of systemic homeostasis. In severe dengue alteration of liver, heart, nervous and hematologic systems associated with severe condition.

Clinical manifestations of cardiac involvement could be from silent disease to severe myocarditis resulting in death. Rhythm abnormalities, hypotension, arrhythmias, myocarditis, myocardial depression with symptoms of heart failure and shock, and pericarditis have been reported. Dengue associated severe organ involvement were cardiovascular, hepatic, renal, as well as central nervous systems, and to some extent, respiratory and muscular systems. The severe organ involvement has been associated with adult dengue, and are likely to occur late in the disease course, but occurs rapidly when it happens, with limited time for optimal clinical management.

Severe organ involvement results in severe dengue disease. Elderly, diabetes, cardiac disorders, asthma, and two or more pre-existing comorbidities were independent risk factors of severe organ involvement.

Keyword: dengue, liver, organ dysfunction, severe dengue

Insecticide resistance in mosquito vectors of dengue virus in Indonesia



Tri Baskoro Tunggul Satoto^{1,2}, Ajib Diptyanusa², Widiarti³, Tri Wibowo Ambargarjito³, Winarno⁴

Insecticide resistance has emerged as one of the major problems facing dengue vector control in Indonesia. Steadily increasing number of dengue cases despite routine vector control measures in many provinces in Indonesia demonstrated possible insecticide resistance on mosquito vectors. An updated database on insecticide resistance monitoring is essential to support insecticide resistance management and operational decisions for effective vector control. During the study, database was obtained from published paper through Google Scholar, PubMed, and unpublished reports that have been officially issued by the Directorate General of Disease Prevention and Control, Ministry of Health of Indonesia. Insecticide resistance status among major dengue vectors in Indonesia was reported, particularly in the two classes of insecticides: pyrethroids and organophosphates. In 2009, resistance against 0.8% malathion in Aedes aegypti was reported in 13 provinces in Indonesia. Subsequently, Aedes aegypti resistance against 0.8% malathion and 0.75% permethrin in other 15 provinces was found in 2011. In 2015, approximately 76.6% of total 34 provinces in Indonesia have reported Aedes aegypti resistance to either pyrethroids and organophosphates. Hence, the database is important to evaluate the widely used insecticides and their field applications for dengue vector control program in dengue endemic area, including Indonesia. Determination of discriminating dose based on major insecticide resistance situation is also necessary to provide intervention policies in the fight against dengue in Indonesia.

Keyword: insecticide, resistance, dengue, vector

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⁴ Expert Commission Board for Vector Control, Ministry of Health of Indonesia

Implementation Research in Dengue Control

Riris Andono Ahmad^{1,2}



¹Center for Tropical Medicine, Faculty of Medicine, Public Health, Universitas Gadjah Mada ²Department of Biostatistics, Epidemiology and Population Health, Faculty of Medicine, Public Health, Universitas Gadjah Mada

Dengue is a global public health priority with an estimated burden of 390 million infections yearly. Approximately half a million of the cases needed hospitalization due to severe dengue hemorrhagic fever with 2.5% fatal outcome. With no effective treatment available and limited effectiveness of current dengue vaccine, dengue control strategies relay on integrated vector control interventions.

The vector control strategy focuses on combining use of on larva breeding site elimination, biological or chemical larvicide and insecticide intervention. However, such interventions require complex implementation strategies to be able to ensure the sustainable implementation and resulting in positive impact of reduction in dengue transmission.

Implementation research focuses on addressing the bottleneck of implementation and in dengue control means developing intervention packages that ensures the acceptability and adoption of intervention by community which lead to sustainability of intervention. This presentation aims to discuss factors that influence the degree of community engagement and participation in Dengue control

Keyword : Dengue control, Vector control, Implementation Research, Community Participation

The implementation research on tropical diseases in South East Asia: Lessons learnt and way forward



Ari Probandari^{1,2}

¹Centre for Tropical Medicine, Faculty of Medicine, Universitas Gadjah Mada, Yogyakarta, Indonesia ² Department of Public Health, Faculty of Medicine, Universitas Sebelas Maret, Surakarta, Indonesia

Universitas Gadjah Mada Yogyakarta acts as a Regional Training Center for WHO Tropical Diseases Research. One of the functions as a Regional Training Center for WHO Tropical Diseases Research is arranging a postgraduate program on international health with a focus on implementation research on tropical diseases research since 2015. In the program, the students should conduct and report implementation research as a requirement for Master of Public Health degree.

This session aims to discuss lessons learned from the existing implementation research conducted by the students in Universitas Gadjah Mada and relevant publications. The session highlights the spectrum of implementation research on tropical diseases has been conducted in South East Asia and explore the gap for further studies. Recommendations related to the capacity building of implementation research for South East Asia are discussed.

Keyword: implementation research, tropical diseases, capacity building

Friday 14 December 2018

09.00-10.30 Room B

\$35: Machine Learning in Public Health

Chairpersons:

1. Saranath Lawpoolsri





2. Wirichada Pan-ngum

Invited Speakers:



Large-scale detailed mapping of dengue vector breeding sites using street view images

Peter Haddawy

Faculty of Information and Communication Technology, Mahidol University, Thailand



Mapping malaria risks by drone: case studies using aerial and satellite-based data in Southeast Asia and Africa

Kimberly Fornace

London School of Hygiene and Tropical Medicine



Bayesian network decision model for supporting dengue diagnosis

Saranath Lawpoolsri

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

Large-Scale detailed mapping of dengue vector breeding sites using street view images



Faculty of ICT, Mahidol University

Peter Haddawy

In this talk, I present a pipeline to detect potential dengue vector breeding sites from geotagged images to create highly detailed dengue risk maps at unprecedented scale. The approach is implemented and evaluated using Google Street View images which have the advantage of broad coverage and of being somewhat historical so that the data can be aligned with other types of data for analysis. Containers comprising eight of the most common breeding sites are detected in the images using convolutional neural network transfer learning. Over a test set of images the object recognition algorithm has an accuracy of 0.91 in terms of F-score. Container density counts are generated and displayed on a decision support dashboard. We carry out extensive analyses of the approach over three provinces in Thailand. We show that the container density counts agree well with manual container counts, with larval survey data, and with dengue case data. To delineate conditions under which the density counts are indicative of risk, we analyze a number of factors affecting agreement with larval survey and dengue case data. We conclude that creation of container density maps from geotagged images is a promising approach to providing detailed information on potential breeding sites at large scale.

Keyword: dengue, risk mapping, geotagged images, convolutional neural nets

Mapping malaria risks by drone: case studies using aerial and satellite-based data in Southeast Asia and **Africa**



Kimberly Fornace

London School of Hygiene and Tropical Medicine

For infectious diseases with environmental drivers such as malaria, identifying high risk areas to effectively target interventions requires spatially and temporally accurate data on the geographic areas where transmission occurs. Geospatial data can be acquired from different sources, such as satellite and aerial- based remote sensing and ground-based GPS surveys. Increasingly, unmanned aerial vehicles (UAVs or drones) are used to collect high resolution data in real time for relatively low costs. We present examples of the use of drones for malaria studies across a range of contexts, including mapping land cover change to identify malaria risks in Malaysia and the Philippines, identifying wildlife disease hosts using thermal cameras in Borneo and mapping malaria vector breeding sites in Burkina Faso. Availability of different sensors to collect multispectral and thermal data increases the range and utility of data collected as well as the applicability of different analysis methods. However, despite these benefits, the use of UAVs can be limited by logistical constraints and are often most effective when integrated with more traditional satellitebased remote sensing.

Keyword: Mapping malaria, drone, aerial and satellite-based data, Southeast Asia and Africa

Bayesian network decision model for supporting dengue diagnosis



Saranath Lawpoolsri¹, Chaitawat Sa-Ngamuang¹, Peter Haddawy²

Making diagnosis for dengue infection is a challenge for physician. Commonly, dengue diagnosis relies mostly on clinical manifestation and basic laboratory tests, such as complete blood count (CBC). However, these clinical and basic laboratory characteristics of dengue infection are sometimes difficult to differentiate with other causes of acute febrile illnesses, particularly at the early stage of infection. Hence, the validity of clinical dengue diagnosis may depend on physician's experience. Currently, there are specific laboratory tests for dengue infection, including NS1 rapid test, serology test, and PCR. However, the use of these specific laboratory test is still limited due to high cost, lack of equipment, and uncertain validity. As patients with dengue disease require a proper fluid management, misdiagnosis of dengue may lead to severe complications. In addition, patients may unnecessarily expose to antibiotic while waiting for the confirmation. Machine learning has been recently applied to assist physician's diagnosis decision. Bayesian Networks (BN), one of machine learning techniques, is a model construction that link among different factors reflecting causal relationship network for dengue diagnosis. Previous data on patients' demographic, clinical manifestation, and laboratory results are used to train and test for the validity of the BN. For the final BN model, the probability of having dengue infection will be computed when entering related clinical and laboratory findings of a patient. The constructed BN for dengue diagnosis showed comparable performance with infectious diseases specialists. The BN would be useful to assist physicians in dengue diagnosis, particularly in limited resource settings.

Keyword: Dengue

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Friday 14 December 2018

09.00-10.30 Room C

\$36: Systems biology and innovative healthcare for tuberculosis

Chairpersons:

1. Supachai Topanurak





2. Wirongrong Chierakul

Invited Speakers:



WGS of *M. tuberculosis* reveal strong associations between genotypes and ethnicity: Its implication in TB control

Prasit Palitapongarnpim

Department of Microbiology, Faculty of Science, Mahidol University



Integrated human and pathogen genomic information for tuberculosis control **Surakameth Mahasirimongkol**

Department of Medical Sciences, Ministry of Public Health

(No Abstract)



Mining through gene expression profiles for novel biomarkers for tuberculosis **Nusara Satproedprai**

Department of Medical Sciences, Ministry of Public Health



Whole genome sequencing for detection and surveillance of drug-resistant tuberculosis

Areeya Disratthakit

Department of Medical Sciences, Ministry of Public Health

WGS of M. tuberculosis reveal strong associations between genotypes and ethnicity: Its implication in TB control



Prasit Palittapongarnpim

Department of Microbiology, Faculty of Science, Mahidol University

Controlling tuberculosis, a major health problem worldwide, is still problematic, partly due to the lack of good vaccines. Preliminary evaluation of vaccine candidates is generally done using the H37Rv as the challenging strain. The strain is only distantly related to most clinical strains. We studied 1170 isolates of Mycobacterium tuberculosis in Chiangrai, isolated from pulmonary patients during 2001-2011 by WGS. The relative prevalence of various lineages was 41, 45, 1 and 13 % Lineage 1 to Lineage 4. Further classification to sublineages were done based on previously published schemes. An exceptionally large number of L1 allowed us to classify them into 18 sublineages. Several rare and novel sublineages of L2 were identified in large numbers. Chiangrai was a relatively unusual place in the world where the Ancestral Beijing strains were more common than the Modern Beijing strains, different from Bangkok in the South. The lineages and sublineages associated with age, ethnicity, HIV infection and drug resistance. The frequencies of sublineages of L1 in various countries, inferred from published spoligotype data, were compared, which revealed strong correlations throughout the Indian subcontinent and Island SEA. However, the profiles of strains circulating the Mainland SEA were different between countries, which used official languages belonging to different families. This finding supported the hypothesis that *M. tuberculosis* co-evolve well with the hosts. As the H37Rv strain belonged to L4.9, the sublineage not circulating in SEA, development of vaccines for the regions should include L1 and L2 strains in the testing

Keyword: Mycobacterium tuberculosis, whole genome seguencing, coevolution, Beijing strains, spoligotypes.

Mining through gene expression profiles for novel biomarkers for tuberculosis



<u>Nusara Satproedprai</u>¹, Tassamonwan Chaiyasung¹, Natthakul Bunneung¹, Nuanjun Wichukchinda¹, Hideki Yanai², Reiko Miyahara², Katsushi Tokunaga³ and Surakameth Mahasirimongkol¹

In the past decade, high throughput methods provide us a global look at the transcriptome of host response against tuberculosis and allow researchers to capture the global picture of the immune response against an infection at different state. Traditionally, TB infection is classified into 2 distinct states which are latent TB infection and active TB disease. However, recent studies have shown that latent TB infection can be further stratified into different states that challenges the classical paradigm of TB infection. Insight into immune response at different states could guide to new interventions and treatment that help ending TB. In addition, the distinct patterns of gene expression that are exclusive to active Tuberculosis disease has been found and lead to identification of novel host biomarkers for diagnosis of TB. These novel gene expression biomarkers can also be used for differentiating stage of TB infection and monitoring the response to anti-tuberculosis treatment. Our team has developed a novel method for diagnosis of active TB by quantification of gene expression biomarkers in blood using droplet digital PCR. This talk will discuss on method development, usage of newly developed assay and how this method give a look at different stage of TB infection and disease.

Keyword: Tuberculosis, Gene Expression, RNA biomarker, Diagnosis

¹ Medical Genetics Center, Medical Life Sciences Institute, Department of Medical Sciences

² Fukujuji Hopspital, Japan Anti-Tuberculosis Association

³ Department of Human Genetics, School of International Public Health, The University of Tokyo

Whole genome sequencing for detection and surveillance of drug-resistant tuberculosis



Areeya Disratthakit¹, Saijai Smithikarn², Pundharika Paiboonsiri¹, Nuanjun Wichukchinda¹, Natthakan Thipkrua³, Krairerk Suthum³, Samarn Futrakul³, Koapong Tossapornpong⁴, Kittima Noppakaorattanamanee⁵, Itthipon Jarasolan⁴, Phalin Kamolwat², Surakameth Mahasirimongkol¹

Background: Whole genome sequencing (WGS) offers an effective approach for rapid detection of drug-resistant tuberculosis and high resolutions of tuberculosis outbreak investigation.

Method: Using next-generation sequencing, the genomes of 953 *Mycobacterium tuberculosis* clinical isolates in Thailand were sequenced. Bioinformatics pipeline was developed and applied to determine antituberculosis drug resistance, genotypes and genotypic relationship based on single nucleotide variations among these genomes.

Results: WGS provided sensitivity, specificity, positive and negative predictive values at 80.0-100 %, 88.6-100%, 80.0-100% and 89.1-100%, respectively, for detecting resistance to first-line and second-line anti-tuberculosis drugs. Genotype analysis revealed that Lineage 1 (Indo-Oceanic) was predominant in Thailand. The analysis of single-nucleotide polymorphisms provided a molecular evidence of specific strain of Beijing family causing MDR-TB outbreak. Total turnaround time for results was 7 days when the sequencing was performed on purified genomic DNA from culture.

Conclusions: We demonstrated the potential to utilize whole genome analysis for shortening time to detect drug-resistant tuberculosis including resistance to the second-line anti-tuberculosis drugs and early confirmation of tuberculosis outbreaks in Thailand.

Keyword : Tuberculosis, Whole Genome Sequencing, Outbreak, Drug resistance

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³ The Office of Diseases Prevention and Control 5, Department of Diseases Control, Ministry of Public Health, Thailand

⁴ Makarak Hospital, Ministry of Public Health, Thailand

⁵ Paholpolpayuhasena Hospital, Ministry of Public Health, Thailand

Friday 14 December 2018

11.00-12.30 Watergate Ballroom

\$37: Closing Session / Sornchai Looareesuwan Medal Lecture

Chairperson:

Pratap Singhasivanon



Keynote Speaker:



New tools in the NTDs armoury **Prof. Donald Peter McManus**QIMR Berghofer Medical Research Institute, Brisbane, Australia

New tools in the NTDs armoury



McManus DP

QIMR Berghofer Medical Research Institute, Brisbane, Australia

The Neglected Tropical Diseases (NTDs) are a group of parasitic/bacterial diseases that cause substantial morbidity for more than one billion people globally. Affecting the world's poorest people, NTDs cause severe disability, hinder growth, productivity and cognitive development, and often end in death; children are disproportionately affected. Asia is a NTD hot spot claiming some of the highest infection rates in the world, second only to that of sub-Saharan Africa. Approximately one-third of the world's parasitic worm infestations occur in this region. In this Keynote Address I will provide an overview of my past nearly 50 years' research to find the way to prevent and control helminthiases of humans and animals. My visionary approach continues to link basic and applied research, and my commitment to international field and laboratory studies with a multi-skilled team has translated into workable, innovative and practical control strategies for parasitic worm infections. I will emphasise my laboratory's recent studies on the development of novel interventions for the control of schistosomiasis and intestinal worm infections in Asia, tools that are important for the integrated control of these insidious diseases. My group's research in pathogen genomics, vaccine development/trialling, molecular diagnostics, and the outcomes of a successful video-based health educational intervention package ("The Magic Glasses"), tested in cluster-randomised controlled trials in China, the Philippines and Vietnam, will be featured. With decades of transformative-research contributions, my ultimate goal is the global elimination of these parasitic worms that are the cause of such extensive human suffering.

Keyword: Neglected Tropical Diseases, Schistosomiasis, Intestinal worms



JOINT INTERNATIONAL TROPICAL MEDICINE MEETING

2018



12 - 14 DECEMBER 2018 AMARI WATERGATE HOTEL, BANGKOK, THAILAND

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Organizers

HEALTH EDUCATION

Hellellells

- Faculty of Tropical Medicine, Mahidol UniversitySEAMEO TROPMED Network
- TROPMED Alumni Association
- The Parasitology and Tropical Medicine Association of Thailand

Co-organizers

Department of Disease Control Ministry of Public Health (MOPH)

Mahidol - Oxford Tropical Medicine Research Unit (MORU)

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Poster No.: 1

Parasite clearance and post-treatment submicroscopic parasitemia in patients treated with atovaquone-proguanil in combination with artesunate



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Parasite clearance is one indicator of reduced drug susceptiEility and a marker for artemisinin resistant phenotype Eut data on parasite clearance post treatment with atovaquoneproguanil (AP) in the settings of multidrug resistance in CamEodia remains limited. Light microscopy (LM) and qPCR targeting 18s rRNA expression indicative of *Plasmodium* species were performed to estimate parasite clearance, suEmicroscopic parasitemia, and treatment outcomes following treatment with AP and comEination of AP with AS (ASAP). Out of 149 evaluaEle volunteers, 76 received treatment with AP and 73 were treated with ASAP. On admission, the median parasite density was 7.7x10³ and 8.1x10³ parasite/µl in AP and ASAP arms, respectively. The failure rate was similar for AP (n=8) and ASAP (n=6) groups. The number of volunteers parasitemic on D3 was higher than reported in earlier studies with 37 (51%) volunteers in ASAP and 28 (37%) in AP arm having submicroscopic parasitemia. By week 1, all volunteers had cleared their parasitemia by LM, but 47% and 18% volunteers had submicroscopic parasitemia in AP and ASAP arms, respectively. None of the 32 volunteers with undetectable parasitemia at 72 hrs failed treatment, compared to 10 failures (20%) in volunteers with positive blood film, and 4 failures (6%) in volunteers with submicroscopic parasitemia on D3. The addition of AS in the settings of confirmed artemisinin resistance resulted in more rapid parasite clearance by the PCR. Additional studies are needed to confirm the predictive value of negative parasitemia by PCR on D3 on the treatment success post AP and ASAP combinations.

Keyword: Submicroscopic parasitemia, Treatment failure, Atovaquone-Proguanil, Artesunate

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Poster No.: 2

Spatiotemporal modeling of relative risk of malaria infection along Thailand-Myanmar border: the Hlaingbwe Township and Tha-Song-Yang District



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The challenging for the global goal of malaria eradication is still focused on the malaria transmission along international borders- the so-called border malaria. In order to get a clear picture of border malaria transmission, more sophisticated tools are required to implement the targeted control measures to control the spread of resistance and to prevent the reintroduction of parasites. Spatiotemporal modeling of relative risk of malaria disease in this study could serve as a useful tool for surveillance and forecasting. The objective of the study was to generate smoothed estimates of relative risk applying hierarchical Bayesian spatiotemporal Zero-Inflated Poisson (ZIP) model, including covariates age, sex and interaction between age and sex. Data used to develop the model were extracted from malaria surveillance systems during January-December 2016, along the international Thailand-Myanmar border, the Hlaingbwe Township and Tha-Song-Yang District. WinBUGs software version 1.4.3 was used for the data analysis and ArcMap software version 10.4.1 for the disease mapping. The risk mapping revealed disease clustering both within and along the Thai-Myanmar border (upper and lower parts) of the Tha-Song-Yang District, but also mainly in the upper and inner border area of the Hlaingbwe Township. Some apparent hot spot appeared along the Thai-Myanmar border and some scattered over the areas which is far away from the border area in both Tha-Song-Yang District and Hllaingbwe Township. The presented maps emphasized the importance of preventive actions for malaria in high-risk border areas for the common goal of malaria elimination by the two countries.

Keyword: Spatiotemporal, Border malaria, Thailand, Myanmar

Poster No.: 3

Relapse pattern in vivax malaria in Nepal



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Nepal has been clustered with malaria infection cases, especially in the southern bordered with India, and the infections are mostly due to *Plasmodium* vivax. Therefore, the main objective of this study is to determine the relapse patterns. A total of 206 microscopically confirmed *P. vivax* mono-infection patients were enrolled and randomized into two treatment arms: chloroguine alone and chloroguine plus primaguine. Blood samples were tested for microscopy, and qualitative G6PD testing by care start rapid card. Follow ups were made on 1, 3, 7, 14, 21, 28 days and in between 1-2 months intervals up to twelve months. Collected filter paper blood spots (pre and post treatment) were analyzed by semi-nested PCR and genotyped by three microsatellite markers (3.27, 3.502 and MS8). Of the total 206 cases, 12% (25/206) showed relapse during follow-up period. The relapse in CQ alone arm (22/25; 21.8%) was significantly higher than CQ+PQ arm (3/25; 2.9%) (p<0.005). Out of 25 cases, 48% showed early relapse (in ≤ 90 days) and 52% showed late relapse (in \geq 90days). The frequency of most common alleles and heterozygosity (He) of three microsatellite markers 3.27, 3.502 and MS8 were 15.38%, 25.93% and 7.69% and 0.853, 0.949, and 0.989, respectively. Of 25 *P. vivax* cases (D0+DR), 8 paired (32%) were found homologous; 8 paired (32%) were found heterologous, and 9 paired (36%) could not be differentiated. Of 16 genetically categorized paired samples, homologous genotypes were more widely distributed in late relapse cases. Microsatellite genotyping of *P. vivax* cases showed high genetic diversity.

Keyword: Plasmodium vivax / CQ/ CQ+PQ/ Relapse / Microsatellite genotyping

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Poster No.: 4

How are the Village Health Volunteers delivering malaria testing and treatment services and what are the challenges they are facing? - a mixed methods study in Myanmar



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Background: Village Health Volunteers (VHVs) play a key role in delivering community based malaria care especially in hard-to-reach areas in Myanmar. It is necessary to assess their performance and understand the challenges encountered by them forto effectively engage them in community management of malaria. This mixed methods study was conducted to: i) understand the cascade of malaria services (testing, diagnosis, referral and treatment of malaria) provided by the VHVs under the National Malaria Control Programme (NMCP) in Myanmar in 2016, and compare with other health care providers, ii) explore the challenges in delivery of malaria services by VHVs.

Methods: A sequential mixed methods study was designed with a quantitative followed by a descriptive qualitative component. The quantitative study was a cohort design involving analysis of secondary data available from NMCP database whereas the qualitative part involved 16 Focus Group Discussions (08 each with community and VHVs) and 14 Key-Informant Interviews with program stakeholders in four selected townships.

Results: Among 444,268 cases of undifferentiated fever identified by VHVs in 2016, 444190 were tested using Rapid Diagnostic Test. Among those tested, 20,375 (4.6%) cases of malaria were diagnosed, of whom 16,910 (83.0%) received appropriate treatment, with 7,323 (35.96%) were treatment within 24 hours. Of all malaria cases, 296 (1.5%) were complicated, of whom, 79 (26.7%) were referred to the higher facility. More than two-thirds of all cases were falciparum malaria (13,970, 68.6%) followed by vivax (5,619, 27.6%). Primaquine was given to 83.64% of all cases. VHVs managed 34.0% of all undifferentiated fever cases, 35.96% of all malaria cases and identified 38.0% of all Plasmodium falciparum cases reported under NMCP. The key barriers identified are: work related (challenges in reporting, referral, management of malaria especially primaquine therapy, and lack of community support) and logistics related (challenges in transportation, financial constraints, time and shortage of drugs and test kits). On the other hand they also enjoy good community support and acceptance in most areas.

Conclusion: VHVs play an important role in malaria carediagnosis and management in Myanmar, especially in hard-to-reach areas. More programmatic support to VHVs is needed in terms of logistics, transportation allowance and supervision to improve their performance.

Keyword: community health workers; Midwife; rapid diagnostic test; undifferentiated fever

Poster No.: 5

FTY720 restores endothelial cell permeability induced by malaria sera



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Increased endothelial cell (EC) permeability in severe Plasmodium falciparum malaria contributes to major complications of severe malaria. This study explored EC permeability in malaria, and evaluated the potential use of FTY720 to restore EC permeability. ECs were incubated with sera from malaria patients (P. vivax, uncomplicated and complicated P. falciparum malaria). Cellular permeability was investigated using a fluorescein isothiocyanate (FITC)dextran permeability assay. FTY720, an analogue of sphingosine-1-phosphate (S1P), was tested for its potential action in maintaining EC integrity. ECs with from malaria patients incubated sera complicated P. falciparum showed higher fluorescein leakage compared with ECs incubated with sera from P. vivax (p < 0.001) and uncomplicated P. falciparum (p < 0.001). ECs pretreated with FTY720 before incubation with malaria sera had significantly decreased fluorescein leakage compared with no FTY720 treatment. In addition, FTY720 treatment significantly reduced fluorescein leakage for both uncomplicated (at 45 min) (p = 0.015), and complicated P. falciparum malaria (15 min) (p = 0.043). The permeability increase induced by complicated P. falciparum sera was significantly reversed and prevented by FTY720 in vitro. FTY720 may have clinical applications to protect against endothelial barrier dysfunction in severe P. falciparum malaria.

Keyword: malaria/ *Plasmodium falciparum*/ endothelial cells/ cell permeability/ sphingosine-1-phosphate/ S1P/ FTY720

Poster No.: 6

Spatio-temporal Analysis of Malaria Cases along China-Myanmar Border



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OBJECTIVE: To analyse the spatio-temporal distribution pattern of malaria cases along China-Myanmar border in Yunnan Province, China.

METHOD: Malaria data in 2011-2016 were extracted from China's malaria surveillance information system. The data were analyzed using Microsoft Excel and ArcGIS.

RESULTS: There were a total number of 2,117 malaria cases during the 6 years across 18 counties along China-Myanmar border in Yunnan. An average annual incidence was 0.06/1,000. Although with an overall trend of decreasing from 0.13/1,000 in 2011 to 0.03/1,000 in 2016, there was significant variation among different counties. The high-risk areas mainly clustered in central part (west of Yunnan) along the border. There were 314 indigenous cases and 1803 imported cases accounted for 12.14% and 87.86%, respectively. Most of imported cases came from Myanmar (92.12%, 1661/1803). Number of counties with indigenous cases decreased from 17 to 1, with only 1 case in Yingjiang county in 2016. The imported cases reached the peak in May and the indigenous cases in June. About 78% of the patients aged between 15 to 54 years old and about 85% were male. **CONCLUSION:** The number of malaria cases, particularly indigenous cases in

Yunnan decreased from 2011 to 2016 indicates a good prospect for achieving the goal of malaria elimination in 2020 for China. However, the burden of interrupting malaria transmission still unevenly distributed throughout the border area. Spatio-temporal mapping of malaria risk area with ArcGIS technique developed in this study will provide useful information for targeted intervention during malaria elimination phase.

Keyword : Malaria, China-Myanmar border, Spatio-temporal distribution, Risk map

Poster No.: 7

Antimicrobial susceptibility patterns of *Salmonella* species in a tertiary care hospital of Western Nepal: Are first line antibiotics still effective?



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Background: Enteric fever remains significant cause of morbidity and mortality in developing countries like Nepal. Large number of cases remained undiagnosed due to lack of trained laboratory personnel and poor laboratory facilities. Increasing resistance to antimicrobials among *Salmonella* species is a challenge for clinicians. This study was aimed to determine the drug resistance pattern of *Salmonella* species.

Methods: This hospital based study was conducted over a period of ten years between 2008 to 2017 at Manipal Teaching Hospital, Pokhara, Nepal. Blood and stool samples from suspected patients were collected. Isolation, identification and antibiotic susceptibility testing was performed by standard microbiological techniques.

Results: Total 105 isolates of *Salmonella* species were cultured from the blood and stool samples. *Salmonella enterica serovar paratyphi* A, being the most common accounting for 48.6% (51/105) followed by *Salmonella enterica serovar typhi* 36.2% (38/105), other *Salmonella* species 10.5% (11/105) and *Salmonella enterica serovar paratyphi* B 4.7% (5/105). Patients were between age group of 2 years to 67 years. Most of the isolates were cultured from the patients of age group of 15-30 years. The susceptibility pattern of *Salmonella* species to chloramphenicol, ceftriaxone, ciprofloxacin, gentamicin, cotrimoxazole, and ampicillin was 90.4%, 85.7%, 86.6%, 78%, 79%, and 42.8% respectively.

Conclusion: The susceptibility of *Salmonella* species to ciprofloxacin and chloramphenicol was as effective as ceftriaxone. Findings of this study highlight the need for continuous surveillance of antimicrobial susceptibility pattern before shifting to higher generation of antibiotics for the treatment of enteric fever.

Keyword: Enteric fever, Drug resistance, Salmonella, Blood culture

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Poster No.: 8

Investigating of knockdown resitance (Kdr) mutation in dengue vector *Aedes aegypti* cypermethrin resistance from dengue endemic area in Medan City, North Sumatera Province, Indonesia



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Background: Dengue is health problem in Medan where the annual incidence rate is above the national target. Tanjungrejo Village Lk. XIX are the highest dengue cases area compared to other Lingkungan, whereas Lk. XXII was dengue free area for the past two years. Cypermethrin insecticide is commonly used in dengue vector control. Major mechanism of cypermethrin insecticide is the presence of Kdr mutation in *Ae. aegypti* VGSC gene.

Objective: Monitoring resistance status of *Ae. aegypti* against cypermethrin and detection of mutation in *Ae. aegypti* VGSC gene.

Method : Eggs of *Ae. aegypti* was collected using 400 ovitraps (indoor and outdoor). Resistance status of *Ae. aegypti* against cypermethrin was determined based on CDC bottle bioassay method and detection of mutation in *Ae. aegypti* VGSC gene was determined based on PCR method and DNA sequencing.

Results : Knockdown percentage of *Ae. aegypti* from Lk. XIX was 76.67% and Lk. XXII was 97.67% after exposure to cypermethrin diagnostic dose for 30 minutes. Knockdown time (KT $_{99}$) of *Ae. aegypti* Lk. X1X was 79.64 minutes and Lk. XXII was 40.54 minutes respectively. Mutations were found in domain II segment 6 (S989P and V1016G) and domain III segment 6 (F1534C). Combination mutations (S989P+V1016G) and (F1534C+V1016G) were found from *Ae. aegypti* Lingkungan XIX, whereas Lk. XXII only found V1016G mutation.

Conclusion : Ae. aegypti Lk. XIX has been resistant whereas Ae. aegypti Lk. XXII was susceptible to cypermethrin insecticide. Combination mutations found in Ae. aegypti resistant whereas one point mutation in Ae. aegypti susceptible to cypermethrin insecticide.

Keyword : Aedes aegypti, resistance, cypermethrin, mutation

Poster No.: 9

Knowledge, attitude and stigma of leprosy: a community based cross-sectional study in Nepal



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Background: Though Nepal declared leprosy elimination in 2010, it is identified as public health problem for the past 2 years and its burden is constantly rising in Terai communities with 3000 new leprosy patients being diagnosed each year. Community's perception is very important for prevention and control of leprosy and enhancing quality of life of leprosy patients. Poor knowledge, unfavorable attitude and associated stigma create a hindrance to prevention and control of leprosy.

Objective: To assess knowledge and attitude of the communities towards leprosy and associated stigma with leprosy.

Methods: Community-based cross-sectional study was conducted in Dhanusha and Parsa. 424 individuals were interviewed using semi-structured schedule. Data was analyzed using both descriptive and statistical analysis SPSSv20.

Results: Only 31% of the respondents had good knowledge. Around 30% knew that leprosy can lead to deformities, 55.5% believed it is caused by bacteria, and 13% believed it is due to curse. Around 8% of the respondents believed that leprosy is transmitted by having sexual contact with leprosy patients. Overall, 65% had unfavorable attitude towards leprosy. Knowledge and attitude were associated with age and education (p<0.01). There was significant positive correlation between knowledge and attitude towards leprosy. EMIC scale showed high level of stigma attached to leprosy in $2/3^{rd}$ of the respondents.

Conclusions: More than two-third of the respondents were highly stigmatized, with poor knowledge and negative attitude towards leprosy. With increasing knowledge there'd be increasing favorable attitude towards leprosy. Awareness to reduce stigmatizing behaviors and improve community knowledge of and attitude towards leprosy should be emphasized.

Keyword: Knowledge, Attitude, Stigma, Community, Leprosy

Poster No.: 10

Prevalence and associated factors of *Enterobacteriaceae* producing extended spectrum beta-lactamase carriers in Thai rural area, 2018.



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Enterobacteriaceae producing extended spectrum beta-lactamase (ESBL) are bacteria live in gastrointestinal tract, resist to 3rd generation cephalosporins. Its prevalence in rural community of Thailand 2012 was 65.7%, higher than similar researches conducted in other countries. The study of associated factors for ESBL carriers is important for preventing spread and decreasing the prevalence.

A cross-sectional study was conducted to determine the prevalence and associated factors of being *Entertobacteriaceae* ESBL carriers among healthy population of Sakeow Province, Thailand 2018. Stool culture on selective agar was used as screening test and combination disk as confirmation test. MALDI-TOF was used to identify the species of ESBL colony. Associated factors were assessed by online questionnaire then matched with the culture result.

Among 455 of volunteers, *Enterobacteriaceae* ESBL carriers prevalence was 73.8%. The predominated organism was *Escherichia coli* (72.6%). Married or living as spouse have more chance to be carriers (3.9 times) compare to living without partners. Having elementary education and above have more chance of being carriers (2.7 times) compare to people with education below elementary. Having domestic mammals in the house have less chance of being ESBL carriers (0.4 times) compare to not having domestic mammals.

The public health protocol of controlling antibiotic use in human and livestock is not enough to control the spreading of this germ. To reduce the prevalence in community we should focus on human-to-human spreading. Basic hand hygiene after using toilet and after farming should be raised to the community awareness.

Keyword : Enterobacteriaceae, ESBL, E coli, Antibiotic-resistant bacteria, Community based, Thailand

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Poster No.: 11

Development of dengue virus serotype specific Nonstructural protein 1(NS1) capture immunochromatographic assay



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Dengue virus (DV) is an arbovirus that has shown a rapid geographical spread. A prompt diagnosis is crucial for a reduction of mortality with a timely manner and adequate management of severe dengue cases. Four DV serotypes (DV1-4) are classified and each of amino acid level differs by approx. 40%. Currently, the method of extracted RNA reverse transcription and PCR amplification is a standard for the DV serotype determination, however, it requires some time, so the rapid detection system has been desired for long.

We obtained anti-NS1 mouse monoclonal antibodies and developed rapid detection systems. We successfully developed serotype-specific immune chromatographic systems of DV NS1. All of these systems were able to detect 10^4 copies/mL virus in 15 min and no cross-reaction among different DV serotypes was observed. We also confirmed no reaction against Chikungunya, Japanese encephalitis, Sindbis, and Zika viruses. These assay systems would accelerate both the DV diagnosis and epidemiological research in the DV endemic areas.

Keyword: Dengue virus, immunochromatography, point-of-care

Poster No.: 12

Eexpression of gene encoding merozoite surface protein 1 Plasmoidum falciparum (PfMSP1-19kDa) in Escherichia coli BL21 (DE3)



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Background: *Plasmodium falciparum* merozoite surface protein 1 19kDa is referred as a vaccine candidate against the erythrocyte phase of *P. falciparum*. It is a potential antigen to trigger immune response to inhibit the merozoite invasion of red blood cell (RBC). Many researches study about the production of PfMSP- $\mathbf{1}_{19}$ and its imunological evaluation have been published from several endemic malaria countries, but the production of PfMSP- $\mathbf{1}_{19}$ from indonesian strain have not been studied.

Objective: The objective of this study was to express merozoite surface protein 1_{19} gene from *Plasmodium falciparum* on *Escherichia coli* BL21 (DE3), as the initial study of PfMSP- 1_{19} antigen development in Indonesia.

Methods: Amplification of Pfmsp1₁₉ gene using GoTaq Green mix amplification kit. Fresh amplification product of Pfmsp1₁₉ gene was cloned on pET SUMO vectors and transformed in $E.\ coli$ Mach1 competent cell. The insert DNA from positif colonies were analysis using Sanger sequencing method. Recombinant gene was expressed on $E.\ coli$ BL21 (DE3) induced with IPTG. Recombinant protein was analyzed using SDS-PAGE and western blotting.

Result: cloning of Pfmsp- $\mathbf{1}_{19}$ gene was successfully performed, with 10 positive colonies containing recombinant plasmid pET SUMO-Pfmsp $\mathbf{1}_{19}$. Based on the sequencing analysis of insert DNA from positive colonies, 2 colonies have correct in sequence and orientation accordance with Genebank database. The expression results were detected by western blotting analysis with antiHis tag antibody at the size of about 34 kDa. The desired protein band should be detected at a size of about 23 kDa.

Conclusion: Pfmsp1₁₉ gene was successfully cloned in pET SUMO vector but it was not expressed well in *E. coli* BL21(DE3).

Keyword : Cloning, Expression, PfMSP-1₁₉, *Plasmodium falciparum*, *Escherichia coli* BL21 (DE3)

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Poster No.: 13

Malaria case investigation review in Thailand, 2012-2017



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Under the national malaria elimination strategy, Thailand has adopted the 1-3-7 benchmark such as all malaria cases should be notified within one day, investigated within three days, and responded to within seven days. Case investigation is conducted to determine the source of infection and implement the appropriate response. We reviewed the case investigation data and measured the proportions of indigenous (infection acquired in the village of residence including surrounding areas) and imported (outside the village of residence) malaria cases. Logistic regression was used to measure adjusted odd ratios (AORs) for the explanatory variables. Between October 2012 and September 2017, 94,486 malaria cases (61% Plasmodium vivax, 37% P. falciparum, and 2% of mixed or other species) were analysed. Overall, there was a significant increase in case investigation coverage rate from 81% in 2013 to 96% in 2017 (p=0.001) resulting from the implementation of the 1-3-7 benchmark. In 2013, Pv cases were more frequently investigated than Pf cases (85% vs 77%, respectively), but this difference converged to reach 96% for Pf and 97% for Pv in 2017. The proportion of indigenous cases increased by 86% for all species from 37% in 2012 to 69% in 2017. In 2012, the proportion of investigated indigenous cases for Pf was greater than for Pv (47% vs. 29%, respectively), but this difference tended to converge up to 68% for both species. Over the study period, the investigation rate for passively detected cases also increased from 85% to 97% (p=0.001). Although the overall investigation rate was significantly greater in higher burden provinces (>100 cases per year, p=0.001) than in provinces with lower malaria burden, Pattani and Ubon Ratchathani provinces accounted for 35% of the subjects not investigated in 2017, resulting from malaria outbreaks and limited vertical malaria program resources. Despite a recent increase in case investigation rates in these two provinces, the coverage in 2017 remained lower than in other provinces (AOR=0.12, AOR=0.46, respectively, p=0.001), while no other significant risk was detected. It is recommended that the national program strengthens the capacity of the Surveillance and Rapid Response Teams (SRRT) to conduct case investigations in identified provinces with lower case investigation rates and implement the 1-3-7 strategy to achieve the malaria elimination targets.

Keyword : Malaria elimination, surveillance

Poster No.: 14

Health problems among Myanmar and Laos workers in Samut Sakhon, Thailand



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Introduction: There are increased numbers of workers from Myanmar and Laos migrated to Thailand in a past decade. There is no previous data of health problems and health care seeking behaviors among these ethnics during working in Thailand. This study aims to identify health problems and health care seeking behaviors among Myanmar and Laos workers.

Methods: A questionnaire-based survey was conducted among Myanmar and Laos workers who have been in Thailand during 3 months to 7 years regarding their health problems and health care seeking behaviors. This study was conducted at the Migrant Check-Up Clinic, Krathumbaen Hospital, Samut Sakhon during March to August 2018.

Results: A total of 767 migrant workers were enrolled. Six hundred (78%) workers were Myanmar and 167 (22%) were Laos. The mean age was 29.1±7.2 years (range 18-55 years). Seven hundred and twelve (92.8%) persons were factory workers, Myanmar (95.5%) and Laos (83.2%). The overall prevalence of health problems was 27.1% (19.2% vs 5.7%, p-value <0.01, Myanmar and Laos respectively). The top three health problems were respiratory tract symptom (13.7%), diarrhea (13.2%), and tooth decay (12.6%). Respiratory tract symptom was the most common symptom requiring health care seeking services in both groups (37.8% vs 33.3%, Myanmar and Laos respectively). During check-up, chest radiographic abnormalities were found in 9 out of 767 workers and all abnormalities were pulmonary infiltration.

Conclusions: Overall 27.1% of workers experienced health problems during their stay in Thailand. Respiratory tract symptom was the most common health problems in both groups.

Keyword: Health problems, Myanmar, Laos

Poster No.: 15

Optimal target concentrations of piperaquine against placental malaria



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Dihydroartemisinin-piperaquine is an alternative antimalarial drug for intermittent preventive treatment in pregnancy (IPTp). Several pharmacokinetic studies showed that malaria treatment in pregnancy using dihydroartemisinin-piperaquine may not need dose adjustment. However, there are limited information on the long-term IPTp regimen. In this study, the pharmacokinetics of piperaquine as IPTp in 366 Kenyan pregnant women and 101 Indonesian pregnant women were evaluated. Also, the relationship between the pharmacokinetic parameters and the placental malaria outcome was investigated.

Pregnant women received the standard 3-day oral treatment of dihydroartemisinin-piperaquine monthly until delivery. Venous plasma samples from Kenya and dried-blood-spot samples from Indonesia were collected before each subsequent dose (i.e. trough level), breakthrough symptomatic malaria, and at delivery. Piperaquine concentrations in the samples were measure using solid phase extraction followed by liquid chromatography coupled with tandem mass spectroscopy. Piperaquine pharmacokinetic properties were evaluated using nonlinear mixed-effects modelling. The pharmacokinetic model and parameter estimates were guided and stabilised using prior information. Placental malaria outcomes were evaluated using logistic regression modelling.

The pharmacokinetic properties of piperaguine were described using a flexible transit absorption model followed by three disposition compartments. Gestational age showed no impact on the pharmacokinetic parameters of piperaquine. Only 3.26% (3/92) of Indonesian pregnant women and 31.7% (112/353) of Kenyan women were positive for placental malaria at delivery. Piperaguine concentrations were statistically significant determinants for placental malaria. In conclusion, this study evaluated the pharmacokinetic properties of piperaquine and its relationship to malaria during intermittent preventive treatment in pregnancy. High piperaquine exposure was associated with a protective efficacy against placental malaria, and maintaining piperaguine trough concentrations above the estimated target value is needed to protect against malaria during pregnancy.

Keyword: Piperaguine; Intermittent Preventive Treatment in pregnancy (IPTp); Placental Malaria; Pharmacokinetic model; Nonlinear mixed-effects modelling

Poster No.: 16

Susceptible status and resistance mechanism of *Aedes* aegypti to malathion and cypermetrin in endemic dengue area from Palu City, Central Sulawesi, Indonesia



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Background. Dengue often causes outbreaks in several districts/cities in Indonesia. In 2016, Palu City had the highest number of DHF cases in Central Sulawesi Province, 2 people died from Balaroa Village. Balaroa Village is categorized dengue endemic. It has been reported that *Ae. aegypti* mosquitoes in Palu City has been resistant to insecticide malathion and cypermethrin insecticides, but the resistance mechanism is not well known.

Objectives. The study aimed to determine the resistance status to malathion and cypermethrin and the resistance mechanism.

Methods. Aedes aegypti collected from endemic dengue area (Balaroa Village) was reared to adult. The resistance status of Ae. aegypti to malathion and cypermethrin was performed based on the CDC bottle bioassay. The metabolic resistance mechanism was performed based on the level of nonspecific esterase activity. The target site resistance mechanism was performed using PCR and sequencing of DNA VGSC gene.

Results. The susceptibility status of *Ae. aegypti* to malathion and cypermethrin were moderately resistant and resistant respectively in dengue endemic area. The nonspecific esterase activity increased with average absorbance value (AV) was 0.639. It was found double point mutation at S989P and V1016G and a single point mutation at target site V1016G in IIS6 VGSC gene.

Conclusion. Aedes aegypti from dengue endemic area was resistant to malathion and cyperpethrinn, the nonspecific esterase activity increased and the two alleles have a role in the occurrence of cypermethrin resistance

Keyword : Aedes aegypti, malathion, cypermethrin, esterase, VGSC gene mutation

Poster No.: 17

Human population movement patterns in malaria hotspots on the Thai-Myanmar border



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Human population movement (HPM) patterns are important with regard to malaria transmission, perhaps especially in areas approaching malaria elimination. Individuals can acquire malaria from outdoor activities and then transmit while traveling or upon returning to their villages. Areas that have achieved local elimination can experience reintroductions through HPM. This study aimed to characterize and quantify HPM, and determine the effect of HPM on malaria infections, in malaria hotspots on the Thai-Myanmar border. The study was conducted in four villages of Tha Song Yang District, Tak Province and Sangkhlaburi District, Kanchanaburi Province; two sub-districts with persistently high malaria incidence. Participants were surveyed using travel questionnaires during the dry (March) and wet (May) seasons of 2018. HPM patterns were quantified and determined the association with malaria by logistic regression. Trips were more common in the dry season. In both seasons, there were more longer trips without overnight stays to almost all places in Tha Song Yang when compared to Sangkhlaburi, with the exception of overnight trips in the wet season. Model adjusted odds ratios (AOR) indicated an increased risk of malaria relative to the number of days doing outdoor activities in the dry season, especially trips to areas on the Myanmar side (AOR=1.11, 95%CI 1.03-1.17), forests (AOR=1.08, 95%CI 1.03-1.13), and overnight trips (AOR=1.10, 95%Cl 1.02-1.19). In order to effectively and rapidly eliminate malaria, people with high risk movement patterns should be prioritized for screening as part of the targeted malaria elimination programme and closely monitored as part of national malaria surveillance.

Keyword: Human population movement, malaria hotspot, Thai-Myanmar border

Poster No.: 18

Expression, purification and activity sssay of trehalose phosphate phosphatase from *Burkholderia pseudomallei*



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Burkholderia pseudomallei is a Gram-negative intracellular bacillus. It is a causative agent of melioidosis, a lethal disease endemic in tropical areas, especially in northeast Thailand and northern Australia. B. pseudomallei resists to many antibiotics, so the treatment requires special antibiotics for a long period of time. Up to now, there are no effective vaccines available. Trehalose and trehalose biosynthesis pathways have been found to play important roles in pathogenicity of many organisms. In B. pseudomallei, when treA, a gene encoding trehalase enzyme which catalyzes trehalose breakdown, was deleted, the pathogen has reduced virulence. This suggests that enzymes in trehalose biosynthesis pathway could serve as potential drug targets for melioidosis treatment. In this study, we aim to express, purify and determine the enzyme activity of trehalose phosphate phosphatase (TPP), a member of trehalose synthesis pathway (TPS/TPP pathway) that found to be absent in mammals. The tpp gene from B. pseudomallei was successfully cloned into pET28a expression vector. The recombinant pET28a-tpp was transformed and expressed in E. coli BL21 (DE3) under induction of IPTG. After that, the protein was purified to homogeneity by Co²⁺ affinity chromatography and the purity of protein was checked by SDS-PAGE. The phosphatase activity of TPP was measured using Phosphate Assay Kit. It was demonstrated that purified TPP was able to catalyze the phosphate release from trehalose-6- phosphate. In summary, we are able to express and purify TPP from B. pseudomallei with expected activity. This purified TPP can be used in the functional study or crystallization to gain more information regarding the role *B. pseudomallei* TPP in the future.

Keyword : Burkholderia pseudomallei, Trehalose phosphate phosphatase, Protein expression, Enzyme activity

Poster No.: 19

Phylogenetic analysis of dengue viruses isolated from clinical cases in Southern Thailand.



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In a few decades, Dengue virus (DENV) has become the most prevalent arbovirus in the world particularly for people living in urban areas in intertropical countries.

There are four distinct DENV serotypes (DENV-1 to 4). Based on the genomic variability, strains of each serotype of DENV are themselves divided into different genotypes. This genetic variability within the serotypes is attributed to the high mutation rate of DENV. The phylogenetic analysis of the variants allows the monitoring of the spatio-temporal dissemination of each DENV strain, showing the rise of a specific genotype or highlight a shift of genotype. These events may be associated with changes in virulence, vector competence and geographical adaptation for instance.

In Thailand, the DENV remains a burden with recurrent epidemics in the country particularly in the southern region. Due to its geographical location and its position as a regional communication hub, this makes this region one of the hot spots of DENV circulation in South East Asia.

The goal of this study is to determine the genetic variability of DENV isolated from clinical cases and circulating in Southern Thailand during the period 2015-2016.

Finally, this study provides a spatio-temporal phylogenetic follow-up and the precise identification of DENV variants that could help for understanding how epidemics are triggered, evaluate the dynamic of dissemination and identifying strains involve in severe dengue cases in South Thailand.

Keyword: Dengue virus, Southern Thailand, phylogenetic, arbovirus

Poster No.: 20

Lesson learned during dengue outbreaks in Thailand, 2013-2018



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Thailand has experienced the largest dengue outbreaks for more than five decades, with a record number of people infected by the Aedes mosquito-borne disease and 74 deaths so far this year (September 2018). Dengue is more prevalent in heavily populated areas with a change in weather patterns and rapidly urbanization have contributed to more getting infections among the target population. This review presents in brief from selected epidemiologic observations on outbreak of dengue occurring in Thailand during the period of 2013-2018. Data are collected from the National Disease Surveillance (Report 506) from Bureau of Epidemiology, Ministry of Public Health. There are three dengue outbreaks occurred in 2013, 2015 and 2018 throughout the country. After analyzing the three outbreaks have found the risk factors affected dengue morbidity and mortality were from dengue cases mostly have late hospital admission and delay treatment and patients with underlying non-communicable diseases associated with patients' death due to dengue. Nevertheless, the three outbreaks have found following prominent themes in the response efforts namely effectively entomological surveillance for dengue, timely detection of illness, rapidly risk communication that engages the community, correct information and timely activated of a rapid response called as Emergency Operating Center (EOC) at all provinces of Thailand. However, the public health authorities urgently need to be involved in the clinical practice guidelines for dengue treatment and laboratory testing promptly as well as provide accurate information and engage the local community in vector control for preventing the outbreaks and more effective dengue prevention and control.

Keyword: dengue, outbreak response, Thailand

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Poster No.: 21

Dengue outbreaks in Bhutan: epidemiological characteristics, risk factors and strategic challenges in disease prevention, a review



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Dengue is transmitted by infected Aedes mosquitoes and it is one of the most significant public health burden in tropical and subtropical countries. This seasonal virus has been increasingly detected in traditionally few non-endemic areas in South-western part of Bhutan since 2004 till date. Here, I have done a systematic review of few dengue outbreak reports to summarize information regarding the epidemiology, clinical characteristics, risk factors and serotype distribution, and strategic challenges in dengue prevention. With an incubation period of 4-10 days (mean 7 days), patients developed fever, headache, body ache, myalgia, arthralgia, nausea or vomiting. Hematemesis and altered mental status and other co-existing morbidities such as typhoid fever, common cold, UTI were recorded. Among many, sanitation, personal and social behavior were found to be the main risk factors for the exposure. Bhutanese traditional dress worn by males is also found as risk factor for dengue. Males were affected most compared to females associated with the nature of outdoor activities. The median age of the cases was 26 years ranging from 2 to 67 years with the highest cases observed in the age group of 30-45 years. All the documented dengue outbreak virus was mainly caused by DENV-2 and 3 relating to those of north India strains. Dengue surveillance need to be reinforced in all endemic areas, timely case notification, proper entomology surveillance, adequate and timely community participation with other stake holders, capacity building on dengue management, and need of frequent public awareness on dengue were the challenges addressed.

Keyword: Bhutan, Myaliga, Arthralgia, Hematemesis, UTI, DENV-2 &3, India

Poster No.: 22

Dengue case management at a Malaysian hospital: insights from an ethnographic study



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Dengue is estimated to pose a risk to half of the world's population. In Malaysia, dengue is a major cause of morbidity and infectious disease mortality, with an annual upward trend in nationally reported cases. Diagnosis and management remain a challenge; to date there is insufficient evidence to inform optimal clinical management; and reported deficiencies in adherence to World Health Organization and national guidelines. There is a dearth of qualitative research exploring why implementing guidelines is difficult.

In 2017, an ethnographic study at an urban public hospital in Malaysia explored day-to-day dengue case management, with a focus on the barriers and facilitators in the implementation of clinical practice guidelines.

The study employed ethnographic, qualitative methods, specifically direct observation, interviews and focus group discussions with doctors and nurses in two hospital departments. Fieldnotes and verbatim transcripts were analysed using a modified thematic content analysis approach.

Findings identified a gap between the uptake of guideline recommendations and actual practice. The diagnosis of dengue was complex and some dengue deaths were perceived by doctors to be "preventable." Recommendations from the study include enhanced training for clinicians across departments, improved communication between doctors, and suggested additions to the current guidelines.

This study provides novel insights on the implementation of dengue case management guidelines in practice, the role of formal guidelines and insights into how case management could be strengthened. The findings from this research may be generalisable to other tertiary care settings in dengue endemic countries.

Keyword: Dengue, Malaysia, Clinical practice guidelines

Poster No.: 23

Dengue: An emerging disease and its challenge in Nepal

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Dengue, is the emerging vector borne diseases in Nepal caused by the bite of infected aedes aegypti mosquitoes. It is emerged in the form of Dengue Fever (DF), Dengue Hemorrhagic Fever (DHF) and Dengue Shock Syndrome (DSS). First suspected incidence of dengue was identified in 2004. Sine then major outbreak occurred in 2006, 2010, 2013 and 2016. Initially most of the case were found to be imported from neighboring country India but now suspected indigenous cases are also beginning to seen. Though dengue is more common in southern terai belt of Nepal, now it is more apparent in middle hilly region. Each year, it is expected to outbreak in post monsoon seasons from September to November. Government is undertaking different measure to control its trend and epidemic but challenges still exist there in different form. Rapid increase in unplanned urbanization, increase in temperature and open cross border issue e.t.c are remaining as challenge in management of dengue in Nepal. Dengue is expanding in rapid pace so, immediate action should be taken in time. This paper aims to review dengue situation and existing challenges of dengue in Nepal with necessary intervention needed to minimize effects of this disease.

Keyword: Dengue, Trend, Challenge in Nepal

Poster No.: 24

Molecular epidemiological investigation revealed serotype switching during major dengue outbreaks in Nepal



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Background: Global expansion of dengue virus (DENV) is a serious public health concern. Although DENV introduced in 2006, molecular epidemiology remains largely unclear in Nepal. We uncovered it through serotype/genotype analysis of circulating strains.

Methods: We employed the archived serum samples (n = 972) collected during 2007-2015 from DENV infected individuals with linked clinical and demographic data. Serotyping was performed by reverse transcription PCR, and complete envelope (E) gene sequences of all four DENV serotypes were identified and analysed.

Results: During the study period, dengue affected at least 25 districts in Nepal with an estimated case fatality rate of 1.5%. Majority were secondary infections (67%) and adults (81%) with 13% severe manifestations. DENV was also detected in the hill districts - possibly adapted towards higher altitudes (>1400 meters). All four serotypes were identified; however, a serotype switching pattern was observed during major outbreaks. While DENV-3 was the major one in 2007-8, DENV-1 and -2 caused larger outbreaks in 2010-11 followed by a predominance of DENV-2 in 2013-14, and a re-emergence of DENV-1 in 2015. Nepal DENV 1 strains belonged to genotype-V and formed two distinct clades. DENV 2, 3, and 4 strains were clustered into cosmopolitan genotype, genotype-III, and genotypes-I/ IIB, respectively. M-L trees revealed that the vast majority of Nepal DENV strains were closely related to contemporaneous India strains suggesting India as the most plausible origin due to physical proximity, extensive cross-border activities and similar geo-climatic features.

Conclusions: DENV serotype switching occurred in Nepal during the major outbreaks. We have also outlined genetic diversity of DENV serotypes in Nepal. This information is useful in epidemic preparedness and in the understanding of DENV evolutionary trends at regional and global level. These findings also underscore the need of cross-border collaboration in dengue control.

Keyword: Dengue epidemiology, dengue virus, serotype switching, genotypes, Nepal

Poster No.: 25

Epidemiology and Clinical Characteristics of Dengue Deaths in Thailand, 2018: Adults were at Higher Risk.



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In 2018, Thailand has been attacked with dengue epidemics. During January to September, a total of 59,140. Cases were reported. Morbidity Rate was 89.48/100,000 populations which highest in the past three years. Eighty cases were fatal led to an unusual high case fatality rate (CFR), 0.13%.

We reviewed dengue dead cases to describe epidemiological characteristics and determine risk factors of deaths in terms of demographic data, underlying diseases, and clinical manifestations. Of those 80 dengue deaths, 59.5% were female. CFR by age groups were about 0.10% in children and young adults, 0 - 34 years old. However, CFR were 3 - 4 times higher in middle age group and elderly, 35 or older. Most of them were from central region 50%. Forty percent of adult cases had underlying conditions i.e. obesity, diabetes, hypertension, hematological diseases, and alcoholism that led to severe liver, cardiovascular, or renal impairment. Nineteen cases presented with specific symptoms apart from high grade fever such as diarrhea or upper respiratory illness. All of them were firstly diagnosed to be other diseases caused to the delayed proper dengue management. Completed blood count on admission showed hemoconcentration, however, patients with anemia such as thalassemia or G-6-PD deficiency were not detected hemoconcentration. There were 32 cases that did not present low white blood cells as dengue case definition probably due to bacterial co-infections complications. Most of cases were diagnosed dengue within 4 days after onset of illness and died within 7 days.

Thailand has taken steps to reduce deaths from dengue problems such as provide training to health care workers, communicate with private clinics and drugstores to avoid NSAID prescription to any patient presenting with fever. Clinical practice guideline was also revised by the multidisciplinary experts, pediatrics, infectious medicine, and critical care teams to cover dengue management in adults.

Keyword: Dengue Dead Case

Poster No.: 26

ONE HEALTH STUDY OF JAPANESE ENCEPHALITIS VIRUS VECTORS' PREFERENCE IN CAMBODIA



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Background: The incidence of mosquito borne diseases are influenced by mosquito host selection. For the determination of the Japanese encephalitis (JE) vector species and their trophic behaviour, collection of mosquitoes straight from the baited net can be considered the most representative method.

Objectives: To analyse the feeding behaviour of the main JE vectors using two methodologies, i.e. baited traps and PCR analysis of mosquito blood meals.

Materials/Methods: Double nets for five different baits: cow, chicken, pig, human and empty were used to trap mosquitoes in a rural area of Cambodia for five consecutive nights. Mosquitoes were collected four times a night. In another method, the blood-fed mosquitoes were analysed using PCR.

Results: In total 12,573 mosquitoes of six different species and one genus were captured. *Culex vishnui* (36.7 %) followed by Anopheles genus (31.9 %) and *Culex tritaeniorhynchus* (30.4 %) were the most trapped mosquitoes. The mosquitoes trapped were 12.4 % in chicken, 49.3 % in cow, 12.6 % in human, 20.2 % in pig, and 5.3 % in empty trap. Trap-cow attracted the most mosquitoes and hence had positive effect on the number of trapped mosquitoes. Mosquito species were found to have opportunistic behaviour..

Conclusions: This suggests mosquito have wide opportunity to acquire and transmit viruses from animal to human. Most mosquito species were found in cow and having blood-fed from cow. The finding of Culex species mosquitoes attracted to animals endorses for the transdisciplinary involvement and potential One Health approach to implement the control and intervention of JE.

Keyword: mosquitoes, trophic behavior, Cambodia

Poster No.: 27

Knowledge, attitude, and practice study on japanese encephalitis, dengue, and zika among long term expatriates from non-endemic countries residing in Thailand



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Background/Objectives: Increasing number of long term expatriates from non-tropical countries staying in Thailand pose a unique health risks on mosquito-borne *flavivirus* infection including Japanese encephalitis (JE), dengue, and Zika. There is limited study focusing on those diseases among expatriates. This study aimed to determine the knowledge, attitude and practice among long term expatriates residing in Thailand.

Method: This was a questionnaire based study, implemented on westerner expatriates living in Thailand. Questionnaires were collected in Bangkok and Chiang Mai public areas during December 2017 to August 2018

Results: 591 expatriates were participated in this study. 85.8% came from Europe and America with median stay in Southeast Asia equal to 53 and 42 months, respectively. 213 participants (36%) were vaccinated with JE vaccine. Participants who were vaccinated with JE vaccine were more likely to have good knowledge on JE when compared to non-vaccination group (43.2% vs 10.6%, p<0.001). Health care provider, friends/family/relatives, and social medias were the main source of knowledge sought by expatriates. DEET and citronella repellent were frequently used among expatriates residing in Thailand. Seeking pre-travel consultation with GP doctor (OR=1.66, 95% CI 1.06-2.60) and travel medicine expert (OR=2.62, 95% CI 1.61-4.26) were associated with better knowledge and better attitude on mosquito-borne diseases.

Conclusion: Only the minority of expatriate in Thailand had good knowledge on JE. Those with history of JE vaccination had significantly better knowledge and attitude. Adequate pre travel preparation on common mosquito-borne diseases are urgently needed among expatriates before residing in the endemic area.

Keyword: Japanese encephalitis, Dengue, Zika, Knowledge, Attitude, Practice

Poster No.: 28

Migration pathways and the mechanisms of Japanese encephalitis virus into/from Okinawa, Japan



University of the Ryukyus

Mika SAITO, Masaru MIZUYAMA

[Objective]

Japanese encephalitis is caused by Japanese encephalitis virus (JEV) which belongs to mosquito-borne flavivirus. It poses a public health concern because of its high mortality rate, serious symptoms and sequelae in human, and expanding distribution areas. JEV cannot be easily eradicated, because the zoonotic transmission cycle. Therefore, risk assessments, including identifying the transmission pathways of JEV from surrounding countries and areas, are critical. To clarify the migration pathways and mechanisms of JEV Okinawa clusters, phylogenetic analysis was performed with Okinawa and domestic/foreign JEV strains. [Materials & Methods]

A phylogenetic tree was constructed with the sequence (1,500 nucleotides) of the E regions from 83 Okinawa and 366 domestic/foreign JEV strains isolated in different years. The strength of the relationship between clusters, including the Okinawa strains, and other regions was weighted with Bayes factors (BF) to predict the pathways on a map.

[Results]

Four Okinawa strains were mainly identified over time: Okinawa clusters OKN1 (G3), 2 (G3), 3 (G1), and 4 (G1). Relationships (BF>3) were substantiated between OKN1 and Osaka (BF = 32.7), between OKN2 and Osaka (BF = 21,802), Zhejiang province (China), Vietnam, and Korea, between OKN3 and Oita (BF = 5.7), and between OKN4 and Nagasaki (BF = 18,781). The tree shape and the isolation years demonstrated pathways from Okinawa to Osaka (OKN2) and from Nagasaki to Okinawa (OKN4). [Discussion]

In spite of the sampling biases, our analysis strongly suggested a northward pathway for OKN2 and a southward pathway for OKN4. In addition, the migration pathways predicted in the analysis overlapped with the East Asian-Australasian flyway of migratory birds. The migration pathways of the Okinawa clusters are discussed based on the seasonality of migration and the period of virus activity.

Keyword: Japanese encephalitis virus, phylogenetic analysis, migratory pathway

Poster No.: 29

Systematic review and meta-analysis: association between hepatitis B surface antigen levels and the risk of hepatocellular carcinoma in patients with chronic hepatitis B infection



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Background

The role of hepatitis B surface antigen (HBsAg) levels in predicting the risk of developing hepatocellular carcinoma (HCC) has remained unclear. The aim of this study was to obtain the most up-to-date estimated measure of the association between HBsAg levels and the development of HCC in patients.

Methods

We performed a systematic review by searching for relevant studies on PubMed, Scopus, ProQuest and the Cochrane Central Register of Controlled Trials from January 2002 to November 2017. We presented the effects of HBsAg levels at each cut-off value as the odds ratios (ORs) at 95% confidence interval (CI). We also investigated HCC and its potential risk factors including HBeAg, and HBV DNA. We registered our protocol with the International Prospective Register of Systematic Reviews (PROSPERO) with the registration number CRD42018081138.

Results

We selected 10 studies representing 12 541 cases. At the 100 IU/ml cut-off, the OR for HCC at the high HBsAg level versus the low level was 4.99 (95% CI, 3.01–8.29) with high inconsistency ($I^2=79\%$). At the 1,000 IU/ml threshold, the pooled OR for HCC at the high HBsAg versus the low level was 2.46 (95% CI, 2.15–2.83) with low variance. We also found correlations between the risk of HCC and male gender (OR=2.12), hepatitis B eantigen positivity (OR=2.99), or hepatitis B (HBV) viral load \geq 2000 IU/ml (OR=4.37).

Conclusion

Our study revealed that HBsAg levels \geq 100 IU/ml, and notably >1000 IU/ml, are associated with an increased risk of HCC development.

Keyword : Hepatitis B surface antigens, hepatocellular carcinoma, chronic hepatitis B infections, meta-analysis

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Poster No.: 30

A study of the serum cross reactivity to ZIKA virus among Indian febrile patients



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Dengue and ZIKA virus (ZIKV) have overall 56% of sequence homology. Studies indicate that exposure of one or more flaviviruses leads to the development of the cross-reactive immune response. Despite India having all four Dengue serotypes circulating, no ZIKV transmission has been reported. Therefore, it is a unique setting to study Dengue antibody response that are cross reactive to ZIKV in India.

In this study we analyzed children with acute febrile Dengue and asked- (a) Whether these patients have developed antibodies that can cross react to ZIKV? (b) Whether the cross reactive antibodies are induced in primary or secondary dengue infection? (c) Does this cross reactive antibody response is biased towards a particular Dengue serotype?

We observed that patients with primary Dengue infection characterized by only IgM antibodies, have no binding antibodies to ZIKV. Primary Dengue patients with IgM>IgG and secondary Dengue patients showed higher ZIKV binding antibodies. Our data showed that evolution of Dengue induced IgG response results in cross reactive binding antibodies to ZIKV at febrile phase. We observed association in the level of Dengue IgG to the ZIKA binding IgG. We had repeat bleed at convalescence for 57 of the 91 patients and observed that the level of these cross reactive antibodies rises at convalescence. Detection of dengue serotype specific ZIKV binding antibody response on the limited number of samples we had, revealed a bias towards DV1 in these Indian patients. These results will have significant impact on Dengue vaccine testing and evaluation that India is poised to implement in future.

Keyword: Dengue, Human immune response, ZIKA, antibody

Poster No.: 31

Risk Perception Regarding Rabies in Cattles in North-East Population, Thailand.



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A buffalo in a North-East province of Thailand died of unknown causes. When it died, livestock officials told the owner to bury it after they cut off the head, which was sent for lab tests to determine the cause of the death. However, the buffalo owner and neighbors were dissected the buffalo before burying it, then sold and shared the meat among villagers. Some villagers consumed the raw meat. Two day after, a lab test confirmed the buffalo had died from rabies. Moreover, there were three buffalos had died which villager also dissected and sold in this community and nearby. In addition, there were many of animals had tests positive to rabies virus. Is this mean, people in these communities at risk of rabies? How terrible, not just people at risk but also health care service has to pay amount of money for rabies jabs to contact and consume buffalo with rabies. The researchers went to field for in-dept interview and focus group discussion found that villager beliefs and perceives that these buffalos can eat. It's not dangerous, because it's animal in communities, relative's cattle, look nice to eat and it was sold in low-priced. This situation, related organizations need to concern about risk perception regarding rabies in cattle? In Thailand, more than 1,200 animal heads had positive to rabies and 16 humans had died because rabies, in 2018. Disseminating and delivery the right information of rabies, truly, timely and through appropriate channels may help people protect themselves from rabies.

Keyword: Risk perception, Rabies, Risk analysis, Risk Communication

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Poster No.: 32

A CASE REPORT: HAEMATOLOGICAL AND CYTO-HISTOPATHOLOGICAL FEATURES OF DOMESTIC CHICKEN THAT NATURALLY-INFECTED WITH VISCEROTROPIC VELOGENIC NEWCASTLE DISEASE VIRUS (VVDNV) IN TERBAN MARKET, YOGYAKARTA, INDONESIA



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Newcastle Disease (ND) is a minor zoonotic respiratory disease caused by Avian Paramyxovirus serotype-1 virus which is highly contagious and found worldwide that affects both wild and domestic avian. The aim was to report haematological and cytohistopathological features in domestic chicken that naturally-infected by Viscerotropic-Velogenic Newcastle Disease Virus (VVDNV). Methods used in this study including tracking historical record in the market, clinical signs inspection, blood sampling (routine haematology), necropsy and post-mortem examinations (lung and trachea were used for virus isolation). Based on tracking, chicken were brought from traditional farms in Kulonprogo district. Based on microbiological examination, the chicken has been confirmed to be infected by NDV that containing \geq 4HAU (confirmed positive hemagglutination inhibition specified NDV-antiserum). The clinical signs from the chicken were bilateral fascial oedema with serous exudate (infraorbital sinus), plaque in the oral cavity, anorexia, pale pial and combs, also presented white and green diarrhea. Haematological findings, the chicken had normochromic macrocytic anemia, reticulocytosis, leukocytosis, left shift heterophilia, monocytosis, hypoproteinemia, hyperfibrinogenemia, thrombocytocytosis. Cytopathological features, the exudates from infraorbital sinus and trachea were examined which resulted with predominantly lymphocytes, macrophages, nondegenerative heterophils as well as degenerative heterophils. In histopathological features, chicken had necrotic haemorrhages alongside digestive organs including proventriculus, caecum, intestine; followed by mucosal epithelial hyperplasia, submucous oedema in trachea; and white pulp depletion and large numbers of hemosiderin pigments in the spleenic tissue. In conclusion, the chicken was infected by VVDNV which was severely damaging the digestive organs and mildly the respiratory organs.

Keyword: Domestic chicken, Newcastle disease virus, viscerotropic, haematology, cytohistopathology

Poster No.: 33

Seroprevalence Of Humanimmunodeficiency Virus , Hepatitis B Virus and Hepatitis C Virus infections in Wasted-Blood Sample



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DSMRC1

Nowdays Human immuno Deficiency virus (HIV), Hepatitis B (HBV), Hepatitis C (HCV) infection are major public health problems in developing country causing coonsiderable morbidity and mortality. Many risk behaviour and routes of transmission for these infections are identical. In Myanmar there has been no study for seroprevalence low risk population such as patient with non communical diseases. in this study Overall seroprevalence rate among 1000 waste-blood samples was HIV (2.3%), HBV (5.0%), HCV (1.1%), HIV -HBV coinfection (0.3%), HIV -HCV co-infection (0.1%), and HBV-HCV co-Infection (0.1%), there was no HIV-HBV-HCV c0-infections. HBV was the highest and HCV was the lowest sreoprevalence in these three infectious diseases. While HIV-HBV co-infection was the highest seroprevalence co-infection. In Murad et al. study, seroprevalence of HBV and HCV among pregnaant women were 10.8% and 8.5 % respectively but there was no HBV-HCV co-infection. In Sethi et al. study, seroprevalence among 7884 blood donors was HIV 90.19%), HBV (0.63%), HCV (0.20%), HIV-HBV co-infection (0.01%), and HIV-HCV co-infection (0.01%). In comparison of present study and above studies, there were some differeces which may be due to difference study populations sample selection snd nationality. This study evaluated HIV, HBV, HCV, HIV-HBV, HIV-HCV and HBV-HCV co-infection in waste-blood samples for tested for non communicable diseases. Therefore, everybody, especially health care workers should pay more attention on handling of blood samples or body fluids of patients not only with communicable diseses but also with non-communicable diseases.

Keyword : HIV = Human immunodeficiency Virus; HBV = Hepatitis B Virus; HCV = Hepatitis C Virus

Poster No.: 34

Profiling the upper respiratory tract microbiota of patients living with HIV, TB and HIV/TB from Myanmar



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HIV and TB are the world's leading infectious killers due to opportunistic bacterial infections which occur more frequently in HIV and TB patients. Using next-generation sequencing technology, the author conducted a preliminary study to profile the upper respiratory tract microbiota. This study was a crosssectional descriptive study on naso- and oropharyngeal swabs from 36 participants. The subjects were properly explained and consent was taken. Nasopharyngeal swab and oropharyngeal swab specimens were collected using flexible swab strips with transport medium. Bacterial microbiome DNAs were extracted by using DNA microbiome extraction Kit and then sequenced by nextgeneration 16s rRNA amplicon sequencing. Mean age was 37±7.49 years. There were 20 (55.56%) male and 16 (44.44%) female patients in this study. We found that the upper respiratory tract bacterial communities in HIV treatmentnaive patients and HIV/TB patients were dominated by Streptococcaceae, whereas Staphylococceaceae was dominant in HIV patients on treatment. Due to the limited resolution of the 16s rRNA gene among closely related species, the VITEK 2 system was employed for the identification of them as Streptococcus pneumoniae and Staphylococcus aureus. The abundance of Veillonellaceae was observed in TB patients and HIV treatment-naive patients. Considering results, this study lays the vivid foundations for basic information warranting further studies to gain insight into the prevention and treatment of bacterial infections in the respiratory tract associated with HIV, TB and HIV/TB including the use of an innovative approach such as probiotics.

Keyword : Microbiome, Bacterial infections, Next-generation sequencing, probiotics

Poster No.: 35

CO-INFECTION OF HUMAN T LYMPHOTROPIC VIRUS TYPE 1 AND 2 IN HIV INFECTED PATIENTS



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Human T Lymphotrophic viruses (HTLV) belong to Retroviridae family, genus Deltaretrovirus are transmitted sexually and vertically, firstly by breastfeeding, as well as parenterally. Prevalence of HTLV infection ranging from 0.5 to 20% in population is defined as endemic and less than 0.1% is non-endemic. Dual Human immunodeficiency virus (HIV) and HTLV infection is a frequently occur in HTLV endemic countries. This dual infection of HIV and HTLV-1 may accelerate progression to AIDS and other complications of HIV infection and increase risk of developing adult T cell leukaemia/lymphoma (ATL) and HTLV-1 associated myelopathy/tropical spastic paraparesis (HAM/TSP). Although Antiretroviral therapy (ART) is recommended for all HIV-infected persons regardless of the CD4 count, ART treatment is considered with high priority conditions including HIV/HTLV co-infection according to panel on ART guidelines for adult and adolescent. However, HTLV infection cannot be controlled by ART. This study was to explore HTLV 1/2 co-infection in 94 HIV infected patients where 39 (41.5%) were male and 55 (58.5%) were female. Most patients were receiving ART within 4 months after the diagnosis of HIV infection. HTLV testing was performed by Maglumi 800 Imunology Analyzer and HTLV-1/2 serostatus of all participants was non-reactive (less than 1.0 index/ml). Since testing for HTLV is not routinely performed in outpatient of HIV clinics, we are aware for this coinfection. HTLV infection carriers remain asymptomatic throughout life, so that we recommend screening assays for HTLV infection in blood donation and organ transplantation cases.

Keyword : Human T Lymphotrophic Virus, Human Immunodeficiency Virus, co-infection, CD4 count

Poster No.: 36

Tuberculosis Outbreak Investigation And Prevalence In The Home Destitute, Phitsanulok Province.



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On November 30th, 2017, ODPC2 staffs were informed 5 cases of tuberculosis (TB) patients in the shelter of home destitute in Wang Thong district. The investigation team of tuberculosis was recruited for planning. The purposes of this study were to confirm and monitor TB outbreak, to assess the severity of situation and to find close contacts and control the spread of TB. This is a descriptive and analytic study, using the retrospective data, medical records and prevalence statistics. Relevant data collection was including present and past illness history, interviewing with close contacts. Screening for TB was performed by verbal screening, chest radiography and sputum examination. Results were found that TB prevalence of the most recent screening in 2014 was 0.004 %. In November 2017, there were 479 people in home destitute. Five patients with confirmed/suspected TB were detected. Two confirmed TB cases died in November 2017. After active case finding, 422 people were performed chest radiography, 77 of them (16.1%) were diagnosed of TB suspected case. Sputum collection for X-pert diagnosis was done in 71 people and 9 samples were confirmed of smears positive pulmonary TB. At the end of the study, the prevalence of pulmonary TB was 1.89%, significantly higher than the past 3 years. We found a problem with the ventilation system in bedrooms which increased risk of TB spreading. There is a need for TB screening every year and should have a TB screening project plan with continuous support of budget.

Keyword: tuberculosis, TB, outbreak investigation

Poster No.: 37

The Implementation of National Operation Center Tuberculosis (NOCTB) Policy for Ending TB in Thailand: Lesson learned from Health Region10th, Ubon Ratcathani



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Thailand is one of 14 of TB High Burden Country Lists in Global. The burden is result from TB. TB with HIV, and MDRTB. This situation was stimulated the department of Disease Control (DDC), to formulate NOCTB policy and implement to 77 provinces on late 2017. This study was to describe the implementation of NOCTB in Health Region 10th Ubon Ratchathani. The policy was implement in 5 provinces by the commitment of the director of Health Region 10th and helath networks. Two major results were: (1) The provincial health office was established the NOCTB in order to command the NOCTB policy, comprehensive care service to TB patient, and risk communication of TB and guideline of TB working by the cooperation of various health networks in order to ending TB. And (2) three appropriate innovations were extracted from best practice hospitals in Health Region 10th to fight with TB. Firstly, the 4S model was helping for searching and screening of TB new case. Secondly and thirdly were the 3Cs model and 2-2-2 model that supporting system approach and TB case management to enhance the successful outcome treatment of TB. Three innovations, 4s, 2-2-2, and 3Cs model, were contributed to the 33 community hospitals in 5 provinces where TB success rate was lower than 85%. It was function as the innovation tools of TB care team to fight with TB. This study was confirmed that NOCTB policy was implemented by the cooperation of various health networks and supported by appropriately innovation.

Keyword: TB, NOCTB, Ending TB

Poster No.: 38

Varicocele due to tuberculosis: the importance of differential diagnosis in an endemic area



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Introduction

Extrapulmonary tuberculosis accounts for more than 20% of cases involving genitourinary system in about 6%. Tuberculosis of the spermatic cord sparing the testis and the epididymis is very rare.

Case report

A 45-year-old man presented with an increasing painless swelling in the left scrotum for 4 months without other associated symptoms. On examination, there was an approximately 3×2.5 cm hard lump in the left side of the scrotum in the upper pole of the testis with small hydrocele. Laboratory data were normal including AFP, β-hCG and LDH. USG of the scrotum showed left varicocele with bilateral minimal hydrocele. CECT abdomen and pelvis showed bilateral hydrocele with normal testes, left varicocele and bilateral inquinal lymphadenopathy. Surgery was planned for excision of the lump ± orchidectomy with inguinal lymph node biopsy via high inguinal approach. At surgery, an approximately 4x2 cm left spermatic cord hard tumour engulfing the vessels and the vas deferens just proximal to the testis was found associated with thrombosis of the testicular vein, secondary varicocele, minimal hydrocele and multiple left inquinal lymph nodes. Excisional biopsy of the left spermatic cord lump and inquinal lymph nodes was done. Histopathological report showed reactive lymphadenitis from the inquinal lymph nodes and necrotizing granulomatous lesion suggesting tuberculosis from left spermatic cord lump.

Conclusion

Though very rare, tuberculosis should be considered as a differential diagnosis in case of spermatic cord or testicular tumour in tuberculosis endemic countries so that unnecessary orchidectomy can be prevented.

Keyword : Tuberculosis, spermatic cord, varicocele, hydrocele, testis

Poster No.: 39

Unfolding a mystery: Erythema Induratum as a rare epiphenomenon to tubercular appendicitis



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Tuberculosis is endemic in several countries, including the Philippines. Erythema Induratum of Bazin (EIB) is classified as a tuberculid, and is characterized by a chronic nodular eruption usually on the legs of women. EIB, along with the other tuberculids pose a diagnostic challenge because the organisms are not found in smears or cultures taken from the lesion. Usually a focus of infection is found elsewhere and is difficult to identify. We report a case of tuberculid EIB with active tuberculosis of the appendix which to the best of our knowledge, has not been reported.

A 40-year-old female was referred because of erythematous nodules on both legs for more than 5 years. Physical examination revealed tender, erythematous nodules, hyperpigmented patches and scars on both legs. She was previously diagnosed as a case of prurigo nodularis and erythema nodosum. A skin biopsy was performed and revealed a lobular type of panniculitis with focal granulomas and vasculitis, consistent with Erythema induratum. Mantoux test demonstrated an exaggerated reaction at 20 mm. One day after, she experienced right lower quadrant pain, underwent appendectomy which showed tubercular appendicitis on biopsy.

Anti-tubercular therapy for 6 months was given. There was complete resolution of the nodules, leaving atrophic and hyperpigmented scars. Residual hyperpigmentation was evident on the purified protein derivative (PPD) site after 6 months. Repeat abdominal CT scan with contrast did not show calcifications in the previous area of the appendix, which ruled out persistent TB infection.

This report highlights the clinical course, cutaneous manifestations, laboratory abnormalities and histopathological features of EIB, which will heighten awareness among primary care workers of this tuberculid's key features.

Keyword: Tuberculosis, Erythema Induratum of Bazin, Tuberculid

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Poster No.: 40

Contamination of *Burkholderia pseudomallei* in environment near patient's residence in Buriram, northeast Thailand



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Melioidosis is a fatal infectious disease caused by Gram-negative bacterium Burkholderia pseudomallei. The routes of B. pseudomallei infection are the inoculation during exposure to soil or environmental water, ingestion by eating contaminated food or drinking untreated water, and inhalation by outdoor exposure to bacterial aerosol. Tracking individual cases to the environmental sources where patients are suspected to be exposed in endemic area is needed for a better understanding of B. pseudomallei infection. We investigated the presence and quantity of B. pseudomallei from environmental samples near a patient's residence and where patient was suspected to be exposed. A 53 years old, Thai male melioidosis patient admitted to Buriram Hospital located in Buriram province, northeast Thailand was enrolled to the present study in 2018. B. pseudomallei was isolated from primary culture of his blood and pus samples. Environmental samples including 18 soil, 15 rhizosphere and 9 water samples were collected from environment near patient's residence and where patient was suspected to be exposed. Quantitative culture on Ashdown agar was performed and B. pseudomallei isolates were identified using latex agglutination test and MALDI-TOF Mass Spectrometry. B. pseudomallei were detected in 23.8 % (10/42) of all samples in which 7 positive samples were distributed at where patient was suspected to be exposed and 3 positive water samples collected from near patient's house. Overall, 5.6 % (1/18) was found in soil samples, 55.6 % (5/9) in water samples, and 26.7 % (4/15) in rhizosphere samples. Of 5 positive water samples, 2 samples were collected from a pond and 3 samples were collected from a rain jar, a pump well and a dug well near patient's house. The mean and standard deviation of B. pseudomallei from water, rhizosphere and soil samples were 5.3 ± 4.8 CFU/ml, 80 ± 42.4 CFU/g and 125 CFU/g, respectively. Water sample was significantly associated with the detection of B. pseudomallei compared to soil and rhizosphere samples (P < 0.05). Clinical and environmental isolates will be then genotyped to identify source of infection. These data will provide insights into the epidemiology of the B. pseudomallei in Thailand.

Keyword: Melioidosis, *Burkholderia pseudomallei*, sources of melioidosis, environment near patient's residence

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Poster No.: 41

Study of *Burkholderia pseudomallei* pathogenesis in human neuronal cell



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Melioidosis is an infectious disease caused by B. pseudomallei, the gramnegative facultative intracellular bacillus. This disease is endemic in northern Australia and southeast Asia including Thailand. For clinical symptoms of melioidosis, the most common presentation is pneumonia. Meanwhile, melioidosis cases can present other clinical manifestations such as central nervous system (CNS) or neurological melioidosis. Although the neurological melioidosis is rare condition, it has often been criticizes as high mortality rate of melioidosis cases. At present, there are increasing reports of neurological melioidosis; but mechanical understanding on how B. pseudomallei affect the nervous system is still poorly understood. In this study, we investigated the pathogenesis of B. pseudomallei in human neuronal cells focusing on bacterial ability in invasion and intracellular replication. The result showed that B. pseudomallei has the ability of invasion and intracellular replication in human neuronal cells (SH-SY5Y cell line). Our finding provides a basic knowledge for understanding on the neurological melioidosis. However, further investigations of B. pseudomallei pathogenic mechanism of neuronal cell are still needed for discovery the strategy to protect or decrease the damage of neuronal cells in neurological melioidosis patients.

Keyword: neurological melioidosis, SH-SY5Y cell, invasion, MNGC formation

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Poster No.: 42

FLOOD-RELATED LEPTOSPIROSIS OUTBREAK, UPPER SOUTHERN THAILAND, 2017



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Background: Upper Sothern Thailand experienced widespread floods in January 4th, 2017. One week later, a number of leptospirosis increased sharply with 5 fatal cases were reported. We started outbreak investigations with aims to confirm diagnosis and outbreak, recommend control and prevention measures.

Materials/methods: Active case finding, a case was defined as a person who had fever plus myalgia and exposed to flood water and mud during January 6th – February 12th, 2017. Behavioral data were collected and lab investigations included PCR, MAT and IFA. Environmental survey together with collection of samples from domestic animals, rodents, soils and water for PCR and culture.

Results: A total of 151 and confirmed outbreak, 5 died. Of those, 30.46% were lab-confirmed. Median age was 40 years (Range 7, 80), 79.49% were male. Number of cases peak at second week after flooding. Clinical manifestations was fever (98.67%), myalgia (81.25%) and headache (78.13%). Risk behaviors included contacted with flood water and mud (96.88%), unprotective boots (84.37%) and contacted with flood water over 6 hours (81.25%). Serovar Shermani is most common in both patients and domestic animals. Leptospira spp. was also detected in 6 soil samples (100%).

Conclusions: A lab-confirmed leptospirosis outbreak occurred in area following the severe floods. After aggressive surveillance and control implementation, the outbreak was terminated on February 12th 2017, when cases had decrease to baseline level and no fatal case reported. Therefore, interventions should be implemented in the affected farm to prevent and control the spread of Leptospira to animals, humans and environment.

Keyword: Leptospirosis, Flooding, Upper Southern Thailand

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Poster No.: 43

Detection of Carbapenem resistant genes among multidrug-resistant *Klebsiella* pneumoniae from respiratory specimens in Prapokklao Hospital, Chanthaburi province, Thailand.



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Carbapenem resistant Klebsiella pneumoniae (CRKP) are spreading worldwide and growing problem causing severe and difficult to treat hospital epidemics associated with high mortality rates. The most important mechanism of carbapenem resistance in K. pneumoniae is the production of carbapenemases by KPC, VIM, NDM, IMP and OXA-48 types. This study investigated the antibiotic resistance pattern and the prevalence of Carbapenem resistant genes in K. pneumoniae producing CRE in respiratory tract infections patient. One hundred and twelve K. pneumoniae isolates from Respiratory tract specimens in the Prapokklao Hospital, Chanthaburi province during 2016-2018. The isolated bacteria were evaluated Disc diffusion antimicrobials susceptibility test, Carbapenem MIC test Strip (Liofilchem®) and molecular characterization of beta-lactamase (bla) genes, including carbapenemase genes were detected by PCR. The results showed K. pneumoniae were highly of Multi-drugs resistant (MDR). There were resistant to 3rd Cephalosporins, Piperacillin-tazobactam, Ampicillin-sulbactam, Amoxicillin-clavulanate, Ciprofloxacin, Gentamicin and Trimethoprim-sulframethoxazole. The Carbapenem resistant rate was 92% for Ertapenem, 80% for Meropenem and 80% were resistant both Ertapenem and Meropenem. For bla genes characterization, there were 100% positive of CRKP gene. The majority of the CRKP were positive for the bla_{NDM} (84%) and bla_{IMP} (81%), and lower positive for the bla_{VIM} (1.8%) and bla_{KPC} (0.9%). These results suggest that K. pneumoniae isolated from respiratory samples were high resistant to carbapenem antibiotic and produce enzyme carbapenemases, mostly bla_{NDM} and bla_{IMP} . It is urgent to establish surveillance, antibiotic stewardship program and infection control measures to prevent further spread of Carbapenem resistant Klebsiella pneumoniae (CRKP).

Keyword : Carbapenem resistant *Klebsiella pneumoniae,* Antimicrobial resistant, Carbapenemase, betalactamase (*bla*) genes.

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Poster No.: 44

Cycling of brucellosis at wildlife-livestock and human interface in Nepal



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Brucellosis is a zoonosis that manifests its most significant global burden on vulnerable pastoralist communities. In Nepal, annual outbreaks are associated with severe impact on human and animal health and the livestock economy. We studied the geographic suitability of Brucellosis across Nepal and its associated environmental features using a biogeographical application of machine learning. Both biotic and abiotic features were found to contribute to risk across multiple scales of influence, but the wildlife-livestock interface appears to be the dominant feature in delineating its suitability. To a lesser but non-trivial extent, the loss of forest and environment appears to influence brucellosis risk. These findings show that the wildlife-livestock interface plays an important role in the cycling of brucellosis in Nepal, and that anthropogenic ecotones, or zones of transition, may be particularly relevant spaces for the emergence of this interface and subsequent anthrax transmission. Prevention efforts targeted toward blocking the wildlife-livestock interface, particularly within anthropogenic ecotones, may yield successes in reducing ongoing transmission between animal hosts and subsequent zoonotic transmission to humans.

Keyword : Brucellosis, wildlife, livestock, humans, environment

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Poster No.: 45

Childhood leprosy in post elimination era; A difficult challenge to face in Nepal



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Leprosy is a chronic infectious, potentially disabling social disease with stigma. The most vulnerable group is children as they reflect transmission and the efficiency of control programs.

Objectives:

To study the epidemiological and clinical trends of childhood cases of leprosy **Methods**: A retrospective study was done among childhood leprosy all over Nepal from leprosy registry during 2010-2016.

Results: A total of 19206 new cases were registered, of whom 1177 (6.12%) were children. National prevalence is below the leprosy elimination cut-off, but trend is gradually increasing in recently(from 0.77 to 0.82/10000), reflecting the active transmission. The mean age of the children was 10.5 (SD 3.35 years) with a male preponderance (3.9:1). History of close contact with leprosy was present in 20 %. The average slit skin smear positivity was in 27% patients. The multi-bacillary leprosy among child comprised of 38% and pauci-bacillary leprosy comprised 62% where as among total new cases MB cases were significantly higher (p < 0.005). Neuritis occurred in 21% and grade II disability at the time of diagnosis was noted in 3.5% of total patients including children. Lepra reactions treated in referral centre were observed with ratio of 2.75:1 between Type 1 and Type 2. There were no cases of relapse among children.

Conclusions: Increasing childhood leprosy with high multibacillary status continue to present in alarming numbers suggests possible gaps in the leprosy elimination programs. We focus on importance of continuous efforts for early case detection, treatment and follow-up of contacts of leprosy cases.

Keyword: Childhood Leprosy, Nepal, Leprosy Elimination

Poster No.: 46

Trend of Elimination of Leprosy from Bangladesh: Learning from 1998 to Current Era

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Background:

WHO declared elimination of leprosy from Bangladesh in 1998. Statistics up to 2015 sates the prevalence rate varied between 0.86- 0.21/10,000. The slow reduction of prevalence rate creates curiosity to find the underlying cause where a recent study conducted by Lepra* detected 3140 new cases in only 10 districts in 2017 with a 11% of severely disabled people. It's alarming, as these 11% people remain undiagnosed in previous year. This study aims to find out the gaps in case detection and way forward from the existing literature in the context of Bangladesh.

This is a literature review following systematic review approach. Both journal articles and grey materials relevant to leprosy elimination program was reviewed to explore the gaps in case detection and how to address that. A matrix was prepared to extract data from the literature and framework analysis was done to draw the result.

Result:

The study findings revealed that, 58% cases were detected passively or through referral system in 2013 and it doesn't differ much in previous years. Declared elimination resulted cut of budget severely for training and resource allocation resulting 42% of the health staff didn't know about MDT.

- Passive mode of case detection causing more undetected hidden cases may result sudden outbreak. Active case detection strategies should be adopted according to the Global Leprosy Strategy. Further studies recommended to find country specific strategies.
- Poor knowledge of cardinal signs and mode of transmission is another alarming sign for the country. Both hidden and detected cases causing new cases and more cases remain undetected. Further campaign and educational program should be included and studied frequently.
- Disability prevention and rehabilitation, reduction of social stigma and creating employment opportunity should be bundled in the treatment package to reduce vulnerability of the affected people to fight leprosy holistically.

Conclusion:

It's evident that there are several gaps in the leprosy elimination program and should be identified and acknowledged sooner to avoid further outbreak.

*A UK-based international charity working to beat leprosy

Keyword: Leprosy, MDT

Poster No.: 47

The study of *Orientia tsutsugamushi* strain in chigger mite and liver/spleen from trapping rat in northern part by used Polymerase chain reaction



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The objective of this survey research was to find out the *Orientia tsutsugamushi* strain in chiqger mite and liver/spleen of reservoir host by used Polymerase chain reaction technique; PCR in the corny areas of scrub typhus, in the three provinces of northern Thailand including Tak province Chainhg mai province and Chaing rai province. The sample of serum that collected from all captured rats used to detect an immunity level by using Immunofluorescence antibody: IFA while chigger mites and sample of liver and spleen of captured reservoir host were detected for Orientia tsutsugamushi strain by using the Polymerase chain reaction; PCR technique and identification species the chigger mites collected from the reservoir hosts. The result shown that percent trap success was 8.6 i.e. 60 trap success of 694 total animals traps. The rodents capture are 98.3 % (59 rats in total) and 1.7 of Tupaia glis (1 rodent). The immunity against Orientia tsutsugamushi from IFA test the infected rate were 11.86% (positive 7 sample). By using PCR technique, we detected *Orientia tsutsugamushi* strain in liver and spleen only one sample (1.67%) from Rattus tanezumi code RCR1 in Chaing rai province. By using Blast technique comparing between sequenced DNA lines and nucleotide in gen-bank, we found that 99% of *Orientia tsutsugamushi* strain similar as FPW 2049 strain in the patient in Tak province with 94% similar as standard strain Gilliam. The result of this research pointed out that the reservoir host could be found in the corny areas of scrub typhus because there is no disease control in those area. Most of public health officers focused on patient treatment. However for decreasing the rate of patient with scrub typhus, they should research and survey on the reservoir host and the vector and implementing disease control along with developing patient treatment.

Keyword: Orientia tsutsugamushi strains, scrub typhus chiggers' mite, liver/spleen, PCR

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Poster No.: 48

Factors Associated with Serological Response to Treatment in Syphilis



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Background: Non-treponemal titers are used to monitor serological response after syphilis treatment. This study aims to determine factors associated with serological response to treatment in syphilis.

Method: This is a descriptive study of syphilis patients who visited Bangrak STIs Center between 1 January 2007 and 31 December 2016. Syphilis patients with VDRL titer tested at baseline and at least one VDRL follow-up titer were included in the study. Univariate analysis was conducted to determine factors associated with serological cure.

Results: Out of 497 syphilis patients, approximately half of the patients (51.3%) presented to the clinic with secondary syphilis, followed by late latent and latent syphilis with unknown duration (31%). HIV co-infection with syphilis were found in 42.3% of the patients. Regarding the serological outcome, 62.1% had serological cure, 2.2% non-response, 4.6% treatment failure or reinfection, 9.9% serofast status and 21.2% were undetermined due to loss follow-up. HIV co-infection and syphilis stage were significantly associated with different serological outcomes (p=0.017 and p<0.001 respectively). Diagnosis with early syphilis and high baseline titer (\geq 1:32) were also associated with serological cure (RR 1.25, 95% CI 1.07-1.46 and RR 1.14, 95% CI 1.03-1.26 respectively). Patients with no sexual risks were more likely to achieve serological cure than those with 2 or more risks (RR 3.59, 95% CI 1.64-7.86).

Conclusion: HIV co-infection and syphilis stages affect the serological response after syphilis treatment. Patients with low sexual risks, early syphilis and high baseline titer ($\geq 1:32$) were associated with serological cure.

Keyword: syphilis, VDRL, serological response, treatment outcome

Poster No.: 49

UNPRECEDENTED CASE STUDY: CYTO-HAEMATOPATHOLOGICAL FINDINGS FROM UNEXPECTED COMPLEX INFECTIONS BY CHLAMYDIA SP, CYTAUXZOON FELIS AND MYCOPLASMA HEMOFELIS IN INDONESIAN MIXED-BREED CAT



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The common clinical symptoms from chlamydial infection in cat from this study are conjunctivitis, rhinitis, and mild form of pneumonia. These bacteria have a unique developmental cycle involving extracellular form (elementary bodies) and intracellular (reticulate bodies). Elementary bodies initiate infection by attaching to receptors on the surface of host cells. Chlamydophila felis has been identified as an important cause of conjunctivitis in cats and occasionally in humans (considered to be zoonotic pathogen). This study was aimed to confirm clinical and laboratory finding using cytological and hematological evaluation of cat that chronically and persistently infected with Chlamydia. The animal that studied was shown main clinical symptoms such as bilateral conjunctivitis with ocular discharge, rhinitis and sneezing. Conjungtival swab, nasal and tracheal discharge were used as cytological samples to detect chlamydial inclusion bodies (both elementary and reticulate) with Giemsa-stained smears. Blood sample were used for fine blood smear examination and complete blood count routine hematology. Cytological examination were shown both elementary and reticulated bodies within the epithelial cells from conjungtival swab and tracheal discharge, therefore from nasal discharge were only shown degenerative neutrophils with proteinaceous materials. Blood smear examination were found hemotropic mycoplasma (suspected as Mycoplasma hemofelis) organism on the surface of erythrocytes. Another blood parasite that were found Cytauxzoon felis with signet ring form in the erythrocytes. Routine hematological findings were shown several important changes such as anemia macrocytic hypochromic, polychromatophilia, mild leucocytosis, hyperproteinemia, hyperfibrinogenemia, trombocytopenia, neutrophilia left shift,basophilia, eosinophilia and lymphocytosis.

Keyword : Cat, cyto-haematopathology, chlamydial infection, cytauxzoon felis, hemotropic mycoplasma

Poster No.: 50

Cryptococcal Meningitis In People Living With Human Immunodeficiency Virus In Nepal



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Background: Cryptococcal meningitis is an opportunistic fungal infection that occurs primarily among Human Immunodeficiency Virus (HIV) infected persons. The objective of this study is to diagnose cryptococcal meningitis in people living with HIV (PLHIV) and to compare available laboratory techniques in confirmation of cryptococcal infection.

Methods: This cross-sectional study was conducted from Jan 2017 to July 2018 among 72 PLHIV with clinically suspected meningitis. Cerebrospinal fluid (CSF) specimens collected by the attending physicians were processed with India ink staining, cryptococcal antigen lateral flow immunoassay and fungal culture at National Public Health Laboratory, Nepal following standard protocols. The cryptococcal isolates were identified observing colony characteristics, India ink staining, phenol-oxidase production and urea hydrolysis. The data were analyzed using IBM SPSS-21 software and a p-value of <0.05 was considered significant.

Results: The laboratory confirmed cryptococcal meningitis cases were between 24 and 69 years of age (median age 39 years) with 87.5%(12/14) of cases being male. *Cryptococcus* was detected in 19.44% (14/72) by cryptococcal antigen lateral flow immunoassay, 16.66% (12/72) by india ink staining and 8.33%(6/72) by culture. Cryptococcal antigen detection was found to be more sensitive compared to India ink staining and CSF culture.

Conclusions: High percentage of cryptococcal meningitis among PLHIV warrants early microbiological diagnosis for better management of cases. Cryptococcal antigen detection by immunoassay should be the priority test for laboratory diagnosis of cryptoccal meningitis in PLHIV. Alternatively, very simple and economic India ink staining of CSF specimens could be used in resource limited settings like Nepal.

Keyword: Cryptococcal meningitis, Human Immunodeficiency Virus, culture, India ink staining, cryptococcal antigen

Poster No.: 51

Candida parapsilosis isolated from environment and the important virulence factors



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Candida parapsilosis, although, is a human commensal of epithelial and mucosal tissues. This species is also frequently isolated from environments. C. parapsilosis is notable for the ability to form biofilms on medical devices. Therefore, it is frequently associated with nosocomial outbreaks. In addition, ability of *C. parapsilosis* to produce secrete proteinase and phospholipase can causes more severe infection. The present study aimed to determine biofilm formation using crystal violet staining and hydrolytic enzyme production using spot assay on relevant agar medium of C. parapsilosis isolated from environment. In total, 8 of 33 isolates (24.24%) obtained from environment were C. parapsilosis. Biofilm formation of the isolated C. parapsilosis was variable. All of the isolates revealed the higher biofilm formation at room temperature (30°C) compared to 37°C. All C. parapsilosis isolates showed moderate to high activity of proteinase but no activity of phospholipase. In contrast to biofilm formation, proteinase production of the isolates were increased at 37°C. In conclusion, temperature is one important factor affecting biofilm formation and proteinase production. The formation of the biofilm is beneficial for the isolates to live in the hostile environment. However, production of proteinase is possibly more important for *C. parapsilosis* to cause infection in human.

Keyword : Candida parapsilosis, Biofilm formation, Proteinase, Phospholipase, Virulence factor

Poster No.: 52

A 54 Year Old Female with Malarial Myocarditis: First Case Report from Indonesia



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Myocarditis is inflammation of myocardium and broad range of etiologies such as infectious, autoimmune, hypersensitivity; toxins, systemic diseases and vasculitis. Malaria is one of the commonest parasitic diseases in the tropics since ages including Various cardiac complications of malaria include pericardial effusion, bundle branch block, cardiomyopathy and myocarditis. Myocarditis is extremely rare complication of *P. falciparum* malaria. In the similar context we report a case of Plasmodium vivax induced myocarditis in 54 year old female presented with shortness of breath, shock condition suspected cardiogenic shock. Patient had fever since 10 days before examination, at that time she was admitted at other private hospital. The fever accompanied with shivering and sweating. Patient also complained with athralgia in all over her body, and diarrhea only in the first few days. History of travelling to endemic area in the last few month was denied. On examination, the blood pressure was 90/50 mmHg with Norepinefrin and Dobutamin. Rhonki in right side of the lung. On workup there is leucocytosis, Echocardiography showed LV concentric hypertrophy and Diastolic function. Anti salmonella Thyphi IgM was positive +6 therefore the patient was treated with empirical antibiotic for thyphoid besides standard therapy for cardiogenic abnormalities. In the last two days of hospitalization patient was checked for malaria and ICT showed PAN-pLDH positive, otherwise Pf HRP-2 and Pvax PLDH negative. Interestingly Nest-PCR for Malaria revealed P. vivax. Unfortunately before treating with standard malarial theraphy the patient died due to respiratory failure and acute lung oedema.

Keyword: myocarditis, malaria, *P. vivax*

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Poster No.: 53

Mixed Infection of *Plasmodium falciparum* and *Plasmodium vivax* with severe malaria presentation at eliminated region Indonesia



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Mixed infection of *Plasmodium falciparum* and *Plasmodium vivax* is common in endemic area of Indonesia. This kind of infection tends to decrease the severity of disease. Here, we report three patients who suffered from severe malaria infection. after overnight camping at Teluk Asmara Beach, southern part of Malang District, East Java Province, Indonesia. The first two patients were referred to dr. Saiful Anwar General Hospital Malang. The first was a 13-year-old female with a clinical diagnosis of distributive shock and obesity. While the second was an 18-year-old female, who suffered from acute kidney injury and decrease of consciousness. The last patient, 18-year-old male, was referred to Karsa Husada Hospital Batu with suspected Dengue Hemorrhagic Fever. All patients exhibited thrombocytopenia, anemia, icteric, and were diagnosed as severe malaria due to mixed infections of P. falciparum and P. vivax by rapid test. Examination on blood smear revealed that only the second patient suffered from mixed infection, others were single infection of P. falciparum and this observation similar to nest PCR result. Real-time PCR confirmed strong expression of *P. falciparum* on all patients instead there was an unspecific target for P.vivax. All patients were then treated using WHO standard therapy. The second patient was re-admitted one month later due to a recrudescence with severe falciparum malaria and recovered after combination of oral quinine and doxycycline therapy. This report encourages us to be aware of mixed malarial infections and drug resistance incidences especially in eliminated region.

Keyword: severe malaria, triple mixed malarial infections, anti-malarial drug resistance

Poster No.: 54

Bacterially expressed *Plasmodium falciparum* EBA-140 and its immunoreactivity as a malaria vaccine candidate antigen



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Causing half a million deaths each year, malaria due to Plasmodium falciparum remains one of the most life-threatening tropical diseases. P. falciparum antigens involved in erythrocyte recognition and invasion during the merozoite stage are likely targets of protective immune responses. Erythrocyte-binding antigen 140 (EBA-140), a member of the Pf erythrocyte binding antigen (EBA) family, is one of the prospective candidates for malaria vaccine development. Notably, natural antibody responses against the EBA-140 ligand have been found in individuals in malaria-endemic areas. In the study, we selected EBA-140 from the genes involved in malaria by P. falciparum strain FCH/4 using the genomic database PlasmoDB and synthesized a codon-optimized full-length EBA-140. This 3284bp gene was cloned into peT30-a(+) vector with a 6xHis tag. After transformation in BL21(DE3) E. coli cells and pilot protein expression, the recombinant EBA-140 was purified using the Ni-NTA agarose column. Purified protein fractions at about 120kDa in size were eluted out at 250mM imidazole. To further confirm the identity of the concentrated elution fraction, Western blot was used to determine its specificity to antibodies in the malaria-infected serum samples. The purified recombinant EBA-140 was tested against both malarianegative and malaria-infected serum samples where the measured immunoreactive properties proved that the recombinant EBA-140 may be considered for inclusion in some multicomponent blood-stage vaccines. As there is no preventive vaccine available for malaria yet, studies of immunoreactivity of Pf EBA ligands such as EBA-140 are of great importance.

Keyword : Malaria, EBA-140, vaccine development, blood-stage malaria, protein purification

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Poster No.: 55

Prevalence of Plasmodium falciparum piperaquine resistance markers in Northeastern Thailand, 2013-2015



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Plasmodium falciparum resistance to piperaguine (PPQ) emerged rapidly in northern Cambodia, and as Thailand has used dihydroartemisinin-PPQ (DHA-PPQ) as the first-line malaria treatment since 2015, any geographical spread of antimalarial drug resistance must be closely monitored particularly in areas bordering Cambodia. Multiple copies of the plasmepsin II (pfpm2) gene have been associated with piperaguine resistance, and a novel single nucleotide polymorphism (SNP), PfCRT F145I, has recently been implicated in DHA-PPQ treatment failure in Cambodia. During 2013-2015, we conducted a study in collaboration with the Royal Thai Army (RTA) in Srisaket Province along the Thai-Cambodian border, collecting 112 P. falciparum isolated from soldiers presenting with uncomplicated malaria. We then determined the prevalence of the PfCRT F145I SNP, K13 genetic polymorphisms (SNPs indicative of artemisinin resistance), by Sanger sequencing and, pfpm2, and Pfmdr1 gene copy numbers, by real time PCR. We found an overall prevalence of 16.96% for PfCRT F145I (19/112), while the most frequent K13 mutation was C580Y (95/112, 84.82%) followed by R539T (16/112, 14.29%). Half had multiple pfpm2 gene copy number (58/112, 51,79%) with fewer having multiple *Pfmdr1* copy number (4/112, 3.57%). A total of 11.6% (13/112) had both PfCRT F145I and multiple pfpm2 copy numbers. All samples collected in 2014-2015 with either the PfCRT F145I SNP or multiple pfpm2 copy numbers harbored K13 mutations. This identification of samples from Thailand carrying the PfCRT F145I mutation is similar to the pattern in the Cambodia isolates leading up to DHA-PIP treatment failure and warrants continued surveillance.

Keyword : F145I piperaquine resistance marker

Poster No.: 56

Malaria: Country Economic Destruction



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Malaria is one of the mist important challenge to global public health. Based on the World Malaria Report 2017, 91 countries report a total of 216,000,000 cases of the malaria in 2016, the global talky of malaria death reached 455,000 deaths. In this periode all other region have also report case increase. The economy growth of countries that racing the severity of malaria in 1965 in the next 25 years ia much lower, otherwise a much higher economy growth ia owner by countries that successfully reduce malaria afterward. Malaria can disrupt economy growth in several ways. First, it is a demographic effect that is directly observable from high mortality, whereas the indirect effect is to cause high fertlity and large numbes of families. Second, effect on human capital, children have the greatest burden of morbidity and mortality due to malaria. Children who survive from malaria dan have long-term effect on their physical and mental health. Third, the impact of malaria on tourism and foreign direct Investment. Fourth, malaria can limit the internal movement of the population within a country that can affect in development constrain. Besides affecting macroeconomic sector, malaria certainly affects micreconomics as well. Malaria generally associated with negative impact on the socioeconomic development of the countries. Therefore, this review aim to know the malaria impact on the economy and possibility to become the burden of the country.

Keyword : Malaria, economic, burden, country, destruction

Poster No.: 57

Assessment of capacity and Readiness of Provincial Health Staff for Moving towards Malaria Elimination in Thailand



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Malaria Elimination is an important policy and plan undertakings by Ministry of Public Health, Thailand in this century. The Bureau of Vector Borne Disease, Department of Disease Control, Thailand, has also targeted the entire country to be malaria free zone by the year 2024, together with 10 other countries in Southeast Asia. The Malaria Control Program of Thailand was operated as a vertical program in the past; but nowadays it has been integrated in the provincial health system. Due to this transformation, we would like to assess the knowledge and attitude of program staff on malaria elimination and to identify related training needs. It was carried out as a cross sectional qualitative study during November 2014 - August 2015. Data were collected through questionnaire survey and in-depth interview. Participants in the study were 61 health personnel from 48 public health offices in 3 provinces, Trat, Ranong and Tak. It was found that the basic knowledge of participants was at the middle level with the score range was 9-16 out of 20. The training needs included advanced courses on drug resistance and case investigation. We recommended to promote the role of district and subdistrict health personnel to learn and apply quality malaria detection and treatment activities at district health promotion hospitals and community health facilities. In conclusion, this assessment should be useful to plan and develop effective curriculum for public health staff in order to achieve malaria elimination. Key words: knowledge, attitude, public health personal, malaria elimination, provincial health systems.

Keyword : knowledge, attitude, public health personal, malaria elimination, provincial health systems.

Poster No.: 58

A LOW MALARIA PREVALENCE AND LIMITED LARVAL SITES SUGGEST THAT MALARIA ELIMINATION IS POSSIBLE IN TWO DISTRICTS OF LAMPUNG PROVINCE: PESAWARAN AND SOUTH LAMPUNG, INDONESIA



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Introduction: Three years of Annual Parasite Incidence data (2016: 0.40, 2015: 0.49, 2014: 0.40), demonstrate malaria transmission is low, heterogenous and endemic in Lampung province. South Lampung and Pesawaran remain the primary malaria foci in the province. This study aims to characterize epidemiological and entomological aspects of transmission towards elimination strategic decisions in the area.

Methods: Malaria prevalence and incidence studies were conducted from August 2008 to September 2009. Prevalence was determined in 15 sub-villages in each district using rolling cross sectional surveys, while incidence density was measured in cohorts of elementary schoolchildren. During the same period, larval sites of *Anopheles* vectors were identified and characterized using the WHO standard dipping technique and morphological identification of adults. Genotyping of *Plasmodium falciparum* was performed using nested PCR employing *merozoite surface protein-1* (*MSP1*) and *merozoite surface protein-2* (*MSP2*), from the highest endemic village.

Result: Overall malaria prevalence was low (1.3%). Mean prevalence in 30 subvillages was 1.1%, ranging from 0-5% with the highest prevalence in Sukajaya Lempasing. Incidence density was also low (0.16/person-year). Primary larval sites for the main vector- *Anopheles sundaicus*, were man-made (neglected fish ponds and seed tanks), had surface area of 0.5-10,000 m². Genotyping result demonstrated that almost all *P. falciparum* infections were monoclonal (MSP-1=97%=31/32 and MSP-2=100%=24/24). **Conclusion:** Near clonality of parasites, the presence of few, fixed and findable larval sites, low incidence as well as prevalence indicates that malaria elimination is feasible in these areas with the use of vector and parasite-based interventions.

Keyword: Malaria, prevalence, incidence, larval, Lampung

Poster No.: 59

Medical Analyst Performance in Malaria Diagnosis is Related with Age and Working Experience but not Gender, Workplace Location, and Training Experience at Malaria Endemic Area



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As first-line laboratory service provider at a malarial endemic area, medical analyst's knowledge and skill are important in guarantying speed and accuracy of malaria diagnosis. Knowledge and skill in identifying Plasmodium are crucial as early as at Primary Health Care. Here we conducted the blood smear training according to standardize Ministry of Health of Indonesia's Blood Smear Examination Training Manuals. Fifty medical analysts who enrolled were asked to answer questioners and pretest which was constructed from training manuals. Training consisted of thick and thin blood smear examination procedure lecture followed by practical work. Medical analyst's knowledge and skill were evaluated after the training. Several factors were also analyzed in terms of their relationship with the medical analyst's knowledge and skill. As many as 37 medical analysts met the inclusion criteria. Age and working experience (years) of medical analysts had a positive significant correlation with their knowledge (p=0.029, r=0.360; p=0.001, r=0.528 respectively). Meanwhile, gender (male or female), workplace location (urban or rural area), and training experience didn't affect their knowledge. Furthermore, none of the above factors significantly affected the medical analyst's skill and performance in determining parasite species. The after-training evaluation showed significant improvement of medical analyst's knowledge and skill performances (p<0.05). Age of medical analyst in conjunction with working period are most related factors which may reflect medical analyst's experience and performance in malaria diagnosis. Therefore, accurate malaria diagnosis is mainly achieved by repeated practice of blood smear examination.

Keyword: malaria, medical analyst, training, performance

Poster No.: 60

Malaria in the primary school textbook



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Malaria kills about a half million people in 2016. Many organisations and researchers have made efforts to fight against malaria through several aspects such as searching and developing vaccines, new drugs, developing simple test kits, controlling mosquitoes, increasing peoples' awareness, etc. To increase peoples' awareness, early exposure to proper information is effective, therefore, health education to primary school pupils is a useful tool. However, some countries do not have health subject in their curriculum, hence, the challenge to conduct it. In Kenya, the curriculum does not have health subject, however, they included health topics in science and language classes to give the information to pupils. Science, English and Kiswahili textbooks were examined by two researchers. First, contents related to malaria were extracted individually by each researcher. Then, the extracted contents were compared and discussed if there were any disagreement. Lastly, the quality of contents were examined. A total of 64 textbooks; 16 science, 24 English and 24 Kiswahili textbooks, were examined. Of these 9 textbooks (2 science, 6 English and 1 Kiswahili textbooks) mentioned malaria. The contents of information varied from transmission/vector, causative agent, signs and symptoms, to treatment and prevention. There were no misinformation found. Science, English and Kiswahili textbooks in Kenya contained several information on malaria. The topic of malaria in English and Kiswahili textbooks were narrative, therefore it allowed pupils to simulate experience and helped pupils to understand well. Including malaria topics to the ordinal subjects, especially language class, will be one of the ways to increase pupils' understanding and peoples' awareness, which contribute to the fight against malaria.

Keyword: malaria, health education

Poster No.: 61

Case series of human *Plasmodium knowlesi* infection in southern border of Thailand



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Although *Plasmodium knowlesi* (*P. knowlesi*) infection in human can be found throughout the Southeast Asia, it has been restricted mainly to Malaysian Borneo. During November 2017 to April 2018, however, six cases of *P. knowlesi* malaria were identified in Songkhla (5) and Narathiwat (1), southern provinces of Thailand located near Peninsular Malaysia. Despite the early diagnosis of dengue, influenza, or *P. falciparum* or *P. vivax* malaria, all cases were confirmed to be positive for *P. knowlesi* by expert microscopy, nested-PCR, and quantitative PCR. All patients received anti-malarial treatment and recovered without complications. This unprecedented number of *P. knowlesi* malaria, observed within six months, is a clear sign to the emerging threat of *P. knowlesi* in the affected and neighboring areas, including the jungle inhabited by the potential *P. knowlesi* simian host.

Keyword : *Plasmodium knowlesi*, Malaria, Southern Thailand, Malaysian border, Imported case

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Poster No.: 62

THE EFFECT OF *Toxoplasma gondii* PROFILIN EXPOSURE ON REACTIVE OXYGEN SPECIES LEVELS IN OBESE WISTAR RAT MODEL

(STUDY OF ASSOCIATION BETWEEN ADIPOCYTE DISFUNCTION AND *Toxoplasma gondii* iNFECTION)



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Background: Obesity, as a major cause of metabolic syndrome, remains a prominent global health issue. Chronic inflammation, including *Toxoplasma gondii* infection, is known to trigger reactive oxygen species (ROS) production and adipocyte dysfunction, leading to obesity. Our previous study demonstrated the significant association between in vitro *T. gondii* profilin exposure and increased ROS levels in adipocytes. **Objectives:** To assess the in vivo effects of *T. gondii* profilin exposure on ROS levels in obese wistar rat model.

Materials and methods: This study was a true experimental post-test only control group design. Wistar rats were divided into 6 treatment groups; normal diet group given profilin at doses of 15 μ g/mL, 30 μ g/mL, and 45 μ g/mL, and hypercaloric diet group given profilin at the same doses. Wistar rats with normal diet and no profilin exposure were used as control. ROS levels were determined by enzyme-linked immunosorbent assay (ELISA).

Results: Our study showed no significant difference in ROS levels from the six treatment groups (p> 0.05). However, there was an increase in the average body weight that was significant before and after given treatment (p = 0.001).

Conclusion: *T. gondii* profilin exposure did not have significant affect on ROS levels in obese wistar rat models compared to normal control, although accompanied by a significant increase in weight of the treatment groups. Further research on rats model with *T. gondii infection* is required to fulfill the current gap of knowledge.

Keyword : *Toxoplasma gondii* profilin, reactive oxygen species, obese wistar rat model, hypercaloric diet

Poster No.: 63

The Effect of *Toxoplasma gondii* Profilin Exposure to the Level of Leptin in Rattus Norvegicus Wistar Strain Rats Given Normal and Hypercaloric Diet



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Obesity is an abnormal accumulation of body fat and has multiple etiologies including an infection. Based on previous study, there is a possible association between Toxoplasma gondii infection and obesity. T.gondii is classified as zoonotic disease and has a profilin-like protein recognized by Toll-like Receptor stimulates pro-inflammatory cytokines which (TLR-11) and inflammation of the host cell and possibly associated with leptin level. This research is done to know the effect of exposure to *Toxoplasma gondii* profilin on leptin level in Rattus Norvegicus Wistar Strain rats given normal and hypercaloric diet. This experiment was done at Pharmacology and Parasitology Laboratory of Medical Faculty Brawijaya University for rats maintenance, intervention and leptin level measurement. For the positive control groups, the tested concentrations of *T.gondii* profilin was 15µg/ml, 30µg/ml, and 45µg/ml on two group of rats, consuming normal and hypercaloric diet. The result was analyzed using one way ANOVA and showed a significant difference between Toxoplasma gondii profilin and leptin level (p=0.001 $<\alpha$), (alpha=0.05). The Pearson correlation showed that there is a positive and a strong correlation between T.gondii profilin and leptin level in Wistar rats given normal diet (R=0.557), with no significant effect (p=0.087> α); whereas a negative direction and a strong correlation between *T.gondii* profilin and leptin level in Wistar rats given hypercaloric diet (R=-0.616), with a significant effect (p=0.014 $<\alpha$). The conclusion is Toxoplasma gondii profilin increase the leptinl evel in rats given normal diet but decrease in rats given hypercaloric diet.

Keyword: Toxoplasma gondii profilin, leptin, hypercaloric diet

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Poster No.: 64

Cryptosporidiosis among immunocompromised patients: prevalence, symptomatology, and laboratory findings in one single institution



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Cryptosporidium sp., as neglected tropical infection, is one of the independent predictors of mortality among HIV/AIDS patients. The prevalence increases along with the downslope of CD4+ cell count. The study aimed to reveal the prevalence, symptomatology, and laboratory findings of Cryptosporidiosis among HIV/AIDS patients in one tertiary referral care, Haji Adam Malik General Hospital, Medan, Indonesia and Parasitology Department, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia. Symptomatology was noted using short-questionnaire, and laboratory findings were obtained from hospital medical record registry on the same day of admission. We enrolled 24 patients were suffered from HIV infection for certain period of time and more than oneweek diarrhea including 18 males and 6 females. Routine feces examination using wet mount, Kinyoun-gabet, and trichrome staining was performed for all samples in. Our study found that 8 of 24 patients were positive with Cryptosporidium sp. while its symptomatology including abdominal cramp (66.7%), nausea and vomiting (70.8%), and fever (62.5%) is prevalent from our study. We obtained significant association between CD4 cell count (p= 0.033, OR 0.086, 95% CI 0.008-0.878), duration of diarrhea (p=0.032, OR 0.111, 95% CI 0.016-0.789), and abdominal pain (p=0.005, OR 0.048, 95% CI 2.372-185.930) with cryptosporidiosis by using Fisher exact test. Correlation between laboratory findings and its symptomatology could increase awareness related to mortality of the infection particularly in among HIV/AIDS patients since its management remains questionable.

Keyword: Cryptosporidium sp., cryptosporodiosis, HIV/AIDS

Poster No.: 65

Isolation of Trypanosoma evansi for in vitro cultivation



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Isolation of live trypanosome were conducted using 3 different methods; 1. Low speedcentrifugation 2. High speed centrifugation and 3.DE52 isolation. HMI9 media (Hirumietal..1989) was modified as 4 different solutions: 1. HMI9 Sol I. 2.HMI9 Sol II. 3. HMI9 Sol III and 4. HMI9 Sol IV. Comparison of 3 isolation methods found that DE52 isolation method was completely separated trypomastigote from erythrocytes. Comparison of four different cultivation media solutions showed that HMI9 Soll is the best condition for cultivation of T.evansi. T.evansi TECRY 4M, anisolate from a beef cattle from Rayong in 2009 was successfully cultivated and multiplied in HMI9 Soll at 37 °C, 5% CO2, 75% humidity. The growth level of parasite was suddenly increased at the 8 th sub-passage (23 times). Growth level of TEC RY 4M reached up to 26 times when compared to initial parasite concentration. TEC RY 4M T. evansi that strain can be survived and multiplied continuously in cultivation media. The parasite concentration can be reached up to 2.8 x 106 trypanosomes/ml within 48-96 hours. This is the first report of in vitro cultivation of T. evansi that isolate. This study is useful for future antigen production, drug sensitivity test, diagnostic kit development and cell metabolism studies. Using of laboratory animals for production of *T. evansi* trypomastigote antigen was replaced by in vitro cultivation which reducing cost and laboratory animal facilities. Interestingly, we have noticed that T. evansi density may affect survival rate and time of sub-cultivation which is need future investigations.

Keyword : *Trypanosoma evansi*, Thai strain, *In vitro*, Surra

Poster No.: 66

Protease activities of *Blastocystis* sp. from farm animals and water samples in the Philippines



Davin Edric V. Adao^{1,2} and Windell L. Rivera^{1,2}

The potential pathogenicity of the gastrointestinal protozoan *Blastocystis* sp. is an important aspect of the study of human gut microbiota. It is commonly encountered in humans with high prevalence and found in animals and water samples. Thus, transmission of potentially pathogenic *Blastocystis* sp. is possible via zoonotic, anthroponotic, or waterborne routes. The pathogenicity of this protozoan is linked to high activities of cysteine proteases but recent studies have shown the possibility of lateral gene transfer and thus, possible presence of other proteases linked to pathogenicity. This study aimed to identify other types of proteases (serine, aspartic, metalloprotease) in waterborne and farm animal Blastocystis sp. samples. Blastocystis sp. were separated from their accompanying bacteria in xenic cultures and protease activities were measured using azocasein assay with appropriate protease inhibitors. Four (4) water samples were positive for serine and aspartic proteases while only 3 of these 4 were positive for metalloprotease activity. None of the accompanying microorganisms of these *Blastocystis* sp. samples were positive for any type of protease activity. Serine proteases are commonly associated with the pathogenic protozoa Entamoeba histolytica. Additionally, aspartic proteases are commonly associated with the pathogenic yeast Candida albicans while metalloproteases are commonly associated with pathogenic bacteria such as *Vibrio* spp. These results show that other types of proteases may be present in *Blastocystis* sp. and in turn, this enteric protozoa may have other effects on host gut health and microbiota.

Keyword : *Blastocystis,* protease activity, azocasein assay

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Poster No.: 67

Subtype Distribution of *Blastocystis* Isolated from Humans and Associated Animals in an Indigenous Community with Poor Hygiene in Peninsular Malaysia



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Blastocystis is one of the most common parasites inhabiting in small intestines of human and animals. Currently, human Blastocystis isolates are classified into nine subtypes (STs) based on the phylogeny of their small subunit ribosomal RNA gene. Although its pathogenicity has been remaining controversial, the possibility of zoonotic transmission was recognized since eight of the nine STs have been reported in both humans and animals. A cross-sectional study was conducted to determine the prevalence and subtype distribution of *Blastocystis* isolated from humans and associated animals in an indigenous community with poor hygiene in Malaysia, where the risk of parasitic infection is high. A total of 275 stool samples were collected, submitted to DNA extraction and amplified by PCR assay. The Blastocystis-positive amplicons were then purified and sequenced. Phylogenetic tree of positive isolates, reference strains and outgroup were constructed using maximum likelihood method based on Hasegawa-Kishino-Yano+G+I model. The prevalence of Blastocystis infection among humans and domestic animals by PCR assay were 18.5% (45/243) and 9.4% (3/32), respectively. Through molecular phylogeny, 48 isolates were separated into six clusters containing isolates from both hosts. Among human isolates, ST3 (53.3%) was the predominant subtype, followed by ST1 (31.1%) and ST2 (15.6%). Chicken and cattle had lower proportions of ST6 (33.3%), ST7 (33.3%) and ST10 (33.3%), that were barely seen in humans. The distinct distributions of the most important STs among the host animals examined, as well as humans demonstrate that there is host specificity in the lifecycle of Blastocystis.

Keyword : Blastocystis, host specificity, molecular epidemiology, subtype, Malaysia

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Poster No.: 68

Survelliance of *Naegleria fowleri* in Bangkok and Neighboring provinces



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N. fowleri is a causative agent of fulminant brain infection, also known as primary amoebic meningoencephalitis (PAM). Survey of N. fowleri amoeba has been carried out since 1997, due to the first case of PAM was reported in Srisaket province. Isolation and identification of *Naegleria* species in 237 water samples from Bangkok, Nakhon Nayok, Nakhon Pathom, and Rachaburi during 2016-2017 were investigated. The results revealed that the water samples from Bangkok, Nakhon Nayok, Nakhon Pathom, Rachaburi yielded 33% (79/237) Naegleria spp. at 37°C, heat tolerant Naegleria spp.at 24.89% (59/237). Among Naegleria spp. 9.7% (23/237) N. fowleri. was isolate at 37°C and 42°C from Wang Lang, Wat Rakhang, Nang Rong Waterfall, Pha Wang Palace, Prapa Maha Sawat, Bo Khlueng Hot Spring, Nine-level Waterfall. In fresh preparation, Naegleria spp. showed semicircular pseudopod with active progressive and directional movement. In Trichrome & staining, Naegleria spp. showed large nucleous with halo and sucker apparatus in electron micrograph.PCR amplification demonstrated that Naegleria spp. had 450-bp Genus specific ITS gene and 350-bp species specific Nf gene, whereas pathogenic N. fowleri had also 360-bp virulent nfa1 gene.Conclusion, N. fowleri was isolated and identified in Bangkok, Nakhon Nayok, Nakhon Pathom, and Rachaburi. The increasing knowledge of N. fowleri distribution in Thailand should be alerted the health professionals.

Keyword: NAEGLERIA FOWLERI, BANGKOK, NEIGHBORING PROVINCES

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Poster No.: 69

Genotypic identification of *Acanthamoeba* spp. associated with corneal infections in Malaysia



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Acanthamoeba spp. is an opportunistic protist, which is ubiquitously distributed in the environment. This amoeba is the most commonly associated parasitic infection amongst healthy contact lens users, causing an infection known as Acanthamoeba keratitis. Data on the genotype associated with clinical cases in Malaysia is rather scarce, thus this study aimed to determine the genotype variation in Acanthamoeba spp. isolated from corneal scraping of Acanthamoeba keratitis patients diagnosed in our laboratory. Genotype characterization was done by amplifying the 18S rDNA using PCR and sequencing the Acanthamoeba diagnostic fragment 3(DF3) using the primer pair JDP1F and JDP2R. The sequences were aligned with the corresponding sequence to a range of 20 known isolates, genotype T1-T120 and subjected into phylogenetic analysis. The study shows, out of 23 isolates studied, 91.3% (21) were analysed as T4 genotype and 4.35% (1) each for genotype T3 and T5. This finding shows T4 is the most common genotype causing Acanthamoeba keratitis in Malaysia.

Keyword: Acanthamoeba, genotype, Acanthamoeba keratitis

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Poster No.: 70

Histopathological variation of thyroid gland in infected mice with *Trichinella spiralis*



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Up to now, Trichinellosis with severe complications and inadequate treatment was the remaining problem of public health consequence of pathogenesis and pathology that caused by consumption raw and undercooked meat with encysted larvae containing first stage larvae of Trichinella spiralis which larvae stage spread to various internal organs and tissues in which resulting inflammatory reaction and serious complications that cause by immune response between host and parasite interaction and lead to cause of death such as myositis, myocarditis. Therefore, the interesting point focused on an inflammatory reaction of the thyroid gland and tissues. This study design was performed in female ICR mice model infected with 450 Trichinella spiralis larvae and histopathological study with Hematoxylin and Eosin staining technique and determine under microscopic examination on study period. The results of this study demonstrate that the thyroid gland and tissues in infected mice on 13th,18th and 21st DPI showed an acute inflammatory reaction yielded 9.09% to 100% (p-value<0.05) such as perithyroidal capsule (100%),thyroidal capsule (81.81%), interstitial tissues (50%) and thyroid follicle (9.09%). Therefore, infection of *Trichinella spiralis* should be realized that even though low dose infection (450 larvae) could be induce an inflammatory reaction with consequence in serious complication in thyroid gland and functional thyroid gland such as metabolism. The futher proper development study should be concern for clinical useful and treatment together with prevention of serious complication in trichinellosis.

Keyword : Thyroid gland, *Trichinella spiralis*, Inflammatory reaction, Histopathology, Hematoxylin and Eosin staining

Poster No.: 71

An alteration of histology in the periorbital tissue of infected mice with *Trichinella spiralis*



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Trichinellosis is an important public health problem with worldwide distribution caused by Trichinella spiralis. Ocular clinical manifestations often appear in early stage during post infection, include periorbital and facial edema, conjunctivitis that resulting from an inflammatory reactions in which host and parasites interaction after *T.spiralis* infection. Therefore, the interesting point focused on an inflammatory reactions in the periorbital tissue of infected mice. This study was performed in mice model and infected with *T.spiralis* larvae. An inflammatory reactions grading was evaluated histology with hematoxylin and eosin staining technique under microscopic examination. The results showed an acute inflammatory reactions in the periorbital tissue of infected mice on day 13^{th} , 21^{st} , and 35^{th} DPI 9.09% to 100% (*p-value*<0.05) as extraocular muscle(100%), eyelid (36-54%), blood vessels(9-54%), and nerve(27-36%). In conclusion, this study indicates that infected mice with low dose of *T.spiralis* (450 larvae) could be induce an inflammatory reactions in the periorbital tissue after the first week of infection. The further proper study should be development for investigation in suspect case with periorbital edema in which serious complications such as myocarditis should be concern during early after T.spiralis infection.

Keyword : Periorbital tissue, Ocular manifestation, *Trichinella spiralis*, Inflammatory reaction, Histology, Hematoxylin and Eosin staining (H&E).

Poster No.: 72

Epidemiology and Control of Soil Transmitted Helminthes in Nepal



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Objective: The objective of this paper is to explore the Epidemiology and Control of Soil Transmitted Helminths in Nepal.

Findings & Discussion: Initially, there was no national data on worm infestation it is estimated that more than 50% of the children and adolescents are suffering from intestinal worms in 2004 in Nepal. All districts in Nepal are considered to be endemic for STH, based on district-level studies carried out in the 1990s and 2000s. Research Triangle Institute funded a local NGO, conduct a National STH prevalence survey in fiscal year 2014/015. The results indicated that national STH prevalence is 20.7%, with a disease-specific prevalence 14.6% for roundworms, 4.7% for hookworms, and 5% for Trichuris. The highest prevalence of STH was found in the Mid-Western Development Region (27.7%), followed by the Western Development Region (26.5%).

Following programs were conducted by Government of Nepal to control & prevent STHs in Nepal; Biannual Deworming Tablet Distribution to the Children aged 12-59 months, School Health & Nutrition Program which consists of Biannual School Deworming to all the School-aged children. Distribution of Albendazole tablet for pregnant women during Antenatal checkup, In Mass Drug Administration Campaign, Albendazole tablet also added with the objective of provide deworming through albendazole to endemic communities especially to children.

Conclusion: Government of Nepal fully committed to control and eliminate the STHs infection. It constantly works by joint coordination with various nongovernment agencies to eliminate STHs infection from Nation. The epidemiology of STHs was going decreased compared to previous data.

Keyword: Soil Transmitted Helminths, Nepal

Poster No.: 73

Associated Factors of *Strongyloides stercoralis* Infection in Rural Area of Central Thailand



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Strongyloides stercoralis is a soil-transmitted helminth transmitted by contacting soil contains infective filariform larvae. Together with the ability to cause autoinfection within host and lack studies for risk factors, infection control is considerably challenging especially in the agricultural-based community in rural Thailand.

Cross-sectional study was performed during 2017 in 6 villages of Phraploeng District in Chachoengsao Province, central Thailand. Risk factors were obtained by questionnaires. Stool specimen were prepared with simple smear, Kato-katz technique and formalin ether concentration technique methods. Positive results were diagnosed by detection of rhabditiform larvae under light microscope. Multiple logistic regression analysis was conducted for assessing risk factors of infecting *S.stercoralis*.

1267 subjects participated the study. Mean age was 43.2 ± 22.9 years and 56.5% were male. Majority of occupation was agricultural-based. Prevalence of *S. stercoralis* infection was 3.8% and hookworm infection was 1.3%. Independent associated factors for acquiring the infection were male gender (OR=1.96, 1.08-3.56 95%CI), aging ≥ 60 years (OR=2.38, 1.01-5.56 95%CI) and co-infected with hookworm (OR=9.56, 2.90-31.45 95%CI). Agricultural-based work was not statically associated with the infection.

Prevalence of *S.stercoralis* infection and its association with hookworm coinfection could pose a health threat in the community. Although there is no statistical evidence for the association of agricultural-based work and the infection, direct soil contactmight link to population background along with identified risks, male and elderly age. Further longitudinal and qualitative studies could be performed to address additional risk factors of *S.stercoralis* infection.

Keyword: -

Poster No.: 74

Lymphatic Filariasis in Nepal



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Lymphatic Filariasis (LF), also known as Elephantiasis, is a parasitic infection caused by *Wuchereria brancrofti*, *Brugia malayi* and *Brugia timori* nematode worm transmitted to humans through the bite of infected *Aedes*, *Culex*, *Anopheles* and *Mansonia* mosquitoes. It is regarded as one of the public health problem in Nepal. According to the LF mapping conducted in Nepal in 2001, 2005 and 2012; the prevalence of LF was found to be an average of 13%. The survey also identified sixty-one district (among 75 districts) of Nepal as endemic to LF.

Although the disease has been detected in various ecological zone ranging from the hilly region to the plain flatlands in the country, predominantly more LF cases are detected in the plains. The disease is more prevalent in the rural areas; predominantly affecting the poor sector of the community.

Mass Drug Administration is the main strategy adopted by Nepal for the control and elimination of LF. The government has targeted to eliminate LF by 2020. MDA was initiated in 2003 from Parsa district of Nepal, which then gradually scaled up to cover all the endemic districts, achieving 100% coverage by 2013. Since 2015, post MDA has been initiated in at least five districts and morbidity management in selected high endemic districts. It has been targeted that all the districts will complete the six rounds of MDA by 2018. Various surveys carried out since the beginning of MDA have shown considerable improvements and achievements in terms of reducing the prevalence of LF, thus significantly reducing sufferings and preventing disabilities due to LF.

Keyword : Lymphatic Filariasis, Nepal, Mass drug administration

Poster No.: 75

PREVALENCE, INFECTION INTENSITY AND RISK FACTORS OF OPISTHORCHIS VIVERRINI INFECTION IN RURAL AREA OF CENTRAL THAILAND.



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Opisthorchis viverrini(OV) infection is a food-borne trematode infection through the consumption of uncooked cyprinoid fish containing metacercariae. Infected cases could be unaware of the infection because of asymptomatic clinical presentation and chronic infection is strongly associated with cholangiocarcinoma. In Thailand, uncooked cyprinoid fish is popular in the North and Northeastern region as a traditional dish especially *Koi pla*(Chopped raw fish mixed with spicy ingredients).

The study was conducted in Phra-plerng sub district in Sa Kaeo Province, Central Thailand in 2015 using cross-sectional design. The study areas composed of Central and Northeastern descendants. Stool specimen was examined with 3 methods; direct smear, modified Kato-Katz and FECT aimed to measure prevalence and intensity of OV infection. Infection intensity was measured as EPG(eggs per gram) and risk behaviours were assessed by questionnaires. Zero-inflated model was used for zero-excess data from EPG.

Study areas comprised of 5 villages with 1267 participants. Overall prevalence of OV infection was 9.4%. The prevalence was significantly higher in Village Moo 9(p < 0.001) where most of villagers are Northeasterners. Male gender increased risk of acquring infection(OR = 2.8, 95% CI: 1.1 – 7.5). Infection intensity showed overdispersion with mean EPG = 3.2 and SD = 28.1. Zero-inflated negative binomial model showed that male gender, increasing age and *Koi pla* consumption were associated with increasing EPG(p < 0.05).

Modelling zero-excess and overdispersion for infection intensity could help shaping more robust analysis. Up-to-date information on risk factors are valuable for targeting intervention to high risk population.

Keyword: Prevalence, infection intensity, risk factors, *Opisthorchis viverrini*

Poster No.: 76

PREVALENCE OF THE LIVER FLUKE OPISTHORCHIS VIVERRINI AND MINUTE INTESTINAL FLUKES BASE ON HUMAN COPRO-DNA DIAGNOSIS IN UPPER NORTHERN REGION OF THAILAND

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The objective of this study was to study the prevalence rates of liver fluke and minute intestinal flukes in the fecal samples of inhabitants in the upper northern region of Thailand, using the copro-DNA diagnosis. The study was conducted in eight provinces in this region from April to September 2017. The Kato-Katz and PCR techniques were used for detecting eggs or larva in fecal samples. The overall prevalence of helminth infections among 1,500 samples was 12.9%. The most common helminthes were Opisthorchis viverrini-like eggs representing 11.5% (172/1,500), followed by Strongyloides larva, Taenia eggs, hookworm eggs, Trichuris eggs, and mixed parasitic worms with rates of 0.9%, 0.5%, 0.4%, 0.2%, and 1.0%, respectively. Furthermore, Lamphun was the most prevalent of Ov-like eggs, followed by Nan, Chiang Mai, Phrae, Lampang, Phayao, and Chiang Rai Provinces with rates of 21.0%, 18.0%, 17.0%, 16.7%, 7.1%, 7.0%, and 6.0%, respectively. Among 172 samples, 126 (73.26%) were positive for Haplorchis taichui DNA (PCR product size of 186 bp), whereas all samples were negative for O. viverrini. The results indeed reflect the real situation of problems regarding liver and minute intestinal flukes in the upper northern region of Thailand. Therefore, it is important to provide knowledge on the consumption behaviors to inhabitants in these areas.

Keyword: copro-DNA, liver fluke, minute intestinal fluke, prevalence of helminthes

Poster No.: 77

Paragonimiasis in Umphang District, western Thailand: case series



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Paragonimiasis is the most common lung parasite worldwide. It is a food-borne parasitic disease endemic in Asia. We reviewed the clinical and laboratory findings of six cases of paragonimiasis in Thailand including three children aged 3, 4, and 10 years, and three adults aged 55, 60, and 65 years. All were hill-tribe who lived in districts near the Thai-Myanmar border in western Thailand. All presented with chronic cough for 2 weeks to one year, 4 patients had blood stained sputum or hemoptysis. The chest x-rays revealed reticulonodular infiltrations in all, and two patients had pleural effusion. Eosinophilia was found in 4 cases. The diagnosis was made by identification of the eggs in the fresh sputum in all. All were also worked-up for tuberculosis with negative results. The habit of eating raw or undercooked crabs or crayfish was likely the causes of infestation. All of the patients received health education and praziquantel treatment with fully clinical response. Paragonimiasis should be in the differential diagnosis of the hemoptysis, particularly with eosinophilia.

Keyword : Paragonimiasis, *Paragonimus heterotremus, Paragonimus pseudoheterotremus,* Thailand

Poster No.: 78

Metagonimus miyatai infection: Improvement of Inflammatory bowel disease in experimental mice model



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Inflammatory bowel disease (IBD) is characterized by chronic inflammatory disorder of gastrointestinal tract, strongly associated with Immunomodulation. Helminth therapy has been promising to treatment method of IBD and other allergy disorder. In this study, we found effective parasite to ameliorate IBD among several intestinal parasites in an experimental model of colitis. To establish the animal model of DSS-induced colitis, oral administrated in C57BL/6 mice of dextran sulfate sodium (DSS). Six kinds of parasites were infected into each mice, and then colitis were induced. To measured the degree of ameliorating inflammation, we analyzed the weight loss, stool consistency, gross bleeding. And then, we studied whether parasites infection could remission effect on colitis in mice model according to several DPI. The results showed that M. miyatai was most effective ameliorating colitis than other intestinal parasites in DSS-induced colitis mice. And we found that infection with M. miyatai decrease the clinical severity such as weight loss, shortening of colon and histological score by 28 day post infection compared to 7 day post infection and control. Our finding indicate that the preventive application of M. miyatai may be effective in colitis in experimental mice model.

Keyword: Inflammatory bowel disease, Metagonimus miyatai

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Poster No.: 79

PREVALENCE OF SCHISTOSOMIASIS MEKONGI BASED ON STOOL EXAMINATION AND ELISA TECHNIQUE IN LAO PDR



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The blood fluke, Schistosoma mekongi is prevalent along Mekong river basin in a province, Champasak, in the southern part of Laos. In 2017, WHO adopted a new strategy that accelerated the elimination of Asian schistosomiasis in the Western Pacific Region, i.e., transmission interruption by 2025 and eradication by 2030. Presently, stool examination by Kato-Katz method is used as a standard diagnostic method for S. mekongi. However, sensitivity of the Kato-Katz method may be insufficient to detect a light infection. In this study, we estimated the prevalence among people who lived in the endemic areas, using the Kato-Katz method and a serological test: ELISA. A Cross-sectional study was conducted from September, 2016 to August, 2017 in Khong and Mounlapamok districts, Champasak province. Seven highest prevalent villages were selected as sentinel sites and 7 villages were randomly selected as spot check sites. Stool samples (n=1,950) were examined by the Kato-Katz method to find the parasite's eggs. Blood samples (n=2,601) were collected on filter papers and examined by the ELISA to detect anti-Schistosoma antibody using S. japonicum soluble egg antigen. The prevalence of *S. mekongi* ranged from 0.0% to 10.3% with one case (0.05%) of heavy-intensity infection by the Kato-Katz method. On the other hand, the prevalence of *S. mekongi* antibody was much higher (2.06%-53.3%) by the ELISA. To accelerate the elimination of *S. mekongi* in the endemic areas, the basic diagnostic method alone, such as the Kato-Katz method, may not be sufficient to monitor the prevalence precisely. Therefore, more sensitive techniques, such as the ELISA should be efficiently utilized in Laos.

Keyword : Schistosomiasis, *Schistosoma mekongi*, Kato-Katz method, ELISA, Laos

Poster No.: 80

Prevalence Of Parasitic Infection Among The Children In Bhairahawa



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Intestinal parasitic infections are one of the common public health problems of Nepal.In Nepal, 50% of diarrhoeal diseases among children is due to parasites, diarrhoea being major killer of Nepalese children. This study was carried out to determine the prevalence of parasitic infection among the children visiting Pakhlihawa secondary school Rupandehi, Bhairahawa Nepal. A total of 133fecal samples from the students were examined by direct smear wet mountand concentration technique to enhance the rate of recovery of parasite. Result was correlated with their socioeconomic status and hygienic behavior and Body mass index (BMI) The chi-square test was used for analytical assessment. The prevalence rate was 63.20%, girls being highly infected (61.90%) than boys (38.09 %). Single parasitic infection was detected in 74 (88.09%) children, while 10 (11.90%) children had mixed infection. The commonest helminthic parasite was found to be Ascaris lumbricoides (82.71%; n=67) followed by Hymenolepis nana (7.40% n=6;) and Trichuris trichura (1.23%; n=1). Among the protozoan Entaamoeba histolytica accounts (66.66%; n=2) and Giardia lamblia (33.33%) ;n=1) The highest positive rate was found among children of 0-4 years .Infection rate was higher among the children between BMI 10 to 20 (67.44%). Children drinking water from pond were more infected than those drinking water from boaring and handpump. (p < 0.05). Intestinal parasitic infection was found among 63.20% school children. Higher rate of infection was found in malnourished children. This study has shown that hygiene and education are closely associated with the prevalence of intestinal infections.

Keyword: parasitic infections, children

Poster No.: 81

FIRST DETECTION OF *DENGUE* VIRUS ON *AEDES AEGYPTI* AND *AEDES ALBOPICTUS* IN ENDEMIC AND NON ENDEMIC AREA, MIMIKA, PAPUA



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Background: *Dengue* hemorrhagic fever in Papua has increased in the last 3 years as well as in Mimika Regency. According to Mimika Public Health Office, there was no dengue cases before 2015. Virology surveillance on vectors can be used as an early warning systems to prevent an outbreak. Characteristics of *dengue* virus recently become very important by mapping the serotype which is circulating in a region. *Dengue* viruses are persistent up to filial F7 (descendant to the 7th generation). Transovarial transmission has been indicates that potentially support the large number of DHF cases in an area.

Method: This study was descriptive observational and used spatial approach. Research subjects were eggs, larvae, pupae, and imago. Virus detection using RT-PCR. Sample for RNA isolation was performed from the head-thorax of all *Aedes aegypti* and *Aedes albopictus*.

Results: Aedes aegypti and Aedes albopictus in endemic area (Mimika Baru District) proved transovarial transmission by dengue virus type-1. Non endemic area (Kuala Kencana District) have not proven. Minimum infection rate (MIR) of dengue virus on Aedes aegypti is higher than Aedes albopictus in endemic area. While MIR in non endemic area is 0, no dengue virus found on mosquitoes.

Conclusion: A positive result by RT-PCR examination indicates that there has been a vertical transmission from the female mosquito to its eggs, both inside and outside the house. *Aedes albopictus* in endemic area has been proven transovarial and potentially transmitted *dengue* virus.

Keyword: Aedes spp, Dengue Virus Detection, RT-PCR

Poster No.: 82

Presence of dengue virus in field caught *Aedes aegypti* and *Aedes albopictus* (Diptera: Culicidae) in northeastern Thailand



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Objective

Dengue is an important mosquito-borne disease endemic in most tropical countries. In Thailand, *Aedes aegypti* is the main vector involved in dengue virus (DENV) transmission. *Aedes albopictus* is also widespread and plays an important role in dengue transmission. The objective of this study was to determine the presence of different DENV serotypes in *Aedes* mosquitoes collected in dengue transmission areas of northeastern Thailand.

Methodology

Adult *Aedes* mosquitoes were collected using battery-driven mechanical aspirators in households, selected based on patients with suspected dengue and surrounding households in 2016-2018. A total of 282 households in four provinces were included. Individual mosquitoes were cut and abdomens pooled and processed for DENV detection using 300-500 mg extracted RNA in RT-PCR. DENV serotypes were confirmed from individual head and thoraces by nested RT-PCR.

Results

A total of 879 *Aedes* mosquitoes were collected and identified of which 97.2% were *Ae.aegypti* and 2.8% *Ae.albopictus*. The average *Aedes* mosquito density was 2.9 females/household. The proportion of DENV positive pools were 67.2%. The estimated individual mosquito infection rate was 3.9%. All four serotypes were detected; the most frequent being DENV-1 (34.1%). KhonKaen had the highest percentage of dengue positive mosquitoes of the four provinces.

Conclusion

All four DENV serotypes are co-circulating in study area. Understanding the movement of different dengue serotypes within a region is useful for planning control strategies. Entomological and virological surveillance, vector density and DENV infected vectors in the field caught may be used for developing dengue prediction and early warning system for dengue outbreaks.

Keyword: dengue, serotype, *Aedes*, co-circulating

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Poster No.: 83

Insect vectors and their infecting viral agents in the zoological parks in Thailand



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With a unique assemblage of various free roaming and captive wildlife, both domestic and exotic animal species, humans and insect vectors, zoos provide suitable environments for maintenance and establishment of transmission cycles of local and exotic arboviruses. With the aims to identify the potential insect vectors inhabiting in the zoos, and to identify the viral agents circulating in biting flies in the zoological parks of Thailand, biting flies were collected in the zoological parks located in Northern (Chiang Mai), and Northeastern (Khon Kaen) and the central (Bangkok) regions of Thailand. Collections were carried during May 11-18 and September 22-26. Biting flies will be collected by using to different of traps, Light (at night time) and BG Sentinel Traps (at night and day time). Among the mosquito species, important zoonotic and human pathogen vectors have been identified, such as Ae. aegypti, Aedes albopictus, Armigeres spp., and Mansonia spp. Furthermore, Phlebotomine and Culicoides flies have been identified. Thus, the usefulness of the presented data for risk management of virus infections in animals and humans (visitors and zoo staffs) for the appropriated Implementation of preventive and control strategies to minimize zoonotic transmission will be discussed.

Keyword: Biting flies, Zoological Parks, Viral agents

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Poster No.: 84

BREEDING HABITAT CHARACTERISTICS And GEOGRAPHICAL DISTRIBUTION of LARVAE of *Anopheles* sp. IN THE WORKING AREA RONDOMAYANG BAMBALAMOTU SUBDISTRICT HEALTH CENTERS NORTH MAMUJU REGENCY OF WEST SULAWESI PROVINCE



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Background: The existence of indegeneous and introduced cases indicates that most of the areas in West Sulawesi Province were receptive, therefore understanding of habitat characterization and geographical distribution become important in the epidemiology of malaria vector infectious disease that it can be used as a basic in the control efforts.

Objective: To identified habitats characterization and geographical distribution of *Anopheles sp.*

Method: Survey of Anopheles.sp larval were conducted at selected location based on endemic area of malaria.

Result: A total Of 65 potential habitat were sampled, 47(72.31%) were found positive of *Anopheles Sp* larvae, positive percentage: river side (100%), kobakan (85.71%), ditch (85%), pond (60%) with slow water movement and stagnant. Water temperature was 27°C to 28°C, pH was 4 to 6, Salinity was 0‰. Presence of vegetation and natural predator. Density of larvae: river side (4.13/dip), ditch (2.77/dip), kobakan (1.74 /dip) and pond (0.66 /dip). 14 species mosquito have been found such as: *An.tesselatus, An. ludlowae, An. vagus, An. kochi, An. flavirostris, An. aconitus, An. maculatus, An. sulawesi, An. crowfordi, An. sinensis, An. leucosphyrus Group, An. barbirostris, An. barbumrosus, <i>An. subpictus.* Distribution geografic of *Anopheles Sp* larvae on different topography with species composition and distribution of patients within 500m from habitat.**Conclusion**: Characterization of breeding habitat of *Anopheles sp* in the work area of Rondomayang health centre was supported the existence of vector and species diversity due to environmental and climate factors that support indegeneous malaria cases and introduced cases still existed.

Keyword : Anopheles sp, habitats, distribution, malaria vectors.

Poster No.: 85

Metaphase karyotype of *An. maculatus* s.l. from Java, Indonesia and crossing experiment with *An. maculatus* s.s. from Thailand (Diptera : Culicidae)



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The present study reports the metaphase karyotype of *Anopheles maculatus* s.l. from Java, Indonesia and crossing experiments with *An. maculatus* s.s. from Thailand in order to determine the genetic compatiEility. The larval metaphase karyotype of *An. maculatus* s.l. Java is different from other members in the Maculatus Group reported previously. The X chromosome is acrocentric. The short arm is heterochromatic, whereas the opposite arm consists of a euchromatic portion and centromeric heterochromatin of approximately equal length. The heterochromatic Y chromosome is small telocentric. Reciprocal crosses yielded F_1 hybrids from both directions, but the egg hatchability was low. All hybrid adult males were completely sterile, but the ovaries of hybrid females looked normal. Backcrosses between F_1 hybrids and *An. maculatus* s.l. Java showed low egg hatchability. Adult males were partially sterile with abnormal (enlarged head) and inactive spermatozoa, while the ovaries of adult females looked normal. This study provides evidence that *An. maculatus* s.l. from Java, Indonesia is genetically distinct from *An. maculatus* s.s.

Keyword: Metaphase karvotype, *Anopheles maculatus*, Crossing experiments

Poster No.: 86

Study of Influence of Water Types on Oviposition Response of *Toxorhynchites splendens* Mosquitoes (Diptera: Culicidae)



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Toxorhynchites larvae, the natural predator coexisting with mosquito larvae, are recognized as a potential biological control agent for Aedes mosquitoes. However, cannibalism among Toxorhynchites larvae is a major problem to sustain *Toxorhynchites* population in environment. The ability of *Toxorhynchites* females to discriminate the breeding sites containing Aedes larvae and to avoid other Toxorhynchites larvae could be critical to biocontrol program. Additionally, bacterial microorganisms living in different types of water might be a factor of *Toxorhynchites* oviposition success. To determine the oviposition selection of Tx. splendens females on water types as breeding sites: dechlorinated water containing fish food (FF), Ae. aegypti larval rearing water (AeL), Tx. splendens larval rearing water (TxL), and dechlorinated water (DC) as control. The oviposition response of gravid mosquitoes was assessed by determining the number of eggs laid and bacterial isolates by bacterial culture and microbiological methods. The oviposition response of the FF (38%) and AeL (28%) exhibited a preference for egg-laying while the TxL (8%) was the least selection for egg-laying of the gravid mosquitoes when compared with the control (p<0.05). Tx. splendens females showed clearly avoiding response to the TxL. While these females lay more eggs in the tentative Ae. aegypti breeding sites, Ae. aegypti breeding water and dechlorinated water respectively. However, gram stains and density of bacteria in the different water types might related to the factor of ovipositing selection. Gram negative bacilli, high density of bacteria, mild acidic (pH 6.5), and Aedes larvae nutrient are the most suitable condition for *Toxorhynchites* oviposition.

Keyword : Aedes, bacteria, breeding, oviposition bioassay, *Toxorhynchites*

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Poster No.: 87

The successful establishment of sand flies *Phlebotomus* papatasi (Diptera: Psychodidae) at the AFRIMS Insectary, Thailand



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Phlebotomus papatasi, the main vector of Leishmaniasis, has a wide distribution in the Old World. Rearing and colonization of this species is highly specialized undertaking. The aim of this study was to establish sand flies *P. papasi* colony in laboratory, and report the duration of each stage under controlled laboratory conditions. In this study, P. papasi could be colonized for more than 4 successive genearations at the Armed Forces Research Institute of Medical Sciences (AFRIMS), Thailand. The original colony was established from progenies obtained Walter Reed Army Institute of Research (WRAIR) (Silver Spring, MD, USA). Blood feeding rates on direct animal of *P. papasi* were 92.1 (F1), 84.6 (F2), 89.2 (F3) and 86.7% (F4), respectively. The female fecundity was 46-56 eggs/female (2nd-4th generation). The life cycle of *P. papasi*, from egg to adult, occurred in 37.6 ± 1.1 days. The average longevity was determined to be in 38.2+8.9 days for unfed females and 22.6+3.6 days for engorged females, while the males lived for an average of 41.8+10.9 days. This is the first successful colonization of P. papatasi for consecutive generations as a laboratory strain in AFRIMS, Thailand.

Keyword: Phlebotomus papatasi, sand fly, Leishmaniasis, colonization, AFRIMS

Poster No.: 88

TanRabad: Software Suite for Enhancing National Dengue Surveillance System in Thailand.



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Dengue fever is a major public health problem and causes significant morbidity and mortality every year. Early warning system by using intergraded data management such as epidemiological and entomological data is a crucial factor to deal with dengue outbreak. TanRabad is a software suite for supports the mission of health officers to enhance dengue surveillance prevention and control strategy. It consists of 4 key core applications: TanRabad-SURVEYmobile application that supports real-time larval survey data collection; TanRabad-WATCH- web application which visualizes disease epidemics and consolidating entomological indices on map and table; TanRabad-REPORT- web application that supports the production of routine-used reports relevant to disease epidemic and entomological indices; and TanRabad-BI- web application that contributes to the generation of reports related to disease epidemic and entomological indices based on users' perspective. After testing and deployment by an agency under Department of Disease Control, TanRabad has shown several essential functions that strengthening national dengue surveillance system: (i) timely and effective identification high-risk container; (ii) clearly illustrate the outbreak area by using comprehensives data management including epidemiological and entomological matters; (iii) data analysis that useful for national program authorities to set up and planning a potential strategy for dengue prevention and control. In conclusion, Tanrabad has been the online platform that will be standardized dengue surveillance system in Thailand. It will improve and fulfill other aspects such as outbreak investigation and the prediction of a dengue epidemic to ensure that the severity of dengue infection in Thailand will be reduced in the future.

Keyword: TanRabad, Dengue, Dengue Surveillance

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Poster No.: 89

HOST PREFERENCE AND CIRCUM SPOROZOITE PROTEIN (CSP) Plasmodium spp AT Anopheles spp IN WORKING AREA GEBANG HEALTH CENTER DISTRICT PURWOREJO



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Introduction: DistrictPurworejo is one of the districts in Central Java with 547 malaria cases (0.57%) in 2012 and has increased to 803 cases in 2013-2014. According to Gebang Public Health Center, there were 14 malaria cases in 2017 and 46 malaria positive cases in 2018 (From January to March) based on Rapid Diagnostic Test (RDT) and microscopic examination in the laboratory.

Method:This research was descriptive and used cross-sectional study design. The research was started from March until April 2018. Human landing was applied indoor and outdoor the houses to catched the mosquitoes, also resting methodwas applied indoor and near the livestock cages in Tlogosono Village, GebangSubdistrict, PurworejoDistrict. ELISA Method was performfor host preferences examination and to detect CSP *Plasmodium* spp. **Results:**There were 3 species found from 25 mosquitoes caught on the field, such as *An. balabacensis, An. Maculatus* and *An. vagus.* The result of host preferences ELISA examination shows that 7 *Anopheles* spp positive contained human blood. The result of CSP ELISA examination for malaria vector reconfirmation shows that 2 samples were *An. balabacensis;* 1 samplepositive contains *P. falciparum* and 1 sample was positive contains *P. vivax.* The other species was *An. vagus;* 1 sample was positive contains *P. falciparum* and 2 samples were positive contains *P. vivax.*

Conclusion:Host preferens of *Anopheles* spp in the working area of Gebang Public Health Center has a tendency to sucked the human blood. The HBI of *Anophelesbalabacensis*was 50% (zooanthropofilic), *Anopheles maculatus*and *Anopheles vagus* was 25% (zoofilic). Malaria vectors confirmation inthe working area of Gebang Public Health Center were *Anopheles balabacensis*and *Anopheles vagus*. They werecompeteon transmitting the *Plasmodium falciparum* and *Plasmodium vivax*, meanwhile *Anopheles maculatus*showed negative result.

Keyword: Anophelesspp, Preference Blood Feeding, CircumSporozoitProtein, ELISA

Poster No.: 90

Novel application of Bxb1 integrase for target gene modifications in *Plasmodium falciparum*



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The low transfection efficiency, lack of wide range of selectable markers and haploid genome with high A/T content makes genetic manipulation challenging in *Plasmodium falciparum*. While CRISPR and other strategies have significantly advanced DNA transfection of *Plasmodium* parasites, each method has several limitations. Importantly, the ability to introduce the full range of modifications (epitope tagging, site-directed mutagenesis, and indels) remains challenging and is often confounded by off-target effects at other genomic sites. Despite the progress in gene manipulation strategies, gene modifications in an essential target gene are still a significant challenge. Here, we report a novel application of Bxb1 integrase that, together with a silent intronic attB, permits robust and simplified modification of a target gene. Briefly, the strategy involves introducing a short attB sequence in the intron of the gene of interest. The attB is silent, and does not interfere with splicing or protein function, and is readily amenable to recombination with an incoming attP plasmid, enabling rapid and specific target gene modifications. We describe the range applications where this strategy can be used, and also specific cases where it can be preferred over CRISPR-Cas9 and other strategies.

Keyword : malaria, DNA transfection, intron, attB, attP, Bxb1 integrase, gene editing

Poster No.: 91

Development and Evaluation of Attenuated Korea Vaccinia Viral Vectored Vaccines Expressing CSP and MSP1₃₃ of *Plasmodium vivax*



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Relapse and recurrence of vivax malaria is still a major issue in temperate regions including Korea. For the development of viral vectored vaccines against vivax malaria, we constructed recombinant Korea vaccinia viral vector, KVAC103. Then, two KVAC103-vectored vaccines, KVAC-PvCSP and KVAC-PvMSP1₃₃, each expressing the circumsporozoite protein and 33 kDa fragment of merozoite surface protein-1 of Plasmodium vivax, respectively, were generated. Mice were subcutaneously inoculated twice with the viruses, with a three-week interval between injections, and cellular as well as humoral immune responses, including memory B cell response, were examined. Serial inoculation of them elicited strong IgG production in mice. CD3+, CD4+ and CD8+ T-cells were increased by the vaccination in hepatocytes, but not in splenocytes of mice vaccinated with KVAC-PvCSP. In the mice vaccinated with KVAC-PvMSP1₃₃, CD3+, CD4+ and CD8+ T-cells were increased slightly only in slenocytes. These results suggest that KVAC103-based vaccination may be useful for targeting various stages of vivax malaria.

Keyword : *Plasmodium vivax*, Malaria, Vaccine, Vaccinia virus, KVAC103, Circumsporozoite protein, Merozoite surface protein-1

Poster No.: 92

Bioanalytical method development of anti-malarial drugs in clinical blood samples using LC-MS/MS



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The treatment and prevention of malaria disease is mainly dependent on chemotherapy and chemoprophylaxis. It is crucial to be able to quantify antimalarial drugs in clinical samples, in order to describe and understand the pharmacological properties and the relationship between drug exposure and therapeutic effect. Clinical drug concentrations are also needed to distinguish between true treatments failures due to resistant development and subtherapeutic dosing. Here, we present important considerations and recommendations when developing bioanalytical methods for quantifying antimalarial drugs in clinical blood samples using LC-MS/MS. Several factors, such as molecular drug structure, sample matrix (blood vs plasma), sensitivity issues, extraction technique, sample storage, high-throughput implementation and instrumentation, must be evaluated for its impact on the drug determination. We have summarized these challenges, ranging from blood sample collection to drug quantification and reporting, to achieve a reliable quantification method.

Keyword: Antimalrial drugs, LC-MS/MS, bioanalyticl method, blood sample

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Poster No.: 93

The Model Development of ARV Service to Support Drug Adherence for HIV/AIDS People (PHA) in North-eastern part, Thailand



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This study was aimed to develop the model of ARV service to support drug adherence for PHA in North-eastern part, Thailand. The study area was ARV clinic in 5 provincial hospitals. Target group were the service provider and the core group of PHA who working in ARV clinic: 25 people, PHA who provide the ARV service, 330 people and the representative of public health form provincial health office, 5 people. Data was collected by interview belong to the research tools. Quantitative data was analyzed by MRA and qualitative data was by content analysis.

The factor effecting to CD4 level (p-value < 0.05) were time of ARV treatment and provide income. The model of ARV service to support drug adherence for PHA in ARV clinic was the service comprise 4 components; the service that was coverage with the dimensions of physical mental and societal, continuously service from the hospital to the family and community, service by the integrated team of professional of public health, and service by one stop service. The process of service was divided in 3steps; the preparedness of the PHA, the ARV service within the clinic, and the referral system to serve the continuous service from the ARV clinic to the family and community. The provider was the public health personnel and the PHA core group who had direct experience from ARV treatment and PHA specific group: MSM and youth group.

Keyword: Model Development, ARV, HIV/AIDS

Poster No.: 94

Development of an UPLC-QToF method for quantitative analysis of primaquine and its metabolites in human plasma and urine.



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For over 60 years, primaguine (PQ) has been used for radical cure of relapsing vivax malaria but its active metabolites are still poorly characterized. Recent evidence suggests that 5,6 orthoguinone is a stable surrogate marker for an unstable PQ active metabolite, 5-hydroxyprimaguine. An ultraperformance liquid chromatography (UPLC) coupled with quadrupole time-offlight (QToF) analysis method was developed to measure PQ concentrations and carboxyprimaguine (cPQ) and 5,6-orthoguinone (OQ), in human plasma and urine. The assay was validated using stable isotope labeled-PQ (SIL-PQ) as an internal standard. Chromatographic separation were performed on 2.1x50 mm Waters ACQUITY BEH C₁₈ column with a gradient mobile phase of 5mM ammonium acetate pH 4.5 in water and acetonitrile, at flow-rate 0.4 ml/min over 5-min run-time. The analytes were extracted from plasma and urine by protein precipitation using acetonitrile. Selective mass/charge transitions were monitored for PQ (260.19 to 175.21), cPQ (275.15 to 175.21), OQ (260.15 to 147.17) and SIL-PQ (264.21 to 179.24). The method was proved to be accurate and precise at the linearity range of 2.85-63.4, 10.0-300 and 10.0-120 ng/ml, for PQ, cPQ and OQ, respectively, with correlation coefficient (r^2) of > 0.995 and the limits of detection 0.24, 1.92 and 5.73 ng/ml for PO, cPO and OO, respectively. Analyte recovery and matrix effect were greater than 90%, with intra- and interday accuracy and precision less than 10% CV of plasma. The 3 cycles of freezethaw, stability, and full validation of urine are ongoing. Developed methods can be applied to pharmacokinetic studies of patients treated with PQ.

Keyword: UPLC, QToF; Method development; Validation

Poster No.: 95

Optimization of blood feeding success: effects of female density, surface area of membrane and preparing females prior to feeding of *Anopheles belenrae* and *An. pullus* in the laboratory



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Anopheles belenrae and An.pullus, members of the Anopheles Hyrcanus Group (Culicidae, Diptera), were captured in the Republic of Korea (ROK) and successfully colonized at the Armed Forces Research Institute of Medical Sciences, Thailand (AFRIMS) in 2016. These species are very hard to breed because they do not blood feed satisfactorily using the normal membranefeeding method. The purpose of this study was to provoke bloodfeeding behavior of An. belenrae and An. pullus by artificial feeding with human blood in an insectary. This study evaluated various factors; female density (50 and 100 females), membrane surface area (28.8 cm² and 30.2 cm²), and preparing females in a dark environment prior to feeding. Anopheles belenrae showed a satisfactory feeding response at densities of 100 females per membrane surface area of 30.2 cm² (69.8%) and 28.8 cm² (65.4%). Moreover, the maximum feeding rate of An. belenrae achieved was 73% when females were prepared prior to blood feeding in a dark condition for 30 minutes. Anopheles pullus displayed a significant difference in the feeding rate when offered blood through a membrane surface area of 30.2 cm² at densities of 50 females (85.2%) and 100 females (80.7%). Meanwhile, the feeding rate of An. pullus was reduced when females were prepared prior to blood feeding in a dark condition (79.9%). Engorgement by An. dirus was always greater than in An. belenrae and An. pullus by membrane feeding. These results demonstrated that the effect of these factors influence the membrane feeding response of An. belenrae and An. pullus.

Keyword : Anopheles belenrae, Anopheles pullus, membrane-feeding, female density, surface area, dark environment

Poster No.: 96

CLONING AND EXPESSION GENE ENCODING PfMSP-1 19 kDa IN CELL-FREE SYSTEM



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Background: PfMSP-1 19 kDa is a protein-encoding gene on the merozoite surface of *P. falciparum*. These proteins play a role in the pathogenesis of malaria and can induce protective immune responses and can form antibodies when malaria infections occur. Antibodies PfMSP-1 19 kDa can be used to determine differences in seroprevalence and antibody levels at each site.

Objectives: To expression PfMSP-1 19 kDa gene to obtain a protein recombinant as vaccine candidate as well as serological tests.

Methods: The methods used include amplification gene PfMSP-1 19 kDa, ligation into pET SUMO vector, transformation to a competent cells of *E. coli* One Shot®Mach1™-T1^R, culture competent cell in agar plate LB medium, DNA insert analysis, sequencing, protein expression in cell-free system, and analysis of expression results with SDS-PAGE and western blot.

Result and Discussion: The amplification results show a single band size 279 bp. Cloning was successful with the formation of white colonies of 19 clones. DNA insert analysis results in 10 clones containing DNA recombinant. Sequencing results obtained 2 clones that have a sequence and orientation in accordance with Genebank. Analysis of expression results, not found protein with molecular weight according to target protein. Protein expression failure can occur because of differences in the target genes and host used, the absence of post-translational processes in *E. coli* causing errors in folding proteins

Conclusion: Cloning gene was successfully performed in the SUMO pET vector. Protein expression is not successful in cell-free systems.

Keyword: cloning, protein expression, gene encoding PfMSP-1 19kDa.

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Poster No.: 97

Perception and beliefs in poultry farmers' mind: An underrepresented social dilemma in implementation of Antimicrobial Resistance (AMR)



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Background: Poultry is considered as a major hub to spread the Antimicrobial resistance (AMR) in the environment and human. Despite lots of initiatives, the social context and perception as well as beliefs of poultry farmers require further attention for effective intervention in developing countries like Bangladesh.

Methods: We conducted an advocacy program among 30 poultry farmers in a rural area in Bangladesh in July 2018 to know about their perception and beliefs about AMR and antibiotic use.

Results: The farmers bear a false belief that antibiotic works for all types of pathogen like virus, bacteria, fungus and majority of them use it as both therapeutic and prophylactic measures. They give an antibiotic dose to the entire flock within $\mathbf{1}^{\text{st}}$ week of life as the preventive dose, mostly Amoxicillin, Oxytetracycline or Enrofloxacillin. The most interesting cause behind using this preventive dose remains in the lack of trust between farmers and the DOC (day one chicks) supplier (hatcheries/agents). Because, they are not aware of the quality of the DOC (e.g the grading) and the pursuing of the agents for use of antibiotics increases their confusion. Again, the government practitioners are less willing to explain the treatment modalities and less favourable in manners.

Conclusion: A social intervention model comprising open communication, motivation, knowledge, skill and firm implementation of regulation should be adopted at all levels of stakeholders in the poultry value chain to tackle the current alarming AMR situation and the model must be unique considering the sociocultural context of the particular country.

Keyword: AMR, Implementation research, Poultry, Social Belief

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Poster No.: 98

Dermatological Conditions Among Thai Travelers Returning From International Travel: A Preliminary Report



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Introduction: Dermatological condition is one of the three most common health problems in returned travelers. However, no study among Thai travelers has been done. The objectives of this study are to determine the spectrum and impact of skin problems among Thai travelers returning from an international travel.

Methods: A prospective observational study was conducted among short-term Thai travelers who attended Travel Clinic, Hospital for Tropical Diseases, Mahidol University, during February to August, 2018. Questionnaires was collected at the day of the first visit. A telephone interview about travel-related skin problems was done on 7 and 14 days after their return. In addition, the Thai version of Dermatology Life Quality Index (DLQI) has been used to determine the impact of dermatological conditions.

Results: 140 Thai travelers were enrolled. The mean age was 36.53 ± 11.56 years (range 18-70 years) and 51.4% of participants were female. The most common destination was Asia (37.1%) followed by Africa (27.1%). The average trip duration was 13.47 days. Overall, 30.7% of participants developed skin problems during their trips. Common skin problems were dry skin (11.4%), arthropod bites (4.3%), and sunburn (3.6%). Approximately 46.4% presented impairment of quality of life. The main dimensions affected were symptoms and feelings.

Conclusions: One third of Thai travelers experienced dermatological conditions during international travel. With such a high proportion, travel medicine practitioners should advise about risk and prevention of the problems to all travelers attending a pre-travel consultation.

Keyword: DERMATOLOGICAL CONDITIONS, SKIN PROBLEMS, THAI TRAVELERS, RETURNED TRAVELERS, INTERNATIONAL TRAVEL

Poster No.: 99

Pharmacokinetic study of primaquine in plasma and urine of healthy Cambodian adults



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Elimination of *Plasmodium vivax* in Cambodia will require widespread administration of a 2-week course of oral primaguine (PQ) to clear hepatic hypnozoites. Two human host factors may impact the success of radical cure treatment: G6PD deficiency and polymorphisms in the hepatic cytochrome P450 2D6 enzyme. The latter can result in reduced or no enzyme activity (Intermediate Metabolizer [IM] and Poor Metabolizer [PM] phenotypes, respectively) leading to PQ failure. We have previously reported on the various CYP2D6 genotypes prevalent in a subset of 40 Cambodians and found 55% allelic frequency of the reduced activity 2D6*10 allele, most often paired with a normal activity allele or another reduced allele. In 2017,27 of these volunteersparticipated in a primaquine pharmacokinetic study. All of the volunteers were predicted to have normal activity i.e., be Extensive Metabolizers (EMs) with a CYP2D6 AS-A score of 1, 1.5 or 2, except one volunteer with the genotype *5/*10 with duplication (DUP), who could be predicted to be either an EM or IM phenotype. Plasma and urine primaguine and its metabolite levels were measured by UPLC-QToF over 24 hours after oral administration of single 15 mg dose of primaquine. Initial results show the mean PQ $t_{1/2}$, C_{max} , T_{max} , and AUC values for EMs to be 5.4 hr, 64.3 ng/mL, 2.7 hr and 559.6 ng/ml*hr and the *5/*10 DUP volunteer to be 5.3 hr, 101.2ng/ml, 2hr and 809.5 ng/ml*hr, respectively, suggesting an IM phenotype. Full pharmacokinetic analysis of primaguine metabolites in both plasma and urine will be presented.

Keyword: vivax

Poster No.: 100

A review of self-medication with antibiotics in Indonesia : current status and policy



Meuthika Noor Fitriyana¹

Antibiotic resistance is one of the most emerging public health problems today due to its negative impacts on both health and economic sectors. The threat of this problem is growing extensively all over the world. Some factors are driving the development of resistance including the inappropriate use of antibiotics through self-medication that are commonly practiced among the Indonesian population. This review article aims to summarize literature on self-medication with antibiotics use and the policy regarding this in Indonesia. There is no reliable national data on self-medication with antibiotics in the country. Several studies have shown that the practices is still happening in different areas of Indonesia. Lack of knowledge, previous successful experience, limited access to health care facilities, affordable antibiotics, pharmacy's staff limited qualification and weak implementation of government regulation are mentioned in those studies as the determinants. General guidance of antibiotic use is mentioned in the regulation of the Health Ministry of the Republic of Indonesia No. 2406/Menkes/per/XII/2011. Nevertheless, antibiotics can still be purchased without a prescription (over-the-counter) in pharmacies, drug stores, and stalls. Therefore, surveillance of antibiotic use and sales is urgently needed to be implemented at the national level as well as reinforcement of the existing regulation on antibiotic use.

Keyword: antibiotic resistance, self-medication, policy

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Poster No.: 101

Contribution of protein stability to clinical manifestations of G6PD variants



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Glucose-6-phosphate dehydrogenase (G6PD) is an enzyme that catalyzes the first and rate-limiting step in the pentose phosphate pathway, providing reducing power to all cells in the form of reduced nicotinamide adenine dinucleotide phosphate (NADPH). NADPH is necessary for protection of the cells against oxidative stress, especially in the red blood cells where G6PD is the only source of NADPH. G6PD deficiency is a hereditary genetic defect which is one of the most prevalent polymorphisms and enzymopathies in human, affecting approximately 400 million people worldwide. G6PD deficiency is commonly found in malaria endemic areas, including Thailand. Unfortunately, malaria drugs such as primaguine, tafenoguine, and sulfanilamide have been reported to cause hemolysis in G6PD-deficient individuals. Additionally, different point mutations in G6PD gene result in different levels of enzyme activity and stability, leading to different severity of clinical manifestations. To understand the molecular mechanisms underlying the clinical features of G6PD deficiency, biochemical properties and stability of 11 G6PD variants which include 3 single, 7 double and 1 triple variants were investigated. G6PD variants were constructed, expressed, purified and biochemically characterized. The results obtained from this study provide useful information regarding the enzyme activity and stability of G6PD variants which is beneficial for a better understanding of clinical manifestations of G6PD deficiencies.

Keyword: G6PD deficiency, enzyme activity, G6PD variants, hemolysis

Poster No.: 102

EFFICIENCY OF ANYPLEX[™] SYSTEM FOR MTB, MDR-TB AND XDR-TB DETECTION COMPARED WITH STANDARD CULTURE METHOD IN CLINICAL SPUTUM SPECIMEN



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Nowadays molecular biology technique is used for several infectious diagnostics because of its high sensitivity, high specificity, and uncomplicated, time effectiveness and could be used for screening test. This study aimed to evaluate Anyplex[™] System (Seegene, Korea) by Anyplex[™] MTB/NTM Real-time Detection, Anyplex[™] II MTB/MDR Detection and Anyplex[™] II MTB/XDR Detection with culture method and drug susceptibility testing using BACTEC[™] MGIT[™] 960 System. Three hundred and sixty three sputum which obtained from laboratory of the Office of Disease Prevention and Control 5th, Ratchaburi were cultured for Mycobacterium tuberculosis (MTB) and then undergone the standard drug susceptibility testing. Those samples were also tested for MTB, MDR-TB and XDR-TB detection by Anyplex[™] System. The result shows 243 (66.94%) MTB consensus detected and these MTB samples were 12 (4.94%) MDR-TB detected and all of MDR-TB was 1 (8.33%) XDR-TB detected. The Anyplex[™] System shows 100%, 100% and 100% sensitivity, 91.67%, 100% and 100% specificity, 96.05%, 100% and 100% positive predictive value and 100%, 100% and 100% negative predictive value for detection of MTB, MDR-TB and XDR-TB, respectively. In conclusion, Anyplex[™] System; its simple, convenient and short TAT technique, could be the high performance method for TB diagnostic and its resistant detection. This method can help to proper treatments for tuberculosis patients for decreasing the incident rate of TB.

Keyword : MDR-TB, XDR-TB, Anyplex[™] System

Poster No.: 103

Development and clinical evaluation of a highly accurate yellow fever non-structural protein 1 (NS1) rapid diagnostic test



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We developed a rapid diagnostic test (RDT) kit for detecting antigen against vellow fever virus (YFV) using monoclonal antibody to the non-structural protein 1 (NS1) of YFV. YF, Dengue (DENV), Zika (ZIKV), Chikungunya (CHIK) and Mayaro (MAYV) viruses were cultured using the Vero cell line. NS1 protein was purified from the cultured YFV to boost antibodies in mice. Monoclonal antibody to NS1 was selected and conjugated with colloidal gold to produce the YFV NS1 RDT kit. Sensitivity and specificity YFV RDT were determined using positive and negative samples from monkeys from Brazil and negative blood samples from Korea. Cross reactions with ZIKV NS1 and DENV NS1 were evaluated, and YFV specific 3A11, 4H5, 3B7, 6C11 and 3C4 clones were selected. Among these, 3A11 and 3B7 clones showed the most sensitive, and this pair was used in the RDT kit. The diagnostic accuracy of YFV NS1 RDT was fiarly high; specificity was 100% and no false positive was detected. No cross reactions were found with DENV type 2 (DENV2), DENV type 3 (DENV3), ZIKV, CHIK and MAYV. This YFV NS1 RDT kit is very simple to use, rapid to assay, and very sensitive and highly specific. Therefore, it would serve as a choice of method for point-of-care diagnosis and large scale surveys of YFV infection under clinical or field conditions worldwide in endemic areas in addition to the confirmation after vaccine tiral.

Keyword : Yellow fever, Flavivirus, diagnostics, RDT, monoclonal antibody, envelope, NS1, cross reaction

Poster No.: 104

Factors associated with non-adherence to iron supplements among pregnant women in southernmost provinces of Thailand: a hospital-based survey



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Anemia during pregnancy, due to iron deficiency, is a maternal problem worldwide. Iron supplements through ante-natal care (ANC) were successfully implemented in Thailand, but maternal anemia had not declined in the southernmost provinces. The hospital-based longitudinal study was conducted during January to September 2015. Pregnant women with 2nd and 3rd trimester gestational age were enrolled in the study. A self-administrated guestionnaire, including socio-demographic, obstetric, iron supplement intake, side effects, and maternal health knowledge, was utilized. Hemoglobin levels were then collected twice, 20 weeks apart. The prevalence of non-adherence to iron supplements was 42%. The main cause of the non-adherence was pregnant women did not give attention to taking iron supplements during their pregnancy. The study's participants (16.9%) showed lack of knowledge regarding the benefits of iron supplements. Four significant factors associated with the non-adherence to iron supplements (p<0.05) were found as follows: gestational age, educational levels, food intake, and belief in iron supplements' benefits. The non-adherence to iron supplements factors were earlier gestational age (OR=2.12, p=0.036), higher than secondary educational levels (OR=0.34, p=0.032), followed food intake recommendations more than 80% (OR=0.15, p=0.037), and poorly understood the benefits of the iron supplements (OR=205.55, p<0.001). In addition, iron supplements adherence was shown to be inconsistent with the second hemoglobin levels. The prevalence of non-adherence to iron supplements in the southernmost provinces of Thailand was high. Effective health education about the iron supplements' benefits and food intake during pregnancy should be advocated especially to women in early gestational pregnancy.

Keyword : Non-adherence, Iron Supplements, Pregnant Women, Southernmost Provinces of Thailand

Poster No.: 105

Vaccination and Maternal Literacy: Experience of Expanded Program on Immunization Coverage during 1993-2014 in Bangladesh



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Background:

The Expanded Program on Immunization (EPI) are designed to balance maximization of vaccine efficacy with high population coverage to achieve high levels of vaccine effectiveness. Immunization currently prevent 2-3 million deaths every year. Immunization prevents deaths every year in all age groups diphtheria, tetanus, pertussis (whooping cough), and measles. An additional 1.5 million deaths could be avoided if global vaccination coverage improves.

Methods:

Data were extracted from the Demographic and Health Survey of Bangladesh (BDHS). We choose the EPI coverage BDHS data from 1993 to 2014. The surveys were conducted on 12-23 months old children.

Results:

The result showed that the maternal education was positively associated with children's likelihood of being fully vaccinated. In 1993-1994, 79% mothers had completed their secondary education and gradually it increased with the time (1999-2000:73%, 2004: 92%, 2007: 93% and 2011: 97%). As a result, in 2014, 95% of mothers had completed their secondary education. At the same time children's vaccine coverage were 59%, 60%, 73%, 82%, 86% and 84% according to year 1993-1994, 1999-2000, 2004, 2007, 2011 and 2014 respectively. So, from the above results we can say that there is a strong relation between mother's education and childhood vaccination. The higher maternal education, the higher vaccination coverage.

Conclusion:

Educational status of the parents was significantly associated with children\'s vaccination status. Among children where only one parent, either mother or father (but not both) will literate, they will likely to be appropriately vaccinated.

Keyword : EPI, Maternal Literacy, Vaccination, Bangladesh.

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Poster No.: 106

Introduction of the project to improve school sanitary system and health education for primary schools in Kandal Steung District, Cambodia



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Infectious diseases are major cause of deaths in Cambodia. 48.3% of deaths are related with infectious diseases. It is important to prevent the infectious diseases, but many people luck of knowledge about how to prevent the infectious diseases. Our project team focused on the improvement of school sanitary system and school health education for keeping healthy about physical and mental health for children in Kandal Steung District, Cambodia. Firstly we checked sanitary conditions for the primary schools in Kandal Steung District. Totally 63 primary schools in the district, only 18 schools had toilets. Furthermore, 4schools toilets were broken and all schools were insufficient toilets compare with pupils number. We are planning to construct new toilets for the model schools, and at the same time, we made the school health education plan for teachers. We invited teachers to japan to study Japanese helth education systems during September to October, 2017. We also made textbooks for health education in Kumel (Cambodian language). On near future, Model on raising awareness and educating health will be implemented and school health leaders will be trained in Kandal Steung District. And organized executing system that allows trained school health leaders to be active in schools and surrounding regions not only Kandal Steung District, but also all Cambodia.

Keyword: School health, Toilets, Primary school, Kandal Steung, Cambodia

Poster No.: 107

Community Mobilization on Health is initiated by Cambodia-Thailand Collaboration for Fighting Malaria and Dengue Project



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This procedure aims to ensure that Malaria and Dengue control is sustainable in the village by training the community leaders, village chiefs and volunteers, then encouraging them to transfer what they have learned from the project to other people in the community.

Twenty-four volunteers from four villages were trained on Malaria and Dengue, including: signs and symptoms, vector transmission, and especially the preventive methods of malaria-dengue infection. Malaria- and Dengue-infected case experience was raised as to impact on people, such as, economic impact, death if late or no treatment, and waste or loss of time. The possible methods to protect malaria and dengue were explained and guided by the local focal person in community, and these methods were effectively applied and implemented by villagers themselves, during the project period. As a result, Malaria has decreased notably from year to year, and since 2015, with almost no local malaria transmission in the project areas (BorNhok1, BorNhok2, BorNhok4 and Prak1).

We conclude that there are some crucial contributory factors responsible for the above result, which are: the improvement of awareness and behavior change of villagers, the improvement of economic evolution, improvement of infrastructure, LLIN/LLIBN distribution, Abate/temephos application, good hygiene and sanitation, Malaria Net Work (VMW/MMW) and strong support from relevant stakeholders, Public Health service and especially strong support from the Provincial of Health Department, Ratanakiri and Cambodia-Thailand Collaboration for Fighting Malaria and Dengue Project.

Keyword: Community Mobilization, Cambodia-Thailand, Malaria and Dengue

Poster No.: 108

Access of Health Care Among Waria (MTF) Positive HIV Related to HIV-AIDS Services in Center Yogyakarta, Indonesia: Qualitative Study



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Background: HIV-AIDS is an infection that is growing rapidly all over the globe, in 2016 counted 36.7 million people in the world living with HIV, in 2016 Indonesian with HIV was 232.323. Waria (MTF) is one of the key population that are vulnerable infected HIV because most of MTF work as sex workers. Total of MTF in Indonesia is 38.928 and HIV prevalence among transgender is 24.8%. However, until now still not known exactly how access to health care for MTF with HIV, and the objectives of this study were to describe the access of MTF in center Yogyakarta.

Methods: A descriptive qualitative using in-depth interview about access MTF to health services related to HIV-AIDS, conducted to MTF positive HIV in KEBAYA Yogyakarta with total number 23, between November-December 2017. Data was analyzed by thematic framework and validity test was done by using triangulation strategy.

Results: All respondents revealed that access to health services related to HIV-AIDS in center Yogyakarta is easy, such as the availability of ARV, social health insurance for treatment, although there are obstacles system which requiring have the ID card of Yogyakarta, and distances to service location. In addition, peer group support (KEBAYA) also has a positive impact in treatment, social life and psychological.

Conclusion: MTF positive HIV in Yogyakarta can easily access health services, because the system is fast, comprehensive, sustainable, attitude of health workers friendly to MTF with HIV and there is support from the government so the health services provided free of charge.

Keyword: Keywords: Waria (MTF), HIV, health care services, Indonesia

Poster No.: 109

Improving Patient Vital Sign Collection and Record Management at Triage Ward, KRONGTES Health Centre, Mondulkiri Province, Cambodia



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Ten health centers (HC) of Mondulkiri provincial health department had been evaluated on health care service quality in April 2017 with scoring marks ranged from 2.3 to 3 (maximum = 5). Of the ten HCs only Krongtes HC got the lowest score (1 score) that was targeted for quality improvement.

Problem Analysis using Ishikawa diagram, three root causes were found including 1)Irregular monitoring/supervision 2) no maintenance system and 3) Lack of the need-supply analysis. In term of Barrier and Aid Analysis, it found that Meeting to set up maintenance system and Meeting with OD technical team for monitoring and supervision planning were no barrier. However, Hands-on training on need-supply data analysis found that most of the new practices were in the old system and Lack of experienced staffs. Macro Flow Chart of Out-Patients to HFs and Micro Flow Chart of Vital Sign Taken in HFs were purposed and implemented. After the TQM implementation, vital sign collection and record management at triage ward of Krongtes Health Center was increased from 1 to 2 points (September 2017). Factors associated with successfulness of the project implementation were mainly regular meeting to get support from health management team and kept them updated about project results, working as a team with each individual's full responsibility for the success or failure of any activities, recording lessons learnt from the practice and sharing them among all of the team members, and crucially applying regular monitoring or supervision for timely problem solving and for ensuring things done as planned.

Keyword : Record Management, Triage Ward, KRONGTES Health Centre, Mondulkiri Province, Cambodia

Poster No.: 110

Heavy metal contamination near industrial estate areas in Phra Nakhon Si Ayutthaya province, Thailand and human health risk assessment



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Industrial activity is one of the significant sources of environmental contamination with heavy metals, especially in developing countries. And flood can also lead the distribution of toxic substances to the environment, regarding Thailand flood in 2011 as some industrial estates are affected, leading to the concern about heavy metal from industrial wastewater contamination. We aimed to measure the levels of Cd, Cr, Cu, Ni, Mn, Pb, and Zn in river and stream water, sediment, and fish collected from the area around the industrial estates in Uthai District and Bangpa-in District of Phra Nakhon Si Ayutthaya Province following the floods of 2011. The results revealed that heavy metal levels in water did not exceed Thailand surface water quality standards, except for Mn levels at one sampling site. Metal levels in sediment and fish samples also did not exceed published standards. The hazard quotient for fish consumption were highest for Ni (0.2178) in Trichopodus trichopterus collected from the area near the industrial estate in Bangpa-in District, while the hazard index from Cd, Cr and Cu exposure were 0.86966 which was lower than 1, indicating that the health risks for these seven metals were within acceptable ranges.

Keyword: Heavy metals, industrial estate, Ayutthaya, risk assessment, hazard quotient, hazard index

Poster No.: 111

DOWN REGULATED HOST GENES AFFECTED BY HPV E7 PROTEIN AS SURROGATE GENES FOR CERVICAL CANCER DIAGNOSIS



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Cervical cancer is the fourth most common cancer-related to death in women globally which is mostly caused by human papillomavirus (HPV) infection and considered as a sexual transmitted disease. It causes more than 270,000 deaths annually, 85% of cases highly occur in developing and underdeveloped countries. The oncogenic HPV E7 protein has been found to play an important role for cervical carcinogenesis by affecting host gene expression mechanism. This study aims to screen and investigate the effect of HPV E7 protein on host gene expression level advocating for cervical cancer diagnosis.

E7 and Empty vector plasmid were transfected into HEK293 cell line, mammalian cell expression system. Host total protein was extracted and determined E7 protein expression by western blot analysis, then continue proceeded protein sample preparation for Mass Spectrometry analysis by trypsin digestion. Analyzed proteins were identified and quantitated properly by proteome discoverer program in order to compare protein level between two conditions (E7 transfection and control). Protein characterization was also performed. Twenty-five targeted proteins were validated further by qRT-PCR to determine gene expression in RNA level. E7 and Empty vector plasmid were transfected again into HEK293 cell line so that to perform RNA extraction and qRT-PCR. Another two cell lines, SiHa (HPV positive cervical cancer cell line) and C33A (HPV negative cervical cancer cell line) were also maintained and extracted RNA to verify gene expression level together with E7 transfected HEK293 and control.

The normalized gene expression level result showed four down regulated gene candidates *PTMS*, *C1QBP*, *HIST1H1D* and *ZMYM6* presented in E7 transfected HEK293 and SiHa cell lines when compared with C33A cell line and control contributing these four genes as surrogate genes for cervical cancer. Consequently, investigating down regulated host genes caused by HPV E7 protein will provide a better understanding of cervical cancer carcinogenesis, lighting up the new way for therapeutic approaches and discovering new gene candidates for cervical cancer screening programs.

Keyword: HPV E7, cervical cancer, host gene

Poster No.: 112

APPLICATION OF OPSONOPHAGOCYTIC KILLING ASSAY (OPKA) FOR ASSESSMENT OF FUNCTIONAL ANTIBODY AMONG CHILDREN VACCINATED WITH PNEUMOCOCCAL VACCINE



Witawat Tunyong¹, Weerawan Hattasingh², Yuvadee Mahakunkijcharoena¹ and **Thareerat Kalambaheti**¹*

INTRODUCTION *Streptococcus pneumoniae* causes serious bacterial pneumonia as well as invasive pneumococcal diseases (IPD) in children. Vaccination of Pneumococcal conjugate vaccine and measurement their immune response were necessary. The Opsonophagocytic killing assay (OPKA) was one of the assays for evaluating the functional antibody response to pneumococcal vaccines.

AIM: The multiplex OPKA assay, using double serotypes per one serum sample was applied to reveal an immune response.

METHODS: Pneumococcal conjugate vaccine (PCV) contains many different pneumocaccal polysaccharide, thus detection of antibody to many pneumococcal strains were required. A pair of serotypes were selected; one strain was induced to be resistant to streptomycin, while another strain was induced to be resistant to optochin, and these two strains were mixed and used as panel antigen. One pair of bacterial strains can then simultaneously react with one sera sample. The principle of this assay was to set up the reaction between serum and its specific pneumococcal serotype for 30 mins. The immuno-competent cell HL-60 (macrophage cell line) was then added to engulf the immune complex. The guinea pig sera (as complement source) was included to promote lysis of bacterial cell. The surviving bacteria were counted incomparable to the control well that used same material, but not included specific sera. The opsonization titre was defined as the serum dilution resulting in a reduction of half the number of colonies from control wells.

RESULT AND DISCUSSION; A multiplexed OPKA reduced the reagents, and the necessary amount of serum. This protocol could applied to any pneumococcal serotypes.

Keyword : Streptococcus pneumoniae, Pneumococcal vaccine, Opsonophagocytic killing assay

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Poster No.: 113

A model of human helminthiasis prevention and control process: A case study at Phufa development setting, Nan Province



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This qualitative research aim to study the process of helminthiasis prevention and control model in human which was a case study at Phufa development aera, Nan province. The research question is "What is the helminthes prevention and control process in the human?"

Methods: Qualitative research methods were used for data collection from 12 member of networks and stakeholders of helminthes problem solving process in the community and school by in-depth interview featured with document study and non participatory observation. The data were analyzed by content analysis for conclusion.

Result: helminthes prevention and control model in the human consisted of two elements which was supporting. Firstly, there are the significance development activities in 3 target settings namely capacity building in caregivers, community health leaders and students, set a learning process in the school and communities, providing health education program, health communications, health behavior campaign, supporting to the learning process, behavior controlling on diseases prevention, environment and reservoir host improvement, social organization and stool examinations. Furthermore, there is the enabling factor for development processes which were organization's policies, positive reinforcement, social support, teamwork strengthens, learning process, participation, and social capitals.

Suggestion: Diseases's prevention and control model should be suitable framework for community and target group contexts by applying the activities that fitted. Focusing on learning activities that cover all dimension of diseases control; host agent and environment with the participation and supporting from related networks.

Keyword: Helhminthiasis, Diseases prevention and control model, Participation

Poster No.: 114

Strategic Evaluation Under "Saving Animals and Human Lives from Rabies Project" following the Determination of Professor Dr. Her Royal Highness Princess Chulabhorn Mahidol, ODPC 7



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Introduction: As rabies is one of the most important public health concern and Thailand has committed to be rabies free country by year 2020. Furthermore, the "Saving Animals and Human Lives from Rabies Project" following the Determination of Professor Dr. Her Royal Highness Princess Chulabhorn Mahidol has established comprise of 6 stake holders and 8 strategies since 2016 and Office of Disease and Prevention Control 7 (ODPC 7) has been working together with all relevant stake holders to eliminate the disease. However, the project has not been evaluated. This study aims to evaluate process and barrier of the project and rise with recommendations.

Methodology: This study was an evaluation study. The project was evaluated in 4 dimensions which were input, process, output and feedback. The subject composed of: administrators (12), Health officers (72), Livestocks (38), SOA (72), Public officers (4) and people (510). Data were collected by questionnaires, interviewing, focus group and document. For analyzed by number and percentage.

Result: On the first strategy: Input showed budget, personnel, material were insufficient. The process found officers had a plan and results as planned was 56.3, 40.0 %. Output: numbers of registered and vaccinated animals was 65.6 %. The 2nd strategy revealed 3 animal dwells in the area, but those place were below standard. The 3rd strategy revealed input on budget, personnel, vaccine was insufficient. The process found officers had a plan and results as planned was 60.9, 53.1 %. The output showed all risk group received vaccine. The 4th strategy showed input on budget personnel and material were insufficient. Process, the number of registered pet in Thai Rabies Net was78.3 %. For the output, number of local pet whose registered was58.2%. Local rules of pet control was 22.3%. Research team has summarized and reflected on information to related personal for fix problem. Therefore, compensation should be paid for local volunteers as an incentive to work for animal Rabies vaccination in the field. The national-level government agency should have a plan for Rabies vaccine stockpile to ensure that 20% of related agencies have adequate supplies.

Keyword: Evaluation of Strategic Plans, Rabies Prevention and Control Program

Poster No.: 115

Imported Respiratory Tract Infections (RTIs) among traveler to Thailand during 2015-2017



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The international tourist has increased significantly public health concerns particularly travelling to join mass gathering events. Respiratory Tract infections (RTIs) are one of public health concerns among tourist due to fast spreading and severe health condition. Such condition led to a need of surveillance system. In 2012, Thai Ministry of Public Health established the Middle East Respiratory Syndrome (MERS) surveillance system for Emerging Infectious Diseases (EID) for the betterment of prevention and control. Understanding the epidemiological pattern of RTIs among traveler can provide necessary information to prevention and control preparedness of imported RTIs.

This study aimed to calculate a prevalence of RTIs and to describe epidemiological characteristics of RTIs derived from the MERS surveillance data during 2015-2017.

A total of 1,353 travelers captured in the system were male (50.4%), in the age group between 55-64 years (22.7%), and the mean of age was 46.5 years. Thai travelers were 3 times higher than foreigners. Of all travelers, 53.2% of the travelling purposes were to participate the Hajj and Umrah ceremonies. There were 369 cases (27.3%) of influenza-like illness (ILI) presenting cough (76.7%), fever (46.7%), and sore throat (44.0%). Out of them, 142 cases (10.5%) were tested with PCR.

Most of travelers reported via the system were the old pilgrims attending the Hajj. The RTIs in the traveler was highly diverse and most infections were vaccine preventable diseases such as influenza. With a highly effective surveillance system, there has never been any outbreak of EID such as MERS reported in Thailand.

Keyword: Imported respiratory tract infections, Traveler

Poster No.: 116

Utilization of traditional and complementary medicine in Indonesia: results of a national survey in 2014-15



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Background: The use of traditional and complementary health care has increased in recent years in Association of Southeast Asian (ASEAN) member states, including Indonesia. The aim of this study was to estimate the prevalence of traditional and complementary medicine use and its correlates in Indonesia.

Methods: Participants were 31415 adults, 15 years and older, who took part in the cross-sectional Indonesia Family Life Survey (IFLS-5) in 2014-15.

Results: One in four participants (24.4%) had used a traditional practitioner and/or traditional medicine in the past four weeks and 32.9% had used complementary medicine in the past four weeks. In adjusted logistic regression analysis, older age, being a Muslim, residing in an urban area and Java, being unhealthy, having a chronic condition, having depression symptoms, sleep disturbance, and high social support or capital were associated with both current traditional practitioner and/or medicine use and complementary medicine use. In addition, lower education, being very religious, and having inadequate health care access were associated with current traditional medicine use, while higher education, higher economic status, tobacco use, and higher life satisfaction were associated with current complementary medicine use.

Conclusion. The study shows a high prevalence of traditional and complementary medicine use in Indonesia. Sociodemographic and health related factors such as older age, socioeconomic status, religion, religiosity, urban residence, poor physical and mental health status were found to be associated with traditional and complementary medicine use.

Keyword : Utilization; Traditional medicine; Self-treatment; Household survey; Indonesia

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Poster No.: 117

Social vulnerability factors of WARIA to HIV infection in Yogyakarta, Indonesia: a qulitative study



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Introduction: Waria (Transgender women) is one of several key populations associated with HIV / AIDS transmission with high prevalence in Indonesia. However, there is little information about HIV among waria groups in Indonesia. Social factors are one of the factors that cause a group to become more susceptible to HIV infection, but still little known to waria groups. This study aimed to identify social factors that cause waria vulnerable to HIV infection.

Methods: We conducted a qualitative study using in-depth interviews of 23 HIV positive waria incorporated in KEBAYA [Great Family of Waria Yogyakarta], Indonesia. We perform thematic analysis to identify, analyze and report themes. Analysis of the data on the qualitative study is reinforced by the test triangulation with key informants.

Findings: Respondents revealed several things, such as lack of social acceptance of gender identity and HIV-positive status; the difficulty of getting access to health, education and jobs because of their gender identity is not legally recognized; as well as the stigma attached to HIV-positive waria groups. It will continue and make it easier for them to engage in sex work. The involvement of waria in sex work puts the risk of HIV infection higher in this group.

Conclusions: Social factors that cause waria groups are more vulnerable to HIV infection is social acceptance related of gender identity, the social stigma and barriers to access to education/health/work due to non-recognition of their identity legally. These single or multiple social factors can increase the vulnerability of waria to HIV infection.

Keyword: waria; HIV; vulnerability; qualitative; Indonesia

Poster No.: 118

RAMSAY HUNT SYNDROME IN MULTIPLE MYELOMA PATIENT: A RARE CASE REPORT



<u>Puji Rahman</u>¹, Nadya Barus¹, Robert Sinto², Widayat Djoko S²

Background: Ramsay Hunt Syndrome (RHS), also called Herpes Zooster Oticus is a reactivation of Varicella Zooster Virus in the geniculate ganglion. RHS often occurs in immunocompromized patients, is a severe and rare complication of VZV, characterized by the appearance of symptoms of unilateral erythematous vesicle rash on the face, ears and / or cavity with otalgia, facial paralysis and hearing loss. These symptoms will improve with antiviral and steroid treatment immediately in less than 72 hours.

Case Presentation: A 55-year-old man with a history of multiple myeloma and undergoing 4th cycle VAD chemotherapy, came to the emergency room with complaints of severe facial pain for 5 days, vesicles appeared on the left side of the face which ruptured pus, extended to the ears, nose, and around eye. The patient also complained of tinnitus, decreased appetite due to swallowing pain, and blurred vision. Symptoms improve with steroids, antiviral drugs and additional antibiotics for the treatment of secondary infections.

Conclusion: RHS is a rare case but requires immediate treatment to improve outcomes and prevent secondary infections. Early intervention using antiviral and corticosteroids showed significant improvement in patients. Symptom follow-up after treatment is very important because some cases of pain will persist and require a tappering dose of corticosteroids.

Keyword: Ramsay Hunt Syndrome, Varicella Zooster Virus, multiple myeloma

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Poster No.: 119

The effectiveness of innovative method for insecticide impregnation of mosquito-net used in Myanmar



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The present study is to develope and establish new method for insecticide impregnation by characterizing and comparing two deltamethrin impregnation method and qualitatively determining the deltamethrin retained in these mosquito-nets. The conventional method being used in Myanmar at present is known as "dip-it yourself method" in which personel protection is important and causes laborious close contact with harmful insecticide. In this study, two mosquito-nets were impregnated with 10 ml of deltamethrin per 2 L of clean water (0.5% v/v) by conventional "dip-it yourself method" taking 30 minutes for each mosquito-nets. Then, another two mosquito-nets were impregnated with the same concentration of deltamethrin by new innovative apporach called "washing-machine method" using 35 L AW-A800MS Toshiba washing machine taking 10 minutes for two mosquito-nets simutaneously. Resudual amount of deltamethrin in mosquito-nets impregnated with both methods were determined using LC-20AD Shimadzu HPLC analyzer at 245 nm and compared. The results showed mean concentration of 6.2 ± 0.2 mg/L compared to 15.2 ± 0.2 mg/L from roofs area, 9.3±1.5 mg/L compared to 13.7±3.8 mg/L from sides area and 8.9 ± 1.9 mg/L statistically significant (p<0.01). Yhis study demonstrated that higher quantity of deltamethrin resudual amounts was detected in mosquito-nets using washing machine method compared to that of conventional method on their corresponding sides. Furthermore, this new method was convenient, time-saving and safer so that new innovative method should be considered.

Keyword : Mosquito-nets, Deltamethrin, Impregnation, Conventional, Waashing machine, HPLC

Poster No.: 120

Determination of Primaquine and Carboxyprimaquine in Breast Milk by using LC-MS/MS



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Primaquineis the first-line therapy for the radical cure of vivax malaria, and single low dose is recommended for transmission blocking in low endemic areas. However, primaquine is not recommended for use in lactating women due to safety concerns of the breastfeeding infant and the risk of severe hemolysis in people with glucose-6-phosphate dehydrogenase deficiencies. It is therefore critical to measure the drug concentration of primaquine in breastmilk in order to assess the safety concerns for the breastfeeding infant. The objective of this study was to develop a bioanalytical method for quantification of primaquine and carboxyprimaquine, in breast milk using liquid chromatography mass spectrometry..

A bioanalytical method for the determination of primaguine and carboxyprimaguine in breast milk was developed and validated using phospholipid removal plate and tandem mass spectrometry (MS/MS). Primaguine and carboxyprimaguine were analysed on Hypersil Gold C18 column (150×2.1 mm, 5 mm). The mobile consisted of acetronitrileammonium acetate at a flow rate 0.5 mL/min. The quantitation was carried out using LC-MS/MS with electrospray ionisation in MRM mode. The method demonstrated good linearity, ranging from 1.14-519 ng/mL for primaguine and 4.88-5000 ng/ml for carboxyprimaguine. Primaguine was stable in human breast milk during five freeze/thaw cycles, at ambient temperature for at least 48 hours and at 4°C for at least 48 hours. However, carboxyprimaguine was unstable in human breast milk during five freeze/thaw cycles, at ambient temperature for at least 24 hours and at 4°C for at least 48 hours. The method was evaluated according to the US FDA guidelines with respect to accuracy, precision, recovery, stability and matrix effects. The developed method was implemented and applied successfully in a pharmacokinetic study to assess the exposure to primaguine in lactating women and breastfeeding infants. The clinical trial demonstrated that concentrations of primaguine in breast milk were very low and therefore very unlikely to cause adverse effects in the breastfeeding infant.

Keyword: primaquine, breasting feeding, lactating women, malaria, Mass Spectrometrty,